No. 24-1819

IN THE

United States Court of Appeals for the Third Circuit

ASTRAZENECA PHARMACEUTICALS, LP, *ET AL.*,

Plaintiffs-Appellants,

v.

XAVIER BECERRA, *ET AL.*,

Defendants-Appellees.

On Appeal from the United States District Court
for the District of Delaware
No. 23-cv-00931-CFC, Chief Judge Colm F. Connolly

JOINT APPENDIX – VOLUME I OF II (JA01- JA52)

Brian M. Boynton
Principal Deputy Assistant Attorney General
Michael S. Raab
Lindsey Powell
Steven A. Myers
David L. Peters
Catherine Padhi
Attorneys, Appellate Staff
United States Department of Justice
Civil Division, Room 7712
950 Pennsylvania Avenue, NW
Washington, DC 20530
(202) 514-5091

Counsel for Defendants-Appellees

Catherine E. Stetson
Susan M. Cook
Danielle Desaulniers Stempel
Claire Adkins Rhodes
HOGAN LOVELLS US LLP
555 Thirteenth Street, N.W.
Washington, D.C. 20004
(202) 637-5600
cate.stetson@hoganlovells.com

Counsel for Plaintiffs-Appellants

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTRAZENECA PHARMACEUTICALS LP and ASTRAZENECA AB, Plaintiffs, v. XAVIER BECERRA, in his official capacity as SECRETARY OF HEALTH AND HUMAN SEVICES, and CHIQUITA BROOKS-LASURE, in her official capacity as ADMINISTRATOR OF THE CENTERS FOR MEDICARE & MEDICAID SERVICES, Defendants.	Civ. No. 23-931-CFC

Daniel M. Silver, Alexandra M. Joyce, MCCARTER & ENGLISH LLP, Wilmington, Delaware; Catherine E. Stetson, Susan M. Cook, Marlan Golden, HOGAN LOVELLS US LLP, Washington, D.C.

Counsel for Plaintiffs

Jacob Laksin, UNITED STATES DEPARTMENT OF JUSTICE, Wilmington, Delaware; Brian D. Netter, Brian M. Boynton, Michelle R. Bennett, Alexander V. Sverdlov, Stephen M. Pezzi, Christine L. Coogle, Cassandra M. Snyder, UNITED STATES DEPARTMENT OF JUSTICE, Washington, D.C.

Counsel for Defendants

MEMORANDUM OPINION

March 1, 2024
Wilmington, Delaware

COLM F. CONNOLLY
CHIEF JUDGE

The plaintiffs in this action—AstraZeneca Pharmaceuticals LP and AstraZeneca AB (collectively, AstraZeneca)—challenge the constitutionality of the Drug Price Negotiation Program (the Program) created by the Inflation Reduction Act of 2022, Pub. L. No. 117-169, (the IRA or the Act) and the lawfulness of certain guidance promulgated by the Centers for Medicare and Medicaid Services (CMS) to implement the Program. They have sued the Secretary of Health and Human Services (the Secretary) and the Administrator of CMS (together with the Secretary, the Government).

Pending before me are the parties' cross motions for summary judgment. D.I. 18; D.I. 21. Because AstraZeneca does not have Article III standing to challenge the lawfulness of the guidance and because it has not identified a property interest protected by the Constitution that is put in jeopardy by the Program, I will deny AstraZeneca's motion and grant the Government's motion.

I.

A.

Medicare is a federally funded health insurance program administered by the Secretary through CMS for individuals who are 65 or older and for some younger

individuals who have certain disabilities. *See generally* 42 U.S.C. § 1395 *et seq*. The Medicare statute is divided into five "Parts" labeled A through E. Two of those Parts are relevant here. Part B provides Medicare beneficiaries with, among other things, coverage for certain drugs administered as part of a physician's service and drugs furnished for use with certain durable medical equipment. 42 C.F.R. § 410.28. Drugs covered by Part B are usually not self-administered. *See Part B Drugs and Biologicals*, CENTERS FOR MEDICARE & MEDICAID SERVICES, https://www.cms.gov/cms-guide-medical-technology-companies-and-other-interested-parties/payment/part-b-drugs [https://perma.cc/7XR4-7JGA] (last modified Sept. 6, 2023). Part D provides beneficiaries with prescription drug coverage. 42 U.S.C. § 1395w–101 *et seq*.; 42 C.F.R. pt. 423. In 2021, approximately 49 million Medicare beneficiaries filled prescriptions covered by Part D. The cost of those prescriptions totaled $200 billion. *See* John E. Dicken, *MEDICARE PART D: CMS Should Monitor Effects of Rebates on Drug Coverage and Spending*, Government Accountability Office, 1 (Sept. 19, 2023), https://www.gao.gov/assets/gao-23-107056.pdf [https://perma.cc/VRW4-YNK4].

To access Part D's coverage, a Medicare beneficiary must enroll in a Part D plan established and administered by a private insurance company (referred to in

Part D as a "sponsor"). *Pharm. Care Mgmt. Ass'n v. Mulready*, 78 F.4th 1183, 1188 (10th Cir. 2023). As the court explained in *Mulready*,

> each plan sets terms for its beneficiaries to use the plan's prescription-drug benefits. These terms include what drugs the plan covers (the formulary), how much the plan will pay for those drugs (the cost-sharing terms), and at which pharmacies beneficiaries can have prescriptions filled (the pharmacy network). Together, the formulary, cost-sharing terms, and pharmacy network comprise the plan's prescription-drug-benefit design or structure.

Id.

As originally enacted in 2003, Part D barred the Secretary (and thus CMS) from "interfer[ing] with the negotiations between drug manufacturers and pharmacies and [prescription drug plan] sponsors" and from "requir[ing] a particular formulary or institut[ing] a price structure for the reimbursement of covered part D drugs." 42 U.S.C. § 1395w-111(i) (2003). But in 2022, in provisions contained in the IRA (codified in relevant part at 42 U.S.C. §§ 1320f–1320f-7 and 26 U.S.C. § 5000D), Congress directed the Secretary, through CMS, to "establish a Drug Price Negotiation Program." 42 U.S.C. § 1320f(a). To carry out the Program, the IRA requires CMS to "enter into agreements with manufacturers of selected drugs" and to "negotiate . . . maximum fair prices for such selected drugs" for defined "price applicability period[s]." *Id.* Notwithstanding the Program's title and its mandates that CMS "negotiate"

maximum fair prices and reach "agreements" with drug manufacturers, the IRA imposes ceilings on the maximum prices of the drugs selected for the Program, § 1320f-3(c); directs CMS to "aim to achieve the lowest maximum fair price for each selected drug," § 1320f-3(b)(1); and levies excise taxes on all sales of a drug selected for the Program in the event the manufacturer of the drug wants to continue to participate in Medicare and Medicaid but won't agree with CMS's maximum fair price determinations for that drug, 26 U.S.C. § 5000D(b). Congress intended the price ceiling, negotiation, and tax provisions in the Program to result in lower prices for Part B and Part D drugs that lack generic competition and account for a disproportionate share of Medicare's expenses. *See* D.I. 19 at 5; D.I. 22 at 6–7.

The Program operates in cycles. Each price applicability period begins on January 1 of the "initial price applicability year" and ends "with the last year during which the drug is a selected drug" subject to the negotiated maximum fair price. 42 U.S.C. §§ 1320f(b)(1)–(2). The Program's first price applicability period—the period at issue in this case—begins on January 1, 2026. For ease of reference, I will call this period "the 2026 price period," and I will similarly identify all other price periods by reference to their initial price applicability year.

For each price period, the Act requires CMS to (1) use a mandated methodology to select a specific number of drugs for negotiating a maximum fair price, (2) publish a list of those selected drugs not later than a specified "selected drug publication date," and (3) engage with the manufacturers of the selected drugs in a negotiation process that has mandated steps and deadlines. *See* §§ 1320f–1320f-3.

The Act directs CMS to begin the process of selecting the drugs for negotiation by identifying the universe of "qualifying single source drugs." As relevant here, § 1320f-1(e)(1)(A) of the Act defines a "qualifying single source drug" as a Part D drug

> (i) that is approved [by the United States Food and Drug Administration (FDA)] and is marketed pursuant to such approval;
>
> (ii) for which, as of the selected drug publication date with respect to such initial price applicability year, at least 7 years will have elapsed since the date of such approval; and
>
> (iii) that is not the listed [brand] drug for any [generic drug] that *is* approved [by the FDA] and *marketed* . . . .

§ 1320f-1(e)(1)(A) (emphasis added).[1]

The Act next requires CMS to identify within this universe of drugs "negotiation-eligible drugs." For the 2026 and 2027 price periods, the negotiation-eligible drugs are the 50 qualifying single source drugs with the highest total Medicare Part D expenditures over a specified 12-month period. § 1320f-1(d)(1)(A). For subsequent price periods, the negotiation-eligible drugs are the 50 qualifying single source drugs with the highest total Medicare Part B and Part D expenditures over a specified 12-month period. § 1320f-1(d)(1)(A).

The Act requires CMS to rank the negotiation-eligible drugs according to total expenditures (with the highest total expenditures having the highest ranking) and to select and publish a list of a specific number of the highest-ranking drugs no later than a selected drug publication date specified in the Act for each price period. The Act mandates that CMS base its total expenditure determinations using "data that is aggregated across dosage forms and strengths of the drug." § 1320f-1(d)(3)(B); *see also* § 1320f-5(a)(2). The number of drugs to be selected varies by year. CMS must select 10 drugs for the 2026 price period, 15 drugs for the 2027 and 2028 price periods, and 20 drugs for all subsequent price periods.

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[1] Qualifying single source drugs also include certain FDA-approved biological products. Because the IRA's provisions relating to biological products have no bearing on this case, I do not discuss them.

§ 1320f-1(a)–(b). If the number of negotiation-eligible drugs for any price period is fewer than the specified number of selected drugs for that period, CMS is to select "all" negotiation-eligible drugs for negotiation. *See* § 1320f-1(a).

Congress took pains to ensure that CMS—and only CMS—selects the drugs covered by the Program. The IRA expressly states that "[t]here shall be no administrative or judicial review of . . . [t]he selection of drugs under section 1320f-1(b) of this title, the determination of negotiation-eligible drugs under section 1320f-1(d) of this title, and the determination of qualifying single source drugs under section 1320f-1(e) of this title." § 1320f-7(2).

Once CMS publishes the list of selected drugs, the manufacturers of those drugs must decide whether to enter into an agreement with CMS to negotiate the maximum fair price of the drug. The Act requires CMS to enter into such negotiation agreements with willing manufacturers by dates specified in the statute for each price period. § 1320f-2(a). The Act does not require manufacturers to enter into negotiation agreements but it provides them a powerful incentive to negotiate a maximum fair price with CMS: If a manufacturer of a selected drug wants to continue to participate in Medicare, it must either agree to negotiate a maximum fair price for that drug or pay an excise tax of at least 65% and up to

95% on all (i.e., both Medicare and non-Medicare) sales of the drug. 26 U.S.C. § 5000D.

CMS and the manufacturers that do enter into negotiation agreements are required under the Act to follow a specified negotiation process that includes the making of offers and counteroffers by deadlines set by the statute. The Act directs CMS to "develop and use a consistent methodology and process" that "accord[s]" with the Act's specified negotiation process and that "aims to achieve the lowest maximum fair price for each selected drug." 42 U.S.C. § 1320f-3(b)(1).

The negotiation process mandated by the Act begins with the submission of pricing and other related data by the manufacturer to CMS on a date prescribed by the statute. § 1320f-2(a)(4); § 1320f-3(b)(2)(A). CMS is then required—again by a date set by the statute for each price period—to make "a written initial offer that contains [its] proposal for the maximum fair price of the drug and a concise justification" of the proposal. § 1320f-3(b)(2)(B). "Not later than 30 days after" receiving the initial offer, the manufacturer must either accept such offer or propose a counteroffer. § 1320f-3(b)(2)(C). The Act requires CMS to "respond in writing to such counteroffer," § 1320f-3(b)(2)(D), but it does not say when CMS must do so.

For each price period, the Act specifies a date when the negotiations between CMS and the manufacturers of the selected drugs "shall end." § 1320f-3(b)(2)(E). If the parties have not agreed on a price by that date, the manufacturer is deemed to be noncompliant and subject to the excise tax penalties under 26 U.S.C. § 5000D.

If CMS and a manufacturer agree on a maximum fair price for a selected drug, the manufacturer must provide "access to such price" to Medicare beneficiaries beginning on January 1 of the initial price applicability year. 42 U.S.C. § 1320f-2(a)(1). Once a drug is selected for the Program, it remains in the Program for sale to Medicare beneficiaries at the negotiated price. Certain changes to the drug, not relevant here, can trigger renegotiation and a new maximum fair price beginning in 2028, or the drug can be removed from the Program starting the first year that begins at least nine months after CMS determines that a generic version of the drug is approved and marketed. §§ 1320f-1(c)(1); 1320f-3(f).

If a manufacturer has agreed to a maximum fair price with the Government, but then fails to make the selected drug available to Medicare beneficiaries at that price, it is subject to civil penalties under § 1320f-6(a). Each time a manufacturer distributes a selected drug at a price above the drug's maximum fair price it "shall

be subject to a civil monetary penalty equal to ten times the . . . difference between the price for such drug . . . and the maximum fair price." § 1320f-6(a)(2).

B.

Congress directed CMS to implement the Program through "instruction or other forms of program guidance." Pub. L. No. 117-169, § 11001(c). CMS issued initial guidance in March 2023 and then, after receiving public comment, published revised guidance (the Guidance) on June 30, 2023. The Guidance expressly states that it applies only to the 2026 price period. D.I. 20-2 at 1–2.

Two provisions in the Guidance are relevant here. Both provisions address how CMS will determine whether a drug constitutes a qualifying single source drug. Under the first provision, CMS "will identify a potential qualifying single source drug using . . . all dosage forms and strengths of the drug with the same active moiety and the same holder of a New Drug Application (NDA), inclusive of products that are marketed pursuant to different NDAs." D.I. 20-2 at 99 (footnote omitted). As explained in the Guidance, "[t]his approach to identifying a potential qualifying single source drug aligns with the requirement in [42 U.S.C. § 1320f-1(d)(3)(B)] of the Act to use data aggregated across dosage forms and strengths of the drug, including new formulations of the drug." D.I. 20-2 at 100. CMS also deemed this approach "appropriate" based on its observation that "new

dosage forms or different routes of administration of the same active moiety/active ingredient have been submitted by the same NDA[-]holder and approved under different NDAs . . . ." D.I. 20-2 at 100.

The second relevant Guidance provision explains how CMS will determine if a generic drug "is marketed" under § 1320f-1(e)(1)(A)(iii). As noted above, § 1320f-1(e)(1)(A)(iii) excludes a brand drug from being designated as a qualifying single source drug if an FDA-approved generic version of the brand drug "is marketed." The Guidance provides that CMS will deem a generic drug to be marketed "when the totality of the circumstances . . . reveals that the manufacturer of that drug or product is engaging in bona fide marketing of that drug or product." D.I. 20-2 at 102. CMS explained in the Guidance that without this provision, a generic drug manufacturer "could launch into the market a token or de minimis amount of a generic drug . . . for the selected drug and the manufacturer of that selected drug could claim that the [maximum fair price] should no longer apply." D.I. 20-2 at 72.

Under the Guidance, the "totality of the circumstances" CMS will consider in determining whether a generic drug has been bona fide marketed "includ[es]" Prescription Drug Event (PDE) data and Average Manufacturer Price (AMP) data, D.I. 20-2 at 3, 165. PDE data are drug cost and payment information submitted to

CMS by drug plan sponsors every time a Medicare beneficiary fills a prescription under Medicare Part D. *See Questions and Answers on Obtaining PDE Data*, CENTERS FOR MEDICARE & MEDICAID SERVICES, https://www.cms.gov/medicare/prescription-drug-coverage/prescriptiondrugcovgenin/downloads/partdclaimsdataqa.pdf [https://perma.cc/QJ5E-ALKG]. AMP is "the average price paid to manufacturers by wholesalers for drugs distributed to retail community pharmacies and retail community pharmacies that purchase drugs directly from the manufacturers." D.I. 20-2 at 76 n.23. It is calculated using manufacturer sales transaction data and is provided to CMS on a monthly and quarterly basis. D.I. 20-2 at 76 n.23. The Guidance expressly states that the "use of [PDE and AMP] data is not exhaustive, and [that] all data and other information will be reviewed in totality in monitoring if manufacturers of these applicable generic drugs . . . engage in bona fide marketing." D.I. 20-2 at 7. The Guidance also provides that "[t]he determination [of] whether a generic drug or biosimilar is being bona fide marketed on an ongoing basis is a totality-of-the-circumstances inquiry that will not necessarily turn on any one source of data." D.I. 20-2 at 77.

II.

On August 25, 2023—almost two months after CMS published its Guidance—AstraZeneca Pharmaceuticals LP (but not AstraZeneca AB) initiated

this lawsuit with the filing of the original Complaint. D.I. 1. Four days later, on August 29, 2023, CMS published the list of the Program's ten selected drugs for the 2026 price period. AstraZeneca's Farxiga is one of those drugs. It is the only AstraZeneca drug on the list. *See* D.I. 19 at 6; D.I. 21-2 at 3.

Farxiga was approved by the FDA and is marketed under a single NDA to treat indications relating to diabetes, heart disease, and chronic kidney disease. D.I. 19 at 6; D.I. 21-2 at 4. Its active moiety is dapagliflozin. D.I. 19 at 6. Between June 2022 and May 2023, approximately 799,000 Medicare Part D enrollees used Farxiga, and Farxiga accounted for approximately $3,268,329,000 of Part D's gross covered prescription drug costs during that 12-month period. *Medicare Drug Price Negotiation Program: Selected Drugs for Initial Price Applicability Year 2026*, CENTERS FOR MEDICARE & MEDICAID SERVICES, https://www.cms.gov/files/document/fact-sheet-medicare-selected-drug-negotiation-list-ipay-2026.pdf [https://perma.cc/T6W5-G6BU].

AstraZeneca alleges, and the Government does not dispute, that the FDA has granted tentative approval to 17 generic manufacturers to market generic versions of Farxiga and that Farxiga "will experience generic competition sometime between October 2025 and Summer 2026." D.I. 20 ¶ 27. The FDA grants a generic drug tentative approval if the generic drug is "ready for approval before the

expiration of any patents or exclusivities accorded to the [brand] reference listed drug product[.]" *Drugs@FDA Glossary of Terms*, U.S. FOOD & DRUG ADMINISTRATION, https://www.fda.gov/drugs/drug-approvals-and-databases/drugsfda-glossary-terms [https://perma.cc/Q88Y-KUWB] (last updated Nov. 14, 2017).

On September 26, 2023, AstraZeneca filed the operative Amended Complaint. The Amended Complaint is identical to the original Complaint in all material respects with two exceptions. First, the Amended Complaint added AstraZeneca AB as a Plaintiff. D.I. 16-2 at 1; D.I. 16-2 ¶ 24. Second, the Amended Complaint added an allegation that CMS had listed Farxiga as one of the ten selected drugs for the Program's 2026 price period. D.I. 16-2 ¶ 22.

The Amended Complaint has three claims. Counts I and II allege that CMS's Guidance violates the Administrative Procedure Act (APA), 5 U.S.C. § 706(2). D.I. 19 ¶¶ 49, 123–30. Count III alleges that the IRA is unconstitutional and violates AstraZeneca's Fifth Amendment right to due process.[2]

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[2] The IRA addressed a broad array of topics such as energy production, carbon emissions, and corporate taxes that have nothing to do with the Drug Price Negotiation Program. Although AstraZeneca's challenge to the IRA focuses solely on the constitutionality of the Program, AstraZeneca asks in its Amended Complaint for "[a] declaration pursuant to 28 U.S.C. § 2201 that the IRA is unconstitutional and violates the Due Process Clause of the United States

Pursuant to a stipulated order, on the same day it filed its Amended Complaint, AstraZeneca filed a motion for summary judgment in its favor on all counts in the Amended Complaint pursuant to Federal Rule of Civil Procedure 56. D.I. 18. Less than a week later—on October 1, 2023—AstraZeneca entered into an agreement with CMS to participate in the Program and negotiate a maximum fair price for Farxiga for the 2026 price period. *Medicare Drug Price Negotiation Program: Manufacturer Agreements for Selected Drugs for Initial Price Applicability Year 2026*, CENTERS FOR MEDICARE & MEDICAID SERVICES, https://www.cms.gov/files/document/fact-sheet-medicare-selected-drug-negotiation-list-ipay-2026.pdf [https://perma.cc/2F7N-4F5U].

On November 1, 2023, the Government filed an opposition to AstraZeneca's summary judgment motion and "cross-move[d] for summary judgment on all claims pursuant to Rule 56." D.I. 21. I heard oral argument on the competing motions on January 31, 2024. D.I. 64.

Constitution." D.I. 16 at 43–44. Neither party addressed the issue of severability. Since I conclude that AstraZeneca's due process claim fails as a matter of law, I need not and do not address severability.

III.

A court must grant summary judgment "if the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). The parties agree that there are no disputes with respect to any material fact and that their motions present purely legal questions. D.I. 13.

IV.

I turn first to AstraZeneca's APA claims. Both claims challenge how CMS interpreted in its Guidance the Act's definition of "qualifying single source drug" in § 1320f-1(e)(1)(A). In Count I, AstraZeneca alleges that the Guidance's interpretation of that term "improperly overrode the statutory definition" by "embrac[ing] *all* dosage forms and strengths of *any* drug marked by the manufacturer with the same active moiety or ingredient" even if those different forms and strengths were approved under different NDAs. D.I. 16 ¶¶ 49, 59, 60, 126 (emphasis in the original). In AstraZeneca's view, § 1320f-1(e)(1)(A) "directs that each Qualifying Single Source Drug must be identified by reference to its *individual* approval . . ., i.e., its distinct NDA" and "[a]ny other reading—including the one based on common active moiety or common active ingredient espoused by

CMS—contradicts the plain text of the statute and therefore must be set aside." D.I. 19 at 16 (emphasis in the original).

In Count II, AstraZeneca alleges that CMS's requirement that a generic drug be marketed in a bona fide way to be deemed "is marketed" under § 1320f-1(e)(1)(A)(iii) "impermissibly expanded the requirements that must be met before a drug is deemed to have generic competition such that it is ineligible for selection or negotiation." D.I. 16 ¶ 52; *see also* D.I. 16 ¶¶ 51, 134; D.I. 19 at 19. According to AstraZeneca, the ordinary and accepted meaning of "marketing" is "exposure for sale in a market," and if a generic drug is exposed for sale in any way or quantity the reference brand drug cannot be a selected drug for negotiation under the Program. D.I. 19 at 20.

The Government argues that I lack jurisdiction over these claims for two reasons: first, because AstraZeneca has not established and cannot establish Article III standing to assert the claims; and second, because § 1320f-7 of the IRA expressly precludes judicial review of CMS's selection of a drug for negotiation under the Program and its underlying determinations that a drug is a qualifying single source drug and a negotiable-eligible drug.

A.

Article III of the Constitution limits the jurisdiction of federal courts to "Cases" and "Controversies." *Lujan v. Defs. of Wildlife*, 504 U.S. 555, 559 (1992). "Part of the case-or-controversy requirement is the requirement that plaintiffs have standing to sue." *Yaw v. Delaware River Basin Comm'n*, 49 F.4th 302, 310 (3d Cir. 2022). To establish standing "a plaintiff must show (i) that he suffered an injury in fact that is concrete, particularized, and actual or imminent; (ii) that the injury was likely caused by the defendant; and (iii) that the injury would likely be redressed by judicial relief." *TransUnion LLC v. Ramirez*, 594 U.S. 413, 423 (2021).

The plaintiff, as the party invoking federal jurisdiction, bears the burden of establishing standing. *Id.* And "[w]hile generalized allegations of injury may suffice at the pleading stage [to meet that burden], a plaintiff can no longer rest on such mere allegations in response to a summary judgment motion, but must set forth specific facts by affidavit or other evidence." *Pa. Prison Soc'y v. Cortes*, 508 F.3d 156, 161 (3d Cir. 2007) (internal quotation marks and citation omitted). Because "standing is not dispensed in gross, a plaintiff who raises multiple causes of action must demonstrate standing for each claim he seeks to press." *In re*

Schering Plough Corp., 678 F.3d 235, 245 (3d Cir. 2012) (internal quotation marks and citation omitted).

As an initial matter, AstraZeneca does not allege that CMS's selection of Farxiga for negotiation under the Program constitutes the injury for which it seeks redress in this action. That makes sense, because neither element of the Guidance's "qualifying single source drug" definition challenged by AstraZeneca could have had any bearing on CMS's decision to designate Farxiga as a selected drug. Farxiga is approved and marketed under a single NDA and no generic version of Farxiga is marketed in any manner or quantity. Thus, Farxiga satisfies *AstraZeneca's* interpretation of the statutory definition of "qualified single source drug," and, as a result, the selection of Farxiga is not a cognizable injury that could be remedied with a decision in AstraZeneca's favor.

In its briefing, AstraZeneca argued that it has standing to pursue its APA claims because the Guidance "ha[s] harmed and will continue to harm" it in three other ways. D.I. 58 at 5. At oral argument, AstraZeneca barely mentioned these three alleged harms and instead argued that a fourth harm it suffered gives it standing to assert Counts I and II. I address the four harms AstraZeneca has alleged in turn.

1.

AstraZeneca contends first that it has standing to bring Count I because CMS's interpretation of "qualifying single source drug" "decreases the incentives for AstraZeneca to look for additional uses for FARXIGA's single-ingredient active moiety for patients in need." D.I. 58 at 19. In AstraZeneca's telling:

> Under CMS's Guidance, the agency will effectively treat FARXIGA and any new product with the same single-ingredient active moiety approved under a distinct NDA as the same drug—even if that new product is approved years after FARXIGA and after extensive research and financial investment. Thus, a new drug product or therapy with the same single-ingredient active moiety as FARXIGA—even if it is approved under a different NDA . . . under FDA's rules—will immediately be subject to the Maximum Fair Price for FARXIGA, without regard to the statutory seven-year minimum that would otherwise apply before a drug is selected for price negotiation. This eliminates incentives for AstraZeneca to further innovate new uses for FARXIGA's single-ingredient active moiety, which in turn will narrow patient access to new treatments.

D.I. 61 at 6–7 (citations and footnote omitted).

A loss or diminishment of an incentive to do something, however, is not a concrete injury. To determine whether an alleged intangible harm is sufficiently concrete to constitute an injury-in-fact, courts "assess whether the alleged injury to the plaintiff has a 'close relationship' to a harm 'traditionally' recognized as providing a basis for a lawsuit in American courts." *TransUnion*, 594 U.S. at 424

(quoting *Spokeo, Inc. v. Robins*, 578 U.S. 330, 340 (2016)). "That inquiry asks whether plaintiffs have identified a close historical or common-law analogue for their asserted injury." *Id.* AstraZeneca has not identified, and I am not aware of, any court decision that has recognized a tort for loss or diminishment of an incentive to do something. Nor has AstraZeneca identified any harm traditionally recognized as providing a basis for a lawsuit that is analogous to or has a close relationship with a loss or diminishment of an incentive. This failure should come as no surprise. AstraZeneca's theory of injury is unprecedented and understandably so. Were courts to adopt AstraZeneca's "disincentivizing" theory of standing, they would open their doors to plaintiffs whose only complaint was that they disliked a law or government action. If AstraZeneca had its way, the merits of every "sin tax" could be challenged in never-ending lawsuits brought by disgruntled smokers, gamblers, oenophiles, and (at least in Philadelphia) soda drinkers.

But even if AstraZeneca's alleged "decreases in incentives" to develop new uses of Farxiga could be deemed sufficiently concrete, it would still not satisfy the "actual or imminent" requirement for an injury-in-fact. To be an imminent harm, the "threatened injury must be *certainly impending*." *Clapper v. Amnesty Int'l USA*, 568 U.S. 398, 409 (2013) (emphasis in the original). "[A]llegations of

possible future injury are not sufficient." *Id.* (internal quotation marks and citation omitted) (emphasis in the original). As the Court held in *Clapper*, a plaintiff "cannot manufacture standing merely by inflicting harm on [itself] based on [its] fears of hypothetical future harm that is not certainly impending." 568 U.S. at 416. In this case, AstraZeneca's alleged injury is premised on a hypothetical scenario that could only be realized *if* AstraZeneca were to develop a new formulation or use of Farxiga's active moiety, *if* the FDA approved that new formulation or use under a new NDA, and *if* Farxiga were still a selected drug for the Program at that (unknown) time. The fact that the word "if" is required to describe AstraZeneca's alleged injury demonstrates that the harm it complains of is neither actual nor certainly impending. *See Reilly v. Ceridian Corp.*, 664 F.3d 38, 43 (3d Cir. 2011) (finding plaintiffs failed to allege an imminent injury-in-fact where "we cannot now describe how [plaintiffs] will be injured in this case without beginning our explanation with the word 'if.'"); *Storino v. Borough of Point Pleasant Beach*, 322 F.3d 293, 297–98 (3d Cir. 2003) (finding plaintiffs failed to allege imminent injury-in-fact where "one cannot describe how the [plaintiffs] will be injured without beginning the explanation with the word 'if'").

In addition, the record evidence shows that the hypothetical scenario upon which AstraZeneca's stated harm is premised is extremely *unlikely* to occur. For

starters, the odds of winning FDA approval are slim for any new drug. AstraZeneca itself acknowledges that "very few early drug candidates are ever approved or commercialized," D.I. 19 at 2, and "[e]ven when a drug shows early promise in clinical trials, the rigorous drug approval process means very few of these research efforts result in a new drug or indication," D.I. 58 at 2. According to the declarant of the sole affidavit submitted by AstraZeneca in support of its motion, "[i]t can take decades . . . to shepherd a single potential new therapy through clinical trials" and "only one of every 5,000 compounds that enters preclinical testing will achieve FDA approval—a failure rate of 99.98%." D.I. 60 ¶ 7.

The odds of the FDA approving a new indication of Farxiga in the near future appear especially unlikely, as AstraZeneca concedes that its only clinical trials involving Farxiga's active moiety are "focused on 'combination product' therapies that would not be impacted by [the Guidance's] definition of a Qualifying Single Source Drug." D.I. 60 ¶ 23. But even if AstraZeneca could eventually win FDA approval of a new indication for Farxiga's active moiety at some future date, the record evidence provides no basis to believe that any new indication would be approved in a new NDA; and thus there is no basis to believe that CMS's definition of a qualifying single source drug would come into play if a

new indication were approved. If anything, the record suggests the opposite, as AstraZeneca says it "has developed multiple new uses for FARXIGA, resulting in FDA approvals to treat heart disease and chronic kidney disease, in addition to diabetes," D.I. 58 at 7–8, but none of these new uses were approved in a new NDA, D.I. 21-2 at 4. Finally, even if AstraZeneca could eventually obtain FDA approval for a new indication that met the criteria for a new NDA—perhaps "decades" from now—it would be highly unlikely that Farxiga would not have generic competition at that time and thus highly unlikely that it would still meet the definition of a qualifying single source drug. AstraZeneca insists, and the Government does not dispute, that 17 generic manufacturers have already received tentative approval to launch a Farxiga generic drug and that Farxiga "will experience generic competition sometime between October 2025 and Summer 2026." D.I. 60 ¶ 27.

For all these reasons, AstraZeneca's alleged harm in the form of decreases in incentives to develop new uses of Farxiga does not give it standing to assert Count I.

2.

AstraZeneca next argues that it has standing to assert Count II because the Guidance's bona fide marketing test will soon cause it an injury-in-fact in the form

of simultaneous "generic competition *and* mandatory pricing" "for months" after generic versions of Farxiga enter the market. D.I. 58 at 9 (emphasis in the original). According to AstraZeneca, "[t]he statute directs that if a generic product is 'approved and marketed' before or during [initial price applicability year] 2026, FARXIGA will be released from the Maximum Fair Price." D.I. 58 at 8 (citing §§ 1320f-1(e)(1)(A)(iii)–(B)(iii)). In AstraZeneca's words:

> The IRA is a heavy-handed statute that imposes a significant burden on manufacturers. The one critical concession the statute gives to AstraZeneca and other manufacturers is that when a drug product faces generic competition, the drug is no longer subject to the IRA's price controls. CMS's "bona fide marketing" test annihilates that statutory protection. Under the agency's test, AstraZeneca will have to sell FARXIGA at the agency's compelled below-market price, despite also facing generic competition for that same product between October 2025 and Summer 2026, unless and until the agency decides the generic product has been marketed in a sufficiently "robust and meaningful" manner.

D.I. 58 at 43–44. AstraZeneca says that CMS cannot comply with this statutory directive if it applies the bona fide marketing test because the reporting of the PDE data that CMS has said it will rely on to determine if there has been bona fide marketing of a generic drug "moves at a glacial pace." D.I. 19 at 27. In AstraZeneca's view, "[b]ecause that data is delayed by numerous months, FARXIGA's generic competitor will not satisfy the agency's 'bona fide marketing'

standard for months after generic entry—assuming the agency finds the generic's marketing sufficiently 'bona fide' even then." D.I. 58 at 9.

There are many flaws in this argument. To begin with, its legal premises are wrong. Neither § 1320f-1(e)(1) nor any other section of the Act requires the "release" of a drug selected for negotiation for the 2026 price period from the Program's maximum fair price if a generic version of that drug is approved and marketed before or during 2026. It is also not accurate to say that the Act "conce[des]" or even suggests in any way that a selected drug is not subject to the Act's price controls if it faces generic competition.

As discussed above, § 1320f-1(e)(1) defines the universe of qualifying single source drugs from which the negotiation-eligible drugs and ultimately the selected drugs are chosen. Section 1320f-1(c)—not § 1320f-1(e)(1)—governs the removal of drugs from the Program once they have been selected. Section 1320f-1(c)(2) provides that a selected drug "shall not be subject to the negotiation process" if CMS determines that a generic version of the drug has been approved by the FDA and marketed "before or during the negotiation period." 42 U.S.C. § 1320f-1(c)(2)(B). Under § 1320f-1(c)(1), if no generic version of the selected drug has been approved and marketed by the end of the negotiation period, then that selected drug is deemed a selected drug for the initial price applicability year

and for "each subsequent year beginning before the first year that begins at least 9 months after the date on which the Secretary determines at least one drug or biological product" has been approved and marketed.

The negotiation period for the 2026 price period began on October 1, 2023, and ends on August 1, 2024. *See* §§ 1320f(b)(4); 1320(d)(2)(A)–(B). Thus, under the express terms of the Act, if no generic version of a drug selected for the 2026 price period enters the market before August 1, 2024, then the selected drug is subject to any negotiated maximum fair price for the entirety of 2026 even if a generic drug later enters the market before or during 2026. And if no generic drug enters the market before April 1, 2026, then the selected drug is subject to any negotiated maximum fair price for the entirety of 2027 even if a generic drug enters the market between April 1, 2026 and December 31, 2027. In both scenarios, the selected drug is simultaneously subject to generic competition and mandatory pricing.

In this case it is undisputed that no generic version of Farxiga will enter the market before October 2025. Accordingly, since there will not be an approved generic version of Farxiga on the market by August 1, 2024, it is not the "agency's test" but rather the Act itself that requires AstraZeneca to "have to sell FARXIGA at the agency's compelled below-market price, despite also facing generic

competition for that same product between October 2025 and Summer 2026." D.I. 58 at 43–44. That alleged harm, therefore, cannot meet the causation and redressability requirements for standing, as it was not caused by the Guidance and could not be remedied by vacating the Guidance.

To the extent AstraZeneca meant to imply in its briefing that it would be injured by having to face generic competition and mandatory pricing simultaneously in 2027 because delays in PDE data reporting will prevent CMS from determining before April 1, 2026 that Farxiga had been subjected to bona fide marketing of generic competition, that harm does not constitute an actual or imminent injury sufficient to create standing. First, a generic version of Farxiga would have to be on the market before April 1, 2026 for Farxiga to be exempted from the negotiated maximum price in 2027. But whether a generic would be on the market by that date is speculative. AstraZeneca says that Farxiga "will experience generic competition *sometime* between October 2025 and Summer 2026." D.I. 20 ¶ 27 (emphasis added). AstraZeneca has not alleged, let alone established, that a generic version of Farxiga *will* be on the market before April 1, 2026. *See Clapper*, 568 U.S. at 409 ("Although imminence is concededly a somewhat elastic concept, it cannot be stretched beyond its purpose, which is to

ensure that the alleged injury is not too speculative for Article III purposes—that the injury is certainly impending.").

Second, AstraZeneca's allegation that CMS will "delay" "for months" after the market entry of a Farxiga generic competitor its determination of whether that competitor was bona fide marketed is also speculative. The Guidance expressly states that CMS's totality-of-the-circumstances inquiry "will not necessarily turn on any one source of data" and that "all data and other information will be reviewed in totality" to determine whether a manufacturer has engaged in bona fide marketing. D.I. 20-2 at 6, 77. AstraZeneca does not allege or suggest that CMS's receipt of these alternative sources of information would be "delayed." AstraZeneca also does not allege—and there is no reason to infer from the record evidence—that a delay in PDE reporting would affect the timing of CMS's determination that a generic drug had been bona fide marketed any more than such a delay would affect the timing of CMS's determination that a generic drug met AstraZeneca's definition of marketed. AstraZeneca does not allege, for example, that CMS would not consider PDE data to determine whether a generic drug had been exposed for sale (AstraZeneca's definition of "marketing").

Third, AstraZeneca has not alleged, let alone established, that Farxiga will experience generic competition that is exclusively marketed at a de minimis level

insufficient to qualify as bona fide marketing. And accepting as true AstraZeneca's allegations that 17 manufacturers have received tentative FDA approval to enter the market and that Farxiga will experience generic competition no later than Summer 2026, it is highly unlikely that all 17 of those manufacturers would market their drugs in only a de minimis manner.

In sum, AstraZeneca has not established that the harm it alleges it has suffered and will continue to suffer from CMS's bona fide marketing requirement creates standing to assert Count II.

3.

AstraZeneca also argues that it has standing to assert both of its APA claims because its "current decision-making about other drugs has been and will continue to be negatively affected by CMS's Guidance." D.I. 58 at 11. In AstraZeneca's words:

> Within the next three years, 50 more drug products will be selected [by CMS] for negotiation. As a large U.S. pharmaceutical company, AstraZeneca will very likely have products on that list. As it makes plans to develop and commercialize new versions of these and other products, AstraZeneca has no rational choice but to take the agency's current policies into account. That causes AstraZeneca harm now.

D.I. 58 at 11 (citations omitted).

The harm alleged here is too vague to establish a cognizable injury. *Nat'l Shooting Sports Found. v. Att'y Gen. of New Jersey*, 80 F.4th 215, 219 (3d Cir. 2023). The Guidance is only for the 2026 price period, and Farxiga is the only AstraZeneca drug selected for that period. AstraZeneca does not say or suggest in any way how its decision-making about other drugs has been or could be "negatively affected" by the Guidance. Nor does it say or suggest in any way how "tak[ing] the agency's current policies into account" causes it harm as it "makes plans to develop and commercialize" other drugs.

This alleged harm of negatively affected decision-making for price periods beyond 2026 also fails to meet the causation and redressability requirements for standing. AstraZeneca cannot trace an injury it might suffer in price periods that begin in 2027 and beyond to guidance that by its express terms governs only the 2026 price period. And vacating the Guidance could not provide AstraZeneca any relief with respect to its decision-making regarding other drugs that might be selected under future guidance that has not been released.

4.

At oral argument, AstraZeneca effectively abandoned the standing arguments it made in its briefing. Instead, it argued that the counteroffer of a maximum fair price for Farxiga that the Act requires it to submit to CMS on March

2, 2024 "supplies the basis for [AstraZeneca's] standing." D.I. 64 at 8:5–9. Its counsel explained this standing theory as follows:

> . . . [I]n order to make a counteroffer to the Government's price offer . . ., AstraZeneca needs to know what is the value of this product [Farxiga] that we have.
>
> The value of that product, among other things, depends on a couple of key components. One of them is, what is coming down the pipeline . . . that might, under the Government's construction of the guidance, be treated as the exact same drug and shunted into the same price? That's going to affect our valuation of the product right now, this product, Farxiga.
>
> The exact same calculus comes into play with respect to our other merits APA argument, which is the bona fide marketing requirement. If this drug, as should be, is taken back out of the price negotiation after generics come on the market, which 17 of them are poised to do as our declarant points out, that affects our valuation of the drug right now because we will understand that, in the world of the statute, this drug should be taken back out of the price program after a year.
>
> But *because the CMS has chosen to interpret the statute in two very faulty ways, we are not able to make that kind of valuation. We have no idea whether the value will be higher or lower because we don't know the impact of CMS's flawed guidance on our ability to negotiate.*
>
> *So we, essentially, have to walk in over the next 30 days to this counteroffer, based on a flawed definition*

> *that affects our ability to value our product. That is the reason that we have standing.*

D.I. 64 at 8:15–9:21 (emphasis added).

Of course, AstraZeneca *does* "know the impact of CMS's [allegedly] flawed guidance on [its] ability to negotiate." AstraZeneca described in detail in a 44-page Amended Complaint and 100 pages of briefing the content of the Guidance it challenges and the reasons why it contends that Guidance is unlawful. It cannot credibly argue that it is unable to understand the Guidance or how the Guidance applies as written to Farxiga.

The only uncertainty relating to the Guidance comes from the filing of this lawsuit. Because AstraZeneca seeks by this lawsuit a declaration that the IRA is unconstitutional and vacatur of the Guidance, so long as the suit is pending, AstraZeneca can say with a straight face that it has "no idea whether the value [of Farxiga] will be higher or lower." A plaintiff, however, cannot create standing to file a suit by filing the suit. *See Fair Hous. Council of Suburban Phila. v. Montgomery Newspapers*, 141 F.3d 71, 80 (3d Cir. 1998) ("[T]he pursuit of litigation alone cannot constitute an injury sufficient to establish standing under Article III."). To hold otherwise would eviscerate the Constitutional requirement of standing.

Accordingly, the injury articulated by AstraZeneca at oral argument is insufficient to confer standing for either of its APA claims.

* * * *

Because AstraZeneca has failed to identify a cognizable injury-in-fact that is caused by the Guidance and could be redressed by vacatur of the Guidance, it has not established the requisite standing to allege Counts I and II of the Amended Complaint and I will therefore dismiss those claims for lack of jurisdiction.

B.

Having determined that I lack jurisdiction over Counts I and II under Article III, I need not (and arguably cannot) address whether § 1320f-7 precludes judicial review of those claims.

V.

I turn next to AstraZeneca's claim that the IRA violates its Fifth Amendment due process rights. The Fifth Amendment prohibits the government from depriving a person of "life, liberty, or property, without due process of law." U.S. Const. amend. V.

AstraZeneca alleges in Count III that the IRA violates its right to due process "by directing the Secretary to fix [selected drug] prices at the 'lowest' level, without affording adequate procedural safeguards," D.I. 16 ¶ 143;

"strip[ping] manufacturers of any ability to meaningfully negotiate a reasonable price for their products," D.I. 16 ¶ 144; "dispens[ing] with traditional hearing and notice-and-comment rulemaking procedures," D.I. 16 ¶ 144; and "vest[ing] [CMS] with unchecked authority to finalize its decisions without any process for administrative or judicial review," D.I. 16 ¶ 144. The Government does not challenge AstraZeneca's standing to assert this claim, *see* D.I. 66, but it says that I should grant it summary judgment on Count III because AstraZeneca is not legally compelled to provide Medicare beneficiaries with drugs and therefore the IRA's imposition of caps on the amount the Government will reimburse AstraZeneca for drugs sales does not deprive AstraZeneca of a protected property interest for purposes of the Fifth Amendment. *See* D.I. 22 at 44–45.

A.

Before addressing the merits of Count III, I consider whether I have the authority to do so. Even if jurisdiction is not contested, I am obligated to assure myself of jurisdiction under Article III. *Trump v. Hawaii*, 585 U.S. 667, 697 (2018); *Wayne Land & Min. Grp., LLC v. Del. River Basin Comm'n*, 959 F.3d 569, 574 (3d Cir. 2020). For that reason, after oral argument, I ordered the parties to submit supplemental briefs "addressing whether Plaintiffs have standing to assert Count III." D.I. 65. Unfortunately, the Government ignored my order, and instead

of addressing in its supplemental brief whether AstraZeneca has standing, it merely reiterated that it "ha[s] not argued (and do[es] not now argue) that Plaintiffs lack standing to bring Count III." D.I. 66 at 2.

I had ordered the supplemental briefing because I had thought it might help me navigate the fine line between standing and the merits with respect to AstraZeneca's due process claim. As the Seventh Circuit observed in *Protect Our Parks, Inc. v. Chicago Park District*, 971 F.3d 722, 736 (7th Cir. 2020), "it is not unusual for the distinction between standing and the merits to cause conceptual trouble when a plaintiff alleges the deprivation of a dubious property or liberty interest." The court noted in *Protect Our Parks* that "when the existence of a protected property interest is an element of the claim, deciding whether the interest exists *virtually always* goes to the merits rather than standing." *Id.* (emphasis added). Notably, the court did not say that deciding whether the interest exists *always* goes to the merits. But unfortunately, the court in *Protect Our Parks* did not provide, and I have not been able to find in any other case, helpful guidance to determine *when* the question of whether the interest exists goes to the merits as opposed to *when* that question goes to standing. In this case, at the summary judgment stage of the litigation, distinguishing the issue of whether AstraZeneca has established a deprivation of a property interest that meets the injury-in-fact,

causation, and redressability requirements for standing from the issue of whether AstraZeneca has established a deprivation without due process of a property interest protected by the Constitution poses an epistemological question I'm not capable of answering. This being "one of those cases where the line between standing and the merits is rather fine but makes little practical difference," *Matushkina v. Nielsen*, 877 F.3d 289, 291 (7th Cir. 2017), I will assume I have jurisdiction and proceed to the merits. *Cf. Trump*, 585 U.S. at 682–83 ("assum[ing] without deciding that plaintiffs' statutory claims [were] reviewable" and that Court "ha[d] authority" to "address[ ] the merits of plaintiffs' statutory claims" when "[t]he justiciability of plaintiffs' challenge under the [statute] present[ed] a difficult question"); *but see id.* (noting that "[t]he Government d[id] not argue that [its justiciability] argument goes to the Court's jurisdiction").

B.

"[T]he first inquiry in every due process challenge is whether the plaintiff has been deprived of a protected interest in 'property' or 'liberty.'" *Am. Mfrs. Mut. Ins. Co. v. Sullivan*, 526 U.S. 40, 59 (1999). To have a protected property interest, "a person clearly must have more than an abstract need or desire" and "more than a unilateral expectation of it. He must, instead, have a legitimate claim of

entitlement to it." *Town of Castle Rock, Colo. v. Gonzales*, 545 U.S. 748, 756, (2005) (quoting *Bd. of Regents of State Colls. v. Roth*, 408 U.S. 564, 577 (1972)).

Distilled to its essence, the property interest AstraZeneca contends merits protection under the Fifth Amendment's due process clause is the ability to sell its drugs to Medicare at prices above the ceiling prices and negotiated maximum fair prices established by the IRA. The central and oft-repeated allegation in the Amended Complaint is that "the Program is designed to coerce manufacturers to submit to government-imposed price controls." D.I. 16 ¶ 94. *See also* D.I. 16 ¶ 1 ("This case is about a statute and guidance designed to cut costs to the federal government at great cost to innovation and the country's most vulnerable patients. The Inflation Reduction Act enacted sweeping changes to drug pricing under Medicare, jettisoning a market-based approach in favor of a new scheme of price controls established by the federal government."); D.I. 16 ¶ 13 ("The IRA jettisons . . . market-based solutions in favor of price controls set by the federal government."); D.I. 16 ¶ 16 ("Selected products are subject to statutory price ceilings defined to require deep cuts from the current, market-based prices. For nearly all drugs, there is no floor. The Secretary could decide that Medicare should pay only a penny for a particular drug, and the manufacturer would have to sell at that price . . . ."); D.I. 16 ¶ 19 ("[T]he IRA forces manufacturers to engage

in purported 'negotiations' but affords them no bargaining power, no meaningful opportunity to walk away, and no ability to protect their interests against a so-called 'maximum fair price' capped at an amount drastically below actual fair market value."); D.I. 16 ¶ 32 ("Historically, innovator manufacturers have been able to sell their products both commercially and under Medicare at prices dictated by market dynamics. That market-driven dynamic has now come to a crashing halt with the passage of the IRA."); D.I. 16 ¶ 38 ("The price is capped at a fraction of reference prices specified by statute and defined by the Guidance to be as low as possible, and the agency can insist that the 'maximum fair price' be set lower than the cap."); D.I. 16 ¶ 117 ("The IRA's design mandates that its targeted price controls must be trained on the most revolutionary therapies . . . ."); D.I. 16 ¶ 142 ("The IRA deprives AstraZeneca of . . . [its] common law right to sell its products at market prices free from arbitrary and inadequately disclosed governmental constraints."); D.I. 16 ¶ 143 ("The IRA deprives AstraZeneca of those property interests by directing the Secretary to fix prices at the 'lowest' level, without affording adequate procedural safeguards.").

AstraZeneca alleges in two paragraphs of the Amended Complaint that it also has a protected interest in undefined "patent rights." D.I. 16 ¶¶ 91, 142. But it never identifies a patent or explains how the IRA affects or could affect a patent

right. AstraZeneca does not allege that the IRA authorizes or will result in the seizure or threatened seizure of its patents, and it could not credibly allege that the Government's refusal to purchase a drug at the price demanded by AstraZeneca constitutes patent infringement. Although I pressed AstraZeneca on the issue at oral argument, its counsel was unable to articulate a coherent theory of why or how the IRA affects patent rights. *See* D.I. 64 at 38:6–39:8; D.I. 64 at 54:19–55:5; D.I. 64 at 62:15–65:5. But in any event, AstraZeneca alleges in the Amended Complaint that the IRA deprives it of these putative patent rights "by directing the Secretary to fix prices at the 'lowest level,' without affording adequate procedural safeguards" and "strip[ping] manufacturers of any ability to meaningfully negotiate a reasonable price for their products." D.I. 16 ¶¶ 143–44. And in its briefing, AstraZeneca similarly argues that the IRA deprives it of "protected interests in its patented drugs and the revenue it derives therefrom . . . by compelling sales of its products at well-below market prices." D.I. 19 at 29. Thus, the property interest encompassed by AstraZeneca's alleged "patent rights" is at bottom the ability to sell products to Medicare beneficiaries at prices above what the IRA requires.

No one, however, is entitled to sell the Government drugs at prices the Government won't agree to pay. *See Coyne-Delany Co. v. Cap. Dev. Bd.*, 616 F.2d 341, 342 (7th Cir. 1980) ("No one has a 'right' to sell to the government that

which the government does not wish to buy."). Just like private individuals and businesses, "the Government enjoys the unrestricted power to produce its own supplies, to determine those with whom it will deal, *and to fix the terms and conditions upon which it will make needed purchases*." *Perkins v. Lukens Steel Co.*, 310 U.S. 113, 127 (1940) (emphasis added). Neither the IRA nor any other federal law requires AstraZeneca to sell its drugs to Medicare beneficiaries. On the contrary, "participation in the Medicare program is a voluntary undertaking." *Livingston Care Ctr., Inc. v. United States*, 934 F.2d 719, 720 (6th Cir. 1991); *see also Dayton Area Chamber of Com. v. Becerra,* 2023 WL 6378423, at *11 (S.D. Ohio Sept. 29, 2023) ("[P]articipation in Medicare, no matter how vital it may be to a business model, is a completely voluntary choice.").

The IRA simply establishes maximum prices the Government will pay for selected drugs. These prices are lower than the prices CMS has been paying for the selected drugs. The whole point of the Program is to lower the prices of selected drugs that lack generic competition and account for a disproportionate share of Medicare's expenses. Understandably, drug manufacturers like AstraZeneca don't like the IRA. Lower prices mean lower profits. Drug manufacturers like AstraZeneca desire the old pricing regime, and they lobbied and perhaps expected Congress not to pass the IRA in 2022. Yeganeh Torbati and Jeff

Stein, *Lobbyists are Rushing to Influence the Democrats' Spending Bill*, THE WASHINGTON POST (Aug. 5, 2022), https://www.washingtonpost.com/business/2022/08/05/inflation-reduction-act-lobbyists/ [https://perma.cc/N5DN-R5FP]. But AstraZeneca's "desire" or even "expectation" to sell its drugs to the Government at the higher prices it once enjoyed does not create a protected property interest. *Castle Rock*, 545 U.S. at 756. And because AstraZeneca has no legitimate claim of entitlement to sell its drugs to the Government at any price other than what the Government is willing to pay, its due process claim fails as a matter of law. *Id.*

AstraZeneca insists that "participation in the Drug Price Negotiation Program is anything but voluntary" and that the Third Circuit "intimated as much" in *Sanofi Aventis U.S. LLC v. HHS*, 58 F.4th 696 (3d Cir. 2023). In support of this assertion, it points to dicta in *Sanofi* that "[t]he federal government dominates healthcare" and "uses [its] market power to get drug makers to subsidize healthcare." D.I. 58 at 48 (quoting *Sanofi,* 58 F.4th at 699). But neither that dicta nor anything else the Third Circuit said in *Sanofi* suggests in any way that drug manufacturers are required to participate in the Program or any other part of Medicare.

Sanofi did not mention let alone discuss the IRA or the Program. At issue in *Sanofi* was the lawfulness of regulations issued to implement the so-called 340B Program created by the Veterans Health Care Act of 1992, Pub. L. No. 102-585, 106 Stat. 4943 (1992), codified at 42 U.S.C. §§ 256b; 1396r-8. Like the IRA's Program, the 340B Program conditions drug manufacturers' participation in Medicare on their offering certain drugs at capped prices. In the case of the 340B Program, "drug makers that want to take part in Medicare or Medicaid must offer their drugs at a discount to certain healthcare providers . . . that typically care for low-income and rural persons." *Sanofi*, 58 F.4th at 699. The court took note in *Sanofi* of the fact that Medicare and Medicaid account "for almost half the annual nationwide spending on prescription drugs," and that the Government "uses that market power to get drug makers to subsidize healthcare" by conditioning their participation in Medicare on selling drugs to the healthcare providers of low-income and rural patients at below-market prices. *Id.* This observation makes sense, and there is nothing sinister in the Government wielding its market power to obtain lower prices or set "conditions upon which it will make needed purchases." *Perkins*, 310 U.S. at 127. The opportunity to sell drugs to 50% of the potential market for prescription drugs provides a powerful incentive for a manufacturer to agree to sell certain drugs to certain healthcare providers at below-market prices.

The Government can offer that incentive because of its market power. But it does not follow, and the court did not say or imply in *Sanofi*, that the 340B Program or any other law requires a drug manufacturer to participate in the 340B Program or any other Medicare program.

The IRA's Drug Price Negotiation Program operates much like the 340B Program. The IRA offers a powerful incentive—the opportunity to sell products to more than 49 million Medicare and Medicaid beneficiaries—to induce drug manufactures to participate in the Program and negotiate with CMS maximum fair prices for selected drugs. That incentive is not, as AstraZeneca contends, "a gun to the head." D.I. 58 at 50. It is a potential economic opportunity that AstraZeneca is free to accept or reject.

Because AstraZeneca's participation in Medicare is not involuntary, AstraZeneca does not have a protected property interest in selling drugs to the Government at prices the Government will not agree to pay. Accordingly, AstraZeneca's due process claim fails as a matter of law.

VI.

For the reasons stated above, I lack jurisdiction to hear Counts I and II; and, because AstraZeneca has not identified the deprivation of a constitutionally protected property interest, Count III fails as a matter of law. I will therefore deny

AstraZeneca's Motion for Summary Judgment (D.I. 18) and grant Defendants' Motion for Summary Judgment (D.I. 21).

The Court will enter an order consistent with this Memorandum Opinion.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTRAZENECA PHARMACEUTICALS LP and ASTRAZENECA AB, Plaintiffs, v. XAVIER BECERRA, in his official capacity as SECRETARY OF HEALTH AND HUMAN SEVICES, and CHIQUITA BROOKS-LASURE, in her official capacity as ADMINISTRATOR OF THE CENTERS FOR MEDICARE & MEDICAID SERVICES, Defendants.	Civ. No. 23-931-CFC

ORDER

At Wilmington on this First day of March in 2024, having considered the parties' cross-motions for summary judgment, it is hereby ORDERED that Plaintiffs' Motion for Summary Judgment (D.I. 18) is DENIED; and it is further

ORDERED that Defendants' Cross-Motion for Summary Judgment (D.I. 21) is GRANTED.

CHIEF UNITED STATES DISTRICT JUDGE

IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

ASTRAZENECA PHARMACEUTICALS LP and ASTRAZENECA AB, Plaintiffs, v. XAVIER BECERRA, in his official capacity as SECRETARY OF HEALTH AND HUMAN SEVICES, and CHIQUITA BROOKS-LASURE, in her official capacity as ADMINISTRATOR OF THE CENTERS FOR MEDICARE & MEDICAID SERVICES, Defendants.	Civ. No. 23-931-CFC

JUDGMENT IN A CIVIL CASE

For the reasons stated in the Court's Memorandum Opinion and Order of March 1, 2024;

IT IS ORDERED that judgment is entered in favor of Defendants and against Plaintiffs.

Dated: 3.1.24

Chief Judge

(By) Deputy Clerk

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTRAZENECA PHARMACEUTICALS LP and ASTRAZENECA AB, Plaintiffs, v. XAVIER BECERRA, in his official capacity as SECRETARY OF HEALTH AND HUMAN SERVICES, and CHIQUITA BROOKS-LASURE, in her official capacity as ADMINISTRATOR OF THE CENTERS FOR MEDICARE & MEDICAID SERVICES, Defendants.	Civil Action No. 23-931-CFC

NOTICE OF APPEAL

Notice is hereby given that Plaintiffs AstraZeneca Pharmaceuticals LP and AstraZeneca AB hereby appeal to the United States Court of Appeals for the Third Circuit from the Court's March 1, 2024 Memorandum Opinion (D.I. 70), Order denying Plaintiffs' motion for summary judgment and granting Defendants' cross-motion for summary judgment (D.I. 71), and corresponding Judgment (D.I. 72), and

from all orders, opinions, decisions, and rulings prior to the entry of the order that merge therein.

Respectfully submitted,

Dated: April 29, 2024

McCarter & English, LLP

Catherine E. Stetson*
Susan M. Cook*
Marlan Golden*
HOGAN LOVELLS US LLP
555 Thirteenth Street, NW
Washington, D.C. 20004
Tel: (202) 637-5600
cate.stetson@hoganlovells.com
susan.cook@hoganlovells.com
marlan.golden@hoganlovells.com

*admitted pro hac vice

/s/ Daniel M. Silver
Daniel M. Silver (#4758)
Alexandra M. Joyce (#6423)
Renaissance Centre
405 North King Street, 8th Floor
Wilmington, DE 19801
(302) 984-6300
dsilver@mccarter.com
ajoyce@mccarter.com

Attorneys for Plaintiffs

CERTIFICATE OF SERVICE

I certify that the foregoing Joint Appendix was filed with the Clerk using the appellate CM/ECF system on July 15, 2024. All counsel of record are registered CM/ECF users, and service will be accomplished by the CM/ECF system. I also hereby certify that pursuant to Third Circuit Local Appellate Rule 30.1, four paper copies of the foregoing Joint Appendix were sent on today's date via overnight Federal Express to the Clerk of this Court.

July 15, 2024

/s/ Catherine E. Stetson
Catherine E. Stetson
HOGAN LOVELLS US LLP
555 Thirteenth Street, N.W.
Washington, D.C. 20004
(202) 637-5600
cate.stetson@hoganlovells.com

Counsel for Plaintiffs-Appellants

No. 24-1819

IN THE

United States Court of Appeals for the Third Circuit

ASTRAZENECA PHARMACEUTICALS, LP, *ET AL.*,

Plaintiffs-Appellants,

v.

XAVIER BECERRA, *ET AL.*,

Defendants-Appellees.

On Appeal from the United States District Court
for the District of Delaware
No. 23-cv-00931-CFC, Chief Judge Colm F. Connolly

JOINT APPENDIX – VOLUME II OF II (JA53- JA322)

Brian M. Boynton
Principal Deputy Assistant Attorney General
Michael S. Raab
Lindsey Powell
Steven A. Myers
David L. Peters
Catherine Padhi
Attorneys, Appellate Staff
United States Department of Justice
Civil Division, Room 7712
950 Pennsylvania Avenue, NW
Washington, DC 20530
(202) 514-5091

Counsel for Defendants-Appellees

Catherine E. Stetson
Susan M. Cook
Danielle Desaulniers Stempel
Claire Adkins Rhodes
HOGAN LOVELLS US LLP
555 Thirteenth Street, N.W.
Washington, D.C. 20004
(202) 637-5600
cate.stetson@hoganlovells.com

Counsel for Plaintiffs-Appellants

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTRAZENECA PHARMACEUTICALS LP, 1800 Concord Pike Wilmington, DE 19803, and ASTRAZENECA AB, S-151 85 Södertälje, Sweden, Plaintiffs, v. XAVIER BECERRA, in his official capacity as SECRETARY OF HEALTH AND HUMAN SERVICES, 200 Independence Avenue, S.W. Washington, DC 20201, and CHIQUITA BROOKS-LASURE, in her official capacity as ADMINISTRATOR OF THE CENTERS FOR MEDICARE & MEDICAID SERVICES, 7500 Security Boulevard Baltimore, MD 21244, Defendants.	Civil Action No. 1:23-cv-931-CFC

AMENDED COMPLAINT

AstraZeneca Pharmaceuticals LP and AstraZeneca AB (collectively, AstraZeneca) brings this Complaint challenging certain aspects of the drug pricing negotiation provisions of the Inflation Reduction Act of 2022, Pub. L. 117-169 (IRA), as well as recent guidance issued by the Centers for Medicare & Medicaid Services (CMS) purporting to implement the statute.

PRELIMINARY STATEMENT

1. This case is about a statute and guidance designed to cut costs to the federal government at great cost to innovation and the country's most vulnerable patients. The Inflation Reduction Act enacted sweeping changes to drug pricing under Medicare, jettisoning a market-based approach in favor of a new scheme of price controls established by the federal government. The IRA's drug pricing provisions, however, run headlong into the goals of the Orphan Drug Act, a federal statute designed to encourage manufacturers to invest in new therapies for rare (or "orphan") diseases.

2. It is not uncommon for an orphan drug to have multiple designations for multiple different rare conditions, as is the case with AstraZeneca's LYNPARZA® (olaparib) and SOLIRIS® (eculizumab), both of which provide important therapeutic options for patients with a variety of rare diseases. The IRA nominally exempts orphan drugs from its drug pricing program – so long as the drug is designated for the treatment of a single orphan condition. 42 U.S.C. § 1320f-1(e)(3)(A). Should a drug be designated for a second orphan condition – as is often the case – the exemption no longer applies, meaning that an orphan-protected drug product could immediately be selected for negotiation and subject to the resulting price controls in as little as two years. The losers in this cost-cutting exercise, in the end, will be the patients who need new therapies for their rare diseases.

3. Innovator pharmaceutical companies take on enormous risks in developing new drug products. It takes vast amounts of time and the support of significant monetary investment to identify, test, and develop any new drug candidate. Even when a drug shows early promise in clinical trials, the United States Food and Drug Administration (FDA)'s rigorous drug approval process means very few of those early drug candidates are ever approved and commercialized.

Studies estimate that only *one* out of every 5,000 compounds that enters preclinical testing will achieve FDA approval – a failure rate of 99.98%.[1]

4. The most important constituents depending on that high-risk, low-probability drug development marathon are patients, whose well-being – and sometimes lives – depend on the efficacy and safety of the therapies available to treat them. There is one subset of patients, in particular, for whom drug makers' research and investment choices may spell life or death: individuals with what are called "orphan diseases" – rare illnesses or afflictions shared by a vanishingly small cohort in the United States.

5. Orphan diseases are generally defined as conditions that affect fewer than 200,000 people in the entire country – less than the population of Sussex County, Delaware. They vary in name recognition; cystic fibrosis and Lou Gehrig's disease are orphan illnesses. So are eosinophilic esophagitis and peritoneal cancer. Individually, these diseases are extremely rare. But collectively, they number over seven thousand, affecting about 30 million Americans and 400 million people worldwide. Half of these patients are children.

6. Until the 1980s, individuals with rare diseases had very few options for drug product treatment. The process for pharmaceutical manufacturers to discover, test, and secure approval of a drug was so challenging that very few manufacturers would take that risk for a small patient population. That is why drug products designed to treat rare diseases are called "orphan drugs": There was little incentive for manufacturers to "adopt" and develop them, given the costs associated with research and development and the low odds of crossing the finish line with FDA approval.

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[1] Sandra Kraljevic et al., *Accelerating Drug Discovery*, 5 Eur. Molecular Biology Org. Reps. 837, 837 (2004), *available at* https://bit.ly/2Y2gwEK.

7. In 1983, Congress passed the Orphan Drug Act, a law designed to create incentives for manufacturers to discover, sponsor, and market drugs for rare-disease patient populations. The Orphan Drug Act does so by providing, among other things, seven years of marketing exclusivity to sponsors of approved drug products covering orphan indications. Importantly, in this context, the Orphan Drug Act does not limit the number of orphan designations a drug may receive, or constrain the resulting market exclusivity by the number of orphan indications that are approved. Nor is a product ineligible for orphan exclusivity simply because it is also approved for non-orphan uses.

8. The Orphan Drug Act has been successful. Since 1983, FDA has approved approximately six hundred distinct drug products designed to treat orphan conditions suffered by tens of millions of Americans. NORD, *New Study Investigates the Number of Available Orphan Products, Generics, and Biosimilars* (Mar. 25, 2021), *available at* https://rarediseases.org/new-study-investigates-the-number-of-available-orphan-products-generics-and-biosimilars/. As one FDA historian put it, "the Orphan Drug Act finally provided for many of those orphaned among blockbuster treatments a hope of their own." FDA, *The Story Behind the Orphan Drug Act*, *available at* https://www.fda.gov/industry/fdas-rare-disease-day/story-behind-orphan-drug-act.

9. Upon enactment, patients of rare diseases had reason to be optimistic, because the Orphan Drug Act facilitated market-based incentives to support the development of new therapies for their orphan conditions.

10. Indeed, many cancer medicines in the U.S. launch first in an orphan indication and broaden their use over time to additional populations. One example of this is AstraZeneca's drug LYNPARZA® (olaparib), a small-molecule cancer medicine approved in 2014 in the U.S. for a small group of late-line ovarian cancer patients. Pre-approval, FDA designated LYNPARZA as

an orphan drug for that indication. Additional trials added small groups of breast and pancreatic cancer patients, with the most recent indication in prostate cancer approved just this year – nine years later. If the IRA had been in place, significant disincentives would have existed for pursuing the late-line ovarian cancer approval in the U.S., an indication which has benefited patients in great need of this unique medicine for their rare condition.

11. Another example is Alexion (AstraZeneca Rare Disease)'s SOLIRIS® (eculizumab), which has received approval to treat four rare diseases, including debilitating and potentially life-threatening neuromuscular and hematological diseases. First approved in 2007 in paroxysmal nocturnal haemoglobinuria (PNH), a rare chronic blood disorder, historic dynamics enabled continued research investment to support further innovation, resulting in a U.S. approval more than a decade later in neuromyelitis optica spectrum disorder (NMOSD), a rare autoimmune disease that affects the central nervous system. The IRA would have deterred the continued development of this life-changing medicine for patients with rare diseases beyond its initial indication.

12. The work done by the Orphan Drug Act is far from over. Even with the gains made following its passage, more than 90% of orphan diseases have no treatment options. The Orphan Drug Act encourages manufacturers to research and develop drugs for small patient populations. But the Orphan Drug Act did not – and could not – relieve the risk manufacturers take when they embark on the process of research and discovery. Manufacturers still confront daunting odds for each and every product they attempt to perfect and bring to market. They accept those odds because they understand that *if* they discover a compound, *if* it can be made into a drug that proves safe and efficacious, *if* it obtains regulatory approval, and *if* it reaches patients and fulfills a medical need, the product *might* earn market-based returns.

13. Enter the IRA. Medicare – which covers approximately 20% percent of the entire U.S. population – has long relied on market-driven pricing incentives to control prescription drug costs. The IRA jettisons these market-based solutions in favor of price controls set by the federal government. Specifically, Congress has purported to delegate to CMS the authority to unilaterally select drugs and biologics lacking generic competition for a purported "negotiation" with their manufacturers after such drugs have been on the market for a specified period, and then to dictate a "maximum fair price" (sometimes referred to as "MFP") for each selected drug product that cannot exceed a statutory ceiling. 42 U.S.C. § 1320f-1.

14. To be clear, there is no actual negotiation involved: A manufacturer may either consent to the agency's dictated price or face an extreme tax penalty of up to 95% of the drug's gross U.S. revenues on the drug – including non-Medicare sales. *Id.* § 1320f-5(a)(6); 26 U.S.C. § 5000D.[2] Manufacturers thus have no real choice but to accede to the agency's unilaterally dictated price or terminate its Medicare Part D agreements and Medicaid rebate agreement – not just for the drug in question, but for *all* of the manufacturer's drugs.

15. Congress paired the scale of this market intervention with a breathtakingly expansive grant of implementation authority to CMS. The IRA authorizes CMS to implement the particulars of this program through guidance, without any notice or opportunity to comment afforded to drug manufacturers – or, for that matter, patients themselves. Pub. L. 117-169, Title I, § 11002(c); 42 U.S.C. § 1320f-1. As if that was not enough, the statute also purports to shield

[2] The Internal Revenue Service recently issued a notice that it "intend[s] to propose regulations" interpreting this provision, "including how taxpayers would report and pay" this excise tax. *See* IRS Notice 2023-52, "Section 5000D Excise Tax on Sales of Designated Drugs; Reporting and Payment of the Tax" (Aug. 4, 2023). The IRS notice indicates that the tax penalty *may* be limited to Medicare sales. *See id.* at 3.

several key aspects of the new drug pricing program from judicial review, including the selection of a particular drug product for negotiation and the determination of a "maximum fair price." 42 U.S.C. § 1320f-7.

16. The IRA is designed to result in steep discounts. Selected products are subject to statutory price ceilings defined to require deep cuts from the current, market-based prices. For nearly all drugs, there is no floor. The Secretary could decide that Medicare should pay only a penny for a particular drug, and the manufacturer would have to sell at that price or assume massive liabilities.

17. Multiple lawsuits have been filed challenging the constitutionality of the IRA. There is little question that the statute's draconian regime violates a number of constitutional protections, including basic due process principles, as explained later. CMS compounded the injury, however, when it purported to implement the program through guidance.

18. In March and June 2023, CMS issued two Medicare Drug Price Negotiation Program guidance documents detailing how the agency planned to execute these sweeping changes, with the first tranche of selected drugs to be identified no later than September 1. The two guidance documents (collectively referred to as the Guidance Documents) violate the Administrative Procedure Act (APA) for at least two reasons: They override the statutory definition of "Qualifying Single Source Drug," such that the term impermissibly includes two different drugs approved at different times, and they add a new "bona fide marketing" requirement that sweeps drugs into the selection process even when they have generic competition, and keeps them subject to the discounted price longer.

19. These statutory violations only serve to compound the due process problems inherent in the IRA itself. On the front end, the IRA forces manufacturers to engage in purported

"negotiations" but affords them no bargaining power, no meaningful opportunity to walk away, and no ability to protect their interests against a so-called "maximum fair price" capped at an amount drastically below actual fair market value. Then, on the back end, it purports to preclude affected manufacturers even from seeking judicial review. 42 U.S.C. § 1320f-7. In sum: Manufacturers have no meaningful right to participate or be heard from beginning to end. The cumulative effect of these provisions violates the procedural due process guarantees of the Fifth Amendment.

20. The IRA also undermines the Orphan Drug Act by radically reducing the market incentives for pharmaceutical manufacturers to invest in new drug candidates and new indications for existing therapies, like LYNPARZA and SOLIRIS. This is especially the case when it comes to treatments targeting orphan indications: While the IRA exempts orphan drugs from selection for their first orphan designations, it *removes* that exemption once the drug receives any *additional* orphan designations. By reducing manufacturers' ability to recoup their investment on new orphan indications for existing drugs post-approval, the IRA disincentivizes the very research and development the Orphan Drug Act was intended to – and for the last four decades, did – spur. The IRA's stingy approach to orphan products generates real risk that future treatment breakthroughs will be jeopardized, particularly for therapies with the potential to treat multiple orphan conditions, undermining patient access to meaningful treatment options and life-saving therapies.

21. These are not hypothetical harms. They are already happening. *See* Joe Grogan, *The Inflation Reduction Act Is Already Killing Potential Cures*, Wall Street Journal (Nov. 3, 2022), *available at* https://www.wsj.com/articles/the-inflation-reduction-act-killing-potential-cures-pharmaceutical-companies-treatment-patients-drugs-prescriptions-ira-manufacturers-11667508291?ns=prod/accounts-wsj.

22. CMS has identified the first ten drugs selected for negotiation, including AstraZeneca's FARXIGA. Once that process starts, it moves quickly. The manufacturer then must enter into an agreement to "negotiate" by October 1, 2023. AstraZeneca therefore seeks expedited briefing in this administrative record-based case to allow for an early decision.

PARTIES

23. AstraZeneca is a biopharmaceutical company focusing on the discovery, development, manufacturing, and commercialization of medicines.

24. Plaintiff AstraZeneca Pharmaceuticals LP is a limited partnership organized in Delaware with its principal place of business in Wilmington, Delaware. Plaintiff AstraZeneca AB is a company operating and existing under the laws of Sweden, with its principal place of business at S-151 85 Södertälje, Sweden.

25. Defendant Xavier Becerra is the Secretary of the U.S. Department of Health and Human Services (HHS). Defendant Becerra maintains an office at 200 Independence Avenue, S.W., Washington, D.C. 20201.

26. Defendant Chiquita Brooks-LaSure is the Administrator of CMS and is responsible for administering the guidance and statutory provisions challenged here on behalf of the Secretary. Defendant Brooks-LaSure maintains an office at 7500 Security Boulevard, Baltimore, Maryland, 21244.

JURISDICTION AND VENUE

27. Jurisdiction in this Court is grounded upon and proper under 28 U.S.C. § 1331, in that this civil action arises under the laws of the United States; 28 U.S.C. § 1346, in that this case involves claims against the federal government; 28 U.S.C. § 1361, in that this is an action to compel officers of the United States to perform their duty; and 28 U.S.C. §§ 2201–2202, in that

there exists an actual justiciable controversy as to which AstraZeneca requires a declaration of its rights by this Court and injunctive relief to prohibit Defendants from violating laws and regulations.

28. Venue is proper in this Court under 28 U.S.C. § 1391(e) because this is a civil action in which Defendants are officers of the United States acting in their official capacities.

FACTUAL BACKGROUND

I. Statutory and Regulatory Background

A. Medicare and FDA's Drug Approval Process

29. The Medicare program, enacted in 1965, provides health insurance for individuals 65 years of age and older, some individuals with disabilities under age 65, and individuals with certain conditions such as end-stage renal disease. Medicare Part B covers enrolled beneficiaries for, in relevant part, drugs and biologicals administered by physicians and other health care providers. Medicare Part D, which is optional, helps cover enrolled beneficiaries for the cost of non-physician-administered drugs. In totality, approximately 20 percent of all Americans are covered by Medicare.

30. All "new drugs" must be approved by FDA before being introduced or delivered for introduction into interstate commerce. 21 U.S.C. §§ 355(a), 331(d). A "new drug" may be a drug product that has never been approved, or it may be an approved drug product with a change, such as a new intended use or indication, or a different strength or dosage form. 21 U.S.C. § 321(p). Innovator drugs are typically approved under a New Drug Application (NDA) or a Biologics License Application (BLA).

31. Innovator pharmaceutical companies invest tremendous resources into pursuing a new drug candidate in the hopes that it might provide new therapeutic options for patients that can

save their lives, or at least make them better. The process is arduous, however, and only a scant few early drug candidates are ever approved and commercialized. For that reason, innovator drugs are often rewarded with periods of marketing exclusivity and patent rights.

32. Historically, innovator manufacturers have been able to sell their products both commercially and under Medicare at prices dictated by market dynamics. That market-driven dynamic has now come to a crashing halt with the passage of the IRA.

B. Congress Passes the IRA

33. In August 2022, President Biden signed the IRA, which made sweeping changes to health care, tax, and climate laws. Relevant here, the IRA provides for a "Drug Price Negotiation Program" that lowers the Medicare Parts B and D prices of certain drugs and biologics that lack generic or biosimilar competition, starting in 2026.

34. Starting September 1, 2023, the Secretary is directed each year to select a specified number of "negotiation-eligible" drugs with the highest total Part B or D expenditures over a specified preceding 12-month period. 42 U.S.C. § 1320f-1(b)(1)(A). CMS must rank these "negotiation-eligible" drugs in order of the highest total Medicare expenditures during that period and must select an increasing number of the highest ranked drugs for the Program each year. *Id.* § 1320f–1(a)-(b). The number of drugs selected for price-setting is cumulative. Once a drug is selected, it remains selected until the first year that begins at least nine months *after* the date on which CMS determines that a generic version of the drug is approved and marketed. *Id.* § 1320f–1(c)(1). Thus, for the first initial price applicability year (aptly known as "IPAY"), 2026, CMS will select up to ten Part D drugs. For 2027, CMS will select up to fifteen more Part D drugs, on top of the ten drugs previously selected. For 2028, CMS will select up to fifteen more Part B or D

drugs. And for 2029 and each year thereafter, CMS will select up to twenty more Part B or D drugs. *Id.*

35. To be eligible for selection and negotiation, a drug must be a "Qualifying Single Source Drug." 42 U.S.C. § 1320f-1(d)(1). That term is expressly defined in the statute, and the definition has several parts. First, for the first IPAY, the drug must be "a covered part D drug (as defined in section 1395w-102(e) of this title [the Medicare statute])." 42 U.S.C. § 1320f-1(e)(1). Second, the drug is required to be a drug approved by FDA, and at least 7 years must have elapsed "since the date of such approval." *Id.* § 1320f-1(e)(1)(A). And third, the drug must not be the reference listed drug for a generic drug that has been "approved and marketed." *Id.* The same is true for biological products, except the applicable time period is 11 years from the date of "such licensure" by FDA, and no biosimilar must have been "licensed and marketed." *Id.* § 1320f-1(e)(1)(B).

36. Orphan drugs are nominally exempt from selection – but only so long as the drug is designated for the treatment of a single orphan condition and all approved indications are limited to the treatment of that one orphan condition. 42 U.S.C. § 1320f-1(e)(3)(A). In other words, orphan drugs are only exempt so long as they have a single orphan designation. Should a drug even be designated for the treatment of a second orphan condition, as is often the case with orphan therapies, the exclusion no longer applies, and the market benefits of the seven years of exclusivity promised by the Orphan Drug Act is effectively a nullity, as the product could be selected for negotiation immediately and subject to the resulting price controls in as little as two years.

37. Once a manufacturer's drug is selected for negotiation, the manufacturer must enter into an agreement to negotiate the price of the drug. 42 U.S.C. § 1320f-3(a). The agency then purportedly "negotiate[s]" with the manufacturer over a "maximum fair price" for the selected

drug, with the agency ultimately having the final say with a take-it-or-leave-it offer. *Id.* This is a negotiation in name only. The IRA directs CMS to "develop and use a consistent methodology and process . . . for negotiations . . . that aims to achieve the *lowest* maximum fair price for each selected drug." *Id.* § 1320f–3(b)(1) (emphasis added).

38. The "maximum fair price" contemplated by the IRA, however, is neither maximum nor fair. The price is capped at a fraction of reference prices specified by statute and defined by the Guidance to be as low as possible, and the agency can insist that the "maximum fair price" be set lower than the cap. 42 U.S.C. § 1320f-3(c). The "maximum fair price" will be adjusted each subsequent year by an inflation factor for a specified preceding 12-month period.

39. Once CMS has imposed a maximum fair price for a selected drug, the statute provides that the manufacturer must provide "access to such price" to a wide variety of individuals and entities participating in Medicare. *Id.* § 1320f–2(a)(1). These participants include all eligible Medicare beneficiaries who are dispensed drugs under Medicare Parts B and D; all "pharmacies, mail order services, and other dispensers" that dispense drugs to Medicare beneficiaries; and all "hospitals, physicians, and other providers of services and suppliers" that furnish or administer drugs to Medicare beneficiaries. *Id.* § 1320f–2(a)(1)(A)-(B); *see id.* § 1320f(c)(2).

40. Manufacturers that fail to provide the required access to the maximum fair price are subject to a civil monetary penalty of ten times the difference between the price the manufacturer actually charges and the maximum fair price, multiplied by the total number of units sold. *Id.* § 1320f–6(a).

41. None of this process occurs at arm's length. Any manufacturer that declines to enter into negotiations, or declines to agree with CMS on a "maximum fair price," is subject to penalty in the form of an escalating and punitive "excise tax." 26 U.S.C. § 5000D(b). The statute

suggests this tax can be as high as 95% of the *total* U.S. revenues for the drug. *Id.* § 5000D(a). The penalty continues to accrue every day until the manufacturer acquiesces to CMS's demands (or until the drug in question ceases to be a selected drug).

42. The penalty is calculated based on an "applicable percentage," which starts at 65% and increases by 10% for each successive quarter that the manufacturer is out of compliance, to a maximum of 95%. *Id.* § 5000D(d). The statute provides that the penalty is "in an amount such that the applicable percentage is equal to the ratio of (1) such tax, divided by (2) the sum of such tax and the price for which so sold [sic]." *Id.* § 5000D(a). The excise-tax penalty thus represents a multiple of the manufacturer's total revenues from the drug in question, not merely its profits.

43. The IRA provides for the "[s]uspension" of the excise-tax penalty, but only if the manufacturer terminates its Medicare Part D agreements and Medicaid rebate agreement – not just for the drug in question, but for *all* of the manufacturer's drugs. 26 U.S.C. § 5000D(c); *see id.* § 5000D(c)(1) (providing that the penalty is suspended only during a period in which "none of the drugs of the manufacturer … are covered by an agreement" under certain programs within Medicare Part D and the manufacturer has terminated "all applicable agreements," including agreements necessary for the manufacturer's drugs to be payable under Medicare and Medicaid). Terminating the Medicaid rebate agreement would also result in all of the manufacturer's products losing Part B coverage. 42 U.S.C. § 1396r–8(a)(1). Thus, in order to suspend application of the tax penalty, a pharmaceutical manufacturer must entirely cease participation in both Medicare and Medicaid, withdrawing the availability of its products to potentially millions of patients. This draconian "alternative" to negotiation is no alternative at all – at least for a manufacturer that hopes to keep its doors open.

44. Manufacturers that disagree with the selection of their drug or with the price dictated by CMS are, according to the IRA, out of luck. Congress included in the statute a provision purporting to preclude judicial review for certain key aspects of the drug price negotiation program, including the "selection of drugs," the "determination of qualifying single source drugs," and the "determination of a maximum fair price." 42 U.S.C. § 1320f-7.

C. CMS Issues Guidance Implementing The IRA

45. On March 15, 2023, CMS issued an initial guidance document detailing how the agency planned to execute these sweeping changes for the first year of the program. CMS, *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026* (Mar. 15, 2023) (the Initial Guidance).

46. The foundational policies governing the selection of drugs subject to negotiation for IPAY 2026 are set forth in Section 30 of the Initial Guidance. Leaning into the IRA's power-grab, CMS issued Section 30 in final form, with no opportunity for manufacturers or impacted patients to comment. Initial Guidance at 2, 5.

47. On June 30, 2023, CMS released another guidance document representing the agency's final word on implementation of the Drug Price Negotiation Program before the selection of the first year's list of drugs occurs by September 1, 2023. CMS, *Medicare Drug Price Negotiation Program: Revised Guidance, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026* (June 30, 2023) (the Final Guidance). The Final Guidance doubled down on the most problematic aspects of Section 30.

48. The Guidance Documents violate the IRA in at least two ways.

49. First, CMS impermissibly overrode the statutory definition of an individual "Qualifying Single Source Drug" (QSSD). The statutory text makes clear that whether a drug constitutes its own Qualifying Single Source Drug depends on whether it has been approved under a separate New Drug Application (NDA) or licensed under a separate Biologics License Application (BLA). 42 U.S.C. § 1320f-1(e). In its Guidance Documents, however, CMS has defined a Qualifying Single Source Drug to embrace *all* dosage forms and strengths of *any* drug marketed by the manufacturer with the same active moiety or ingredient – greatly expanding the universe of products that are lumped together and treated as a single "drug." Initial Guidance at 8; Final Guidance at 99.

50. The agency's interpretation has material consequences for manufacturers: Two products with the same active moiety – including one approved years after the first – will run on the same selection clock, based on the approval or licensure date of the earlier approved product. Medicare expenditures on both products will be aggregated for purposes of ranking the qualifying single source drug for selection for negotiation. In addition, the negotiated maximum fair price will apply across both products.

51. Second, CMS impermissibly expanded the requirements that must be met before a drug is deemed to have generic competition such that it is ineligible for selection or negotiation. The IRA sets up two alternative pathways for moderating the prices of those drugs with the highest levels of Medicare spending: market-based competition in the form of a generic or biosimilar competitor, or failing that, price controls. The IRA specifies two objective criteria for a generic drug or biosimilar to render a brand name drug ineligible for selection and negotiation: the generic drug must be "approved" (or in the case of biologics, "licensed") and it must be "marketed." 42 U.S.C. §§ 1320f-1(e)(1)(A) and (B). Both of these requirements are a check-the-box, point-in-

time determination: A drug is either approved or it is not, and it is either marketed or it is not. A drug is approved when FDA grants an application or licensure for the product, and it is marketed when it has been launched by its manufacturer and enters the commercial marketplace for sale.

52. In its Guidance Documents, however, CMS has created an entirely new and different test: CMS will subjectively assess the generic or biosimilar biological product over time in order to determine whether it has been the subject of "bona fide marketing." Initial Guidance at 62; Final Guidance at 101–102. The agency's subjective "bona fide marketing" test finds no support in the statutory text.

53. The combined effect of these two definitions has vast real-world consequences. The agency's broad definition of Qualifying Single Source Drug benefits the Medicare program at the expense of pharmaceutical manufacturers in several important ways. First, two distinct drugs that were evaluated and approved by FDA under entirely separate drug approval processes will nevertheless have their Medicare sales aggregated for purposes of selection so long as they share the same "active moiety" and have the same NDA-holder, increasing the likelihood that the aggregated products will cross the $200 million sales threshold for eligibility. Second, the agency's approach means that some new drug products could be subject to selection and negotiation *immediately* upon approval, contrary to the prohibition on selecting products until "at least 7 years will have elapsed since the date of [FDA] approval." 42 U.S.C. § 1320f–1(e)(1)(A)(i)-(ii). Under the agency's approach, the clock would begin to run from when FDA approved the *first* product with the same active moiety, rather than the date mandated by statute: the date of approval of a newer, otherwise distinct drug product.

54. The breadth of CMS's Qualifying Single Source Drug definition has one downside for the Government, however, which CMS has grudgingly recognized: It means that a generic for

any one version of the drug is sufficient to render *all* forms of the drug ineligible for negotiation. Initial Guidance at 10; Final Guidance at 12, 102. In such a scenario, one form of the drug may have its price moderated by competition, while others will not, but the generic entrant nevertheless disqualifies the drug, as a whole, from negotiation. CMS therefore added the qualitative and subjective "bona fide" overlay to the statutory "marketed" determination to draw out and delay the date by which any generic entrant disqualifies a drug from negotiation. In doing so, CMS crafted bespoke definitions of two key terms that together work to endow CMS with boundless, and extra-statutory, discretion that transcends even Congress's generous grant of authority.

55. Both of these provisions are unlawful.

II. CMS's Guidance Violates The Administrative Procedure Act

56. Agency action violates the APA when it contravenes the text of an agency's governing statute. *See Natural Res. Def. Council v. EPA*, 643 F.3d 311, 323 (D.C. Cir. 2011); *Orion Rsrvs. Ltd. P'ship v. Salazar*, 553 F.3d 697, 703 (D.C. Cir. 2009); *Bennett v. Donovan*, 4 F. Supp. 3d 5, 13 (D.D.C. 2013); *Lone Mountain Processing, Inc. v. Secretary of Labor*, 709 F.3d 1161, 1164 (D.C. Cir. 2013).

57. In addition, agency action is arbitrary and capricious under the APA when the agency fails to adequately explain a deviation from prior policy, *Steenholdt v. FAA*, 314 F.3d 633, 639 (D.C. Cir. 2003), or ignores evidence bearing on the issue, *Butte County v. Hogen*, 613 F.3d 190 (D.C. Cir. 2010). Agency action also is arbitrary and capricious when the agency entirely "fail[s] to consider an important aspect of the problem, offer[s] an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise." *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983).

58. CMS has violated all of these maxims here.

Qualifying Single Source Drug

59. First, CMS's definition of a "Qualifying Single Source Drug" violates the statute by impermissibly aggregating different drug products approved under different NDAs (or in the case of biologicals, different BLAs).

60. In Section 30 of the Guidance Documents, CMS specified that two drug products with the same active moiety are treated as the same Qualifying Single Source Drug, even if they were approved under distinct NDAs. Initial Guidance at 8; Final Guidance § 30.1 at 99. Similarly, two biological products with the same active ingredient are treated as the same Qualifying Single Source Drug, even if they were licensed under distinct BLAs. *Id.*

61. That has profound implications for drug manufacturers when they have two drugs approved under different applications that share the same active moiety or active ingredient: such products – including one approved years after the first – will run on the same seven- or eleven-year selection clock, based on the approval or licensure date of the *earlier* approved or licensed product. That means that some new products will be subject to selection and negotiation *immediately* upon approval, contrary to the statutory prohibition on selecting products until "at least 7 years will have elapsed since the date of [FDA] approval." 42 U.S.C. § 1320f–1(e)(1)(A)(i)-(ii). Under the agency's approach, the clock will begin to run from when FDA approved the *first* product with the same active moiety, rather than from the date of approval of the newer product, as Congress required. Medicare expenditures on both products will be aggregated for purposes of ranking the qualifying single source drug for selection for negotiation. And the negotiated maximum fair price will apply across both products.

62. None of this is what Congress intended. Under the plain language of the statute, two products are the same Qualifying Single Source Drug *only* where the two products share the same NDA or BLA. This statutory mandate is expressed in several different ways.

63. First, the statute defines the term "Qualifying Single Source Drug" by reference to "a covered part D drug," as that term is defined in the Medicare statute. 42 U.S.C. § 1320f-1(e)(1). The definition of a "covered Part D drug," in turn, cross-references the definition of a "covered outpatient drug" in the Medicaid Drug Rebate Program (MDRP) statute. *Id.* § 1395w-102(e)(1). Under that definition, whether a single source drug is a distinct "covered outpatient drug" is based on whether the product is approved pursuant to a distinct NDA or BLA. *Id.* §§ 1396r–8(k)(2), (k)(7)(A)(iv).

64. The *only* exception to this MDRP standard – that a drug is defined by its NDA or BLA – comes in context of line extensions, which involve new formulations of a drug. Congress specifically amended the MDRP statute to treat line extensions as the same "covered outpatient drug" even if they were approved under different NDAs or BLAs. Patient Protection and Affordable Care Act of 2010, § 2503, Pub. L. No. 111-148, 124 Stat. 119 (codified at 42 U.S.C. § 1396r–8(c)(2)(C)). Congress knew about this "line extension" exception to the one-NDA-one-drug standard when it created the IRA because it included that exception in the new law, but it did so selectively: Congress chose *not* to include this exception in the IRA's drug pricing negotiation program but *did* expressly do so in its Part D inflation rebate provision. 42 U.S.C. § 1395w-114a(b)(5)(B). Congress therefore must be presumed to have specifically chosen *not* to include that exception in connection with the Drug Price Negotiation Program.

65. The IRA further defines a Qualifying Single Source Drug as a drug approved by FDA and for which "at least 7 years will have elapsed since the date of *such approval*." 42 U.S.C.

§ 1320f-1(e)(1)(A) (emphasis added). The definition is the same for a biological product, except the applicable time period is "at least 11 years will have elapsed since the date of *such licensure*." 42 U.S.C. § 1320f-1(e)(1)(B) (emphasis added). This language directs that each Qualifying Single Source Drug be identified by reference to its *individual* approval or licensure, i.e., its distinct NDA or BLA. Any other reading – including the one based on common active moiety or common active ingredient espoused by CMS – contradicts the plain text of the statute.

66. Finally, the statutory definition of "Qualifying Single Source Drug" is grounded in FDA's framework for approving and licensing drugs and biologics, and such framework distinguishes among drugs and biologics via distinct applications. By expressly cross-referencing the FDA framework in the Qualifying Single Source Drug definition, Congress clearly intended that CMS rely on such framework in distinguishing among qualifying single source drugs.

67. In fact, by excluding from selection "the listed drug for any drug that is approved and marketed under section 355(j)" – i.e., the reference drug for an approved and marketed generic – the IRA necessarily uses "drug" in reference to a single, specific NDA. This is because, under the Federal Food, Drug, and Cosmetic Act, sponsors of generics apply for approval by identifying a specific NDA for the reference drug. FDA, in turn, approves generics based on that specific NDA. By excluding listed drugs from the Qualifying Single Source Drug definition, therefore, the IRA confirms that "drug" means "drug marketed pursuant to a specific NDA."

68. CMS's approach will pull drugs into the queue for "negotiation" significantly earlier than the statutorily prescribed approach, based on the approval date of another drug. The Final Guidance also dramatically increases the chance that an individual drug will be among the highest-spend drugs selected for "negotiation" because its Medicare expenditures will be

aggregated with the Medicare expenditures of a distinct – and potentially statutorily ineligible – drug.

69. The agency's definition of this arcane term – Qualifying Single Source Drug – will have real-world consequences for patients as well. It works to discourage pharmaceutical manufacturers from investing time and money to discover whether an active ingredient used in an existing drug could also be used in a new product to address distinct patient populations, especially those with orphan conditions. Even if the new product is approved under a distinct application or licensure, CMS will consolidate any Medicare expenditures for the two products, thereby increasing the likelihood of selection of *both* products for the draconian Drug Price Negotiation Program. Perhaps worse, the new product could be deemed eligible for selection *immediately* upon approval, if it comes more than 7 years after approval of the initial product (11 years for a biological product). The agency's approach thus incentivizes manufacturers not to innovate.

70. This approach was so concerning that stakeholders submitted comments opposing this definition, despite CMS's admonition that the definition was final as issued and that comments should not be submitted. Initial Guidance at 2, 5. The Final Guidance acknowledges that these problems were nevertheless brought to CMS's attention through comments submitted on the Initial Guidance. The agency's response only underscores the absurdity of its statutory interpretation. To justify redefining Qualifying Single Source Drugs, the Final Guidance does not ground its approach in the definition of a Qualifying Single Source Drug itself, but rather invokes the IRA's "Use of Data" provision, and the provision requiring CMS to "compute and apply the [Maximum Fair Price] across different strengths and dosage forms of a selected drug," 42 U.S.C. § 1320f-5(a)(2). Neither provision justifies the agency's approach.

71. CMS reasons in its Guidance Documents that an expansive definition of Qualifying Single Source Drug "aligns with" the IRA's "Use of Data" provision, 42 U.S.C. § 1320f–1(d)(3)(B). *See* Final Guidance § 30.1 at 100. The "Use of Data" provision proves the opposite. That provision specifies that "the Secretary shall use data that is aggregated across dosage forms and strengths" of a Qualifying Single Source Drug, "including new formulations ***of the drug***, such as an extended-release formulation, and not based on the specific formulation or package size or package type ***of the drug***" in determining whether a Qualifying Single Source Drug satisfies any of the selection criteria. 42 U.S.C. § 1320f–1(d)(3)(B) (emphases added). The emphasized phrases above are important. The provision only applies when the different dosage forms, strengths, and formulations under consideration involve the ***same*** Qualifying Single Source Drug. The identification of the Qualifying Single Source drug is a predicate determination. If the products are not the same drug, then the Use of Data provision is not triggered.

72. CMS also points toward a statutory provision requiring the agency to "compute and apply the [Maximum Fair Price] across different strengths and dosage forms ***of a selected drug*** and not based on the specific formulation or package size or package type of such drug," *id.* § 1320f-5(a)(2) (emphasis added). Again, the emphasized language is important. To be consolidated, the different strengths and dosage forms must all be "of a selected drug" – that is, they must qualify as the same drug. This provision also would be unnecessary if all products sharing the same active moiety or ingredient were already consolidated into the same Qualifying Single Source Drug.

73. For all of these reasons, CMS's definition of what constitutes a distinct Qualifying Single Source Drug is unlawful.

Bona Fide Marketing

74. The Guidance Documents also purport to overwrite the statutory requirements governing the generic competition that renders a drug ineligible for selection or negotiation.

75. Whether a generic has been "marketed" has far-reaching consequences under the Program. Under the IRA, a drug that is the listed reference product for an approved and "marketed" generic cannot be a Qualifying Single Source Drug, and therefore cannot be selected for "negotiation." *See* 42 U.S.C. § 1320f–1(e)(1). The IRA also requires CMS to remove a selected drug from the selected drug list on January 1 of the first "subsequent year" (i.e., a year after the initial price applicability year) that begins at least 9 months after CMS determines that a generic has been approved and "marketed." *Id.* § 1320e(c)(1). CMS also must cease "negotiations" if, after a drug has been selected but before the end of the "negotiation period," a generic version is approved and "marketed." *Id.* § 1320f–1(c)(2).

76. The statutory test for these off-ramps is simple. The IRA requires that a generic drug be "approved and marketed," or in the case of a biological biosimilar product, "licensed and marketed." 42 U.S.C. §§ 1320f-1(e)(1)(A) and (B).

77. CMS, however, adds both language and substance in the Guidance Documents: it "will consider a generic drug . . . to be market*ed*" only if certain sources of data "reveal[ ] that the manufacturer of that drug or product is engaging in bona fide market*ing* of that drug." Final Guidance § 30.1 at 102 (emphases added). In other words, generic competition will be subjected to CMS's bespoke and ongoing "bona fide marketing" test – a subjective, multi-factor inquiry based on the "totality of the circumstances." Initial Guidance at 62; Final Guidance at 101–102. The agency said that it plans to review data over a 12-month period and make a "holistic inquiry"

based on the "totality of the circumstances" about "whether a generic drug or biosimilar is marketed on a bona fide basis." Initial Guidance at 62; Final Guidance at 101–102.

78. The end result is that even a drug with generic competition on the market may be selected for negotiation, forced to go through negotiation, and then subject to a Maximum Fair Price if CMS concludes that the generic competition is not "bona fide" enough. This expanded qualitative standard enables CMS to slow-walk a drug's disqualification from the Drug Price Negotiation Program. Such delays, dressed up as "bona fide" determinations, become particularly important to CMS in the context of a Qualifying Single Source Drug definition that draws in products subject to multiple NDAs (or BLAs), which can be disqualified from negotiation eligibility when a generic for only one version of the drug is marketed.

79. This problem is compounded by the agency's further decision to monitor, "after such determination is made, whether meaningful competition *continues to exist* in the market by ongoing assessments of whether the manufacturer of the generic drug . . . is engaging in bona fide marketing." Final Guidance § 90.4 at 170 (emphasis added). There is no statutory basis for the agency to conduct ongoing monitoring after a generic competitor is approved and marketed. Yet, the agency threatens to withdraw its prior determinations that a drug is disqualified from selection or price controls based on the agency's unilateral determination at some later time that there is insufficiently "meaningful" competition between the innovative and generic versions of a drug.

80. CMS intends to conduct such monitoring by reviewing a number of factors, including but not limited to "whether the generic drug or biosimilar biological product is regularly and consistently available for purchase through the pharmaceutical supply chain and whether any licenses or other agreements between a Primary Manufacturer and a generic drug or biosimilar manufacturer limit the availability or distribution of the selected drug." *Id.* CMS also intends to

"analyze the share of generic drug or biosimilar biological product units identified in [Medicare claims] data as a percentage of total units of Part D expenditures, as well as whether manufacturers are reporting units of the selected drug as part of their [Average Manufacturer Price (AMP)] reporting responsibilities under section 1927(b)(3)(A) of the Act, and the trend in reporting of such AMP units." *Id.*

81. As part of this ongoing monitoring process, CMS "reserves the right to also use other available data and informational sources on market share and relative market competition of the generic drug or biosimilar." *Id.* If CMS determines through monitoring that a generic drug manufacturer is not engaged in bona fide marketing after a previous determination that there was an approved and marketed generic, "the drug/biologic could be eligible for negotiation in a future price applicability year." *Id.* at 78.

82. None of that is allowed by the statute. CMS cannot supplant the statutory reference point – the date a product is "marketed" – with a wholly extra-statutory standard tied to the agency's subjective and ongoing assessment of adequate utilization. The plain meaning of the statutory phrase "approved . . . and . . . marketed" makes clear that Congress intended this to be a check-the-box inquiry. Marketing is "[t]he act[] . . . of bringing or sending a product or commodity to market." Oxford English Dictionary, Definition of Marketing, *available at* https://www.oed.com/view/Entry/114186?rskey=36dfg4&result=2&isAdvanced=false#eid (last accessed Aug. 23, 2023). Whether a product is "marketed" is an objective point-in-time determination based on when the product enters the commercial marketplace for sale. Once the product has entered the marketplace, it has been "marketed." That is true regardless of its utilization.

83. Indeed, one other section of the *Initial* Guidance – the provision listing the data that manufacturers must submit to CMS – actually defined "marketing" in accordance with the plain meaning of the term: "[T]he introduction or delivery for introduction into interstate commerce of a drug product." Initial Guidance at 82. CMS deleted that definition in the *Final* Guidance without explanation, an implicit acknowledgement of the sharp contrast between the accepted, objective definition and CMS's new, entirely subjective "bona fide marketing" standard.

84. The objective, point-in-time meaning of "marketing" is consistent with the approach CMS has taken with regard to the same statutory term in numerous other contexts, including other provisions of the IRA itself. With respect to the IRA's Part B inflation rebate, CMS has proposed to determine when a product is "marketed" by reference to the "date of first sale" that the manufacturer must report for average sales price (ASP) purposes, which likewise is an objective point-in-time determination. CMS, Medicare Part B Inflation Rebates Paid by Manufacturers: Initial Memorandum, at 13–14 (Feb. 9, 2023). It also is consistent with the meaning of the term "marketing" as used in FDA regulations. *See* 21 C.F.R. § 314.3(b) (defining "commercial marketing" in relevant part as "the introduction or delivery for introduction into interstate commerce of a drug product").

85. For purposes of the IRA's Part D inflation rebates, CMS similarly proposed to determine when a product is "marketed" by reference to its "market date" as reported under the MDRP. CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, at 18–19 (Feb. 9, 2023); FDA, National Drug Code Directory (July 22, 2022). In turn, CMS's longstanding policy under the MDRP has been to define "marketed" by reference to the date on which a product "is available for sale." *Announcement of Medicaid Drug Rebate Program*, 83 Fed. Reg. 12,770, 12,784 (Mar. 23, 2018) (MDRP National Rebate Agreement); *see*

also 42 C.F.R. § 447.502. That meaning is echoed in the agency's pending proposed MDRP rule, where CMS has proposed to define a drug's "market date" as the "date on which the . . . drug was first sold." *Updates Under the Medicaid Drug Rebate Program*, 88 Fed. Reg. 34,238, 34,292 (May 26, 2023). The Final Guidance reinforced the relevance of these MDRP definitions when it explained that CMS will evaluate "bona fide" marketing using sales volume data reported under the MDRP. Final Guidance at 2, 101–102. In doing so, CMS highlighted the paradox of its bona fide marketing standard: CMS will evaluate whether a drug is "marketed" for purposes of the Drug Price Negotiation Program by reference to MDRP sales volume data – which can be reported to the MDRP only once the drug qualifies as being "marketed" such that its sales volume can be reported in the first place.

86. This same problem plays out in reference to the second data set CMS will rely upon in determining whether a drug is "marketed." In addition to Medicaid data, CMS has stated it will also evaluate Part D program Prescription Drug Event (PDE) data in effectuating its bona fide marketing standard. PDE data is summary claims data generated when a Part D plan sponsor fills a prescription under Medicare Part D. CMS has recognized that the date on which a product is "release[d] onto the market" triggers certain coverage-related obligations on the part of Part D plans. CMS requires that Part D plan sponsor Pharmacy & Therapeutics committees "make a reasonable effort to review a new FDA approved drug product (or new FDA approved indication) within 90 days of its release onto the market and . . . make a decision on each new FDA approved drug product (or new FDA approved indication) within 180 days of its release onto the market, or a clinical justification will be provided if this timeframe is not met." Prescription Drug Benefit Manual, ch. 6 § 30.1.5 (rev. Jan. 15, 2016). All of this means that, like with the MDRP data, CMS

will have already recognized that a product has been released onto the market by the time PDE data show product utilization.

87. None of this is authorized by the statute. It is clear that Congress used the phrase "approved and marketed" intentionally, to refer to the first time a generic product enters the marketplace. CMS may not override the bright-line test imposed by the statute in favor of a subjective standard that effectively gives the agency unlimited discretion to determine whether and when a product is sufficiently subjected to "bona fide" generic competition.

88. This is especially so given that Congress has demonstrated that it knows how to establish a subjective "bona fide" standard as well as a standard requiring the availability of a drug broadly in the market and on a nationwide basis. 42 U.S.C. § 1396r–8 (k)(1)(B)(i)(II) (as amended by Pub. L. No. 111–148, § 2503(a)(2) (2010)) (amending the MDRP statute to specify that only "bona fide" service fees are exempt from the calculation of average manufacturer price); § 1396r-8(e)(5) (as amended by Pub. L. No. 111-148 § 2503(a)(1)) (amending the MDRP statute to direct the calculation of a drug's federal upper limit using "pharmaceutically and therapeutically equivalent multiple source drug products . . . available for purchase by retail community pharmacies on a nationwide basis"). Congress did neither here. "[W]here Congress knows how to say something but chooses not to, its silence is controlling." *Animal Legal Def. Fund v. U.S. Dep't of Agric.*, 789 F. 3d 1206, 1217 (11th Cir. 2015).

89. One further note about the Qualifying Single Source Drug and "bona fide marketing" tests. These two provisions do not operate wholly independently. CMS's insistence on combining drugs approved under separate NDAs as a single "Qualifying Single Source Drug" and then evaluating whether a generic product is sufficiently marketed exacerbates the problems created by both unlawful positions. A generic drug is tied to a particular NDA. If FDA approves

a generic drug that references one NDA, the generic will *not* be rated therapeutically equivalent to the other product approved under a different NDA or automatically substitutable for that product under state substitution laws. Thus, one form of the drug may have its price moderated by competition, while others will not, but the generic entrant nevertheless disqualifies the drug as a whole from negotiation. CMS's addition of the qualitative and subjective "bona fide" overlay to the "marketed" determination thus allows the agency to further orchestrate (and delay) the date by which any generic entrant disqualifies a drug from negotiation.

III. The IRA Violates The Due Process Clause

90. The agency's unlawful implementation of the IRA only compounds an already unlawful statutory scheme.

91. Drug manufacturers have at least two property interests implicated by the IRA: their property rights in their drug products and their patent rights. The IRA undermines both, without providing notice or an opportunity to be heard, either before or after the deprivation. Agency action that deprives a person or entity of a property interest, without an opportunity to be heard, is unconstitutional. *See Propert v. District of Columbia*, 948 F.2d 1327, 1333 (D.C. Cir. 1991).

92. The IRA has due process problems from the beginning of its process to its very end. On the front end, the statute contemplates that the first few years of the Drug Price Negotiation Program will be instituted through agency guidance rather than the standard notice-and-comment rulemaking. To compound this problem, CMS dropped the key aspects of the selection and negotiation provisions for the first year of the program (IPAY 2026) on regulated entities through guidance that was finalized as soon as it was announced, with no formal opportunity for comment. The overreach evidenced by CMS's adoption of its Qualifying Single Source Drug and bona fide marketing positions amply demonstrates CMS's embrace of this unbridled authority.

93. Once a drug is selected, the IRA forces manufacturers to engage in purported "negotiations" but affords them no leverage, no meaningful opportunity to walk away, and no ability to protect their interests. It then directs CMS to unilaterally impose a "maximum fair price" for selected drugs that is drastically below the actual fair market value of the product.

94. Manufacturers that disagree with the selection of their product or the fairness of the price proffered by the agency have no leverage to push back. Although the Drug Price Negotiation Program is designed to mimic a negotiation – including use of terms like "offer," "counteroffer," and "negotiation," 42 U.S.C. § 1320f–3 – the statute uses these terms to conceal the true nature of the process. In reality, the Program is designed to coerce manufacturers to submit to government-imposed price controls. The Program is enforced through an "Excise Tax Imposed on Drug Manufacturers During Noncompliance Periods." IRA § 11003 (codified at 26 U.S.C. § 5000D(b)(1)–(4)). A manufacturer who fails to enter into a Program agreement (at the initiation of the "negotiation" period) or who fails to "agree[]" to the ultimate price that CMS sets is subject to a steep and escalating daily penalty, 26 U.S.C. § 5000D(b), which the statute suggests applies to each sale of the subject drug, *id.* § 5000D(a). The penalty continues to accrue every day until the manufacturer acquiesces to CMS's demands (or until the drug in question ceases to be a selected drug). The penalty maxes out at 95% of total U.S. revenues for the product – not just for Medicare sales but for *all* sales. *Id.* § 5000D(d). Moreover, it applies to total *revenues* from the drug in question, not merely its *profits*. *Id.*

95. There is no easy off-ramp for manufacturers who do not wish to negotiate. While the IRA provides for the "[s]uspension" of the punitive excise-tax penalty, that happens only if the manufacturer terminates both its Medicare Part D agreements and Medicaid rebate agreement – not just for the drug in question, but for *all* of the manufacturer's drugs. *Id.* § 5000D(c); *see id.*

§ 5000D(c)(1). That would result in loss of access to important medicines for a significant amount of the U.S. population. It is simply not a choice that any manufacturer can afford to make lightly.

96. On the back end, the statute purports to preclude affected manufacturers from exercising their constitutional right to judicial review of a number of critical inputs, among them the drug selected and the price set. 42 U.S.C. § 1320f-7. While Congress has authority to define the scope of judicial review, that power cannot be exercised to "cut off all review of an allegedly unconstitutional statute" that may result in a property deprivation. *Feinberg v. Fed. Deposit Ins. Corp.*, 522 F.2d 1335, 1341–42 (D.C. Cir. 1975); *see also Marozsan v. United States*, 852 F.2d 1469, 1478 (7th Cir. 1988).

97. The IRA does not just preclude manufacturers from negotiating or challenging the government's price-fixing process. It also hollows out other statutory incentives.

98. The Orphan Drug Act, 21 U.S.C. §§ 360aa-360ee, provides a seven-year period of marketing exclusivity to remedy the lack of pharmaceutical options for rare diseases or conditions. Before the Act, it was difficult to justify the expense involved in pursuing drug candidates intended to treat rare diseases or conditions. *See, e.g.*, HHS, Office of Inspector General, The Orphan Drug Act: Implementation and Impact, Report OEI-09-00-00380 at 7 (May 2001). The incentives provided by the Orphan Drug Act include grants, tax credits, and, most importantly, a seven-year marketing exclusivity period. Those incentives work. Since passage of the Orphan Drug Act, more than 600 products to treat rare disease have been approved by FDA, providing important treatment options for tens of millions of Americans.

99. The IRA excludes orphan drugs from selection – but only so long as the drug is designated for the treatment of a single orphan condition and all approved indications are limited to the treatment of that one orphan condition. 42 U.S.C. § 1320f-1(e)(3)(A). Should a drug be

designated for a second orphan condition, which often happens, the exclusion no longer applies. Final Guidance at 102. This significantly undermines the value of any subsequent orphan designation. By rendering such orphan drugs eligible for selection as soon as they come off their seven-year marketing exclusivity for the first approval, the IRA undermines the very incentive structure that was designed to promote innovation.

100. Take, for example, AstraZeneca's drug LYNPARZA. LYNPARZA is an orphan drug that was first approved in 2014 and designed to treat a rare type of ovarian cancer. Over the next 8 years, AstraZeneca continued to invest in the drug, engaging in research and development efforts that led to additional orphan indications for fallopian tube cancer, peritoneal cancer, and rare pancreas cancer. Each one of these additional approved indications has saved or extended lives. Had the IRA's negotiation eligibility clock been in effect then, only a fraction of current LYNPARZA patients would benefit from the drug now: Investors would not have supported the continued research and development that made possible its additional orphan approvals. This would have had a particular impact on minority communities, who are disproportionately impacted by ovarian, prostate, and breast cancers.

101. Another example is SOLIRIS. SOLIRIS received orphan exclusivity in 2001 for treatment of idiopathic membranous glomerular nephropathy; in 2003 for treatment of paroxysmal nocturnal hemoglobinuria; in 2009 for treatment of atypical hemolytic uremic syndrome; in 2011 for treatment of Shiga-Toxin producing escherichia coli hemolytic uremic syndrome; in 2013 for treatment of neuromyelitis optica; in 2014 for treatment of Myasthenia Gravis; and in 2022 for treatment of Guillain-Barré syndrome. Each new indication was spurred by additional research and development efforts spawned by the incentives provided by the Orphan Drug Act.

102. The IRA's application to drugs with more than one orphan designation will disincentivize companies from investing in follow-on indications in distinct orphan diseases, and prioritize orphan conditions with the largest populations. Neither of these outcomes is good for patients. As several health policy experts recently explained, the IRA "may lead pharmaceutical manufacturers to develop more single-indication orphan drugs (which are not subject to negotiations) rather than follow-on indications. Our analysis suggests that the potential for foregone follow-on indication approvals for serious illness and unmet needs could be nontrivial." Chambers et al., *Follow-On Indications for Orphan Drugs Related to the Inflation Reduction Act*, JAMA Network Open (2023). The Rare Disease Company Coalition, for its part, similarly explained that "Unfortunately, by making orphan products with a second designation eligible for drug price negotiation, this provision will disincentivize further investment in rare disease research and development." *Revised Inflation Reduction Act Guidance Increases Risk of Rare Disease Drug Development* (June 30, 2023).

103. Any one of these problems is independently concerning. Collectively, they immobilize manufacturers like AstraZeneca from participating in any meaningful way in a true "negotiation," prevent AstraZeneca from challenging in any meaningful way the IRA's Drug Price Negotiation Program, and sap AstraZeneca of the resources needed to invest in further rare disease research. The overall scheme unlawfully deprives manufacturers of fundamental due process rights under the Fifth Amendment.

IV. CMS's Actions Cause Concrete And Imminent Harm To AstraZeneca and Patients

104. AstraZeneca has been and will continue to be harmed absent preliminary relief, as explained below.

105. Pharmaceutical manufacturers like AstraZeneca discover and develop life-saving and life-enhancing medicines that are distributed, prescribed, and used across the nation and around the world. The cost of developing such groundbreaking drugs is stunning.

106. The unlawful activities complained of herein – the due process problems of the IRA coupled with CMS's unlawful definitions of "Qualifying Single Source Drug" and "marketed" – collectively discourage innovation and punish manufacturers who take risks on small patient populations or unconventional therapies.

107. That in turn harms patients, particularly patients of rare and orphan diseases, because the incentive structure that was designed to encourage innovation is compromised by the IRA's imposition of price controls on therapies that seek to treat more than one orphan condition.

108. AstraZeneca markets FARXIGA® (dapagliflozin) tablets, which was approved by FDA in 2014 to improve glycemic control in adults with type 2 diabetes. Generic entry is expected in the near future. CMS's determination of when generic entry constitutes "bona fide marketing" will directly impact when any maximum fair price sunsets for FARXIGA.

109. AstraZeneca's cancer medication LYNPARZA® (olaparib) was approved in capsule form in 2014. It has since been discontinued. AstraZeneca subsequently invested in developing a formulation that was better tolerated by patients, and a tablet form of the drug was approved by FDA under a separate NDA in 2017. The tablet product allowed patients to reduce the number of pills they must take per day, making it far more convenient for patients and improving adherence to the prescribed treatment, with the goal of improving patient outcomes.

110. CMS's definition of "Qualifying Single Source Drug" would render the LYNPARZA tablet and capsule as *the same* Qualifying Single Source Drug, because the capsule and tablet forms of LYNPARZA contain "the same active moiety." That is so even though the

two products were approved under unique NDAs, and even though the capsule that started the negotiation clock, three years before approval of the tablet, is no longer marketed. Under CMS's test, the tablet form would immediately be eligible for selection on September 1, 2023, even though it has not yet been approved for seven years as contemplated by the statute.

111. AstraZeneca's drug CALQUENCE® (acalabrutinib), a leukemia medicine, was approved in capsule form in 2017 and in 2022 in tablet form under a different NDA. The tablet product expanded the patient population able to benefit from CALQUENCE because, unlike the capsule, it may be taken with gastric acid-reducing agents, including proton pump inhibitors, antacids, and H2-receptor antagonists. FDA viewed the products to be different enough that it warranted unique NDAs, and the IRA accordingly mandates that the products be treated separately. But CMS's definition would treat the two products – approved under separate NDAs – as a single Qualifying Single Source Drug. Under the language of IRA, the tablet form will be ineligible as a Qualifying Single Source Drug until at least February 1, 2030, because that is the first selection date seven years after CALQUENCE was "marketed pursuant to such approval" – i.e., pursuant to its 2022 approval. But under CMS's test, the capsule and tablet forms would *both* be eligible for selection in 2025 for IPAY 2027, even though the tablet will not have been approved for seven years as contemplated by the statute.

112. Because AstraZeneca has developed and markets a number of drug products that are well-represented within the Medicare program, it faces an especially serious risk of injury from the IRA and CMS's unlawful implementation thereof. Compounding this risk, these drugs are some of AstraZeneca's most successful products. AstraZeneca thus has an acute interest in ensuring protection of its rights.

113. Because the IRA eschews any process for meaningful negotiation or challenging selection of a drug or the maximum fair price once set, the IRA's effects are felt even before a company is formally subjected to the law's drug-price controls. Indeed, due to the speed at which CMS is moving to reorder the Medicare drug pricing landscape pursuant to the IRA, AstraZeneca has already been required to take significant steps to fundamentally reposition its business operations and investments in pipeline products in response to CMS's Guidance Documents.

114. Take research and development activities that once seemed like reasonable investments. As a matter of IRA-driven economic necessity, many of those projects must now be abandoned. The average cost of successfully bringing a drug to market now stands at $2.3 billion. *See* Deloitte, *Seize the Digital Momentum: Measuring the Return from Pharmaceutical Innovation 2022* at 12 (Jan. 2023).[3] That *average* figure does not include the costs associated with research and development activities for failed or abandoned drugs – which is far and away the norm in the high-risk enterprise of pharmaceutical innovation.

115. As previously noted, manufacturers developing new drugs face daunting odds. Of the therapies approved for patient use, only one-third manage to cover their cost of development, much less to provide an economic return significant enough to allow for continued investment and innovation. *See* John A. Vernon et al., *Drug Development Costs When Financial Risk Is Measured Using the FAMA-French Three-Factor Model*, 19 J. Health Econ. 1002, 1004 (2009).

116. The improper approach to identifying qualifying single-source drugs set forth in Section 30 drastically undermines AstraZeneca's ability to recoup investments on its existing drugs. In particular, it makes the impending selection of LYNPARZA and CALQUENCE

[3] *Available at* https://www2.deloitte.com/content/dam/Deloitte/uk/Documents/life-sciences-health-care/deloitte-uk-seize-digital-momentum-rd-roi-2022.pdf.

significantly more likely, which forces AstraZeneca to make irrevocable resource-allocation decisions now – even prior to selection.

117. The harms wrought by the IRA are already beginning to pile up. AstraZeneca must labor under the assumption – starting now – that its most successful current and future products will be subjected to the IRA's scheme. The IRA's design mandates that its targeted price controls must be trained on the most revolutionary therapies: Those drugs that are not only therapeutically groundbreaking, but are also widely prescribed because of their significant benefit to patients.

118. Those same products fund the bulk of AstraZeneca's research and development capabilities. Like other manufacturers, AstraZeneca is making the painful decision to suspend ongoing research and development activities. The Guidance Documents eliminate incentives for research and development of new treatment applications for existing drugs. Under the improperly broad definition of Qualifying Single Source Drug set forth in Section 30, a manufacturer has no reason to invest years and billions of dollars of resources researching whether an active ingredient or active moiety in an existing drug could also be used to treat a separate disease. If the manufacturer identifies such an application, the new drug's eligibility for negotiation will be tied with the eligibility timeline of the existing drug.

119. The prospects for future innovation are even more dire. Already, AstraZeneca has reckoned with the delayed launch of cancer drugs, and certain other of the company's product development plans have been shelved entirely. *See* Biocentury, AstraZeneca May Defer U.S. Cancer Drug Launches in Response to IRA.[4]

[4] *Available at* https://www.biocentury.com/article/645834/astrazeneca-may-defer-u-s-cancer-drug-launches-in-response-to-ira (Nov. 10, 2022).

120. For example, last year AstraZeneca was forced to begin making preparations to curb its investment in pipeline products in anticipation of the IRA's expected impact. *See* Reuters, "AstraZeneca's Soriot warns new U.S. drug price law will hurt innovation."[5]

121. These harms are bad for AstraZeneca, but they are also bad for patients and for public health. The IRA delivers a death blow to the incentive structure that has encouraged pharmaceutical companies to continue to innovate, looking for new treatment therapies and new improvements on their existing drugs. That in turn means fewer new treatment options for patients, who rely on new therapies to save their lives and improve their lives. Nobody will feel the impact on incentives more than patients of rare and orphan diseases.

122. Absent prompt judicial relief, AstraZeneca will be forced to make even further irreversible cutbacks to its business operations and its level of investment in life-saving and life-extending products.

COUNT I
(Administrative Procedure Act — Qualifying Single Source Drug)

123. AstraZeneca realleges, reasserts, and incorporates by reference herein each of the foregoing allegations as though set forth fully herein.

124. The APA prohibits CMS from implementing its statutory mandate in a manner that is unlawful, arbitrary, capricious, an abuse of discretion, or contrary to law. 5 U.S.C. § 706(2)(A).

125. CMS's unlawful definition of a Qualifying Single Source Drug constitutes agency action in excess of statutory jurisdiction, authority, or limitations, or short of statutory right, in violation of 5 U.S.C. § 706(2)(C).

[5] *Available at* https://www.reuters.com/business/healthcare-pharmaceuticals/astrazenecas-soriot-warns-new-us-drug-price-law-will-hurt-innovation-2022-08-23/ (Aug. 24, 2022).

126. The statute makes clear that two drugs approved under separate NDAs or BLAs count as two separate Qualifying Single Source Drugs. CMS's Guidance Documents, however, purport to lump multiple Qualifying Single Source Drugs together for purposes of selection and assessment of a maximum fair price. That is unlawful.

127. CMS's finalized Guidance documents – undertaken in accordance with its statutory mandate to implement the first year of the program through guidance – constitute final agency action for which AstraZeneca has no other adequate remedy within the meaning of 5 U.S.C. § 704.

128. Both AstraZeneca and the patient population will be irreparably harmed unless the agency's definition of a Qualifying Single Source Drug is set aside.

129. There is no mechanism by which AstraZeneca can be made whole for the injuries described herein. AstraZeneca is without an adequate remedy at law because of the unique nature of the harm it would suffer absent injunctive relief.

130. The intent of Congress will be served by an Order vacating CMS's unlawful definition of Qualifying Single Source Drug. In addition, the public interest will be served by such an Order.

COUNT II
(Administrative Procedure Act — Bona Fide Marketing)

131. AstraZeneca realleges, reasserts, and incorporates by reference herein each of the foregoing allegations as though set forth fully herein.

132. The APA prohibits HHS from implementing its statutory mandate in a manner that is unlawful, arbitrary, capricious, an abuse of discretion, or contrary to law. 5 U.S.C. § 706(2)(A).

133. CMS's interpretation of the statutory "approved . . . and . . . marketed" (or in the case of biological products, "licensed . . . and . . . marketed") requirement constitutes agency

action in excess of statutory jurisdiction, authority, or limitations, or short of statutory right, in violation of 5 U.S.C. § 706(2)(C).

134. The statute just says "approved . . . and . . . marketed" or "licensed . . . and . . . marketed." That is a point-in-time inquiry tied to product launch. The statute does not support a backward-looking, "holistic" inquiry into the utilization of the generic drug after entering the market.

135. CMS's "bona fide marketing" standard – implemented in accordance with its statutory mandate that the first year of the program should be implemented through guidance – constitutes final agency action for which AstraZeneca has no other adequate remedy within the meaning of 5 U.S.C. § 704.

136. Both AstraZeneca and the patient population will be irreparably harmed unless the agency's "bona fide marketing" standard is set aside.

137. There is no mechanism by which AstraZeneca can be made whole for the injuries described herein. AstraZeneca is without an adequate remedy at law because of the unique nature of the harm it would suffer absent injunctive relief.

138. The intent of Congress will be served by an Order vacating CMS's unlawful "bona fide marketing" standard. In addition, the public interest will be served by such an Order.

COUNT III
(Fifth Amendment — Due Process)

139. AstraZeneca realleges, reasserts, and incorporates by reference herein each of the foregoing allegations as though set forth fully herein.

140. The Fifth Amendment's Due Process Clause prohibits the government from depriving a person or entity of a constitutionally protected property interest without following constitutionally sufficient procedures.

141. At its core, the Due Process Clause requires notice and an opportunity to be heard "at a meaningful time and in a meaningful manner." *Armstrong v. Manzo*, 380 U.S. 545, 552 (1965); *see also Mathews v. Eldridge*, 424 U.S. 319, 333 (1976). Due process requires procedural protections to prevent, to the extent possible, an erroneous deprivation of property. *See Gilbert v. Homar*, 520 U.S. 924, 930–932 (1997).

142. The IRA deprives AstraZeneca of two constitutionally protected property interests: its investment-backed patent rights and common-law right to sell its products at market prices free from arbitrary and inadequately disclosed governmental constraints. And the statute works this deprivation upon AstraZeneca involuntarily.

143. The IRA deprives AstraZeneca of those property interests by directing the Secretary to fix prices at the "lowest" level, without affording adequate procedural safeguards.

144. Even the most rudimentary of these procedural safeguards are absent from the statutory scheme. On the front end, the IRA strips manufacturers of any ability to meaningfully negotiate a reasonable price for their products. The IRA also dispenses with traditional hearing and notice-and-comment rulemaking procedures, freeing CMS of any obligation to consider the input of affected drug manufacturers, providers, or patients. On the back end, the statute vests the agency with unchecked authority to finalize its decisions without any process for administrative or judicial review, leaving AstraZeneca without any meaningful opportunity to be heard. 42 U.S.C. § 1320f-7.

145. The statute's lack of ex-ante procedural protections, combined with its refusal to supply any ex-post process for parties affected by its decisions, pushes the agency's scheme beyond the perimeter of constitutionally mandated due-process safeguards.

146. AstraZeneca's purported "option" to avoid the Drug Price Negotiation Program's reach by forgoing all Medicare and Medicaid reimbursement is no option at all. Even if it were possible for a manufacturer to withdraw from the programs in time to avoid the application of the maximum fair price, these programs account for a gargantuan percentage of the pharmaceutical market. It simply is not an economically viable course for manufacturers to withdraw from both programs.

147. The risk of erroneous deprivation resulting from the IRA's lack of process is substantial, and the Government has no legitimate interest in shielding CMS's decisions from public input or judicial review.

148. The IRA's drug price control program is therefore unconstitutional under the Fifth Amendment and should be enjoined.

PRAYER FOR RELIEF

For the foregoing reasons, AstraZeneca prays for the following relief:

A. A declaration pursuant to 28 U.S.C. § 2201 that CMS's definition of a Qualifying Single Source Drug is unlawful, arbitrary, and capricious under the APA;

B. A declaration pursuant to 28 U.S.C. § 2201 that CMS's "bona fide marketing" standard is unlawful, arbitrary, and capricious under the APA;

C. An order vacating and setting aside the definitions of "Qualifying Single Source Drug" and "Bona Fide Marketing" set forth in the Guidance Documents;

D. A declaration pursuant to 28 U.S.C. § 2201 that the IRA is unconstitutional and

violates the Due Process Clause of the United States Constitution;

E. Preliminary and permanent injunctive relief barring Defendants from applying the drug pricing provisions of the IRA to AstraZeneca;

F. An order awarding AstraZeneca its costs, expenses, and attorneys' fees incurred in these proceedings pursuant to 28 U.S.C. § 2412; and

G. Such other and further relief as the Court deems just and proper.

Dated: September 26, 2023

Respectfully submitted,

OF COUNSEL:

Catherine E. Stetson
Susan M. Cook
Marlan Golden
HOGAN LOVELLS US LLP
555 Thirteenth Street, NW
Washington, D.C. 20004
Tel: (202) 637-5600
cate.stetson@hoganlovells.com
susan.cook@hoganlovells.com
marlan.golden@hoganlovells.com

McCarter & English, LLP

/s/ Daniel M. Silver
Daniel M. Silver (#4758)
Alexandra M. Joyce (#6423)
Renaissance Centre
405 North King Street, 8th Floor
Wilmington, DE 19801
(302) 984-6300
dsilver@mccarter.com
ajoyce@mccarter.com

Attorneys for Plaintiffs AstraZeneca Pharmaceuticals LP and AstraZeneca AB

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTRAZENECA PHARMACEUTICALS LP and ASTRAZENECA AB, Plaintiffs, v. XAVIER BECERRA, in his official capacity as SECRETARY OF HEALTH AND HUMAN SERVICES, and CHIQUITA BROOKS-LASURE, in her official capacity as ADMINISTRATOR OF THE CENTERS FOR MEDICARE & MEDICAID SERVICES, Defendants.	Civil Action No. 23-931-CFC

DECLARATION OF JIM ADER

1. I, Jim Ader, submit this Declaration on behalf of AstraZeneca Pharmaceuticals LP and AstraZeneca AB (collectively, AstraZeneca) in opposition to Defendants' Cross-Motion for Summary Judgment.

2. I am over the age of 18. Except as expressly indicated, the facts stated herein are based upon my personal knowledge, including my work at AstraZeneca,

and my general experience in the pharmaceutical industry. If called to testify, I could truthfully and competently testify to those facts.

3. I am the Vice President of U.S. Market Access at AstraZeneca, where I have been employed for 24 years. I have more than 31 years of experience in the pharmaceutical industry. During that time, I have held a variety of roles in market access and sales at several different pharmaceutical companies.

4. In my current position, I lead the U.S. Market Access team across AstraZeneca's BioPharmaceutical Business Unit. I also serve as a member of the US Leadership Team.

5. As a result, I am familiar with the concrete and imminent harm that will befall AstraZeneca as a direct result of CMS's implementation of the Drug Price Negotiation Program (DPNP) provisions of the Inflation Reduction Act (IRA).

6. AstraZeneca is a global, science-led, patient-focused pharmaceutical company. We are dedicated to transforming the future of healthcare by unlocking the power of what science can do for people, society and the planet.

7. AstraZeneca therefore invests significant time and money to identify, test, and develop new drug candidates with the goal of helping patients live longer and better lives. It can take decades and hundreds of millions of dollars to shepherd a single potential new therapy through clinical trials. Even when a drug

shows early promise, FDA's rigorous drug approval process means very few of those early drug candidates are ever approved and commercialized. Studies estimate that only one of every 5,000 compounds that enters preclinical testing will achieve FDA approval—a failure rate of 99.98%.

8. On August 29, 2023, the Centers for Medicare & Medicaid Services (CMS) selected AstraZeneca's drug product FARXIGA® (dapagliflozin) for negotiation under the Drug Price Negotiation Program.

9. On or before October 1, 2023, as required by the statute, AstraZeneca signed a Manufacturer Agreement drafted by CMS that spells out how the negotiation process will play out. Exhibit 1. The Agreement gave the agency unilateral authority to make changes to its terms to reflect changes in "law, regulation, or guidance." *Id.* at IV.B. Any breaches of the Agreement or failures to meet the requirements of the Drug Price Negotiation Program will result in "civil monetary penalties and an excise tax, as applicable." *Id.* at IV.J.

10. On or before February 1, 2024, CMS will send out an initial offer of a Maximum Fair Price, and AstraZeneca will be forced to respond before **March 2, 2024**.

11. AstraZeneca therefore is forced to make a number of decisions now about its willingness to go forward with its participation in the program—and it has no choice but to do so based on the policies that CMS has announced will apply in

the first initial price applicability year (IPAY), 2026. If AstraZeneca were to withdraw from both Medicare and Medicaid participation—not just for FARXIGA, but for all of its drug products—it would have an enormous financial consequence for the company. Medicare and Medicaid collectively cover 30% of the American population and 50% of all U.S. prescription drug sales.

12. The penalty is particularly high for those AstraZeneca drug products that cater to patient populations disproportionately covered by Medicare Part B. For example, AstraZeneca's IMFINZI® (durvalumab), an immunotherapy designed to treat certain cancers, is heavily Medicare-dependent. The vast majority of its patient population—over 50%—is comprised of Medicare beneficiaries.

13. Medicare and Medicaid collectively account for approximately more than 40% of AstraZeneca's gross revenues in the U.S. .

14. AstraZeneca, no less than any other drug manufacturer, can ill afford to withdraw from federal programs that make up approximately half of all spending in the prescription-drug market.

HARMS DUE TO QUALIFYING SINGLE SOURCE DRUG DEFINITION

15. CMS's Qualifying Single Source Drug definition harms AstraZeneca in several ways. First, the agency's policy ensures that if any future therapies share the same active moiety as a selected drug product, those products will immediately be subject to the Maximum Fair Price the agency has already established for the selected product.

16. It is a core value of AstraZeneca to follow the science and continuously explore new potential uses of the active moieties of its already-approved drug products. To be clear, AstraZeneca must still devote a lot of work, effort, time, and resources to obtaining approval for a new indication for or formulation of an already-approved active moiety, often including clinical trials. By subjecting two or more AstraZeneca products approved under separate New Drug Applications (NDAs) or Biologics License Applications (BLAs) to the same Maximum Fair Price, CMS's Qualifying Single Source Drug definition diminishes incentives for AstraZeneca to invest in future therapies and treatments for the active moiety of a selected drug product.

17. FARXIGA provides a good example. FDA first approved FARXIGA in 2014 as an adjunct to diet and exercise to improve glycemic control in adults with Type 2 diabetes. AstraZeneca's continued investment in FARXIGA has resulted in subsequent FDA approvals over the years to treat a variety of diseases.

Each of these supplemental approvals has saved and improved patients' lives by making available new treatments that FDA has found to be safe and effective.

18. In October 2019, FDA approved FARXIGA as a treatment to reduce the risk of hospitalization for heart failure in adults with Type 2 diabetes and established cardiovascular disease or multiple cardiovascular risk factors. The approval was a significant development for Type 2 diabetes patients; heart failure is often one of the first cardiovascular complications a Type 2 diabetes patient will experience, and FDA's supplemental approval allowed physicians to act sooner by prescribing FARXIGA, thereby reducing patients' risk of hospitalization for heart failure.

19. In May 2020, FDA further approved FARXIGA as a treatment to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure (New York Heart Association class II-IV) with reduced ejection fraction. This approval gave physicians a new treatment option to greatly improve outcomes in heart-failure patients with reduced ejection fraction.

20. FDA again issued new approvals in April 2021, approving FARXIGA as a treatment to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end-stage kidney disease, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression. This milestone approval marked the most significant advancement in

the treatment of chronic kidney disease in more than two decades. It gave patients and physicians a new and effective treatment option to combat an often debilitating and life-threatening disease.

21. Just this past spring, in May 2023, FARXIGA was approved as a treatment to reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure. This most recent FDA approval made it possible for patients across the full spectrum of heart failure, regardless of left ventricular ejection fraction status, to benefit from FARXIGA.

22. So far, all of these additional approvals were associated with the original NDA for FARXIGA. However, if there are enough differences between the original formulation and/or indication and the new formulation and/or indication, or in the drug products themselves, FDA will require a new therapy to be approved under a new NDA.

23. While clinical trials are currently focused on "combination product" therapies that would not be impacted by the agency's definition of Qualifying Single Source Drug, there are other ongoing drug development efforts involving the same active moiety as FARXIGA where one development pathway could result in the product being treated as the same QSSD as FARXIGA under CMS's position.

24. Another example is AstraZeneca's drug LYNPARZA® (olaparib), a small-molecule cancer medicine that was first FDA-approved in capsule form in 2014. Over time, AstraZeneca continued to invest in the drug, developing a formulation that was better tolerated by patients, resulting in FDA approval for a tablet form under a different NDA in 2017. The tablet form expanded the patient population able to benefit from the active ingredient, because it could be taken with certain other medicines.

25. Similarly, AstraZeneca's drug CALQUENCE® (acalabrutinib), a leukemia medicine, was approved in capsule form in 2017. FDA separately approved a tablet form of CALQUENCE under a different NDA in 2022. The tablet formulation expanded the patient population able to benefit from CALQUENCE because, unlike the capsule, it may be taken with gastric acid-reducing agents.

26. CMS's definition of Qualifying Single Source Drugs dramatically alters manufacturers' incentives to invest in such follow-on therapies using a previously approved active moiety. Under the agency's approach, a product approved under a different NDA with the same active moiety as a selected drug product will now be treated as the same drug, and immediately become subject to the Maximum Fair Price. Under the agency's definition, AstraZeneca would have

no incentive to spend years and a steep financial investment researching alternative treatment uses for the active moiety of a selected product.

HARMS DUE TO BONA FIDE MARKETING STANDARD

27. FARXIGA will experience generic competition sometime between October 2025 and Summer 2026. FDA has already granted tentative approval to 17 generic versions of FARXIGA. A tentative approval means that FDA has determined that the product meets the requirements for approval but must await expiration of either patent rights or market exclusivity periods before it may lawfully enter the market. Once all patents and exclusivities for FARXIGA expire, FDA will convert the tentative approvals to final approvals and there will be no legal impediment to the generic products entering the market.

28. If AstraZeneca is forced to sell FARXIGA at the agency's compelled below-market price while *also* facing generic competition, the financial losses suffered by AstraZeneca will be significant. That harms AstraZeneca—and in turn will adversely affect AstraZeneca's ability to invest in follow-on therapies as well as other drug products, to the detriment of patients.

HARMS DUE TO IMPACT ON DRUG DEVELOPMENT EFFORTS

29. These harms are not limited to the impact on FARXIGA. Over the next three years, CMS will select up to 50 additional drugs to be eligible for the

Drug Price Negotiation Program. That selection process will very likely sweep up more of AstraZeneca's drug products.

30. For example, AstraZeneca's CALQUENCE is a potential candidate for selection in 2025 for IPAY 2027. Thus, even pre-selection, AstraZeneca has to make investment decisions now on research development of follow-on therapies for new indications and improvements to the drug itself.

31. Because it is unclear whether CMS will ever change its policies on the issues challenged in this lawsuit, AstraZeneca must assume those policies will continue absent judicial intervention.

32. AstraZeneca has thus been forced to make decisions now based on the agency policies currently in place. In this way, the policies will impact the company's drug development and commercialization for years to come.

I declare under penalty of perjury pursuant to 28 U.S.C. § 1746 that the foregoing is true and correct.

DocuSigned by:
James Ader
9B159FC660504BB...

December 1, 2023

MEDICARE DRUG PRICE NEGOTIATION PROGRAM AGREEMENT
(hereinafter referred to as the "Agreement")

Between

the Centers for Medicare & Medicaid Services (CMS), pursuant to delegated authority of the Secretary of Health and Human Services

And

[Full Name of Manufacturer]
(hereinafter referred to as the "Manufacturer")

For

[Name of Selected Drug]
(hereinafter referred to as the "Selected Drug")

WHEREAS, pursuant to sections 1191 through 1198 of the Social Security Act ("the Act"), as set forth in the Inflation Reduction Act (IRA), Pub. L. 117-169, CMS is responsible for the administration of the Medicare Drug Price Negotiation Program (hereinafter referred to as the "Negotiation Program"), which sets forth a framework under which manufacturers and CMS may negotiate to determine a price (referred to as "maximum fair price" in the Act) for selected drugs in order for manufacturers to provide access to such price to maximum fair price eligible individuals; and

WHEREAS, CMS has designated the Manufacturer as the Primary Manufacturer, as defined in applicable guidance or regulations adopted in accordance with section 1193 of the Act, of the Selected Drug, and CMS has included the Selected Drug on the list of selected drugs published on [Date]; and

WHEREAS, the Manufacturer, if it reaches agreement with CMS, intends to provide access to the determined price pursuant to section 1193 of the Act and in accordance with how the price is computed and applied across different strengths and dosage forms of the Selected Drug as identified by CMS and updated, as applicable, in accordance with sections 1194(f), 1195(b), and 1196(a)(2) of the Act and applicable guidance and regulations, including where the Selected Drug is sold or marketed by any Secondary Manufacturers as defined in applicable guidance or regulations;

NOW THEREFORE, CMS, on behalf of the Department of Health and Human Services, and the Manufacturer, on its own behalf, in accordance with sections 1191 through 1198 of the Act, and all applicable guidance and regulations, hereby agree to the following:

I. Definitions

All terms included in this Agreement shall have the meaning given to them under the provisions of sections 1191 through 1198 of the Act and any applicable guidance and regulations implementing those provisions, except where such terms are expressly defined in this Agreement.

II. CMS and Manufacturer Responsibilities

CMS shall administer the Negotiation Program and the Manufacturer agrees to comply with all applicable requirements and conditions for the Negotiation Program set forth in sections 1191 through 1198 of the

Act and all applicable guidance and regulations implementing those provisions and any changes to the Act that affect the Negotiation Program.

Without limiting the foregoing, CMS and the Manufacturer agree:

a) During the negotiation period for the initial price applicability year for the Selected Drug, in accordance with section 1194 of the Act and applicable guidance and regulations CMS and the Manufacturer shall negotiate to determine (and, by not later than the last date of such period, agree to) a maximum fair price for the Selected Drug of the Manufacturer in order for the Manufacturer to provide access to such price—
   i. to maximum fair price eligible individuals who with respect to the Selected Drug are described in subparagraph (A) of section 1191(c)(2) of the Act and are dispensed the Selected Drug (and to pharmacies, mail order services, and other dispensers, with respect to such maximum fair price eligible individuals who are dispensed the Selected Drug) during, subject to paragraph (b) of this section, the price applicability period; and
   ii. to hospitals, physicians, and other providers of services and suppliers with respect to maximum fair price eligible individuals who with respect to the Selected Drug are described in subparagraph (B) of section 1191(c)(2) of the Act and are furnished or administered the Selected Drug during, subject to paragraph (b) of this section, the price applicability period.

b) As applicable, CMS and the Manufacturer shall, in accordance with section 1194 of the Act and applicable guidance and regulations, renegotiate (and, by not later than the last date of the period of renegotiation, agree to) the maximum fair price for the Selected Drug, in order for the Manufacturer to provide access to such maximum fair price (as so renegotiated)—
   i. to maximum fair price eligible individuals who with respect to the Selected Drug are described in subparagraph (A) of section 1191(c)(2) of the Act and are dispensed the Selected Drug (and to pharmacies, mail order services, and other dispensers, with respect to such maximum fair price eligible individuals who are dispensed the Selected Drug) during any year during the price applicability period (beginning after such renegotiation) with respect to such Selected Drug; and
   ii. to hospitals, physicians, and other providers of services and suppliers with respect to maximum fair price eligible individuals who with respect to the Selected Drug are described in subparagraph (B) of section 1191(c)(2) of the Act and are furnished or administered the Selected Drug during any year during the price applicability period (beginning after such renegotiation) with respect to such Selected Drug.

c) Subject to paragraph (f) of this section and in accordance with applicable guidance and regulations, access to the maximum fair price (including as renegotiated pursuant to paragraph (b) of this section), with respect to such a Selected Drug, shall be provided by the Manufacturer to—
   i. maximum fair price eligible individuals, who with respect to the Selected Drug are described in subparagraph (A) of section 1191(c)(2) of the Act, at the pharmacy, mail order service, or other dispenser at the point-of-sale of the Selected Drug (and shall be provided by the Manufacturer to the pharmacy, mail order service, or other dispenser, with respect to such maximum fair price eligible individuals who are dispensed the Selected Drug), as described in paragraph (a)(i) or (b)(i) of this section, as applicable; and
   ii. hospitals, physicians, and other providers of services and suppliers with respect to maximum fair price eligible individuals who with respect to the Selected Drug are described in subparagraph (B) of section 1191(c)(2) of the Act and are furnished or administered the Selected Drug, as described in paragraph (a)(ii) or (b)(ii) of this section, as applicable.

d) The Manufacturer shall submit to CMS, in a form and manner specified by CMS and in accordance with applicable guidance and regulations, for the negotiation period for the price

applicability period (and, if applicable, before any period of renegotiation pursuant to section 1194(f) of the Act), and for section 1192(f) of the Act, with respect to the Selected Drug—

i. information on the non-Federal average manufacturer price (as defined in section 8126(h)(5) of title 38, United States Code) for the Selected Drug for the applicable year or period;
ii. information that CMS requires to carry out the negotiation (or renegotiation) process under sections 1191 through 1198 of the Act; and
iii. information that CMS requires to carry out section 1192(f) of the Act, including rebates under section 1192(f)(4) of the Act.

e) The Manufacturer shall comply with requirements determined by CMS to be necessary for purposes of administering the Negotiation Program and monitoring compliance with the Negotiation Program, including in accordance with applicable guidance and regulations.
f) Under this Agreement and in accordance with applicable guidance and regulations, the Manufacturer—
   i. Shall not be required to provide access to the maximum fair price under paragraph (c), with respect to the Selected Drug and maximum fair price eligible individuals who are eligible to be furnished, administered, or dispensed the Selected Drug at a covered entity described in section 340B(a)(4) of the Public Health Service Act, to such covered entity if the Selected Drug is subject to an agreement described in section 340B(a)(1) of such Act and the ceiling price (defined in section 340B(a)(1) of such Act) is lower than the maximum fair price for such selected drug; and
   ii. Shall be required to provide access to the maximum fair price to such covered entity with respect to maximum fair price eligible individuals who are eligible to be furnished, administered, or dispensed the Selected Drug at such entity at such ceiling price in a nonduplicated amount to the ceiling price if such maximum fair price is below the ceiling price for the Selected Drug.
g) In accordance with section 1193(c) of the Act and applicable guidance and regulations, information submitted to CMS under the Negotiation Program by the Manufacturer that is proprietary information of such Manufacturer, as determined by CMS, shall be used only by CMS or disclosed to and used by the Comptroller General of the United States to carry out such Negotiation Program, unless otherwise required by law.

III. Effective Date, Term and Termination

a) This Agreement shall have an effective date of the date this Agreement is signed by both parties.
b) The term of this Agreement shall be from the effective date until the termination date, which shall be the earlier of the first day that the Selected Drug is no longer a selected drug pursuant to CMS' determination in accordance with section 1192(c) of the Act and applicable guidance and regulations, or the date that the Agreement is terminated by either party in accordance with applicable guidance and regulations.
c) Notwithstanding the termination of this Agreement, certain requirements and obligations shall continue to apply in accordance with applicable guidance and regulations.

IV. General Provisions

a) This Agreement contains the entire agreement of the parties with respect to the subject matter of this Agreement and supersedes all prior oral and written representations, agreements, and understandings of the parties. If CMS and the Manufacturer reach agreement on a price for the Selected Drug pursuant to section II(a) or II(b) of this Agreement, CMS and the Manufacturer shall execute an addendum setting forth the price for the Selected Drug that will apply for purposes of this Agreement.

b) CMS retains authority to amend this Agreement to reflect changes in law, regulation, or guidance. When possible, CMS shall give the Manufacturer at least 60-day notice of any change to the Agreement.
c) Any notice required to be given by either party pursuant to the terms and provisions of this Agreement shall be sent by email. CMS shall provide the appropriate email address for notice in guidance, rulemaking, or other publications. The Manufacturer shall provide the appropriate email address(es) for notice to CMS in a form and manner specified by CMS.
d) Nothing in this Agreement shall prohibit the Manufacturer from transferring the Selected Drug and obligations of this Agreement to another entity in accordance with applicable guidance and regulations.
e) Nothing in this Agreement shall limit the Manufacturer from providing access under the Medicare program to a price lower than the price determined pursuant to this Agreement.
f) In signing this Agreement, the Manufacturer does not make any statement regarding or endorsement of CMS' views, and makes no representation or promise beyond its intention to comply with its obligations under the terms of this Agreement with respect to the Selected Drug. Use of the term "maximum fair price" and other statutory terms throughout this Agreement reflects the parties' intention that such terms be given the meaning specified in the statute and does not reflect any party's views regarding the colloquial meaning of those terms.
g) Nothing in this Agreement shall be construed to require or authorize the commission of any act contrary to law. If any provision of this Agreement is found to be invalid by a court of law with competent jurisdiction, this Agreement will be construed in all respects as if any invalid or unenforceable provisions were eliminated, and without any effect on any other provision.
h) No failure by any party to insist upon the strict performance of any requirement, obligation or condition of this Agreement shall constitute a waiver of any such requirement, obligation or condition.
i) This Agreement shall be construed in accordance with Federal law and any ambiguities shall be interpreted in the manner that best effectuates the statute. Any litigation relating to this Agreement, to the extent that jurisdiction and a cause of action would otherwise be available for such litigation, shall be resolved in Federal court. Actions by the Manufacturer for damages are not permitted pursuant to this Agreement, and the Manufacturer's remedies for any breach are limited to termination of the Agreement or other action consistent with applicable statutes, regulations, or guidance.
j) CMS and the Manufacturer acknowledge and agree that in accordance with section 1197 of the Act and 26 U.S.C. § 5000D, the Manufacturer may be subject to civil monetary penalties and an excise tax, as applicable, for failure to meet the requirements of the Negotiation Program, including violations of this Agreement.
k) Neither party shall be liable for failure to perform its obligations under this Agreement if such failure is occasioned by a contingency beyond such party's reasonable control, including, but not limited to, lockouts, riots, wars, fires, floods or storms (a "Force Majeure Event"). A party claiming a right to excused performance under this section shall promptly notify the other party in writing of the extent of its inability to perform, which notice shall specify the Force Majeure Event that prevents such performance and include a timeline for remediation. The party failing to perform shall use reasonable efforts to avoid or remove the cause of the Force Majeure Event and shall resume performance under the Agreement promptly upon the cessation of the Force Majeure Event.

V. Signatures

FOR THE MANUFACTURER

A. By signing this Agreement, the Manufacturer agrees to abide by all provisions set forth in this Agreement and acknowledges having received notice of potential penalties for violation of the terms of the Agreement.

B. The undersigned individual hereby attests that he or she is authorized by the Manufacturer to execute this Agreement with regard to the Selected Drug and to legally bind the Manufacturer on whose behalf he or she is executing the Agreement to all terms and conditions specified herein. The undersigned individual further attests that he or she has obtained access in the CMS Health Plan Management System (CMS HPMS) as an authorized representative to be signatory for the Manufacturer and that the individual's CMS HPMS access credentials contain the same information regarding the undersigned individual as the information set forth below.

By:

Print Name: _____

Signature: _____

Title: _____

Date: _____

P-Number: _____

Manufacturer Address: _____

_____

FOR THE CENTERS FOR MEDICARE & MEDICAID SERVICES

By:

Print Name: _____

Signature: _____

Title: _____

Date: _____

Addendum 1: Negotiated Maximum Fair Price

MEDICARE DRUG PRICE NEGOTIATION PROGRAM AGREEMENT
NEGOTIATED MAXIMUM FAIR PRICE ADDENDUM
(hereinafter referred to as the "Addendum")

Between

the Centers for Medicare & Medicaid Services (CMS), pursuant to delegated authority of the Secretary of Health and Human Services

And

[Full Name of Manufacturer]
(hereinafter referred to as the "Manufacturer")

For

[Name of Selected Drug]
(hereinafter referred to as the "Selected Drug")

WHEREAS, the Manufacturer has in effect a Medicare Drug Price Negotiation Agreement (the "Agreement"), which the Manufacturer entered into with CMS on [Date], to negotiate to determine a price (referred to as "maximum fair price" in the Social Security Act ("the Act")) for the Selected Drug under the Negotiation Program; and

WHEREAS, the Manufacturer and CMS have engaged in negotiation of the price for the Selected Drug in accordance with the negotiation process set forth in section 1194 of the Act and applicable guidance and regulations; and

WHEREAS, the Manufacturer and CMS now agree to a price for the Selected Drug, as published by CMS in accordance with section 1195(a) of the Act and updated in accordance with sections 1195(b) and 1196(a)(2) of the Act and applicable guidance and regulations, which will apply for purposes of the Agreement;

NOW THEREFORE, the Manufacturer and CMS agree to this Addendum, such that the following terms are hereby incorporated as part of the Agreement:

a) The parties agree to a price of [$] for the Selected Drug per 30-day equivalent supply, weighted across dosage forms and strengths.

b) The parties agree that the price set forth in clause (a) shall apply to the dosage forms and strengths of the Selected Drug as identified on the list of National Drug Codes (NDCs) maintained by CMS as may be updated with information from the manufacturer in accordance with section 1193 of the Act and applicable guidance and regulations.

c) The parties agree that the price set forth in clause (a), which in accordance with section 1196(a)(2) of the Act and applicable guidance and regulations is computed and applied by CMS across the different strengths and dosage forms of the Selected Drug as set forth

in clause (b), is binding and shall apply as specified in the Agreement and in accordance with the Act and any applicable guidance and regulations.

Signatures

FOR THE MANUFACTURER

A. By signing below, the Manufacturer agrees to this Addendum to the Agreement and acknowledges having received notice of potential penalties for violation of the terms of the Addendum and the Agreement.

B. The undersigned individual hereby attests that he or she is authorized by the Manufacturer to execute this Agreement with regard to the Selected Drug and to legally bind the Manufacturer on whose behalf he or she is executing the Agreement to all terms and conditions specified herein. The undersigned individual further attests that he or she has obtained access in the CMS Health Plan Management System (CMS HPMS) as an authorized representative to be signatory for the Manufacturer and that the individual's CMS HPMS access credentials contain the same information regarding the undersigned individual as the information set forth below.

By:

Print Name: _____

Signature: _____

Title: _____ _____

Date: _____

P-Number: _____

Manufacturer Address: _____

_____

FOR THE CENTERS FOR MEDICARE & MEDICAID SERVICES

By:

Name: _____

Signature: _____

Title: _____

Date: _____

Addendum 2: Renegotiated Maximum Fair Price

MEDICARE DRUG PRICE NEGOTIATION PROGRAM AGREEMENT
RENEGOTIATED MAXIMUM FAIR PRICE ADDENDUM
(hereinafter referred to as the "Addendum")

Between

the Centers for Medicare & Medicaid Services (CMS), pursuant to delegated authority of the Secretary of Health and Human Services

And

[Full Name of Manufacturer]
(hereinafter referred to as the "Manufacturer")

For

[Name of Selected Drug]
(hereinafter referred to as the "Selected Drug")

WHEREAS, the Manufacturer has in effect a Medicare Drug Price Negotiation Agreement (the "Agreement"), which the Manufacturer entered into with CMS on [Date], to negotiate to determine a price (referred to as "maximum fair price" in the Social Security Act ("the Act")) for the Selected Drug under the Negotiation Program and agreed to such a price on [Date(s)]; and

WHEREAS, the Manufacturer and CMS have engaged in renegotiation of the price for the Selected Drug in accordance with the renegotiation process set forth in section 1194 of the Act and applicable guidance and regulations; and

WHEREAS, the Manufacturer and CMS now agree to a renegotiated price for the Selected Drug, as published by CMS in accordance with section 1194(f)(4) of the Act and updated in accordance with sections 1194(f)(4) and 1196(a)(2) of the Act and applicable guidance and regulations, which will apply for purposes of the Agreement; and

NOW THEREFORE, the Manufacturer and CMS agree to this Addendum, such that the following terms are hereby incorporated as part of the Agreement:

a) The parties agree to a price of [$] for the Selected Drug per 30-day equivalent supply, weighted across dosage forms and strengths.
b) The parties agree that the price set forth in clause (a) shall apply to the dosage forms and strengths of the Selected Drug as identified on the list of National Drug Codes (NDCs) maintained by CMS as may be updated with information from the manufacturer in accordance with section 1193 of the Act and applicable guidance and regulations.
c) The parties agree that the price set forth in clause (a), which in accordance with section 1196(a)(2) of the Act and applicable guidance and regulations is computed and applied by CMS across the different strengths and dosage forms of the Selected Drug as set forth in clause (b), is binding and shall apply as specified in the Agreement and in accordance with the Act and any applicable guidance and regulations.

Signatures

FOR THE MANUFACTURER

A. By signing this, the Manufacturer agrees to this Addendum to the Agreement and acknowledges having received notice of potential penalties for violation of the terms of the Addendum and the Agreement.

B. The undersigned individual hereby attests that he or she is authorized by the Manufacturer to execute this Agreement with regard to the Selected Drug and to legally bind the Manufacturer on whose behalf he or she is executing the Agreement to all terms and conditions specified herein. The undersigned individual further attests that he or she has obtained access in the CMS Health Plan Management System (CMS HPMS) as an authorized representative to be signatory for the Manufacturer and that the individual's CMS HPMS access credentials contain the same information regarding the undersigned individual as the information set forth below.

By:

Print Name: _____

Signature: _____

Title: _____ _____

Date: _____

P-Number: _____

Manufacturer Address: _____

_____

FOR THE CENTERS FOR MEDICARE & MEDICAID SERVICES

By:

Name: _____

Signature: _____

Title: _____

Date: _____

DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

CENTER FOR MEDICARE

DATE: June 30, 2023

TO: Interested Parties

FROM: Meena Seshamani, M.D., Ph.D., CMS Deputy Administrator and Director of the Center for Medicare

SUBJECT: Medicare Drug Price Negotiation Program: Revised Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026

This memorandum provides interested parties with the revised Medicare Drug Price Negotiation Program guidance for initial price applicability year 2026. It includes four sections:

A. An introduction, which begins on page 1.
B. A summary of changes and clarifications to the initial memorandum released on March 15, 2023, which begins on page 2.
C. A summary of the public comments received in response to the initial memorandum, and the Centers for Medicare & Medicaid Services' (CMS') responses, which begins on page 8.
D. Revised guidance that establishes final policies on the topics discussed for initial price applicability year 2026, which begins on page 92 and for which a table of contents appears on page 94.

CMS may supplement this guidance with further program instruction to explain how these policies will be implemented during initial price applicability year 2026 (e.g., technical instructions for data submissions).

A. Introduction

Sections 11001(c) and 11002(c) of the Inflation Reduction Act (IRA) direct the Secretary to implement the Medicare Drug Price Negotiation Program (hereafter the "Negotiation Program") for 2026, 2027, and 2028 by program instruction or other forms of program guidance. In accordance with the law, on March 15, 2023, CMS issued an initial memorandum for implementation of the Negotiation Program for initial price applicability year 2026. CMS also voluntarily solicited comments on a number of key aspects of the initial memorandum. The 30-day comment period for the initial memorandum began March 15, 2023 and concluded April 14, 2023. CMS received more than 7,500 comment letters in response to the initial memorandum, representing a wide range of views from academic experts and thought leaders, consumer and patient organizations, data vendors/software technology entities, health plans, health care providers, health systems, individuals, labor unions, pharmaceutical and biotechnology

manufacturers, pharmacies, pharmacy benefit managers (PBMs), state governments, trade associations, venture capital firms, and wholesalers.

CMS will make public copies of the timely comment letters that CMS received on the Inflation Reduction Act website at https://www.cms.gov/inflation-reduction-act-and-medicare in July 2023. Comment letters from individuals not representing organizations will have the name, address, and contact information of the individual removed for privacy purposes. Additionally, substantively duplicative letters (e.g., submitted as part of a coordinated advocacy campaign) will be combined into a single document.

After consideration of the comments received, CMS is making certain changes to the policies described in the initial memorandum in this revised guidance for initial price applicability year 2026. These comments also may be considered in development of program guidance for initial price applicability years 2027 or 2028 of the Negotiation Program, for which CMS also intends to solicit comments. CMS will develop its policies for 2029 and all subsequent initial price applicability years of the Negotiation Program through notice-and-comment rulemaking. The public will have an additional opportunity to submit comments as part of that rulemaking process, and comments submitted in response to the initial memorandum may be considered as part of that rulemaking process.

CMS is providing a summary of significant comments that it received in response to the initial memorandum, as well as the agency's response to those significant comments, which begins on page 8. CMS is not responding in this document to all 7,500 comments that it received, but instead is addressing those significant comments that have prompted a revision or a clarification of its policies under the Negotiation Program, or that otherwise raised a significant issue warranting a response that would explain to the public the agency's resolution of that question.

B. Summary of Changes and Clarifications in Revised Medicare Negotiation Guidance

CMS received many constructive, thoughtful, and helpful comments from consumer and patient groups, manufacturers, pharmacies, individuals, and other interested parties on the initial Medicare Drug Price Negotiation Program Guidance that was released on March 15, 2023. This section provides a summary of the key changes and clarifications made to the initial memorandum based on these comments and other feedback. CMS provides responses to the comments received in section C of this revised guidance and has made corresponding changes and clarifications to the policies described in the initial memorandum, as summarized below.

Section 30 – Identification of Selected Drugs for Initial Price Applicability Year 2026: In section 30 of this revised guidance, CMS has made clarifications to policies detailed in section 30 of the initial memorandum, including:

- Bona Fide Marketing of a Generic Drug: CMS has clarified in section 30.1 of this revised guidance the process it will use to determine if bona fide marketing of a generic drug or biosimilar competitor to a potential qualifying single source drug is occurring for the purposes of drug selection. CMS will review both Prescription Drug Event (PDE) data and Average Manufacturer Price (AMP) data reported by manufacturers. The determination whether a generic drug or biosimilar is marketed on a bona fide basis will be based on a totality of the circumstances, including PDE and AMP data.

- Orphan Drug Exclusion: CMS has clarified in section 30.1.1 of this revised guidance that a drug that has designations from the U.S. Food and Drug Administration (FDA) for more than one rare disease or condition will not qualify for the Orphan Drug Exclusion, even if the drug has not been approved for any indications for the additional rare disease(s) or condition(s) and that CMS will only consider active designations and active approvals when evaluating a drug for the Orphan Drug Exclusion; that is, CMS will not consider withdrawn orphan designations or withdrawn approvals as disqualifying a drug from the Orphan Drug Exclusion. CMS does not have the statutory authority to change the starting date from which qualifying single source drug status is determined, regardless of whether the drug or biological product was previously eligible for the Orphan Drug Exclusion under 1192(c)(3)(A) of the Social Security Act ("the Act").
- Exception for Small Biotech Drugs and Biosimilar Delay: CMS has clarified in sections 30.2.1 and 30.3.1 of this revised guidance the scope of the data that CMS will use to calculate the Small Biotech Drug Exception, which patents and litigation will be considered related to the Biosimilar Delay determination and how CMS will evaluate the manufacturing schedule for the marketing of the Biosimilar, as well as how, for both the Small Biotech Exception and the Biosimilar Delay, CMS will protect information from disclosure and communicate to the public whether there were successful requests.

Section 40 – Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026: CMS has made the following changes and clarifications to policies detailed in section 40 of the initial memorandum:

- Manufacturer Negotiation Agreement: CMS revised section 40.1 to establish a process for a Primary Manufacturer that is unwilling to enter into an Agreement for the Negotiation Program to expedite its termination from the Medicare Coverage Gap Discount Program and the Manufacturer Discount Program. The revised guidance also specifies that a Primary Manufacturer may terminate its Agreement with CMS at any time, provided the conditions for termination are met, as described in section 40.6 of this revised guidance.
- Data Submission, Confidentiality, and Data Use Provisions: CMS revised section 40.2.2 of the guidance to state that CMS will not publicly discuss ongoing negotiations prior to the release of the explanation of the maximum fair price (MFP) unless a Primary Manufacturer publicly discloses information regarding the negotiation process. Primary Manufacturers may choose to publicly disclose information regarding ongoing negotiations at its discretion. In addition, CMS will treat as proprietary certain data submitted by a Primary Manufacturer of a selected drug in accordance with sections 1194(e)(1) and 1194(e)(2) of the Act, but if a Primary Manufacturer chooses to disclose any material that is made public that CMS has previously deemed to be proprietary information of that Primary Manufacturer, CMS will no longer consider that material proprietary. CMS removed the data destruction requirements under the confidentiality policy pertaining to Primary Manufacturers in section 40.2.2 of this revised guidance. Section 40.2.3 of the revised guidance also provides that CMS will provide the Primary Manufacturer an opportunity for corrective action in the event a submission is incomplete or inaccurate.
- Public Explanation of MFP: CMS will publish a public explanation of the MFP for initial price applicability year 2026 for each selected drug by March 1, 2025 that will include a narrative explanation of the negotiation process, the agreed-upon MFP, and redacted

information regarding the section 1194(e) data received, exchange of offers and counteroffers, and the negotiation meetings, if applicable.

- Use of Medicare Transaction Facilitator (MTF): CMS clarified in section 40.4 of this revised guidance that it intends to engage with an MTF to facilitate the exchange of data between pharmaceutical supply chain entities to help effectuate access to the MFP through a retrospective refund model. CMS is also exploring allowing the use of a standardized refund amount from the manufacturers to the pharmacies under a retrospective refund model and confirms it will require the use of a 14-day prompt pay standard for the refund from manufacturers to pharmacies and other dispensing entities to reimburse dispensing entities for passing through the MFP.
- Suggestion of Error: CMS clarified in section 40.5 of this revised guidance that if a Primary Manufacturer in good faith believes that CMS has made an error in the calculation of the ceiling or the computation of MFP across dosage forms and strengths, the Primary Manufacturer can submit a suggestion of error. CMS will respond to suggested errors within 30 days.
- Manufacturer Ownership Transfer of Selected Drugs: CMS clarified in section 40.7 of this revised guidance the Primary Manufacturer's ongoing responsibilities if the Primary Manufacturer of a selected drug transfers ownership of one or more New Drug Application(s) (NDA) / Biologics License Application(s) (BLA) of the selected drug to another entity, unless and until the Primary Manufacturer transfers all the NDAs / BLAs of the selected drug that it holds to an entity and such acquiring entity assumes responsibility as the new Primary Manufacturer as evidenced by a novation that meets certain criteria.

Section 50 – Negotiation Factors: In the revised guidance, CMS reaffirmed that it will not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill. CMS also clarified that, for initial price applicability year 2026, it will review cost-effectiveness measures and studies that use such measures to determine whether the measure used may be considered in accordance with section 1194(e)(2) of the Act. However, while such measures may be considered, they will not be used to adjust the initial offer if the measure does not provide relevant information or is not permitted in accordance with section 1194(e)(2) of the Act and section 1182(c) of the Act. CMS has also noted that outcomes such as changes to productivity, independence, and quality of life will be considered when these outcomes correspond with a direct impact on the individuals taking the selected drug or therapeutic alternative(s) and are permitted by section 1194(e)(2) of the Act.

Section 60 – Negotiation Process: CMS has revised the guidance to provide additional detail about how CMS will use the days' supply field in PDE data to calculate a 30-day equivalent supply using the methodology described in 42 C.F.R. § 423.104(d)(2)(iv)(A)(2) when calculating the MFP ceiling (described in section 60.2 of this revised guidance) and using the Wholesale Acquisition Cost (WAC) ratio to apply the MFP across dosage forms and strengths (described in section 60.5 of this revised guidance). As described in section 60.3.2 of this revised guidance, when comparing prices of therapeutic alternatives for purposes of informing a starting price for the initial offer, CMS may use an alternative methodology for calculating a 30-day equivalent

supply when appropriate. In addition, the following revisions were made in this section of the guidance:

- Limitations on Offer Amount: CMS has revised section 60.2 of this revised guidance to use the single ceiling per 30-day equivalent supply across all dosage forms and strengths of the selected drug. CMS has also clarified that the time period for determining whether a selected drug is an extended- or long-monopoly drug runs from NDA approval to the start of the applicable initial price applicability year and clarified that PDE units will be used when averaging non-Federal average manufacturer price ("non-FAMP") across 11-digit National Drug Codes (NDC-11s).
- Unmet Medical Need: In section 60.3.3.1, CMS has revised the definition of unmet medical need to further align with FDA's "Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics."[1]
- Addition of Manufacturer and Patient-Focused Meetings: To facilitate communication with manufacturers, CMS has described in section 60.4 that a CMS-manufacturer meeting will be added to the overall MFP negotiation process that would occur in Fall 2023 after the October 2, 2023 manufacturer data submissions, so that the manufacturer has an opportunity to present the data elements submission and share new information on the section 1194(e)(2) factors, if applicable, with CMS. In addition, CMS will be holding patient-focused listening sessions in Fall 2023 after the October 2, 2023 deadline for patients and other interested parties to share patient-focused input on therapeutic alternatives and other section 1194(e)(2) data regarding selected drugs.
- Negotiation Process: CMS revised section 60.4.3 to clarify that CMS will respond in writing no later than 30 days after receipt of a manufacturer's counteroffer regardless of whether CMS accepts or rejects the counteroffer. CMS has clarified that, to effectuate any MFP agreed upon by CMS and the Primary Manufacturer, both CMS and the Primary Manufacturer must sign and execute an Addendum to the Agreement. CMS also clarified in section 60.4.4 of the revised guidance that if an agreement on an MFP is not reached by the statutory end of the negotiation period, the Primary Manufacturer will enter a period during which an excise tax potentially may be assessed. The Primary Manufacturer can end this period by agreeing to an MFP or sending a notice terminating all of its applicable agreements under the Medicare and Medicaid programs and establishing that none of the Primary Manufacturer's drugs are covered by an agreement under section 1860D-14A or section 1860D-14C of the Act.
- Publication of MFPs for Selected Drugs: CMS clarified in section 60.6 of the revised guidance that CMS will publish the following on the CMS website by September 1, 2024 for all initial price applicability year 2026 selected drugs where an MFP was agreed upon: the selected drug, the initial price applicability year, and the MFP pricing file (which would be updated annually to show the inflation-adjusted MFP for a selected drug). CMS will strive to publish the explanation of the MFP earlier than March 1, 2025, if feasible.
- Manufacturer Delay in Negotiation Process: CMS has clarified in section 60.8 of the revised guidance that, if a Primary Manufacturer is delayed in meeting one or more deadlines related to the negotiation process, CMS will continue to engage in the negotiation process, as described in section 60.4. If delays occur such that the MFP is established after the end of the

[1] FDA Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics, May 2014. See: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/expedited-programs-serious-conditions-drugs-and-biologics.

negotiation period, CMS will follow timelines consistent with this revised guidance and take the time to complete the negotiation process as described.

Section 70 – Removal from the Selected Drug List Before or During Negotiation, or After an MFP is in Effect: In accordance with the policy clarification in section 30, CMS clarified that, in addition to monitoring PDE data for a selected drug, CMS will use AMP data reported by manufacturers to determine whether bona fide marketing is occurring when the agency undertakes the process of deselecting a selected drug and monitoring for the continued bona fide marketing of a generic drug or biosimilar. CMS will consider an approved generic drug or licensed biosimilar biological product to be marketed when the totality of the circumstances, including these data, reveals that the manufacturer of the generic drug or biosimilar biological product is engaging in bona fide marketing of that drug or product.

In addition, the revised guidance clarifies that status as a selected drug is unaffected by whether the Primary Manufacturer effectuates or terminates the Agreement to participate in the Negotiation Program or divests of the selected drug.

Section 80 – MFP-Eligible Individuals: CMS clarified in section 80 of this revised guidance that for initial price applicability year 2026, an MFP for a selected drug must be provided to a Medicare beneficiary who uses their Part D plan (including a Medicare Advantage Prescription Drug (MA-PD) plan under Medicare Part C or an Employer Group Waiver Plan) if Part D coverage is provided under such plan for such selected drug. The MFP is not required to be made available to a Medicare beneficiary who uses other sources of prescription drug coverage, such as a plan that receives the Retiree Drug Subsidy, prescription drug discount cards, or cash. For initial price applicability year 2026, CMS does not expect manufacturers to provide access to the MFP of a selected drug to hospitals, physicians, and other providers of services and suppliers with respect to a drug furnished or administered to MFP eligible individuals enrolled under Part B, including an individual who is enrolled in an MA plan.

Section 90 – Manufacturer Compliance and Oversight: CMS made revisions to note that, while the statute clearly requires that the manufacturers of selected drugs are responsible for providing access of the MFP to MFP-eligible individuals and to pharmacies, mail order services, and other dispensers, CMS intends to engage with an MTF to facilitate the exchange of data between supply chain entities to verify eligibility of MFP-eligible individuals such that the MFP can be effectively passed through by the manufacturer to pharmacies, mail order services, and other dispensers. CMS also intends to explore options to facilitate retrospective payment exchange between interested parties to help effectuate access to the MFP.

Consistent with the changes and clarifications noted in sections 30 and 70 of this summary, CMS has also reaffirmed in section 90.4 of this revised guidance that it intends to monitor whether the manufacturer of a generic drug or biosimilar for the selected drug is engaging in "bona fide marketing" of the product by reviewing both PDE data and AMP data. CMS has also clarified that use of these data is not exhaustive, and all data and other information will be reviewed in totality in monitoring if manufacturers of these applicable generic drugs and biosimilars continue to engage in bona fide marketing.

Section 100 – Civil Monetary Penalties (CMPs): In the revised guidance, CMS has provided additional details on the CMP Notification that will be sent to the Primary Manufacturer, an opportunity for corrective action in applicable circumstances, additional details on CMP calculations, and information regarding the payment and appeals processes. CMS will provide an opportunity for corrective action prior to imposing CMPs in some circumstances, providing, for example, a Notice of Potential Noncompliance that includes an opportunity for the Primary Manufacturer to correct or mitigate noncompliance in applicable situations. CMS also revised the guidance to adopt a definition for "knowingly" that is consistent with language used by the Office of the Inspector General in administration of CMPs at 42 C.F.R. § 1003.110 such that "knowingly" means that a person, with respect to an act, has actual knowledge of the act, acts in deliberate ignorance of the act, or acts in reckless disregard of the act, and no proof of specific intent to defraud is required. CMS has also removed the "knowingly" requirement as related to the submission of false information under the Manufacturer Agreement.

Section 110 – Part D Formulary Inclusion of Selected Drugs: The revised guidance has clarified that the statute requires Part D plans to include on their formularies all dosage forms and strengths of the selected drug that constitute a covered Part D drug and for which the MFP is in effect and has established the agency's expectations for how this requirement will be met for initial price applicability year 2026.

Section 120 – Application of Medicare Part B and Part D Prescription Drug Inflation Rebate Programs to Selected Drugs: In the revised guidance, CMS has reaffirmed that selected drugs will also be subject to the Part D drug inflation rebate, but clarified that the MFP for a selected drug is not included in the AMP for the selected drug and thus will not affect the Part D inflation rebate calculation (see section 1927(k)(1)(B)(i)(VI)).

Appendix C – Definitions for Purposes of Collecting Manufacturer-Specific Data: After consideration of the comments on this guidance and the Negotiation Data Elements Information Collection Request (ICR) (CMS-10847 / OMB 0938-NEW), CMS has revised certain definitions in Appendix C. For example, CMS has revised the definition of non-FAMP in Appendix C to clarify that any restatements of the non-FAMP made in any applicable manufacturer non-FAMP submissions to the Department of Veterans Affairs must be reflected in the non-FAMP submitted to CMS as part of the section 1194(e)(1) data submission. CMS has consolidated several research and development (R&D) cost categories in Appendix C and has revised the R&D-related definitions by, for example, requiring reporting of acquisition costs as part of R&D rather than market data and revenue and sales volume data. CMS has also revised Appendix C to clarify that CMS will consider both a Primary Manufacturer's global and U.S. revenue when determining whether to adjust the preliminary price based on manufacturer-submitted data. In addition, CMS has revised the definition related to patents and exclusivities to provide clarification about the types of patents and patent applications that CMS considers to be "related to" the selected drug.

CMS removed certain definitions in Appendix C that are no longer needed due to deletions and revisions to information requested in the 30-day public notice for comment on the Negotiation Data Elements Information Collection Request, including 340B ceiling price, 340B prime vendor program price, manufacturer average net unit price to Part D plans, and quarterly total U.S. unit

volume. CMS revised the definition of unmet medical need and clarified when CMS will consider caregiver perspectives and outcomes such as changes to productivity, independence, and quality of life.

CMS directs interested parties to the 30-day public notice for comment on the Negotiation Data Elements ICR for revisions to ICR instructions and questions that are out of scope for this revised guidance.

C. Summary of Public Comments on the Initial Medicare Drug Price Negotiation Program Memorandum and CMS' Responses

CMS Statutory Authority to Issue Program Instruction and to Issue Section 30 of the Initial Memorandum as Final

Comment: Many commenters stated that CMS should use notice-and-comment rulemaking procedures to implement sections of the IRA. Specifically, a few commenters suggested that by issuing policy through program instruction, CMS violated the Administrative Procedure Act (APA) and the Medicare statute, which require use of notice procedures in certain circumstances and 60 days for comment. Relatedly, a few commenters stated that CMS violated the Due Process Clause of the U.S. Constitution by releasing section 30 of the initial memorandum as final without soliciting comments. Commenters asserted that in relying on the strict statutory deadlines for implementing the Negotiation Program as the rationale for issuing section 30 of the initial memorandum as final, CMS has not shown "good cause" to issue section 30 as final. In addition, a couple of commenters indicated that by issuing section 30 as final, CMS exceeded the scope of what Congress permitted in statute and engaged in *ultra vires* conduct.[2] Some commenters stated that it was improper for CMS to establish substantive obligations without providing notice and opportunity for comment, with one of these commenters further stating that such obligations are invalid and unenforceable because the guidance did not go through rulemaking procedures. A couple of commenters also wrote that the fact that CMS published the initial memorandum seven months after the IRA was enacted does not exempt it from providing opportunities for comment. Several commenters specifically requested that CMS use notice-and-comment rulemaking to codify the negotiation process for initial price applicability years 2027 and beyond. Other commenters recommended that CMS finalize the guidance well in advance of the selected drug publication date for initial price applicability year 2026 to provide interested parties with adequate time to review this revised guidance and conform their actions accordingly.

Response: Sections 11001(c) and 11002(c) of the IRA state that CMS "shall implement" the Negotiation Program "for 2026, 2027, and 2028 by program instruction or other forms of program guidance." Thus, the initial memorandum is not subject to the notice-and-comment requirements of the APA or the Medicare statute. The terms "program instruction" and "program guidance" are terms of art that Congress routinely uses in Medicare statutes to refer to agency pronouncements other than notice-and-comment rulemaking. The statutory directive in sections 11001(c) and 11002(c) thus specifies that CMS shall follow policymaking procedures that differ from the notice-and-comment procedures that would otherwise apply under the APA or the

[2] *Ultra vires* means "beyond the powers," and is used to describe actions taken by governmental bodies that exceed the scope of power given to them by law.

Medicare statute. Congress underscored this directive by placing the Negotiation Program in the newly-enacted Part E of Title XI of the Social Security Act.

Even if the notice-and-comment procedures of the APA and the Medicare statute were applicable, the use of those procedures would be impracticable, unnecessary, and contrary to the public interest, and CMS thus had good cause to depart from those procedures. CMS solicited public comment on many key aspects of the initial memorandum, and also concluded, as stated in the initial memorandum, that in light of the complexity of the actions that must be undertaken in advance of the statutorily-mandated publication of the selected drug list by September 1, 2023, there was good cause to issue parts of the initial memorandum as final, including section 30, without soliciting public comment and without a delayed effective date. CMS reiterates this good-cause justification in this final guidance. CMS also has good cause to issue this revised guidance as final in advance of the statutory September 1, 2023, publication date of the selected drug list for initial price applicability year 2026. CMS agrees with the commenters who encouraged CMS to finalize the guidance well in advance of September 1, 2023 in order to allow interested parties advanced notice of the final policies for the Negotiation Program for initial price applicability year 2026. In particular, manufacturers need to take a number of actions well in advance of September 1, 2023, to prepare for the possibility that a drug that they manufacture will be included on the selected drug list for initial price applicability year 2026. For example, manufacturers may need to engage in internal discussions regarding whether the manufacturers would choose to participate in the Negotiation Program if their drug is included on the selected drug list published on September 1, 2023, review the template Medicare Drug Price Negotiation Program Agreement and guidance to understand Negotiation Program requirements for participating manufacturers in advance of the statutory deadline of October 1, 2023, for entering agreements, and gather information for potential submission to CMS by the statutory deadline of October 2, 2023. In addition, for the reasons explained below, the deadline for a biosimilar manufacturer to submit a delay request under section 1192(f) of the Act was May 22, 2023. CMS could not have proceeded through notice-and-comment rulemaking and still provided interested parties with guidance sufficiently far in advance of these deadlines to allow them adequate time to complete their preparations for potential participation in the Negotiation Program.

Although section 30 was issued as final in the initial memorandum due to these timing constraints, CMS received many comments on section 30. In this guidance, CMS summarizes and responds to those comments, and CMS revised section 30 to help clarify, as needed, the policies it will follow to implement the selection of drugs for initial price applicability year 2026. CMS will continue to consider these comments as it develops guidance and rulemaking for future years of the Negotiation Program.

CMS also disagrees that the use of program guidance to implement the Negotiation Program for initial price applicability year 2026 or the issuance of section 30 as final violates the Due Process Clause of the U.S. Constitution. To the contrary, the reason CMS has undertaken efforts to finalize this guidance well before September 1, 2023, is to ensure that interested parties have advance notice about the procedures CMS will use to implement the Negotiation Program in accordance with the statute. The statute expressly directs CMS to use program guidance rather than notice-and-comment rulemaking to implement the Negotiation Program for 2026, 2027, and 2028, and, even so, through the publication of the initial memorandum, CMS ensured that

interested parties were given notice of and an opportunity to comment on many key aspects of the procedures CMS intends to follow in advance of any selection or negotiation for initial price applicability year 2026. And as explained, although CMS did not solicit comment on section 30, it received many comments on that section and revised to clarify the section in light of those comments.

Further, since enactment of the IRA in August 2022 CMS has engaged with interested parties through various platforms. On January 11, 2023, CMS issued a memorandum outlining how CMS will approach implementation of the Negotiation Program for initial price applicability year 2026, including engagement with the public; program guidance; information collection requests; and a timeline outlining key dates.[3] CMS considered the feedback it received through this engagement in the development of the initial memorandum for the Negotiation Program. Following the issuance of the initial memorandum in March 2023, CMS continues to engage with interested parties, with the intention to engage interested parties throughout implementation of the Negotiation Program.

Between September 2022 and March 2023, CMS accepted 104 meetings with interested parties representing the views of consumer and patient organizations, health care providers, health plans, PBMs, pharmaceutical and biotechnology manufacturers, pharmacies, researchers and academic experts, and wholesalers. In these meetings, CMS leadership and staff received feedback on implementation of the Negotiation Program ranging from policy concerns, questions requiring clarification, and recommendations on policy or operations. CMS also received 129 written materials totaling more than 1,100 pages submitted by pharmaceutical and biotechnology manufacturers and their trade associations, researchers and academic experts, consumer and patient organizations, and health plans and their trade associations, among other interested parties, before publishing the initial memorandum. Based on CMS' tracking of meeting agendas and materials provided, interested parties commonly provided feedback on key Negotiation Program topics including how to identify qualifying single source drugs for negotiation, how to apply the Orphan Drug Exclusion, how to operationalize requests by a biosimilar sponsor to delay selection and negotiation of a biological product that is a reference product for biosimilar market entry, and how to effectuate the MFP. Additionally, CMS leadership participated in 22 speaking engagements on IRA implementation hosted by interested parties. In addition to meetings with interested parties on specific issues of importance to the individual company or organization, CMS has held monthly one-hour calls open to all pharmaceutical and biotechnology manufacturers since December 2022. During these monthly calls, CMS staff provide an overview of recent IRA activities and take questions from manufacturer participants. In addition, in Fall of 2022, CMS established an IRA webpage for all program policies and updates and created an IRA mailbox (IRARebateandNegotiation@cms.hhs.gov) to receive queries from the public related to implementation of the Part B and Part D Inflation Rebate Program and the Negotiation Program. For example, CMS has received queries through the IRA mailbox from interested parties on how to ensure beneficiaries have access to the MFP through their Part D plan.

[3] CMS memorandum, *Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026.* Accessible at https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf.

Through external meetings with interested parties, monthly IRA calls with pharmaceutical and biotechnology manufacturers, and the IRA mailbox, interested parties have had multiple touchpoints with CMS. Therefore, CMS disagrees that it has not provided opportunity for interested parties to engage with CMS on policies that may impact their business operations and patients. CMS remains committed to ongoing engagement efforts with interested parties and plans to meet with the Primary Manufacturer of each selected drug as well as hosting patient-focused listening sessions on the selected drugs in Fall 2023, as described in section 60.4 of this revised guidance.

Identification of Qualifying Single Source Drugs for Initial Price Applicability Year 2026 (Section 30.1)

Comment: CMS received many comments on its reading of the statute to aggregate all dosage forms and strengths of a drug with the same active moiety and the same holder of the NDA or of a biological product with the same active ingredient and the same holder of the BLA, for the purposes of identifying potential qualifying single source drugs. Some commenters stated that this approach is consistent with the clear statutory instruction to aggregate across dosage forms and strengths. A couple of commenters stated that this policy is critical to prevent gaming. In their view, this reading of the statute will prevent pharmaceutical manufacturers from engaging in "product hopping," attempting to shift use of their products away from those with an MFP to those without an MFP, based solely on modest or minor modifications, a practice which increases revenue for pharmaceutical companies. Other commenters asserted that this approach is not supported by the statute and that the statute defines a qualifying single source drug in reference to a distinct NDA or BLA.

Response: Section 1192(d)(3)(B) of the Act directs CMS to "use data that is aggregated across dosage forms and strengths of the drug, including new formulations of the drug, such as an extended release formulation, and not based on the specific formulation or package size or package type of the drug" for purposes of determining whether a qualifying single source drug is a negotiation-eligible drug. Similarly, section 1196(a)(2) of the Act directs CMS to establish procedures "to compute and apply the maximum fair price across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug." The aggregation rules under sections 1192(d)(3)(B) and 1196(a)(2) are clear, and are designed to ensure that the Negotiation Program delivers benefits to the Medicare program and its beneficiaries as intended by the law. Because different dosage forms and strengths, as well as different formulations, of an active moiety / active ingredient can be approved or licensed under multiple NDAs or BLAs, the suggestion from commenters to define a qualifying single source drug in reference to a distinct NDA or BLA is inconsistent with sections 1192(d)(3)(B) and 1196(a)(2) of the Act. Contrary to the views of some commenters, section 1192(d)(3)(B) refers to the aggregation of data "across dosage forms and strengths of the drug, including new formulations of the drug," thereby necessarily establishing that the statutory negotiation procedures apply more broadly than to a distinct NDA or BLA. Unlike the views offered by some commenters, CMS' understanding of the statutory language gives full effect to all relevant provisions of the statute, including sections 1192(e), 1192(d)(3)(B), and 1196(a)(2) of the Act; CMS is applying an interpretation of the statute that follows the statutory criteria for the identification of a qualifying single source drug under section 1192(e) of the Act and,

consistent with sections 1192(d)(3)(B) and 1196(a)(2) of the Act, gives effect to the statutory policy that a drug that may be selected for negotiation includes multiple dosage forms and strengths and formulations of that drug.

CMS agrees with commenters that complying with the statutory requirement to identify a qualifying single source drug using data that is aggregated across different dosage forms and strengths, as described in the initial memorandum, will decrease incentives for pharmaceutical manufacturers to engage in "product hopping." This statutory requirement ensures that products by the same sponsor with the same active moiety / active ingredient are subject to the same processes under the Negotiation Program, and that a manufacturer is therefore limited in its ability to shift use of its products away from those with an MFP to those without an MFP, based on modest or minor modifications. Reducing "product hopping" is consistent with the purpose of the statute, which is to ensure that the Negotiation Program delivers benefits to the Medicare program and its beneficiaries. For the above reasons, in this revised guidance, CMS maintains the approach described in the initial memorandum for identifying potential qualifying single source drugs.

Comment: Some commenters raised questions about how CMS will treat products that have different formulations or routes of administration within the same qualifying single source drug, given the policy to define a qualifying single source drug based on active moiety or active ingredient. Some commenters expressed concerns that aggregation will limit pharmaceutical innovation, including innovation for rare diseases and conditions, and commenters urged CMS to consider the patient perspective on whether new formulations demonstrate an improvement to patient care. In contrast, one commenter was concerned that aggregating products with different indications and/or routes of administration into the same qualifying single source drug could be problematic because one product with different indications and/or routes of administration from the other products within a potential qualifying single source drug could have a generic or biosimilar competitor that would disqualify all products from the Negotiation Program.

Response: CMS thanks these commenters for their input. CMS is committed to recognizing the clinical benefit of products, including products with different formulations or routes of administration from other products that are aggregated as part of the same qualifying single source drug, and directs readers to section 60.3.3 of this revised guidance, which details CMS' approach to adjusting the starting point for an initial offer based on clinical benefit.

CMS appreciates the concern raised that a generic or biosimilar competitor for one product within a potential qualifying single source drug will disqualify all products within that potential qualifying single source drug from the Negotiation Program. However, as explained above, the statute directs CMS to aggregate across dosage forms and strengths of the drug, and CMS must apply that requirement faithfully not only for purposes of identifying the qualifying single source drug, but also for purposes of disqualifying products with generic or biosimilar competition that satisfies the relevant statutory criteria.

CMS is committed to ensuring that the statutory criteria are satisfied for any such disqualification, including the requirement that a generic or biosimilar be "marketed." This is particularly important given that a drug or biological product will not be considered a qualifying

single source drug for initial price applicability year 2026 if such competition is determined to exist at the time of drug selection; if such determination occurs after drug selection, it will cause a selected drug (1) to be no longer subject to the negotiation process or (2) to cease to be a selected drug, depending on the timing of such determination. CMS directs readers to section 90.4 of this revised guidance, which details how CMS will monitor whether a generic drug or biosimilar competitor is engaging in bona fide marketing such that a potential qualifying single source drug is disqualified from participation in the Negotiation Program.

Comment: Many commenters asserted that the distinct time periods for when a drug versus biological product will be eligible for negotiation are arbitrary and that CMS should implement the Negotiation Program so that, for any drug or biological product to qualify as a qualifying single source drug, at least 11 years must have elapsed since the drug or biological product was approved or licensed, respectively.

Response: Section 1192(e)(1)(A)(ii) of the Act states that for a drug product to be considered a qualifying single source drug, at least 7 years must have elapsed since the drug product was approved by the FDA.[4] Section 1192(e)(1)(B)(ii) of the Act states that for a biological product to be considered a qualifying single source drug, at least 11 years must have elapsed since the biological product was licensed by the FDA.[5] CMS is implementing the program in accordance with these statutory requirements.

Comment: A couple of commenters expressed support for CMS' reading of the statute in the initial memorandum on fixed combination drugs with two or more active moieties / active ingredients, which treats the distinct combination of active moieties / active ingredients as one active moiety / active ingredient for the purpose of identifying qualifying single source drugs. One commenter raised a concern that this reading, while sensible in some cases, creates a gaming opportunity for manufacturers to seek approval of fixed combination drugs with one active moiety / active ingredient in common and market them in a way that could influence volume for each fixed combination drug in an effort to avoid selection. For example, a sponsor might market a fixed combination drug that contains active moiety / active ingredient X and Y and a fixed combination drug that contains active moiety / active ingredient X and Z. The commenter encouraged CMS to aggregate sales for fixed combination drugs with other dosage forms containing the newest active moiety / active ingredient if the products are made by the same manufacturer.

Response: CMS appreciates commenters' support for its understanding of the statutory language and acknowledges the concern outlined by one commenter. CMS believes that a fixed combination drug is distinct in its composition from the individual active moieties / active ingredients and in this revised guidance maintains its approach on fixed combination drugs,

[4] For drug products, to determine the date of approval for a potential qualifying single source drug with more than one FDA application number, section 30.1 of this revised guidance specifies that CMS will use the earliest date of approval of the initial FDA application number assigned to an NDA for the active moiety for which the manufacturer is the holder of the NDA.

[5] For biological products, to determine the date of approval for a potential qualifying single source drug with more than one FDA application number, section 30.1 of this revised guidance specifies that CMS will use the earliest date of licensure of the initial FDA application number assigned to a BLA for the active ingredient for which the manufacturer is the holder of the BLA.

which treats the distinct combination of active moieties / active ingredients as one active moiety / active ingredient for the purpose of identifying qualifying single source drugs.

Orphan Drug Exclusion from Qualifying Single Source Drugs (Section 30.1.1)

Comment: Many commenters asked CMS to clarify that the 7- or 11-year periods prior to eligibility as a qualifying single source drug would begin on the date the Orphan Drug Exclusion ceases to apply to a drug or biological product. That is, a drug or biological product could not become a qualifying single source drug until 7 or 11 years had passed between the date on which the drug or biological product, respectively, loses eligibility for the Orphan Drug Exclusion and the selected drug publication date.

Response: CMS does not have the statutory authority to change the starting date from which qualifying single source drug status is determined. Sections 1192(e)(1)(A)(ii) and (B)(ii) of the Act require CMS to use the date of the approval or licensure of the drug or biological product to determine whether the product is a qualifying single source drug that may be selected for negotiation if it meets all other Negotiation Program eligibility criteria, regardless of whether the drug or biological product previously qualified for an exclusion under section 1192(e)(3)(A) of the Act. CMS has added language to section 30.1.1 of this revised guidance to clarify the timing that CMS will use to identify qualifying single source drugs.

Comment: Many commenters asserted that drugs or biological products with multiple orphan designations (for multiple rare diseases or conditions) that are approved only for indications within the scope of a single rare disease or condition should qualify for the Orphan Drug Exclusion. A few commenters remarked that designating a drug under section 526 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for a rare disease is done very early in the drug development process and is important to unlocking Orphan Drug Act incentives. These commenters expressed concern that the current Orphan Drug Exclusion policy in the Negotiation Program will stymie innovation for drugs or biological products and discourage sponsors from seeking designations for more than one rare disease or condition.

Response: CMS thanks these commenters for their feedback. Section 1192(e)(3)(A) of the Act describes a drug that qualifies for the Orphan Drug Exclusion as a "drug that is designated as a drug for only one rare disease or condition under section 526 of the FD&C Act and for which the only approved indication (or indications) is for such disease or condition." CMS therefore does not have the statutory authority to exclude a drug under the Orphan Drug Exclusion that has designations for multiple rare diseases or conditions, even if the drug has been approved only for indication(s) within a single rare disease or condition. CMS has added a clarification about designations for multiple rare diseases or conditions to section 30.1.1 of this revised guidance, which addresses how CMS will implement this exclusion.

Comment: A couple of commenters urged CMS to interpret the term "rare disease or condition" with sufficient breadth to capture designations and approved indications for different mutations or subtypes of one disease. Commenters noted that this interpretation would allow a drug or biological product to seek designations and approvals for sub-conditions within the same rare

disease or condition and remain eligible for the Orphan Drug Exclusion and would preserve incentives for drug development across sub-conditions.

Response: CMS will follow the statutory directive in section 1192(e)(3)(A) of the Act to consider orphan designations and approvals within the scope of the same rare disease or condition. As clarified in section 30.1.1 of this revised guidance, CMS will consult with the FDA as needed to determine whether a drug is designated under section 526 of the FD&C Act for, or has approved indications for, one or more rare diseases or conditions, as part of determining whether a drug meets the requirements in section 1192(e)(3)(A) of the Act to qualify for the Orphan Drug Exclusion.

Comment: Commenters offered contrasting perspectives on whether CMS should consider orphan designations that have been withdrawn when evaluating a drug or biological product for the Orphan Drug Exclusion. Some commenters asserted that CMS should not consider withdrawn designations. In contrast, one commenter recommended that CMS should consider withdrawn designations because a manufacturer could withdraw a designation that is not yet FDA-approved so that a drug or biological product could qualify for the Orphan Drug Exclusion.

Response: CMS appreciates this feedback. CMS understands that a drug or biological product may be designated for a rare disease or condition early in the drug development process, and that designation might not always result in FDA-approved indications that fall within the scope of that designation, and that a manufacturer may choose to withdraw the designation. Similarly, there may be situations where, for example, a manufacturer decides to request that FDA withdraw approval of an indication. In accordance with section 1192(e)(3)(A) of the Act, only designations and approvals active at the time of identifying qualifying single source drugs will be considered for purposes of determining a drug's eligibility for the Orphan Drug Exclusion to best reflect the status of the drug at the time it is evaluated for qualifying single source drug eligibility. As such, CMS has clarified in section 30.1.1 of this revised guidance that it will not consider withdrawn orphan designations or withdrawn approvals when evaluating a drug for the Orphan Drug Exclusion.

Comment: A few commenters raised questions as to whether a potential qualifying single source drug will qualify for the Orphan Drug Exclusion if some but not all dosage forms and strengths of that potential qualifying single source drug meet the Orphan Drug Exclusion criteria. One commenter requested that, when a drug or biological product loses eligibility for the Orphan Drug Exclusion, CMS carve out the original approval(s) that qualified for the Orphan Drug Exclusion from the resulting qualifying single source drug. Another commenter requested that potential qualifying single source drugs that qualify for the Orphan Drug Exclusion must qualify across all dosage forms and strengths. An additional commenter asked whether a fixed combination drug will qualify for the exclusion if only one of the two active moieties / active ingredients qualifies for the Orphan Drug Exclusion.

Response: The initial memorandum states that, in order to qualify for the Orphan Drug Exclusion, "all dosage forms and strengths and different formulations of the qualifying single source drug described in section 30.1 of this memorandum must meet the criteria for exclusion." In this revised guidance, CMS maintains this requirement. Because section 1192(e)(3)(A) of the

Act is an exclusion from the definition of qualifying single source drug under section 1192(e)(1) of the Act, CMS must consider whether the drug, including all products that constitute the potential qualifying single source drug, meets the statutory criteria for the Orphan Drug Exclusion.

Comment: A few commenters expressed concern that the FDA Orphan Drug Product designation database and the FDA approvals database will not allow CMS to identify whether an indication falls within an orphan designation. To alleviate this concern, commenters recommended that CMS consult with FDA and consider written communications between FDA and the manufacturer during the review and approval process. Commenters also suggested that CMS establish a pathway for manufacturers and other interested parties to demonstrate that an indication falls within an orphan drug designation.

Response: CMS appreciates these comments. CMS believes that consulting the FDA Orphan Drug Product designation database and approvals on the FDA website, in addition to consultation with FDA as needed, will allow CMS to successfully implement the Orphan Drug Exclusion. CMS will monitor this approach to ensure that it accurately operationalizes the Orphan Drug Exclusion.

Comment: A few commenters requested that CMS support the development of diagnosis codes for rare diseases and disorders; support early dialogue between payers and rare disease manufacturers; and create new payment and service delivery models with the Center for Medicare and Medicaid Innovation (CMMI) that bolster innovation in the treatment of rare diseases or conditions.

Response: CMS noted in the initial memorandum that CMS is considering whether there are additional actions that CMS might take in its implementation of the Negotiation Program to support orphan drug development, and CMS directs readers to the discussion in section 60.3.3 of how it will consider unmet medical need and the impact of a selected drug on specific populations when developing the initial offer. CMS notes, however, that these specific requests related to CMMI, diagnosis code development, and other payers' interactions with manufacturers are outside the scope of this revised guidance.

Low-Spend Medicare Drug Exclusion from Qualifying Single Source Drugs (Section 30.1.2)

Comment: A few commenters provided feedback on CMS' description of how it will calculate the Low-Spend Medicare Drug Exclusion. One commenter supported the approach that CMS detailed in the initial memorandum. Another commenter recommended that CMS include rebates in the calculation of Total Expenditures under Part B and Part D for purposes of the Low-Spend Medicare Drug Exclusion. One commenter recommended that CMS exclude beneficiary cost sharing under Part B and net out Direct and Indirect Remuneration (DIR) under Part D when calculating total Part B and Part D expenditures for purposes of this exclusion.

Response: For the purposes of the Negotiation Program, Total Expenditures under Part D of Title XVIII are defined in section 1191(c)(5) of the Act as total gross covered prescription drug costs (as defined in section 1860D-15(b)(3) of the Act). The term "gross covered prescription

drug costs" is also defined in the Part D regulations at 42 C.F.R. § 423.308. In the initial memorandum, CMS indicated that it had proposed to update this regulatory definition of gross covered prescription drug costs to eliminate any potential ambiguity in the regulation text and help to ensure there is a consistent understanding of the term for purposes of both the Part D program and the IRA. Since the initial memorandum was issued, CMS has issued a final rule adopting the proposed revisions to 42 C.F.R. § 423.308 (see Contract Year 2024 Policy and Technical Changes to the Medicare Advantage and Medicare Prescription Drug Benefit Programs Final Rule (0938-AU96), 88 Fed. Reg. 22,120, 22,259 (Apr. 12, 2023)).[6] CMS has updated this revised guidance to reflect the issuance of the final rule.

Using PDE data combined with Part B claims data, inclusive of beneficiary cost sharing, to calculate combined Total Expenditures under Part D and Part B will allow CMS to implement the Low-Spend Medicare Drug Exclusion in a manner that aligns with the statute and regulatory policy. CMS will use Part B claims data that are inclusive of beneficiary cost sharing to determine Part B Total Expenditures to maintain consistency with the approach to determining "gross covered prescription drug costs" under Part D, which are defined in the statute and regulations as inclusive of Part D beneficiary cost sharing. CMS has clarified in section 30.1.2 of this revised guidance that, in accordance with section 1191(c)(5) of the Act, expenditures for a drug or biological product that are bundled or packaged into the payment for another service are excluded from the calculation of total allowed charges under Part B for purposes of determining Total Expenditures under Part B.

Comment: One commenter asked CMS to clarify that the 30-day additional period from June 1, 2023 to June 30, 2023 for Part D plan sponsors and Part B providers and suppliers to submit PDE and Part B claims data is a grace period.

Response: As described in section 30.1.2 of this revised guidance, the 30-day period from June 1, 2023 to June 30, 2023 provides time for data to be submitted. In identifying low-spend Medicare drugs for initial price applicability year 2026, CMS will only consider PDE data and Part B claims with dates of service that occur during the 12-month period beginning June 1, 2022, and ending May 31, 2023.

Plasma-Derived Product Exclusion from Qualifying Single Source Drugs (Section 30.1.3)

Comment: Some commenters asked CMS to provide further clarification on which products will be considered plasma-derived for the purpose of the Plasma-Derived Product Exclusion. A couple of commenters asserted that cellular or gene therapies should not be subject to the exclusion. A couple of commenters requested a more holistic approach to identifying plasma-derived products, such as through consultation with FDA and other interested parties.

Response: CMS continues to believe that referring to product information available on the FDA Approved Blood Products website[7] and the FDA Online Label Repository[8] is the best way to

[6] Accessible at: https://www.federalregister.gov/documents/2023/04/12/2023-07115/medicare-program-contract-year-2024-policy-and-technical-changes-to-the-medicare-advantage-program.
[7] See: https://www.fda.gov/vaccines-blood-biologics/blood-blood-products/approved-blood-products.
[8] See: https://labels.fda.gov/.

identify plasma-derived products for the purpose of implementing the Plasma-Derived Product Exclusion in a consistent manner. CMS agrees that there may be specific products where additional insights from FDA would be beneficial, and as noted in section 30.1.3, CMS will also consult with FDA as needed to implement this exclusion.

CMS confirms that cellular and gene therapies are not categorically ineligible for the Plasma-Derived Product Exclusion described in section 1192(e)(3)(C) of the Act, which applies the exclusion to biological products derived from human whole blood or plasma. As described by FDA, cellular therapy products include cellular immunotherapies, cancer vaccines, and other types of both autologous and allogeneic cells for certain therapeutic indications. As further described by FDA, human gene therapy seeks to modify or manipulate the expression of a gene or to alter the biological properties of living cells for therapeutic use.[9] Cellular and gene therapies will be assessed using the same standards as other biological products to determine whether they qualify for the Plasma-Derived Product Exclusion.

Identification of Negotiation-Eligible Drugs for Initial Price Applicability Year 2026 (Section 30.2)

Comment: One commenter asked CMS to clarify whether rebates will be incorporated into the calculations used to rank the 50 negotiation-eligible drugs.

Response: In identifying and ranking the negotiation-eligible drugs for initial price applicability year 2026, CMS will use Total Expenditures under Part D, which are defined at section 1191(c)(5) of the Act as "total gross covered prescription drug costs," as defined in section 1860D-15(b)(3). Section 1860D–15(b)(3) of the Act defines "gross covered prescription drug costs" in relevant part as "the costs incurred under the plan, not including administrative costs, but including costs directly related to the dispensing of covered part D drugs during the year and costs relating to the deductible." The term is also defined in the Part D regulations at 42 C.F.R. § 423.308. As discussed in the Contract Year 2024 Final Rule (see 88 Fed. Reg. 22,120, 22,259 (Apr. 12, 2023)), costs directly related to the dispensing of covered Part D drugs are most logically calculated as the accumulated total of the negotiated prices that are used for purposes of determining payment to the pharmacy or other dispensing entity for covered Part D drugs. Consistent with this policy, CMS will calculate Total Expenditures under Part D for purposes of the Negotiation Program using PDE data and will not consider any rebates or other price concessions not reflected in the negotiated price of the drug on the PDE to identify and rank negotiation-eligible drugs.

[9] See: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products.

Exception for Small Biotech Drugs (Section 30.2.1)[10, 11]

Comment: A couple of commenters requested that CMS create a dispute resolution process so that a manufacturer that disagrees with CMS' determination of its eligibility for the Small Biotech Exception can dispute this determination. One commenter requested that CMS allow small biotech companies to provide additional data after the deadline to support their application for the exception before CMS makes a final determination.

Response: CMS thanks these commenters for their recommendations. CMS requests all information necessary to determine eligibility for the Small Biotech Exception in the Small Biotech Exception ICR Form. Additionally, because of the ambitious statutory deadlines for the Negotiation Program for initial price applicability year 2026, CMS will not accept incomplete or late requests for the Small Biotech Exception for initial price applicability year 2026, including additional data submitted by companies to support their application after the deadline, but before CMS makes a final determination. CMS also declines to create a dispute resolution process for the Small Biotech Exception.

Comment: A couple of commenters requested further detail on the Small Biotech Exception for initial price applicability years 2027 and 2028. Commenters recommended that CMS introduce a streamlined application for manufacturers that had previously received the exception, wherein such manufacturers would only have to attest that they have not been acquired by another entity in order to receive the exception again. One commenter requested clarity on whether manufacturers only have one chance to apply for the Small Biotech Exception or if a manufacturer may submit each year.

Response: This revised guidance establishes the policies CMS will use to implement the Negotiation Program for initial price applicability year 2026. A determination by CMS that a given qualifying single source drug qualifies for the Small Biotech Exception for initial price applicability year 2026 does not mean that this drug will continue to qualify for the Small Biotech Exception for future initial price applicability years. CMS will share the submission process for the Small Biotech Exception for initial price applicability years 2027 and 2028 in future guidance and appreciates the feedback received from commenters.

Comment: One commenter asserted that, for the purpose of identifying drugs that qualify for the Small Biotech Exception for initial price applicability year 2026, CMS must consider whether

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[10] On January 24, 2023, CMS released the Small Biotech Exception ICR (CMS-10844 / OMB 0938-1443) to detail the specific data that CMS is requesting for purposes of implementing this exception. The comment period for the 60-day notice closed on March 27, 2023, and the comment period for the 30-day notice closed on May 24, 2023. Section 30.2.1 of this revised guidance reflects revisions that CMS made in response to feedback from interested parties on the Small Biotech ICR and section 30.2.1 of the initial memorandum. Here, CMS responds to comments on the discussion of the Small Biotech Exception in the initial memorandum that raised inquiries or recommendations not already addressed by revisions to the Small Biotech ICR. To view the Small Biotech ICR Form, a summary of changes made to the Small Biotech ICR in response to comments received during the 60-day and 30-day notice periods, as well as comments received on the Small Biotech ICR and CMS' responses to those comments, please see https://www.reginfo.gov/public/do/PRAViewICR?ref_nbr=202304-0938-016.

[11] On June 2, 2023, CMS released the Small Biotech Exception functionality in CMS HPMS. To request the Small Biotech Exception for a qualifying single source drug for initial price applicability year 2026, manufacturers must submit a Small Biotech Exception request via HPMS by 11:59 p.m. PDT on July 3, 2023.

Total Expenditures for a qualifying single source drug meet the expenditure requirements under either Part B or Part D. If the qualifying single source drug meets the requirements with respect to either Part B or Part D Total Expenditures, then that qualifying single source drug would qualify for the Small Biotech Exception.

Response: CMS appreciates this recommendation but, for initial price applicability year 2026, sections 1191(a) and 1192(d) of the Act require CMS to evaluate whether a qualifying single source drug meets the criteria to be considered a negotiation-eligible drug, including with respect to the Small Biotech Exception, based on Total Expenditures under Part D only.

Comment: One commenter requested that CMS make the Small Biotech Exception permanent rather than exclude small biotech drug products for only the first three years of the Negotiation Program.

Response: The Small Biotech Exception, as required by section 1192(d)(2)(A) of the Act, applies only with respect to initial price applicability years 2026, 2027, and 2028. CMS does not have the authority to make the Small Biotech Exception permanent.

Although the Small Biotech Exception is limited to initial price applicability years 2026, 2027, and 2028, CMS notes that the temporary floor for small biotech drugs described in section 1194(d) applies to qualifying single source drugs described in section 1192(d)(2) with respect to initial price applicability years 2029 and 2030.

Comment: One commenter requested that CMS clarify which 2021 Total Expenditure data it will use to determine eligibility for the Small Biotech Exception.

Response: As described in section 30.2.1 of this revised guidance, CMS will use PDE data for dates of service during the 12-month period beginning January 1, 2021 and ending December 31, 2021 to determine eligibility for the Small Biotech Exception.

Selection of Drugs for Negotiation for Initial Price Applicability Year 2026 (Section 30.3)

Comment: A few commenters requested greater transparency into the process of selecting drugs for negotiation. A couple of commenters requested that CMS notify the manufacturer of a drug that will be selected for negotiation at least 30 days in advance of the selected drug list publication date. One commenter asked that CMS publish the calculations used to determine the list of selected drugs and establish a process for manufacturers to identify concerns in advance of the selected drug publication date. A couple of commenters suggested that CMS establish a pathway for interested parties to provide input into which negotiation-eligible drugs are included on the selected drug list.

Response: For initial price applicability year 2026, the statute requires that CMS publish the selected drug list no later than September 1, 2023. CMS believes that disclosing to manufacturers whether their drug is a selected drug before this date is operationally infeasible due to the time constraints required to meet statutory deadlines and the complexity of the preparation that must be undertaken in advance of the publication of the selected drug list by September 1, 2023 for

initial price applicability year 2026. For example, sections 1191(d)(3)(B) and 1192(d)(1)(A) of the Act require that CMS identify negotiation-eligible drugs for initial price applicability year 2026 using Total Expenditure data during the period beginning on June 1, 2022, and ending on May 31, 2023. As discussed in section 30 of this revised guidance, Total Expenditures under Part D will be calculated using PDE data for dates of service between June 1, 2022 and May 31, 2023. To allow a reasonable time for Part D plan sponsors to submit PDE data, CMS will use PDE data for the dates of service during this 12-month period that have been submitted to CMS by June 30, 2023. The complexity of the data analyses and quality checks that must then be performed on the data prior to September 1, 2023 forecloses the possibility of disclosing to manufacturers whether their drug is a selected drug prior to the statutory selected drug list publication date for initial price applicability year 2026.

Although CMS appreciates the request for a pathway for interested parties to provide input into the selected drug list for initial price applicability year 2026, section 1192(b)(1)(B) of the Act requires that CMS select the highest ranked drugs from the list of negotiation-eligible drugs using Total Expenditures under Part D. CMS is committed to engaging with interested parties throughout the implementation of the Negotiation Program. As detailed earlier in this guidance, CMS solicited input from interested parties throughout the development of the initial memorandum and this revised guidance. Further, CMS refers readers to sections 50.2 and 60.3.3 of this revised guidance, which detail CMS' approach to adjusting the starting point for the initial offer using evidence submitted by the public on therapeutic alternatives to the selected drug, in accordance with section 1194(e)(2) of the Act. CMS also refers readers to section 60.4 of this guidance, which describes how, in response to comments from interested parties, CMS is providing for additional engagement opportunities for interested parties—specifically, meetings with manufacturers and patient-focused listening sessions—after the October 2, 2023 deadline for submission of section 1194(e) data.

Delay in the Selection and Negotiation of Certain Biologics with High Likelihood of Biosimilar Market Entry) (Section 30.3.1)

Comment: One commenter expressed support for a stringent process for assuring that a Biosimilar Manufacturer and Reference Manufacturer cannot have entered into agreements that require or induce the Biosimilar Manufacturer to limit market share, as well as the process for assuring that there is a high likelihood that the Biosimilar will be marketed before September 1, 2025. The commenter urged CMS to apply similar levels of scrutiny to all areas of implementation where proof of competition is required, including the definition of a qualifying single source drug.

Response: CMS appreciates this commenter's perspective. Section 1192(f)(2)(D)(iv) of the Act excludes certain Biosimilar Manufacturers from the Biosimilar Delay if CMS determines that the Biosimilar Manufacturer is the same as the Reference Manufacturer, or that the Biosimilar Manufacturer has entered into any agreement with the Reference Manufacturer that requires or incentivizes the Biosimilar Manufacturer to submit an Initial Delay Request, or that restricts the quantity (either directly or indirectly) of the Biosimilar that may be sold in the United States over a specified period of time. As described in section 90.4 of this revised guidance, CMS plans to monitor whether the manufacturer of a generic or biosimilar competitor of a potential qualifying

single source drug or selected drug is engaging in bona fide marketing when identifying qualifying single source drugs and selected drugs.

Comment: One commenter expressed concern that a Reference Manufacturer will not have transparency into whether a Reference Drug will be a selected drug because the Reference Manufacturer will not know whether a Biosimilar Manufacturer has submitted an Initial Delay Request to delay the inclusion of that Reference Manufacturer's Reference Drug on the selected drug list. The commenter recommended that CMS publish a list of Biosimilar Manufacturers submitting an Initial Delay Request and make CMS' determinations known publicly.

Response: CMS thanks this commenter for raising this issue. The submission of an Initial Delay Request does not guarantee that a Reference Drug would be a selected drug absent the Initial Delay Request, nor does it guarantee that the Initial Delay Request will be granted even if the Reference Drug would be a selected drug absent the Biosimilar Delay. CMS, therefore, will not publish a list of Biosimilar Manufacturers submitting an Initial Delay Request or CMS' determinations. However, as described in section 30.3.1.4 of this revised guidance, CMS will notify each Biosimilar Manufacturer that submits an Initial Delay Request of CMS' determination regarding such request on or after September 1, 2023, but not later than September 30, 2023. CMS will also notify each Reference Manufacturer named in a successful Initial Delay Request and will identify the Reference Drug that would have been a selected drug, absent the successful Initial Delay Request. In recognition that the public has an interest in understanding the impact of the Biosimilar Delay, CMS is clarifying in this revised guidance that it will publish the number of Reference Drugs that would have been selected drugs for initial price applicability year 2026, absent successful Initial Delay Requests, as part of publishing the selected drug list by September 1, 2023.

Comment: Some commenters asserted that the information required from a Biosimilar Manufacturer to demonstrate a high likelihood that the Biosimilar will be licensed and marketed before September 1, 2025 is too narrow. A couple of commenters contended that section 1192(f)(1)(B)(ii)(I)(aa) of the Act directs CMS to consider all documents that a Biosimilar Manufacturer believes support a high likelihood determination. One commenter stated that the Act does not specify that the scenarios described in sections 1192(f)(3)(A) and (B) are the only scenarios under which a high likelihood determination can be made. The commenter noted that other documentation should therefore suffice to demonstrate a high likelihood that the Biosimilar will be licensed and marketed before September 1, 2025.

Response: CMS thanks these commenters for their feedback related to the high likelihood determination. Section 30.3.1.2 of this revised guidance aligns with the statutory language, which requires CMS to identify whether a Biosimilar has a high likelihood of being licensed and marketed within two years after the publication of the selected drug list. CMS believes the information detailed in section 30.3.1.2 will allow CMS to implement the high likelihood provision of the Biosimilar Delay in a manner that benefits the Medicare program by minimizing the likelihood of CMS approving a delay request for a Biosimilar that is not highly likely to become licensed and marketed within two years after the publication of the selected drug list. Further, CMS believes this approach will support robust biosimilar competition.

Comment: One commenter stated that the metrics proposed to assess the operational readiness of a Biosimilar Manufacturer are generally sensible, but filings with the Securities and Exchange Commission (SEC) on future revenues are often subject to significant caveats about uncertainty and changing market conditions. The commenter recommended that CMS consider a more concrete indicator of operational readiness but did not provide any examples.

Response: CMS believes that section 30.3.1.2 of the guidance aligns with the statutory language and that SEC filings, despite any potential uncertainties, represent a meaningful source of information about a manufacturer's plans to manufacture and market a drug. CMS also notes that, in determining whether a Biosimilar Manufacturer will be operationally ready to market the Biosimilar before September 1, 2025, CMS will also consider supporting documentation provided to CMS as part of the Initial Delay Request, such as the copy of the manufacturing schedule submitted to FDA, which as CMS has clarified in section 30.3.1.2 of this revised guidance, must be consistent with public-facing statements and demonstrative of readiness to meet revenue expectations. Further, operational readiness is only one component of the high likelihood determination. To meet the high likelihood threshold, the Initial Delay Request must also demonstrate that an application for licensure under section 351(k) of the Public Health Service Act ("PHS Act") for the Biosimilar has been accepted for review or approved by FDA, and that patents related to the Reference Drug are unlikely to prevent the Biosimilar from being marketed before September 1, 2025.

Comment: One commenter explained that, upon review of a BLA, FDA may issue a Complete Response letter identifying the deficiencies that preclude approval. The applicant will generally work to address the deficiencies and resubmit the section 351(k) BLA, and FDA will generally act on a resubmitted section 351(k) BLA within six months of receipt. The commenter recommended that CMS make clear that a section 351(k) BLA in Complete Response status remains eligible for the Special Rule Delay.

Response: CMS thanks this commenter for the recommended clarification. CMS has clarified in section 30.3.1.2 of the guidance that CMS will consider a section 351(k) application for licensure that has been accepted for review and has received a Complete Response letter to meet the section 1192(f)(3)(A) requirement that a section 351(k) BLA for the biosimilar biological product has been accepted for review by FDA.

Comment: One commenter recommended that CMS collaborate with FDA to identify key milestones that would indicate a high likelihood that a Biosimilar will be licensed and marketed before September 1, 2025.

Response: Both the initial memorandum and revised guidance incorporate technical assistance from FDA along with other federal agencies. To demonstrate there is a high likelihood that a Biosimilar will be licensed and marketed before September 1, 2025, an Initial Delay Request must demonstrate that the Biosimilar meets the high likelihood threshold described in section 30.3.1.2 of the revised guidance. This threshold requires that, for Initial Delay Requests submitted with respect to initial price applicability year 2026, the Biosimilar's application for licensure must be approved or accepted for review by FDA no later than August 15, 2023, and that the Initial Delay Request demonstrate clear and convincing evidence that the Biosimilar will

be marketed before September 1, 2025. The clear and convincing evidence criteria will be satisfied if the Initial Delay Request demonstrates both (1) that patents related to the Reference Drug are unlikely to prevent the Biosimilar from being marketed and (2) that the Biosimilar Manufacturer will be operationally ready to market the Biosimilar. CMS will continue to consult with FDA as needed on its policies for implementing the Biosimilar Delay.

Comment: One commenter stated that the purpose of the manufacturing schedule submitted to FDA during FDA's review of a section 351(k) BLA – and to CMS under section 1192(f)(1)(B)(ii)(III)(aa) of the Act – is to facilitate an FDA inspection of the establishment that is manufacturing the biological product to confirm the establishment is in operation and manufacturing the proposed product. This manufacturing schedule, therefore, does not reflect any post-approval manufacturing dates. The commenter advised CMS to omit the reference to "consistent with the public-facing statements and any revenue expectations" in the revised guidance.

Response: CMS thanks this commenter for offering their perspective on the uses of the manufacturing schedule submitted to FDA during FDA's review of a section 351(k) BLA. CMS has included a clarification in section 30.3.1.2 of this revised guidance that the manufacturing schedule must be consistent with the manufacturer's public-facing statements and demonstrate readiness to meet revenue expectations, in recognition that the schedule does not reflect post-approval manufacturing dates.

Comment: A few commenters remarked that ongoing patent litigation may be irrelevant to a Biosimilar launch. A Biosimilar Manufacturer can carve out indications with active patents from the Biosimilar's labeling, or a Biosimilar can launch at risk. The commenters asserted that active litigation should, therefore, not prevent manufacturers from meeting the high likelihood threshold.

Response: CMS has clarified that an Initial Delay Request for initial price applicability year 2026 only has to meet one of the following criteria to satisfy the patent-related component of the high likelihood determination: (1) there are no unexpired patents relating to the reference product included in the Reference Drug that are applicable to the Biosimilar; (2) one or more court decisions establish the invalidity, unenforceability, or non-infringement of any potentially applicable unexpired patent relating to the reference product included in the Reference Drug that the patent holder asserted was applicable to the Biosimilar; or (3) the Biosimilar Manufacturer has a signed legal agreement with the Reference Manufacturer that permits the Biosimilar Manufacturer to market the Biosimilar before September 1, 2025, without imposing improper constraints on the Biosimilar Manufacturer. For example, if a Biosimilar Manufacturer has carved out a patent-protected indication or method of use from the Biosimilar's labeling, then such patents would not be considered to be "applicable to the Biosimilar." CMS reiterates that the above criteria reflect how CMS will determine if the Initial Delay Request clearly demonstrates that patents related to the Reference Drug are unlikely to prevent the Biosimilar from being marketed before September 1, 2025.

Comment: A few commenters requested that CMS clarify the specific circumstances under which CMS will find that an agreement between a Biosimilar Manufacturer and a Reference

Manufacturer would disqualify a Biosimilar Manufacturer from making an Initial Delay Request. The commenters noted that a signed legal agreement between the Reference Manufacturer and the Biosimilar Manufacturer permitting the Biosimilar Manufacturer to market the Biosimilar may serve as evidence that patents related to the Reference Drug are unlikely to prevent the Biosimilar from being marketed. At the same time, however, for a Biosimilar Manufacturer to meet the requirements for CMS to grant an Initial Delay Request, the Biosimilar Manufacturer and the Reference Manufacturer must not have entered into an agreement that requires or incentivizes the Biosimilar Manufacturer to submit an Initial Delay Request, or that directly or indirectly restricts the quantity of the Biosimilar that may be sold in the United States over a specified period of time.

Response: CMS does not believe that the two agreement types that the commenters raise conflict since it is possible to have an agreement that permits commercialization without either directly or indirectly restricting volume or incentivizing the Biosimilar Manufacturer to submit an Initial Delay Request. CMS reiterates that, consistent with section 1192(f)(2)(D)(iv)(II) of the Act, the Biosimilar Manufacturer and the Reference Manufacturer must not have entered into an agreement that either requires or incentivizes the Biosimilar Manufacturer to submit an Initial Delay Request, or that directly or indirectly restricts the quantity of the Biosimilar that may be sold in the United States over a specified period of time.

Comment: A few commenters expressed concern that the timeline for submitting Initial Delay Requests is unreasonably accelerated and will jeopardize the accuracy of the requests and create a barrier to biosimilar competition, as the timeline effectively eliminates the additional runway for a Biosimilar competitor to come to market between the deadline on May 22, 2023 for a Biosimilar Manufacturer to submit the documentation for its Initial Delay Request and the selected drug list publication date on September 1, 2023. A few commenters also expressed concern that CMS will not permit the Biosimilar Manufacturer to supplement its Initial Delay Request, except if CMS requests follow-up information or if the Biosimilar Manufacturer would like to update CMS on the status of the Biosimilar application for licensure before 11:59pm PT on August 15, 2023. Commenters requested that CMS set the Initial Delay Request submission deadline as close as reasonably possible to the selected drug list publication date and permit broad supplementation of a timely request with late-breaking information.

Response: CMS thanks these commenters for their feedback and reiterates that the statute is clear that an Initial Delay Request submitted with respect to initial price applicability year 2026 must demonstrate that there is a high likelihood that the Biosimilar will be licensed and marketed before September 1, 2025. The Initial Delay Request timeline therefore does not preclude a Biosimilar from coming to market between the deadline on May 22, 2023 for a Biosimilar Manufacturer to submit the documentation for its Initial Delay Request and the selected drug list publication date on September 1, 2023 (though CMS notes that if the Biosimilar launches between May 22, 2023 and September 1, 2023, then CMS may determine the Reference Drug is not a qualifying single source drug based on the process described in section 30.1 of this revised guidance). Further, the Initial Delay Request deadline has already been set as close to the selected drug publication date as is administratively feasible. CMS adopted this timeline under the authority granted to it in section 1192(f)(1)(B)(ii) of the Act to set the time, form, and manner of Biosimilar Delay requests, and has exercised this authority to establish a timeline

(which is described in section 30.3.1.4 of the revised guidance) that allows CMS to carefully review the Initial Delay Request documentation and, if applicable, to request follow-up information from the Biosimilar Manufacturer on its Initial Delay Request. The timeline ensures that CMS will have adequate time to review follow-up data and make a well-informed determination. Regarding commenters' requests that CMS permit broad supplementation of a timely request, CMS believes that the timeline described in section 30.3.1.4 allows Biosimilar Manufacturers sufficient opportunity to provide CMS with information during the Initial Delay Request process. CMS is not able to accommodate broad supplementation of an Initial Delay Request given the ambitious statutory deadlines for implementing the Negotiation Program for initial price applicability year 2026. CMS will consider adjusting the Initial Delay Request timeline for initial price applicability year 2027 in future guidance, if feasible.

Comment: A few commenters requested that CMS create a way for a Biosimilar Manufacturer to ascertain, before the Initial Delay Request deadline, whether a Reference Drug is likely to be selected for negotiation. One commenter recommended that CMS enable a Biosimilar Manufacturer to inquire with CMS in advance of the Initial Delay Request deadline. A couple of commenters requested that CMS update the Part D Drug Spending Dashboard more frequently or direct manufacturers to other sources of publicly available information to inform assessments of the likelihood that a Reference Drug will be selected for negotiation.

Response: CMS thanks these commenters for their feedback. CMS must complete all steps of the drug selection process with fidelity, including the identification of negotiation-eligible drugs using PDE data with dates of service during the 12-month period beginning June 1, 2022, and ending May 31, 2023. As described in section 30.2 of this revised guidance, to allow a reasonable amount of time for Part D plan sponsors to submit PDE data, CMS will use PDE data for the dates of service during this 12-month period that Part D plans have submitted to CMS no later than 30 days after May 31, 2023, i.e., by June 30, 2023. Further, to ensure that a potential qualifying single source drug does not have generic or biosimilar competition, CMS will review PDE data for the 12-month period beginning August 16, 2022 and ending August 15, 2023, using PDE data available on August 16, 2023, as well as AMP data for the 12-month period beginning August 1, 2022 and ending July 31, 2023, using the AMP data available on August 16, 2023 for a given generic drug or biosimilar biological product for which a potential qualifying single source drug is the listed drug or reference product. CMS is, therefore, unable to disclose information regarding the selected drug list in advance of the selected drug publication date due to the ambitious statutory deadline for identifying selected drugs and publishing the selected drug list.

CMS appreciates feedback received on the Part D Drug Spending Dashboard. This dashboard allows for a longer claims runout to provide time for claims to be submitted, processed, and finalized than is possible for the data that CMS is statutorily required to use to identify and rank negotiation-eligible drugs. CMS recently announced that it plans to continue its annual updates to the Drug Spending Dashboards to provide the public with comprehensive data on trends related to drug spending for Medicare and Medicaid.[12]

[12] See: https://www.cms.gov/blog/cms-drug-spending-dashboards-and-inflation-reduction-act.

Comment: A couple of commenters asked that CMS notify each Biosimilar Manufacturer that submits an Initial Delay Request of the results of such request in advance of the selected drug publication date. These commenters requested that CMS establish a mechanism by which manufacturers can dispute CMS' determination.

Response: Ambitious statutory deadlines prevent CMS from providing each Biosimilar Manufacturer that submits an Initial Delay Request for initial price applicability year 2026 with advance notice of CMS' determination regarding its request prior to the selected drug list publication date. However, CMS will notify each Biosimilar Manufacturer of CMS' determination on or after September 1, 2023, but not later than September 30, 2023. CMS does not intend to establish a dispute resolution process for Initial Delay Requests.

Comment: One commenter was uncertain whether Appendix B of the initial memorandum includes conflicting information on whether CMS will accept Initial Delay Requests that are incomplete or not timely.

Response: CMS appreciates this request for clarity and confirms that CMS will not accept Initial Delay Requests that are incomplete or not timely. CMS directs readers to section 30.3.1.4 of this revised guidance, which includes a table providing a summary of key dates related to implementation of the Biosimilar Delay for initial price applicability year 2026 as specified in section 30.3.1 of this revised guidance. The deadline for a Biosimilar Manufacturer to email CMS regarding its intent to submit an Initial Delay Request for initial price applicability year 2026 was 11:59 p.m. PT on May 10, 2023.

Comment: One commenter inquired about Question 10 of Appendix B: Template for the Initial Delay Request Form. The commenter remarked that a Biosimilar may qualify for an Initial Delay Request if its section 351(k) BLA is accepted for filing by August 15, 2023. Given FDA's 60-day filing review, the section 351(k) BLA must be submitted no later than June 16, 2023. A Biosimilar Manufacturer that has not yet submitted its section 351(k) BLA by May 22, 2023, but intends to do so by June 16, 2023, must select option (D) on the form detailed in Appendix B of the initial memorandum. The commenter requested that, to guard against any inadvertent disqualification of such Initial Delay Requests, CMS should make clear that selecting this option does not preclude eligibility for the Initial Delay Request.

Response: Selecting option (D) on the form detailed in Appendix B of this guidance does not preclude eligibility for the Initial Delay Request. Biosimilar Manufacturers have until 11:59 p.m. PT on August 15, 2023, to update CMS on the status of the Biosimilar's application for licensure.

Comment: A couple of commenters urged CMS to favor policies that support a robust biosimilars market that drives down prices for patients but did not reference any specific policies. These commenters stated that CMS should consider how to mitigate potential unintended consequences that may disincentivize the development of biosimilars and hinder a robust biosimilars market.

Response: CMS firmly supports a robust biosimilars market and believes that the policies for implementing the special rule to delay selection and negotiation of biologics for biosimilar

market entry will help support biosimilar entry and price competition in the biosimilars market. CMS welcomes input on specific approaches to monitor for potential unintended consequences of these policies and may consider modifications if necessary to mitigate any unintended impact.

Medicare Drug Price Negotiation Program Agreement (Sections 40, 40.1, and 40.6)

Comment: One commenter commented that the statute defines manufacturer by reference to section 1847A(c)(6)(A) of the Act and requested that CMS clarify the definition of Primary Manufacturer as it pertains to the very broad statutory definition.

Response: CMS thanks this commenter for the recommendation. Section 1193(a)(1) of the Act instructs CMS to negotiate with "the manufacturer" to arrive at the MFP for a given selected drug, and the phrase "the manufacturer" appears repeatedly throughout the statutory provisions establishing the Negotiation Program. The best statutory interpretation is to interpret the term "manufacturer" as a single entity for the negotiation process, responsible for negotiating the maximum fair price for a given selected drug. As described in section 40 of this revised guidance and pursuant to section 1191(c)(1) of the Act, to the extent that more than one entity meets the statutory definition of manufacturer for a selected drug for purposes of initial price applicability year 2026, CMS will designate the entity that holds the NDA(s) / BLA(s) for the selected drug to be "the manufacturer" (referred to in this revised guidance as the Primary Manufacturer) of the selected drug.

Comment: Some commenters requested that CMS remove requirements related to Secondary Manufacturers because they view such requirements as inconsistent with CMS' past interpretation of the definition of "manufacturer" in Section 1927(k)(5) of the Act.

Response: CMS appreciates commenters' feedback. In previous interpretations of other provisions of the Act, CMS has expressed concern with burdening manufacturers with no relationship to the holder of an NDA / BLA. In this revised guidance, CMS reiterates its position to exclusively limit any requirements with respect to the terms of the Agreement to manufacturers listed on the NDA / BLA, or manufacturers that market the selected drug pursuant to an agreement with the Primary Manufacturer. Any requirements placed on the Primary Manufacturer by the Negotiation Program to address Secondary Manufacturer actions are solely related to its voluntarily assumed relationship.

CMS also notes that, under the Negotiation Program, Primary Manufacturers enter into an agreement to negotiate an MFP with CMS and to provide access to that MFP for the selected drug, including sales of the selected drug by Secondary Manufacturers. Harm to competition from Primary Manufacturers ensuring MFP availability in sales by Secondary Manufacturers is unlikely because the requirement to provide access to the MFP is mandated by the Negotiation Program and not imposed by the Primary Manufacturer, and because accepting that approach is a requirement of the Negotiation Program. Moreover, the Negotiation Program offers operational flexibility to manufacturers and would not restrict the Primary Manufacturer or Secondary Manufacturer(s) from offering the selected drug at a price lower than the MFP. For these reasons, applying the MFP to sales by Secondary Manufacturers is unlikely to create a situation inconsistent with the antitrust laws.

Comment: In connection with their feedback on the Secondary Manufacturer policies, a few commenters cited the provisions of a 2007 Medicaid Drug Rebate Program (MDRP) rule relating to the treatment of authorized generic drugs. A few commenters also cited a provision from a 2016 MDRP rule relating to the treatment of line extensions.

Response: CMS thanks these commenters for their input. This revised guidance echoes the relationship between manufacturers in the 2007 and 2016 MDRP rules. This revised guidance defines a Secondary Manufacturer as either listed as a manufacturer in the NDA or BLA or marketing the selected drug pursuant to an agreement with the Primary Manufacturer. As it relates to the comments regarding the 2016 MDRP rule, in which the primary concern expressed by commenters involves unrelated manufacturers, CMS notes that the initial memorandum focuses on Secondary Manufacturers with agreements with the Primary Manufacturer thereby limiting the applicability of those concerns. More generally, the 2007 and 2016 MDRP rules suggest that CMS has previously interpreted the statutory definition of "manufacturer" at section 1927(k)(5) of the Act to apply to situations involving multiple manufacturers in a manner that is consistent with the IRA initial memorandum policy of imposing obligations on a Primary Manufacturer with regard to Secondary Manufacturers. Where differences remain under which the Negotiation Program imposes more substantial obligations on the Primary Manufacturer for commercial practices and data of Secondary Manufacturers, these differences are supported by the text, scope, and purpose of the IRA.

Comment: One commenter questioned whether CMS' definition of Secondary Manufacturer could include firms that do not meet the statutory definition of manufacturer with respect to the selected drug but have a marketing agreement in place with the Primary Manufacturer.

Response: CMS thanks this commenter for their input. As described in section 40 of this revised guidance, for initial price applicability year 2026, CMS will refer to any entity other than the Primary Manufacturer that meets the statutory definition of manufacturer, under section 1191(c)(1) of the Act, for a drug product included in the selected drug, and that either (1) is listed as a manufacturer in an NDA or BLA for the selected drug or (2) markets the selected drug pursuant to an agreement with the Primary Manufacturer, as a Secondary Manufacturer. Secondary Manufacturers will include any manufacturer of any authorized generics and any repackager or relabeler of the selected drug that meets these criteria, including those entities that have a marketing agreement with the Primary Manufacturer. A firm that does not meet the statutory definition of a manufacturer under section 1191(c)(1) of the Act does not meet CMS' definition of a Secondary Manufacturer.

Comment: Several commenters requested that CMS provide a comment period for the Medicare Drug Price Negotiation Program Agreement (herein referred to as the "Agreement") to allow manufacturers and the public the opportunity to review and comment on the Agreement. A few commenters expressed concern that lack of advance notice could result in a manufacturer's inability to establish appropriate processes prior to the Agreement's effective date, resulting in possible noncompliance. A couple of commenters also stated that there are only three options for manufacturers within the Negotiation Program under the IRA: sign the Agreement, pay the excise tax, or leave Medicare and Medicaid. Manufacturers expressed concern with the lack of options available to a manufacturer that chooses not to sign the Agreement.

Response: In section 40 of the initial memorandum, CMS included descriptions of and solicited comments on the Agreement requirements to provide interested parties an opportunity to comment on these requirements. Given the thoughtful and extensive comments CMS received on these requirements, CMS determined to set forth the parameters of the manufacturer's obligations under the Negotiation Program in this revised guidance, while reserving for the Agreement certain general provisions and term and termination provisions. The decision to not separately repeat the program requirements in the Agreement means that the program requirements applicable to a manufacturer of a selected drug that enters into an Agreement for initial price applicability year 2026 are preserved and presented in this revised guidance for which there has been public notice and comment. In light of the complexity of the actions the agency must undertake in advance of the Agreement being signed by the statutory deadline of October 1, 2023, CMS will not provide a comment period on the Agreement. However, CMS will make reasonable efforts to make the final text of the Agreement available to the public before the selected drug list is published for initial price applicability year 2026. Please see the responses to comments below for a discussion of the options available to manufacturers who choose not to participate in the Negotiation Program.

Comment: One commenter asked that CMS provide manufacturers with information on how CMS plans to monitor compliance with the Agreement and allow for manufacturers to provide feedback on this information.

Response: The initial memorandum and subsequent revised guidance provide information on how CMS plans to monitor compliance with the Agreement, including the requirements within this revised guidance. As described in section 90.1 of this revised guidance, CMS will provide information about the negotiation process to the Primary Manufacturer of each selected drug. CMS anticipates this information will include operational and statutory timelines, procedural requirements, system instructions, IRA resources, and contact information. During the negotiation period, CMS plans to track and monitor progress during all steps of the process and engage in direct communications with each Primary Manufacturer, including as it relates to compliance. CMS is committed to supporting compliance with program requirements and will provide written reminders and warnings of potential noncompliance (described in section 90.1 of this revised guidance). Following the conclusion of negotiations, CMS plans to monitor compliance related to the Primary Manufacturer's obligations to provide access to the MFP, as described in section 40.4 and section 90.2 of this revised guidance.

As described in section 40.5 of this revised guidance, in monitoring compliance, CMS may engage in auditing processes to verify the accuracy and completeness of any information provided by the Primary Manufacturer, as well as any data related to the Primary Manufacturer providing access to the MFP, including where the selected drug is provided by any Secondary Manufacturer(s).

Comment: A few commenters stated that CMS should not require Primary Manufacturers to submit points of contact for the Agreement within five calendar days of publishing selected drugs, as this process is not included in statute. Commenters noted that CMS should state its

authority in developing this timeline and clarify implications of noncompliance with this timeline.

Response: CMS thanks these commenters for their feedback. CMS revised its policy in section 40.1 of this revised guidance regarding providing points of contact. CMS recommends but does not require this action be taken within five days following publication by CMS on September 1, 2023 of the list of selected drugs and prior to the Agreement being signed to facilitate communication between CMS and the Primary Manufacturer and support efficient effectuation of the Agreement. Primary Manufacturers must provide points of contact by October 1, 2023 at the time that the Agreement is signed.

Comment: A few commenters suggested that CMS consider different ways to designate a Primary Manufacturer other than the holder of the NDA / BLA, given scenarios like split licensures and acquisitions. Commenters recommended CMS consider using the FDA product labeler ID to determine the manufacturer for purposes of negotiating the MFP.

Response: When an application to market a new drug or biological product for human use is submitted to the FDA, the NDA / BLA that is submitted lists only one sponsor. The policy for identifying the Primary Manufacturer with responsibility for the selected drug based on the holder of the NDA / BLA for the selected drug under the Negotiation Program is consistent with the FDA regulatory framework under which the single sponsor of the NDA / BLA in its application describes the manufacturing process and lists the facilities that will produce the sponsor's product. In section 1191(c)(1) of the Act, the statute adopts the definition of "manufacturer" established in section 1847A(c)(6)(A) of the Act. CMS understands that the holder of an NDA or BLA can enter into agreements regarding the sale of drugs approved under a particular NDA or BLA with other entities that may also meet this statutory definition of "manufacturer." CMS must find a mechanism to identify the appropriate manufacturer for purposes of negotiation and ensure other aspects of the Negotiation Program apply to the selected drug. In addition, section 1193(a)(1) of the Act instructs CMS to negotiate with "the manufacturer" to arrive at the MFP for a given selected drug and the term "the manufacturer" appears repeatedly throughout the statutory provisions establishing the Negotiation Program. The best statutory interpretation is to interpret the term "manufacturer" as a single entity for the negotiation process, responsible for negotiating the maximum fair price for a given selected drug. Thus, the most effective way to determine the "manufacturer" described in section 40 of this revised guidance, and the signatory of the Agreement, is to identify the NDA / BLA holder as the Primary Manufacturer.

Comment: Many commenters made recommendations pertaining to the Agreement and how it applies to Secondary Manufacturers. Commenters recommended CMS require all Secondary Manufacturers to sign the same Agreement that applies between Primary Manufacturers and CMS. A few commenters suggested that Secondary Manufacturers sign a unique Agreement with CMS in addition to the Agreement between Primary Manufacturers and CMS. A few commenters were supportive of CMS' policy to enter into an Agreement with only the Primary Manufacturer.

Response: Given that section 1193(a)(1) of the Act instructs CMS to negotiate with "the manufacturer" to arrive at the MFP for a given selected drug to which "the manufacturer" would provide access in accordance with the statute, and given that the term "the manufacturer" appears repeatedly throughout the statutory provisions establishing the Negotiation Program, the best statutory interpretation is to interpret the term "manufacturer" as a single entity for the negotiation process, responsible for negotiating a single maximum fair price for a given selected drug. Thus, in accordance with section 1193(a)(1) of the Act and other statutory references to "the manufacturer," CMS will enter into an Agreement with "the manufacturer" of a selected drug, where "the manufacturer" is the NDA / BLA holder as described in section 40 of this revised guidance. CMS has adopted the designations of "Primary Manufacturer" and "Secondary Manufacturer," respectively, to establish a process to negotiate the maximum fair price with "the manufacturer" to align with the meaning of the statutory language and establish responsibilities and requirements of the Primary Manufacturer related to data collection and submission and MFP availability for the selected drug sold by the Secondary Manufacturer(s).

Comment: One commenter asked CMS to clarify whether a Primary Manufacturer is only responsible for data submission and MFP availability for sales of the selected drug by a Secondary Manufacturer when there is a contractual agreement between the two parties.

Response: CMS thanks this commenter for their question. For initial price applicability year 2026, a Primary Manufacturer will be responsible for data submission and MFP availability for sales of the selected drug by a separate manufacturer of the selected drug if that separate manufacturer is a Secondary Manufacturer as described in section 40 of this revised guidance. An entity is a Secondary Manufacturer if it meets the statutory definition of a manufacturer for the selected drug and either (1) is listed as a manufacturer in an NDA or BLA for the selected drug or (2) markets the selected drug pursuant to an agreement with the Primary Manufacturer. Specifically, any manufacturer that qualifies as a Secondary Manufacturer for initial price applicability year 2026 will have an existing relationship with a Primary Manufacturer. A Secondary Manufacturer will include any manufacturer of any authorized generics and any repackager or relabeler of the selected drug.

Comment: A few commenters stated that CMS should allow each Secondary Manufacturer to participate in all negotiation activities, including negotiation meetings, and have access to all written correspondence between the Primary Manufacturer and CMS. If CMS chooses not to allow this, the Primary Manufacturer should be allowed to share any and all documentation with the Secondary Manufacturer.

Response: The best statutory interpretation is to interpret the term "the manufacturer" as a single entity for the negotiation process responsible for negotiating a single maximum fair price for a given selected drug. In addition, section 1193(a)(1) of the Act instructs CMS to negotiate with "the manufacturer" to arrive at the MFP for a given selected drug, and the phrase "the manufacturer" appears repeatedly throughout the statutory provisions establishing the Negotiation Program. Congress's use of the singular definite article demonstrates that, for any one selected drug, the "manufacturer" with which CMS negotiates is a single entity. Thus, CMS believes that the most effective way to determine the "manufacturer" described in section 40 of the guidance and the signatory of the Agreement, is to identify the NDA / BLA holder as the

Primary Manufacturer. CMS has adopted the designations of "Primary Manufacturer" and "Secondary Manufacturer," respectively, to establish a process to negotiate an MFP with a single manufacturer to align with the meaning of the statutory language "the manufacturer," and establish responsibilities and requirements of the Primary Manufacturer related to data collection and submission and ensuring MFP availability for selected drug sold by the Secondary Manufacturer(s).

As described in section 40.2.2 and 60.6.1 of this revised guidance, CMS does not intend to publicly discuss the negotiation process prior to the public explanation of the MFP being released, unless a Primary Manufacturer discloses information that is made public. If a Primary Manufacturer discloses information that is made public regarding any aspect of the negotiation process prior to the explanation of the MFP being released by CMS, CMS reserves the right to publicly discuss the specifics of the negotiation process regarding that Primary Manufacturer. Primary Manufacturers engaged in negotiating an MFP with CMS are reminded that statements to or discussions with other Primary Manufacturers also engaged in the MFP negotiation process with CMS could negatively impact the competitive process for each independent MFP negotiation. Primary Manufacturers should consider the antitrust implications of any such actions. CMS will protect the confidentiality of any proprietary information from Primary Manufacturers or Secondary Manufacturers (described in section 40.2.1) as required under section 1193(c) of the Act and other applicable law. If a Primary Manufacturer chooses to disclose any material that is made public that CMS has previously deemed to be proprietary information of that Primary Manufacturer, CMS will no longer consider that material proprietary consistent with section 40.2.1 of this revised guidance. Neither the IRA nor this revised guidance prevents Primary Manufacturers from disclosing any information to Secondary Manufacturers.

Comment: One commenter stated that CMS should revise the National Drug Rebate Agreement and the Coverage Gap Discount Program Agreement, and work with the Health Resources and Services Administration (HRSA) to revise the Pharmaceutical Pricing Agreement, to permit immediate termination from all applicable federal programs in the event that an agreement on an MFP cannot be reached or a manufacturer is dissatisfied with the MFP.

Response: CMS thanks this commenter for their recommendation. CMS has clarified in section 40.6 of the revised guidance that a Primary Manufacturer that decides not to participate in the Negotiation Program may voluntarily terminate the Medicare Drug Price Negotiation Program Agreement if it also ceases participation in the Medicaid Drug Rebate Program, the Medicare Coverage Gap Discount Program, and the Manufacturer Discount Program through the end of the price applicability period for the selected drug. CMS has also clarified in section 40.1 of the revised guidance that a Primary Manufacturer that elects not to participate in the Medicare Drug Price Negotiation Program may take similar measures to cease its participation in the Medicaid Drug Rebate Program, the Medicare Coverage Gap Discount Program, and the Manufacturer Discount Program. Sections 40.1 and 40.6, as revised, set forth the procedures for the Primary Manufacturer to initiate termination processes under the Medicare and Medicaid programs and the steps CMS will take to facilitate an expeditious termination of the Primary Manufacturer's agreements under the Medicare Coverage Gap Discount Program and the Manufacturer Discount Program, as applicable. As a result of these procedures, any manufacturer that declines to enter an Agreement for the Negotiation Program may avoid incurring excise tax liability by submitting

the notice and termination requests described herein 30 days in advance of the date that excise tax liability otherwise may begin to accrue. Moreover, any manufacturer that has entered into an Agreement will retain the ability to promptly withdraw from the program prior to the imposition of civil monetary penalties or excise tax liability.

Manufacturer Data Submission, Proprietary Information, and Confidentiality (Section 40.2)

Comment: Several commenters requested that CMS not publish any proprietary information in the MFP public explanation and continue to provide strong protections to proprietary data otherwise collected under Part D. Several commenters also stated that CMS should give manufacturers the opportunity to review, raise concerns, and designate any information therein that is confidential and proprietary in advance of the publication of the public explanation of the MFP. A few commenters stated that CMS should clarify that any proprietary information shall be disclosed or exclusively used by CMS or the Comptroller General of the United States only for IRA-related purposes, and not used or disclosed for any other reason, regardless of whether the requirements of the Freedom of Information Act (FOIA) are satisfied.

Response: Section 1193(c) of the Act requires that information submitted to CMS by the manufacturer of a selected drug that is proprietary information, as determined by CMS, shall be used only by CMS or disclosed to and used by the Comptroller General of the United States for purposes of carrying out the Negotiation Program. CMS is committed to protecting confidential and proprietary information obtained from manufacturers throughout the negotiation process. In addition, CMS is also committed to protecting information that is obtained from Prescription Drug Plans (PDPs) and MA-PD plans that will inform the negotiation process. For initial price applicability year 2026, as described in section 40.2.1 of this revised guidance, CMS will treat information on non-FAMP as proprietary, as well as treat certain data elements submitted by a Primary Manufacturer of a selected drug in accordance with sections 1194(e)(1) and 1194(e)(2) of the Act as proprietary, if the information constitutes confidential commercial or financial information of the Primary Manufacturer or a Secondary Manufacturer that meets the requirements set forth under Exemptions 3 and/or 4 of FOIA (5 U.S.C. § 552(b)(3), (4)). In addition to the protections under the FOIA for trade secrets and commercial or financial information obtained from a person that is privileged or confidential, the Trade Secrets Act at 18 U.S.C. § 1905 requires executive branch employees to protect such information. CMS understands commenters' concerns pertaining to the confidentiality of proprietary information and will protect confidential and proprietary information as required by applicable law. However, if a Primary Manufacturer chooses to disclose any material that is made public that CMS has previously deemed to be proprietary information of that Primary Manufacturer, CMS will no longer consider that material proprietary consistent with section 40.2.1 of this guidance.

Comment: Some commenters stated that CMS should remove, or at least modify, the data destruction requirements within the confidentiality policy for manufacturers following the deselection of a selected drug. One commenter stated that CMS should consider removing the 30-day timeline for data destruction, or let manufacturers petition for an extension. Other commenters stated that CMS should impose parallel data destruction requirements or revise the policy to align with other federal programs.

Response: After reviewing these comments and further consideration of the issue, CMS has removed the data destruction requirements under the confidentiality policy described in section 40.2.2 of this revised guidance pertaining to Primary Manufacturers.

Comment: Many commenters requested that CMS clarify whether specific data elements submitted by Primary Manufacturers (including, where applicable, Secondary Manufacturer data submitted by the Primary Manufacturer) will be released publicly. Commenters asked that CMS aggregate and release information about prior Federal financial support, approved patents, exclusivities, approvals, aggregate estimates or deidentified research and development costs, historic sales, volume of sales, revenue, and market data of selected drugs. Commenters requested that CMS clarify that information that is publicly available will not be deemed proprietary.

Response: CMS thanks these commenters for their input. As stated in section 40.2.2 of the revised guidance, CMS revised the confidentiality policy for the negotiation process in response to comments received and further consideration of the issue. In the interest of balancing transparency and confidentiality, CMS has made revisions in the guidance pertaining to what information CMS will keep confidential and for how long. As described in section 40.2.2 and 60.6.1 of this revised guidance, as a part of the public explanation of the MFP published in March 2025, CMS will make public a narrative explanation of the negotiation process and the agreed-upon MFP and share redacted information regarding the section 1194(e) data received, exchange of offers and counteroffers, and the negotiation meetings. CMS maintains that any information submitted by manufacturers that constitutes confidential commercial or financial information of the Primary Manufacturer or a Secondary Manufacturer will be considered proprietary and will be redacted.

A Primary Manufacturer may choose to publicly disclose information regarding any aspect of the negotiation process at any time, including prior to the public explanation of the MFP being released by CMS. Of note, while CMS generally plans to wait to release information about the negotiation process until CMS publishes the public explanation of the MFP, if the Primary Manufacturer chooses to disclose information prior to the publication of the public explanation of the MFP, CMS may decide to make early disclosures about the negotiation process as well.

Comment: One commenter stated that CMS should clarify what elements of the Biosimilar Initial Delay Request will be exempt from any FOIA requests or disclosures.

Response: CMS revised section 30.3.1 of this revised guidance to clarify that information in an Initial Delay Request and in a Small Biotech Exception ICR Form that is a trade secret or confidential commercial or financial information will be protected from disclosure if the proprietary information meets the requirements set forth under Exemptions 3 and/or 4 of FOIA (5 U.S.C. § 552(b)(3), (4)).

Comment: One commenter stated that CMS should clarify that the existence and status of a pending NDA or BLA, in addition to information contained in a pending NDA or BLA, will be treated as proprietary information.

Response: As stated in the initial memorandum, for initial price applicability year 2026, CMS will treat certain data elements submitted by a Primary Manufacturer of a selected drug in accordance with section 1194(e)(1) of the Act as proprietary if the information constitutes confidential commercial or financial information of the Primary Manufacturer or a Secondary Manufacturer. It is CMS' presumption that a pending NDA or BLA would qualify as proprietary under this standard.

Comment: One commenter asked CMS to release the full negotiation records five to ten years after the patents for a selected drug expire.

Response: As stated in section 40.2.2 of this revised guidance, CMS revised the confidentiality policy for the negotiation process in response to comments received and after further consideration of the issue. In the interest of balancing transparency and confidentiality, CMS has made revisions in the guidance pertaining to what information CMS will keep confidential and for how long. As described in sections 40.2.2 and 60.6.1 of this revised guidance, as a part of the public explanation of the MFP published in March 2025, CMS will make public a narrative explanation of the negotiation process and the agreed-upon MFP and share redacted information regarding the section 1194(e) data received, exchange of offers and counteroffers, and the negotiation meetings.

At this time, CMS is issuing guidance for implementation of initial price applicability year 2026 and does not foresee that CMS would subsequently provide additional disclosure in the manner the commenter is suggesting. CMS will continue to consider whether such additional disclosure is appropriate in the future.

Comment: One commenter asked CMS to clarify the consequences for violating the requirements of confidentiality for both manufacturers and CMS.

Response: CMS thanks this commenter for their input. In the interest of balancing transparency and confidentiality, CMS revised the confidentiality policy for the negotiation process in response to comments received and further consideration of the issue. CMS does not intend to publicly discuss the negotiation process prior to the public explanation of the MFP being released, unless a Primary Manufacturer chooses to discuss the negotiation publicly. If a Primary Manufacturer discloses information that is made public regarding any aspect of the negotiation process prior to the explanation of the MFP being released by CMS, CMS reserves the right to publicly discuss the specifics of the negotiation process regarding that Primary Manufacturer. Primary Manufacturers engaged in negotiating an MFP with CMS are reminded that statements to or discussions with other Primary Manufacturers also engaged in the MFP negotiation process with CMS could negatively impact the competitive process for each independent MFP negotiation. Primary Manufacturers should consider the antitrust implications of any such actions.

The Trade Secrets Act at 18 U.S.C. § 1905 requires executive branch employees to protect proprietary information. If a Primary Manufacturer chooses to disclose any material that is made public that CMS has previously deemed to be proprietary information of that Primary

Manufacturer, CMS will no longer consider that material proprietary consistent with section 40.2.1 of this revised guidance.

Comment: One commenter asked how CMS will enforce the confidentiality requirements for individuals who no longer work at a manufacturer of a selected drug or at CMS.

Response: CMS thanks this commenter for their question. In the interest of balancing transparency and confidentiality, CMS revised the confidentiality policy for the negotiation process in response to comments received and further consideration of the issue. Primary Manufacturers have the authority to determine how former employees may use or discuss its proprietary information as it pertains to the Negotiation Program. CMS employees that leave CMS are informed prior to their departure that they are not permitted to disclose nonpublic information obtained as a result of CMS employment that has not been released to the public.

Comment: Many commenters stated that the confidentiality policy as described in the initial memorandum violates the First Amendment rights of manufacturers, is not supported by statute, or is not necessary to administer or monitor compliance with the Negotiation Program. One commenter asked that CMS align the confidentiality policy so manufacturers and CMS are bound by the same confidentiality standards. Many commenters raised concerns that the confidentiality policy would prevent manufacturers from disclosing to their board and investors pertinent information related to the negotiation process. One commenter asked CMS to make all offers and counteroffers public. A few commenters were supportive of CMS' confidentiality policy as it is consistent with private sector negotiation processes.

Response: CMS thanks these commenters for their input. As stated in section 40.2.2 of the revised guidance, CMS revised the confidentiality policy for the negotiation process in response to comments received and upon further consideration of the issue. In the interest of balancing transparency and confidentiality, CMS has made revisions pertaining to which information CMS will keep confidential and for how long in the revised guidance. As described in sections 40.2.2 and 60.6.1 of the revised guidance, as a part of the public explanation of the MFP published in March 2025, CMS will make public a narrative explanation of the negotiation process and the agreed-upon MFP and share redacted information regarding the section 1194(e) data received, exchange of offers and counteroffers, and the negotiation meetings. CMS maintains that any information submitted by manufacturers that constitutes confidential commercial or financial information of the Primary Manufacturer or a Secondary Manufacturer will be considered proprietary and will be redacted.

A Primary Manufacturer may choose to publicly disclose information regarding any aspect of the negotiation process at any time, including prior to the explanation of the MFP being released by CMS. Of note, while CMS generally plans to wait to release information about the negotiation process until CMS publishes the explanation of the MFP, if the Primary Manufacturer chooses to disclose information about the negotiation process prior to the publication of the public explanation of the MFP, CMS may decide to make early disclosures about the negotiation process as well. If a Primary Manufacturer chooses to disclose any material that is made public that CMS has previously deemed to be proprietary information of that Primary Manufacturer,

CMS will no longer consider that material proprietary consistent with section 40.2.1 of this revised guidance.

Comment: One commenter stated that CMS should allow manufacturers to negotiate the scope and terms of any confidentiality policies, including whether manufacturers may publicly discuss the Negotiation Program, as a part of the broader negotiation process.

Response: CMS thanks this commenter for their input. In the interest of balancing transparency and confidentiality, CMS made revisions in the guidance to clarify that a Primary Manufacturer may publicly disclose information regarding the Negotiation Program, as described in section 40.2.2 of this revised guidance. In section 40.2 of this revised guidance, CMS describes a confidentiality policy that applies to all Primary Manufacturers of selected drugs who choose to sign an Agreement. Adopting a standard confidentiality policy allows CMS to focus the negotiations on the statutory goal of negotiating to achieve agreement on the lowest MFP and creates uniform protection of information determined to be proprietary as well as transparency upon the release of the explanation of the MFP.

Comment: One commenter asked CMS to consider revising the policies for classification and handling of proprietary data in the coming years and re-evaluate whether this approach should be applied to a narrower set of data elements.

Response: CMS thanks this commenter for their input and will take the comment under advisement as CMS considers policies for future years of the Negotiation Program.

Comment: A few commenters asked how CMS plans to secure manufacturer-submitted data. Commenters asked CMS to outline a cybersecurity policy regarding how CMS plans to implement safeguards to protect manufacturer-submitted data, how such data will be stored, and a process for alerting manufacturers of any breach or erroneous use.

Response: CMS thanks these commenters for their comments on safeguarding data submitted by manufacturers. Primary Manufacturers will submit the information to CMS via the Health Plan Management System ("CMS HPMS"). The CMS HPMS adheres to all applicable policies, procedures, controls, and standards required by the Department of Health and Human Services (HHS)/CMS information security and privacy programs to ensure the confidentiality, integrity, and availability of manufacturer information and government information systems. The CMS HPMS system is the primary CMS system for exchange of information between CMS and Medicare Advantage and Medicare Prescription Drug Plans, and as such is designed to receive and keep confidential proprietary and commercially sensitive information.

As required by CMS, the CMS HPMS integrates security into every aspect of the system development life cycle. The CMS HPMS is subject to the agency's Security Assessment and Authorization (SA&A) process, a rigorous methodology during which the system must demonstrate a sound and comprehensive information security posture. In order to achieve and maintain an Authority to Operate (ATO), the CMS HPMS routinely undergoes system penetration testing as well as a Security Control Assessment (SCA), where independent auditors

perform a detailed assessment to ensure that the system's security controls meet the CMS Acceptable Risk Safeguards (ARS).

An individual must apply for and obtain a CMS-issued user account and password in order to access the CMS HPMS. In addition to the CMS-issued user ID and password, internal CMS staff must use an HHS identification badge (referred to as a PIV card) when accessing the website on the CMS network, while all users accessing the system from outside of the CMS network must use multi-factor authentication. The CMS HPMS further employs role-based access, ensuring that each user is granted access only to those functions required by their position.

The CMS HPMS is hosted at a CMS approved cloud service provider. The system is protected by a suite of firewall and intrusion detection services, including Akamai Content Delivery Network (CDN), which serves as an additional web application firewall that offers robust distributed denial of services protection and access control. The CMS HPMS utilizes a multi-zone architecture comprised of a presentation zone, an application zone, and a data zone, designed to provide further defense against security attacks. CMS will employ encryption at rest in the database for sensitive manufacturer data (e.g., proprietary information, including trade secrets and confidential commercial or financial information) in addition to encryption in transit.

The CMS HPMS adheres to the CMS Information Security Incident Handling Procedures, which are supplemented by the CMS HPMS Security Incident Handling Procedures. These documents outline the procedures for managing known or suspected security or privacy incidents, including, but not limited to, roles and responsibilities, escalation procedures, and guidelines for notifying impacted individuals or organizations.

Negotiation and Agreement to an MFP and Renegotiation in Later Years (Section 40.3)

Comment: One commenter noted that CMS has not outlined the specific conditions under which a renegotiation will occur in subsequent years.

Response: CMS thanks this commenter for the comment. This guidance includes details regarding the Negotiation Program for initial price applicability year 2026. CMS will provide additional information in the future for initial price applicability years 2027 and beyond, including renegotiation, which will be implemented for initial price applicability year 2028 and subsequent years, in accordance with the statute.

Access to the MFP (Sections 40.4 and 90.2)

Comment: One commenter expressed concern that the MFP would be adopted as a reference price by non-Medicare payers. For example, commercial plans and PBMs might use a selected drug's MFP to inform negotiations or to establish payment and reimbursement amounts for the selected drug outside of the Medicare program.

Response: The IRA directs CMS to negotiate an MFP for each selected drug for the Medicare program and requires the manufacturers of such drugs to make the MFP available to MFP-eligible individuals. As discussed in section 80 of this revised guidance, for initial price

applicability year 2026, Primary Manufacturers of selected drugs must provide access to the MFP for a selected drug to Medicare beneficiaries who use their Part D plan (including an MA-PD plan under Medicare Part C or an Employer Group Waiver Plan, but not a plan that receives the Retiree Drug Subsidy) if Part D coverage is provided under such plan for such selected drug. The Negotiation Program does not regulate payment rates by payers outside of the Medicare program (e.g., in the commercial markets). CMS will publish the MFP for each selected drug, as required by law. The MFP for each selected drug could be published by pharmaceutical pricing database companies and could be used by other payers for reimbursement and other purposes. Payers will continue to have discretion to consider Medicare payment rates among other considerations in establishing their own payment policies. CMS notes that Medicare already establishes and publishes payment rates for drugs under Part B using the Average Sales Price (ASP) methodology that may be used by other payers (such as state Medicaid programs), and Medicaid also publishes various pharmaceutical pricing benchmarks, such as the National Average Drug Acquisition Cost (NADAC) file and Federal Upper Limits (FULs) for multiple source drugs, that may be used by other payers.

Comment: Many commenters provided perspectives and recommendations regarding CMS' policies in the initial memorandum to monitor access to the MFP. Many commenters recommended CMS require manufacturers to use a retrospective MFP refund approach to adjust reimbursement to pharmacies, mail order services, and other dispensing entities for dispensing a selected drug to an MFP-eligible individual. Many commenters recommended CMS help effectuate a retrospective refund model by contracting with a third-party administrator (TPA) or clearinghouse to facilitate data and/or payment exchange between entities in the supply chain so pharmacies, mail order services, and other dispensing entities receive retrospective refunds in a timely manner. Many commenters recommended that, in contracting with a TPA, CMS include processes to allow manufacturers to avoid providing the 340B price and an MFP refund for the same unit(s) of a selected drug dispensed to an MFP-eligible individual.

Response: CMS thanks these commenters for the recommendations. CMS intends to engage with a Medicare Transaction Facilitator (MTF) to facilitate the exchange of data between supply chain entities to verify eligibility of MFP-eligible individuals. CMS appreciates the value of the role an MTF could play in supporting the identification of selected drugs dispensed to MFP-eligible individuals to facilitate appropriate retrospective reimbursement by manufacturers. CMS is also exploring options to facilitate retrospective payment exchange between interested parties to help effectuate access to the MFP. CMS is committed to the goal of ensuring prompt payment to dispensers for pass through of the MFP, consistent with other prompt pay rules in Part D.[13] Pursuant to section 40.4 of this revised guidance, CMS requires that the MFP be passed through to dispensers within 14 days of the manufacturer receiving sufficient information to verify that an individual is eligible for access to the MFP. With respect to the establishment of a process to allow manufacturers to avoid providing a 340B price and an MFP for the same unit of drug, CMS understands the value of the identification of 340B units for the Negotiation Program and the Part D Drug Inflation Rebate Program. CMS intends to examine options with respect to identification of 340B units and intends to work with HRSA accordingly. CMS has revised sections 40.4 and 90.2 of this revised guidance to include further detail regarding access

[13] See 42 C.F.R. § 423.520, Prompt Payment by Part D Sponsors, which requires Part D sponsor payment to pharmacies within 14 days after receiving a Part D claim and determining that the Part D claim is a clean claim.

to the MFP and will provide more information in advance of initial price applicability year 2026.

Comment: Some commenters recommended that CMS define the amount of the MFP refund that is due from the manufacturers to the pharmacies. Some advocated for a retrospective "true up" payment from the manufacturer to the dispensing entity, using a standardized amount, such as the difference between a publicly reported pricing metric (such as WAC) and the MFP, rather than a dispensing entity's actual acquisition cost for the selected drug. One commenter recommended CMS use the annual non-FAMP as the standardized metric.

Response: CMS thanks these commenters for their recommendation. The majority of the comments received from supply chain entities on this topic, including manufacturers and pharmacies, supported the use of a standardized, published pricing metric to calculate the refund due from the manufacturer to the pharmacy or other dispenser for the pass through of the MFP. After reviewing the comments and further consideration of the topic, CMS is exploring the option of allowing manufacturers to use a standardized refund amount, such as the WAC of the selected drug minus the MFP (WAC-MFP). CMS plans to provide further information regarding this topic in technical guidance before initial price applicability year 2026.

Comment: Some commenters recommended CMS regularly monitor whether Primary or Secondary Manufacturers are compliant with the requirements of the Negotiation Program, including providing access to the MFP. One commenter recommended CMS create an online option and phone options for reporting violations related to access to the MFP with respect to MFP-eligible individuals. One commenter recommended CMS set a time limit to respond to individuals reporting violations, report the number of complaints CMS receives, and create an ombudsman to serve as a point of contact for individuals submitting complaints.

Response: CMS thanks these commenters for their recommendations, including those relating to the importance of having multiple avenues for reporting violations and timely resolution of investigating such complaints. As further described in sections 40.4 and 90.2 of this revised guidance, CMS will closely monitor the Primary Manufacturers' compliance with the terms of the Agreement and other aspects of the Negotiation Program, including whether the Primary Manufacturer is ensuring that the MFP is available for the selected drug sold by Secondary Manufacturers, where applicable. CMS will establish procedures by which individuals, as well as pharmacies, mail order services, and other dispensing entities, will be able to report instances to CMS in which the MFP should have been made available but was not. CMS will respond to reports of violations in a timely manner, and plans to issue more information on reporting procedures in advance of initial price applicability year 2026.

Comment: A few commenters recommended that CMS establish a financially viable model for pharmacy reimbursement when a pharmacy dispenses a selected drug to an MFP-eligible individual, including by requiring a dispensing fee that covers a pharmacy's business operation costs to dispense a selected drug. A couple of commenters recommended that CMS clarify that claims paid for a selected drug must be excluded from pharmacy DIR or other fees imposed by entities in the supply chain. A couple of commenters recommended CMS prohibit PBMs, Part D plan sponsors, or other entities in the supply chain from charging administrative fees to

manufacturers or pharmacies for providing access to a selected drug. One commenter recommended CMS require higher dispensing fees for entities dispensing a selected drug.

Response: CMS thanks these commenters for their recommendations. Under section 1860D-2(d)(1)(D) of the Act, as amended by section 11001(b) of the IRA, the negotiated prices used in payment by each Part D plan sponsor for each selected drug must not exceed the applicable MFP plus any dispensing fees for such drug. CMS intends to allow manufacturers to use either a prospective upfront discount model or a retrospective refund model to make the MFP available. After reviewing the comments and further consideration of the topic, CMS is working with interested parties to explore developing a standard retrospective rebate model process that would allow for the pass through of the MFP for a selected drug by manufacturers to dispensing entities for dispensing a selected drug to an MFP-eligible individual. As noted above, CMS intends to engage with an MTF to facilitate the exchange of data between pharmaceutical supply chain entities to verify eligibility of MFP-eligible individuals under a retrospective rebate model. As described in section 40.4 of this revised guidance, neither Primary Manufacturers nor their contracted entities shall charge any transaction fee to dispensing entities for the pass through of the MFP to the dispenser.

Provided that Part D plans comply with all applicable requirements, plan sponsors retain flexibility in determining the fees paid or charged to pharmacies, including dispensing fees. However, CMS is committed to the goal of assuring prompt payment to pharmacies and other dispensers for passing through the MFP, consistent with other prompt pay rules in Part D, and is requiring manufacturers to pass through the MFP within 14 days of confirming an individual is eligible for the MFP. Please refer to sections 40.4 and 90.2 of this revised guidance for more information.

Comment: Some commenters recommended CMS collaborate with interested parties to implement a single process for manufacturers to provide access to the MFP that works for entities across the pharmaceutical supply chain. A few commenters recommended CMS work with interested parties in the pharmaceutical supply chain to develop standards for facilitating the transaction of the MFP refund.

Response: CMS thanks these commenters for their recommendations. Consistent with section 40.4 of this revised guidance, Primary Manufacturers must provide access to the MFP by either (1) ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP, or (2) providing retrospective reimbursement for the difference between the dispensing entity's acquisition cost and the MFP. However, CMS notes that the majority of the commenters support the retrospective rebate or refund approach. CMS intends to engage with an MTF that could assist with data facilitation in a retrospective rebate model. CMS has been working with, and plans to continue working with, interested parties to explore processes for facilitating data exchange while minimizing burden.

Comment: A few commenters supported the options CMS outlined in the initial memorandum for providing access to the MFP. One commenter recommended CMS incentivize manufacturers to prospectively effectuate access to the MFP by making the MFP available to dispensing entities at the point of acquisition of a selected drug. One commenter recommended CMS require

manufacturers to create secondary NDCs for selected drugs and make secondary NDCs available to wholesalers at the MFP.

Response: CMS thanks these commenters for their recommendations. The majority of commenters supported a retrospective refund or rebate approach to making pharmacies, mail order services, and other dispensers whole with respect to the pass through of the MFP. CMS intends to engage with an MTF to help facilitate data exchange to confirm MFP-eligibility to provide access to the MFP using a retrospective approach for pharmacies, mail order services, and other dispensers. CMS is not requiring manufacturers to create secondary NDCs for selected drugs and the assignment of labeler codes is the responsibility of the FDA. Moreover, the NDCs for the dosage forms and strengths of a selected drug will be published on the CMS website, and CMS expects that pharmaceutical drug pricing compendia will also publish them.

Comment: Some commenters recommended CMS share detailed Part D claims data with manufacturers to verify that an individual is eligible to receive a selected drug at the MFP. One commenter recommended CMS minimize the data shared with manufacturers and other entities in the supply chain while facilitating access to the MFP.

Response: CMS thanks these commenters for their recommendations. CMS agrees that a Primary Manufacturer should be able to verify that a selected drug was dispensed to an MFP-eligible individual. As further described in sections 40.4 and 90.2 of this revised guidance, after consideration of the comments, CMS plans to release more information in advance of initial price applicability year 2026 regarding how CMS might support and facilitate data exchange between pharmaceutical chain entities.

Comment: A couple of commenters recommended that CMS require Primary Manufacturers to report the MFP of a selected drug and the effective date for the MFP in standard drug pricing compendia.

Response: CMS thanks these commenters for their recommendation. CMS will publish the MFP at the per-unit level for the dosage forms and strengths for a selected drug and keep this list up-to-date over time on the CMS IRA website. CMS anticipates that various drug pricing compendia will decide to include the MFP in their pricing files.

Comment: Some commenters recommended CMS remove or lengthen the requirement for retrospective payment to dispensing entities be made within 14 days, due to operational complexities. Some commenters recommended CMS clarify that the 14-day reimbursement requirement begins when the claim is verified for an MFP-eligible individual. One commenter recommended that CMS clarify that the 14-day reimbursement period begins when the Primary Manufacturer receives the request for reimbursement.

Response: CMS thanks these commenters for their recommendations. CMS will apply the standards set forth in current Part D prompt pay reimbursement regulations regarding payment by plan sponsors to pharmacies to manufacturers for their pass through of the MFP for selected drugs. That is, CMS will require that a Primary Manufacturer ensure that pharmacies, mail order services, and other dispensers are reimbursed timely for the pass through of the MFP within 14

days of verifying eligibility of an MFP-eligible individual. This will ensure that pharmacies are paid for the claim for the selected drug in the same timeframe as if the entire claim would have been filled through the regular Part D process. Please see sections 40.4 and 90.2 of this revised guidance for more information.

Comment: Many commenters made recommendations regarding CMS policy relating to non-duplication of the MFP and the 340B ceiling price. One commenter recommended CMS clarify that the same unit(s) of a drug dispensed to an MFP-eligible individual is not eligible for a duplicate 340B discount. A few commenters wrote that it is burdensome for pharmacies and dispensing entities to identify 340B units proactively or retroactively to avoid duplication of the MFP and 340B ceiling price. Some commenters recommended CMS contract with a TPA to identify 340B units at the point of sale or during retrospective reimbursement. A few commenters recommended CMS condition claims payment for units of selected drugs on including an accurate 340B or non-340B claim modifier. A few commenters recommended CMS work with HRSA to ensure the MFP for a selected drug is not applied to a drug that was acquired at the 340B ceiling price. Some commenters recommended CMS implement an oversight system to audit selected drug units dispensed at the MFP and identify if the same units of a selected drug were acquired at the 340B ceiling price.

Response: CMS thanks these commenters for their recommendations. CMS reiterates, as described in section 40.4.1 of the initial memorandum, that a manufacturer that provides an MFP for a unit of a selected drug is not also required to provide a 340B discount on that same drug if the MFP is lower than the 340B ceiling price (and vice versa, that the MFP does not need to be made available if the 340B ceiling price is lower). That is, these price concessions are not cumulative.

Further, CMS understands the interest in ensuring compliance with the statutory requirement to avoid duplication of the MFP and the 340B ceiling price for a selected drug. CMS also notes the interest in requiring that all Part D claims be marked as either 340B or non-340B to ensure that there is no duplication of 340B prices with the pass through of the MFP. At this time, CMS is examining options with respect to identification of 340B units in consultation with HRSA and interested parties. In addition to any policies or procedures that CMS may adopt in this regard, CMS will also work with HRSA to ensure the MFP is made available where appropriate in a nonduplicated amount to the 340B ceiling price.

Comment: A few commenters recommended CMS create accessible materials that list the MFP for a selected drug and the date the MFP applies for Medicare beneficiaries to reference to understand access to the MFP. A few commenters recommended CMS incorporate information about the MFP of a selected drug into various beneficiary outreach materials.

Response: CMS thanks these commenters for their recommendations. CMS is committed to helping Medicare beneficiaries understand access to a negotiated MFP for a selected drug during the price applicability period. CMS will publish on its website the MFP at the per unit (e.g., tablet) level for each NDC-11 associated with the selected drug. CMS will also develop accessible materials to educate Medicare beneficiaries, as well as the health care providers and other organizations that serve them, on benefits related to the Negotiation Program.

Comment: One commenter recommended CMS reduce the need for Primary Manufacturers to retain any records relating to sales of the selected drug to entities that dispense the selected drug to MFP-eligible individuals, including pharmacies, mail order services, and other dispensers for units of selected drug. The commenter recommended CMS reduce the timeframe from ten years to six years from the date of sale due to the burden and costs associated with retaining these records.

Response: CMS thanks this commenter for the recommendation. CMS believes ten years is a reasonable requirement for record retention for these sales to align with the statute of limitations period under the False Claims Act.[14]

Suggestion of Error and Corrective Actions and Compliance (Sections 40.2.3 and 40.5)

Comment: Some commenters asked CMS to consider a dispute resolution process for any disputes on claims-level data, including 340B claims. A few commenters suggested that CMS delay reimbursement during any dispute resolution process. A few commenters suggested that if CMS does not create a dispute resolution process, that CMS develop stewardship principles within the Negotiation Program, including for facilitating access to the MFP.

Response: CMS thanks these commenters for their recommendations. CMS notes that it intends to engage with an MTF to facilitate the exchange of data between pharmaceutical supply chain entities to support the verification of dispensing of a selected drug to an MFP-eligible individual. CMS believes that engaging with an MTF to facilitate data transfer for eligibility purposes could minimize the potential for claims-level disputes. With respect to the Primary Manufacturer's obligation to provide access to the MFP, requirements are described in sections 40.4 and 90.2 of this revised guidance. CMS is also providing Primary Manufacturers with a corrective action process, detailed in section 40.2.3 of this revised guidance.

Comment: A few commenters asked that CMS establish a dispute resolution process that would apply to various aspects of the Negotiation Program. One commenter asked that the dispute resolution process be established prior to the September 1, 2023, deadline for publication of selected drugs.

Response: CMS thanks these commenters for their recommendations. Section 1198 of the Act prohibits administrative or judicial review of CMS' determinations of drug selection, unit determination, and the determination of MFP. CMS recognizes that Primary Manufacturers, at times, may disagree with CMS regarding certain calculations during the negotiation process. Therefore, if a Primary Manufacturer in good faith believes that CMS has made an error in the calculation of the ceiling for the selected drug or the computation of MFP across dosage forms and strengths, section 40.5 of this revised guidance notes that the Primary Manufacturer can submit a suggestion of error. Additionally, sections 40.2.3 and 100.2 of this revised guidance have been revised to provide an opportunity for corrective action in certain circumstances in which a violation of a requirement could result in a CMP being issued.

[14] 31 U.S.C. § 3731(b).

Comment: A commenter asked that CMS allow for broader stakeholder input in any dispute resolution process that is created.

Response: CMS thanks the commenter for their recommendations. After considering feedback from multiple interested parties for initial price applicability year 2026, CMS updated section 40.5 of this revised guidance to allow Primary Manufacturers the opportunity to suggest potential errors to CMS in the event that the Primary Manufacturer has a good faith belief that CMS has made an incorrect calculation. Further, CMS updated section 100.2 of this revised guidance to describe how Primary Manufacturers will have an opportunity to correct identified incompleteness or inaccuracies in certain manufacturer-submitted information in instances in which a violation of a data submission requirement could result in the imposition of a CMP. CMS will continue to evaluate those processes for future years.

Other Provisions in the Agreement (Section 40.7)

CMS solicited comment on this section, but did not receive any comments that are not otherwise addressed elsewhere (see the Medicare Drug Price Negotiation Program Agreement (Sections 40, 40.1, and 40.6) section above).

Negotiation Factors (Section 50)

Comment: Many commenters supported the use of certain cost-effectiveness measures to gain insight into the relationship between cost and effectiveness for a selected drug and its therapeutic alternative(s). Cost-effectiveness measures mentioned by commenters included Equal Value of Life-Years Gained (evLYG), Equal Value Life-Year (evLY), and Health Years in Total (HYT) and alternative methods recommended for assessing cost-effectiveness included Generalized Risk-Adjusted Cost-Effectiveness (GRACE) and Generalized Cost-Effectiveness Analysis (GCEA). Some commenters recommended convening experts to advise CMS on whether such metrics or methods are appropriate for assessing clinical benefit within the context of negotiation. Some commenters requested CMS clarify that the use of such measures is permitted when evaluating clinical benefit.

Response: CMS appreciates these commenters' responses and suggestions. CMS indicates in section 50.2 of this revised guidance that CMS will review cost-effectiveness measures and studies that use such measures for initial price applicability year 2026 to determine if such measures are permitted under section 1194(e) of the Act. CMS may use content in a study that uses a cost-effectiveness measure if it determines that the cost-effectiveness measure used is permitted in accordance with the law. A measure will not be used to adjust the initial offer if the measure does not provide information related to the negotiation factors described in section 1194(e) of the Act or is used in a manner that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than the life of an individual who is younger, nondisabled, or not terminally ill, in accordance with section 1194(e)(2) and section 1182(e) of Title XI of the Act. CMS clarifies in this revised guidance that it will not use Quality-Adjusted Life Years (QALYs) to determine any offer.

Comment: Many commenters interpreted the initial memorandum as stating a CMS decision not to use QALYs when assessing clinical benefit of a selected drug and its therapeutic alternative(s) and supported such a decision.

Response: CMS appreciates these commenters' feedback and reaffirms that QALYs will not be used in the Negotiation Program. CMS will consider studies that use QALYs only when they contain other content that is relevant and permitted under section 1194(e)(2) of the Act and section 1182(e) of Title XI of the Act.

Comment: Some commenters urged CMS not to use any metrics of cost-effectiveness or clinical effectiveness because the metric and/or the underlying data or assumptions used to develop the metric may be discriminatory. Some commenters stated that CMS should adopt a full prohibition on the use of QALYs and/or "similar measure[s]" under the relevant prohibition in the Patient Protection and Affordable Care Act.

Response: CMS reaffirms that QALYs will not be used in the Negotiation Program to adjust CMS offers. In response to feedback received on whether any measures may be permissible under section 1194(e)(2) and section 1182(e) of Title XI of the Act, CMS revised section 50.2 of this revised guidance to indicate CMS will review and consider cost-effectiveness measures and studies that use such measures for initial price applicability year 2026. However, while such measures may be reviewed, they will not be used to adjust the initial offer if the measures do not provide information related to the negotiation factors described in section 1194(e) of the Act or are prohibited under section 1194(e)(2) of the Act, or under section 1182(e) of the Act.

Comment: Regarding CMS' intent to use data that can be separated from the use of QALYs within a given study, a couple of commenters requested clarification on how CMS would separate such evidence from QALYs. A few commenters requested that CMS not consider any study referencing QALYs in determining the initial offer.

Response: Per section 1194(e)(2) of the Act, comparative clinical effectiveness research may not be used "in a manner that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill." CMS will not, per section 1182(e) of Title XI of the Act, use QALYs but may review the underlying data, results, or other content in studies that employ QALYs. By doing so CMS may glean important insights into the outcomes associated with the drug under consideration. For example, a study using QALYs to examine the cost-effectiveness (i.e., reviewing the cost per outcome) of drug A compared to drug B for the treatment of cardiovascular disease will describe the population of interest and quantify the outcomes. Factors in the study that do not treat extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or terminally ill, such as demographic information, blood pressure, cardiovascular events, and mortality before and after starting drug A versus starting drug B may provide important data to CMS about the clinical benefit of drug A when compared to drug B. Reviewing demographic information and outcomes, such as in this example, does not require CMS to review the results of the QALY calculation but may still provide important clinical information.

This approach aligns with CMS' decision to not use QALYs in the Negotiation Program while also enabling CMS to review and consider relevant information.

Comment: Many commenters requested that CMS simplify the process by which the public, including patients and caregivers, can submit information on the negotiation factors described in section 1194(e)(2) of the Act and the Negotiation Data Elements ICR (CMS-10847 / OMB 0938-NEW). Commenters requested additional time for submissions and clarity on the format in which information should be submitted to ensure usability for the submission of factors related to sections 1194(e)(1) and 1194(e)(2) of the Act.

Response: CMS appreciates commenters' feedback. Due to the statutory timeline of the negotiation period, including the requirement under sections 1191(d)(5)(B) and 1194(b)(2)(B) of the Act for CMS to issue an initial offer by February 1, 2024, it is not feasible to extend the timeframe for the submission of information under section 1194(e)(2) of the Act. However, as described in section 60.4 of this revised guidance, CMS will host patient-focused listening sessions that will be open to the public, including patients, beneficiaries, caregivers, consumer and patient organizations, and other interested parties, to share patient-focused input on the therapeutic alternative(s) and other section 1194(e)(2) information regarding selected drugs. These patient-focused listening sessions will occur in Fall 2023 after the section 1194(e) data submission, which will give patients and other interested parties additional time to prepare their feedback. Regarding the standardization of submissions, CMS expects a wide range of data to be appropriately submitted as part of the process and does not seek to limit the types of data submitted based on format. CMS will review submissions in alignment with sections 50 and 60 of this revised guidance.

Comment: Some commenters supported CMS' decision to open the submission of section 1194(e)(2) factors to the public. Some commenters suggested evaluating bias in information submitted or requiring a conflict of interest disclosure.

Response: CMS appreciates commenters' feedback. As described in section 50.2 of this revised guidance, CMS will consider, among other factors, the source of information, whether the study has been through peer review, as well as risk of bias during review. CMS also requires that declarative statements submitted via the Negotiations Data Elements ICR be supported by cited evidence unless the submission is a description of personal experience. This approach focuses on the merit of the information provided.

Comment: One commenter suggested requiring an executive summary of manufacturer-submitted data and another suggested requiring manufacturers to report rebates at the drug level.

Response: CMS appreciates commenters' suggestions. The comment suggesting that CMS require an executive summary of manufacturer-submitted data is out of scope for the Negotiation Program guidance and will be considered for the revised Negotiation Data Elements ICR. Regarding the comment suggesting manufacturers be required to report rebates at the drug level, CMS consulted with subject matter experts and representatives of the pharmaceutical and biotechnology industry in developing the definitions described in Appendix C of this guidance to align with statutory data collection requirements and other federal programs.

Comment: A few commenters suggested that CMS validate manufacturer data using independent data sources or suggested a third-party entity validate manufacturer data instead of CMS. One commenter recommended that CMS specify that submissions may be audited to ensure accuracy.

Response: CMS will validate manufacturer-submitted data to the extent possible, including via audit as deemed appropriate, pursuant to compliance monitoring activities under section 1196(b) of the Act.

Comment: Some commenters stated that the Negotiation Data Elements ICR included unclear expectations or data formatting inconsistent with current manufacturer approaches to tracking such data. A few commenters stated this could generate risk for the manufacturer and that a standard data format should be clarified. One commenter requested that CMS clarify that only the Primary Manufacturer is responsible for submitting data on factors described in section 1194(e)(1) of the Act.

Response: The Primary Manufacturer is responsible for providing manufacturer-submitted data described in section 1194(e)(1) of the Act and section 50.1 of this revised guidance. More information on what must be reported can be found in Appendix C of this revised guidance. Comments on formatting are out of scope for the Negotiation Program guidance and will be considered in the revised Negotiation Data Elements ICR.

Comment: A couple of commenters requested that CMS accept any information provided by a manufacturer of a selected drug even if such information is not tied to a specific statutory factor.

Response: CMS will accept information as outlined in this revised guidance and the Negotiation Data Elements ICR in accordance with statutory requirements.

Comment: One commenter requested manufacturer data submissions be provided to CMS on a rolling basis to permit adequate time to compile accurate and complete data given the relationship between inadequate submissions and CMPs. Another commenter requested sufficient time for manufacturers to evaluate requests for information and price offers from CMS before a manufacturer is determined to be noncompliant and/or enforcement actions are taken. This commenter suggested that CMS has flexibility to establish the timeframe between publication of the selected drug list (September 1, 2023 for initial price applicability year 2026) and submission of data required under section 1194(e) of the Act (stated in the initial memorandum as October 2, 2023), particularly given the resulting tax liability for failure to submit data.

Response: CMS appreciates commenters' concerns regarding deadlines. Pursuant to sections 1191(d)(5)(A) and 1194(b)(2)(A) of the Act, Primary Manufacturers must submit the manufacturer-specific data described in sections 1193(a)(4)(A) and 1194(e) of the Act to CMS by October 2, 2023 for initial price applicability year 2026. CMS will use data submitted by the Primary Manufacturer and other interested parties when developing the initial offer for a selected

drug along with CMS analyses and assessments of evidence as described in section 50.2 of this guidance. CMS is abiding by the statutory deadlines in this revised guidance.

Comment: One commenter requested that CMS clarify that consideration of manufacturer average net unit price will not trigger a future renegotiation of MFP.

Response: Renegotiation is out of scope for this revised guidance for initial price applicability year 2026 and will be addressed in future guidance or rulemaking, as appropriate.

Establishment of a Single MFP for Negotiation Purposes (Section 60.1)

Comment: Some commenters expressed concern with CMS' proposal to use a 30-day equivalent supply to apply the MFP across dosage forms and strengths, particularly for drugs with irregular intervals, topicals, and drugs taken for acute symptoms. Some commenters requested that CMS provide alternative options, consult with manufacturers on the methodology to be used for a selected drug, and/or work with interested parties to better understand how 30-day equivalent supplies are calculated for those medicines that have irregular or varied dosing schedules.

Response: CMS appreciates commenters' feedback and requests for clarity. This revised guidance provides additional detail about how CMS will use the days' supply field in PDE data to calculate 30-day equivalent supply using the methodology described in 42 C.F.R. § 423.104(d)(2)(iv)(A)(2) when calculating the MFP ceiling (described in section 60.2 of this revised guidance) and using the WAC ratio for initial price applicability year 2026 to apply the MFP across dosage forms and strengths (described in section 60.5 of this revised guidance). For purposes of weighting across dosage forms and strengths, CMS believes that calculating a 30-day equivalent supply, using the days' supply field, is feasible for the high-expenditure, single source Part D drugs that might be subject to negotiation for initial price applicability year 2026. As described in section 60.3.2 of this revised guidance, when comparing prices of the therapeutic alternative(s) for purposes of informing a starting price for the initial offer, CMS may use an alternative methodology for calculating a 30-day equivalent supply when appropriate.

Limitations on Offer Amount (Section 60.2)

Comment: A few commenters opposed the approach described in the initial memorandum, which these commenters asserted would result in the ceiling being applied twice. One commenter agreed with CMS that an MFP should be calculated specific to dosage forms and strengths and account for the variation in prices "specific to each dosage form and strength of the selected drug," but proposed negotiating multiple MFPs per drug by calculating the ceiling for the lowest unit of measure of a selected drug and establishing a metric from which CMS may negotiate a percent of the MFP ceiling to arrive at the published MFP per lowest unit of measure.

Response: CMS appreciates commenters' feedback. CMS disagrees that the procedure that it described in the initial memorandum would have applied the MFP ceiling twice. However, after consideration of the comments, for initial price applicability period 2026, CMS has revised section 60.2 of the guidance to use the single ceiling per 30-day equivalent supply across all

dosage forms and strengths of the selected drug. This approach aligns with the concept of negotiating an MFP for a whole selected drug across multiple dosage forms and strengths (as identified on the list of NDC-11s of the selected drug in the CMS HPMS, per section 40.2 of this revised guidance) subject to a single MFP ceiling, and then applying that MFP across dosage forms and strengths as required under section 1196(a)(2) of the Act. As discussed in the response to comments under section 60.5 below, CMS intends to monitor the practical effect of its procedures for applying the MFP across the dosage forms and strengths of the selected drug to inform its use of its section 1196(a)(2) authority for initial price applicability years after 2026.

Comment: A few commenters recommended that CMS revise the non-FAMP calculation to use the four quarters of the fiscal year, as opposed to the calendar year, to align with the Veterans Health Care Act of 1992 and reduce burden on manufacturers. Relatedly, commenters recommended that CMS develop mechanisms to account for anomalies in the non-FAMP and to permit restatements of the average non-FAMP due to data or other errors identified after the fact.

Response: Section 1194(c)(6) of the Act defines average non-FAMP to mean "the average of the non-Federal average manufacturer price... for the 4 calendar quarters of the year involved." As a result, the statutory language requires that the calendar year be used to calculate the average non-FAMP. CMS has revised the definition of non-FAMP in Appendix C to clarify that any restatements of the non-FAMP made in any applicable manufacturer non-FAMP submissions to the Department of Veterans Affairs (VA) must be reflected in the non-FAMP submitted to CMS as part of the section 1193(a)(4)(A) manufacturer data submission. Section 50.1.1 and Appendix C of this guidance discuss how manufacturers should report non-FAMP to CMS in cases where there are no data or data are insufficient to calculate non-FAMP for at least one calendar quarter of 2021.

Comment: A few commenters requested clarification as to whether the time period for determining if a selected drug is an extended or long-monopoly drug runs to the start of the applicable initial price applicability year or selected drug publication date. Commenters noted that the initial memorandum is inconsistent, applying the length of time one way when describing the initial delay request made by a biosimilar manufacturer (i.e., to the start of the initial price applicability year) and another when determining the monopoly type as well as the applicable percent specified for the purposes of establishing a ceiling (i.e., to the selected drug publication date).

Response: CMS thanks these commenters for their careful review of the initial memorandum and appreciates their flagging this inconsistency. CMS has revised section 60.2.3 of this guidance to clarify that the time period for determining whether a selected drug is an extended- or long-monopoly drug runs to the start of the applicable initial price applicability year, as specified in sections 1194(c)(4)(A) and 1194(c)(5)(A) of the Act, respectively. However, CMS notes that, as discussed in section 60.2.3 of this guidance, the definition of "extended-monopoly drug" under section 1194(c)(4)(B)(ii) of the Act expressly excludes a selected drug for which a manufacturer has entered into an Agreement with CMS with respect to an initial price applicability year that is before 2030. CMS interprets this to mean that no selected drug will be considered an extended-monopoly drug for purposes of calculating the ceiling prior to initial price applicability year 2030.

Comment: A couple of commenters requested that CMS clarify whether unit refers to non-FAMP units or PDE units in the calculation of the annual non-FAMP for the dosage forms and strengths of the selected drug.

Response: CMS thanks these commenters for their careful review of the initial memorandum and appreciates the requests for clarification. CMS has revised section 60.2.3 of this guidance to clarify that PDE units will be used when averaging non-FAMP across NDC-11s. This is consistent with the use of PDE units to average NDC-9[15] non-FAMP amounts to a whole drug non-FAMP amount.

Comment: A few commenters disagreed with CMS' intent to use DIR data in calculating the "sum of the plan-specific enrollment weighted amounts" for purposes of determining the MFP ceiling. These commenters claim that the "plan specific enrollment weighted amount" is defined by reference to the Part D negotiated price, which does not include price concessions from manufacturers.

Response: Section 1194(c)(2)(A) of the Act states that the "plan-specific enrollment weighted amount" for a Part D or MA-PD plan with respect to a covered Part D drug is calculated using the negotiated price of the drug under the plan "net of all price concessions received by such plan or pharmacy benefit managers on behalf of such plan," and as such CMS plans to use DIR data, including information on manufacturer rebates and other price concessions collected through DIR reporting, in calculating the "sum of the plan-specific enrollment weighted amounts" under section 1194(c)(1)(B) of the Act.

Comment: One commenter recommended that CMS provide manufacturers with an opportunity to review and reconcile CMS' data for the MFP ceiling calculation for a selected drug. One commenter expressed concern that CMS is engaging in various conversion calculations to move from data at the NDC-11 level to the NDC-9 level to the whole drug level without providing sufficient detail to interested parties.

Response: CMS appreciates commenters' feedback. As discussed in section 60.4 of this revised guidance, CMS will provide the Primary Manufacturer information on the calculation of the statutorily-determined ceiling price. However, CMS is not able to provide manufacturers with all data used in ceiling calculations, as some of the calculations use proprietary information.

Comment: One commenter suggested that CMS should consider that the manufacturer-specific factors in section 1194(e)(1) of the Act could constitute the floor for price negotiations while the factors in section 1194(e)(2) could constitute the ceiling, keeping in mind the statutory ceiling in section 1194(c).

Response: As the commenter notes, section 1194(c) of the Act provides a specific formula for the calculation of the ceiling on the MFP for a selected drug, which is further described in section 60.2 of this guidance. The statute also requires CMS to consider the nine factors

[15] In this guidance, the NDC-9 refers to the first two segments of the NDC-11 that represent the labeler code and product portions of the NDC and indicate a drug's dosage, form, and strength regardless of the package size.

described in sections 1194(e)(1) and 1194(e)(2) when developing the initial offer. The statute does not direct CMS to use the manufacturer-submitted data or the section 1194(e)(2) data to establish a floor or ceiling, respectively, for price negotiations.

Methodology for Developing an Initial Offer (Section 60.3)

Comment: Many commenters recommended that CMS set the initial offer at or near the ceiling for all or a subset of selected drugs; for example, drugs that have provided therapeutic advancements, filled an unmet need, or otherwise demonstrated significant patient benefit; drugs under patent protection; small molecule drugs; and all drugs for initial price applicability year 2026 and for several subsequent price applicability years thereafter.

Response: CMS appreciates commenters' input. Section 1194(b)(1) of the Act instructs CMS to develop and use a consistent methodology and process for negotiations that aims to achieve agreement on the lowest MFP for each selected drug and in doing so, to consider the nine factors described in sections 1194(e)(1) and 1194(e)(2) of the Act. Offering the ceiling without a more thorough review of those statutory factors, including manufacturer-submitted data, may not achieve that objective and is inconsistent with the statutory directive.

Comment: CMS received many comments related to the identification of therapeutic alternative(s). Some commenters expressed concern regarding CMS' intent to use the price of the therapeutic alternative(s) in developing the offer starting point, including that drugs would be identified as the therapeutic alternative(s) based on cost rather than clinical appropriateness and that patients' needs will be overlooked when identifying the therapeutic alternative(s). A few commenters also noted that drugs in certain classes have few equivalent or substitutable alternatives. Some commenters were generally supportive of CMS' approach to identifying the therapeutic alternative(s), including limiting comparators to pharmaceutical alternatives, identifying therapeutic alternative(s) by indication, and considering off-label use when appropriate. However, a few commenters opposed CMS' approach to consider off-label use when identifying the therapeutic alternative(s). One commenter recommended that CMS identify no more than two comparators, one of which should be the lowest cost alternative and the other the most commonly used alternative. Another commenter stated that there is variability in how different entities define therapeutic categories, which results in different combinations of drugs in that therapeutic category. Many commenters recommended that CMS provide manufacturers, health care providers, and patients with the opportunity to participate in the selection of the therapeutic alternative(s).

Response: CMS appreciates commenters' feedback. As described in section 60.3.1 of this guidance, CMS will identify the therapeutic alternative(s) based on clinical appropriateness and consideration of various sources of evidence including clinical guidelines, peer-reviewed literature, drug compendia, and data submitted by manufacturers and the public, and not based on the cost of therapeutic alternative(s). CMS also may consult with FDA in the process of identifying other approved therapies for the same indication and with health care providers, patients or patient organizations, and academic experts to ensure that the appropriate therapeutic alternative(s) are selected. CMS expects that the negotiation offer/counteroffer exchange, as well as the negotiation meetings, will offer an opportunity for discussion about the therapeutic

alternative(s) with manufacturers. Further, as described in section 60.4 of this guidance, CMS will provide additional engagement opportunities for interested parties via manufacturer data submission-focused meetings and patient-focused listening sessions after the October 2, 2023 deadline for submission of information on the section 1194(e) data. CMS will provide additional information about these engagement opportunities at a later date.

Comment: Some commenters requested clarification as to whether generic drugs and biosimilars may be included as the therapeutic alternative(s). A few commenters opposed such inclusion because it would enable CMS to undervalue medicines. A few commenters expressed support for including generic and biosimilar therapeutic alternative(s) to establish the starting point for the initial offer.

Response: CMS appreciates commenters' feedback. As described in sections 60.3.1 and 60.3.2 of this guidance, CMS will consider the range of Part D net prices and/or ASPs of therapeutic alternative(s) for the selected drug, including prices of generic and biosimilar therapeutic alternative(s) if clinically appropriate.

Comment: Some commenters expressed support for CMS' proposal to consider the Part D net price or ASP of therapeutic alternative(s) for the selected drug as the starting point for the initial offer. A few commenters had concerns that considering Part D net prices would result in an inflated starting point and recommended CMS use the lowest net price or ASP as the starting point or the manufacturing cost and adjust based on clinical benefit. Another commenter recommended that CMS go beyond the net price of therapeutic alternative(s) to include all health system costs associated with the selected drug and its therapeutic alternative(s). One commenter recommended that if there are multiple therapeutic alternatives, CMS should use the highest-value alternative. Some commenters proposed additional options for the offer starting point, including using the MFP ceiling as the starting point or using comparative effectiveness to establish a price range or threshold for the initial offer.

Response: CMS understands concerns that using the Part D net price or ASP of a therapeutic alternative for the selected drug may result in a higher starting point; however, using net price(s) and ASP(s) of therapeutic alternative(s) enables CMS to start developing the initial offer within the context of the cost and clinical benefit of a group of drugs that treat the same disease or condition. As described in section 60.3.2 of this guidance, CMS will consider the range of Part D net prices and/or ASP(s) of therapeutic alternative(s), which may include consideration of generics and biosimilars as well as on- and off-label use (if such use is included in nationally recognized, evidence-based guidelines and recognized in CMS-approved Part D compendia). Some of the proposed alternatives for determining an offer starting point would not consider the clinical benefit provided by the selected drug relative to its therapeutic alternative(s). For example, if CMS were to use the MFP ceiling for the selected drug as the starting point, all adjustments to the starting point would be decreases, which could limit CMS' ability to adjust the starting point to recognize superior clinical benefit of the selected drug compared to therapeutic alternative(s). Rather than using manufacturing costs as a starting point, CMS will adjust the preliminary price based on manufacturer-specific data elements, including but not limited to the unit costs of production.

Comment: A couple of commenters indicated that CMS' intent to cap the offer starting point at the MFP ceiling is inconsistent with the statute. These commenters noted that the statute only requires that CMS not make an initial offer or accept a counteroffer that is above the statutory ceiling, and that limiting each step of the initial offer development process at the ceiling would lower the amount CMS could subsequently adjust based on other statutory factors (i.e., manufacturer-submitted data and clinical benefit).

Response: CMS appreciates commenters' feedback. CMS believes that the statute grants CMS flexibility to determine the amount of the initial offer, provided that the offer does not exceed the ceiling. Specifically, section 1194(b)(2)(F) of the Act requires that CMS may not make an offer or agree to a counteroffer for an MFP that exceeds the ceiling, but does not prohibit CMS from applying the ceiling when determining the starting point of the initial offer. Further, section 1194(b)(1) of the Act instructs CMS to develop and use a consistent methodology and process for negotiations that aims to achieve agreement on the lowest MFP for each selected drug. CMS' approach of using the Part D net price or ASP of the therapeutic alternative(s), as applicable, as the starting point to determine the initial offer only if it is lower than the ceiling is consistent with this directive. As discussed in section 60.3 of this revised guidance, CMS will further adjust the starting point by the other factors specified in section 1194(e) of the Act.

Comment: CMS received many comments regarding its intent to use the Federal Supply Schedule (FSS) or Big Four price[16] as an offer starting point for selected drugs with no therapeutic alternative(s) or for selected drugs with therapeutic alternative(s) with Part D net prices and/or ASPs greater than the statutory ceiling. Some commenters disagreed with CMS' approach, noting that these prices do not reflect market prices because of certain required discounts. Other commenters were concerned that if Medicare uses these prices, it could put upward pressure on the FSS and Big Four prices, or manufacturers would be less willing to provide price concessions to the Big Four.

Response: CMS thanks these commenters for their remarks and understands the concerns raised. As discussed in section 60.3 of this revised guidance, CMS will use FSS/Big Four prices in situations where the selected drug has no therapeutic alternative(s) or the price of the therapeutic alternative(s) exceeds the ceiling. CMS believes use of FSS/Big Four prices is appropriate in these situations, as these prices are publicly available and are reflective of prices available to other federal payers.

Comment: A commenter requested that CMS limit downward adjustments related to prior Federal financial support to an amount proportional to the amount of prior Federal financial support as a share of total investment in research and development (R&D) in the selected drug.

Response: CMS appreciates these suggestions. As described in section 60.3.4 of this guidance, for each selected drug, CMS may consider each factor outlined in section 1194(e)(1) in isolation or in combination with other factors. With respect to prior Federal financial support specifically,

[16] The Big Four price is the maximum price a drug manufacturer is allowed to charge the "Big Four" federal agencies, which are the Department of Veterans Affairs (VA), Department of Defense (DoD), the Public Health Service, and the Coast Guard. See section 8126 of title 38 of the U.S. Code. See: https://www.cbo.gov/publication/57007.

CMS will consider the extent to which the Primary Manufacturer benefited from such Federal financial support with respect to the selected drug. For example, CMS may consider adjusting the preliminary price downward if funding for the discovery and development of the drug was received from Federal sources.

Comment: Many commenters indicated the definition of unmet medical need provided in section 60.3.3.1 of the initial memorandum was too narrow and should include situations where patients may not respond to or tolerate available treatments or disease burden remains significant. Some commenters suggested the definition should consider populations with disparities in outcomes or access. Some commenters proposed adopting the definition of unmet need from the FDA's expedited review programs. One commenter suggested looking to the National Comprehensive Cancer Network (NCCN) definition. A couple of commenters suggested looking to the framework used for New Technology Add-On Payments (NTAP). Many commenters recommended incorporating the patient perspective and/or broader societal or public health benefits when determining whether a selected drug fulfills an unmet medical need. A few commenters suggested reviewing unmet medical need across a product's lifecycle. A couple of commenters suggested reviewing unmet medical need at the time of FDA approval.

Response: CMS appreciates commenters' feedback and has reviewed the variety of definitions and frameworks suggested. After consideration of these comments, CMS revised the definition of unmet medical need to further align with section 1194(e)(2)(D) of the Act and FDA's "Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics" to include drugs that may have a therapeutic alternative but the existing alternative does not adequately address the condition or disease indicated (as described in section 60.3.3.1 of this revised guidance). Because the FDA guidance was issued in May 2014 and includes nonbinding recommendations, CMS will consider the guidance a reference and will consider any updates concerning unmet medical need that may be issued by FDA. CMS encourages patients and other interested parties to submit their perspective on how a selected drug meets an unmet medical need through the Negotiation Data Elements ICR submission and in the patient-focused listening sessions that will be held in Fall 2023, per revised section 60.4. More information on patient-focused listening sessions is forthcoming.

CMS also appreciates comments suggesting unmet medical need should be evaluated across a product's lifecycle. CMS will evaluate unmet medical need as of the time the section 1194(e)(2) data is submitted, which aligns with CMS' approach to reviewing manufacturer costs and data, therapeutic alternative(s), and other negotiation factors.

Comment: Many commenters supported using clinical benefit as the primary means for developing the initial offer. A few commenters stated CMS should deemphasize distribution costs when reviewing manufacturer-submitted data. A commenter suggested manufacturer-submitted data only be considered for selected drugs that provide fewer clinical benefits than the therapeutic alternative(s).

Response: CMS appreciates commenters' support for using clinical benefit to inform the initial offer. CMS is required to consider the factors described in section 1194(e) of the Act, as applicable to the selected drug, but there is flexibility to use these factors to inform the initial

offer and final offer, if applicable, in such a way as to recognize the unique characteristics of a selected drug. Regarding distribution costs, as described in section 60.3 of this guidance, CMS will adjust the starting point for the initial offer based on factors related to clinical benefit and then consider manufacturer-submitted data for additional adjustments, as appropriate. CMS also notes that the information submitted by the manufacturer and the public as well as information gathered through CMS' analysis will be considered in totality.

Comment: A few commenters suggested CMS should apply special considerations when evaluating orphan drugs or apply an upward adjustment for drugs with orphan indications, drugs that represent a significant therapeutic advance, and drugs that address an unmet medical need(s).

Response: As noted in the guidance, CMS will consider the totality of evidence when developing the initial offer. If a selected drug represents a significant therapeutic advance or addresses an unmet medical need, all other factors held constant, the initial offer for that selected drug would be higher than if this were not the case. CMS continues to explore whether there are additional actions that can be taken in the Negotiation Program to support orphan drug development, and CMS appreciates continued input from interested parties on this topic.

Comment: Many commenters requested additional detail on how negotiation factors, including those submitted by the Primary Manufacturer, would be weighted and how evidence would be evaluated and prioritized, stating additional transparency is needed. Many commenters suggested developing or adopting an existing framework for evaluating submitted information. A commenter requested CMS define "therapeutic advance."

Response: CMS appreciates commenters' feedback and recognizes the importance of balancing transparency and confidentiality in the negotiation process. CMS believes it is important to maintain flexibility when considering how each negotiation factor contributes to the initial offer and final offer, if applicable, which may be impacted by the unique characteristics of each selected drug, the populations each selected drug is intended to treat, and information that may emerge from meaningful discussions with manufacturers, patients, and patient representatives. Regarding therapeutic advance, CMS will determine whether a selected drug represents a therapeutic advance by examining improvements in outcomes for the selected drug compared to its therapeutic alternative(s) as described in section 60.3.3.1 of this revised guidance. CMS also included considerations for how evidence will be prioritized in section 50.2 of the initial memorandum and this revised guidance.

Comment: Many commenters recommended that real-world evidence,[17] information from clinical experts, and/or patient and caregiver perspectives be prioritized when reviewing negotiation factors. A few commenters suggested both qualitative and quantitative approaches be used to review negotiation factors and develop an initial offer. One commenter noted that CMS

[17] Real-world evidence is clinical evidence about the usage and potential health benefits or risks of a medical product derived from real-world data. Real-world data are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. From *Framework for FDA's Real-World Evidence Program*, December 2018. See: https://www.fda.gov/media/120060/download.

should consider the limitations of real-world evidence, particularly real-world evidence based on patient registry data and the limitations of data from electronic health records and billing records.

Response: CMS agrees with commenters on the importance of real-world evidence as well as the limitations of such evidence, as with any type of data. CMS also agrees with commenters on the importance of the perspective of clinicians, patients, and caregivers. CMS included real-world evidence and consultation with clinical experts and academic researchers in the initial memorandum and, as described in section 60.4 of this revised guidance, CMS will host patient-focused listening sessions that would be open to the public, including patients, beneficiaries, caregivers, consumer and patient advocacy organizations, and other interested parties, to share patient-focused input on therapeutic alternative(s) and other section 1194(e)(2) data regarding selected drugs. CMS may also consider the caregiver perspective to the extent that it reflects directly upon the experience or relevant health outcomes of the patient taking the selected drug. As noted in the initial and revised guidance, CMS will take a qualitative perspective when reviewing a selected drug and consider the evidence, including real-world evidence, clinical input, and patient and caregiver input, in totality. By employing a qualitative approach to information review rather than a more formulaic quantitative approach, CMS is able to preserve flexibility in negotiation, including the ability to consider nuanced differences between different drugs that might not be captured in a more thoroughly pre-specified quantitative approach.

Comment: A few commenters noted that CMS should include the caregiver experience and equity as factors in the negotiation process. A couple of commenters requested that for specific populations, CMS relax data prioritization standards to ensure underserved and underrepresented populations are considered. One commenter recommended that CMS prioritize studies that include individuals from diverse racial and ethnic backgrounds.

Response: CMS thanks these commenters for their feedback. Health equity is the first pillar of the CMS Strategic Plan, which builds health equity into the core functions of CMS, including the Negotiation Program.[18] As noted in the initial memorandum, CMS will consider information related to a selected drug within specific populations. In this revised guidance, CMS clarified that this includes underserved and underrepresented populations, as applicable, that may be experiencing disparities in health outcomes or access to the selected drug. As noted above, CMS will also consider the caregiver perspective to the extent that input reflects directly upon the experience or relevant health outcomes of the patient taking the selected drug. This information will be collected using the Negotiation Date Elements ICR and is open to the public. All applicable negotiation factors will be considered in totality for each selected drug.

Comment: Some commenters suggested that the negotiation factors be expanded to include adherence, convenience, societal impact, caregiver burden, independence, lost wages, travel expenses, costs to patients, medical costs, value of hope, cost of side effects, and other indirect costs. One commenter recommended that CMS de-prioritize or exclude indirect health benefits and instead focus solely on health outcomes to develop the initial offer.

Response: CMS agrees that factors such as adherence and convenience (as applicable to patient experience and outcomes) are important to consider for a selected drug. CMS views such factors

[18] See: https://www.cms.gov/cms-strategic-plan.

as directly related to patient experience and as such, considers these to be included in the factors outlined in the guidance. CMS appreciates commenters' suggestions to add broader societal, economic, and public health factors to those that will be considered during negotiation. Upon reviewing commenters' suggestions for additional factors, CMS revised the guidance to include consideration of both health outcomes and other outcomes when evaluating the benefit of the selected drug and therapeutic alternative(s). Outcomes such as changes to productivity, independence, and quality of life will be considered to the extent that these outcomes correspond with a direct impact on individuals taking the drug and are permitted in accordance with section 1194(e)(2).

Comment: Some commenters recommended using Multi-Criteria Decision Analysis (MCDA) as a framework for evaluating evidence related to a selected drug and its therapeutic alternative(s).

Response: CMS appreciates this suggestion. Due to the statutory timeline, conducting a full MCDA is not feasible. CMS will consider whether the general approach used in MCDA can serve as an informative framework for evaluating evidence.

Comment: A few commenters suggested that CMS share its literature review and other materials related to the selected drug and its therapeutic alternative(s) with the manufacturer of the selected drug.

Response: Per section 1194(b)(2) of the Act and this revised guidance, CMS will provide each manufacturer of a selected drug with an initial offer and a concise justification of the factors used to develop the offer.

Comment: Many commenters stated that CMS should not decrease the initial offer based on existing patents and exclusivities provided by the FD&C Act or PHS Act and recommended the initial offer be increased in cases where a drug has existing patents and exclusivities. Many commenters are concerned that a downward adjustment based on patents and exclusivities will stifle innovation, may impact patient access, disincentivize R&D, and work against the purpose of the patent system. A few commenters believe a downward adjustment based on patents and exclusivities exceeds CMS' statutory authority. A few commenters noted that CMS' action may constitute "a taking requiring just compensation" under the Fifth Amendment's Takings Clause and stated that patents are a constitutionally protected property right.

Response: CMS appreciates commenter feedback on adjusting the initial offer price based on patents and exclusivities provided by the FD&C Act or PHS Act ("exclusivities"). The statute explicitly directs CMS to consider data on approved patents and exclusivities in its determination of the amount of the initial offer. CMS does not believe that its implementation of this statutory mandate constitutes a taking or otherwise implicates or violates the Fifth Amendment Takings Clause. CMS also notes that the example provided in the initial memorandum was intended to provide an illustrative example of how such data could be considered in developing an initial offer. However, as discussed in section 60.3.4 of this revised guidance, following further consideration of the issue, CMS has omitted the example provided in the initial memorandum. This revised guidance clarifies CMS' belief that this information will support CMS' consideration of the 1194(e)(1) and 1194(e)(2) factors described in section 60 of this revised

guidance. For instance, patents and exclusivities may inform CMS' understanding of therapeutic alternatives and other available therapy for the purposes of adjusting for clinical benefit, including consideration of whether the selected drug represents a therapeutic advance or meets an unmet medical need. More specifically, in light of exclusivities, there may be no other available therapy aside from the selected drug that adequately addresses treatment or diagnosis of a condition; consideration of such information would be relevant to CMS' consideration of the extent to which the selected drug addresses an unmet medical need for that condition.

Comment: Many commenters requested that CMS develop additional opportunities for patient, caregiver, and clinician input throughout the negotiation process, particularly to provide input on therapeutic alternative(s) to the selected drug, patient-reported outcomes, health outcomes, whether the drug fulfills an unmet medical need, weighing evidence, and benefits and impacts of the selected drug. Many commenters requested a structured, standardized means for such input to be provided such as roundtables, an advisory or stakeholder panel, listening sessions, town halls, additional meetings, or creating a patient ombudsman to engage with interested parties. A few commenters pointed to FDA's Patient-Focused Drug Development program as one that CMS can adopt or model. Some commenters requested that patients be recognized in this revised guidance as subject matter experts. Some commenters requested that patients and clinical experts be included early and throughout the negotiation process to provide input on therapeutic alternative(s) and negotiation factors such as outcomes of importance and care preferences.

Response: CMS appreciates commenters' recommendation to incorporate additional opportunities for patient, caregiver, and clinician input. In this revised guidance, patients and caregivers have been added as interested parties with whom CMS may consult. CMS will host patient-focused listening sessions that will be open to the public, including patients, beneficiaries, caregivers, consumer and patient advocacy organizations, health care providers, and other interested parties to share patient-focused input on therapeutic alternative(s) and other data on the factors in section 1194(e)(2) for a selected drug and its therapeutic alternative(s). These patient-focused listening sessions will occur in Fall 2023 after the section 1194(e) data submission, which will give patients and other interested parties additional time to prepare their feedback. CMS may draw from the principles and strategies in FDA's "Patient-Focused Drug Development – Collecting Comprehensive and Representative Patient Input" guidance when facilitating patient-focused listening sessions. Additional information is forthcoming.

Negotiation Process (Section 60.4)

Comment: Some commenters suggested that interested parties should be allowed to submit new section 1194(e) data after the October 2, 2023 initial price applicability year 2026 deadline when there is good cause. Commenters also said that not allowing new data submission until the negotiation meetings could result in an inefficient process. One commenter also mentioned that some new data may be in formats that are not conducive to meetings, such as graphs and charts.

Response: CMS recognizes the interest of manufacturers to be involved early in the negotiation process beyond the section 1194(e) data submission due on October 2, 2023. CMS also recognizes the value of current and future patient and other interested parties' input in the negotiation process as well as throughout the implementation of the Negotiation Program. CMS

revised this guidance to allow for meetings after the section 1194(e) data submission deadline of October 2, 2023, where manufacturers can provide context for their submissions, and listening sessions where patients and interested parties can provide input as CMS begins reviewing data.

First, CMS would meet with the Primary Manufacturer of each selected drug once after the October 2, 2023 deadline so that the manufacturer has an opportunity to present its section 1194(e) data submission and share its perspective. These meetings will occur in Fall 2023. Primary Manufacturers may bring materials to facilitate discussion and CMS may request any materials presented afterwards. Primary Manufacturers are limited to sharing 50 pages (or a combination of pages, slides, and/or charts totaling 50 pages) of material, in order to focus the discussion on issues that can reasonably be discussed within the scope of the meeting, anticipating that these materials may contain cross-references to other material, particularly other material already submitted to CMS. This material is meant to provide context on the Primary Manufacturer's 1194(e)(1) submission and may also be used to share any new information regarding the section 1194(e)(2) data that has been identified following the October 2nd data submission.

Second, CMS will host patient-focused listening sessions for the selected drugs that would be open to the public, including patients, beneficiaries, caregivers, consumer and patient organizations, and other interested parties to share patient-focused input on therapeutic alternatives and other section 1194(e)(2) data regarding selected drugs. Interested parties may also use these listening sessions to orally share new information regarding the section 1194(e)(2) data that has been identified since the October 2nd deadline. These patient-focused listening sessions will occur in Fall 2023 after the section 1194(e) data submission deadline, which will give patients and other interested parties additional time to prepare their input. Additional information about these listening sessions will be shared in the future.

Manufacturers are required to provide information on the non-FAMP and information required to carry out negotiation (i.e., the section 1194(e)(1) data), by October 2, 2023 for initial price applicability year 2026. CMS expects Primary Manufacturers to submit information that is complete and accurate by this deadline. Information shared during the Primary Manufacturer meetings described above and materials shared afterwards should only contextualize the Primary Manufacturer's October 2nd section 1194(e)(1) submission; new section 1194(e)(1) data will not be considered. But, as described above, new information on section 1194(e)(2) data will be considered. Similarly, patients, beneficiaries, caregivers, consumer and patient advocacy organizations, and other interested parties may provide contextual information on their October 2nd section 1194(e)(2) data submission and/or share new section 1194(e)(2) data.

Comment: Some commenters recommended that CMS should allow negotiation meetings to happen throughout the negotiation period (i.e., between the publication of the selected drug list through the conclusion of negotiations), and not just in the situation when a manufacturer's counteroffer is rejected. A few commenters suggested specific periods during the negotiation process where CMS should hold meetings with manufacturers of selected drugs, such as after drug selection and prior to the initial offer.

Response: In response to comments requesting the opportunity to provide additional section 1194(e) data submissions to inform CMS' initial offer and negotiations after October 2, 2023, concerns about the tight timeline for data submission, and recommendations to remove any meeting caps and allow meetings throughout the negotiation period, CMS has revised this guidance to allow for manufacturer meetings and patient-focused listening sessions after the October 2, 2023 deadline. CMS would hold one meeting with the Primary Manufacturer of each selected drug to allow the Primary Manufacturer to provide context for the section 1194(e) data submission as CMS reviews the submitted data and develops its initial offer. The patient-focused listening sessions will be open to patients, beneficiaries, caregivers, consumer and patient advocacy organizations, and other interested parties and will invite attendees to share patient-focused input on therapeutic alternatives and other section 1194(e)(2) data regarding selected drugs. Manufacturer meetings and patient-focused listening sessions will occur in Fall 2023. CMS will schedule the meeting with the Primary Manufacturer once the selected drug list is published, and more information will be forthcoming from CMS regarding the patient-focused listening sessions after the selected drug list is published.

Comment: Some commenters stated that limiting negotiation meetings to a maximum of three meetings is restrictive and recommend that CMS allow for more exchanges throughout the negotiation period. One commenter asked that CMS make the meetings more transparent through recorded minutes, records of attendees, and allow any interested party to participate.

Response: The timeline for the negotiations extends from February 1, 2024, the statutory deadline for CMS to make the initial offer on a selected drug to a manufacturer, to July 31, 2024, a total of six months. The statutory deadline for the conclusion of negotiations is August 1, 2024. Up to three negotiation meetings with the manufacturer can occur. During these meetings, the Primary Manufacturer may provide context on the section 1194(e) data submission and additional relevant input on CMS' initial offer and the Primary Manufacturer's counteroffer as CMS reviews data and develops its final offer. Additional meetings (i.e., more than the maximum of three) during the negotiation period after the Primary Manufacturer's counteroffer, if applicable, are not feasible due to time constraints.

As part of the public explanation of the MFP, CMS will publish redacted information on any negotiation meetings that occur if a Primary Manufacturer's counteroffer is rejected.

As mentioned in the responses to the comments directly above, CMS is adding one meeting for each manufacturer and listening sessions for other interested parties after the data submission deadline and before CMS' initial offer is made. These meetings will allow Primary Manufacturers and other interested parties to share their perspectives as CMS reviews data and develops initial offers.

Comment: A few commenters suggested that CMS provide justifications for counteroffer responses and not just initial offers.

Response: CMS thanks these commenters for their feedback. Section 1194(b)(2)(D) of the Act requires that CMS provide the manufacturer with a written response to the manufacturer's counteroffer. CMS believes that if CMS declines the Primary Manufacturer's counteroffer and

offers a meeting, the first meeting between CMS and the Primary Manufacturer will provide an opportunity for CMS to explain its rationale for not accepting the manufacturer's counteroffer.

Comment: Some commenters asked that CMS' justification of its initial offer be meaningful and explain how CMS arrived at the offer. Commenters mentioned that the justification should include sources CMS referenced, section 1194(e) data considered and how they were weighted, therapeutic alternatives considered, interested parties consulted, and benefits and impacts of the drugs considered. One commenter asked that CMS issue a template for the initial offer justification in the final guidance.

Response: CMS thanks these commenters for their feedback and will consider the suggestion to include the information listed in the comment above when developing initial offers and concise justifications for selected drugs. Section 1194(b)(2)(B) of the Act directs CMS to provide a "concise justification" to the Primary Manufacturer when the initial offer is made. CMS will include information that helps the Primary Manufacturer understand the range of evidence and other information submitted pursuant to section 1194(e) that CMS found compelling in developing its initial offer. Because this information will be shared with the Primary Manufacturer, CMS believes the concise justification will be meaningful and provide information that will enable the manufacturer to develop its counteroffer. CMS does not plan on issuing a template for the initial offer or the concise justification but will release redacted information regarding the initial offer with the MFP explanation no later than March 1, 2025.

Comment: One commenter suggested that CMS issue a confidential report to manufacturers alongside the initial offer and concise justification. This confidential report would make manufacturers aware of section 1194(e)(2) data submitted by other interested parties and allow manufacturers to use that information in counteroffers, if applicable, and in future data submissions.

Response: CMS understands that manufacturers may benefit from awareness of section 1194(e)(2) data submitted by other interested parties during the negotiation period and that all interested parties would value receiving access to this information ahead of data submission for initial price applicability year 2027. CMS revised this guidance to state that CMS will aim to share with the Primary Manufacturer of a selected drug the section 1194(e)(2) data received from other interested parties during the negotiation period when feasible. These data will be appropriately redacted and will not include proprietary information, protected health information (PHI) / personally identifiable information (PII), or information that is protected from disclosure under other applicable law. If an MFP is reached during the negotiation period, CMS will issue the public explanation of the MFP no later than March 1, 2025. As part of this public explanation, CMS will share redacted information regarding the section 1194(e) data received, exchange of offers and counteroffers, and the negotiation meetings, if applicable. This redacted information will not contain any proprietary data, as described in section 40.2.1 of this guidance, PHI / PII, or other information that is protected from disclosure under other applicable law. However, as described in section 40.2.1, if a Primary Manufacturer chooses to disclose any material that is made public that CMS has previously deemed to be proprietary information of that Primary Manufacturer, CMS will no longer consider that material proprietary and will not redact it in the public explanation.

Comment: A few commenters asked CMS to commit to responding to counteroffers within 30 days of receipt. Commenters also recommended CMS give manufacturers at least 30 days to review and comment on CMS' response to counteroffers and asked CMS to consider these comments before setting the MFP.

Response: Section 60.4.3 of this revised guidance reaffirms the statement from section 60.4.4 of the initial memorandum that CMS will provide a written response to the manufacturer's counteroffer, if applicable, no later than 30 days after the receipt of the manufacturer's counteroffer. CMS made minor revisions to section 60.4.3 to clarify that CMS will respond in writing no later than 30 days after receipt of a manufacturer's counteroffer regardless of the nature of the response.

CMS declines to revise the guidance to allow manufacturers 30 days to review and comment on CMS' response to counteroffers. If a manufacturer's counteroffer is rejected, negotiation meetings with the Primary Manufacturer and CMS will span from approximately April 1, 2024 to June 28, 2024. This period exceeds 30 days and will give Primary Manufacturers the opportunity to comment on CMS' response to the counteroffer in negotiation meetings.

If applicable, CMS will issue a "Notification of Final Maximum Fair Price Offer" no later than July 15, 2024, and require Primary Manufacturers to respond to this final offer by July 31, 2024. Although this turnaround is less than 30 days, it will come at the end of approximately six months of negotiations (February 2024-July 2024) where there will have been ample opportunity for the Primary Manufacturer to review the initial offer, respond in writing via a counteroffer, and consider the discussions that occurred within the context of up to three negotiation meetings, including any additional proposals for an MFP made by CMS.

Comment: A couple of commenters recommended CMS establish a definition for "meeting" and consider adopting a policy similar to the 2017 FDA guidance "Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products: Guidance for Industry," which details meeting criteria and has definitions for different tiers of meetings.

Response: CMS thanks these commenters for their feedback. CMS has updated the description of meeting criteria in section 60.4.3 of this guidance to provide more information on the number of permitted attendees, length of each meeting, meeting scope, and meeting logistics. CMS believes that the meetings as part of the negotiation process under the Negotiation Program have a different purpose than FDA's formal meetings under the user fee agreements and therefore has taken a different approach when defining its meeting standards.

Comment: One commenter suggested CMS allow Secondary Manufacturers to participate in the negotiation process, including negotiation meetings.

Response: CMS thanks this commenter for this feedback. As described in section 60.4.3 of this memorandum, negotiation meetings would be attended solely by representatives of both the Primary Manufacturer and of CMS. CMS will defer to the Primary Manufacturer to identify its preferred representatives it plans to have attend any negotiation meetings.

Comment: One commenter stated that if CMS and a manufacturer engage in bona fide negotiations that result in no agreement, then the MFP should be set at the ceiling.

Response: CMS believes that this suggestion does not align with the statute. The statute envisions a period of negotiations that are expected to result in an agreement between the two parties on MFP by a certain date. The statute does not provide a "default" option if negotiations are not successful. This recommendation is inconsistent with the framework of the statute and would undermine the purpose of the Negotiation Program if manufacturers are assured the ceiling as long as they engage in good faith efforts to negotiate on an MFP.

Comment: One commenter suggested CMS consider issuing further guidance in the future on how data will be used in the negotiation process to determine MFP, as this may promote reaching agreements during negotiations.

Response: CMS will consider the totality of evidence throughout the negotiation period, including when developing the initial offer, reviewing a possible counteroffer, and participating in negotiation meetings when applicable. CMS will leverage the negotiation data described in section 50 to inform the methodology described in section 60.3 and the negotiation process described in section 60.4. Additional documents, such as the various ICRs associated with the Negotiation Program and this revised guidance, provide more detail related to the negotiation process and how data will be used.[19]

Application of the MFP Across Dosage Forms and Strengths (Section 60.5)

Comment: Some commenters indicated that CMS' methodology for calculating the MFP and applying it across dosage forms and strengths is overcomplicated, arbitrary, and inconsistent with the statute. Some commenters also opposed CMS' proposal to use a 30-day equivalent supply to apply the MFP across dosage forms and strengths. A few commenters expressed support for CMS' approach to applying the MFP across dosage forms and strengths, including to new NDAs, BLAs, and NDCs.

Response: CMS appreciates commenters' feedback. The statute requires a single price negotiation to agree upon an MFP for a selected drug, and contemplates that CMS will establish "procedures to compute and apply the maximum fair price across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug." As such, CMS will identify one MFP for a selected drug, which it will base on the cost of the selected drug per 30-day equivalent supply, weighted across dosage forms and strengths.

Comment: Some commenters opposed CMS' proposed approach to apply the MFP across dosage forms and strengths by calculating a WAC ratio that represents the WAC of a given dosage form and strength compared to the WAC of the whole drug. A few commenters indicated

[19] For ICRs related to the Negotiation Program, see: https://www.cms.gov/inflation-reduction-act-and-medicare/medicare-drug-price-negotiation.

that WAC is a flawed measure because it does not reflect discounts and that it changes over time. A couple of commenters recommended that CMS consider other price metrics such as AMP.

Response: CMS appreciates commenters' concerns regarding the use of the published WAC. For initial price applicability year 2026, CMS will use the WAC ratio to apply the MFP across dosage forms and strengths of a selected drug and will monitor changes to WAC relative to other pricing data, as well as shifts in utilization across dosage forms and strengths. CMS appreciates the commenters' recommendation to use AMP, but is concerned that using AMP prices in place of WAC could potentially disclose manufacturers' proprietary data. CMS recognizes there may be other ways to apply the MFP to dosage forms and strengths and will monitor whether this policy serves the intent of the Negotiation Program. As noted throughout this revised guidance, the policies described for the Negotiation Program are for initial price applicability year 2026, and CMS may consider additional policies for future years of the Negotiation Program.

Comment: Some commenters requested that for purposes of transparency and clarity, CMS provide to manufacturers the data used in MFP calculations, include example calculations in guidance, and publish a decision-making framework.

Response: CMS agrees with commenters about the importance of clarity and transparency in MFP calculations. CMS believes the discussion in sections 60.2 and 60.5 of this revised guidance sufficiently describes the methodologies CMS will use to calculate a single ceiling for a selected drug and to apply the single MFP negotiated for a selected drug across dosage forms and strengths of the selected drug (as identified at the NDC-11 level on the list of NDC-11s of the selected drug in the CMS HPMS, per section 40.2 of this revised guidance) and as such, this revised guidance does not include example calculations. However, as discussed in section 60.4 of this revised guidance, CMS will provide to the Primary Manufacturer information on the calculation of the statutorily-determined ceiling and application of a single MFP across dosage forms and strengths. However, CMS is not able to provide manufacturers with all data used in MFP calculations, as some of the calculations use proprietary pricing information.

Publication of the MFP (Section 60.6)

Comment: Some commenters recommended that the public explanation of the MFP provide details on the negotiation process, what data were considered, and how they were weighted when arriving at the final MFP. Commenters also suggested CMS share information on methodologies, therapeutic alternatives, outcomes metrics, interested parties engaged, and comparative effectiveness research considered. Several commenters also requested CMS explain how patient experience data and real-world evidence were used and how unmet need was factored in when developing the MFP. Commenters also broadly recommended that the public explanation of the MFP be transparent and detailed.

Response: CMS believes that all interested parties should have a transparent understanding of the process and rationale that CMS and the Primary Manufacturer of the selected drug used when negotiating the MFP and how that reasoning evolved over time. In addition to the data elements required by law to be submitted by the Primary Manufacturer regarding the selected drug, CMS expects robust participation by interested parties in submitting information and participating in

the patient-focused listening sessions for the selected drugs. As required under section 1195(a)(1) of the Act, CMS will publish the public explanation of the MFP for each selected drug no later than March 1, 2025. The public explanation, as described in the revised section 60.6.1 of this guidance, will include a narrative explanation of the negotiation process that occurred with that manufacturer and redacted information regarding the section 1194(e) data received, exchange of offers and counteroffers, and the negotiation meetings, if applicable, in alignment with the confidentiality policy described in section 40.2. CMS will also strive to share the section 1194(e)(2) data submitted by the public with the Primary Manufacturer of a selected drug during the negotiation period. This data will be redacted as per the confidentiality standards described in section 40.2 and will not include proprietary information, PHI / PII, or other information that is protected from disclosure under other applicable law. CMS thanks these commenters for their feedback.

Comment: A few commenters recommended CMS make the publication of the MFP and explanation clear, accessible, and transparently available for the public. These comments mention ensuring the information is easy to read, easy to access, and developed in a consumer-friendly format. A couple of commenters suggested CMS include information on how beneficiaries can access the MFP and provide a process to follow if the MFP is not honored. One commenter suggested a webpage that provides the brand name (proprietary name) and generic name (non-proprietary name) for each selected drug where there is an MFP, MFPs for all dosage forms, and the dates the prices are in effect. Another commenter suggested providing a summary in the public explanation so that patients can understand the negotiation process and what to expect when procuring a medication with an MFP.

Response: CMS thanks these commenters for their feedback regarding the publication of the MFPs of the selected drugs and explanations of those MFPs. As described in section 60.6 of this revised guidance, CMS will publish the following on the CMS website by September 1, 2024 for all initial price applicability year 2026 selected drugs where an MFP was agreed upon: the selected drug, the initial price applicability year, and the MFP pricing file for that selected drug. The MFP file will contain the MFP as applied to each selected drug at the single MFP for a 30-day equivalent supply, NDC-9 per unit price, and NDC-11 per package price and will be updated annually to show the inflation-adjusted MFP for the selected drug. CMS will also publish on the CMS website: when a drug is no longer a selected drug and the reason for that change, and situations in which an MFP between a Primary Manufacturer and CMS is not agreed upon. No later than March 1, 2025, CMS will publish the public explanation of the MFP for each initial price applicability year 2026 selected drug. CMS is committed to providing accessible educational materials to beneficiaries, and the pharmacies, mail order services and other dispensers that serve them, about the MFPs for selected drugs and how they can report a violation if they do not believe that they were able to access the MFP for a selected drug.

Comment: Some commenters urged CMS to provide as much information as legally possible when issuing the public explanation of the MFP. These commenters stated that a high level of transparency will garner confidence that the negotiated MFP is the lowest price that CMS could obtain. One commenter asked that CMS release at minimum non-FAMP, R&D costs and recoupment, and unit costs of production, and distribution. Other commenters stated that the only

information that should be withheld from public explanations are R&D costs, unit costs of production, and certain net pricing information.

Response: CMS thanks these commenters for their feedback. CMS is committed to a negotiation process that is transparent and respects confidentiality of proprietary information. CMS appreciates the need to balance both transparency in the negotiation process to assure interested parties and the public that the negotiations were conducted in a fair manner, and that CMS attempted to achieve agreement on the lowest possible MFP for the selected price for Medicare beneficiaries, with the need to maintain the confidentiality of certain information, including manufacturers' proprietary data. As part of the public explanation of the MFP, CMS will release a narrative explanation of the negotiation process and redacted information regarding the section 1194(e) data received, exchange of offers and counteroffers, and the negotiation meetings, if applicable. All information that CMS publishes as part of the public explanation and any other public documents related to the MFP and negotiation process will abide by the confidentiality policy described in section 40.2 and redact proprietary information, PHI / PII, and information that is protected from disclosure under other applicable law.

Comment: One commenter expressed concern that CMS' definition of R&D costs and recoupment was too narrow and suggested that CMS broaden its scope for R&D costs for failed and abandoned products to include all products in the relevant disease state, not just products with the same active moiety / active ingredient as the selected drug. The commenter also felt that CMS' intent to compare R&D costs and global, net revenue reported resulted in an unfair comparison, as global revenue may include products and indications without FDA approval and be supported by separate clinical trials. The commenter asked, if CMS does not revise the definitions, that CMS explain the calculation methodology and inputs in all publications regarding the negotiation process, especially the public explanation of the MFP. The commenter also said CMS should note where its definitions of concepts may differ from others.

Response: CMS thanks this commenter for this feedback. CMS believes that for the purpose of the Negotiation Program, the definition of R&D costs is sufficiently broad, as reflected in the additional revisions and clarifications made to Appendix C, as noted below. To the extent R&D costs and recoupment inform the final MFP for a selected drug, this information and how it was used will be described, with appropriate redactions for proprietary information, as part of the public explanation of the MFP. For more information on CMS' consideration of R&D costs and recoupment definitions, please see the comment and response section for Appendix C.

Comment: One commenter recommended that CMS carefully evaluate what information to include in the public explanation of the MFP and consider whether requests not to disclose some information are to protect business interests or to undermine a transparent process.

Response: CMS thanks the commenter for this feedback. CMS is committed to a transparent process and will follow the confidentiality policy as described in section 40.2 in this revised guidance when developing the public explanation of the MFP. As discussed earlier in this section, as part of the public explanation, CMS will publish redacted information regarding the section 1194(e) data received, exchange of offers and counteroffers, and the negotiation meetings, if applicable. CMS' publication of this information will abide by the confidentiality

policy described in section 40.2 and redact proprietary information, PHI / PII, and information that is protected from disclosure under other applicable law.

Comment: One commenter suggested CMS limit its disclosure of information in the public explanation of the MFP to only information that is already public information.

Response: CMS thanks the commenter for this feedback. CMS is committed to a transparent process and will follow the confidentiality policy as described in section 40.2 in this revised guidance when developing the public explanation of the MFP.

Comment: Some commenters recommended that CMS allow manufacturers to review the explanation for the MFP before it is published so that manufacturers can provide comments and raise concerns about inadvertent disclosure of confidential information.

Response: CMS recognizes the interests of the manufacturers in making sure that certain data they provided to CMS for the negotiation process remain confidential. The statute does not require disclosure of the explanations of the MFP provided to manufacturers before the explanations are made public. Additionally, section 40.2 of this revised guidance describes the information from manufacturers that CMS will consider and maintain as confidential. CMS does not intend to share the explanations of the MFP with manufacturers before releasing the explanations to the public.

Comment: Many commenters suggested that CMS publish the explanation of MFP for all selected drugs with an MFP before the statutorily defined deadline for initial price applicability year 2026 of March 1, 2025. Some commenters recommended that CMS release the explanations along with the first set of MFPs for selected drugs on September 1, 2024, while other commenters did not specify a date. Commenters suggested an earlier publication so that interested parties can review the explanation and understand CMS' negotiation process ahead of submitting section 1194(e) data for initial price applicability year 2027 by the March 1, 2025 deadline.

Response: CMS thanks these commenters for their feedback. According to the statute, the public explanation of the MFP must be published no later than March 1, 2025 for initial price applicability year 2026 selected drugs. CMS understands commenters' interest in reviewing these public explanations in advance of the deadline for manufacturers of drugs selected for negotiation for initial price applicability year 2027 to submit their information, and will strive to release the public explanation of the MFP as soon as practicable. CMS notes that the policies for initial price applicability year 2027 will be shared in future guidance, including whether the policies adopted for section 1194(e)(2) submissions for initial price applicability year 2026 will apply in a similar manner for initial price applicability year 2027, and if so, when those submissions would be due.

Comment: One commenter recommended that, in addition to the public explanation of the MFP, CMS issue a summary report for all negotiated drugs in initial price applicability year 2026 and provide data on various negotiation outcomes. The commenter also suggested a summary report

and using SSR Health and IQVIA data may avoid confidentiality concerns around data from manufacturers.

Response: CMS thanks these commenters for their feedback. In response to comments, CMS revised section 60.6.1 of this guidance so that the public explanation of the MFP now includes a narrative explanation of the negotiation process and redacted information regarding the section 1194(e) data received, exchange of offers and counteroffers, and the negotiation meetings, if applicable. CMS' publication of this information will abide by the confidentiality policy described in section 40.2 and redact any proprietary information, PHI / PII, and information that is protected from disclosure under other applicable law. CMS believes that, with these revisions, the public explanation of the MFP will be sufficiently comprehensive and will achieve the goals suggested by the commenter.

Comment: One commenter recommended that CMS publish the NDCs along with the list of MFPs for selected drugs. One commenter recommended that when CMS releases MFPs and associated data, the list should include selected drug active moieties / active ingredients, their respective NDCs, and unit-level MFPs in a structured and machine-readable format. The commenter also suggested CMS provide additional context on how CMS will use NDC-9s to calculate the unit-level MFPs for every dosage form and strength of the selected drug and how the structure and formatting of the MFP file release will be affected by FDA's proposed rule on the NDC-12 format.[20]

Response: CMS thanks the commenter for this recommendation. CMS will publish by September 1, 2024 the MFP for each drug selected for initial price applicability year 2026 for which CMS and the Primary Manufacturer have reached an agreement on an MFP. Related to this requirement, CMS will publish the following on the CMS website: the selected drug, the initial price applicability year, the MFP file (which will contain the MFP as applied to each selected drug at the single MFP for a 30-day equivalent supply, NDC-9 per unit price, and NDC-11 per package price and will be updated annually to show the inflation-adjusted MFP for the selected drug), and the explanation for the MFP (published at a later date). The MFP file will be machine-readable and in a .CSV format. While CMS understands FDA has issued a proposed rule regarding changes to the format of FDA-issued NDCs, CMS does not believe that this proposed rule is relevant to the Negotiation Program or the establishment of the MFP for initial price applicability year 2026 because the policy, if finalized as proposed, would take effect five years after the final rule is published.

Exclusion from the Negotiation Process Based on Generic or Biosimilar Availability (Section 60.7) and Establishment of MFPs After the Negotiation Deadline (Section 60.8)

CMS solicited comment on these sections, but did not receive any comments that are not otherwise addressed elsewhere (see the "Bona Fide Marketing" section below).

[20] Revising the National Drug Code Format and Drug Label Barcode Requirements, July 25, 2022, available at https://www.federalregister.gov/documents/2022/07/25/2022-15414/revising-the-national-drug-code-format-and-drug-label-barcode-requirements

Removal from the Selected Drug List (Section 70)

Comment: Some commenters recommended CMS not apply the MFP to a selected drug if CMS determines that a generic drug or biosimilar is approved and marketed after the negotiation period but before the start of initial price applicability year 2026. One commenter recommended that CMS replace a selected drug that is removed from the selected drug list. One commenter recommended that, if a generic drug or biosimilar competitor of a selected drug receives FDA approval or licensure before the end of the negotiation period, CMS should establish a grace period after the negotiation period ends (e.g., 30 days) for CMS to consider whether that generic or biosimilar has been bona fide marketed. One commenter asserted that section 1192(e) of the Act requires CMS to remove a selected drug from the selected drug list if a generic drug or biosimilar is approved and marketed before the start of the applicable initial price applicability year.

Response: CMS thanks these commenters for the recommendations. Section 1192(c), not section 1192(e) of the Act, governs the circumstances under which a selected drug would be removed from the selected drug list after the date that that list is published. Section 1192(c) of the Act requires a selected drug that is included on the selected drug list to remain a selected drug for that year and each subsequent year beginning before the first year that begins at least nine months after the date on which CMS determines the statutory criteria in section 1192(c) are met unless CMS makes the determination before or during the negotiation period that a generic drug or biosimilar product for the selected drug is approved or licensed and is marketed. CMS interprets this requirement such that a drug included on the selected drug list published for initial price applicability year 2026 will remain a selected drug for initial price applicability year 2026 unless CMS determines on or before August 1, 2024 that a generic drug or biosimilar product for the selected drug has been approved for marketing by the FDA, and that bona fide marketing exists for the generic drug or biosimilar product. If CMS determines between August 2, 2024 through March 31, 2026 that bona fide marketing exists for the generic drug or biosimilar, the selected drug would cease to be a selected drug after 2026, and no MFP would apply for 2027.

MFP-Eligible Individuals (Section 80)

Comment: One commenter recommended CMS clarify whether an MFP-eligible individual that is enrolled in Part D can receive a selected drug at the MFP if it is paid under Part B. The commenter also requested clarification that the MFP must be made available to an individual with Part D coverage, even if they choose not to use their insurance. One commenter asked CMS to detail how it will ensure access to an MFP for individuals seeking to obtain a selected drug under Part B or Part C. A couple of commenters recommended that CMS clarify that the MFP for initial price applicability year 2026 only applies when the beneficiary receives a selected drug under Part D and that the MFP does not apply when the beneficiary is administered a selected drug under Part B. One commenter stated that the definition of MFP-eligible individual includes an individual enrolled in a Medicare Advantage (MA) Plan who is furnished or administered the selected drug for which payment may be made under Part B.

Response: CMS thanks these commenters for their recommendations. CMS has clarified in section 80 of the guidance that for initial price applicability year 2026, an MFP for a selected

drug must be provided to a Medicare beneficiary who uses their Part D plan (including an MA-PD plan under Medicare Part C or an Employer Group Waiver Plan, but not a plan that receives the Retiree Drug Subsidy) if Part D coverage is provided under such plan for such selected drug. For initial price applicability year 2026, the MFP is not required to be made available to a Medicare beneficiary who uses other sources of prescription drug coverage, prescription drug discount cards, or cash. CMS has made conforming changes throughout this revised guidance to clarify the scope of the requirement to provide access to the MFP for initial price applicability year 2026. For initial price applicability year 2026, CMS does not expect manufacturers to provide access to the MFP of a selected drug to hospitals, physicians, and other providers of services and suppliers with respect to MFP eligible individuals enrolled under Part B, including an individual who is enrolled in an MA plan.

Bona Fide Marketing (Sections 30.1, 60.7, 70, and 90.4)

Comment: Several commenters supported CMS' proposal to determine whether bona fide marketing exists for a generic or biosimilar to (1) determine whether a drug should be selected as a qualifying single source drug, (2) determine whether a selected drug should be deselected, and (3) monitor in cases where a drug is not selected or after it has been deselected to ensure that bona fide marketing is still occurring. These commenters agreed with this approach to ensure that the presence in the market of a generic drug means that there is meaningful competition. Other commenters said that such monitoring is warranted given manufacturers' past market behavior, and identified certain market-limiting agreements that some brand name manufacturers have entered into with generic drug manufacturers to limit the supply of the generic drug and thus inhibit competition. The commenters maintained that such arrangements justify CMS' proposal to determine whether bona fide marketing of a generic or biosimilar is actually occurring. Some commenters suggested that CMS require that manufacturers attest that they have not entered into any agreements that would limit the market share of the generic or biosimilar products, either implicitly or explicitly. One commenter also suggested that CMS require manufacturers submit all agreements provided to the Federal Trade Commission (FTC).

Response: CMS appreciates the support for its reading of the statute to contemplate a determination by the agency that a generic drug or biosimilar is being marketed on a bona fide basis as part of drug selection, deselection, and monitoring of the Negotiation Program. CMS agrees with these commenters that manufacturers' past behavior warrants CMS review on an ongoing basis as to whether a generic drug or biosimilar is being bona fide marketed. Absent this review, a generic drug or biosimilar manufacturer could launch into the market a token or de minimis amount of a generic drug or biosimilar for the selected drug and the manufacturer of that selected drug could claim that the MFP should no longer apply. This result would be inconsistent with the text of the statute as well as its purpose, which is to lower drug prices for Medicare through either negotiation or price competition. Consistent with this statutory purpose, section 1192(e)(1) of the Act requires that a generic drug or biosimilar "is … marketed" in order for a drug or biological product to be excluded from the definition of a qualifying single source drug, and section 1192(c)(1) likewise requires that a generic or biosimilar "is marketed" in order for a selected drug to be deselected. This terminology demonstrates that Congress contemplated that a generic or biosimilar must have a continuing presence on the market in order to affect CMS' determination whether a drug should be selected as a qualifying single source drug or whether a

selected drug should be deselected. Manufacturers are welcome and encouraged to provide information to CMS about the market for generic drugs or biosimilars for the selected drug.

Comment: Many commenters stated CMS lacks statutory authority to define "marketed" for purposes of selected drug eligibility under the statute, including sections 1192(e)(1), 1192(e)(2)(B), and 1192(c) of the Act[21] differently from the first market date reported by the manufacturer to the Medicare Part D Drug Inflation Rebate Program. Further, these commenters stated that CMS lacks statutory authority to address "bona fide marketing" to implement the statutory requirement of determining if a generic or biosimilar is "approved and marketed" or "licensed and marketed" under sections 1192(c) and (e) of the Act. These commenters also asserted that CMS lacks statutory authority to review product utilization or assess "robust and meaningful competition" as part of a determination of whether a generic or biosimilar is "marketed." In addition, these commenters stated that "marketing" is already a term defined in the pharmaceutical industry, including by FDA and CMS, noting that in Appendix C of the initial memorandum, marketing is defined as the "introduction or delivery for introduction into interstate commerce of a drug product." These commenters stated that any review of "marketing" for purposes of drug selection under section 1192(e) of the Act or deselection under section 1192(c) of the Act must be based on the first "market date." One commenter stated that the IRA is not intended to review market performance across an arbitrary period of time but rather whether a generic or biosimilar is marketed at the point in time of CMS' determination of drug selection. Additionally, some commenters suggested that CMS lacks statutory authority to monitor marketing after a drug/biological is determined ineligible for selection or removed from the selected drug list.

Other commenters suggested that CMS clarify the term "bona fide marketing" and its application to the Biosimilar Delay special rule and drug selection and deselection.

Response: Section 1192 of the Act requires CMS to make a determination whether a generic drug or biosimilar "is marketed" in order to determine whether a listed drug / reference product should be selected as a qualifying single source drug or whether a selected drug should be deselected. Congress purposefully used different terminology in section 1192 than it did in section 1860D-14B of the Act, which established the new Medicare Part D Drug Inflation Rebate Program. In the latter provision, Congress referred to the date that a drug is "first marketed." The absence of similar terminology in section 1192 demonstrates that, for purposes of the Negotiation Program, Congress contemplated that a generic drug or biosimilar would have a continuing presence on the market in order to affect the status of a listed drug / reference product.

Consistent with the purpose of the statute to lower prices for Medicare through negotiation or price competition, the statute contemplates that, in making this determination, CMS would consider whether meaningful competition exists on an ongoing basis between a listed drug or

[21] These determinations include whether a drug/biologic is eligible as a qualifying single source drug under section 30.1 of this guidance and whether a selected drug should be removed under sections 60.7 and 70 of this guidance because either (1) the listed drug has an approved generic drug (under section 505(j) of the Federal Food, Drug, & Cosmetic Act) or (2) the reference product has a licensed biosimilar (under section 351(k) of the Public Health Service Act) that is marketed pursuant to that approval or license.

reference product and a generic drug or biosimilar. This determination requires more than solely token or de minimis availability of the products. For example, CMS is aware of situations in which a manufacturer of a brand name drug or biologic has entered into a market-limiting agreement with a manufacturer of a generic drug or biosimilar, where the generic drug manufacturer agrees to limit production or distribution of the generic version of the drug, such that only a nominal quantity of product is allowed to enter the market. The result is a lack of meaningful price competition, and in that circumstance the generic drug or biosimilar is not "marketed" within the meaning of that term as it is used in the IRA.

Given the Negotiation Program is targeted at single source drugs and biologics that have been on the market for some time, for which no generic drug or biosimilar competition currently exists, the statutory directive would not be met if a qualifying single source drug were to avoid selection or be removed from the selected drug list where generic drug or biosimilar availability is limited by the Primary Manufacturer. It is consistent with the purpose of the statute to remove the MFP for a selected drug only when there is evidence that the selected drug or biological product is subject to meaningful competition. For example, Section 1192(e)(2)(A) of the statute provides that an "authorized generic" drug or biosimilar product "shall be treated as the same qualifying single source drug." Although an authorized generic may appear to be competing with the reference drug, authorized generics are typically marketed by the brand name drug company or another company with the brand company's permission, meaning that the relationship between the brand drug and its authorized generic is not meaningful competition in the way envisioned by Congress.

Whether such competition exists between a listed drug or reference product and a generic drug or biosimilar will depend on the totality of circumstances in existence at the time that CMS performs its function of making the determination whether a generic is being marketed. Accordingly, CMS maintains the approach in this guidance of determining if the manufacturer of the generic/biosimilar is engaged in bona fide marketing of the generic/biosimilar.

For a discussion of CMS' approach to the Biosimilar Delay rule, which under section 1192(f)(1)(A) requires CMS to make the statutory determination that there is a "high likelihood" that a biosimilar "will be licensed and marketed" within the relevant statutory time frame, see section 30.3.1 of this revised guidance.

Comment: Some commenters stated CMS lacks statutory authority to establish metrics of "sufficient quantities" and "market share" to assess bona fide marketing. These same commenters suggested these terms are vague and represent arbitrary requirements. A few commenters suggested specific thresholds that CMS could use to determine if meaningful competition exists. For example, one commenter suggested pulling a threshold from literature on competitive generic markets (which the commenter suggested is at least half of the market for small molecule drugs and at least 25 percent for biosimilars) and based on standardized prescriptions (e.g., a 30-day Part D supply) to estimate the generic drug penetration relative to the total volume of products dispensed in Medicare. Specifically, the commenter suggested the calculation of the number of standardized prescriptions dispensed for the generic product divided by the number of standardized prescriptions dispensed for the selected drug aggregated across all dosage forms and strengths, plus the number of standardized prescriptions dispensed for the

generic/biosimilar. Another commenter suggested a generic/biosimilar was effectively marketed when its market share is within a standard deviation of the mean for a given period of time since market entry and/or if its market share is at or above the mean of uptake at the point in time of CMS review regarding selection or deselection of the product.

One commenter requested CMS carefully consider what bar might be too high for a sufficient market share if certain factors of a market share are out of a manufacturer's control and limit competition, for example, this commenter said certain rebates can limit competitive entry.

Response: The statute requires CMS to determine whether a generic drug or biosimilar has been approved or licensed and is marketed pursuant to such approval or licensure for which the selected drug is the listed drug / reference product. Consistent with the purpose of the statute to lower prices for Medicare through negotiation or price competition, the statute contemplates that, in making this determination, CMS would consider whether meaningful competition exists on an ongoing basis between a listed drug or reference product and a generic drug or biosimilar. This determination requires more than solely token or de minimis availability of the products. However, CMS agrees with the commenter than CMS will not set a single specific numeric threshold for meaningful generic drug or biosimilar competition for selected drugs because CMS does not believe there is one specified threshold that would appropriately capture meaningful competition in the market for every selected drug. As described below, CMS will review multiple data sources to inform its determination whether a generic drug or biosimilar is being marketed on a meaningful basis.

CMS clarified in this revised guidance that these data sources will be reviewed holistically to determine if meaningful competition exists in the market for purposes of: (1) the identification of qualifying single source drugs for initial price applicability year 2026 (see section 30.1), (2) removal from the selected drug list before or during negotiation or after an MFP is in effect (see section 70), and (3) monitoring whether a manufacturer of a generic or biosimilar is engaged in bona fide marketing of a drug/biologic determined ineligible as a qualifying single source drug as described in section 30.1 of this guidance or removed from selection as described in section 70 of this guidance because the selected drug was the listed drug or reference biologic for a generic or biosimilar (see section 90.4). Manufacturers can provide evidence to CMS regarding the market for an approved generic drug or biosimilar that references its drug(s) to inform CMS' monitoring for bona fide marketing after a drug is not selected or after deselection.

Comment: Some commenters expressed concern regarding the time difference between the actual date of marketing and the date of CMS' determination of bona fide marketing using PDE data because of the time lag for sales to be captured in PDE data. One commenter suggested that a 12-month review period is arbitrary and CMS failed to explain why this period was selected to establish if a generic/biosimilar is marketed. Another commenter stated that the initial six months of PDE data after market entry reflect a limited uptake because Part D plan sponsors add the drug to their formulary at the 180-day CMS deadline for Part D formulary inclusion, or not at all, and additionally there is a gradual transition for product uptake by providers and patients. Another commenter stated that CMS was relying on the indicator that shows slowest generic drug uptake by relying on PDE data.

Response: CMS thanks these commenters for their feedback regarding the timing of data review. CMS chose to review data over this 12-month time period for initial price applicability year 2026 because it believes that this time range will provide a sufficient window of opportunity to demonstrate whether a generic drug or biosimilar is marketed on a continuing basis while still allowing for sufficient time for that data to inform the selected drug list published on September 1, 2023 in accordance with section 1192(a) of the Act.

While CMS appreciates commenters' concerns regarding the time lag between a generic drug's availability and the ability to detect it in PDE data resulting from filled Part D prescriptions, CMS understands that generally this timing lag is relatively short as Part D plans are instructed to submit original PDEs to CMS within 30 days following the date the claim is received or date of service (whichever is greater)[22] and the average turnaround time to date of submission is fewer days.

Under Medicare Part D rules, 42 C.F.R. § 423.120(b)(5)(iv) permits immediate substitution of a generic drug for a brand name drug on a Part D formulary, and section 1860D-4(b)(3)(I)(ii) of the Act permits removal of a selected drug if permitted by § 423.120(b)(5)(iv) (or any successor regulation). CMS expects that Part D plans would immediately substitute a generic version of the selected drug for the brand version of the selected drug. In addition, Part D sponsors may add new generic drugs and biosimilars to their formularies at any time. Thus, the Part D rules allow for relatively quick formulary substitution of generic drugs for selected drugs and the addition of generic drug and biosimilar versions of selected drugs such that both should be evident in the PDE data relatively quickly.

Nonetheless, to address commenters' concerns about the implications of any lags in timing of data used and its implications on drug selection, CMS will also review AMP[23] data at the time of the initial qualifying single source drug determination under section 30.1 of this revised guidance, any subsequent removal from selection under sections 60.7 and 70 of this revised guidance, and when monitoring whether a manufacturer of a generic drug or biosimilar is engaged in bona fide marketing of a drug/biologic determined ineligible as a qualifying single source drug as described in section 30.1 of this guidance or removed from selection as described in section 70 of this guidance because the selected drug was the listed drug or reference biologic for a generic drug or biosimilar under section 90.4 of this revised guidance. AMP data may capture sales transactions in the supply chain in situations when use of the generic drugs in Part D plans has not yet become evident in the PDE data. A drug's AMP units (which represent manufacturer sales to retail pharmacies and wholesalers that distribute to retail community

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[22] Timely Submission of Prescription Drug (PDE) Event Records and Resolution of Rejected PDEs, Centers for Medicare & Medicaid Services, October 6, 2011, available at: https://www.hhs.gov/guidance/document/revision-previous-guidance-titled-timely-submission-prescription-drug-event-pde-records.

[23] See definition at Section 1927(k)(1) of the Act. Average Manufacturer Price (AMP) is the average price paid to manufacturers by wholesalers for drugs distributed to retail community pharmacies and retail community pharmacies that purchase drugs directly from the manufacturers. AMP was established under the Omnibus Budget Reconciliation Act of 1990 for the Medicaid Drug Rebate Program and is calculated using manufacturer sales transaction data, which include cash discounts, volume discounts, and other reductions in the actual price paid to the manufacturer. CMS receives AMP data from manufacturers that have an agreement with the Secretary of HHS as specified under Section 1927(a)(1) for all Medicaid-covered outpatient drugs on a monthly and quarterly basis, as well as data on the number of units sold by the manufacturer during those time periods.

pharmacies) are reported monthly to CMS as part of a manufacturer's reporting responsibilities under the Medicaid Drug Rebate Program. PDE data and AMP data will be reviewable once the generic drug is listed in the FDA Orange Book (using at least one dosage form and strength of the selected drug as the listed drug) or the biosimilar is listed in the FDA Purple Book (using at least one dosage form and strength of the selected drug as the reference product).

Comment: A few commenters requested CMS include other data sources in addition to PDE data, such as data from NADAC, IQVIA, and DailyMed data; determinations of national market share; presence at distributors and in group purchasing organization (GPO) contracts; and presence on formularies, to determine the presence of a marketed generic or biosimilar for the selection and/or deselection of a drug or biologic. One commenter requested that CMS permit manufacturers to certify the status of the marketing of generic drugs and biosimilars and determine this marketing status on an ongoing basis.

Response: CMS thanks these commenters for these suggestions of additional sources that may include useful information to demonstrate bona fide marketing of a generic drug or biosimilar. The determination whether a generic drug or biosimilar is being bona fide marketed on an ongoing basis is a totality-of-the-circumstances inquiry that will not necessarily turn on any one source of data. Manufacturers of selected drugs can provide evidence to CMS regarding the market for the generic drug or biosimilar versions of their selected drug(s) to inform CMS' monitoring for bona fide marketing before drug selections are made, or after deselection. In addition to also reviewing AMP data, given commenters' suggestions to include additional examples of such other data that may be used, CMS clarified in sections 70 and 90.4 of this guidance (with application to sections 30.1 and 60.7 by way of cross-reference to the discussion of bona fide marketing), that CMS will use multiple sources, including but not limited to, the examples as described in sections 70 and 90.4 of this revised guidance to determine if bona fide marketing exists of the generic drug or biosimilar under review. This monitoring will ensure that drugs and biologicals ineligible for selection or removed from selection are subject to competition from generic drugs and biologicals that are marketed on a meaningful basis. CMS retains the right to consider other data in monitoring if manufacturers of the applicable generic drug or biosimilar continue to engage in bona fide marketing once a selected drug is deselected.

Comment: A few commenters encouraged CMS to monitor for manufacturing and/or marketing arrangements that intend to limit generic competition. One commenter suggested that a drug or biologic should remain eligible as a selected drug, so long as the drug or biologic otherwise qualifies, in the presence of limited distribution agreements. Another commenter suggested CMS publish arrangements that CMS views as limiting competition as a component of monitoring bona fide marketing. A couple of commenters stated that monitoring of market competition is not within CMS' authority and cited FTC and FDA regulatory frameworks to address biosimilar and generic competition.

Response: CMS thanks these commenters for these suggestions. CMS believes that limited-distribution agreements can in fact limit the supply of an available generic drug. CMS reiterates that, for the purposes of the Negotiation Program, the statute instructs CMS to make a determination whether a generic drug or biosimilar "is marketed," which requires a determination whether the generic drug or biosimilar has a continuing presence on the market.

Congress used this language in furtherance of the purpose of the Negotiation Program, which is to lower costs for Medicare through negotiation or price competition. The statute accordingly contemplates that CMS' determination will turn on a finding whether meaningful market competition for such given generic drug or biosimilar biological product exists. While these market-limiting agreements may make CMS aware of a limitation on meaningful market competition, these agreements do not necessarily inform the agency whether such a limitation is manifesting itself in the marketplace. For this reason, CMS intends to monitor actual conditions in the marketplace through PDE and AMP data. However, as commenters suggest, CMS may consult with FTC to identify the types of agreements or arrangements that limit competition. FDA does not receive agreements of this type in the normal course of its operations.

Comment: One commenter asked what action might result if CMS determines through monitoring that a generic drug/biosimilar manufacturer is not engaging in bona fide marketing after CMS determined that there was an applicable generic drug/biosimilar for which the manufacturer was engaged in bona fide marketing.

Response: If the reason for disqualification as a qualifying single source drug is removed, the drug/biologic could be eligible for negotiation in a future price applicability year.

Comment: One commenter requested CMS evaluate whether its monitoring approach accurately captures true competition and whether any specific types of drug marketing/distribution agreements limit generic competition and include in this review the impact on payers, providers and insurers. A few commenters generally expressed concerns about potential impacts they suggested that the Negotiation Program might have on generic drug markets, which they suggested could broadly include reducing the impact to a manufacturer of being the first filer for generics, promoting pricing via negotiation in lieu of market competition, or deterring generic competition and increasing drug pricing costs to payers in certain drug market segments.

Response: CMS thanks these commenters for their input and will keep these comments in mind as CMS implements the Negotiation Program and monitors for bona fide marketing over time.

Monitoring Compliance and Civil Monetary Penalties (Sections 90.1 and 100)

Comment: Many commenters requested additional details regarding the scope and amount of the CMPs, detailed procedures for determining violations and imposing fines, and a review and appeal process for determinations of noncompliance prior to the imposition of CMPs and initiation of the procedures described in section 1128A of the Act. Additionally, some commenters suggested CMS undertake notice and comment rulemaking to provide the process steps and requirements of involved parties prior to imposing any CMPs, and a few commenters requested that CMS use a single notice and comment rulemaking process to capture all instances of CMP triggers under the IRA. A few commenters instructed CMS to look to examples of CMP application in other CMS programs, including Medicare Advantage and the HHS Office of the Inspector General (HHS OIG), when establishing its procedures for the Negotiation Program. A couple of commenters suggested that the dollar amount required by the IRA for a CMP requires rulemaking under the Excessive Fines Clause of the Eighth Amendment of the U.S. Constitution. A few commenters requested a delay in the implementation of CMPs until rulemaking occurs.

Response: CMS appreciates the concern for ensuring that administration of CMPs under section 1197 of the IRA and in accordance with the requirements of section 1128A of the Act is achieved via defined procedures, and appreciates the suggestions offered by commenters. In this revised guidance, CMS has provided additional information about compliance violations that may result in CMPs being issued; the notification process surrounding compliance violations, including reminders, warnings, Notices of Potential Noncompliance, and formal CMP Notifications; and has provided a series of informative example scenarios on the scope and calculation of CMPs when applicable. CMS has also added detail to the CMP Notification process, following the requirements of section 1128A of the Act. CMS directs commenters to section 100 of this guidance for additional information. CMS reviewed examples of CMP processes in other CMS programs to develop the procedures outlined in this guidance. The amounts of CMPs are defined in section 1197 of the IRA and will be applied accordingly. CMS defines the start date and end dates for calculating violations in section 100.2 of this revised guidance.

Sections 11001(c) and 11002(c) of the IRA provide that the Secretary "shall implement" the Negotiation Program "for 2026, 2027, and 2028 by program instruction or other forms of program guidance." Thus, the initial memorandum is not subject to the notice-and-comment requirement of the Administrative Procedure Act or the Medicare statute. Section 1197 of the Act indicates violations that warrant a CMP. This guidance is consistent with the statutory requirement to use program guidance to implement the Negotiation Program for 2026, 2027, and 2028 and to impose certain penalties for violations of the Negotiation Program.

Comment: Some commenters requested that CMS share information with the Primary Manufacturer in advance of the notice of imposition of a CMP and permit the Primary Manufacturer to cure the violation for which a CMP could be imposed. Some commenters also requested a reasonable time period be specified for this cure period and a process be provided to appeal a finding of noncompliance, including as a means to safeguard against a perceived or actual legal or factual error of CMS.

Response: CMS has added in this revised guidance additional details about how Primary Manufacturers will have an opportunity for corrective action in applicable circumstances. For example, CMS revised section 100.2 of this revised guidance to clarify that CMS may request additional information to administer or monitor compliance with the Negotiation Program in accordance with section 1193(a)(5) of the Act. In addition, CMS will issue a written reminder of the impending deadline for submission of information to include a warning of potential liability for a CMP upon failure to comply with the deadline.

Comment: A few commenters expressed support for the IRA's inclusion of CMPs to support the negotiation of the MFP.

Response: CMS thanks these commenters for their feedback.

Comment: Some commenters raised concerns regarding the application of CMPs to Primary Manufacturers due to the actions of a Secondary Manufacturer that does not provide data

required under section 1194(e)(1) of the Act or the action of other third parties, including pharmacies and providers, that do not provide access to the MFP for MFP-eligible individuals. A few commenters requested CMS limit the imposition of CMPs to only a Primary Manufacturers' actions, or alternatively, refrain from enforcement of the CMP on a Primary Manufacturer for a third party's actions in initial price applicability year 2026. One commenter suggested a Primary Manufacturer be able to raise a defense against a CMP when the violation at issue was committed by a Secondary Manufacturer. A few other commenters supported monitoring and imposition of CMPs on third parties via the Primary Manufacturer, and one commenter encouraged CMS to monitor Secondary Manufacturers directly.

Response: CMS appreciates commenters' feedback regarding the imposition of a CMP on the Primary Manufacturer based on the actions of a Secondary Manufacturer or other third party. Per section 40 of this revised guidance, a Secondary Manufacturer is defined as either (1) a manufacturer listed in an NDA or BLA for the selected drug or (2) an entity that has entered into an agreement with the Primary Manufacturer to market the selected drug. A Secondary Manufacturer will include any manufacturer of any authorized generics and any repackager or relabeler of the selected drug that meet these criteria. As such, a Primary Manufacturer may be required to request data from a Secondary Manufacturer including non-FAMP, current unit costs of production and distribution, and certain market data elements. As described in section 1193 of the Act (described in section 40 of this revised guidance) and included in the Manufacturer Agreement, the Primary Manufacturer is also responsible for ensuring access to the MFP for MFP-eligible individuals and to pharmacies, mail order services, and other dispensers that dispense the selected drug to an MFP-eligible individual. Because CMS is entering into the Agreement with the Primary Manufacturer, it is the Primary Manufacturer that will be responsible for adhering to the terms of the Agreement. CMS believes the Primary Manufacturer, based on its arrangements with Secondary Manufacturer(s), can reasonably ensure that the Primary Manufacturer can comply with its Negotiation Program obligations with regards to data submission and ensuring the availability of the MFP for the selected drug sold by a Secondary Manufacturer(s). CMS is not aware of circumstances where a Secondary Manufacturer can operate without a formal arrangement of the Primary Manufacturer, through which the Primary Manufacturer can ensure compliance by the Secondary Manufacturer.

As is clarified in section 100 of this revised guidance, CMS will provide an opportunity for corrective action in certain instances of potential violation prior to imposing CMPs, which may provide Primary Manufacturers an opportunity to mitigate noncompliance related to Secondary Manufacturers in applicable situations.

Comment: One commenter requested CMS identify a pathway by which third parties could provide information regarding potential violations to CMS for investigation, while another commenter suggested an online form and toll-free phone number be established for consumer complaints on MFP availability.

Response: CMS appreciates commenters' feedback. CMS will establish a dedicated telephone line and/or e-mail inbox for interested parties to report any perceived MFP availability violations. Section 90.1 provides additional information regarding monitoring of manufacturer compliance. CMS anticipates providing more information on public monitoring in the future.

Comment: Several commenters requested CMS provide information about how CMS will interpret the term "knowingly" with regard to knowingly providing false information under section 100.3 of this guidance and as applicable to violations of the Agreement under section 100.2 of this guidance. Some commenters requested that CMS interpret "knowingly" based on a plain meaning of the term or uses by other CMS programs, OIG and the False Claims Act, while others requested CMS require "actual knowledge" of the act or omission.

Response: CMS appreciates these comments. After considering the comments received, CMS has adopted a standard for "knowingly" within the context of the Negotiation Program that conforms with the HHS OIG definition at 42 C.F.R. § 1003.110. Specifically, "knowingly" is interpreted to mean that a person, with respect to an act, has actual knowledge of the act, acts in deliberate ignorance of the act, or acts in reckless disregard of the act, and no proof of specific intent to defraud is required. CMS adopts this standard for "knowingly" in section 100.3 of this revised guidance for purposes of whether a manufacturer knowingly provides false information under the procedures to apply the aggregation rule in section 1192(d)(2)(B) of the Act for the Small Biotech Exception and whether any Biosimilar Manufacturer knowingly provides false information under the procedures to apply the aggregation rule in section 1192(f)(1)(C) of the Act for the Biosimilar Delay, as provided in section 1197(d) of the Act.

In applying CMPs, CMS intends to use discretion such that CMPs are reserved for instances of substantive noncompliance. These violations do not necessarily require the violation to be "knowing." Based on statutory requirements, CMS has clarified in section 100.2 that CMS maintains the authority to issue CMPs for substantive violations of the Agreement even in cases that violations are not "knowing."

Comment: Several commenters raised concerns that the detailed and numerous Primary Manufacturer data submission requirements under the Agreement will result in violations of compliance unintended by the Primary Manufacturer unless CMS allows for Primary Manufacturers to submit data based on a reasonable assumption of the IRA statutory data requirements.

Response: CMS appreciates commenters' feedback regarding the perceived potential for CMP liability based on unintended noncompliance with data submission requirements as set forth in section 1194(e)(1) and section 50 and Appendix C of the initial memorandum. As previously noted, CMS clarified in section 100 of this revised guidance that CMS will provide manufacturers with an opportunity, via the Notice of Potential Noncompliance, for corrective action in certain instances of potential violation prior to determining whether to impose a CMP. CMS has also provided responses regarding data submissions within the responses to Appendix C comments, including revisions to Appendix C definitions in response to commenters' requests for clarifications (e.g., unit type for non-FAMP, patents to be included). CMS also directs commenters to the 30-day notice for public comment on the Negotiation Data Elements ICR (CMS-10847 / OMB 0938-NEW), which incorporates revisions to instructions in response to comments CMS received in response to the 60-day notice for public comment. CMS is not adopting the recommendation that Primary Manufacturers submit a statement of reasonable assumptions with submissions under section 1194(e)(1) of the Act or otherwise use reasonable

assumptions in lieu of the definitions in Appendix C of this revised guidance. Submitted data must align with the instructions in CMS' Negotiation Data Elements ICR and the definitions in Appendix C of this guidance to ensure that the data submitted by Primary Manufacturers are based on consistent definitions and scope.

Part D Formulary Inclusion of Selected Drugs (Section 110)

Comment: Many commenters expressed support for requiring selected drugs to be included on Part D formularies. Several other commenters noted that the IRA does not detail how selected drugs should be included on formularies; therefore, CMS should confirm plan formulary flexibilities for selected drugs. A few commenters also requested CMS clarify when the formulary inclusion requirement would not apply, such as when a selected drug is excluded from negotiation because of the introduction of a generic or biosimilar competitor. Additionally, a couple of commenters expressed concern that mandating inclusion of selected drugs on Part D formularies—without establishing guardrails to ensure beneficiary access—could create perverse incentives because plans could place selected drugs on less favorable tiers compared to non-selected drugs. Finally, a couple of commenters requested CMS clarify that it will not require that Part D formularies include every dosage form and strength of a selected drug, noting that plans could comply with the IRA if only one dosage form and strength of the selected drug is included. One commenter stated Congress did not intend that every dosage form and strength of a selected drug be included on formularies.

Response: CMS appreciates commenters' feedback and agrees with commenters about the importance of ensuring meaningful beneficiary access to selected drugs and their MFPs and ensuring that plans do not engage in gaming behavior. CMS shares concerns that Part D sponsors may be incentivized in certain circumstances to disadvantage selected drugs by placing selected drugs on less favorable tiers compared to non-selected drugs, or by applying utilization management that is not based on medical appropriateness to steer Part D beneficiaries away from selected drugs in favor of non-selected drugs. CMS expects Part D sponsors to provide their enrollees with meaningful access to selected drugs and will use its comprehensive formulary review process to assess any practices that may undermine beneficiary access to selected drugs, as discussed in section 110 of this guidance. CMS maintains a robust, clinical formulary review process to ensure that all Part D plan formularies comply with statutory and regulatory requirements, including the requirement under section 1860D-11(e)(2)(D)(i) of the Act that CMS may only approve a Part D plan if it "does not find that the design of the plan and its benefits (including any formulary and tiered formulary structure) are likely to substantially discourage enrollment by certain Part D eligible individuals under the plan." Further, if CMS identifies that Part D sponsors are not providing beneficiaries with meaningful access to selected drugs, CMS may consider implementing new requirements for future contract years. CMS believes this approach will provide Part D sponsors with the flexibility to continue to manage costs when clinically appropriate while allowing CMS to monitor practices that may undermine enrollee access to selected drugs and inform further action, as necessary.

Section 1860-D-4(b)(3)(I) of the Act requires Part D plan formularies to include each covered Part D drug that is a selected drug under section 1192 of the Act for which an MFP is in effect with respect to the year. Accordingly, all dosage forms and strengths of the selected drug that

constitute a covered Part D drug and for which the MFP is in effect must be included on formulary. In response to the comments requesting clarification on when the formulary inclusion requirement would cease to apply, CMS refers readers to section 70 of this revised guidance, which, in accordance with section 1192(c) of the Act, details when a selected drug will cease to be a selected drug because CMS determines that a generic or biosimilar competitor to the selected drug has been approved or licensed and marketed pursuant to such approval or licensure. CMS notes that, as specified by section 1860D-4(b)(3)(I)(ii) of the Act, nothing shall prohibit a Part D sponsor from removing a selected drug from a formulary if such removal would be permitted under 42 C.F.R. § 423.120(b)(5)(iv) (or any successor regulation).

Comment: A couple of commenters stated CMS should require selected drugs to be placed on lower (preferred) formulary tiers, noting that this would reduce out-of-pocket costs for beneficiaries. A couple of commenters recommended CMS ensure parity between selected drugs and non-selected drugs, such as requiring plans to cover selected drugs on the most favorable tier as any brand name drug in the therapeutic class. One commenter stated CMS should require plans to place selected drugs on lower or equivalent tiers as their competitors. A few commenters indicated that selected drugs should be placed on formulary tiers with copayments rather than coinsurance to help beneficiaries plan for their drug expenses. One of these commenters added CMS should prohibit plans from placing selected drugs on tiers that require coinsurance. Finally, one commenter recommended CMS use the specialty tier cost threshold to determine tier placement of selected drugs. Specifically, selected drugs with monthly costs less than the specialty tier threshold could be placed on the lowest generic tier and selected drugs with monthly costs greater than the threshold could be placed on higher copayment tiers.

Response: CMS appreciates commenters' feedback. For contract year 2026, CMS is not implementing explicit tier placement requirements for selected drugs, but section 110 of this revised guidance indicates how CMS will use its formulary review process to assess potentially concerning review findings. CMS generally expects that Medicare beneficiaries taking selected drugs will benefit from the lower negotiated MFPs. While CMS understands that not all selected drugs and drug classes will present Part D sponsors and their Pharmacy & Therapeutics (P&T) Committees with the same formulary considerations and might not warrant the same formulary placement in all situations, CMS is concerned that Part D sponsors may be incentivized in certain circumstances to disadvantage selected drugs by placing selected drugs on less favorable tiers compared to non-selected drugs. To help ensure that beneficiaries have meaningful access to selected drugs and consistent with the agency's statutory obligation to monitor plan compliance with all applicable formulary requirements, CMS will use its formulary review process to assess any instances where Part D sponsors place selected drugs on non-preferred tiers or where a selected drug is placed on a higher tier than non-selected drugs in the same class. As discussed in section 110 of this revised guidance, as part of the annual bid review process, CMS will expect Part D sponsors to provide CMS with a reasonable justification to support the submitted plan design that includes any such practices. This justification should address applicable clinical factors, such as clinical superiority, non-inferiority, or equivalence of the selected and non-selected drugs, as well as the plan design's compliance with applicable statutory and regulatory requirements (e.g., the requirement to have a cost-effective drug utilization management program that bases decisions on the strength of the clinical evidence and standards of practice). As CMS reviews Part D plan formularies to ensure they comply with statutory and regulatory

requirements, pursuant to section 1860D-11(e)(2)(D)(i) of the Act, CMS will only approve a Part D plan bid submitted by a Part D plan sponsor if CMS does not find that the design of the plan and its benefits (including any formulary and tiered formulary structure) are likely to substantially discourage enrollment by certain Part D eligible individuals under the plan. CMS believes this approach will provide Part D sponsors with the flexibility to continue to manage costs through tier placement in a clinically appropriate manner, while allowing CMS to monitor practices that may undermine beneficiary access to selected drugs and inform new requirements for future contract years.

Comment: Many commenters expressed concern that plans will use utilization management not based on medical appropriateness to steer Part D beneficiaries away from selected drugs in favor of non-selected drugs that may be associated with higher rebates. Therefore, commenters suggested CMS should limit or prohibit utilization management for selected drugs. A few commenters asserted that maintaining the ability to use utilization management will best ensure that plans can negotiate effectively with interested parties to lower prescription drug costs.

Response: CMS appreciates commenters' feedback. For contract year 2026, CMS is not implementing explicit utilization management requirements for selected drugs, but section 110 of this revised guidance indicates how CMS will use its formulary review process to assess potentially concerning review findings. CMS shares the commenters' concerns that Part D sponsors may be incentivized in certain circumstances to disadvantage selected drugs by applying utilization management that is not based on medical appropriateness to steer Part D beneficiaries away from selected drugs in favor of non-selected drugs. To help ensure that beneficiaries have meaningful access to selected drugs and consistent with the agency's statutory obligation to monitor plan compliance with all applicable utilization management requirements, CMS will use its formulary review process to assess any instances where Part D sponsors require utilization of an alternative brand drug prior to a selected drug with an MFP (i.e., step therapy) or where Part D sponsors impose more restrictive utilization management (i.e., step therapy and/or prior authorization) for a selected drug compared to a non-selected drug in the same class. As discussed in section 110 of this guidance, as part of the annual bid review process, CMS will expect Part D sponsors to provide CMS with a reasonable justification to support the submitted plan design that includes any such practices. This justification should address applicable clinical factors, such as clinical superiority, non-inferiority, or equivalence of the selected and non-selected drugs, as well as the plan design's compliance with applicable statutory and regulatory requirements (e.g., the requirement to have a cost-effective drug utilization management program that bases decisions on the strength of the clinical evidence and standards of practice). CMS reviews all Part D plan formularies to ensure they comply with statutory and regulatory requirements and, pursuant to section 1860D-11(e)(2)(D)(i) of the Act, will only approve a Part D plan bid submitted by a Part D plan sponsor if CMS does not find that the design of the plan and its benefits (including any formulary and tiered formulary structure) are likely to substantially discourage enrollment by certain Part D eligible individuals under the plan. CMS believes this approach will provide Part D sponsors with the flexibility to continue to manage costs through utilization management in a clinically appropriate manner, while allowing CMS to monitor practices that may undermine beneficiary access to selected drugs and inform new requirements for future contract years.

Comment: Many commenters expressed concern that price negotiation, combined with changes in interested party liability from Part D redesign, will have significant impacts on the structure of Part D and could negatively impact patient access to medicines. These commenters recommended CMS monitor plan formularies and the extent to which plans are using utilization management and tiering for selected drugs. Some commenters also recommended CMS update rules and guidance around plan coverage decisions and create safeguards to ensure patient access to a selected drug.

Response: CMS thanks these commenters for sharing their concerns regarding patient access to selected drugs. CMS agrees with commenters about the importance of beneficiaries having meaningful access to selected drugs. As such, as discussed in section 110 of this guidance and consistent with the agency's statutory obligation to monitor plan compliance with all applicable formulary requirements, CMS will use its formulary review process to assess (1) any instances where Part D sponsors place selected drugs on non-preferred tiers, (2) any instances where a selected drug is placed on a higher tier than non-selected drugs in the same class, (3) any instances where Part D sponsors require utilization of an alternative brand drug prior to a selected drug with an MFP (i.e., step therapy), or (4) any instances where Part D sponsors impose more restrictive utilization management (i.e., step therapy and/or prior authorization) for a selected drug compared to a non-selected drug in the same class. As CMS reviews Part D plan formularies to ensure they comply with statutory and regulatory requirements, pursuant to section 1860D-11(e)(2)(D)(i) of the Act, CMS will only approve a Part D plan if it does not find that the design of the plan and its benefits (including any formulary and tiered cost-sharing structure) are likely to substantially discourage enrollment by certain Part D eligible individuals under the plan. While CMS is not implementing additional tier placement or utilization management requirements for selected drugs for contract year 2026, if CMS identifies that Part D sponsors are not providing beneficiaries with meaningful access to selected drugs, CMS may consider implementing new requirements for future contract years to ensure that Part D sponsors are not undermining beneficiary access to selected drugs.

Application of Medicare Part B and D Prescription Drug Inflation Rebate Programs to Selected Drugs (Section 120)

Comment: A few commenters stated that selected drugs should not be subject to inflation rebates. These commenters pointed to the Part B inflation rebate calculation in statute to assert that Congress did not intend for rebates to apply to selected drugs.

Response: The statute provides that the inflation rebates apply to selected drugs.[24] Specifically, the rebate calculation specified in section 1847A(i)(3)(A)(ii)(I) of the Act references section 1847A(b)(1)(B) of the Act, which includes payment for selected drugs. That is, there is no statutory exemption from inflation rebates for selected drugs. Note that CMS intends to issue final guidance relating to the Part B and Part D inflation rebates later in 2023.

Comment: Commenters requested clarification regarding the application of inflation rebates to selected drugs. One commenter asked CMS to clarify how MFPs will be factored into the inflation rebate calculations for selected drugs under the Part B and Part D programs. Another

[24] See sections 1847A(i) and 1860D-14B of the Act.

commenter urged CMS to issue guidance to ensure that the Negotiation Program and Part B Inflation Rebate Program do not have an interactive effect, and that inflation rebates should only apply when the manufacturer has increased its price.

Response: Section 120 of this guidance clarifies that the MFP for a selected drug is not included in the AMP for the selected drug and thus will not affect the Part D inflation rebate calculation.[25] CMS will provide additional information about how Part B inflation rebates apply to selected drugs in future guidance.

Appendix C: Definitions for Purposes of Collecting Manufacturer-Specific Data

Comment: Some commenters stated that the proposed framework for CMS' data collection and corresponding definitions to capture information required in sections 1194(e)(1) and (2) of the Act lacks the flexibility necessary to accommodate unique characteristics of different drugs/products that will be reviewed through the Negotiation Program. These commenters requested CMS rescind the proposed definitions and permit manufacturers to provide statutorily required data submissions based on reasonable assumptions along with a justification of such assumptions when interpreting the applicable IRA statutory requirements. Some commenters stated that because of the assumptions inherent in responding to a data request, CMS must use notice-and-comment rulemaking to provide information about required data. A few commenters raised concerns about differences between the definitions proposed in the initial memorandum and other pharmaceutical industry and/or government reporting requirements with related terms, and some commenters included specific term examples of these situations (included in other comments below). A couple of commenters expressed broad support for the definitions in Appendix C. Additionally, some commenters requested CMS allow manufacturers to provide supplemental data without text limits. Another commenter requested CMS establish a uniform starting point across data collections and not require data prior to this point because it could unfairly penalize manufacturers for previous pricing practices and data collection before the IRA went into effect.

Response: CMS thanks these commenters for articulating the considerations they will need to address when preparing to conform data submissions to the definitions provided in Appendix C of this guidance. CMS consulted with subject matter experts and federal agencies regarding the terms defined in this guidance. As already discussed herein, CMS engaged (and continues to engage) with interested parties through various platforms since passage of the IRA in August 2022. CMS has considered recommendations and suggestions in revising the definitions included in Appendix C of this guidance, which serve as the basis for the information to be collected under sections 1194(e)(1) and (2) of the Act. CMS is not adopting the recommendation that Primary Manufacturers submit a statement of reasonable assumptions with submissions under section 1194(e)(1) of the Act or otherwise use reasonable assumptions. CMS believes it is important that data submissions reflect the application of consistent standards and definitions to permit appropriate consideration of such data, timely execution of the negotiation process, and enforcement actions, as warranted. As such, data submitted in response to this revised guidance must be based on consistent definitions and scope, as reflected in Appendix C of this revised guidance. CMS appreciates the resources required to meet these submission requirements. On

[25] See section 1927(k)(1)(B)(i)(VI) of the Act.

March 21, 2023, CMS released the Negotiation Data Elements ICR (CMS-10847 / OMB 0938-NEW) to detail the specific data that CMS is requesting for purposes of implementing the negotiation process to determine the MFP. The comment period in response to the 60-day notice closed on May 22, 2023. CMS is releasing a revised version of the Negotiation Data Elements ICR on June 30, 2023, and the 30-day comment period will close on July 31, 2023. The revised ICR is available here: https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847. Comments must be submitted through www.regulations.gov.

Additionally, as explained in response to comments received regarding CMS' statutory authority to issue program instruction, sections 11001(c) and 11002(c) of the IRA state that CMS "shall implement" the Negotiation Program "for 2026, 2027, and 2028 by program instruction or other forms of program guidance"; thus, this revised guidance and corresponding data collection requirements are not subject to the notice-and-comment requirements of the Administrative Procedure Act or the Medicare statute. However, CMS is following requirements pursuant to the Paperwork Reduction Act of 1995 for information collection requests related to the administration of the Negotiation Program.

Comment: A few commenters asked for clarification on the requested data elements related to R&D costs. Some commenters expressed concern that CMS' definition of R&D costs is too narrow and excludes relevant costs such as those related to acquisition, ongoing studies or monitoring of a drug, and costs related to investments in technology that may apply to multiple drugs. One commenter recommended CMS exclude from the definition of R&D costs post-marketing clinical trials that were not completed and limit consideration of spending on abandoned and failed projects to those that were conducted within a narrower timeframe. One commenter expressed concern that the 8.1 percent capital rate specified in the guidance is too low. A few commenters stated CMS' approach for calculating recoupment of R&D costs by comparing global net lifetime revenue for the selected drug with R&D costs attributable to FDA-approved indications of the selected drug is imprecise or flawed and disadvantages the manufacturer.

Response: CMS thanks these commenters for their feedback. After consideration of the comments on this guidance and the Negotiation Data Elements ICR, CMS has revised Appendix C to consolidate several R&D cost categories. Specifically, as revised, the category "Post-Investigational New Drug (IND) Application Costs" includes costs for completed, FDA-required post-marketing trials, which were previously in their own category. The category "All Other R&D Direct Costs" includes costs associated with post-marketing trials that were not completed or were conducted for the purposes of marketing claims, which were previously in their own category. In addition, CMS revised the guidance to require reporting of acquisition costs as part of R&D costs rather than market data and revenue and sales volume data. CMS also revised the definition of basic pre-clinical research costs to clarify that the relevant time period for reporting such costs begins on the later of the date of initial discovery or the date the Primary Manufacturer acquired the right to hold the NDA(s) / BLA(s) of the selected drug. This revision was made to clarify that CMS does not expect the Primary Manufacturer to submit R&D costs for the time period prior to its acquisition of the rights to the selected drug.

Acknowledging that not all costs are mutually exclusive among products and that manufacturer investments can include failed drug candidates, CMS believes that for the purpose of the Negotiation Program, the definition of R&D costs is sufficiently broad. As required in section 1194(e)(1)(A), CMS must consider R&D "costs of the manufacturer related to the [selected] drug." Expanding the definition of such costs to include failures of products with different active moieties / active ingredients or mechanisms of action or in different therapeutic classes or other non-specific innovation-related costs goes beyond considering costs related to the R&D of the selected drug and does not provide a clear accounting of drug-specific R&D expenditures. In defining R&D costs, CMS considered a multitude of sources including government reports, literature searches, the FDA website, and discussions with experts. The definition is intended to be sufficiently broad to accommodate differences in accounting policies and cost allocations across different manufacturers. Manufacturers should submit additional R&D costs not included in other R&D definitions as part of "All Other R&D Direct Costs", as applicable. The 8.1 percent capital rate is consistent with assumptions used by the Congressional Budget Office in an April 2021 study on R&D in the pharmaceutical industry.[26]

CMS appreciates commenters sharing their concerns regarding comparisons of global, lifetime net revenue for the selected drug with R&D costs attributable to FDA-approved indications of the selected drug. CMS understands that R&D occurs globally and, as stated in the Negotiation Data Elements ICR instructions, the Primary Manufacturer must report R&D costs incurred in other countries that are related to the FDA-approved indication of a selected drug. As noted in the ICR and Appendix C of this revised guidance, R&D costs exclude costs associated with applying for and receiving foreign regulatory approvals. In response to commenters' concerns, CMS has revised Appendix C of this guidance, as well as the ICR, to clarify that CMS will consider both a Primary Manufacturer's global and also U.S. revenue when determining whether to adjust the preliminary price based on manufacturer-submitted data. Further, to align reporting of U.S. revenue with global total lifetime net revenue, CMS has (1) eliminated reporting of quarterly gross U.S. revenue and (2) replaced reporting of quarterly net revenue for the selected drug with U.S. lifetime net revenue for the selected drug.

Comment: Some commenters recommended CMS remove federal tax credits from the definition of prior Federal financial support and limit consideration of prior Federal financial support to only products with a patent application containing a Government Interest Statement and/or research where a patent assignee was a U.S. government agency. One commenter recommended that prior Federal financial support exclude indirect federal funding (e.g., provision of funding to a third party which then provides funding to the manufacturer). One commenter suggested including tax credits provided under the Orphan Drug Act and similar subsidies in addition to grants and contracts. Another commenter recommended CMS use broad definitions for "preclinical" and "novel discovery" to capture prior Federal financial support that occurs before a manufacturer acquires a viable drug product.

Response: CMS thanks these commenters for their feedback. CMS disagrees that tax credits should be excluded from the definition of prior Federal financial support. The federal government supports drug research through tax incentives. The statute does not require that CMS

[26] Congressional Budget Office, "Research and Development in the Pharmaceutical Industry," April 2021, available at https://www.cbo.gov/publication/57126.

only consider direct expenditures in prior Federal financial support or only government interest patents. CMS believes that the definition of prior Federal financial support appropriately captures industry and/or government standards in a manner that is consistent with the statutory requirements to use such information.

Comment: Several commenters raised concerns about challenges with obtaining requested information about current unit costs of production and distribution at the drug-specific level, which they stated is inconsistent with reporting requirements of other governmental bodies such as the SEC. One commenter recommended CMS allow manufacturers to use reasonable assumptions based on existing audited financial reports submitted to the SEC and/or generally accepted accounting principles. One commenter noted that it may not be able to obtain some of these data from Secondary Manufacturers. One commenter recommended CMS include channel fees in its definition of distribution costs. Several commenters recommended CMS allow manufacturers discretion to include production and distribution costs that are available to them and provide a narrative rationale for any factors they are not able to include.

Response: CMS appreciates commenters' concerns and feedback. In response to comments, CMS revised Appendix C to note that costs should be determined and reported in accordance with generally accepted accounting principles. CMS believes the Primary Manufacturer, based on its arrangements with Secondary Manufacturer(s), can reasonably ensure that the Primary Manufacturer can comply with its negotiation program obligations with regarding to data submission and ensuring the availability of MFP for selected drug sold by Secondary Manufacturer(s). CMS notes that because the agreement is between CMS and the Primary Manufacturer, it is the Primary Manufacturer's responsibility to submit certain data that will serve as the basis for offers and counteroffers. CMS declines to explicitly include channel fees in its definition of costs of distribution and notes that the definition generally refers to all (direct and allocation of indirect) costs related to packaging, labeling, and shipping operating costs for facilities and transportation. CMS refers commenters to the Negotiation Data Elements ICR for information about submitting explanations of various calculations, including unit production and distribution costs. Finally, CMS notes that the definitions of unit costs of production and distribution are intended to be sufficiently broad to account for various costs associated with producing and distributing drugs or biological products.

Comment: One commenter noted that manufacturers define kits differently than the National Council for Prescription Drug Programs (NCPDP) Billing Unit Standards that are referenced in Appendix C. This commenter recommended including the definition to avoid confusion.

Response: This revised guidance includes a footnote to provide clarification with respect to the definition of kits to be clear that CMS is adopting the NCPDP definition for kits.

Comment: Some commenters disagreed with the scope of patent and exclusivity information that CMS proposed to collect and recommended CMS clarify and narrow the scope of these reporting requirements to, for example, include only U.S. patents and applications directly related to the Primary Manufacturer and/or selected drug. Some commenters also disagreed with the patent-related definitions adopted by CMS. A few commenters requested clarity with respect to certain terms used in this section, including the meaning of patents "linked to" or "relating to"

the selected drug. One commenter recommended removing required reporting of reference product exclusivity for biologics, stating that FDA only makes this determination if there is a regulatory necessity (as opposed to at the time of approval). A few commenters also recommended CMS obtain information about approved patent applications and marketing applications from FDA resources such as the Orange Book and Purple Book and that manufacturers be allowed to reference those sources in their submissions to CMS to reduce burden. One commenter recommended CMS align its terminology and standards with other federal laws and regulations such as those of FDA.

Response: CMS thanks these commenters for their suggestions. In drafting the Patents, Exclusivities, and Approvals section of Appendix C and the Negotiation Data Elements ICR, CMS consulted with the United States Patent and Trademark Office (USPTO) and reviewed the FD&C Act and FDA regulations. After consideration of the comments, CMS has revised Appendix C of this guidance to remove certain definitions and provide additional information about the types of patents and patent applications that CMS considers to be "related to" the selected drug. While CMS understands that certain patent information is submitted to other agencies and is publicly available in the FDA Orange and Purple Books, section 1194(e)(1)(D) of the Act requires that manufacturers submit patent information to CMS. Although some of the requested data may be publicly available, CMS may not be able to ensure that such data are complete or up-to-date. Further, other information required by section 1194(e)(1)(D) of the Act, for example, information about pending patent applications, may not be publicly available. CMS understands that FDA has not made a determination of first licensure for each 351(a) biological product included in the Purple Book and that the absence of a date of first licensure in the Purple Book does not mean that a biological product on the list is not, or was not, eligible for the periods of exclusivity described under the PHS Act. CMS expects that the Primary Manufacturer will report any periods of reference product exclusivity for the selected drug to the extent the determination of exclusivity is listed in the Purple Book.

Comment: A few commenters raised concerns that CMS' definitions in the Market Data Revenue and Sales Volume Data section were too broad and burdensome given the timeframe to collect data from all Secondary Manufacturers. Some commenters opposed CMS' intent to collect certain metrics such as "U.S. commercial average net unit price" and "manufacturer average net unit price to Part D plan sponsors." A few commenters requested CMS withdraw or clarify these metrics. Some commenters also were concerned with CMS requesting data on patient assistance, noting that patient assistance is not a form of price concession or remuneration. One commenter requested CMS remove all reporting of patient assistance or, minimally, clarify that patient assistance programs are defined as charitable free drug programs. One commenter noted the definitions included vague timeframes, which could lead to data discrepancies, and recommended CMS consider including firm dates in definitions. For example, the commenter suggested clarifying "quarterly total U.S. unit volume" and providing a specific quarter on which to report, including which specific quarter in the past five years. One commenter stated that the information collected pursuant to the definitions are considered confidential and proprietary information.

Response: CMS appreciates commenters' concerns. The statute requires CMS to broadly consider market data and revenue and sales data. As noted in guidance, CMS considers these

data to include WAC, Medicaid best price, AMP, FSS price, Big Four price, and U.S. commercial average net unit price, among other data. Data related to these definitions will be considered, in part, as the basis for offers and counteroffers. CMS clarified in Appendix C that patient assistance programs include manufacturer-run patient assistance programs that provide financial assistance such as coupons or copayment assistance or free drug products. In response to comments, CMS removed the metrics "manufacturer average net unit price to Part D plan sponsors" and "quarterly total U.S. unit volume." CMS removed "manufacturer average net unit price to Part D plan sponsors" because CMS does not plan to consider this information for the purposes of developing the initial offer. CMS removed "quarterly total U.S. volume" because CMS collects this information in other questions in the Negotiation Data Elements ICR (CMS-10847 / OMB 0938-NEW). CMS refers interested parties to the revised version of the Negotiation Data Elements ICR that is open for a 30-day public comment period through July 31, 2023. With respect to the comment about confidential and proprietary information, proprietary information, including trade secrets and confidential commercial or financial information, CMS will protect the confidentiality of any proprietary information from Primary Manufacturers or Secondary Manufacturers (described in section 40.2.1) as required under section 1193(c) of the Act and other applicable law.

Timeline for Medicare Drug Price Negotiation Program Initial Price Applicability Year 2026

Date	Milestone
June 30, 2023	Revised Negotiation Program guidance is published by CMS.
July 3, 2023	Latest date to submit Small Biotech Exception request to CMS for initial price applicability year 2026.
September 1, 2023*	CMS publishes list of up to 10 selected drugs for initial price applicability year 2026 of the Negotiation Program.
October 1, 2023*	Latest date for manufacturers of selected drugs to enter into a Medicare Drug Price Negotiation Program Agreement with CMS. Manufacturers of selected drugs without an Agreement in place are referred to IRS.
October 2, 2023*	Manufacturers' section 1194(e)(1) data submissions due to CMS. All voluntary submissions of section 1194(e)(2) data are also due on this date.
Fall 2023	CMS meets with the manufacturer of each selected drug to review data submissions, subject to manufacturer's interest in such meeting.
Fall 2023	CMS holds listening sessions with patients, consumer groups, and other interested parties to obtain input on selected drugs.
February 1, 2024*	Latest date for CMS initial offers to manufacturers for selected drugs, including concise justification of the initial offer.
March 2, 2024*	Latest date for counteroffers from manufacturers, if applicable, assuming initial offer sent to manufacturer by CMS on February 1, 2024.
April 1, 2024	Latest date for CMS to act on manufacturer counteroffer, assuming counteroffer is received by CMS on March 2, 2024. CMS may accept or decline such counteroffer.
April 1, 2024	Latest date for first CMS-manufacturer negotiation meeting to be scheduled if CMS declines the counteroffer, assuming initial offer was sent by CMS on February 1, 2024.

~April 1, 2024 through June 28, 2024	Up to three possible negotiation meetings between the manufacturer and CMS to negotiate MFP for the selected drug. Meetings can begin in late March or April depending on when CMS declines the counteroffer, if applicable, and scheduling.
July 15, 2024	Latest date for final CMS MFP offers to manufacturers if MFP not agreed to during negotiations.
July 31, 2024	Manufacturer response due to CMS regarding final CMS MFP offer.
August 1, 2024*	End of negotiation period for initial price applicability year 2026. Manufacturers of selected drugs without an MFP in place are referred to IRS.
September 1, 2024*	MFPs published for up to 10 selected drugs for 2026 for which MFP agreement has been reached with the manufacturer. CMS will publish the following on the CMS website: the selected drug, the initial price applicability year, and the MFP file (which would be updated annually to show the inflation-adjusted MFP for a selected drug).
March 1, 2025*	CMS publishes explanation of MFP for each selected drug for which MFP agreement has been reached with the manufacturer. CMS will also release redacted information regarding the section 1194(e) data received, exchange of offers and counteroffers, and the negotiation meetings, if applicable.
January 1, 2026*	MFPs for the selected drugs for which MFP agreement has been reached with the manufacturer go into effect.

*Denotes statutory dates

D. Revised Guidance on Medicare Prescription Drug Negotiation Program

10. Introduction

The purpose of this revised guidance is to provide interested parties with information regarding CMS' implementation of sections 11001 and 11002 of the Inflation Reduction Act (IRA) (P.L. 117-169), signed into law on August 16, 2022, which establish the Medicare Drug Price Negotiation Program (hereafter the "Negotiation Program") to negotiate maximum fair prices (MFPs)[27] for certain high expenditure, single source drugs and biological products. The requirements for this program are described in sections 1191 through 1198 of the Social Security Act (hereafter "the Act") as added by sections 11001 and 11002 of the IRA.

Sections 11001(c) and 11002(c) of the IRA direct the Secretary of the Department of Health and Human Services (hereafter "the Secretary") to implement the Negotiation Program for 2026, 2027, and 2028 by program instruction or other forms of program guidance. In accordance with the law, the Centers for Medicare & Medicaid Services (CMS) is issuing this revised guidance for implementation of the Negotiation Program for initial price applicability year 2026.

[27] In accordance with section 1191(c)(3) of the Social Security Act, maximum fair price means, with respect to a year during a price applicability period and with respect to a selected drug (as defined in section 1192(c) of the Act) with respect to such period, the price negotiated pursuant to section 1194 of the Act, and updated pursuant to section 1195(b) of the Act, as applicable, for such drug and year.

This revised guidance is not subject to the notice-and-comment requirements of the Administrative Procedure Act ("APA") or the Medicare statute, due to the requirement in sections 11001(c) and 11002(c) of the IRA to implement the Negotiation Program for 2026, 2027, and 2028 by program instruction or other forms of program guidance. The terms "program instruction" and "program guidance" are terms of art that Congress routinely uses in Medicare statutes to refer to agency pronouncements other than notice-and-comment rulemaking. The statutory directive in sections 11001(c) and 11002(c) thus specifies that CMS shall follow policymaking procedures that differ from the notice-and-comment procedures that would otherwise apply under the APA or the Medicare statute. Congress underscored this directive by placing the Negotiation Program in the newly-enacted Part E of Title XI of the Social Security Act.

Moreover, as explained in the initial memorandum, to the extent that this revised guidance establishes or changes any substantive legal standard, CMS found that notice and public procedure on this revised guidance would be impracticable, unnecessary, and contrary to the public interest in light of the statutory requirement to implement the Negotiation Program for 2026 by program instruction and in light of the complexity of the preparation that must be undertaken in advance of the publication by September 1, 2023 of the selected drug list for initial price applicability year 2026. In particular, manufacturers need to take a number of actions well in advance of September 1, 2023, to prepare for the possibility that a drug that they manufacture might be included on the selected drug list for initial price applicability year 2026. For example, manufacturers may need to engage in internal discussions regarding whether the manufacturer would choose to participate in the Negotiation Program if its drug is included among the selected drug list published on September 1, 2023, review the template Medicare Drug Price Negotiation Program Agreement and guidance to understand Negotiation Program requirements for participating manufacturers in advance of the statutory deadline for entering agreements of October 1, 2023, and gather information for potential submission to CMS by the statutory deadline of October 2, 2023. In addition, for the reasons explained below, the deadline for a biosimilar manufacturer to submit a delay request under section 1192(f) was May 22, 2023. CMS could not have proceeded through notice-and-comment rulemaking and still provided interested parties with guidance sufficiently far in advance of these statutory deadlines to allow them adequate time to complete their preparations for participation in the Negotiation Program. Thus, CMS concluded that there was good cause to issue certain specified parts of the initial memorandum as final (i.e., section 30) without public comment and without a delayed effective date. Although CMS has endeavored to solicit public comment and to respond to comments to the extent that it would be feasible to do so consistent with the statutory deadlines for implementation of the Negotiation Program, CMS also concludes that there is good cause to issue this revised guidance as final without the 60-day period for public comment under the Medicare statute, and without a delayed effective date, in order to meet the statutory deadlines of the Negotiation Program and consistent with the authority provided to CMS in sections 11001(c) and 11002(c) of the IRA. *See* 5 U.S.C. § 553(b)(B) & (d)(3); *see also* section 1871(b)(2)(C) of the Act.

In this revised guidance, CMS has made clarifications and changes to the policies described in the initial memorandum in response to comments and based on CMS' further consideration of the relevant issues, including policies on which CMS did not expressly solicit comment.

This revised guidance describes how CMS will implement the Negotiation Program for initial price applicability year 2026 (January 1, 2026 to December 31, 2026), and specifies the requirements that will be applicable to manufacturers of drugs that are selected for negotiation and the procedures that may be applicable to drug manufacturers, Medicare Part D plans (both Prescription Drug Plans (PDPs) and Medicare Advantage Prescription Drug (MA-PD) Plans), pharmacies, mail order services, and other dispensing entities that dispense drugs covered under Medicare Part D.

If any provision in this revised guidance is held to be invalid or unenforceable, it shall be severable from the remainder of this revised guidance, and shall not affect the remainder thereof, or the application of the provision to other persons or circumstances.

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- 90.1 Monitoring of Manufacturer Compliance
- 90.2 Monitoring of Access to the MFP
- 90.3 26 U.S.C. Section 5000D Excise Tax on Sale of Designated Drugs
- 90.4 Monitoring for Bona Fide Marketing of Generic or Biosimilar Product

- Section 100 – Civil Monetary Penalties
  - 100.1 Failure of Manufacturer to Ensure Access to a Price Less than or Equal to the MFP
  - 100.2 Violations of the Agreement
  - 100.3 Provision of False Information Related to the Small Biotech Exception and the Biosimilar Delay Rule
  - 100.4 Notice and Appeal Procedures
- Section 110 – Part D Formulary Inclusion of Selected Drugs
- Section 120 – Application of Medicare Part B and Part D Prescription Drug Inflation Rebate Programs to Selected Drugs
- Appendix A – Email Template for Biosimilar Manufacturer to Indicate Intent to Submit an Initial Delay Request for Initial Price Applicability Year 2026
- Appendix B – Template for the Initial Delay Request Form
- Appendix C – Definitions for Purposes of Collecting Manufacturer-Specific Data

20. Overview

In accordance with sections 11001 and 11002 of the IRA, which created Part E under Title XI of the Act (sections 1191 through 1198), the Secretary is required to establish the Negotiation Program to negotiate MFPs for certain high expenditure, single source Medicare drugs. With respect to each initial price applicability year, CMS shall (1) publish a list of selected drugs in accordance with section 1192 of the Act; (2) enter into agreements with manufacturers of selected drugs in accordance with section 1193 of the Act; (3) negotiate and, if applicable, renegotiate MFPs for such selected drugs, in accordance with section 1194 of the Act; (4) publish MFPs for selected drugs in accordance with section 1195 of the Act; (5) carry out administrative duties and compliance monitoring in accordance with section 1196 of the Act; and (6) impose civil monetary penalties (CMPs) in accordance with section 1197 of the Act. Section 1198 of the Act establishes certain limitations on administrative and judicial review relevant to the Negotiation Program.

As noted above, in order to facilitate the timely implementation of the Negotiation Program, CMS issued section 30 of the initial memorandum as final, without a comment solicitation (with the exception of the Small Biotech Exception Information Collection Request (ICR),[28] as discussed in section 30.2.1 of this revised guidance). To allow for public input, CMS voluntarily solicited comments on all other sections of the initial memorandum except for section 90.3 (which states that the Treasury Department will issue guidance relating to the excise tax in the coming weeks), and specifically on certain topics in the initial memorandum, including:

- Terms and conditions contained in the manufacturer agreement, including the manufacturer's and CMS' responsibilities (included in section 40 of this revised guidance);

[28] This ICR was approved on May 26, 2023. Small Biotech Exception (CMS-10844; OMB Control No. 1938-1443).

- Approach for considering (1) the manufacturer-reported data elements and (2) evidence about alternative treatments (included in section 60 of this revised guidance);
- Process for the offer and counteroffer exchange between CMS and manufacturers (included in section 60 of this revised guidance);
- Content of an explanation for the MFP (included in section 60 of this revised guidance);
- Method for applying the MFP across different dosage forms and strengths of a selected drug (included in section 60 of this revised guidance);
- Dispute resolution process for specific issues that are not exempt from administrative and judicial review under section 1198 (included in section 40.5 of this revised guidance); and
- Processes for compliance monitoring and imposition of CMPs for violations (included in sections 90 and 100 of this revised guidance).

In this revised guidance, CMS has made clarifications and changes in response to comments and based on CMS' further consideration of the relevant issues, including policies on which CMS did not expressly solicit comment.

30. Identification of Selected Drugs for Initial Price Applicability Year 2026

In order to facilitate the timely implementation of the Negotiation Program in accordance with statutory deadlines, CMS issued section 30 of the initial memorandum as final, without a comment solicitation (with the exception of the Small Biotech Exception ICR, as described in section 30.2.1 of this revised guidance). While CMS did not solicit comment in response to section 30, CMS did receive many thoughtful comments, and based on these comments and further consideration of the relevant issues, CMS identified certain policies where revisions to clarify the policy described in the initial memorandum would facilitate the implementation of the Negotiation Program for initial price applicability year 2026. CMS has noted in section 30, and in the summary of key changes and clarifications, where clarifying revisions were made.

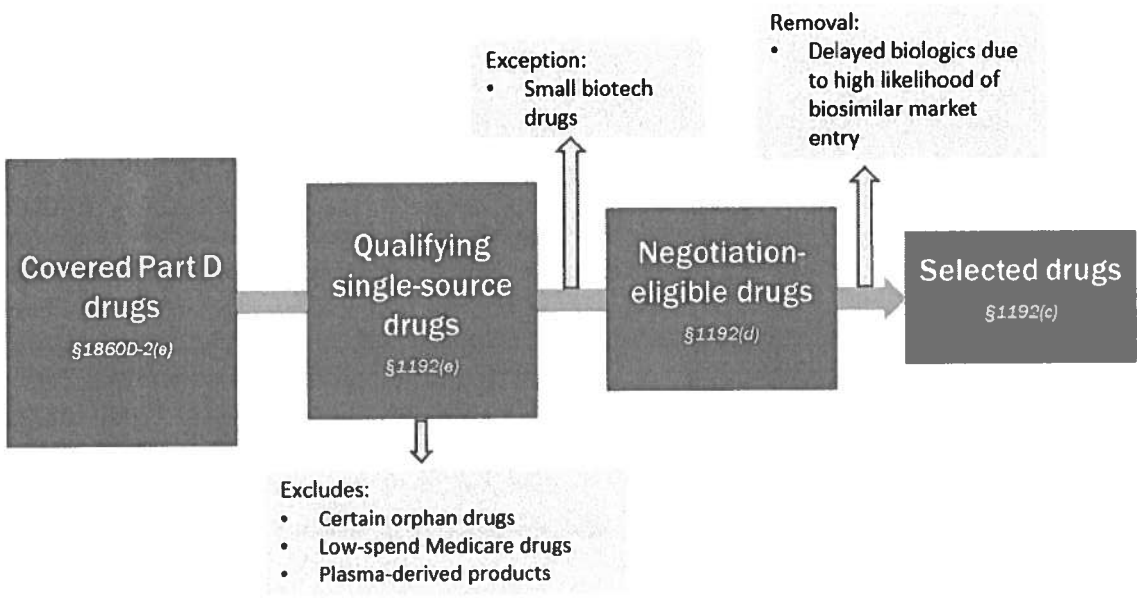
Section 1192 of the Act establishes the requirements governing the identification of qualifying single source drugs, the identification of negotiation-eligible drugs, the ranking of negotiation-eligible drugs and identification of selected drugs, and the publication of the list of selected drugs for an initial price applicability year. First, CMS will identify qualifying single source drugs in accordance with section 1192(e) of the Act, as described in section 30.1 of this revised guidance. CMS will exclude certain drugs in accordance with section 1192(e)(3) of the Act. Next, in accordance with section 1192(d) of the Act, using Total Expenditures[29] under Part D of Title XVIII for these qualifying single source drugs calculated using Part D prescription drug event (PDE) data for dates of service between June 1, 2022, and May 31, 2023, and other information described below, CMS will identify negotiation-eligible drugs for initial price applicability year

[29] For the purposes of the Negotiation Program, Total Expenditures under Part D of Title XVIII are defined in section 1191(c)(5) as total gross covered prescription drug costs (as defined in section 1860D-15(b)(3)). The term "gross covered prescription drug costs" is also defined in the Part D regulations at 42 C.F.R. § 423.308. In the initial memorandum, CMS indicated that it had proposed to update this regulatory definition of gross covered prescription drug costs to eliminate any potential ambiguity in the regulation text and help to ensure there is a consistent understanding of the term for purposes of both the Part D program and the IRA. Since the initial memorandum was issued, CMS has issued a final rule adopting the proposed revisions to 42 C.F.R. § 423.308. (See Contract Year 2024 Policy and Technical Changes to the Medicare Advantage and Medicare Prescription Drug Benefit Programs Final Rule (0938-AU96), 88 Fed. Reg. 22,120, 22,259 (Apr. 12, 2023)).

2026 as described in section 30.2 of this revised guidance (in this step, CMS will also exclude certain drugs in accordance with section 1192(d)(2) and (3) of the Act).

In accordance with section 1192(d)(1) of the Act, CMS will rank negotiation-eligible drugs for initial price applicability year 2026 according to the Total Expenditures for such drugs under Part D of Title XVIII for the 12-month period described above (described in section 30.3 of this revised guidance). In accordance with section 1192(a) of the Act and subject to the Special Rule to delay the selection and negotiation of biologics for biosimilar market entry described in section 1192(f) of the Act, CMS will select the 10 negotiation-eligible drugs with the highest Total Expenditures under Part D of Title XVIII for negotiation for initial price applicability year 2026 (described in section 30.3 of this revised guidance) and publish a list of those ten selected drugs not later than September 1, 2023 (described in section 30.4 of this revised guidance). Figure 1 provides a visual depiction of this process, and detailed guidance pertaining to this process for initial price applicability year 2026 is included below.

Figure 1: Diagram of Process for Selecting Drugs for Negotiation for Initial Price Applicability Year 2026



30.1 Identification of Qualifying Single Source Drugs for Initial Price Applicability Year 2026

For initial price applicability year 2026, in accordance with section 1192(e)(1) of the Act, CMS will define a qualifying single source drug as a covered Part D drug (as defined in section 1860D-2(e) of the Act) that meets the following criteria:

- For drug products, a qualifying single source drug is a drug (1) that is approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and marketed pursuant to such approval; (2) for which, as of the selected drug publication date with respect to a given initial price applicability year, at least 7 years have elapsed since the

date of such approval; and (3) that is not the listed drug for any drug approved and marketed under an Abbreviated New Drug Application (ANDA) under section 505(j) of the FD&C Act.

- For biological products, a qualifying single source drug is a biological product (1) that is licensed under section 351(a) of the Public Health Service Act (PHS Act) and marketed pursuant to such licensure; (2) for which, as of the selected drug publication date with respect to a given initial price applicability year, at least 11 years have elapsed since the date of such licensure; and (3) that is not the reference product for any biological product that is licensed and marketed under section 351(k) of the PHS Act.

Section 1192(d)(3)(B) of the Act states that CMS shall use data that are aggregated across dosage forms and strengths of the drug, including new formulations of the drug, such as an extended release formulation, and not based on the specific formulation, package size, or package type of the drug for purposes of determining whether a qualifying single source drug is a negotiation-eligible drug under section 1192(d)(1) of the Act and applying the exception for small biotech drugs under section 1192(d)(2) of the Act. Similarly, section 1196(a)(2) of the Act directs CMS to establish procedures "to compute and apply the maximum fair price across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug."

Identifying potential qualifying single source drugs:
In accordance with the statutory language cited above, for purposes of the Negotiation Program, CMS will identify a potential qualifying single source drug[30] using:

- For drug products, all dosage forms and strengths of the drug with the same active moiety and the same holder of a New Drug Application (NDA)[31], inclusive of products that are marketed pursuant to different NDAs. The potential qualifying single source drug will also include all dosage forms and strengths of the drug with the same active moiety and marketed pursuant to the same NDA(s) described in the prior sentence that are: (1) repackaged and relabeled products that are marketed pursuant to such NDA(s), (2) authorized generic drugs that are marketed pursuant to such NDA(s), and (3) multi-market approval (MMA) products imported under section 801(d)(1)(B) of the FD&C Act that are marketed pursuant to such NDA(s);
- For biological products, all dosage forms and strengths of the biological product with the same active ingredient and the same holder of a Biologics License Application (BLA),[32] inclusive of products that are marketed pursuant to different BLAs. The potential qualifying single source drug will also include all dosage forms and strengths of the biological product with the same active ingredient and marketed pursuant to the same BLA(s) described in the prior sentence that are: (1) repackaged and relabeled products that are marketed pursuant to such BLA(s), (2) authorized biologic products that are marketed pursuant to such BLA(s), and (3) MMA products imported under section 801(d)(1)(B) of the FD&C Act that are marketed pursuant to such BLA(s).

[30] Throughout this revised guidance, a qualifying single source drug means the specific constituent dosage forms and strengths (at the NDC-9 or NDC-11 level) that are identified as aggregated under the NDA(s) / BLA(s) for the active moiety / active ingredient as outlined in section 30.1 of this revised guidance.
[31] As described in section 505(c) of the FD&C Act.
[32] As described in section 351(a) of the PHS Act.

As an example, entity A holds three NDAs for drug products with the same active moiety approved in NDA-1, NDA-2, and NDA-3. Entity A manufactures and markets three different strengths as an immediate release tablet pursuant to NDA-1, three different strengths as an extended-release tablet pursuant to NDA-2, and three different strengths as a subcutaneous injectable pursuant to NDA-3. Additionally, under an agreement with entity A, entity B repackages three strengths of the immediate release tablets manufactured by entity A and markets them pursuant to NDA-1. In this scenario, all 12 of these drug products, including the repackaged products, will be aggregated as a single potential qualifying single source drug for purposes of identifying negotiation-eligible drugs.

This approach to identifying a potential qualifying single source drug aligns with the requirement in section 1192(d)(3)(B) of the Act to use data aggregated across dosage forms and strengths of the drug, including new formulations of the drug. Consistent with this statutory instruction, this approach is also appropriate because CMS is aware that new dosage forms or different routes of administration of the same active moiety / active ingredient have been submitted by the same NDA / BLA holder and approved under different NDAs or BLAs.

Section 1192(e)(2)(A) of the Act states that an authorized generic drug and the qualifying single source drug that is the listed drug or reference product of that authorized generic drug shall be treated as the same qualifying single source drug. An authorized generic drug is defined in section 1192(e)(2)(B) of the Act as (1) in the case of a drug product, an authorized generic drug (as such term is defined in section 505(t)(3) of the FD&C Act), and (2) in the case of a biological product, a product that has been licensed under section 351(a) of the PHS Act[33] and is marketed, sold, or distributed, directly or indirectly to the retail class of trade under a different labeling, packaging (other than repackaging as the reference product in blister packs, unit doses, or similar packaging for institutions), product code, labeler code, trade name, or trademark.

If a drug is a fixed combination drug[34] with two or more active moieties / active ingredients, the distinct combination of active moieties / active ingredients will be considered as one active moiety / active ingredient for the purpose of identifying qualifying single source drugs. Therefore, all formulations of this distinct combination offered by the same NDA / BLA holder will be aggregated across all dosage forms and strengths of the fixed combination drug. A product containing only one (but not both) of the active moieties / active ingredients that is offered by the same NDA / BLA holder will not be aggregated with the formulations of the fixed combination drug and will be considered a separate potential qualifying single source drug. For example, a long-acting corticosteroid inhaler would not be aggregated with a fixed combination inhaler from the same NDA / BLA holder that contains the same corticosteroid combined with a long-acting beta agonist. In this example, the long-acting corticosteroid inhaler would be considered as a separate potential qualifying single source drug from the fixed combination inhaler.

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[33] CMS is interpreting the reference to "licensed under section 351(a) of such Act" to mean licensed under section 351(a) of the PHS Act. Section 351(a) of the PHS Act addresses the licensure of a biological product.

[34] For purposes of the Negotiation Program, the term "fixed combination drug" has the meaning specified in 21 C.F.R. § 300.50.

Applying statutory criteria for qualifying single source drugs:
In accordance with section 1192(e)(1) of the Act, to be considered a qualifying single source drug, at least 7 years (for drug products) or 11 years (for biological products) must have elapsed between the U.S. Food and Drug Administration (FDA) date of approval or licensure, as applicable, and the selected drug publication date. To determine the date of approval or licensure for a potential qualifying single source drug with more than one FDA application number, CMS will use the earliest date of approval or licensure of the initial FDA application number assigned to the NDA / BLA holder for the active moiety / active ingredient, or in the case of fixed combination drugs, for the distinct combination of active moieties / active ingredients. The selected drug publication date for initial price applicability year 2026 is September 1, 2023, as specified in section 1191(d)(1) of the Act. As such, for initial price applicability year 2026, the initial approval for a drug product to be considered a qualifying single source drug must have been on or before September 1, 2016, and the date of initial licensure for a biological product to be considered a qualifying single source drug must have been on or before September 1, 2012.

For example, if 12 years had elapsed between the original approval for NDA-1 cited in the previous example above and September 1, 2023, then the potential qualifying single source drug defined above would meet this statutory criterion for qualifying single source drugs (even if less than seven years had elapsed between the approval dates for NDA-2 or NDA-3 and September 1, 2023), consistent with the statutory directives in section 1192(d)(3)(B) of the Act to aggregate data across dosage forms and strengths of the drug, including new formulations of the drug.

In accordance with section 1192(e)(1) of the Act, to be considered a qualifying single source drug, a product cannot be the listed drug for any drug approved and marketed under an ANDA under section 505(j) of the FD&C Act, and a biological product cannot be the reference product for any biological product that is licensed and marketed under section 351(k) of the PHS Act. CMS will use FDA reference sources, including the Orange Book[35] and Purple Book,[36] to determine whether a generic drug or biosimilar biological product has been approved or licensed for any of the strengths or dosage forms of the potential qualifying single source drugs for initial price applicability year 2026.

In accordance with section 1192(c) and (e) of the Act for the purpose of identifying qualifying single source drugs for initial price applicability year 2026, CMS is clarifying in this revised guidance that it will review PDE data for the 12-month period beginning August 16, 2022 and ending August 15, 2023, using PDE data available on August 16, 2023, as well as Average Manufacturer Price (AMP)[37] data for the 12-month period beginning August 1, 2022 and ending July 31, 2023, using the AMP data available on August 16, 2023, for a given generic drug or biosimilar biological product for which a potential qualifying single source drug is the listed drug or reference product. The determination whether a generic drug or biosimilar is marketed on a bona fide basis will be a holistic inquiry, but these sources of data over the specified intervals

[35] See: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm.
[36] See: https://purplebooksearch.fda.gov/.
[37] Average Manufacturer Price means, with respect to a covered outpatient drug of a manufacturer for a rebate period (calendar quarter), the average price paid to the manufacturer for the drug in the United States by: (i) wholesalers for drugs distributed to retail community pharmacies; and, (ii) retail community pharmacies that purchase drugs directly from the manufacturer, subject to certain exclusions. See section 1927(k)(1) of the Act.

will be informative for that determination. CMS will consider a generic drug or biosimilar biological product to be marketed when the totality of the circumstances, including these data, reveals that the manufacturer of that drug or product is engaging in bona fide marketing of that drug or product (see section 70 of this revised guidance for additional details). CMS has chosen these time periods to enable CMS to use the most recent possible data to make this determination while still allowing for sufficient time to inform the selected drug list published by September 1, 2023 in accordance with section 1192(a) of the Act.

If any strength or dosage form of a potential qualifying single source drug is the listed drug or reference product, as applicable, for one or more generic or biosimilar biological products that CMS determines are approved and marketed based on the process described in this revised guidance, the potential qualifying single source drug will not be considered a qualifying single source drug for initial price applicability year 2026. If CMS determines that the potential qualifying single source drug will not be considered a qualifying single source drug for initial price applicability year 2026 because a manufacturer of such generic drug or biosimilar biological product has engaged in bona fide marketing of the generic drug or biosimilar biological product, CMS will monitor to ensure continued bona fide marketing of the generic drug or biosimilar biological product based on the approach described in section 90.4 of this revised guidance.

30.1.1 Orphan Drug Exclusion from Qualifying Single Source Drugs

In accordance with section 1192(e)(3)(A) of the Act, CMS will exclude certain orphan drugs when identifying qualifying single source drugs ("the Orphan Drug Exclusion"). Specifically, CMS will exclude a drug or biological product that is designated as a drug for only one rare disease or condition under section 526 of the FD&C Act and for which the only approved indication (or indications) is for such disease or condition. To be considered for the Orphan Drug Exclusion, the drug or biological product must (1) be designated as a drug for only one rare disease or condition under section 526 of the FD&C Act and (2) be approved by the FDA only for one or more indications within such designated rare disease or condition. CMS is clarifying in this revised guidance that a drug that has orphan designations for more than one rare disease or condition will not qualify for the Orphan Drug Exclusion, even if the drug has not been approved for any indications for the additional rare disease(s) or condition(s). CMS further clarifies that it will consider only active designations and active approvals when evaluating a drug for the Orphan Drug Exclusion; that is, CMS will not consider withdrawn orphan designations or withdrawn approvals as disqualifying a drug from the Orphan Drug Exclusion.

In order to qualify for the Orphan Drug Exclusion, all dosage forms and strengths of the qualifying single source drug described in section 30.1 of this revised guidance must meet the criteria for exclusion. CMS will use the FDA Orphan Drug Product designation database[38] and approvals on the FDA website[39] to determine whether a drug meets the requirements in section 1192(e)(3)(A) of the Act to qualify for the Orphan Drug Exclusion. CMS will also consult with FDA as needed, including to determine whether a drug is designated for, or approved for indications for, one or more rare disease(s) or condition(s). In this revised guidance, CMS is clarifying that, in the event that a drug or biological product loses Orphan Drug Exclusion status,

[38] See: https://www.accessdata.fda.gov/scripts/opdlisting/oopd/.
[39] See: https://www.accessdata.fda.gov/scripts/cder/daf/.

pursuant to sections 1192(e)(1)(A)(ii) and (B)(ii) of the Act, CMS will use the date of the earliest approval or licensure of the drug or biological product (as described above in section 30.1) to determine whether the product is a qualifying single source drug that may be selected for negotiation if it meets all other Negotiation Program eligibility criteria, regardless of whether the drug or biological product previously qualified for an exclusion under section 1192(e)(3)(A) of the Act.

As noted in the initial memorandum, CMS is considering whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development, and CMS appreciates continued input from interested parties on this topic. Additional information about how CMS will consider the impact of a selected drug (and its therapeutic alternative(s)) on specific populations as well as the extent to which the selected drug (and its therapeutic alternative(s)) meets an unmet medical need in CMS' development of an initial offer is in section 60.3.3 of this revised guidance.

30.1.2 Low-Spend Medicare Drug Exclusion from Qualifying Single Source Drugs

In accordance with section 1192(e)(3)(B) of the Act, CMS will also exclude low-spend Medicare drugs or biological products with less than $200,000,000 in combined expenditures under Medicare Parts B and D when identifying qualifying single source drugs ("the Low-Spend Medicare Drug Exclusion"). For initial price applicability year 2026, CMS will identify low-spend Medicare drugs as follows:

- CMS will identify PDE data combined with Part B claims data for each potential qualifying single source drug for dates of service during the 12-month period beginning June 1, 2022, and ending May 31, 2023. To allow a reasonable amount of time for Part D plan sponsors to submit PDE data, CMS will use PDE data for the dates of service described above that have been submitted no later than 30 days[40] after May 31, 2023, i.e., by June 30, 2023. To allow a reasonable amount of time for providers and suppliers to submit Part B claims, CMS will use Part B claims data for the dates of service described above that have been submitted no later than 30 days after May 31, 2023, i.e., by June 30, 2023.
- For each potential qualifying single source drug as described in section 30.1 of this revised guidance, CMS will use the PDE data to calculate the Total Expenditures under Part D and CMS will use the Part B claims data to calculate the total allowed charges under Part B, inclusive of beneficiary cost sharing, for purposes of determining Total Expenditures under Part B. CMS is clarifying in this revised guidance that expenditures for a drug or biological product that are bundled or packaged into the payment for another service will be excluded from the calculation of total allowed charges under Part B.
- CMS will exclude from the final list of qualifying single source drugs for initial price applicability year 2026 any drugs for which the sum of Total Expenditures under Part D and Part B is less than $200 million.

[40] For purposes of this revised guidance, CMS defines all days as calendar days unless otherwise specified in statute, guidance, or regulation.

30.1.3 Plasma-Derived Product Exclusion from Qualifying Single Source Drugs

In accordance with section 1192(e)(3)(C) of the Act, CMS will exclude plasma-derived products when identifying qualifying single source drugs as described in section 30.1 of this revised guidance ("the Plasma-Derived Product Exclusion"). For purposes of this exclusion, a plasma-derived product is a licensed biological product that is derived from human whole blood or plasma, as indicated on the approved product labeling. CMS will refer to product information available on the FDA Approved Blood Products website, including the list of fractionated plasma products,[41] and will refer to the FDA Online Label Repository[42] to verify if the product is derived from human whole blood or plasma. CMS will also consult with FDA as needed.

30.2 Identification of Negotiation-Eligible Drugs for Initial Price Applicability Year 2026

In accordance with sections 1192(a) and 1192(d)(1) of the Act, a negotiation-eligible drug for initial price applicability year 2026 is a qualifying single source drug that is among the 50 qualifying single source drugs with the highest Total Expenditures under Part D. CMS will identify the negotiation-eligible drugs for initial price applicability year 2026 as follows:

- CMS will identify all qualifying single source drugs for initial price applicability year 2026 using the process described in section 30.1 of this revised guidance. CMS will exclude any drugs that qualify for the exclusions listed in sections 30.1.1 – 30.1.3 of this revised guidance.
- CMS will identify PDE data for each NDC-11 of a qualifying single source drug for dates of service during the 12-month period beginning June 1, 2022, and ending May 31, 2023. To allow a reasonable time for Part D plan sponsors to submit PDE data, CMS will use PDE data for the dates of service described above that have been accepted no later than 30 days after May 31, 2023, i.e., by June 30, 2023.
- CMS will use this PDE data to calculate the Total Expenditures under Part D for each qualifying single source drug during the 12-month applicable period.
- CMS will (1) remove drugs that are subject to the exception for small biotech drugs, described in section 30.2.1 of this revised guidance; (2) rank the remaining qualifying single source drugs by Total Expenditures under Part D during the applicable 12-month period; and (3) identify the 50 qualifying single source drugs that have the highest Total Expenditures under Part D during the applicable 12-month period.
- These 50 drugs will be considered negotiation-eligible drugs for initial price applicability year 2026.

When two or more qualifying single source drugs have the same Total Expenditures to the dollar under Part D, and such Total Expenditures are the 50th highest among qualifying single source drugs, CMS will rank the qualifying single source drugs based on which drug has the earlier approval or licensure date, as applicable, for the initial FDA application number with its active moiety(ies) / active ingredient(s), until CMS has identified 50 negotiation-eligible drugs. CMS believes that this approach would not be likely to alter which drugs are selected drugs because a maximum of 10 drugs will be selected for initial price applicability year 2026 (see section 30.3 of this revised guidance for details).

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[41] See: https://www.fda.gov/vaccines-blood-biologics/blood-blood-products/approved-blood-products.

[42] See: https://labels.fda.gov/.

30.2.1 Exception for Small Biotech Drugs

In accordance with section 1192(d)(2) of the Act, the term "negotiation-eligible drug" excludes, with respect to initial price applicability years 2026, 2027, and 2028, a qualifying single source drug that meets the requirements for the exception for small biotech drugs ("the Small Biotech Exception"). The statute requires that CMS consider, for Part D drugs, Total Expenditures under Part D for all covered Part D drugs during 2021, Total Expenditures for the qualifying single source drug under Part D during 2021, and Total Expenditures under Part D for all covered Part D drugs for which the manufacturer that had a Coverage Gap Discount Program (CGDP) agreement in effect under section 1860D-14A of the Act for the qualifying single source drug during 2021 also had a CGDP agreement in effect during 2021.[43] To identify and exclude such small biotech drugs, CMS will consider whether, for dates of services in calendar year 2021, the Total Expenditures under Part D for the qualifying single source drug (1) were equal to or less than one percent of the Total Expenditures under Part D for all covered Part D drugs; and (2) were equal to at least 80 percent of the Total Expenditures under Part D for all covered Part D drugs for which the manufacturer of the qualifying single source drug had a CGDP agreement in effect during 2021.

For the purposes of the Small Biotech Exception for initial price applicability year 2026, the aggregation rule at section 1192(d)(2)(B)(i) of the Act requires that CMS treat as a single manufacturer all entities that, as of December 31, 2021, were treated as a single employer under subsection (a) or (b) of section 52 of the Internal Revenue Code (IRC) of 1986 with the entity that had the CGDP agreement for the qualifying single source drug on that date. However, CMS does not have information about which entities were treated as a single employer under the applicable IRC provisions. Therefore, a manufacturer that seeks the Small Biotech Exception for its qualifying single source drug ("Submitting Manufacturer") must submit information to CMS about the company and its products in order for the drug to be considered for the exception. To the extent that more than one entity meets the statutory definition of a manufacturer of a qualifying single source drug, only the holder of the NDA(s) / BLA(s) for the qualifying single source drug may be the Submitting Manufacturer. CMS made this decision to ensure that only the entity with which CMS would negotiate in the event that the qualifying single source drug is selected for negotiation, as described in section 40 of this revised guidance, is able to seek the Small Biotech Exception.

On January 24, 2023, CMS released the Small Biotech Exception ICR (CMS-10844 / OMB 0938-1443) to detail the specific data that CMS is requesting for purposes of implementing this exception. The comment period in response to the 60-day notice closed on March 27, 2023. CMS released a revised version of the Small Biotech Exception ICR on April 24, 2023, and the comment period in response to the 30-day Federal Register notice closed on May 24, 2023. CMS published the final, approved version of the Small Biotech Exception ICR on May 26, 2023.[44]

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[43] For the purposes of this determination, a manufacturer that participated in the CGDP in 2021 by means of an arrangement whereby its labeler codes were listed on another manufacturer's CGDP agreement would be considered to have had an agreement in effect during 2021.

[44] To view the Small Biotech ICR Form, a summary of changes made to the Small Biotech ICR in response to comments received during the 60-day and 30-day notice periods, as well as comments received on the Small Biotech ICR and CMS' responses to those comments, see https://www.reginfo.gov/public/do/PRAViewICR?ref_nbr=202304-0938-016.

The Small Biotech Exception ICR addresses the collection of information for initial price applicability year 2026 only. For initial price applicability year 2026, Sections 1191(a) and 1192(d) of the Act require CMS to evaluate whether a qualifying single source drug qualifies as a negotiation-eligible drug under 1192(d) based on Total Expenditures under Part D only, including with respect to the Small Biotech Exception. As a result, this ICR addresses the collection of information relevant to Total Expenditures only under Part D. Additionally, this ICR does not address the collection of information relevant to the statutory limitation found in section 1192(d)(2)(B)(ii) of the Act (which precludes the application of the Small Biotech Exception to a qualifying single source drug if the manufacturer of that drug is acquired after 2021 by a manufacturer that does not meet the definition of a specified manufacturer under section 1860D–14C(g)(4)(B)(ii) because the earliest effective date specified in that limitation (January 1, 2025) has no impact until initial price applicability year 2027 (the first initial price applicability year with a selected drug publication date after January 1, 2025).

As CMS announced on May 26, 2023, after approval of the ICR, to receive consideration for the Small Biotech Exception for initial price applicability year 2026, the Submitting Manufacturer must submit the Small Biotech Exception ICR Form using the CMS Health Plan Management System (CMS HPMS) by July 3, 2023.[45] CMS will notify the Submitting Manufacturer in September 2023 of the determination of whether the Submitting Manufacturer's qualifying single source drug qualifies for the Small Biotech Exception for initial price applicability year 2026. CMS is clarifying in this revised guidance that information in a Small Biotech Exception ICR Form that is a trade secret or confidential commercial or financial information will be protected from disclosure if the information meets the requirements set forth under Exemptions 3 and/or 4 of the Freedom of Information Act (FOIA) (5 U.S.C. § 552(b)(3), (4)).

CMS will not consider incomplete submissions. Upon receipt of a complete Small Biotech Exception ICR Form, CMS will take the following approach to identify whether a qualifying single source drug qualifies for the Small Biotech Exception:

- CMS will identify the manufacturer that had a CGDP agreement for the qualifying single source drug in effect as of December 31, 2021 ("2021 Manufacturer") based on the information submitted in the Small Biotech Exception ICR Form.
- CMS will use the information submitted in that form to identify the complete set of 11-digit National Drug Codes (NDC-11s)[46] for which any member of the 2021 Manufacturer's controlled group as of December 31, 2021 had a CGDP agreement as of December 31, 2021. "Controlled group" means all corporations or partnerships, proprietorships and other entities treated as a single employer under 26 U.S.C. § 52(a) or (b).
- Using the complete set of NDC-11s for which the 2021 Manufacturer or any member of the 2021 Manufacturer's controlled group had a CGDP agreement in effect on December

[45] On June 2, 2023, CMS released the Small Biotech Exception functionality in CMS HPMS, and manufacturers could begin submitting their requests on that date. To view instructions for requesting the Small Biotech Exception in CMS HPMS, see https://www.cms.gov/files/document/small-biotech-exception-guidance-6223.pdf.

[46] NDC-9 and NDC-11 numbers are identical except for two numbers in NDC-11s that indicate package size. Because of this, NDC-11 is more granular than NDC-9, and multiple NDC-11 numbers can aggregate under a single NDC-9 number.

31, 2021, CMS will identify PDE data for dates of service during the 12-month period beginning January 1, 2021 and ending December 31, 2021.

- Using the PDE data for (1) the qualifying single source drug, (2) the complete set of covered Part D drugs for which the 2021 Manufacturer or any member of the 2021 Manufacturer's controlled group had a CGDP agreement as of December 31, 2021, and (3) all covered Part D drugs, CMS will determine whether:
    - The Total Expenditures under Part D for the qualifying single source drug were equal to or less than one percent of the Total Expenditures under Part D for all covered Part D drugs; and
    - The Total Expenditures under Part D for the qualifying single source drug were equal to at least 80 percent of the Total Expenditures under Part D for all covered Part D drugs for which the 2021 Manufacturer or any member of the 2021 Manufacturer's controlled group had a CGDP agreement in effect during 2021.

  CMS is clarifying in this revised guidance that the Total Expenditures under Part D for all covered Part D drugs will be determined using PDE data for all covered Part D drugs. The Total Expenditures under Part D for the qualifying single source drug and the Total Expenditures under Part D for all covered Part D drugs for which the 2021 Manufacturer or any member of the 2021 Manufacturer's controlled group had a CGDP agreement in effect during 2021 will only include PDE data for NDC-11s with labeler codes associated with the 2021 Manufacturer or any member of the 2021 Manufacturer's controlled group.

For initial price applicability year 2026, the term "negotiation-eligible drug" will exclude any covered Part D drugs that are qualifying single source drugs that meet these criteria to qualify for the Small Biotech Exception.

A determination by CMS that a given qualifying single source drug qualifies for the Small Biotech Exception for initial price applicability year 2026 does not mean that this drug will continue to qualify for the Small Biotech Exception for future initial price applicability years. The Submitting Manufacturer must resubmit a request for the drug to be considered for the exception for initial price applicability years 2027 and 2028. The process for resubmitting a request will be addressed in future guidance.

In this revised guidance, CMS is clarifying that it will publish the number of drugs that applied for and received the Small Biotech Exception for initial price applicability year 2026 as part of publishing the selected drug list on September 1, 2023.

30.3 Selection of Drugs for Negotiation for Initial Price Applicability Year 2026

In accordance with sections 1192(a) and 1192(b) of the Act, CMS will select 10 (or all, if such number is less than 10) negotiation-eligible drugs for initial price applicability year 2026 as follows:

- CMS will rank the 50 negotiation-eligible drugs identified in section 30.2 of this revised guidance by Total Expenditures under Part D (based on the data described in section 30.2 of this revised guidance) in descending order: the negotiation-eligible drug with the highest Total Expenditures under Part D will be listed first and the negotiation-eligible drug with the lowest Total Expenditures under Part D will be listed last.

- CMS will remove any biological products that qualify for delayed selection under section 1192(f) of the Act as described in section 30.3.1 of this revised guidance.
- CMS will select for negotiation the 10 (or all, if such number is less than 10) highest ranked negotiation-eligible drugs remaining on the ranked list for initial price applicability year 2026.
    - In the event that two or more negotiation-eligible drugs have the same Total Expenditures under Part D to the dollar and such Total Expenditures are the 10th highest among negotiation-eligible drugs, CMS will rank those negotiation-eligible drugs based on which drug has the earlier approval or licensure date, as applicable, associated with the initial FDA application number for its active moiety(ies) / active ingredient(s), and select based on that ranking until there are 10 selected drugs (or until all drugs are selected if the number of negotiation-eligible drugs is less than 10).

30.3.1 Delay in the Selection and Negotiation of Certain Biologics with High Likelihood of Biosimilar Market Entry

In accordance with section 1192(b)(1)(C) of the Act, CMS will remove from the ranked list of 50 negotiation-eligible drugs described in section 30.3 of this revised guidance any negotiation-eligible drug for which the inclusion on the selected drug list is delayed in accordance with section 1192(f) of the Act. This section 30.3.1 describes the implementation of section 1192(f) of the Act (the "Biosimilar Delay").

Under section 1192(f)(1)(B) of the Act, the manufacturer of a biosimilar biological product ("Biosimilar Manufacturer" of a "Biosimilar") may submit a request, prior to the selected drug publication date, for CMS' consideration to delay the inclusion of a negotiation-eligible drug that includes the reference product for the Biosimilar (such a negotiation-eligible drug is herein referred to as a "Reference Drug") on the selected drug list for a given initial price applicability year. The Biosimilar Manufacturer eligible to submit the request is the holder of the BLA for the Biosimilar or, if the Biosimilar has not yet been licensed, the sponsor of the BLA submitted for review by FDA. CMS believes that this approach is appropriate because (1) it clearly identifies one manufacturer that may submit a Biosimilar Delay request for a given Biosimilar, avoiding the possibility that CMS would receive two such requests naming the same Biosimilar for the same initial price applicability year, and (2) the status of the application for licensure for the Biosimilar is material to CMS' consideration of a Biosimilar Delay request, as described in this section 30.3.1.

Section 1192(f) of the Act contemplates two potential requests under the Biosimilar Delay: (1) a request to delay the inclusion of a Reference Drug by one initial price applicability year ("Initial Delay Request"), as stated in section 1192(f)(1)(B)(i)(I) of the Act; and (2) a request to delay the inclusion of a Reference Drug for which an Initial Delay Request has been granted for a second initial price applicability year ("Additional Delay Request") as stated in section 1192(f)(1)(B)(i)(II) of the Act.

The following subsections of this section 30.3.1 include details on the implementation of the Biosimilar Delay for initial price applicability year 2026. Topics related to future initial price applicability years (including Additional Delay Requests) will be covered in future guidance.

30.3.1.1 Requirements for Granting an Initial Delay Request for Initial Price Applicability Year 2026

The statute specifies that the following requirements must be met in order for CMS to grant an Initial Delay Request:

1. In accordance with section 1192(f)(1)(A) of the Act, it is required that the Reference Drug would be, absent the Biosimilar Delay, a selected drug for the initial price applicability year.
    - Biosimilar Manufacturers that think that a Reference Drug for their Biosimilar may be a selected drug for initial price applicability year 2026 may submit an Initial Delay Request, and CMS will disregard that application if the Reference Drug would not, in fact, be a selected drug for initial price applicability year. Biosimilar Manufacturers are encouraged to consult publicly available data on expenditures for covered Part D drugs, including data published by CMS, which may allow them to determine the likelihood that a given drug may be a selected drug.
2. In accordance with section 1192(f)(1)(A) of the Act, it is required that the Reference Drug would be an extended-monopoly drug, as defined in section 1194(c)(4) of the Act, included on the selected drug list for the initial price applicability year, absent the Biosimilar Delay. For Initial Delay Requests submitted with respect to initial price applicability year 2026, this means that the Reference Drug must have received its initial BLA licensure between January 1, 2010, and January 1, 2014.
    - Section 1194(c)(4)(B)(ii) of the Act specifies that selected drugs for which a manufacturer had an agreement under the Negotiation Program for an initial price applicability year prior to 2030 are excluded from the definition of extended-monopoly drugs. Importantly, however, an Initial Delay Request must be submitted by a Biosimilar Manufacturer before the selected drug publication date for an initial price applicability year and before the Primary Manufacturer (as defined in section 40 of this revised guidance) of the Reference Drug ("Reference Manufacturer") would have entered into an agreement under the Negotiation Program. Therefore, CMS believes the exception to the definition of "extended-monopoly drug" in section 1194(c)(4)(B)(ii) of the Act will not apply at the time that a delay would be requested for initial price applicability years 2026 through 2029. Accordingly, CMS believes that the Biosimilar Delay under section 1192(f) of the Act is applicable beginning with initial price applicability year 2026. As such, Biosimilar Manufacturers may submit an Initial Delay Request for initial price applicability year 2026, provided that the Reference Drug named in the request will have been licensed for between 12 and 16 years prior to the start of the initial price applicability year on January 1, 2026.
3. In accordance with section 1192(f)(1)(A) of the Act, the Reference Drug must include the reference product identified in the Biosimilar's application for licensure under section 351(k) of the PHS Act that has been approved by the FDA or accepted for review, as described below in section 30.3.1.2 of this revised guidance.
    - Please note that in order for CMS to grant an Initial Delay Request, the licensure application for the Biosimilar does not need to include all of the dosage forms, strengths, and indications for which the Reference Drug has received approval.

4. In accordance with section 1192(f)(2)(D)(iii) of the Act, an Initial Delay Request cannot be granted if more than one year has elapsed since the licensure of the Biosimilar and marketing of the Biosimilar has not commenced.
    - For Initial Delay Requests submitted with respect to initial price applicability year 2026, this requirement means that if the Biosimilar has already received approval by the FDA for its application for licensure under section 351(k) of the PHS Act, the date of such licensure must be on or after September 1, 2022 for a delay to be granted. If the Biosimilar is already licensed and marketed by September 1, 2023, the selected drug publication date for initial price applicability year 2026, the Reference Drug would by definition no longer be a qualifying single source drug and therefore would fail requirement #1 on this list. If the Biosimilar was licensed prior to September 1, 2022 and is not marketed before September 1, 2023, more than one year would have elapsed since the licensure of the Biosimilar without marketing of the Biosimilar having commenced.
5. In accordance with section 1192(f)(2)(D)(iv) of the Act, the Biosimilar Manufacturer must not be the same as the Reference Manufacturer and must not be treated as being the same pursuant to section 1192(f)(1)(C) of the Act.
    - For the purposes of this determination, all persons treated as a single employer under subsection (a) or (b) of section 52 of the IRC of 1986, or in a partnership, shall be treated as one manufacturer, as stated in section 1192(f)(1)(C) of the Act.
    - For the purposes of this determination, "partnership" is defined at section 1192(f)(1)(C)(ii) of the Act as a syndicate, group, pool, joint venture, or other organization through or by means of which any business, financial operation, or venture is carried on by the Reference Manufacturer and the Biosimilar Manufacturer.
6. In accordance with section 1192(f)(2)(D)(iv) of the Act, the Biosimilar Manufacturer and the Reference Manufacturer must not have entered into an agreement that either:
    - requires or incentivizes the Biosimilar Manufacturer to submit an Initial Delay Request; or
    - directly or indirectly restricts the quantity of the Biosimilar that may be sold in the United States over a specified period of time. For Initial Delay Requests submitted with respect to initial price applicability year 2026, CMS will consider any agreement between the Biosimilar Manufacturer and the Reference Manufacturer that directly or indirectly restricts the quantity of the Biosimilar that the Biosimilar Manufacturer may sell during any period of time on or after September 1, 2023 as violating this requirement.
7. In accordance with section 1192(f)(1)(A) of the Act and as described in detail in section 30.3.1.2 of this revised guidance, CMS must determine that there is a high likelihood that the Biosimilar will be licensed and marketed before the date that is two years after the selected drug publication date for the initial price applicability year.

30.3.1.2 High Likelihood

In accordance with section 1192(f)(1)(A) of the Act, CMS will review Initial Delay Requests to determine whether there is a high likelihood that the Biosimilar will be licensed and marketed before the date that is two years after the selected drug publication date for the initial price applicability year. Accordingly, for Initial Delay Requests submitted with respect to initial price

applicability year 2026, CMS must find a high likelihood that the Biosimilar will be licensed and marketed before September 1, 2025, in order to grant the request. If CMS does not find that there is a high likelihood that the Biosimilar will be licensed and marketed before September 1, 2025, based on the criteria described below, CMS will deny the Initial Delay Request.

In accordance with section 1192(f)(3) of the Act, Initial Delay Requests must demonstrate both of the following in order meet the high likelihood threshold:

1. An application for licensure under section 351(k) of the PHS Act for the Biosimilar has been accepted for review or approved by the FDA.[47]
    - For Initial Delay Requests submitted with respect to initial price applicability year 2026, the Biosimilar's application for licensure must be approved or accepted for review by the FDA no later than August 15, 2023, in order to permit CMS time to review the information and finalize the selected drug list prior to the selected drug publication date of September 1, 2023.
    - Please note that if the Biosimilar's application for licensure has not been accepted for review by August 15, 2023, including in the case where the Biosimilar Manufacturer has submitted an application for licensure that has not been accepted for review by the FDA or for which a filing determination is pending, CMS will deny the Initial Delay Request for initial price applicability year 2026.
2. Clear and convincing evidence that the Biosimilar will be marketed before September 1, 2025 (the date that is two years after the selected drug publication date for the initial price applicability year), based on the information from the items described in sections 1192(f)(1)(B)(ii)(I)(bb) and (III) of the Act as submitted to CMS.

For Initial Delay Requests submitted for initial price applicability year 2026, to demonstrate clear and convincing evidence that the Biosimilar will be marketed before September 1, 2025, CMS requires that the information from the items described in sections 1192(f)(1)(B)(ii)(I)(bb) and (III) of the Act as submitted to CMS by the Biosimilar Manufacturer as part of its Initial Delay Request demonstrates both (1) that patents related to the Reference Drug are unlikely to prevent the Biosimilar from being marketed and (2) that the Biosimilar Manufacturer will be operationally ready to market the Biosimilar. These requirements address the two primary contributing factors to delays in marketing of biosimilars approved in the U.S. to date, and so CMS believes that evidence showing that a Biosimilar meets these two requirements is sufficient to establish clear and convincing evidence that the Biosimilar will be marketed.

First, the Initial Delay Request must clearly demonstrate that patents related to the Reference Drug are unlikely to prevent the Biosimilar from being marketed before September 1, 2025. CMS is clarifying in this revised guidance that, in its evaluation of whether this requirement is met, CMS will only consider patents relating to the reference product included in the Reference Drug that are applicable to the Biosimilar. Specifically, CMS will consider this requirement met if (1) there are no unexpired patents relating to the reference product included in the Reference

[47] CMS is clarifying in this revised guidance that it will consider an application for licensure under section 351(k) of the PHS Act that has been accepted for review and that received a Complete Response letter to meet the section 1192(f)(3)(A) requirement that an application for licensure under section 351(k) for the biosimilar biological product has been accepted for review by FDA.

Drug that are applicable to the Biosimilar; (2) one or more court decisions establish the invalidity, unenforceability, or non-infringement of any potentially applicable unexpired patent relating to the reference product included in the Reference Drug that the patent holder asserted was applicable to the Biosimilar; or (3) the Biosimilar Manufacturer has a signed legal agreement with the Reference Manufacturer that permits the Biosimilar Manufacturer to market the Biosimilar before September 1, 2025, without imposing improper constraints on the Biosimilar Manufacturer.[48] CMS will deny all Initial Delay Requests for Biosimilars that do not meet this requirement with respect to at least one reference product included in the Reference Drug. However, active litigation related to another reference product included in the Reference Drug that is not applicable to the Biosimilar will not be disqualifying.

Second, the Initial Delay Request must clearly demonstrate that the Biosimilar Manufacturer will be operationally ready to market the Biosimilar before September 1, 2025. To assess this requirement, CMS will consider the Biosimilar Manufacturer's progress against the actions, activities, and milestones that are typical of the normal course of business leading up to the marketing of a drug as evidenced by both: (1) disclosures about capital investment, revenue expectations, and actions consistent with the normal course of business for marketing of a biosimilar biological product before September 1, 2025, and (2) a manufacturing schedule that is consistent with the public-facing statements and, as clarified in this revised guidance, demonstrates readiness to meet revenue expectations. CMS chose these criteria because they are indicative of operational readiness and should be available in the elements that CMS must consider in making this determination as required by section 1192(f)(1)(B)(ii) of the Act.

In determining whether an Initial Delay Request satisfies the high likelihood threshold, CMS may use all the information described in section 30.3.1.3 of this revised guidance to determine whether an application for licensure under section 351(k) of the PHS Act for the Biosimilar has been accepted for review or approved by the FDA. In accordance with section 1192(f)(3)(B) of the Act, CMS is required to use information from the following items when assessing whether there is clear and convincing evidence that the Biosimilar will be marketed before September 1, 2025:

- All agreements related to the Biosimilar filed with the Federal Trade Commission or the Assistant Attorney General pursuant to subsections (a) and (c) of section 1112 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003;
- The manufacturing schedule for the Biosimilar submitted to the FDA during its review of the application for licensure under section 351(k) of the PHS Act for the Biosimilar; and
- Disclosures (in filings by the Biosimilar Manufacturer with the Securities and Exchange Commission required under section 12(b), 12(g), 13(a), or 15(d) of the Securities Exchange Act of 1934 about capital investment, revenue expectations, and actions taken by the manufacturer that are typical of the normal course of business in the year (or the two years, as applicable) before marketing of a biosimilar biological product) that pertain to the marketing of the Biosimilar, or comparable documentation that is distributed to the shareholders of privately held companies.

[48] As described in section 30.3.1.1 of this revised guidance, an Initial Delay Request will not be granted if the Biosimilar Manufacturer enters into an agreement with the Reference Manufacturer that requires or incentivizes the Biosimilar Manufacturer to submit an Initial Delay Request or directly or indirectly restricts the quantity of the Biosimilar sold in the United States on or after September 1, 2023.

In accordance with section 1198(2) of the Act, there will be no administrative or judicial review of CMS' determinations under section 1192(f) of the Act.

30.3.1.3 Submitting an Initial Delay Request for Initial Price Applicability Year 2026

A Biosimilar Manufacturer intending to submit an Initial Delay Request for initial price applicability year 2026 was required to submit a complete request by 11:59 pm PT on May 22, 2023. The process for Biosimilar Manufacturers to submit an Initial Delay Request, including the required documentation, for initial price applicability year 2026 is detailed below.

A Biosimilar Manufacturer should have submitted an Initial Delay Request for initial price applicability year 2026 only if it (1) plans for its Biosimilar to be licensed and marketed before September 1, 2025, (2) believes its request will satisfy the statutory requirements for granting an Initial Delay Request, as described in section 30.3.1.1 of this revised guidance, and (3) believes that its request demonstrates that there is a high likelihood that the Biosimilar will be licensed and marketed before September 1, 2025, based on the criteria described in section 30.3.1.2 of this revised guidance.[49]

CMS has designed the process for Initial Delay Request submission for initial price applicability year 2026 to allow CMS time to adjudicate all requests in advance of September 1, 2023, the selected drug publication date, and to be operationally feasible. For initial price applicability year 2026, CMS accepted Initial Delay Requests submitted via email and Box[50] as described below, whereas, for future initial price applicability years, CMS plans to issue guidance on use of the CMS HPMS to receive and process these requests. Accordingly, Initial Delay Requests for initial price applicability year 2026 were able to be submitted via the following process:

1. The Biosimilar Manufacturer emailed IRARebateandNegotiation@cms.hhs.gov to indicate its intention to submit an Initial Delay Request for initial price applicability year 2026. The Biosimilar Manufacturer was encouraged to use the template, including subject line and body content, described in Appendix A of this revised guidance. Emails must have been received by 11:59 pm PT on May 10, 2023.
2. Within 5 business days of receipt, CMS responded by providing the Biosimilar Manufacturer with (1) a fillable template for the Initial Delay Request form, available in Appendix B of this revised guidance, and (2) access to a Box folder specific to the Biosimilar Manufacturer's Initial Delay Request. No parties other than the Biosimilar Manufacturer and CMS and its contractors have access to this folder.
3. The Biosimilar Manufacturer must have uploaded a complete Initial Delay Request with the following documentation to the Box folder or using an alternative submission approach approved by CMS by 11:59 pm PT on May 22, 2023. CMS deemed an Initial Delay Request to be complete if it included:

[49] For initial price applicability year 2026, an Initial Delay Request should have been submitted by a Biosimilar Manufacturer that anticipated the reference product for its Biosimilar will be included in one of the ten covered Part D Drugs that will be a selected drug for this initial price applicability year. Biosimilar Manufacturers are encouraged to consult publicly available data on expenditures for covered Part D drugs, including data published by CMS, which may allow them to determine the likelihood that a given drug may be a selected drug for a future initial price applicability year.

[50] See: https://www.box.com/; if a Biosimilar Manufacturer is unable to use Box, it should have included an explanation in its email in step #1 below and request an alternative submission method.

a. A complete Initial Delay Request form using the fillable template that the Biosimilar Manufacturer received from CMS. This template allowed submission of:
    i. information used to identify the Biosimilar Manufacturer, the Biosimilar, the Biosimilar's reference product, and the Reference Manufacturer;
    ii. attestations that the Initial Delay Request meets the statutory requirements listed in section 30.3.1.1 of this revised guidance; and
    iii. information on the status of licensure for the Biosimilar under section 351(k) of the PHS Act;
b. All agreements related to the Biosimilar filed with the Federal Trade Commission or the Assistant Attorney General pursuant to subsections (a) and (c) of section 1112 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003;
c. The manufacturing schedule for the Biosimilar submitted to the FDA during its review of the application for licensure under section 351(k) of the PHS Act, to the extent available; and
d. Disclosures (in filings by the Biosimilar Manufacturer with the Securities and Exchange Commission required under section 12(b), 12(g), 13(a), or 15(d) of the Securities Exchange Act of 1934 about capital investment, revenue expectations, and actions taken by the manufacturer that are typical of the normal course of business in the year (or the two years, as applicable) before marketing of a biosimilar biological product) that pertain to the marketing of the Biosimilar, or comparable documentation that is distributed to the shareholders of privately held companies, to the extent available.

In accordance with section 1192(f)(1)(B)(ii) of the Act, Initial Delay Requests for initial price applicability year 2026 that were not submitted by 11:59 pm PT on May 22, 2023 or that did not include all elements will be denied. CMS is clarifying in this revised guidance that information in an Initial Delay Request that is a trade secret or confidential commercial or financial information will be protected from disclosure if the information meets the requirements set forth under Exemptions 3 and/or 4 of the FOIA (5 U.S.C. § 552(b)(3), (4)).

30.3.1.4 Process and Timing After Submission of an Initial Delay Request for Initial Price Applicability Year 2026

Within 5 business days after the Biosimilar Manufacturer uploaded the required documentation to its Box folder or using an alternative submission approach approved by CMS, CMS sent an email confirming receipt to the email address used by the Biosimilar Manufacturer in its initial email to CMS expressing its intent to submit an Initial Delay Request. In accordance with section 1192(f)(1)(B)(ii)(II) of the Act, after reviewing an Initial Delay Request, inclusive of the materials submitted therein, CMS may request additional information from the Biosimilar Manufacturer as necessary to make a determination with respect to the Initial Delay Request. For initial price applicability year 2026, CMS made any such follow-up request in writing to the Biosimilar Manufacturer via the same email address on or before June 20, 2023. Any such written request specified the additional information required, the format and manner in which the Biosimilar Manufacturer must provide the additional information, and the deadline for providing such information, which will be no later than July 3, 2023. The one exception to these deadlines

is as follows: per section 30.3.1.2 of this revised guidance, for CMS to determine that there is a high likelihood of the Biosimilar being licensed and marketed prior to September 1, 2025, the Biosimilar's application for licensure must be accepted for review or approved by the FDA no later than August 15, 2023. CMS will permit the Biosimilar Manufacturer to update CMS on the status of the Biosimilar's application for licensure before 11:59 pm Pacific Time (PT) on August 15, 2023, in order to enable CMS to use the most recent possible data to make this determination while still allowing for sufficient time to inform the selected drug list published on September 1, 2023, in accordance with section 1192(a) of the Act.

Prior to September 1, 2023, the selected drug publication date for initial price applicability year 2026, CMS will review each Initial Delay Request in the following manner. First, CMS will review each Initial Delay Request to determine whether it includes all of the elements for an Initial Delay Request and was submitted by the applicable deadline in accordance with section 30.3.1.3 of this revised guidance. Second, if an Initial Delay Request includes all required elements and was timely submitted, CMS will review the Initial Delay Request to determine if it meets all of the statutory requirements described in section 30.3.1.1 of this revised guidance, with the exception of the high likelihood requirement. Third, if the Initial Delay Request meets all statutory requirements other than the high likelihood requirement, CMS will review the Initial Delay Request to determine whether it demonstrates a high likelihood that the Biosimilar will be licensed and marketed by September 1, 2025, as described in section 30.3.1.2 of this revised guidance. In considering an Initial Delay Request, CMS will cease consideration upon finding that the Initial Delay Request has failed to meet any of these requirements. For example, if CMS determines an Initial Delay Request was not submitted by the established deadline, CMS will not review that request against other statutory requirements; if CMS determines an Initial Delay Request fails to meet one or more of the statutory requirements described in section 30.3.1.1 of this revised guidance, with the exception of the high likelihood requirement, CMS will not consider whether that Initial Delay Request demonstrates a high likelihood that the Biosimilar will be licensed and marketed before September 1, 2025.

The list of selected drugs published for initial price applicability year 2026 will reflect the results of CMS' determinations with respect to any Initial Delay Requests that are submitted, i.e., a Reference Drug that, absent a successful Initial Delay Request, would have been selected, will not appear on the selected drug list published by September 1, 2023 if it is named in a successful Initial Delay Request.

After completing its review, CMS will notify each Biosimilar Manufacturer that submits an Initial Delay Request for initial price applicability year 2026 in writing of CMS' determination regarding such request. This notification will occur on or after September 1, 2023, but no later than September 30, 2023, and will include a brief summary of CMS' determination, including:

- Whether the Initial Delay Request was successful or unsuccessful; and
- If unsuccessful, the reason CMS determined that the Initial Delay Request was unsuccessful, including but not limited to:
    - failure to submit all elements of the Initial Delay Request by the applicable deadline;
    - failure to meet another statutory requirement for granting a request (other than the high likelihood requirement), including in the case that the Reference Drug would

not have been a selected drug for initial price applicability year 2026 absent the Initial Delay Request; or

- failure to demonstrate a high likelihood that the Biosimilar will be licensed and marketed before September 1, 2025.

CMS will also notify each Reference Manufacturer named in a successful Initial Delay Request using the CMS HPMS to identify the relevant point(s) of contact. Such notification will be in writing and will identify the Reference Drug that would have been a selected drug in initial price applicability year 2026, absent the successful Initial Delay Request. Reference Manufacturers named in unsuccessful Initial Delay Requests will not be notified. In this revised guidance, CMS is clarifying that it will publish the number of Reference Drugs that would have been selected drugs for initial price applicability year 2026, absent successful Initial Delay Requests, as part of publishing the selected drug list on September 1, 2023.

In accordance with section 1192(f)(2)(B) of the Act, CMS must determine whether each Biosimilar named in a successful Initial Delay Request is licensed and marketed during the initial delay period. For successful Initial Delay Requests submitted with respect to initial price applicability year 2026, CMS will make this determination by mid-2024; CMS is still determining the appropriate date by which this determination should be made and plans to publish a specific date in future guidance. The timing, content, and format of this notification will be specified in future guidance.

The following table provides a summary of key dates related to implementation of the Biosimilar Delay for initial price applicability year 2026, as specified in this section 30.3.1:

Date	Deadline / milestone
11:59 pm PT on May 10, 2023	Deadline for Biosimilar Manufacturer to email CMS regarding intent to submit Initial Delay Request for initial price applicability year 2026
11:59 pm PT on May 22, 2023	Deadline for Biosimilar Manufacturer to submit the documentation for its Initial Delay Request as specified in section 30.3.1.3 of this revised guidance
June 20, 2023	Deadline for CMS to request follow-up information for a submitted Initial Delay Request, if applicable
July 3, 2023	Deadline for Biosimilar Manufacturer to submit any follow-up information requested by CMS, if applicable
11:59 pm PT on August 15, 2023	Deadline for Biosimilar application for licensure to be accepted for review or approved by the FDA; deadline for Biosimilar Manufacturer to submit any follow-up information requested by CMS related to the Biosimilar application for licensure
September 1, 2023	Statutory deadline for CMS to publish the selected drug list for initial price applicability year 2026. Along with the selected drug list, CMS will publish the number of drugs that would have been selected drugs, absent successful Initial Delay Requests.
September, 2023	CMS informs each Biosimilar Manufacturer that submitted an Initial Delay Request of the results of such request, in writing; for successful Initial Delay Requests, CMS also informs the Reference Manufacturer
Mid-2024[51]	For successful Initial Delay Requests, CMS determines whether the Biosimilar has been licensed and marketed during the initial delay period

Information on other policies related to section 1192(f) of the Act will be included in future guidance, including, but not limited to:

- the deadline and process for submitting an Initial Delay Request for initial price applicability year 2027;
- the deadline and process for submitting an Additional Delay Request for initial price applicability year 2027, in the event an Initial Delay Request for initial price applicability year 2026 is granted and CMS determines by mid-2024 that the Biosimilar was not licensed and marketed during the initial delay period;[52]
- the criteria for adjudicating Additional Delay Requests;
- the impact of Initial Delay Requests and Additional Delay Requests on the selected drug list for initial price applicability year 2027; and
- the application and calculation of rebates for a Reference Drug for 2026, as applicable.

30.4 Publication of the Selected Drug List

In accordance with section 1192(a) of the Act, CMS will publish the selected drug list for initial price applicability year 2026 no later than September 1, 2023. This list will include the 10 (or all, if such number is less than 10) drugs selected for negotiation for initial price applicability year 2026, including the active moiety / active ingredient for each selected drug, and the list of NDC-9s and NDC-11s for the selected drug that either had PDE utilization in the 12-month period

[51] CMS plans to publish a specific date in future guidance.
[52] CMS plans to publish a specific date in future guidance.

beginning June 1, 2022 and ending May 31, 2023 or that CMS believes are likely to have PDE utilization in the future (for example, NDC-11s associated with recently approved NDAs / BLAs).[53] CMS will post the selected drug list on the CMS IRA webpage and update this list in accordance with the process described in section 40.2 of this guidance.[54]

40. Requirements for Manufacturers of Selected Drugs for Initial Price Applicability Year 2026

In accordance with section 1193(a) of the Act, the Secretary shall enter into agreements with manufacturers of selected drugs. In section 1191(c)(1) of the Act, the Negotiation Program statute adopts the definition of "manufacturer" established in section 1847A(c)(6)(A) of the Act. Section 1193(a)(1) of the Act establishes that CMS will negotiate an MFP with "the manufacturer" of the selected drug. To the extent that more than one entity meets the statutory definition of manufacturer for a selected drug for purposes of initial price applicability year 2026, CMS will designate the entity that holds the NDA(s) / BLA(s) for the selected drug to be "the manufacturer" of the selected drug (hereinafter "Primary Manufacturer").

Likewise, for initial price applicability year 2026, CMS will refer to any other entity that meets the statutory definition of manufacturer for a drug product included in the selected drug and that either (1) is listed as a manufacturer in an NDA or BLA for the selected drug or (2) markets the selected drug pursuant to an agreement with the Primary Manufacturer but is not listed on the NDA or BLA as a "Secondary Manufacturer." A Secondary Manufacturer will include any manufacturer of any authorized generics and any repackager or relabeler of the selected drug that meet these criteria. A manufacturer that is not listed as a manufacturer on the NDA / BLA and without an agreement in place with the Primary Manufacturer would not be considered a Secondary Manufacturer.

In the example described in section 30.1 of this revised guidance, if the potential qualifying single source drug described was selected for negotiation, entity "A" would be considered the Primary Manufacturer while entity "B" would be considered a Secondary Manufacturer either because it was listed as a manufacturer in NDA-1 or if it was not listed as a manufacturer in NDA-1 because it markets the three strengths of the immediate release tablets manufactured by entity A pursuant to an agreement with entity A.

CMS will sign an agreement (a "Medicare Drug Price Negotiation Program Agreement," herein referred to as an "Agreement") with the willing Primary Manufacturer of each selected drug and believes this approach aligns with the statute's requirement to negotiate to determine an MFP with "the manufacturer" of a selected drug in accordance with section 1193(a) of the Act. This Agreement, as described in this section 40, will set forth requirements of the Primary Manufacturer with respect to its participation in the Negotiation Program, including with respect to section 1193(a)(5) of the Act, which requires the Primary Manufacturer to comply with

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[53] CMS acknowledges that, for some selected drugs, the list of NDC-9s and NDC-11s might not reflect all NDCs marketed pursuant to the approved NDA(s) / BLA(s). For example, if a selected drug includes one NDC-9 that has no current or future Part D PDE utilization (e.g., the NDC-9 is utilized only in Part B settings of care), that NDC-9 and associated NDC-11s would not be included on the published list of NDC-9s and NDC-11s of the selected drug for initial price applicability year 2026.

[54] See: https://www.cms.gov/inflation-reduction-act-and-medicare.

requirements set forth in this revised guidance, which CMS has determined are necessary for purposes of administering and monitoring compliance with the Negotiation Program.

CMS will not enter into an Agreement with any Secondary Manufacturer of a selected drug with respect to that drug. As such, under section 1193(a)(4), a Primary Manufacturer that enters into an Agreement must collect and report necessary information applicable to any Secondary Manufacturer(s) as described in section 40.2 of this revised guidance. As the entity that is party to the Agreement, the Primary Manufacturer will be solely responsible for compliance with all provisions of the Agreement and will be accountable for ensuring compliance with respect to units of the selected drug manufactured by the Secondary Manufacturer or marketed by any Secondary Manufacturer pursuant to an agreement with the Primary Manufacturer. In accordance with section 1193(a)(1) of the Act and section 40.4 of this revised guidance, the Primary Manufacturer must ensure that any Secondary Manufacturer(s) make the MFP available to MFP-eligible individuals and to pharmacies, mail order services, and other dispensers. For initial price applicability year 2026, the scope of Primary Manufacturer responsibility to provide access to the MFP for the selected drug is limited to units of such drug sold by the Primary Manufacturer or a Secondary Manufacturer. CMS reiterates that the requirement for Primary Manufacturers to provide access to the MFP applies to all sales of the selected drug to MFP-eligible individuals and to pharmacies, mail order services, and other dispensers that are providing a selected drug to an MFP-eligible individual, as described in section 80 of this revised guidance. Failure to comply with obligations to make the MFP available may result in civil monetary penalties being assessed on the Primary Manufacturer pursuant to section 1197(a) of the Act.

CMS requires that for initial price applicability year 2026, the Primary Manufacturer of a selected drug is the entity that does each of the following:

1. Signs the Agreement with CMS, as described in section 40.1 of this revised guidance;
2. Collects and reports all data required for negotiation under section 1193(a)(4) of the Act, including the negotiation data elements, as described in section 40.2, section 50.1, and Appendix C of this revised guidance;
3. Negotiates an MFP with CMS, as described in section 40.3 of this revised guidance;
4. Ensures the MFP is made available to all MFP-eligible individuals and to pharmacies, mail order services, and other dispensers that dispense the selected drug to those individuals, as described in section 40.4 of this revised guidance; and
5. Responds to CMS requests within specified timeframes with documentation demonstrating compliance and remedial actions, as applicable, pursuant to reports of noncompliance or other CMS compliance and oversight activities, and pays any CMPs for violations, including: violating the terms of the Agreement; providing false information under the procedures to apply the aggregation rule for the Small Biotech Exception or the Biosimilar Delay; failing to pay the rebate amount for a biological product for which inclusion on the selected drug list was delayed but which has since undergone negotiation as described in section 1192(f)(4) of the Act; or not providing access to the MFP to MFP-eligible individuals, pharmacies, mail order services, and other dispensers, as described in section 40.5, section 90, and section 100 of this revised guidance.

Termination of an Agreement for the Negotiation Program is described in section 40.6 of this revised guidance, and other relevant provisions from the Agreement are described in section 40.7. of this revised guidance.

40.1 Entrance into an Agreement with CMS and Alternatives

Section 1193(a) of the Act instructs CMS to enter into agreements with manufacturers of selected drugs for a price applicability period. The deadline for the Primary Manufacturer of a selected drug to enter into an Agreement for initial price applicability year 2026 is October 1, 2023. The Primary Manufacturer must use the CMS HPMS to identify relevant authorized representative(s) and effectuate the Agreement.[55]

CMS recommends, but does not require, that within five days following publication by CMS on September 1, 2023 of the list of selected drugs for an initial price applicability year, the Primary Manufacturer submit to CMS the name(s), title(s), and contact information for the representative(s) authorized to execute the Agreement. CMS recommends taking this action as soon as possible to facilitate timely communication and effectuation of the Agreement. The authorized representative(s) must be legally authorized to bind the Primary Manufacturer to the terms and conditions contained in the Agreement, including any Addenda. The authorized representatives should follow instructions made available on the CMS HPMS webpage to gain access to the CMS HPMS. To be eligible for electronic signature access in CMS HPMS, an authorized representative must be the Primary Manufacturer's Chief Executive Officer, Chief Financial Officer, an individual with equivalent authority to a Chief Executive Officer or Chief Financial Officer, or an individual that has been granted direct delegated authority to perform electronic signatures on behalf of one of the individuals previously noted. CMS notes that it is a requirement of the CMS HPMS that the person accessing the CMS HPMS have a Social Security Number (SSN). An authorized representative of the Primary Manufacturer must access the CMS HPMS and sign the Agreement by October 1, 2023.

The negotiation period for initial price applicability year 2026 will begin on the earlier of two dates: the date on which the Agreement is executed (i.e., signed by both CMS and the Primary Manufacturer) or October 1, 2023. If an Agreement is fully executed before October 1, 2023, the negotiation period (as defined in section 1191(b)(4) of the Act) will begin on the date on which the Agreement is signed by the last party to sign it. If the Agreement is not fully executed by October 1, 2023, then pursuant to 26 U.S.C. § 5000D(b)(1), a period will begin on October 2, 2023, during which the manufacturer could be exposed to potential excise tax liability. CMS will make reasonable efforts to make the final text of the Agreement available to the public before the selected drug list for initial price applicability year 2026 is published.

Section 11003 of the IRA expressly connects a Primary Manufacturer's financial responsibilities under the voluntary Negotiation Program to that manufacturer's voluntary participation in the Medicaid Drug Rebate Program, the Medicare Coverage Gap Discount Program, and the Manufacturer Discount Program. If a Primary Manufacturer decides it is unwilling to enter into an Agreement for the Negotiation Program, it may expedite its exit from the Medicare Coverage Gap Discount Program and the Manufacturer Discount Program by submitting to CMS a notice that incorporates both: (1) a notice of decision not to participate in the Negotiation Program; and

[55] See: https://hpms.cms.gov/app/ng/home/.

(2) a request for termination of the Primary Manufacturer's applicable agreements under the Medicaid Drug Rebate Program, the Medicare Coverage Gap Discount Program, and the Manufacturer Discount Program. When a Primary Manufacturer submits such a notice, CMS will find good cause to terminate the Primary Manufacturer's agreement(s) under the Medicare Coverage Gap Discount Program and the Manufacturer Discount Program, as applicable, pursuant to section 1860D-14A(b)(4)(B)(i) and section 1860D-14C(b)(4)(B)(i) of the Act to expedite the date on which none of the drugs of the Primary Manufacturer are covered by an agreement under section 1860D-14A or section 1860D-14C. CMS has determined (and hereby provides notice) that it will automatically grant such termination requests upon receipt, and that it will expedite the effective date of the Primary Manufacturer's termination of its Medicare Coverage Gap Discount Program and/or Manufacturer Discount Program agreements consistent with the statutory limitation that termination shall not be effective earlier than 30 calendar days after the date of notice to the manufacturer of such termination.

If a Primary Manufacturer has determined it would not be willing to enter into an Agreement for the Negotiation Program if one of its drugs is listed as a selected drug and has submitted a notice of its decision and its request for termination as described above, CMS shall, upon written request from such Primary Manufacturer, provide a hearing concerning its termination request. Such a hearing will be held prior to the effective date of termination with sufficient time for such effective date to be repealed. Such a hearing will be held solely on the papers; because CMS' determination that there is good cause for termination depends solely on the Primary Manufacturer's request for termination to effectuate its decision not to participate in the Negotiation Program, the only question to be decided in the hearing is whether the Primary Manufacturer has asked to rescind its termination request prior to the effective date of the termination. CMS will automatically grant such request from the Primary Manufacturer to rescind its termination request.

40.2 Submission of Manufacturer Data to Inform Negotiation

After entering into an Agreement with CMS and in accordance with section 1193(a)(4) of the Act, the Primary Manufacturer of each selected drug must submit to CMS the following information with respect to the selected drug: information on the non-Federal average manufacturer price ("non-FAMP") (defined in section 8126(h)(5) of title 38, United States Code), as described in section 50.1.1 and Appendix C of this revised guidance, and any information that CMS requires to carry out negotiation, including but not limited to the factors listed in section 1194(e)(1) of the Act, as described in section 50.1 and Appendix C of this revised guidance. This information must be submitted by the Primary Manufacturer to CMS no later than October 2, 2023, for initial price applicability year 2026.

The Agreement must be fully executed, meaning both the Primary Manufacturer and CMS have signed the Agreement, before the Primary Manufacturer may submit the data elements described in this section. While these data elements may not be submitted prior to execution of the Agreement, Primary Manufacturers will be able to access the data elements template in the CMS HPMS, and CMS believes Primary Manufacturers will be able to gather these data prior to the Agreement being executed. By signing the Agreement, a Primary Manufacturer agrees to use the CMS HPMS and comply with all relevant procedures and policies set forth in the CMS HPMS for utilizing the system.

Certain data, as described in section 50.1 and Appendix C of this revised guidance, must reflect any products included in the selected drug marketed by a Secondary Manufacturer(s), and the Primary Manufacturer is responsible for collecting such data from such Secondary Manufacturer(s) and including this information in its submission to CMS.

For each selected drug for initial price applicability year 2026, CMS will populate the CMS HPMS with the list of the NDC-11s published in accordance with section 30.4 of this revised guidance, meaning those NDC-11s of the selected drug that either had Part D PDE utilization in the 12-month period beginning June 1, 2022 and ending May 31, 2023 or which CMS believes are likely to have PDE utilization in the future (for example, NDC-11s associated with recently approved NDAs / BLAs). This list will include any NDC-11s of the selected drug marketed by the Primary Manufacturer and any Secondary Manufacturer. CMS will transmit the list to the Primary Manufacturer of the selected drug. In connection with the data submission described in section 50.1 of this revised guidance, the Primary Manufacturer must provide CMS with information regarding the NDC-11s that may be appropriate to ensure the list is complete and accurate, including but not limited to, whether any NDC-11s associated with the NDA(s) / BLA(s) of the selected drug are missing from the list (e.g., because they are new NDC-11s), including any missing NDC-11s of a Secondary Manufacturer of the selected drug; whether any of the listed NDC-11s are marketed or controlled solely by a manufacturer that is not the Primary Manufacturer or a Secondary Manufacturer; and whether any of the listed NDC-11s have been discontinued. CMS will collect this information in the CMS HPMS as part of the collection of the other data elements described in section 50.1 of this revised guidance and update this list as necessary (e.g., based on supplements from the Primary Manufacturer or other updates).

This list of NDC-11s constitutes the baseline of NDCs of the selected drug as described in section 30 of this revised guidance that will be subject to the negotiation process for initial price applicability year 2026. The NDC-11s on this list will be included in ceiling calculations for initial price applicability year 2026 as described in section 60.2, to the extent data are available to support such calculations. CMS will also use the NDC-11s on this list for the calculations used to apply the MFP across dosage forms and strengths of the selected drug for initial price applicability year 2026 as described in section 60.5 of this revised guidance. In addition, CMS will use the information supplied by the Primary Manufacturer about discontinued NDC-11s as additional context for the data elements described in section 50.1 of this revised guidance (e.g., notice that an NDC-11 has been discontinued may explain why a Primary Manufacturer submitted partial year data for a particular NDC-11 of a selected drug).

The Primary Manufacturer has an ongoing obligation to timely report any changes in this information to ensure the list of NDC-11s of the selected drug in the CMS HPMS remains complete and accurate consistent with this revised guidance and any future guidance and regulations. For example, a Primary Manufacturer must report to CMS any new NDC-11s of the selected drug at least 30 days prior to their first marketed date for any Primary Manufacturer or any Secondary Manufacturer(s) of such selected drug; if CMS believes these new NDC-11s are likely to have PDE utilization in the future, these NDC-11s will be added to the list of NDC-11s of the selected drug. The Primary Manufacturer also must report to CMS the delisting of any NDC-11 of the selected drug that is no longer marketed by the Primary Manufacturer or any

Secondary Manufacturer(s) within 30 days after its discontinuation. Failure of the Primary Manufacturer to provide timely information material to the accuracy of the list of NDC-11s of the selected drug as described in this section 40.2 of the revised guidance will be considered a violation of the Agreement pursuant to section 1193(a)(5) of the Act and may cause the Primary Manufacturer to be subject to civil monetary penalties per section 1197(c) of the Act.

40.2.1 Confidentiality of Proprietary Information

Section 1193(c) of the Act states that CMS must determine which information submitted to CMS by a manufacturer of a selected drug is proprietary information of that manufacturer. Information that is deemed proprietary shall only be used by CMS or disclosed to and used by the Comptroller General of the United States for purposes of carrying out the Negotiation Program. Proprietary information, including trade secrets and confidential commercial or financial information, will also be protected from disclosure if the proprietary information meets the requirements set forth under Exemptions 3 and/or 4 of the FOIA (5 U.S.C. § 552(b)(3), (4)).[56]

CMS will implement a confidentiality policy that is consistent with existing federal requirements for protecting proprietary information, including Exemptions 3 and/or 4 of the FOIA, and that strikes an appropriate balance between (1) protecting the highly sensitive information of manufacturers and ensuring that manufacturers submit the information CMS needs for the Negotiation Program, and (2) avoiding treating information that does not qualify for such protection as proprietary. Thus, for initial price applicability year 2026, CMS will treat information on non-FAMP as proprietary.

For initial price applicability year 2026, CMS will also treat certain data elements submitted by a Primary Manufacturer of a selected drug in accordance with section 1194(e)(1) and section 1194(e)(2) of the Act as proprietary if the information constitutes confidential commercial or financial information of the Primary Manufacturer or a Secondary Manufacturer. Specifically, CMS will treat research and development costs and recoupment, unit costs of production and distribution, pending patent applications, market data, revenue, and sales volume data as proprietary, unless the information that is provided to CMS is already publicly available, in which case it would be considered non-proprietary. CMS will treat the data on prior Federal financial support and approved patent applications, exclusivities, and applications and approvals under section 505(c) of the FD&C Act or section 351(a) of the PHS Act as non-proprietary because CMS understands these data are publicly available.

Pursuant to section 1195(a)(2) of the Act, CMS is required to publish the explanation of the MFP by March 1, 2025, for initial price applicability year 2026 (see section 60.6.1 of this revised guidance). In this public explanation and any other public documents discussing the MFP, CMS will make public the section 1194(e)(1) and section 1194(e)(2) data submitted by the Primary Manufacturer and the public that are determined to be non-proprietary, but will not include any protected health information (PHI) or personally identifiable information (PII). CMS will also make public high-level comments about the section 1194(e)(1) and section 1194(e)(2) data submitted to CMS that are determined to be proprietary, without sharing any PHI / PII or any proprietary information reported to CMS under section 1193(a)(4) for purposes of the negotiation. For example, CMS will not make public the research and development costs

[56] See: https://www.justice.gov/oip/doj-guide-freedom-information-act-0.

reported by a Primary Manufacturer, as CMS would treat that data as proprietary, but CMS may say "the manufacturer has recouped its research and development costs." Any proprietary information obtained during the course of an audit will also remain confidential, except as necessary to use that information in the course of a judicial enforcement proceeding.

40.2.2 Data and Information Use Provisions and Limitations

CMS will not publicly discuss ongoing negotiations with a Primary Manufacturer, except as outlined below. As described in section 60.6.1, CMS will make public a narrative explanation of the negotiation process and share redacted information regarding the section 1194(e) data received, exchange of offers and counteroffers, and the negotiation meetings, if applicable.

Primary Manufacturers may choose to publicly disclose information regarding its ongoing negotiations with CMS at its discretion. If a Primary Manufacturer discloses information that is made public regarding any aspect of the negotiation process prior to the explanation of the MFP being released by CMS, CMS reserves the right to publicly discuss the specifics of the negotiation process regarding that Primary Manufacturer. If a Primary Manufacturer chooses to disclose any material that is made public that CMS has previously deemed to be proprietary information of that Primary Manufacturer, CMS will no longer consider that material proprietary consistent with section 40.2.1 of this guidance. For example, if a Primary Manufacturer chooses to publicly disclose the unit cost of production, CMS will no longer consider the unit cost of production to be proprietary. If the Primary Manufacturer chooses to disclose proprietary information prior to the explanation of the MFP, then it will not be redacted in the explanation of the MFP. Primary Manufacturers negotiating an MFP with CMS pursuant to the process set forth in section 60 are reminded that statements to or discussions with other Primary Manufacturers also engaged in the MFP negotiation process with CMS could negatively impact the competitive process for each independent MFP negotiation. Information exchanges concerning confidential and strategic business negotiations may violate the antitrust laws under certain circumstances and lead to other anticompetitive agreements. Primary Manufacturers should consider the antitrust implications of any such actions.

CMS will prohibit audio or video recording of any negotiation meetings between CMS and a Primary Manufacturer. CMS will maintain written records of the negotiation process, including negotiation meetings, in compliance with applicable federal law, including the Federal Managers Financial Integrity Act and the Federal Records Act. A Primary Manufacturer can maintain its own written record of these exchanges.

40.2.3 Opportunity for Corrective Action Following Information Submission

Recognizing the substantial role that manufacturer-submitted information will play in the negotiation process and in administering and monitoring the Negotiation Program, CMS will provide an opportunity for corrective action in the event a submission is incomplete or inaccurate. Upon receipt of Primary Manufacturer-submitted information – for example, information on the section 1194(e)(1) factors – CMS will review the submission for completeness and accuracy. Should CMS determine a submission is incomplete or contains inaccurate information, CMS will provide a written request that the Primary Manufacturer take corrective action and resubmit the information. CMS will provide five business days for the Primary Manufacturer to correct the submission and/or provide additional information to validate

the accuracy/completeness of the original submission. Following resubmission, CMS may follow up with the Primary Manufacturer to clarify any information included in the resubmission and confirm full accuracy and completeness of the required information.

To facilitate the corrective action process, CMS will provide the Primary Manufacturer with a written request for the corrected information, which will be transmitted to the Primary Manufacturer following CMS' discovery of any inaccurate or incomplete submissions. The written request will include a deadline for resubmitting the information (i.e., the end of the five-business day period). CMS will make efforts to be available to engage with the Primary Manufacturer about the specifics of the request for corrected information and to answer questions and provide clarification. Note that failure to engage in timely corrective action may result in the Primary Manufacturer being subject to civil monetary penalties as authorized under section 1197(c) for failure to submit required information.

40.3 Negotiation and Agreement to an MFP and Renegotiation in Later Years

CMS will use the CMS HPMS to share the initial offer and concise justification, any subsequent offer and justification, and to receive any counteroffer(s) from the Primary Manufacturer of a selected drug. A Primary Manufacturer that signs the Agreement will be required to adhere to the process and deadlines described in section 60 of this revised guidance. CMS will also use the CMS HPMS to share and receive an Addendum to the Agreement, as applicable, in order for CMS and the Primary Manufacturer to effectuate agreement upon the MFP that results from the negotiation process. For example, concurrent with the agency's provision of the initial offer, CMS will populate an Addendum in the CMS HPMS containing the MFP identified in the initial offer; if a Primary Manufacturer wishes to accept CMS' initial offer, it can sign the Addendum in the CMS HPMS. Similarly, concurrent with the Primary Manufacturer's submission of a written counteroffer, the Primary Manufacturer will populate an Addendum in the CMS HPMS containing the MFP identified in the counteroffer and sign the Addendum; if CMS wishes to accept the counteroffer, it will countersign the Addendum in the CMS HPMS. CMS will determine that negotiations have concluded upon execution by both parties of the Addendum setting forth the agreed-upon MFP.

Pursuant to section 1194(f) of the Act, CMS and a Primary Manufacturer may renegotiate the MFP for a selected drug, beginning with 2028. CMS plans to release guidance related to the renegotiation process in future years.

40.4 Providing Access to the MFP

After entering into an Agreement with CMS and in accordance with section 1193(a) of the Act, the manufacturer of a selected drug must provide access to the MFP to MFP-eligible individuals (defined in section 1191(c)(2)(A) of the Act and section 80 of this revised guidance) and to pharmacies, mail order services, and other dispensers with respect to such MFP-eligible individuals who are dispensed that drug during a price applicability period. That is, the manufacturer is required to provide access to the MFP for all dosage forms, strengths, and package sizes of the selected drug (i.e., NDCs included in the MFP file published in accordance with section 60.6 of this revised guidance), including any additional such dosage forms, strengths, and package sizes that may be further included in the MFP file, if coverage is being provided for such dosage forms, strengths, and package sizes under a prescription drug plan

under Medicare Part D or an MA–PD plan under Medicare Part C (including an Employer Group Waiver Plan).

Under section 1860D-2(d)(1)(D) of the Act, as amended by section 11001(b) of the IRA, the negotiated prices used in payment by each Part D plan sponsor for each selected drug must not exceed the MFP plus any dispensing fees for such drug. In Part D, the negotiated price of a drug is the basis for determining beneficiary cost-sharing and for benefit administration at the point of sale. Therefore, the requirement that the price used for beneficiary cost-sharing and benefit administration cannot exceed the MFP (plus dispensing fees) helps to ensure that Part D MFP-eligible individuals will have access to the MFP at the point of sale. Therefore, while section 1193(a) of the Act requires manufacturers to provide access to the MFP to MFP-eligible individuals, as a practical matter, this would be facilitated by Part D plan sponsors in the normal course.

However, section 1193(a) of the Act also requires that the manufacturer of a selected drug provide access to the MFP for the selected drug to pharmacies, mail order services, and other dispensers with respect to MFP-eligible individuals who are dispensed such drugs. CMS requires that the Primary Manufacturer ensures that entities that dispense drugs to MFP-eligible individuals, including pharmacies, mail order services, and other dispensers, have access to the MFP for the selected drug in accordance with section 1193(a) of the Act and as further described in section 90.2 of this revised guidance. CMS defines "providing access to the MFP" as ensuring that the amount paid by the dispensing entity for the selected drug is no greater than the MFP.

Primary Manufacturers must provide access to the MFP in one of two ways: (1) prospectively ensuring that the price paid by the dispensing entity when acquiring the drug is no greater than the MFP; or (2) providing retrospective reimbursement for the difference between the dispensing entity's acquisition cost and the MFP. As part of this obligation, the Primary Manufacturer must ensure the MFP is made available to pharmacies, mail order services, and other dispensers for units of the selected drug for which there is a Secondary Manufacturer. With respect to the second option, CMS plans to issue further information regarding the specific calculation that the manufacturer could use in the determination of the refund to the dispenser. CMS is exploring whether manufacturers could offer a standardized refund amount, such as the Wholesale Acquisition Cost (WAC) of the selected drug minus the MFP (WAC-MFP), in order to meet this obligation.

CMS intends to engage with a Medicare Transaction Facilitator (MTF) to facilitate the exchange of data between pharmaceutical supply chain entities to support the verification of an MFP-eligible individual who is dispensed a selected drug. CMS intends to continue to work with interested parties to identify existing processes and any new processes that would be the most viable for the supply chain to operationalize to ensure that pharmacies, mail order services, and other dispensers have access to the MFP during the price applicability period. CMS will consult with pharmacies, mail order services, and other dispensers, as well as with industry standard development organizations (SDOs), 340B covered entities and related organizations, pharmaceutical/biotechnology manufacturers, and other supply chain participants to understand existing data flows and identify opportunities for increased connectivity and data sharing. CMS is also exploring options to facilitate retrospective payment exchange between manufacturers and

dispensing entities to help effectuate access to the MFP. CMS plans to release more information in advance of initial price applicability year 2026 regarding such issues related to ensuring access to the MFP, including how CMS might support and facilitate data exchange between pharmaceutical supply chain entities.

A Primary Manufacturer must ensure that pharmacies, mail order services, and other dispensers are reimbursed timely. That is, CMS requires that the MFP must be passed through to the dispensers within 14 days of the manufacturer receiving sufficient information to verify that an individual is eligible for access to the MFP. Neither Primary Manufacturers nor their contracted entities shall charge any transaction fees for the data exchanges that would be facilitated through an MTF. Regardless of whether existing processes or new processes are used to facilitate access to the MFP, manufacturers are expected to comply with existing applicable data privacy and security laws. Primary Manufacturers must work with any Secondary Manufacturer of a selected drug to determine how the MFP will be passed through in a manner that complies with applicable data privacy and security laws.

Further, CMS requires that a Primary Manufacturer submit its process for making the MFP available, including to 340B covered entities, for the selected drug in writing to CMS at least 30 days before the start of the initial price applicability year for the selected drug. CMS intends to publish these processes on the CMS IRA website. For initial price applicability year 2026, a Primary Manufacturer of a selected drug must send its process for ensuring MFP availability to CMS in writing by December 2, 2025. A Primary Manufacturer must notify CMS of any changes to its process for making the MFP available at least 30 days before the change goes into effect. CMS will monitor for compliance, and will audit as needed, to ensure that the MFP is being made available for the selected drug (see section 90.2 of this revised guidance for additional details). A Primary Manufacturer must retain for at least ten years from the date of sale any records relating to sales of the selected drug to entities that dispense the selected drug to MFP-eligible individuals, including pharmacies, mail order services, and other dispensers for units of selected drug, in alignment with the statute of limitations period under the False Claims Act.

CMS notes that the Agreement would not restrict the Primary Manufacturer or Secondary Manufacturer(s) from offering to the Part D plans a price lower than the MFP that would be passed through to the beneficiary by the dispenser. CMS reiterates that Primary Manufacturers are responsible for ensuring that the MFP is made available to pharmacies, mail order services, and other dispensers that dispense the selected drug to MFP-eligible individuals, including ensuring that MFP is available for units of the selected drug for which there is a Secondary Manufacturer. Commercial and other payers will continue to have discretion to consider Medicare payment rates among other considerations in establishing their own payment policies.

40.4.1 Nonduplication with 340B Ceiling Price

In accordance with 1193(d) of the Act and as further described in section 90.2 of this revised guidance, the Primary Manufacturer of a selected drug is not required to provide access to the MFP for a selected drug to MFP-eligible individuals who are eligible to be dispensed such selected drug at a covered entity described in section 340B(a)(4) of the PHS Act if the selected drug is subject to an agreement described in section 340B(a)(1) of the PHS Act and the 340B

ceiling price (defined in section 340B(a)(1) of the PHS Act) is lower than the MFP for such selected drug.

A manufacturer that provides an MFP on a selected drug is not also required to provide a 340B discount on that same drug. That is, these price concessions are not cumulative. CMS expects that the ingredient cost component of all Part D prescriptions filled for a selected drug will be no greater than the drug's MFP, including when those prescriptions are filled at 340B covered entities and their contract pharmacies. CMS understands that 340B covered entities and their contract pharmacies currently use different inventory management processes for 340B drugs, such as separate physical drug inventories or a retrospective replenishment model. Regardless of the specific inventory management process used, the same policies regarding the MFP will apply, including that the manufacturer must provide access to the lower of the MFP or 340B ceiling price, such as through a replenished 340B inventory or an MFP refund within 14 days of determining that the selected drug was dispensed to an MFP-eligible individual.

CMS intends to work with the Health Resources and Services Administration, which administers the 340B Drug Pricing Program, to help to ensure that the MFP is made available to 340B covered entities where appropriate and that there is no duplication with the 340B ceiling price.

40.5 Compliance with Administrative Actions and Monitoring of the Drug Price Negotiation Program

Pursuant to CMS' statutory obligation under sections 1191(a)(4), 1196, and 1197 of the Act, CMS will establish a robust program for monitoring compliance with the Negotiation Program. After entering into an Agreement with CMS and in accordance with section 1193(a)(5) of the Act, the Primary Manufacturer must comply with requirements determined by CMS to be necessary for purposes of administering the Negotiation Program and monitoring compliance with the Negotiation Program. For example, CMS anticipates engaging in auditing processes to verify the accuracy and completeness of any information provided by the Primary Manufacturer under the requirements of section 1193(a)(4) of the Act. CMS also may audit any data related to the Primary Manufacturer providing access to the MFP, including where the selected drug is provided by a Secondary Manufacturer. CMS will document all requests for information required to administer or monitor compliance with the Negotiation Program in accordance with section 1193(a)(5) of the Act. Written requests from CMS to the Primary Manufacturer will include a date by which the requested information shall be submitted to CMS. If the Primary Manufacturer fails to submit complete and accurate information to CMS by the deadline stated in a request for information, CMS will consider the Primary Manufacturer in violation of the Agreement and the Manufacturer may be subject to civil monetary penalties as outlined in section 1197(c) of the Act.

CMS will allow a Primary Manufacturer that believes in good faith that CMS has made an error in the calculation of the ceiling or the computation of how CMS will apply a single MFP across dosage forms and strengths to submit a suggestion of error for CMS' consideration. As feasible, CMS will provide information on these calculations to the Primary Manufacturer within 60 days of the Primary Manufacturer's submission of data that complies with the requirements described in section 50.1. A Primary Manufacturer will have 30 days to submit a suggestion of error and may do so by submitting the request via email to IRARebateandNegotiation@cms.hhs.gov with

the subject line "Suggestion of Error for [name of the selected drug]." This notification should include supporting information documenting why the Primary Manufacturer believes that CMS made a mathematical error in its calculations and corresponding steps that should be reviewed. CMS will review and respond within 30 days of receiving the suggestion of error from the Primary Manufacturer if feasible. The suggestion of error process does not imply that a Primary Manufacturer need not comply with Negotiation Program requirements and will not affect any timelines or requirements of the Negotiation Program.

40.6 Termination of the Agreement

In accordance with section 1193(b) of the Act, when the Primary Manufacturer enters into the Agreement described in section 40.1 of this revised guidance, the Agreement will remain in effect, including through renegotiation, as applicable, until the selected drug is no longer considered a selected drug under section 1192(c) of the Act as described in section 70 of this revised guidance unless the Agreement is terminated sooner by the Primary Manufacturer under the conditions specified below. Accordingly, the Agreement will have an effective date as of the date the Agreement is signed by both parties (the "Effective Date"), and the term of the Agreement will be from the Effective Date of the Agreement to the earlier of the first year that begins at least 9 months after the date on which CMS determines that the selected drug is no longer a selected drug under section 1192(c) of the Act or the Agreement is terminated by either party in accordance with this section (the "Termination Date").

In accordance with section 1193(a)(5) of the Act, a Primary Manufacturer may terminate its Agreement with respect to a selected drug with respect to a price applicability period, before reaching an agreement with CMS as to the MFP for the selected drug or after such an MFP is agreed to, if the Primary Manufacturer meets certain conditions for termination consistent with the provisions in 26 U.S.C. § 5000D(c). Specifically, a Primary Manufacturer seeking to terminate its Agreement with respect to a selected drug must submit to CMS a notice of request to terminate. As noted in section 40.1, section 11003 of the IRA expressly connects a Primary Manufacturer's financial responsibilities under the voluntary Negotiation Program to that manufacturer's voluntary participation in the Medicaid Drug Rebate Program and the Medicare Coverage Gap Discount Program and the Manufacturer Discount Program. The provisions enacted at 26 U.S.C. § 5000D give the Primary Manufacturer choices with regard to the Negotiation Program. The Primary Manufacturer may participate in the Negotiation Program. The Primary Manufacturer may opt out of the Negotiation Program and pay the excise tax on the sale of the selected drug during defined periods. Alternatively, the Primary Manufacturer may opt out of the Negotiation Program and avoid the excise tax on sales of the selected drug during the period for which the manufacturer does not have applicable agreements with the Medicare and Medicaid programs and none of its drugs are covered by an agreement under section 1860D-14A or section 1860D-14C of the Act. Promoting continuity in the administration of the Negotiation Program warrants extending parallel options to a Primary Manufacturer with respect to potential CMP liability. A Primary Manufacturer with an Agreement with respect to the price applicability period with respect to a selected drug may opt out of the Negotiation Program and pay CMPs associated with violations of program requirements. Alternatively, a Primary Manufacturer seeking to cease participation in the Negotiation Program through the end of the price applicability period for a selected drug may avoid CMP liability by terminating its Agreement if it also ceases participation in the Medicaid Drug Rebate Program and the Medicare

Coverage Gap Discount Program and the Manufacturer Discount Program through the end of the price applicability period for the selected drug.

Thus, in accordance with section 1193(a)(5) of the Act, CMS has determined that the Primary Manufacturer's notice of termination of the Agreement must incorporate both (1) a request for termination of the Primary Manufacturer's applicable agreements under the Medicaid Drug Rebate Program and the Medicare Coverage Gap Discount Program and the Manufacturer Discount Program, consistent with the requirements as set forth in 26 U.S.C. § 5000D(c)(1)(A)(i), and (2) an attestation that through the end of the price applicability period for the selected drug, the Manufacturer (a) shall not seek to enter into any subsequent agreement with any such program and (b) shall not seek coverage for any of its drugs under the Medicare Coverage Gap Discount Program under section 1860D-14A of the Act or the Manufacturer Discount Program under section 1860D-14C of the Act, consistent with the requirements as set forth in 26 U.S.C. § 5000D(c)(1)(B). A Primary Manufacturer later seeking to re-enter any applicable agreement or obtain coverage for any of its drugs under the Medicare Coverage Gap Discount Program or the Manufacturer Discount Program would be deemed to have provided an invalid attestation that was a condition of termination, and the Agreement would once again become operative as of the date of re-entry into the applicable agreements or coverage for any of its drugs under the Medicare Coverage Gap Discount Program or the Manufacturer Discount Program. If a Primary Manufacturer terminated its Agreement prior to completing the negotiation process and agreeing to an MFP, such process will be initiated or resumed in accordance with the negotiation process described in section 60 of this revised guidance. In addition, the timing of the Primary Manufacturer's decision to resume participation in the Negotiation Program may implicate the renegotiation process beginning with 2028, for which guidance will be forthcoming for future years of the Negotiation Program.

If the conditions for termination of the Agreement for the Negotiation Program described above are met, CMS will terminate such Agreement effective on the first date on which the notices of termination for all applicable agreements have been received and none of the drugs of the Primary Manufacturer are covered by an agreement under the Medicare Coverage Gap Discount Program or the Manufacturer Discount Program. As is noted above, section 11003 of the IRA expressly connects a Primary Manufacturer's financial responsibilities under the voluntary Negotiation Program to that manufacturer's voluntary participation in the Medicaid Drug Rebate Program and the Medicare Coverage Gap Discount Program and the Manufacturer Discount Program. If a Primary Manufacturer determines after executing its Agreement that it is unwilling to continue its participation in the Negotiation Program and provides a termination notice that complies with the requirements in this section 40.6, CMS will find good cause to terminate the Primary Manufacturer's agreement(s) under the Medicare Coverage Gap Discount Program and the Manufacturer Discount Program, as applicable, pursuant to section 1860D-14A(b)(4)(B)(i) and section 1860D-14C(b)(4)(B)(i) of the Act to expedite the date on which none of the drugs of the Primary Manufacturer are covered by an agreement under section 1860D-14A or section 1860D-14C and thus facilitate an expedited Termination Date.

Moreover, consistent with the process described in Section 40.1 above, if a Primary Manufacturer has determined it is unwilling to continue its participation in the Negotiation Program and provides a termination notice that complies with the requirements in this section

40.6, CMS shall, upon written request from such Primary Manufacturer, provide a hearing concerning its termination request for its applicable agreements under the Medicare Coverage Gap Discount Program and the Manufacturer Discount Program, as applicable. Such a hearing will be held prior to the effective date of termination with sufficient time for such effective date to be repealed. Such a hearing will be held solely on the papers; because CMS' determination that there is good cause for termination depends solely on the Primary Manufacturer's request for termination to effectuate its decision not to participate in the Negotiation Program, the only question to be decided in the hearing is whether the Primary Manufacturer has asked to rescind its termination request prior to the effective date of the termination. CMS will automatically grant such request from the Primary Manufacturer to rescind its termination request.

Notwithstanding any termination of the Agreement, the MFP shall continue to apply for any selected drugs that were dispensed prior to the Termination Date. Also, notwithstanding the termination of the Agreement, any confidentiality, record retention, and/or data requirements and any requirements for Primary Manufacturer participation in audit and other Negotiation Program oversight activities shall continue to apply.

40.7 Other Provisions in the Agreement

Additional terms in the Agreement set forth general provisions in accordance with requirements determined by CMS to be necessary for purposes of administering or monitoring compliance with the Negotiation Program. For example, any notice required to be given by the manufacturer or CMS must be sent in writing via email to CMS- and manufacturer-designated email addresses. CMS retains the authority to amend the Agreement to reflect changes in law, regulation, or guidance, and, when possible, CMS will give the Manufacturer at least 60-day notice of any change to the Agreement.

In accordance with section 1193(a)(5) of the Act, if, after entering in an Agreement with CMS, the Primary Manufacturer of a selected drug transfers ownership of one or more NDAs / BLAs of the selected drug to another entity, the Primary Manufacturer remains responsible for all requirements of the Agreement, including the requirement to provide access to the MFP, associated with the transferred NDAs / BLAs unless and until the Primary Manufacturer transfers all the NDAs / BLAs of the selected drug that it holds to an entity and such acquiring entity assumes responsibility as the new Primary Manufacturer. Those steps must be evidenced by a novation to the transferring Primary Manufacturer's original Agreement for the Negotiation Program. The transferring Primary Manufacturer remains responsible for any outstanding Negotiation Program rebate liabilities related to the biosimilar delay provision under section 1192(f) of the Act unless and until such liabilities are transferred to the acquiring entity as the new Primary Manufacturer. The transferring Primary Manufacturer shall provide CMS at least 30 calendar days written notice before the effective date of any such transfer and, if applicable, any novation.

If the Primary Manufacturer of a selected drug transfers all NDAs / BLAs of the selected drug pursuant to the preceding paragraph, such that an acquiring entity assumes responsibility as the new Primary Manufacturer of the selected drug for purposes of the Negotiation Program, CMS recognizes that this transfer of ownership could affect the Primary Manufacturer's potential excise tax liability as well as the impact on the Primary Manufacturer of the statutory suspension

of excise tax provisions and the termination process as described in section 40.6 of this revised guidance. CMS recognizes that whether this transfer of ownership would have these impacts would depend on whether the transfer of the NDAs / BLAs was made to an entity that is not a related party (e.g., not treated as part of the same employer under subsections (a) and (b) of section 52 of the Internal Revenue Code of 1986) and complied with relevant principles of tax law.

If any provision of the Agreement is found to be invalid by a court of law, the Agreement will be construed in all respects as if the invalid or unenforceable provision(s) were eliminated, and without any effect on any other provisions.

50. Negotiation Factors

In accordance with sections 1193(a)(4) and 1194(b)(2)(A) of the Act, the Primary Manufacturer of a selected drug that has chosen to sign the Agreement must submit, in a form and manner specified by CMS, information on the non-FAMP for the selected drug (described in section 50.1.1 of this revised guidance). The Primary Manufacturer must also submit information on certain factors (described in section 1194(e)(1) of the Act and described further in section 50.1 of this revised guidance). The Primary Manufacturer will be responsible for aggregating and reporting information from any applicable Secondary Manufacturer(s). In addition, the statute prescribes that CMS also consider available evidence about therapeutic alternatives to the selected drug(s) (described in section 1194(e)(2) of the Act and described further in section 50.2 of this revised guidance).

While the statute requires that CMS consider manufacturer-specific data for the factors described at section 1194(e)(1) of the Act, the statute does not specify what sources CMS must use for the factors described at section 1194(e)(2) regarding therapeutic alternatives to a selected drug. CMS will consider evidence about therapeutic alternatives relevant to the factors described in section 1194(e)(2) of the Act submitted by members of the public, including manufacturers, Medicare beneficiaries, academic experts, clinicians, caregivers, and other interested parties. CMS believes that by allowing any interested party to submit data, CMS will be best positioned to identify all available, relevant evidence for the factors described at section 1194(e)(2).

CMS published the Negotiation Data Elements ICR in the Federal Register on March 21, 2023. The Negotiation Data Elements ICR describes how CMS will collect the data outlined in sections 1193(a)(4)(A), 1194(e)(1), and 1194(e)(2) of the Act. This ICR includes instructions on how Primary Manufacturers and members of the public may submit relevant data. The comment period for the Negotiation Data Elements ICR closed on May 22, 2023. CMS is releasing a revised version of the Negotiation Data Elements ICR on June 30, 2023, and the 30-day comment period will close on July 31, 2023.

The definitions that CMS is adopting for the purposes of describing the data to be collected for use in the Negotiation Program under sections 1193(a)(4)(A) and 1194(e)(1) of the Act are specified in Appendix C of this revised guidance.

In accordance with sections 1191(d)(5)(A), 1194(b)(2)(A), and 1193(a)(4)(B) of the Act, the data described in sections 50.1 and 50.2 of this revised guidance for drugs selected for initial price applicability year 2026 must be submitted to CMS by October 2, 2023. CMS' determination to

require public submission on the same date as manufacturer submission (i.e., October 2, 2023) serves to enable CMS to consider all submitted evidence in totality and meet the statutory deadline for the initial offer, pursuant to general program administration authority.

50.1 Manufacturer-Specific Data

Section 1194(e) of the Act directs CMS, for purposes of negotiating the MFP for a selected drug with the Primary Manufacturer, to consider certain factors, as applicable to the selected drug, as the basis for determining its offers, as described in section 60 of this revised guidance. These factors include data submitted by the Primary Manufacturer, as specified in section 1194(e)(1) of the Act. Submission of these data by the Primary Manufacturer is required if an Agreement is signed; details related to the submission process are described in section 40.2 of this revised guidance.

These data include the following and are required to be reported by the Primary Manufacturer to CMS by October 2, 2023:

1. Research and development (R&D) costs of the Primary Manufacturer for the selected drug and the extent to which the Primary Manufacturer has recouped those costs;
2. Current unit costs of production and distribution of the selected drug, averaged across the Primary Manufacturer and any Secondary Manufacturer(s);
3. Prior Federal financial support for novel therapeutic discovery and development with respect to the selected drug;
4. Data on pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the FD&C Act or section 351(a) of the PHS Act for the selected drug; and
5. Market data and revenue and sales volume data for the selected drug in the United States for the Primary Manufacturer and any Secondary Manufacturer(s).

The Primary Manufacturer should submit information in the CMS HPMS for the NDC-11s of the selected drug, inclusive of any NDC-11s that the Primary Manufacturer submits for the list of NDC-11s pursuant to section 40.2 of this revised guidance. As noted above, CMS requires the Primary Manufacturer to aggregate data from both the Primary Manufacturer and any Secondary Manufacturer(s) for the following: non-FAMP, current unit costs of production and distribution, and certain data pertaining to market data and revenue and sales volume data for the selected drug.

Please see Appendix C of this revised guidance for a list of definitions that apply for purposes of describing these data to be collected for use in the Negotiation Program.

50.1.1 Non-FAMP Data

The Primary Manufacturer must submit data on non-FAMP for the selected drug for the Primary Manufacturer and any Secondary Manufacturer(s), as required under section 1193(a)(4)(A) of the Act. CMS will be collecting these data through the Negotiation Data Elements ICR described above. Specifically, for initial price applicability year 2026, the Primary Manufacturer must submit the non-FAMP, unit type, and total unit volume for each NDC-11 of the selected drug for the four quarters of calendar year 2021, or in the case that there is not an average non-FAMP price available for such drug for 2021, the non-FAMP, unit type, and total unit volume for each

NDC-11 of the selected drug for the four quarters of the first full calendar year following market entry of such drug. For purposes of determining the applicable year, CMS will consider the average non-FAMP price to be available for a selected drug for calendar year 2021 if the Primary Manufacturer reports at least one quarter of non-FAMP data for at least one NDC-11 of the selected drug in calendar year 2021. As described in Appendix C, when there are at least 30 days of commercial sales data but less than a calendar quarter of data to calculate the non-FAMP in calendar year 2021 (or the first full year following market entry of such drug, when applicable) for a given NDC-11 of such drug, the non-FAMP reported by the manufacturer to CMS for that calendar quarter should reflect the temporary non-FAMP predicated upon the first 30 days of commercial sales data. The temporary non-FAMP should be calculated following the same methodology used to calculate the temporary non-FAMP amount used to determine the Temporary Federal Ceiling Price as described in the Department of Veterans Affairs' (VA) 2023 Updated Guidance for Calculation of Federal Ceiling Prices (FCPs) for New Drugs subject to Public Law 102-585. Any restatements of the non-FAMP made in any manufacturer non-FAMP submissions to the VA must be reflected in the non-FAMP submitted to CMS. The use of these data to calculate the ceiling for the MFP is further described in section 60.2 of this revised guidance. Details on how CMS defines the parameters of the non-FAMP data collection are included in Appendix C of this revised guidance and are also included in the Negotiation Data Elements ICR.

50.2 Evidence About Therapeutic Alternatives for the Selected Drug

As noted above, section 1194(e)(2) of the Act directs CMS to consider evidence about alternative treatments to the selected drug, as available, including:

1. The extent to which the selected drug represents a therapeutic advance compared to existing therapeutic alternatives for the selected drug and the costs of such existing therapeutic alternatives;
2. FDA-approved prescribing information for the selected drug and its therapeutic alternatives;
3. Comparative effectiveness of the selected drug and its therapeutic alternatives, including the effects of the selected drug and its therapeutic alternatives on specific populations (including individuals with disabilities, the elderly, the terminally ill, children, and other patient populations, herein referred to as "specific populations"); and
4. The extent to which the selected drug and the therapeutic alternatives to the drug address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy.

Section 1194(e)(2) of the Act additionally requires that CMS not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill. Information submitted by members of the public, including manufacturers, Medicare beneficiaries, academic experts, clinicians, caregivers, and other interested parties, or other information found by CMS that treats extending the life of individuals in these populations as of lower value will not be used in the Negotiation Program.[57]

[57] Some uses of QALY treat extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill. CMS will not use any QALY in the Negotiation Program.

CMS will review cost-effectiveness measures used in studies relevant to a selected drug to determine whether the measure used is permitted in accordance with section 1194(e)(2), as well as with section 1182(e) of Title XI of the Act. CMS may use content in a study that uses a cost effectiveness-measure if it determines that the cost-effectiveness measure used is permitted in accordance with the law and does not treat extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill. In instances where some, but not all, content in a study is excluded (e.g., QALYs), CMS may still consider content that is relevant and allowable (e.g., clinical effectiveness, risks, harms) under section 1194(e)(2) of the Act and section 1182(e) of Title XI of the Act. CMS requires respondents submitting information to indicate whether their submission contains information from studies that use measures that treat extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill. CMS also requests that respondents submitting information under 1194(e)(2) provide a short description of any cost-effectiveness measures included in the research they are submitting, and how they believe the data avoids treating extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

The Primary Manufacturer and members of the public, including other manufacturers, Medicare beneficiaries, academic experts, clinicians, caregivers, and other interested parties, may submit information on selected drugs and their therapeutic alternatives (specifically pharmaceutical therapeutic alternatives, as described in detail in section 60.3.1 of this revised guidance), including information on whether the selected drug represents a therapeutic advance over its therapeutic alternative(s), prescribing information for the selected drug and its therapeutic alternative(s), comparative effectiveness data for the selected drug and its therapeutic alternative(s), information about the impact of the selected drug and its therapeutic alternative(s) on specific populations, information about patient experience, and/or information on whether the selected drug addresses unmet medical need, as described in section 1194(e)(2) of the Act. Outcomes such as changes to productivity, independence, and quality of life will also be considered when these outcomes correspond with a direct impact on the individuals taking the selected drug or therapeutic alternative and are appropriately measurable and quantifiable.

CMS will additionally review existing literature and real-world evidence, conduct internal analytics, and consult subject matter and clinical experts on these topics (described in section 60.3.1 of this revised guidance) when considering available evidence about alternative treatments to the selected drug. When reviewing the literature from the public and manufacturer submissions as well as literature from CMS' review, CMS will consider the source, rigor of the study methodology, current relevance to the selected drug and its therapeutic alternative(s), whether the study has been through peer review, study limitations, degree of certainty of conclusions, risk of bias, study time horizons, generalizability, study population, and relevance to the negotiation factors listed in section 1194(e)(2) of the Act to ensure the integrity of the contributing data within the negotiation process. CMS will prioritize research, including both observational research and research based on randomized samples, that is methodologically rigorous, appropriately powered (i.e., has sufficient sample size) to answer the primary question

of the research, and structured to avoid potential false positive findings due to multiple subgroup analyses.

CMS will consider research and real-world evidence relating to Medicare populations, including on individuals with disabilities, patients with end-stage renal disease (ESRD), and Medicare-aged populations, as particularly important. In considering impact on specific populations and patients with unmet medical needs, CMS will prioritize research specifically designed to focus on these populations over studies that include outcomes for these populations but for which these populations were not the primary focus.

All information on the factors described in section 1194(e)(2) of the Act related to drugs selected for initial price applicability year 2026 must be submitted to CMS by October 2, 2023.

Please see Appendix C of this revised guidance for a list of definitions that CMS adopted for the purposes of describing these data to be collected for use in the Negotiation Program.

60. Negotiation Process

In accordance with section 1194(b)(1) of the Act, CMS will develop and use a consistent methodology and process for negotiation with the aim of achieving agreement on "the lowest maximum fair price for each selected drug." This section 60 describes the negotiation process, including the development of the written initial offer, the process for making such offer and providing a concise justification to the Primary Manufacturer of a selected drug, the process and requirements for accepting an offer or providing a counteroffer, the potential for up to three negotiation meetings between CMS and the Primary Manufacturer, the conclusion of negotiation, the publication of the MFP, and explanation of the MFP.

60.1 Establishment of a Single MFP for Negotiation Purposes

In accordance with section 1191(c)(3) of the Act, MFP means, with respect to a year during a price applicability period and with respect to a selected drug, the price negotiated pursuant to section 1194 of the Act, and updated pursuant to section 1195(b), as applicable, for such drug and year. CMS interprets this language to refer to negotiation of a single price for a selected drug with respect to its price applicability period. Accordingly, CMS will identify a single price for use at each step in the negotiation process described in this section 60, meaning each offer and counteroffer, described in section 60.4 of this revised guidance, will include a single price, even for a selected drug with multiple dosage forms and strengths. Once the MFP has been agreed upon, section 1196(a)(2) of the Act directs CMS to establish procedures to compute and apply the MFP across different dosage forms and strengths of a selected drug.

For the purposes of determining a single price included in an initial offer (including evaluating clinical benefit compared to the therapeutic alternative(s), as described in section 60.3 of this revised guidance) and conducting the negotiation, CMS will base the single price on the cost of the selected drug per 30-day equivalent supply (rather than per unit – such as tablet, capsule, injection – or per volume or weight-based metric), weighted across dosage forms and strengths. This approach of negotiating a single price across all dosage forms and strengths aligns with the statutory requirement to negotiate an MFP for a selected drug. CMS believes this will also allow for a more direct comparison with the therapeutic alternative(s), which might have different

dosage forms, strengths, and treatment regimens (e.g., daily consumption of tablets versus monthly injections of solutions) than the selected drug.

Section 60.5 of this revised guidance describes the methodology CMS will use to translate the MFP once finalized (which, per above, will be an average price per 30-day equivalent supply for the selected drug) back into per unit (e.g., tablet) prices at the dosage form and strength level for the purposes of publishing per-unit MFPs for the different dosage forms and strengths of the selected drug at the NDC- 9 and NDC-11 levels, as contemplated under section 1196(a)(2). In addition to the description of that methodology included in this revised guidance, CMS will share the inputs behind that methodology specific to the selected drug with the Primary Manufacturer of the selected drug during the negotiation period such that the Primary Manufacturer will have visibility into the implied unit prices based on the MFP for each dosage form and strength throughout the negotiation process (i.e., any offer or counteroffer that identifies a single price would be clearly translatable to per unit prices at the dosage form and strength level). Please see section 60.5 of this revised guidance for details.

60.2 Limitations on Offer Amount

In accordance with section 1194(b)(2)(F)(i) of the Act, in negotiating the MFP of a selected drug, with respect to initial price applicability year 2026, CMS will not make an offer (or agree to a counteroffer) for an MFP that exceeds the ceiling specified in section 1194(c) of the Act. This section 60.2 of this revised guidance provides details on the determination of the ceiling for the MFP and comparison of the ceiling to the MFP.

60.2.1 Determination of the Ceiling for the MFP

In accordance with section 1194(c) of the Act, for initial price applicability year 2026, the ceiling for the MFP for a selected drug shall not exceed the lower of the following:

- As described in section 60.2.2 of this revised guidance, an amount equal to the sum of the plan-specific enrollment weighted amounts; or
- As described in section 60.2.3 of this revised guidance, an amount equal to the applicable percent, with respect to the selected drug, of the average non-FAMP as defined in section 1194(c)(6) of the Act for such drug for calendar year 2021 (or in the case that there is not an average non-FAMP for such drug for calendar year 2021, for the first full year following the market entry for such drug), increased by the percentage increase in the consumer price index for all urban consumers (all items; United States city average) from September 2021 (or December of such first full year following the market entry), as applicable, to September 2022.[58]

CMS interprets the language in section 1194(c)(1)(A) of the Act to mean it should calculate a single amount across all dosage forms and strengths of the selected drug for the sum of the plan-specific enrollment weighted amounts and for the applicable percent of the average non-FAMP in order to determine which one is lower and will serve as the ceiling for the MFP. To determine whether the sum of the plan-specific enrollment weighted amounts or the applicable percent of the average non-FAMP will be used to calculate the ceiling for the MFP, CMS will aggregate the

[58] The September 2021 CPI-U, not seasonally unadjusted, was 274.310; the September 2022 CPI-U, not seasonally adjusted, was 296.808. The percentage increase was 8.202 percent. Data retrieved from https://www.bls.gov/cpi/data.htm on May 16, 2023.

amounts determined for each NDC-11 for the selected drug to calculate a single amount – separately for each methodology – across dosage forms, strengths, and package sizes of the selected drug. These amounts can then be directly compared, and the ceiling for the single MFP of the selected drug (including all dosage forms and strengths) will be the lower amount.

CMS will calculate a single ceiling per 30-day equivalent supply (please see 42 C.F.R. § 423.104(d)(2)(iv)(A)(2) for details on 30-day equivalent supply methodology) across all dosage forms and strengths of the selected drug. Using the price per 30-day equivalent supply to calculate this amount facilitates aggregation across dosage forms and strengths of a selected drug where units (e.g., mg versus ml) and treatment regimens (e.g., daily consumption of tablets versus monthly injections of solutions) differ. Sections 60.2.2 and 60.2.3 of this revised guidance describe the process for calculating the sum of the plan-specific enrollment weighted amounts and for calculating the applicable percent of the average non-FAMP, respectively, and section 60.2.4 describes the selection of the ceiling for the single MFP.

For new NDCs included in the definition of the selected drug that are marketed before the ceiling is calculated, the new NDC will be included in the ceiling calculation (as described in this section) provided that CMS receives non-FAMP price data for at least one calendar quarter in calendar year 2021 (or for the first full calendar year following market entry) and observes PDE days supply, PDE quantity dispensed, and PDE gross expenditures for at least one quarter in calendar year 2022, and DIR amounts for calendar year 2022.

CMS will not include a new NDC in the ceiling calculation if any of the above PDE elements do not have at least one calendar quarter of data in calendar year 2022 or if there are no DIR amounts for calendar year 2022 or the Primary Manufacturer did not submit non-FAMP price data for at least one quarter of calendar year 2021 (or for the first full calendar year following market entry).

60.2.2 Sum of the Plan-Specific Enrollment Weighted Amounts

In accordance with section 1194(c)(1)(B)(i) of the Act, CMS will calculate for a selected drug an amount equal to the sum of the plan-specific enrollment weighted amounts determined using the methodology described in section 1194(c)(2) of the Act. Plan sponsors report Part D PDE data to CMS at the NDC-11 level. Sponsors also report Direct and Indirect Remuneration (DIR) data to CMS at the NDC-11 level in the annual Detailed DIR Report. CMS will use these reported data for plan year 2022, which is the most recent year for which data will be available, for the purpose of determining the sum of the plan-specific enrollment weighted amounts for a selected drug for initial price applicability year 2026.

CMS will include all Part D plans that have PDE data for dosage forms and strengths of the selected drug in this calculation. Because CMS will have no PDE data for Part D plans in the following circumstances, such Part D plans will, by definition, be excluded from the calculation of the plan-specific enrollment weighted amounts: (1) plans that have no utilization for the selected drug and (2) plans that have no enrollment for 2022.[59] CMS will also exclude any PDE

[59] CMS notes that employer sponsored plans that receive the retiree drug subsidy and health plans that offer creditable prescription drug coverage are not included because they are not Part D plans.

records for the selected drug for which the total gross covered prescription drug cost is equal to $0.

CMS will calculate the sum of the plan-specific enrollment weighted amounts in two stages. First, CMS will calculate the sum of the plan-specific enrollment weighted amounts for each NDC-9 associated with NDC-11s included on the list of NDC-11s of the selected drug in the CMS HPMS (see section 40.2 of this revised guidance). Second, CMS will calculate the sum of the plan-specific enrollment weighted amounts across these NDC-9s. The amounts calculated at each stage are for a 30-day equivalent supply (see 42 C.F.R. § 423.104(d)(2)(iv)(A)(2) for details on 30-day equivalent supply methodology).

To determine the sum of the plan-specific enrollment weighted amounts for each NDC-9 and across all NDC-9s of the selected drug, CMS will conduct the following steps.

Steps 1 through 8 will result in the sum of the plan-specific enrollment weighted amounts for each NDC-9 of the selected drug:

1. For each Part D plan, CMS will identify the PDE data for the selected drug for 2022 (that is, PDE records with dates of service during the period beginning on January 1, 2022 and ending on December 31, 2022).
2. For each Part D plan and each NDC-9, CMS will separately sum the negotiated price amounts (as defined in 42 C.F.R. § 423.100), the estimated rebate at point-of-sale amounts (ERPOSA), and units dispensed.
3. For each Part D plan and each NDC-9, CMS will sum the total DIR amounts found in the 2022 Detailed DIR Report and subtract the total ERPOSA calculated in step 2 to avoid double counting price concessions applied at the point of sale.
4. For each Part D plan and each NDC-9, CMS will subtract the total DIR minus ERPOSA amount calculated in step 3 from the total negotiated price amounts calculated in step 2 and then divide by the total units dispensed also determined in step 2. This calculation results in the NDC-9 price per unit, net of all price concessions received by such Part D plan or pharmacy benefit manager on behalf of such Part D plan.
5. Separately, CMS will identify the total number of individuals enrolled in all Part D plans in December 2022 and the total number of individuals enrolled in each Part D plan in that same month.[60] The Part D plans included in both calculations of step 5 will be restricted to Part D plans with at least one PDE record for the selected drug in calendar year 2022.
6. For each Part D plan and each NDC-9, CMS will divide the total number of Part D beneficiaries enrolled in the Part D plan during December 2022 as identified in step 5 by the total number of individuals enrolled in all Part D plans in December 2022 also as identified in step 5, and multiply this quotient by the price per unit, net of all price concessions received by such plan or pharmacy benefit manager on behalf of such Part D plan, calculated in step 4, to arrive at the plan-specific enrollment weighted amount.
7. For each NDC-9, CMS will then sum the amounts calculated in step 6 across all Part D plans to calculate the sum of the plan-specific enrollment weighted amounts.

[60] CMS conducted an analysis of monthly Part D plan enrollment changes during 2022 and determined that monthly enrollment changes were the lowest from November to December, so CMS chose December as the most stable month to identify enrollment. The choice of one month to identify enrollment also allows the weights calculated in step 6 to sum to one.

8. For each NDC-9, CMS will then multiply the sum of the plan-specific enrollment weighted amounts calculated in step 7, which are a per unit price, by the NDC-9 average number of units per 30-day equivalent supply calculated from PDE data for 2022 to yield the price of a 30-day equivalent supply.

Steps 9 through 10 result in the sum of the plan-specific enrollment weighted amounts across all NDC-9s of the selected drug:

9. For each NDC-9, CMS will divide the total 30-day equivalent supply for that NDC-9 by the total 30-day equivalent supply across all NDC-9s, both calculated from 2022 PDE data, and multiply this quotient by the sum of the plan-specific enrollment weighted amounts for a 30-day equivalent supply as calculated in step 8.
10. CMS will then sum amounts calculated in step 9 across all NDC-9s to generate the sum of the plan-specific enrollment weighted amounts for the selected drug for a 30-day equivalent supply.

60.2.3 Average Non-Federal Average Manufacturer Price

In accordance with section 1194(c)(1)(C)(i) of the Act, for initial price applicability year 2026, CMS will calculate an amount equal to the applicable percent, with respect to the selected drug, of the average non-FAMP in calendar year 2021 (or in the case that there is not an average non-FAMP for such drug for calendar year 2021, CMS will use the first full year following the market entry for such drug), increased by the percentage increase in the consumer price index for all urban consumers (all items; United States city average) (CPI-U) from September 2021 (or December of such first full year following the market entry), as applicable, to September 2022.[61]

For this calculation, CMS will use the non-FAMP price and unit volume data, as provided by the Primary Manufacturer, for each NDC-11 included on the list of NDC-11s of the selected drug in the CMS HPMS (see section 40.2 of this revised guidance), for each quarter of calendar year 2021 that is submitted to CMS by the Primary Manufacturer pursuant to section 1193(a)(4)(A) of the Act (as described in section 50.1 of this revised guidance) to calculate an annual average non-FAMP per unit. CMS will use 2022 PDE quantity dispensed and days supply data submitted to CMS at the NDC-11 level by Part D plan sponsors for the following: to calculate an annual average non-FAMP per unit for each NDC-9 of the selected drug, to calculate the annual average non-FAMP per 30-day equivalent supply for each NDC-9 of the selected drug, and to calculate the annual average non-FAMP per 30-day equivalent supply for the selected drug. In order to directly compare the amount calculated based on the applicable percent of average non-FAMP and the amount calculated based on the sum of the plan-specific enrollment weighted amounts (as described in section 60.2.2 above), CMS will base the average non-FAMP calculations on a 30-day equivalent supply and use the same 2022 PDE data for weighting both the sum of the plan-specific enrollment weighted amounts and the average non-FAMP across dosage forms and strengths to determine which amount is lower.

CMS will calculate the applicable percent of the average non-FAMP in two stages to determine the ceiling for the MFP. First, CMS will calculate the applicable percent of the average non-FAMP for each NDC-9 of the selected drug. Second, CMS will calculate the applicable percent

[61] The September 2021 CPI-U, not seasonally adjusted, was 274.310; the September 2022 CPI-U, not seasonally adjusted, was 296.808. The percentage increase was 8.202 percent. Data retrieved from https://www.bls.gov/cpi/data.htm on May 16, 2023.

of the average non-FAMP across NDC-9s of the selected drug. The amounts calculated in each stage are for a 30-day equivalent supply (see 42 C.F.R. § 423.104(d)(2)(iv)(A)(2) for details on 30-day equivalent supply methodology).

To determine the applicable percent of the average non-FAMP for each NDC-9 and across all NDC-9s of the selected drug, CMS will conduct the following steps.

Steps 1 through 9 will result in the average non-FAMP, adjusted for inflation and with the applicable percent applied, for each NDC-9 of the selected drug:

1. To calculate an average non-FAMP that is comparable to the sum of the plan-specific enrollment weighted amounts described in section 60.2.2 of this revised guidance, CMS will compare the non-FAMP unit type (e.g., tablet) to the PDE units (i.e., each, milliliter, and grams). In instances where the units are different, CMS will convert the non-FAMP unit type to the PDE units so that the two amounts (average non-FAMP and sum of the plan-specific enrollment weighted amounts) represent the same quantity of the selected drug.[62]
2. For each NDC-11 and for each quarter during calendar year 2021, CMS will calculate the non-FAMP per unit by dividing the non-FAMP per package by the total number of units per package.
    - Note: If the non-FAMP is missing for all NDC-11s of the selected drug for calendar year 2021 (as described in section 50.1.1 of this revised guidance), CMS will use the non-FAMP for the quarters of the first full calendar year following the market entry for such drug.
3. For each NDC-11 and for each quarter during calendar year 2021, CMS will divide the total unit volume (calculated as the product of the total number of packages sold by the number of units per package from manufacturer-reported non-FAMP data) in that quarter by the total unit volume across all four quarters during calendar year 2021 (also from manufacturer reported non-FAMP data), and multiply this quotient by the non-FAMP per unit calculated in step 2.
    - Note: If the non-FAMP is missing for all NDC-11s of the selected drug for calendar year 2021 (as described in section 50.1.1 of this revised guidance), CMS will use the non-FAMP and total unit volumes for the quarters of the first full calendar year following the market entry for such drug.
4. For each NDC-11, CMS will sum the amounts calculated in step 3 across quarters to calculate the average non-FAMP per unit for that NDC-11 for the calendar year CMS believes steps 3 and 4 are necessary to account for non-FAMP unit volume fluctuations that may occur across quarters.
5. For each NDC-11, CMS will divide the total quantity dispensed for that NDC-11 by the total quantity dispensed for all applicable NDC-11s of the same NDC-9 (both calculated from 2022 PDE data) and multiply this quotient by the average non-FAMP per unit for the calendar year calculated in step 4.
6. For each NDC-9, CMS will sum the amounts calculated in step 5 to calculate the average non-FAMP per unit for that NDC-9 for the calendar year. CMS believes steps 5 and 6 are

[62] PDE units are industry standard National Council for Prescription Drug (NCPDP) defined values of each, milliliter, and grams. See: https://standards.ncpdp.org/Billing-Unit-Request.aspx#:~:text=Billing%20Unit%20Requests,grams%22%20or%20%22milliliters.%22.

necessary to account for fluctuations in quantity dispensed that may occur across NDC-11s of an NDC-9 in the Medicare Part D population.

7. For each NDC-9, CMS will then increase the average non-FAMP per unit for calendar year 2021 calculated in step 6 by the percentage increase in CPI-U (all items; United States city average) from September 2021 until September 2022 as specified in section 1194(c)(1)(C)(i) of the Act.
    - Note: For initial price applicability year 2026, if the non-FAMP is missing for all NDC-11s of the selected drug for calendar year 2021(as described in section 50.1.1 of this revised guidance), and the non-FAMP is based on data from the first full calendar year following the market entry of the such drug, which can only be calendar year 2022, CMS will not apply the CPI-U adjustment.
8. For each NDC-9, after CMS has calculated the average non-FAMP per unit for the calendar year, adjusted for inflation, if applicable, CMS will then apply the applicable percent specified in section 1194(c)(3) of the Act for the monopoly type determined for the selected drug based on its initial approval date (described in section 30.1 of this revised guidance). Applying the applicable percent here, in step 8, results in the same step 11 amount as would result if CMS were to apply the applicable percent to the average non-FAMP per 30-day equivalent supply for the selected drug in step 11. The definition of each monopoly type and the applicable percentage are described below for initial price applicability year 2026. CMS notes that the "extended-monopoly" type is not discussed below because the definition of extended-monopoly drug under section 1194(c)(4)(B)(ii) of the Act expressly excludes a selected drug for which a manufacturer has entered into an Agreement with CMS with respect to an initial price applicability year that is before 2030. CMS interprets this to mean that no selected drug will be considered an extended-monopoly drug for purposes of calculating the ceiling prior to initial price applicability year 2030.

Figure 2: Monopoly Types and Applicable Percentage for Initial Price Applicability Year 2026

Monopoly Type	Definition	Applicable Percentage	Note
Short-monopoly drugs and vaccines (section 1194(c)(3)(A) of the Act)[63]	For initial price applicability year 2026, a selected drug that is not a long-monopoly drug or a selected drug that is a vaccine licensed under section 351(a) of the PHS Act and marketed pursuant to that section.	75%	The first approval date, under section 505(c) of the FD&C Act, associated with the initial FDA application number for the active moiety (or fixed combination drug) must be after January 1, 2010 and before September 1, 2016. The first licensure date, under section 351(a) of the PHS Act, associated with the initial FDA application number for the active ingredient (or fixed combination drug) must be after January 1, 2010 and before September 1, 2012.
Long-monopoly drug (section 1194(c)(5)(A) of the Act)	A selected drug for which at least 16 years have elapsed since the date of approval under section 505(c) of the FD&C Act or since the date of licensure under section 351(a) of the PHS Act, as applicable. The term 'long-monopoly drug' does not include a vaccine that is licensed under section 351(a) of the PHS Act and marketed pursuant to that section.	40%	The first approval date under section 505(c) of the FD&C Act or the first licensure date under section 351(a) of the PHS Act, as applicable, associated with the initial FDA application number for the active moiety / active ingredient (or fixed combination drug) must be on or before January 1, 2010.

9. For each NDC-9, CMS will then multiply the average non-FAMP per unit for the calendar year, adjusted for inflation, if applicable, and with the applicable percent applied as calculated in step 8 by the quotient of the total quantity dispensed divided by the total 30-day equivalent supply (i.e., this quotient represents the average units per 30-day supply equivalent for that NDC-9) calculated from 2022 PDE data to determine the

[63] Because the definition of extended-monopoly drug at section 1194(c)(4)(B)(ii) of the Act expressly excludes a selected drug for which a manufacturer has entered into an agreement with CMS with respect to an initial price applicability year before 2030, for initial price applicability year 2026, any drug, biological product, or vaccine that is not considered a long-monopoly drug will be considered a short monopoly drug.

average non-FAMP for a 30-day equivalent supply. As described above in section 60.2.1 of this revised guidance, CMS believes calculating the average non-FAMP for a 30-day equivalent supply is necessary to account for different units and treatment regimens across dosage forms and strengths.

Steps 10 and 11 will calculate the average non-FAMP per 30-day equivalent supply for the calendar year, adjusted for inflation, if applicable, and with applicable percent applied, across all NDC-9s of the selected drug:

10. For each NDC-9, CMS will divide the total 30-day equivalent supply for that NDC-9 by the total 30-day equivalent supply across all NDC-9s of the selected drug, both calculated from 2022 PDE data, and multiply this quotient by the average non-FAMP per 30-day equivalent supply for the calendar year, adjusted for inflation, if applicable, and with the applicable percent applied, calculated in step 9.
11. CMS will then sum amounts calculated in step 10 across all NDC-9s of the selected drug to calculate the average non-FAMP per 30-day equivalent supply for the calendar year, adjusted for inflation, if applicable, and with the applicable percent applied, for the selected drug.

60.2.4 Selection and Application of the Ceiling for the MFP

CMS will compare the values calculated in step 10 of section 60.2.2 of this revised guidance (sum of the plan-specific enrollment weighted amounts) and step 11 of section 60.2.3 of this revised guidance (applicable percent of the average non-FAMP) and select the lower value as the ceiling for the selected drug. Once CMS has identified whether the ceiling would be determined by the sum of the plan-specific enrollment weighted amounts or the applicable percent of the average non-FAMP, CMS will ensure that the MFP per 30-day equivalent supply, as negotiated through the process described in sections 60.3 and 60.4 of this revised guidance, is no greater than the lower ceiling.

60.3 Methodology for Developing an Initial Offer

Section 1194(e) of the Act directs CMS to consider certain factors related to manufacturer-specific data and available evidence about therapeutic alternative(s) as the basis for determining offers and counteroffers in the negotiation process. The statute requires CMS to provide the manufacturer of a selected drug with an initial offer and a concise justification based on the factors described in section 1194(e) that were used in developing the offer; however, CMS has the discretion to determine how and to what degree each factor should be considered.

As discussed in greater detail below, consistent with section 1194(e) of the Act, for the purposes of determining an initial offer, CMS will (1) identify therapeutic alternative(s), if any, for the selected drug as described in section 60.3.1 of this revised guidance; (2) use the Part D net price for the therapeutic alternative(s) that is covered under Part D and/or the Average Sales Price (ASP) for the therapeutic alternative(s) that is covered under Part B to determine a starting point for developing an initial offer as described in section 60.3.2 of this revised guidance; (3) evaluate the clinical benefit of the selected drug (including compared to its therapeutic alternative(s)) for the purposes of adjusting the starting point using the negotiation factors outlined in section 1194(c)(2) of the Act, including whether the selected drug meets an unmet medical need and the selected drug's impact on specific populations, as described in section 60.3.3 of this revised

guidance (resulting in the "preliminary price"); and (4) further adjust the preliminary price by the negotiation factors outlined in section 1194(e)(1) of the Act (described in section 60.3.4 of this revised guidance) to determine the initial offer price.

Pursuant to section 1194(b)(2)(F) of the Act, CMS will not make any offers or accept any counteroffers for the MFP that are above the statutorily defined ceiling.

60.3.1 Identifying Indications for the Selected Drug and Therapeutic Alternatives for Each Indication

For initial price applicability year 2026, CMS will identify the FDA-approved indication(s) not otherwise excluded from coverage or otherwise restricted under section 1860D-2(e)(2) of the Act for a selected drug, using prescribing information approved by the FDA for the selected drug, in accordance with section 1194(e)(2)(B) of the Act. CMS will consider off-label use when identifying indications if such use is included in nationally recognized, evidence-based guidelines and recognized in CMS-approved Part D compendia.[64]

For each indication of the selected drug, CMS will next identify a pharmaceutical therapeutic alternative(s). CMS considered evaluating non-pharmaceutical therapeutic alternatives; however, for initial price applicability year 2026, CMS will only consider therapeutic alternatives that are drugs or biologics covered under Part D or Part B. CMS believes that pharmaceutical therapeutic alternatives will be the most analogous alternatives to the selected drug when considering treatment effect and price differentials. For purposes of this revised guidance, the term "therapeutic alternative" may refer to one or more therapeutic alternative(s) or a subset of the most clinically comparable therapeutic alternatives.

To identify potential therapeutic alternatives for the indications of a selected drug, CMS will use data submitted by the Primary Manufacturer and the public, FDA-approved indications, drug classification systems commonly used in the public and commercial sector for formulary development, indications included in CMS-approved Part D compendia, widely accepted clinical guidelines, the CMS-led literature review, drug or drug class reviews, and peer-reviewed studies. In addition to brand name drugs and biologics, CMS will consider generic drugs and biosimilars when identifying a therapeutic alternative(s) to a selected drug. CMS will consider off-label use for therapeutic alternatives when identifying indications if such use is included in nationally recognized, evidence-based guidelines and recognized in CMS-approved Part D compendia.

CMS will begin by identifying therapeutic alternatives within the same drug class as the selected drug based on properties such as chemical class, therapeutic class, or mechanism of action before considering therapeutic alternatives in other drug classes. In cases where there are many potential therapeutic alternatives for a given indication of the selected drug, CMS may focus on the subset of therapeutic alternatives that are most clinically comparable to the selected drug for the purpose of developing the initial offer. CMS may consult with FDA to obtain information regarding other approved therapies for the same indication and may also consult with clinicians, patients or patient organizations, and/or academic experts, to ensure that appropriate therapeutic alternatives are identified. If a therapeutic alternative has not yet been incorporated into nationally recognized, evidence-based guidelines, CMS will consider clinical evidence available

[64] CMS-approved Part D compendia are described in Chapter 6, § 10.6 of the Prescription Drug Benefit Manual.

through a literature search and information submitted by the Primary Manufacturer and the public to inform the selection of a therapeutic alternative(s). In all cases, CMS will select therapeutic alternatives based on clinical appropriateness.

60.3.2 Developing a Starting Point for the Initial Offer

CMS considered several options for what price should be used as the starting point for developing the initial offer. Options considered included the use of the Part D net price(s) and/or the ASP(s) of therapeutic alternative(s), if any, to the selected drug, the unit cost of production and distribution for the selected drug, the ceiling for the selected drug (as described in section 60.2 of this revised guidance), a domestic reference price for the selected drug (e.g., the Federal Supply Schedule[65] (FSS) price), or a "fair profit" price for the selected drug based on whether R&D costs have been recouped and margin on unit cost of production and distribution. Under any of these options, the initial offer and final MFP would be capped at the statutory ceiling.

After considering these options and in accordance with section 1194(e)(2)(A) of the Act which directs CMS to consider the cost of therapeutic alternative(s), CMS will use the Part D net price(s) ("net price(s)") and/or ASP(s) of the therapeutic alternative(s) (or a subset of the most clinically comparable therapeutic alternatives) for the selected drug, as applicable, as the starting point for developing the initial offer unless this net price or ASP is greater than the statutory ceiling (described in section 60.2 of this revised guidance), and will then consider adjustments based on section 1194(e)(2) data and manufacturer-submitted data per section 1194(e)(1). CMS intends to identify the price of each therapeutic alternative that is covered under Part D net of all price concessions received by any Part D plan or pharmacy benefit manager on behalf of the Part D plan by using PDE data and detailed DIR report data. In taking this approach, CMS acknowledges that the therapeutic alternative(s) for a selected drug may not be priced to reflect its clinical benefit, however, using net prices and ASPs of therapeutic alternatives enables CMS to start developing the initial offer within the context of the cost and clinical benefit of one or more drugs that treat the same disease or condition. By using the price(s) of the selected drug's therapeutic alternative(s), CMS will be able to focus the initial offer on clinical benefit by adjusting this starting point relative to whether the selected drug offers more, less, or similar clinical benefit compared to its therapeutic alternative(s). The other options considered do not provide a starting point that reflects the cost of therapeutic alternatives in the current market, which is an important factor when considering the overall benefit that a treatment brings to Medicare beneficiaries relative to the other drug(s) available to treat the patient's disease or condition.

When comparing prices of therapeutic alternatives for purposes of informing a starting point for the initial offer, CMS may use an alternative methodology for calculating a 30-day equivalent supply as appropriate. For example, because Part B claims data do not contain a "days' supply" field similar to PDE data, CMS may use an alternative methodology to calculate the price per 30-day equivalent supply for therapeutic alternatives covered under Part B.

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[65] The Federal Supply Schedule (FSS) represents long-term government-wide contracts with commercial companies that provide access to millions of commercial products and services to the government. See: https://www.gsa.gov/buy-through-us/purchasing-programs/gsa-multiple-award-schedule/about-gsa-schedule#:~:text=The%20GSA%20Schedule%2C%20also%20known,reasonable%20prices%20to%20the%20government.

If there is one therapeutic alternative for the selected drug, CMS will use the net price or ASP, as applicable, of the therapeutic alternative (if it is lower than the ceiling) as the starting point to develop CMS' initial offer for the MFP. If there are multiple therapeutic alternatives, CMS will consider the range of net prices and/or ASPs, including the prices of generic and biosimilar therapeutic alternatives, as well as the utilization of each therapeutic alternative relative to the selected drug, to determine the starting point within that range. If the selected drug has no therapeutic alternative, if the prices of the therapeutic alternatives identified are above the statutory ceiling for the MFP (as described in section 60.2 of this revised guidance), or if there is a single therapeutic alternative with a price above the statutory ceiling for the MFP, then CMS will determine the starting point for the initial offer based on the FSS or "Big Four Agency"[66] price ("Big Four price"). If the FSS and Big Four prices are above the statutory ceiling, then CMS will use the statutory ceiling as the starting point for the initial offer. In all cases, this starting point will be subject to adjustments as described further below.

60.3.3 Adjusting the Starting Point Based on Clinical Benefit

To evaluate the clinical benefit conferred by the selected drug compared to its therapeutic alternative(s), as applicable, CMS will broadly evaluate the body of clinical evidence, including data received from the public and manufacturers as described in section 50.2 of this revised guidance, and data identified through a CMS-led literature review. CMS may also analyze Medicare claims or other datasets for utilization patterns of the selected drug versus its therapeutic alternative(s), clinical data, or other information relevant to the selected drug and its therapeutic alternative(s) and may consult with clinicians, patients or patient organizations, academic experts, and/or the FDA. As described in section 60.4 of this revised guidance, CMS will provide additional engagement opportunities for interested parties—specifically, meetings with manufacturers and patient-focused listening sessions—after the October 2, 2023 deadline for submission of section 1194(e)(2) data (further described in section 60.4 of this revised guidance).

This approach provides a pathway for CMS to consider the multitude of information expected from public input, including but not limited to peer-reviewed research, expert reports or whitepapers, clinician expertise, real-world evidence, and patient experience. This approach also provides flexibility for CMS to consider multiple perspectives on the clinical benefit of the selected drug and its therapeutic alternative(s), including potential risks, harms, or side effects, and any unique scenarios or considerations related to clinical benefit, safety, and patient experience.

Once the starting point for the initial offer has been established and evidence on clinical benefit has been considered, CMS will adjust the starting point for the initial offer based on the review of the clinical benefit. CMS will not, per section 1194(e)(2) of the Act, use evidence from comparative effectiveness research in a manner that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual

[66] The Big Four price is the maximum price a drug manufacturer is allowed to charge the "Big Four" federal agencies, which are the Department of Veterans Affairs (VA), Department of Defense (DoD), the Public Health Service, and the Coast Guard. See section 8126 of title 38 of the U.S. Code. See: https://www.cbo.gov/publication/57007.

who is younger, non-disabled, or not terminally ill, and will not, per section 1182(e) of the Act, use QALYs. CMS considered employing both a qualitative approach (e.g., adjusting the starting point upward or downward relative to the clinical benefit offered by the selected drug compared to its therapeutic alternatives) and a more thoroughly pre-specified quantitative approach. CMS will use a qualitative approach to preserve flexibility in negotiation, including the ability to consider nuanced differences between different drugs, for example interactions with other treatments commonly prescribed simultaneously for a condition or disease, and other factors that might not be captured in a more thoroughly pre-specified quantitative approach.

60.3.3.1 Analysis for Selected Drugs with Therapeutic Alternative(s)

To consider comparative effectiveness between a selected drug and its therapeutic alternative(s), CMS will identify outcomes to evaluate for each indication of the selected drug. CMS will consider the identified outcomes, including patient-centered outcomes[67] and patient experience data, when reviewing the clinical benefit of the selected drug and its therapeutic alternative(s). When reviewing such information, as noted above, CMS will not, per section 1194(e)(2), use evidence in a manner that treats extending the life of an individual who is elderly, disabled, or terminally ill as lower value than extending the life of an individual who is younger, non-disabled, or not terminally ill, and will not, per section 1182(e) of the Act, use QALYs. Outcomes such as cure, survival, progression-free survival, or improved morbidity could be considered when comparing the selected drug to its therapeutic alternative(s). Outcomes such as changes in symptoms or other factors that are of importance to patients and patient-reported outcomes will also be identified and considered in determining clinical benefit, if available. Additional outcomes such as changes to productivity, independence, and quality of life will also be considered to the extent that these outcomes correspond with a direct impact on individuals taking the drug, including patient-centered outcomes when available. CMS may also consider the caregiver perspective to the extent that it reflects directly upon the experience or relevant outcomes of the patient taking the selected drug. Relevant outcomes will be identified using the CMS-led literature review and information submitted by manufacturers and the public, including patients and caregivers, through the Negotiation Data Elements ICR described in section 50 of this revised guidance, as well as in the patient-focused listening sessions described in section 60.4.

In all cases, CMS will consider applicable evidence and other input collectively, within the context of the course of care for the condition(s) or disease(s) that the selected drug is indicated to treat, and in accordance with section 50 of this revised guidance. As noted previously, this approach provides flexibility to consider multiple perspectives on the clinical benefit of the selected drug and its therapeutic alternative(s), including potential risks, harms, or side effects, and any unique scenarios or considerations related to clinical benefit, safety, and patient experience.

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[67] A patient-centered outcome is defined as: An outcome that is important to patients' survival, functioning, or feelings as identified or affirmed by patients themselves, or judged to be in patients' best interest by providers and/or caregivers when patients cannot report for themselves. (Source: ISPOR Plenary, Patrick (2013) via FDA's *Patient-Focused Drug Development: Collecting Comprehensive and Representative Input – Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders*, June 2020.) See: https://www.fda.gov/media/139088/download.

CMS will also consider the effects of the selected drug and its therapeutic alternative(s) on specific populations as required by section 1194(e)(2)(C) of the Act. In doing so, CMS will evaluate access, equity, and health outcomes for specific populations. To do so, CMS will seek to identify studies focused on the impact of the selected drug and its therapeutic alternative(s) on individuals with disabilities, the elderly, individuals who are terminally ill, children, and other patient populations among Medicare beneficiaries. Specific populations may include underserved and underrepresented populations, as applicable. Further, CMS will consider whether the selected drug fills an unmet medical need, which CMS will define as treating a disease or condition in cases where no other treatment options exist or existing treatments do not adequately address the disease or condition. CMS will consider each selected drug and its therapeutic alternatives to determine whether the drug fills an unmet medical need at the indication level as of the time the section 1194(e)(2) data is submitted. CMS will consider the nonbinding recommendations in the FDA's "Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics,"[68] as well as any updates that may be issued by FDA in the future, when determining if a selected drug addresses an unmet medical need.

CMS will determine whether a selected drug represents a therapeutic advance by examining improvements in outcomes compared to its therapeutic alternative(s) (e.g., selected drug is curative versus a therapeutic alternative that delays progression). CMS understands that a selected drug can be first in class,[69] however, other drugs may have become available since the selected drug's initial approval. In accordance with section 1194(e)(2)(A) of the Act, CMS will review the analyses detailed above for each indication for the selected drug and its therapeutic alternative(s) and determine, based on the relevant information and evidence, what the difference in clinical benefit is between the selected drug and the therapeutic alternative(s).

As previously noted, CMS will take a qualitative approach to adjusting the starting point based on the unique characteristics of the drug and its therapeutic alternative(s) as well as the patient population(s) taking the selected drug. For each selected drug, the applicable starting point will first be adjusted (i.e., apply an upward or downward adjustment, or no adjustment) based on the totality of the relevant information and evidence submitted and gathered through CMS' analysis based on the clinical benefit the selected drug provides (and then subsequently it will be adjusted by the manufacturer-submitted data described in section 60.3.4). Because the extent of clinical benefit may vary across different indications, CMS may adjust the starting point based on the clinical benefit for an individual indication in cases where the clinical benefit of the selected drug is notably different than the therapeutic alternative(s) for that specific indication.

60.3.3.2 Analysis for Selected Drugs Without Therapeutic Alternatives

Similar to a selected drug with at least one therapeutic alternative, the starting point for a selected drug without a therapeutic alternative will be adjusted based on the totality of relevant information and evidence as detailed above, such as outcomes and impact on specific

[68] FDA Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics, May 2014. See: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/expedited-programs-serious-conditions-drugs-and-biologics.

[69] First in class drugs are those that have a new mechanism of action, defined by the National Cancer Institute as "a term used to describe how a drug or other substance produces an effect in the body." See: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/mechanism-of-action.

populations, submitted through the Negotiation Data Elements ICR and gathered through CMS' analysis of the clinical benefit the selected drug provides.

CMS will consider whether the selected drug fills an unmet medical need separately for each indication. A selected drug will be considered to meet an unmet medical need for an indication included in the analysis when it is used to treat a disease or condition where no other treatment options exist or existing treatments do not adequately address the disease or condition. As noted previously, CMS will consider the nonbinding recommendations in the FDA "Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics," as well as any updates that may be issued by FDA in the future, when considering if a drug addresses an unmet medical need for the purpose of the Negotiation Program. A selected drug may be considered a therapeutic advance when a substantial improvement in outcomes is observed for an indication.

60.3.3.3 Preliminary Price

After the starting point has been adjusted, as appropriate, based on section 1194(e)(2) data submitted by manufacturers and the public through the Negotiation Data Elements ICR and gathered through CMS-led analyses and literature review, the resulting price is referred to as "the preliminary price." As described in section 60.3.4 of this revised guidance, the preliminary price will be adjusted, as appropriate, based on data submitted by the Primary Manufacturer in accordance with section 1194(e)(1) of the Act.

60.3.4 Adjusting the Preliminary Price Based on Consideration of Manufacturer-Specific Data

Under section 1194(e)(1) of the Act, CMS must also consider data reported by the Primary Manufacturer, as described in section 50.1 of this revised guidance. The adjustment to the preliminary price applied on the basis of these data, if any, may be upward or downward, as needed to account for these manufacturer-specific data elements. These data elements are: (1) R&D costs of the manufacturer for the drug and the extent to which the manufacturer has recouped R&D costs; (2) current unit costs of production and distribution of the drug; (3) prior Federal financial support for novel therapeutic discovery and development with respect to the drug; (4) data on pending and approved patent applications or exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the FD&C Act or section 351(a) of the PHS Act for the drug; and (5) market data and revenue and sales volume data for the drug in the United States.

CMS will consider the five elements outlined in section 1194(e)(1) of the Act in totality and apply an upward adjustment, downward adjustment, or no adjustment to the preliminary price. To do this, CMS may consider each factor in isolation or in combination with other factors. CMS provides illustrative examples for the manufacturer-specific data elements below. However, the overall adjustment, inclusive of all five elements taken together, may differ from the example adjustment for any single element viewed in isolation.

In considering element (1) above on R&D costs, CMS will consider the extent to which the Primary Manufacturer has recouped its R&D costs. CMS will compare the R&D costs with the global and U.S. total lifetime net revenue for the selected drug reported by the Primary Manufacturer to determine the extent to which the Primary Manufacturer has recouped its R&D costs. For example, if a Primary Manufacturer has not recouped its R&D costs, CMS may

consider adjusting the preliminary price upward. Conversely, if a Primary Manufacturer has recouped its R&D costs, CMS may consider adjusting the preliminary price downward or apply no adjustment. CMS may use the R&D costs reported by the Primary Manufacturer and the calculated recouped costs, including the assumptions and calculations in the accompanying narrative text, and/or other factors as described in the Negotiation Data Elements ICR and in Appendix C of this revised guidance to adjust the preliminary price.

In considering element (2) on current unit costs of production and distribution, CMS will consider the relationship between the preliminary price and the unit costs of production and distribution. For example, CMS may consider adjusting the preliminary price downward if the unit costs of production and distribution are lower than the preliminary price, or upward if the unit costs of production and distribution are greater than the preliminary price. Again, CMS may consider the assumptions and calculations in the accompanying narrative text submitted by the Primary Manufacturer of the selected drug to determine if an adjustment is appropriate.

In considering element (3) on prior Federal financial support, CMS will consider the extent to which the Primary Manufacturer benefited from Federal financial support with respect to the selected drug. For example, CMS may consider adjusting the preliminary price downward if funding for the discovery and development of the drug was received from Federal sources.

In considering element (4) on patent applications, exclusivities, and applications and approvals for the selected drug, CMS will review the patents and exclusivities reported as it develops its initial offer. CMS believes that this information will support CMS' consideration of the 1194(e)(1) and 1194(e)(2) factors described in section 50 of this revised guidance. For instance, patents and exclusivities may inform CMS' understanding of therapeutic alternatives and other available therapy for the purposes of adjusting for clinical benefit, including consideration of whether the selected drug represents a therapeutic advance or meets an unmet medical need. More specifically, in light of exclusivities, there may be no other available therapy aside from the selected drug that adequately addresses treatment or diagnosis of a disease or condition, and consideration of such information would be relevant to CMS' consideration of the extent to which the selected drug addresses an unmet medical need for that disease or condition.

Finally, in considering element (5) on market data and revenue and sales volume data for the U.S., CMS will consider how the data compare to the CMS preliminary price. For example, if the average commercial net price is lower than the preliminary price, CMS may consider adjusting the preliminary price downward. If the average commercial net price is greater than the preliminary price, CMS may consider adjusting the preliminary price upward.

Appendix C of this revised guidance includes a list of definitions that CMS adopts for the purposes of describing the data to be collected with respect to the data elements listed in section 1194(e)(1) of the Act.

After any adjustments to the preliminary price are made under this section 60.3.4 of this revised guidance, the result is the initial offer.

60.4 Negotiation Process

In accordance with sections 1191(b)(4)(A) and 1191(d)(2)(A) of the Act, and as described in section 40.1 of this revised guidance, the negotiation period begins on the earlier of the date that the Primary Manufacturer enters into an Agreement, or, for initial price applicability year 2026, October 1, 2023. CMS will implement the negotiation process consistent with the requirements of the statute, with the aim of achieving "the lowest maximum fair price for each selected drug" consistent with section 1194(b)(1) of the Act.

After the submission of the section 1194(e) data by manufacturers and other interested parties by October 2, 2023, CMS will host meetings with Primary Manufacturers of selected drugs that have submitted section 1194(e) data and other interested parties. CMS will invite the Primary Manufacturer for each selected drug to one meeting in Fall 2023 after the data submission deadline. The purpose of this meeting will be for the Primary Manufacturer to provide additional context on its data submission and share new section 1194(e)(2) data, if applicable, as CMS begins reviewing the data and developing an initial offer. Primary Manufacturers may bring materials to facilitate discussion and CMS may request any materials presented afterwards. Primary Manufacturers are limited to sharing 50 pages (or a combination of pages, slides, and/or charts and graphs totaling 50 pages) of material, in order to focus the discussion on issues that can reasonably be discussed within the scope of the meeting, anticipating that these materials may contain cross-references to other material, particularly other material already submitted to CMS. CMS will also host patient-focused listening sessions with interested parties. These meetings are intended to bring together patients, beneficiaries, caregivers, and consumer and patient organizations as well as other interested parties to share patient-focused feedback with CMS on therapeutic alternatives and other information as CMS reviews section 1194(e)(2) data submissions and develops an initial offer for each selected drug. More information about these listening sessions will be forthcoming.

CMS acknowledges that Primary Manufacturers may benefit from having access to the section 1194(e)(2) data submitted by other interested parties during the negotiation period. In addition to offering the meetings above, CMS will aim to share redacted section 1194(e)(2) data with the Primary Manufacturer of a selected drug during the negotiation process when feasible. The data will be redacted as per the confidentiality standards described in section 40.2 of this revised guidance and will not include proprietary information, PHI / PII, or information that is protected from disclosure under other applicable law.

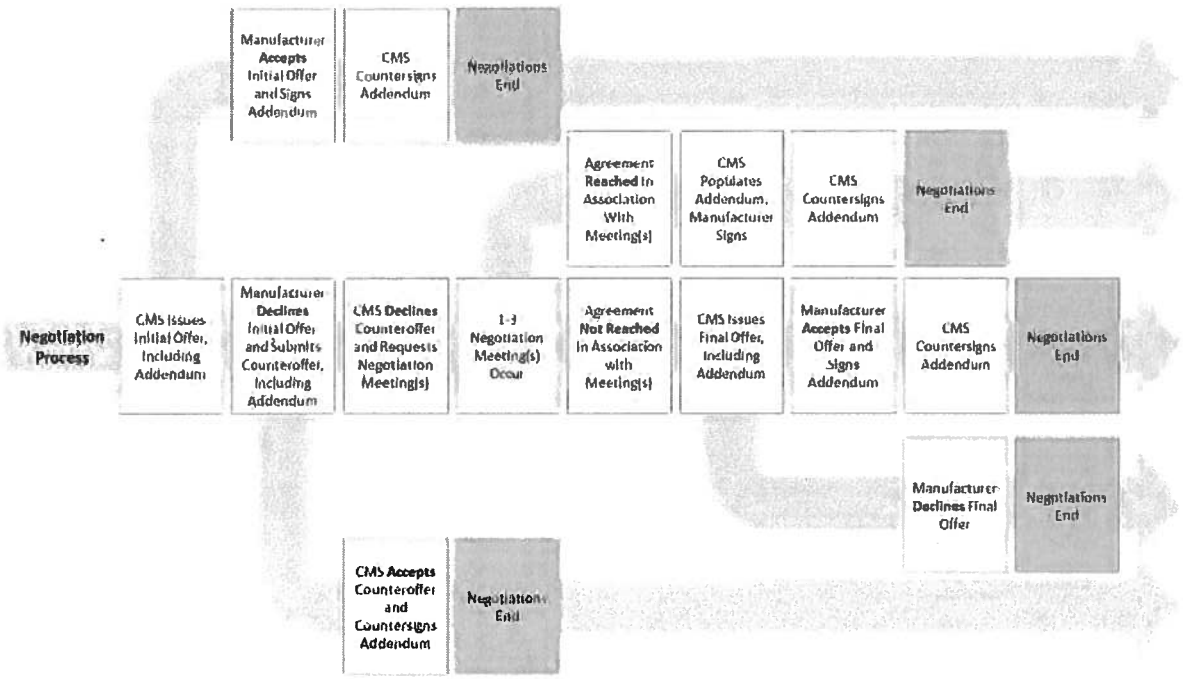
In accordance with sections 1191(d)(5)(B) and 1194(b)(2)(B) of the Act, CMS will make a written initial offer to the Primary Manufacturer with the proposal for the MFP for a selected drug for initial price applicability year 2026 no later than February 1, 2024. This written initial offer will be accompanied by an Addendum to the Agreement populated with the proposal for the MFP, in order for CMS and the Primary Manufacturer to effectuate agreement upon the MFP if such agreement is reached at this stage.

After the written initial offer from CMS is sent to the Primary Manufacturer, the negotiation process may include the following steps, depending on when and whether agreement on the MFP is reached and an offer is accepted:

(1) in accordance with section 1194(b)(2)(C) of the Act, an optional written counteroffer, including an Addendum populated with the counteroffer MFP as described in section 60.4.2 of this revised guidance, from the Primary Manufacturer (if CMS' written initial offer is not accepted by the Primary Manufacturer) that must be submitted no later than 30 days after the date of receipt of the written initial offer from CMS;
(2) in accordance with section 1194(b)(2)(D) of the Act, a written response from CMS to the optional written manufacturer counteroffer, which CMS will provide within 30 days;
(3) if the Primary Manufacturer's written counteroffer is not accepted by CMS, up to three possible in-person or virtual negotiation meetings between the Primary Manufacturer and CMS; and
(4) a final written offer, including an Addendum containing the final offer MFP as described in section 60.4.4 of this revised guidance, made by CMS to the Primary Manufacturer, if no agreement is reached before the end of the negotiation meetings.

Every offer and counteroffer will include an Addendum populated with the offered/counteroffered MFP. If an agreement is reached at any point during the negotiation process by the Primary Manufacturer accepting CMS' written initial offer or final offer (as described in section 60.4.4 of this revised guidance), CMS accepting the Primary Manufacturer's counteroffer, or an agreement being reached in association with the negotiation meetings, the Addendum to the Agreement, as described in section 40.3 of this revised guidance, will be executed by both parties and will constitute agreement on the MFP. Section 60.4.4 of this revised guidance describes how and when the Addendum will be created and signed. The MFP included in the executed Addendum will apply for the selected drug for initial price applicability year 2026 and will be updated according to section 1195(b)(1)(A) of the Act for subsequent years in the price applicability period, as applicable. The diagram below provides a non-exhaustive list of possible paths the negotiation process could take after CMS' initial offer, for a process taking place within the statutorily specified timelines.

Figure 3. Possible Negotiation Paths



During the entire negotiation process, CMS cannot offer or agree to any manufacturer counteroffer that exceeds the statutorily determined ceiling as defined in section 1194(c) of the Act and as described in section 60.2 of this revised guidance.

If the Primary Manufacturer is delayed in meeting one or more deadlines related to establishing the Agreement, submitting required data, and/or submitting the counteroffer, CMS will continue to engage in the negotiation process and will take the time to complete the established process as described in this section. During the period of time from when the Primary Manufacturer fails to meet a deadline until the date the Primary Manufacturer comes into compliance with the negotiation process, CMS will consider the Primary Manufacturer in violation of the Agreement and the Primary Manufacturer may be subject to civil monetary penalties as outlined in section 1197(c) of the Act. Section 90.3 and section 100 of this revised guidance further address possible actions to address noncompliance.

60.4.1 Provision of an Initial Offer and Justification

In accordance with section 1194(b)(2)(B) of the Act, the written initial offer from CMS, provided no later than February 1, 2024, must include a concise justification for the offer based on the data described in section 50 of this revised guidance. The justification will include a qualitative description of the factors from section 1194(e) (further described in sections 50 and 60.3 of this revised guidance) and a description of the methodology that CMS used to determine the initial offer. The information contained in the concise justification will provide the Primary Manufacturer with information on the range of evidence and other information considered pursuant to section 1194(e) that CMS found compelling during the development of the initial offer, thereby providing the Primary Manufacturer the necessary information to build a counteroffer if the Primary Manufacturer decides to reject the initial offer. The initial offer and

justification will not include information that CMS determines to be third-party proprietary pricing information, information that could lead to the calculation of a third party's proprietary information, PHI / PII, other information that is protected from disclosure under other applicable law, or the starting point.

No offer can exceed the statutorily determined ceiling as defined in section 1194(c) of the Act and described in section 60.2 of this revised guidance. As feasible, CMS will provide information on the calculation of the statutorily-determined ceiling and the computation of how CMS will apply a single MFP across dosage forms and strengths of the selected drug to the Primary Manufacturer within 60 days of the Primary Manufacturer's submission of data that complies with the requirements described in section 50.1 of this revised guidance. As described in section 40.2.3 of this revised guidance, CMS may reach out to the Primary Manufacturer for clarity on its data submission if CMS determines the information is not complete or accurate. In situations when additional outreach to the Primary Manufacturer is required to clarify the submitted data, CMS will aim to provide information on the calculation of the statutorily-determined ceiling and computation of how CMS will apply a single MFP across dosage forms and strengths of the selected drug to the Primary Manufacturer as close to 60 days from the initial data submission as feasible. As described in section 40.5 of this revised guidance, a Primary Manufacturer will have 30 days to submit a suggestion of error regarding the calculation of the ceiling and computation of how CMS will apply a single MFP across dosage forms and strengths for CMS' consideration.

60.4.2 Required Components of a Counteroffer

In accordance with section 1194(b)(2)(C) of the Act, the Primary Manufacturer will have no more than 30 days from receipt of the written initial offer from CMS to respond in writing by either accepting the initial offer for the selected drug or making a written counteroffer and providing a justification for such counteroffer based on the data described in section 50 of this revised guidance. Any counteroffer should also respond to the justification provided in CMS' written initial offer. The Primary Manufacturer's response should focus on the elements described in section 1194(c) and indicate the reasons the Primary Manufacturer believes that the information submitted by the Primary Manufacturer on the data in section 1194(e)(1) or (e)(2) of the Act, or other available data related to the selected drug and its therapeutic alternatives as described in section 1194(e)(2) of the Act, does not support the written initial offer made by CMS. Primary Manufacturers may also include in their counteroffer justification new information regarding the selected drug and its therapeutic alternative(s) as described in section 1194(e)(2) that supports the counteroffer MFP.

The Primary Manufacturer should provide a suggested MFP for the selected drug in its written counteroffer. As described in section 60.1 of this revised guidance, the counteroffer MFP should be made consistent with the manner that CMS' written initial offer was made; that is, a single price for the cost of the selected drug per 30-day equivalent supply, weighted across dosage forms and strengths. In accordance with section 1194(b)(2)(F) of the Act, CMS cannot accept a written counteroffer from a manufacturer that exceeds the statutorily determined ceiling as defined in section 1194(c) of the Act and described in section 60.2 of this revised guidance.

On April 18, 2023, CMS published the Drug Price Negotiation Process ICR for 60-day comment to capture information related to the counteroffer that Primary Manufacturers may submit after receiving CMS' initial offer.[70] The Drug Price Negotiation Process ICR includes instructions and a form for Primary Manufacturers to submit written counteroffers in the case where CMS' written initial offer of an MFP for a selected drug is not accepted. The comment period for the Drug Price Negotiation Process ICR closed on June 20, 2023. There will be an additional opportunity to submit comments for 30 days after revisions and re-publication in the Federal Register.

In order for a written counteroffer to be considered complete, a Primary Manufacturer must complete an Addendum in the CMS HPMS in addition to responding to the Drug Price Negotiation Process ICR, as described in section 40.3 of this revised guidance. A completed Addendum would include, but is not limited to, the MFP the Primary Manufacturer is counteroffering and a signature by an authorized representative.

60.4.3 Negotiation Process After Manufacturer Counteroffer

In accordance with section 1194(b)(2)(D) of the Act, CMS will respond in writing to a written counteroffer made by the Primary Manufacturer. Although the statute does not specify a timeframe for CMS' response to the counteroffer, negotiations for initial price applicability year 2026 must end prior to August 1, 2024, i.e., an agreement on MFP for the selected drug must be reached no later than July 31, 2024, to avoid potential excise tax liability under 26 U.S.C. § 5000D(b)(2).

In the case CMS' written initial offer is not accepted, and the Primary Manufacturer submits a written counteroffer, CMS will consider the counteroffer and either accept or reject it in writing within 30 days of receipt of the counteroffer. When considering a counteroffer, CMS will evaluate whether accepting the counteroffer is consistent with the statutory directive to aim to arrive at an agreement that achieves the lowest possible MFP for the selected drug. If CMS' written response to the counteroffer rejects the Primary Manufacturer's written counteroffer, CMS will extend an invitation to the Primary Manufacturer for a negotiation meeting. CMS will offer to hold a minimum of one meeting between CMS and the Primary Manufacturer to discuss CMS' written initial offer, the Primary Manufacturer's written counteroffer, and data considered. After this initial meeting, CMS will give each party (CMS and the Primary Manufacturer) the opportunity to request one additional meeting, resulting in a maximum of three meetings between CMS and the Primary Manufacturer.

The scope for these negotiation meetings will focus on the section 1194(e) data, including the therapeutic alternative(s) for the selected drug, and how they should inform the MFP. During these negotiation meetings, discussion of disputes and program policies regarding the negotiation process will be considered out of scope. CMS and the Primary Manufacturer will each be permitted to bring up to six meeting attendees, and both parties must share its participant lists ahead of each meeting. CMS arrived at this meeting attendee number after considering the roles from each party that would be critical to the conversation while ensuring that the meeting is sized appropriately to encourage active discussion. Additionally, a maximum of six attendees per side

[70] Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (IRA). See: https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10849.

is in line with requirements for similar meetings between government entities and manufacturers. Each meeting will last no more than two hours and may be conducted in-person at CMS or HHS headquarters. CMS believes two hours per negotiation meeting (of which there can be up to three meetings) is sufficient for a fruitful discussion and is appropriate considering time and scheduling constraints. If necessary, due to distance or scheduling challenges, meetings may be held virtually, or may be a "hybrid" arrangement where a portion of attendees are in-person and a portion of attendees are virtual. CMS' notes from negotiation meetings will be retained as part of the meeting record in compliance with applicable federal law including the Federal Managers Financial Integrity Act and the Federal Records Act and will be subject to the confidentiality policy described in section 40.2.1 of this revised guidance. Attendees on behalf of the Primary Manufacturer may take and keep notes of the meetings. Audio and/or video recording of negotiation meetings will not be permitted.

Correspondence regarding negotiation meetings will be conducted over email using the IRARebateandNegotiation@cms.hhs.gov mailbox. CMS will share a meeting agenda with the Primary Manufacturer via email approximately two weeks before the meeting. The Primary Manufacturer may request additions or edits to the agenda as long as they are in scope, as discussed in the paragraph above. Such requests must be submitted via email at least one week ahead of the meeting. CMS will circulate a final agenda two business days prior to the negotiation meeting. If a Primary Manufacturer would like to share materials at a negotiation meeting, such materials should be limited to 20 pages (or a combination of pages, slides, and/or charts and graphs totaling 20 pages), in order to focus the discussion on issues that can reasonably be discussed within the scope of the meeting, anticipating that these materials may contain cross-references to other material, particularly other material already submitted to CMS. Such materials must be submitted via email at least one week ahead of the meeting. Substantive discussion via email will not be permitted, in order for all attendees to benefit from such discussions as part of the negotiation meetings.

The meetings for initial price applicability year 2026 will occur between the time the Primary Manufacturer's written counteroffer is not accepted by CMS, which at the latest will be 30 days after the counteroffer is received, if applicable, and June 28, 2024. There would be about three months' time between CMS' rejection of the Primary Manufacturer's written counteroffer (approximately April 1, 2024) and the deadline for negotiation meetings to conclude (June 28, 2024). CMS requires that all negotiation meetings end no later than June 28, 2024, the last business day that is fifteen days prior to July 15, 2024, to allow CMS sufficient time to prepare a final offer (if an MFP was not reached in association with the negotiation meetings), send that final offer to the Primary Manufacturer by July 15, and to allow the Primary Manufacturer time to consider the final offer and accept or reject the final offer by July 31, 2024, as all negotiations must be concluded prior to August 1, 2024. These dates assume that a Primary Manufacturer is timely in entering into an Agreement, submitting information, and meeting deadlines related to the Negotiation Program.

CMS believes that the negotiation meeting process described above allows for a more efficient and effective approach than preparing and exchanging additional written offers and counteroffers. Negotiation meetings will also allow both parties to discuss any new information consistent with the data described in section 1194(e)(2) of the Act that may have become

available about the selected drug or its therapeutic alternative(s), and that may affect the determination of the MFP. Negotiation meetings will be attended solely by representatives of the Primary Manufacturer and of CMS. A written record will be developed and retained by CMS in compliance with applicable federal laws. The Primary Manufacturer can also develop and retain its own written record. As described in section 40.2.2 of this revised guidance, CMS will not publicly discuss ongoing negotiations with a Primary Manufacturer, including details of the negotiation meetings. Primary Manufacturers may publicly disclose information regarding ongoing negotiations with CMS at its discretion. If a Primary Manufacturer discloses information that is made public regarding any aspects of the negotiation process prior to the explanation of the MFP being released by CMS, CMS reserves the right to publicly discuss the specifics of the negotiation process regarding that Primary Manufacturer.

As described in section 60.6.1 of this revised guidance, in this public explanation, CMS will make public a narrative explanation of the negotiation process and the agreed-upon MFP and share redacted information regarding the section 1194(e) data received, the exchange of offers and counteroffers, and the negotiation meetings while abiding by the confidentiality policy described in section 40.2 of this revised guidance.

When developing this negotiation process, CMS considered using solely a written offer and counteroffer approach. That is, CMS considered providing one written offer and allowing a Primary Manufacturer to make a single written counteroffer, as described in the statute. CMS also contemplated allowing each party to make up to two written offers or counteroffers (i.e., CMS makes an initial offer, Primary Manufacturer possibly makes a counteroffer, CMS possibly makes a second offer, Primary Manufacturer possibly makes a second counteroffer). However, CMS believes that an offer/counteroffer process that includes in-person or virtual meetings (or a hybrid approach) will most effectively facilitate the negotiation process to arrive at an MFP and is more consistent with current industry practices for drug price negotiation.

60.4.4 Determination that Negotiations Have Finished

In accordance with sections 1194(b)(2)(E) and 1191(d)(2)(B) of the Act, all negotiations between CMS and the manufacturer of the selected drug must end prior to August 1, 2024, for initial price applicability year 2026 to avoid potential excise tax liability.

In the event that negotiation meetings occurred and an MFP was not agreed to in association with the negotiation meetings, CMS will send the Primary Manufacturer a "Notification of Final Maximum Fair Price Offer" and an Addendum with the final offer MFP by July 15, 2024. This will serve as the final offer to the Primary Manufacturer for the MFP for the selected drug. This final offer will only be sent if, by July 15, 2024, neither CMS nor the Primary Manufacturer has accepted the latest offer or counteroffer made in writing or agreed upon an MFP in association with the negotiation meetings. If a final offer is sent, the Primary Manufacturer must respond in writing to this final offer by either accepting or rejecting the final offer by July 31, 2024. The following table details CMS' timing for the negotiation process for initial price applicability year 2026:

Date[71]	Milestone
February 1, 2024	Statutory deadline for CMS to send written initial offer to the Primary Manufacturer
30 days after receipt of written initial offer from CMS (March 2nd if the offer is made by CMS on February 1, 2024)	Statutory deadline for the Primary Manufacturer to accept the initial offer or submit a written counteroffer to CMS
30 days after receipt of the manufacturer counteroffer (April 1st if the manufacturer counteroffer is made on March 2, 2024)	Date by which CMS will provide a written response accepting or rejecting the manufacturer counteroffer
Date that the Primary Manufacturer's written counteroffer is not accepted by CMS through June 28, 2024 (the last business day that is fifteen days prior to July 15, 2024)	Negotiation meetings (in-person, virtual, or hybrid, maximum of three possible meetings), if necessary
July 15, 2024	Date by which CMS will issue a "Notification of Final Maximum Fair Price Offer" to the Primary Manufacturer, if the written initial offer or Primary Manufacturer written counteroffer was not accepted and an MFP was not agreed upon in association with the negotiation meetings
July 31, 2024	Date by which the Primary Manufacturer must respond to (i.e., accept or reject) CMS' "Notification of Final Maximum Fair Price Offer," if applicable
July 31, 2024	Statutory deadline for all negotiations to end; CMS will notify the Primary Manufacturer of any failure to meet the deadline and the possible consequences thereof if agreement upon the MFP is not reached by July 31, 2024
August 1, 2024	Statutory end of negotiation period

To formalize agreement on an MFP, CMS and the Primary Manufacturer both sign an Addendum to the Agreement (described in sections 40.3 and 60.4 of this revised guidance) that sets forth the agreed-upon MFP. When CMS prepares a written offer, CMS also completes the Addendum with the offered MFP and sends the Addendum along with the written offer to the Primary Manufacturer via CMS HPMS. If the Primary Manufacturer accepts the written offer, they will sign the Addendum after which CMS will countersign the Addendum. Similarly, a

[71] These dates are contingent on CMS and the Primary Manufacturer meeting the deadlines described in this revised guidance and in statute. If the Primary Manufacturer is delayed in meeting one or more deadlines, CMS will continue to engage in the negotiation process and will take the time to complete the established process as described in this section. If a statutory deadline is missed, the Primary Manufacturer may be subject to a civil monetary penalty or excise tax.

Primary Manufacturer's written counteroffer is not considered complete unless the Primary Manufacturer submits a complete response to the Drug Price Negotiation Process ICR in CMS HPMS, submits an Addendum for the MFP consistent with the counteroffer amount in CMS HPMS, and signs that Addendum. If CMS accepts the written counteroffer, it will countersign the Addendum.[72]

If CMS and the Primary Manufacturer do not agree to an MFP by the statutory end of the negotiation period, the Primary Manufacturer will enter a period during which an excise tax potentially may be assessed. As described in 26 U.S.C. § 5000D(b)(2) and § 5000D(c), the Primary Manufacturer can end the period during which the excise tax may apply by agreeing to an MFP, as described in section 60.8 of this revised guidance, or can meet the statutory criteria for the suspension of tax or may terminate its Agreement in the manner described in section 40.6 of this revised guidance, which includes sending a notice terminating all of their applicable agreements under the Medicare and Medicaid programs and establishing that none of the Primary Manufacturer's drugs are covered by an agreement under section 1860D-14A or section 1860D-14C of the Act.

60.5 Application of the MFP Across Dosage Forms and Strengths

An MFP that is agreed upon as described in section 60.4 of this revised guidance establishes one price for the selected drug. In accordance with section 1196(a)(2) of the Act, CMS has the administrative duty to establish procedures to compute and apply the MFP across different dosage forms and strengths of the selected drug and not based on the specific formulation or package size or package type of such drug.

As described in section 60.1 of this revised guidance, the MFP will reflect a single price for the selected drug per 30-day equivalent supply. To ensure that the MFP is made available to MFP-eligible individuals at the point of sale (and to pharmacies, mail order services, or other dispensers, with respect to such MFP-eligible individuals), however, CMS will publish the MFP at the per-unit (e.g., tablet) level for each NDC-9 and NDC-11 associated with the selected drug.

The following methodology will be used to apply the single MFP across NDC-9s for a 30-day equivalent supply and to calculate an MFP per unit for each NDC-9 of the selected drug. CMS will use a methodology that scales the MFP per unit based on price differentials across different dosage forms and strengths. For initial price applicability year 2026, CMS will use the WAC of the selected drug in this calculation. CMS will first calculate an annual WAC per unit cost for each NDC-11 included on the list of NDC-11s of the selected drug in the CMS HPMS, inclusive of any NDC-11s added by the Primary Manufacturer (see section 40.2 of this revised guidance), from the manufacturer-submitted quarterly WAC per unit and unit volume data, to account for potential variation in unit volume across quarters. The annual WAC per unit for each NDC-11 will then be converted into an amount for a 30-day equivalent supply (using the methodology described in 42 C.F.R. § 423.104(d)(2)(iv)(A)(2)), so that the WAC will be comparable to the negotiated single MFP. CMS will then aggregate the WAC per 30-day equivalent supply for each NDC-11 into a WAC per 30-day supply for each NDC-9 of the selected drug. The WAC per 30-day equivalent supply for each NDC-9 will then be used to calculate a WAC price ratio

[72] In the event that this functionality is delayed in CMS HPMS, CMS will specify an alternative approach for sharing the Addendum in writing.

for each NDC-9 of the selected drug. The ratio derived from the WAC per 30-day equivalent supply for each NDC-9 will then be multiplied by the single MFP for the selected drug to calculate the MFP for a 30-day equivalent supply of each NDC-9 of the selected drug. Lastly, to determine the per unit MFP for an NDC-9, CMS will convert from an MFP for a 30-day equivalent supply to an MFP per unit based on the average number of units in a 30-day equivalent supply.

The following steps provide additional detail regarding the approach CMS will use:

1. For each NDC-11 and calendar quarter, CMS will divide the WAC quarterly units by the total WAC annual units (from- manufacturer submitted data) and multiply this quotient by the quarterly WAC per unit.
    - Note: CMS will use the WAC unit cost for the period beginning January 1, 2022 and ending December 31, 2022 for purposes of this calculation to align with the time period of data used to calculate the ceiling for the MFP.
2. For each NDC-11, CMS will then sum the amounts calculated in step 1 to calculate the annual WAC per unit.
3. For each NDC-11, CMS will divide the quantity dispensed by the total 30-day equivalent supply, both calculated from 2022 PDE data, to calculate the average number of units per 30-day equivalent supply.
4. For each NDC-11, CMS will multiply the WAC per unit calculated in step 2 by the average number of units per 30-day equivalent supply calculated in step 3 to calculate the WAC per 30-day equivalent day supply for that NDC-11.
5. For each NDC-11, CMS will divide the total 30-day equivalent supply for that NDC-11 by the total 30-day equivalent supply across all applicable NDC-11s within an NDC-9 and then multiply this quotient by the amount calculated in step 4.
6. For each NDC-9, CMS will then sum amounts calculated in step 5 across all NDC-11s to calculate the WAC per 30-day equivalent supply for that NDC-9.
7. For each NDC-9, CMS will divide the total 30-day equivalent supply for that NDC-9 by the total 30-day equivalent supply across all NDC-9s and then multiply this quotient by the amount calculated in step 6.
8. CMS will then sum amounts calculated in step 7 across all NDC-9s of the selected drug to calculate the WAC per 30-day equivalent supply for the selected drug.
9. For each NDC-9, CMS will then divide the WAC per 30-day equivalent day supply for that NDC-9 calculated in step 6 by the WAC per 30-day equivalent supply for the selected drug calculated in step 8 to calculate the WAC per 30-day equivalent supply ratio for that NDC-9.
10. For each NDC-9, CMS will multiply the single MFP for the selected drug by the relative WAC per 30-day equivalent supply ratio for that NDC-9 calculated in step 9 to calculate the MFP per 30-day equivalent supply for that NDC-9.
11. For each NDC-9, CMS will divide the MFP per 30-day equivalent supply for that NDC-9 calculated in step 10 by the quotient of the total number of units dispensed divided by the total 30-day equivalent supply to calculate the MFP per unit (e.g., tablet).

CMS will include the MFP per unit price for each NDC-9 of the selected drug, calculated in step 11 of this section 60.5 of this revised guidance, along with corresponding NDC-11 package prices (determined by multiplying the NDC-9 unit price by the number of units per NDC-11 package), in the publication of MFPs as described in section 60.6 of this revised guidance. CMS

recognizes there may be other ways to apply the MFP to dosage forms and strengths and will monitor whether this policy serves the intent of the Negotiation Program. As noted throughout this revised guidance, the policies described for the Negotiation Program are for initial price applicability year 2026, and CMS may consider additional policies for future years of the Negotiation Program.

60.5.1 Application of the MFP to New NDAs / BLAs or NDCs

Based on the definition of a qualifying single source drug described in section 30.1 of this revised guidance, if the Primary Manufacturer for a selected drug receives approval or licensure for a new NDA or BLA, as applicable, for the same active moiety / active ingredient after the drug has been selected, CMS requires that the MFP apply to drug or biological products marketed pursuant to the new NDA or BLA. Similarly, after the drug is selected, if the Primary Manufacturer for such drug receives approval or licensure for a new drug or biological product or NDC that is marketed pursuant to a supplement to an existing NDA or BLA, CMS requires that the MFP apply to such new drug or biological product. Additionally, an NDC that has been marketed pursuant to an applicable NDA or BLA prior to drug selection may lack sufficient PDE or WAC data in 2022 to apply the MFP across that dosage form and strength as described above. To apply the MFP to a new NDC that is marketed for the first time after the MFP is negotiated for a selected drug (including before or after the start of the initial price applicability year) or to an NDC that is marketed prior to MFP negotiation but which lacks either sufficient PDE unit data for calendar year 2022 or sufficient WAC data for calendar year 2022 for CMS to apply the MFP to that dosage form and strength as described above, CMS will determine whether there is an existing, comparable NDC to which the MFP for the selected drug has been applied. If a comparable NDC exists, CMS will impute the quotient of total quantity dispensed to 30-day equivalent supply based on the FDA-approved label associated with the new NDC and will use the same WAC ratio that was calculated for the existing NDC to apply the MFP to the new NDC.

If a comparable NDC does not exist, CMS will impute the quotient of total quantity dispensed to 30-day equivalent supply based on the FDA-approved label associated with the new NDC but will use a WAC ratio of 1.0 to apply the MFP to the new NDC.[73]

60.6 Publication of the MFP

In accordance with section 1191(d)(6) and section 1195(a)(1) of the Act, CMS will publish by September 1, 2024, the MFP for each drug selected for initial price applicability year 2026 for which CMS and the Primary Manufacturer have reached an agreement on an MFP. Related to this requirement, CMS will publish the following on the CMS website: the selected drug, the initial price applicability year, the MFP file, and the explanation for the MFP (published at a later date – see section 60.6.1 of this revised guidance). The MFP file will contain the single MFP for a 30-day equivalent supply of the selected drug, the NDC-9 per unit price, and NDC-11 per package price and will be updated annually to show the inflation-adjusted MFP for the selected drug. CMS will also publish on the CMS website when a drug is no longer a selected drug and

[73] While this guidance is focused on initial price applicability year 2026, CMS notes that in future years, renegotiation of the MFP might be appropriate in the event of certain new NDCs that represent material changes to the selected drug, such as where the new NDC is sought due to changes in the selected drug that result in the addition of a new indication. CMS will provide additional information in the future on renegotiation, which will be implemented for initial price applicability year 2028 and subsequent years, in accordance with the statute.

the reason for that change, and when an MFP between a Primary Manufacturer and CMS is not agreed upon.

60.6.1 Explanation for the MFP

Section 1195(a)(2) of the Act requires CMS to publish an explanation for the MFP no later than March 1 of the year prior to the initial price applicability year, which will be March 1, 2025 for initial price applicability year 2026. CMS will strive to publish these explanations earlier than March 1, 2025, if feasible. The explanation will focus on the section 1194(e) data that had the greatest impact in determining the MFP and include a discussion of the other section 1194(e) data, as applicable. It will also note any data or circumstances that may be unique to the selected drug. Alongside the narrative explanation, CMS will release redacted information regarding the section 1194(e) data received, exchange of offers and counteroffers, and the negotiation meetings, if applicable. CMS will develop and publish the public explanation of the MFP in accordance with the confidentiality policy described in section 40.2 of this revised guidance.

If an agreement for an MFP is not reached for a selected drug, neither an MFP nor a public explanation of the MFP will be published. Instead, CMS will indicate on the CMS website that an MFP has not been agreed upon between the Primary Manufacturer and CMS for the selected drug. In circumstances where an MFP is finalized after the statutory deadline for the conclusion of negotiations, the MFP and the public explanation of the MFP will be posted in accordance with section 60.8 of this revised guidance.

60.7 Exclusion from the Negotiation Process Based on Generic or Biosimilar Availability

In accordance with section 1192(c)(2) of the Act and subject to the timeline and situations discussed in section 70, a selected drug will no longer be subject to the negotiation process, with respect to its initial price applicability year, if CMS determines that at least one generic drug or biosimilar biological product satisfies the following criteria: (1) it is approved under section 505(j) of the FD&C Act with at least one dosage form and strength of the selected drug as the listed drug or licensed under section 351(k) of the PHS Act with at least one dosage form and strength of the selected drug as the reference product, and (2) it is marketed pursuant to such approval or licensure. The approach CMS will take to make this determination is described in section 70 of this revised guidance.

When the drug is no longer subject to the negotiation process based on the criteria in section 1192(c)(2) of the Act, the selected drug will continue to be considered a selected drug with respect to such initial price applicability year with respect to the number of negotiation-eligible drugs on the list published under section 1192(a) of the Act (see section 70 of this revised guidance for additional details).

60.8 Establishment of MFPs After the Negotiation Deadline

Sections 1194(b)(2) and 1191(d)(5)(C) of the Act contemplate that agreement upon an MFP must be reached for initial price applicability year 2026 by August 1, 2024 in order to avoid potential imposition of an excise tax. If negotiations have not ended by this date, the Primary Manufacturer may be subject to an excise tax. As a general matter, if the Primary Manufacturer is delayed in meeting one or more deadlines related to the negotiation process, CMS will continue to engage in the negotiation process described in section 60.4 of this revised guidance.

Certain actions or delays by the Primary Manufacturer may delay the process such that the MFP is established after the end of the negotiation period. If this occurs, in accordance with section 1194(b)(1) of the Act, CMS will follow timelines consistent with the negotiation process established in this revised guidance and take the time to complete the established process so described as appropriate for the selected drug. Likewise, certain actions by the Primary Manufacturer may delay the negotiation process to such an extent that a selected drug has a change in status that is material to CMS' statutory obligations under the negotiation process. If this occurs, in accordance with section 1194(b)(1), when CMS initiates or resumes the negotiation process, CMS will apply the consistent methodology and process with respect to the selected drug based on its status at the time the negotiation process occurs, including beginning in 2028 which may have potential implications with respect to the renegotiation process. Guidance about the renegotiation process will be forthcoming for future years of the Negotiation Program.

If the manufacturer and CMS have completed each step of the negotiation process as detailed in section 60.4 of this revised guidance, including CMS' issuance of a "Notification of Final Maximum Fair Price Offer" and then, after the statutory end of the negotiation period, the Primary Manufacturer of a selected drug wishes to agree to an MFP, the Primary Manufacturer must notify CMS in writing that it would like to accept the last offer of an MFP from CMS, as reflected in the "Notification of Final Maximum Fair Price Offer." In accordance with section 1195(b)(2) of the Act, in the case of a selected drug with respect to an initial price applicability year for which the MFP is determined after the MFPs are published for other selected drugs, CMS shall publish the MFP no later than 30 days after the date such MFP is so determined. In accordance with section 60.6 of this revised guidance, CMS will publish the MFP and the MFP explanation on the CMS website. CMS will follow timelines consistent with the established process for publishing the public explanation of the MFP and will not expedite its timeline due to late action from the Primary Manufacturer.

70. Removal from the Selected Drug List Before or During Negotiation, or After an MFP is in Effect

In accordance with section 1192(c) of the Act, a selected drug will no longer be subject to the negotiation process and will cease to be a selected drug, subject to the timeline and situations discussed below, if CMS determines (1) the FDA has approved a generic drug under section 505(j) of the FD&C Act that identifies as its reference-listed drug a product that is included in the selected drug, or the FDA has licensed a biosimilar biological product under section 351(k) of the PHS Act that identifies as its reference product a product that is included in the selected drug; and, (2) the generic drug or biosimilar biological product, as applicable, is marketed pursuant to such approval or licensure.

The approval (or licensure, as applicable) and marketing of an authorized generic drug (which includes authorized generic drugs and certain biological products as defined in section 1192(e)(2) of the Act) would not qualify as meeting the statutory requirement that a generic drug or a biosimilar biological product is being marketed. In accordance with section 1192(e)(2)(B)(i) of the Act, an authorized generic drug as defined in section 505(t)(3) of the FD&C Act is treated as the same qualifying single source drug as a qualifying single source drug that is the listed drug, for the purposes of the Negotiation Program. Likewise, section 1192(e)(2)(B)(ii) of the Act indicates that the same rule applies to a biological product that is approved under section 351(a)

of the PHS Act and is marketed, sold, or distributed directly or indirectly to the retail class of trade under different labeling or packaging (other than repackaging as the reference product in blister packs, unit doses, or similar packaging for use in institutions), product code, labeler code, trade name, or trademark.

The determination whether a selected drug should not be subject to the negotiation process and ultimately removed from the selected drug list will be informed by CMS' review of PDE and AMP data for the generic drug or biosimilar biological product for which the selected drug is the listed drug or reference product on a monthly basis as described below. CMS will consider an approved generic drug or licensed biosimilar biological product to be marketed when the totality of the circumstances, including these data, reveals that the manufacturer of the generic drug or biosimilar biological product is engaging in bona fide marketing of that drug or product.

After the selected drug is removed from the selected drug list, CMS will monitor the manufacturers of such generic drugs or biosimilar biological products to ensure they continue to engage in bona fide marketing of the generic or biosimilar biological product based on the process described in section 90.4 of this revised guidance.

Starting in October 2023, and repeated each month thereafter, CMS will take the following approach in its review of data to inform its determination whether the statutory criteria in sections 1192(c)(1)(A) and 1192(c)(1)(B) of the Act for an approved generic drug or licensed biosimilar to be marketed pursuant to such approval or licensure are being met.

First, CMS will use FDA reference sources, including the Orange Book and Purple Book, to determine whether a generic drug or biosimilar biological product is approved or licensed for any strength(s) or dosage form(s) of a selected drug for initial price applicability year 2026.

Second, if CMS determines that a generic drug or biosimilar biological product has been approved or licensed, CMS will begin by reviewing the PDE and AMP data with dates of service during the most recent 12-month period available to determine if the manufacturer of the generic drug or biosimilar biological product has engaged in bona fide marketing of that drug or product. For example, when CMS performs this assessment in October of 2023, CMS will use PDE and AMP data with dates of service from October 2022 through September 2023. When CMS performs this assessment in November 2023, CMS will use PDE and AMP data for dates of service from November 2022 through October 2023.

The determination whether a generic drug or biosimilar is being bona fide marketed is a totality-of-the-circumstances inquiry that will not necessarily turn on any one source of data. Additional relevant factors may include whether the generic drug or biosimilar biological product is regularly and consistently available for purchase through the pharmaceutical supply chain and whether any licenses or other agreements between a Primary Manufacturer and a generic drug or biosimilar manufacturer limit the availability or distribution of the selected drug, as articulated further in section 90.4.

Per section 1192(c)(2) of the Act, if CMS makes a determination regarding generic drug or biosimilar biological product availability on or after the selected drug publication date, and

before the end of or during the negotiation period for an initial price applicability year, the selected drug will not be subject to the negotiation process for the negotiation period, and an MFP will not be established. Accordingly, for initial price applicability year 2026, if CMS makes this determination between September 1, 2023, and August 1, 2024, the drug will remain a selected drug through 2026, but no MFP will apply and the drug will not be replaced with another selected drug.

In accordance with section 1192(c)(1) of the Act, a selected drug that is included on the list of selected drugs for an initial price applicability year will remain a selected drug for that year and each subsequent year beginning before the first year that begins at least nine months after the date on which CMS determines the statutory criteria in section 1192(c) are met. Accordingly, if CMS makes this determination between August 2, 2024, and March 31, 2026, for a drug selected for initial price applicability year 2026, then the drug will cease to be a selected drug on January 1, 2027, and the MFP will apply for 2026. If CMS makes this determination between April 1, 2026, and March 31, 2027, then the selected drug will cease to be a selected drug on January 1, 2028, and the MFP will apply for 2026 and 2027. These results are summarized in the following table:

Date on which CMS determines that a generic drug or biosimilar biological product is approved and marketed	**Result with respect to selected drug for the Negotiation Program**
September 1, 2023 through August 1, 2024 (which includes the Negotiation Period for the initial price applicability year 2026)	Selected drug remains a selected drug for initial price applicability year 2026, though MFP does not apply; selected drug ceases to be a selected drug on January 1, 2027.
August 2, 2024 through March 31, 2026	Selected drug remains a selected drug and MFP applies for initial price applicability year 2026; selected drug ceases to be a selected drug on January 1, 2027.
April 1, 2026 through March 31, 2027	Selected drug remains a selected drug and MFP applies for initial price applicability year 2026 and calendar year 2027; selected drug ceases to be a selected drug on January 1, 2028.

Without regard to whether the Primary Manufacturer decides to execute an Agreement as discussed in section 40.1 of this revised guidance, to terminate an Agreement as discussed in section 40.6, or to transfer ownership of the selected drug as discussed in section 40.7, a selected drug remains a selected drug until CMS determines otherwise under the criteria set forth in section 1192(c) of the Act.

In all cases, after CMS determines the statutory criteria in section 1192(c) for generic competition are met for a selected drug, CMS will publish such information on the CMS website.

80. MFP-Eligible Individuals

For initial price applicability year 2026, in accordance with section 1191(c)(2) of the Act, the term "maximum fair price eligible individual" means, with respect to a selected drug, the

following: in the case such drug is dispensed to the individual at a pharmacy, by a mail order service, or by another dispenser, an individual who is enrolled in a prescription drug plan under Medicare Part D or an MA–PD plan under Medicare Part C (including an Employer Group Waiver Plan), if Part D coverage is provided under such plan for such selected drug. The MFP is not required to be made available to a Medicare beneficiary who uses other sources of prescription drug coverage, such as a plan that receives the Retiree Drug Subsidy, prescription drug discount cards, or cash.[74] For initial price applicability year 2026, CMS does not expect manufacturers to provide access to the MFP of a selected drug to hospitals, physicians, and other providers of services and suppliers with respect to a drug furnished or administered to MFP eligible individuals enrolled under Part B, including an individual who is enrolled in an MA plan.

90. Manufacturer Compliance and Oversight

In accordance with section 1196(b) of the Act, CMS will monitor compliance by a Primary Manufacturer with the terms of the Agreement and establish a mechanism through which violations of such terms shall be reported.

90.1 Monitoring of Manufacturer Compliance

CMS will closely monitor the Primary Manufacturer's compliance with the terms of the Agreement and other aspects of the Negotiation Program. Following the publication of selected drugs for each initial price applicability year, CMS will provide information about the negotiation process to the Primary Manufacturer of each selected drug (see section 40 of this revised guidance for additional details). CMS anticipates this information will include operational and statutory timelines, procedural requirements, systems instructions, IRA resources, and contact information.

During the negotiation period, CMS will track and monitor progress during all steps of the process and engage in direct communications with each Primary Manufacturer. To facilitate successful Negotiation Program operations and support manufacturer compliance with Program requirements, CMS will issue reminder letters prior to manufacturer deadlines with warnings of potential applicability of excise taxes (see 26 U.S.C. § 5000D for additional information regarding the excise tax) or CMPs (see section 100 of this revised guidance), written requests for corrective action when applicable (see section 40.2.3 of this revised guidance), written notification that a Primary Manufacturer may be subject to enforcement action as applicable, and written confirmation that a Primary Manufacturer may no longer be subject to enforcement action as applicable.

Failure of a Primary Manufacturer to comply with certain Negotiation Program deadlines and other requirements of the Negotiation Program may result in potential excise tax liability (see 26 U.S.C. § 5000D). As described in section 100 of this revised guidance, failure of a Primary Manufacturer to comply with certain Negotiation Program deadlines and other requirements of the Negotiation Program could result in CMPs.

[74] CMS notes that employer sponsored plans that receive the retiree drug subsidy and health plans that offer creditable prescription drug coverage are not included because they are not Part D plans.

90.2 Monitoring of Access to the MFP

In accordance with section 1193(a)(3)(A) of the Act, under the Agreement with CMS with respect to a price applicability period, access to the MFP with respect to such a selected drug shall be provided by the Primary Manufacturer to MFP-eligible individuals at the pharmacy, mail order service, or other dispenser at the point of sale, and to the pharmacy, mail order service, or other dispenser with respect to such MFP-eligible individuals who are dispensed the selected drug.

Further, in accordance with section 1193(a)(5) of the Act, which requires that the manufacturer comply with requirements determined by the Secretary to be necessary for purposes of administering the program and monitoring compliance with the program, and section 40.4 of this revised guidance, CMS requires that the Primary Manufacturer establish safeguards to ensure the MFP is available to MFP-eligible individuals and to pharmacies, mail order services, and other dispensers on units of the selected drug for which there are Secondary Manufacturers. CMS reiterates that the requirement for the Primary Manufacturer to provide access to the MFP applies to all sales of the selected drug by a Secondary Manufacturer to MFP-eligible individuals and to pharmacies, mail order services, and other dispensers that are providing a selected drug to an MFP-eligible individual, as discussed in section 80 of this revised guidance.

As described in section 40.4 of this revised guidance, CMS is considering the potential to engage with an MTF to facilitate the exchange of data between supply chain entities to support the verification of MFP eligibility of an individual who is dispensed a selected drug. Each component of the pharmaceutical supply chain may have a role in making the MFP available to MFP-eligible individuals, but it is ultimately the Primary Manufacturer's responsibility to ensure access to the MFP. There are various methods by which dispensing entities and MFP-eligible individuals can determine whether they are accessing the MFP for a selected drug.

For example, under section 1195(a) of the Act, the MFP for a selected drug will be published by CMS, giving the public and other interested parties an opportunity to know the MFP for each selected drug, as well as the explanation for each MFP (see section 60.6 of this revised guidance for additional details). Under section 1191(d)(6), the MFPs for selected drugs for initial price applicability year 2026 must be published by September 1, 2024. In addition, CMS anticipates that pharmaceutical database compendia will publish the MFPs for selected drugs such that they would become more knowable and accessible to pharmaceutical purchasers. CMS believes such transparency of the MFPs for selected drugs will help dispensing entities and MFP-eligible individuals to know the MFP for a selected drug and determine whether they are able to access the MFP.

In accordance with section 1196(a)(3)(A) of the Act, as well as section 1196(b), which requires that the Secretary establish a mechanism by which violations of the terms of the Agreement shall be reported, CMS will establish procedures for reporting suspected violations related to access to the MFP with respect to MFP-eligible individuals who are enrolled in Medicare Part D plans and the pharmacies, mail order services, and other dispensers that provide selected drugs to MFP-eligible individuals. As part of this process, CMS may establish a toll-free phone line and email box where an individual or a dispenser could communicate information to CMS regarding an incident in which the MFP was not provided to an MFP-eligible individual or the applicable

pharmacy, mail order service, or other dispenser. CMS anticipates the submissions would likely include the name of the individual reporting the incident, the nature of the incident, the date the incident occurred, the name of the drug, the manufacturer of the drug, and contact information for follow-up.

Upon receipt of a report of a suspected violation, CMS will review the submissions, investigate reports of potential noncompliance, and if appropriate, impose CMPs on the Primary Manufacturer if CMS determines the Primary Manufacturer failed to provide an MFP-eligible individual or an eligible dispenser access to the MFP for the selected drug, including in cases where there are one or more Secondary Manufacturers of the selected drug. CMS would also expect manufacturers and other interested parties to report instances in which a dispenser was not passing through the MFP to an MFP-eligible individual, or a dispenser was extending the MFP to non-MFP-eligible individuals.

As described in section 40.4.1 of this revised guidance and consistent with section 1193(d) of the Act regarding the manufacturer's Agreement with CMS, a manufacturer with a Pharmaceutical Pricing Agreement (PPA) with the Secretary under the 340B program is not required to provide a 340B covered entity with access to the MFP of a selected drug with respect to an MFP-eligible individual who is eligible to be dispensed such selected drug at the covered entity if the 340B ceiling price is lower than the MFP for such selected drug.

CMS is also aware that it is conceptually possible for an entity that meets the statutory definition of a manufacturer, but that is not the Primary Manufacturer or a Secondary Manufacturer, to market one or more drug or biological products pursuant to one or more NDA(s) or BLA(s) included in the selected drug. For example, it is possible for an entity to purchase one or more drug or biological products included in the selected drug from a wholesaler, repackage or relabel such products, and then re-market them pursuant to one or more NDA(s) or BLA(s) included in the selected drug. CMS believes it would be appropriate for the MFP to be made available to all MFP-eligible individuals and to all pharmacies, mail order services, and other dispensers with respect to MFP-eligible individuals who are dispensed units of the selected drug. However, for initial price applicability year 2026, CMS is limiting the scope of Primary Manufacturer responsibility to provide access to the MFP for the selected drug to units of such drug sold by the Primary Manufacturer or a Secondary Manufacturer. CMS will monitor to determine if there are sales of selected drug to MFP-eligible individuals by manufacturers other than Primary Manufacturer and Secondary Manufacturers and consider whether other mechanisms are needed to promote access to MFP to Medicare-eligible individuals in these circumstances. CMS continues to seek feedback on how it might achieve this goal, interested parties can send feedback on this topic to IRARebateandNegotiation@cms.hhs.gov.

90.3 26 U.S.C. Section 5000D Excise Tax on Sale of Designated Drugs

The IRS will administer the excise tax. CMS understands that the Treasury Department will issue guidance relating to the excise tax in the coming weeks.

90.4 Monitoring for Bona Fide Marketing of Generic or Biosimilar Product

If CMS determines that either:

(1) a potential qualifying single source drug will not be considered a qualifying single source drug for initial price applicability year 2026 because any strength or dosage form of a potential qualifying single source drug is the listed drug or reference product, as applicable, for one or more generic drugs or biosimilar biological products that CMS determined are approved or licensed and marketed based on the process described in section 30.1 of this revised guidance, or

(2) a selected drug is no longer subject to the negotiation process and ceases to be a selected drug because (a) the FDA has approved a generic drug under section 505(j) of the FD&C Act that identifies as its reference listed drug a product that is included in the selected drug, or the FDA has licensed a biosimilar biological product under section 351(k) of the PHS Act that identifies as its reference product a product that is included in the selected drug; and, (b) the generic drug or biosimilar biological product, as applicable, is marketed pursuant to such approval or licensure in accordance with section 1192(c) of the Act and under the process described in sections 60.7 and 70 of this revised guidance,

then CMS will monitor, after such an above determination is made, whether meaningful competition continues to exist in the market by ongoing assessments of whether the manufacturer of the generic drug or biosimilar is engaging in bona fide marketing. Such monitoring by CMS may include, but is not limited to, whether the generic drug or biosimilar biological product is regularly and consistently available for purchase through the pharmaceutical supply chain and whether any licenses or other agreements between a Primary Manufacturer and a generic drug or biosimilar manufacturer limit the availability or distribution of the selected drug.

CMS is aware that marketing or other agreements between the Primary Manufacturer and generic drug or biosimilar manufacturers may limit the availability of the generic drug or biosimilar for purchase through the pharmaceutical supply chain, and CMS will attempt to identify when such agreements exist as a factor in determining whether bona fide marketing exists, although such agreements would not by themselves be dispositive of that determination. CMS notes that any agreements limiting the availability of a selected drug may be subject to scrutiny and potential enforcement under antitrust laws (including laws prohibiting unfair methods of competition) as well as laws prohibiting unfair or deceptive acts or practices in or affecting commerce.

In addition, CMS will analyze the share of generic drug or biosimilar biological product units identified in PDE data as a percentage of total units of Part D expenditures, as well as whether manufacturers are reporting units of the selected drug as part of their AMP reporting responsibilities under section 1927(b)(3)(A) of the Act, and the trend in reporting of such AMP units. CMS reserves the right to also use other available data and informational sources on market share and relative market competition of the generic drug or biosimilar.

100. Civil Monetary Penalties

In accordance with section 1197 of the Act, Primary Manufacturers of selected drugs that enter into an Agreement may be subject to CMPs for (1) failure to ensure access to a price that is less than or equal to the MFP for MFP-eligible individuals and pharmacies, mail order services, and

other dispensers who dispense the selected drug with respect to MFP-eligible individuals, (2) failure to pay the rebate amount for a biological product for which inclusion on the selected drug list was delayed but has since undergone negotiation, as described in section 1192(f)(4) of the Act, (3) violation of certain terms of the Agreement, and (4) the provision of false information as described in section 1197(d) of the Act.

CMS' primary goal is to successfully administer all aspects of the Negotiation Program; CMS intends to exercise the authority to impose CMPs for instances of noncompliance that substantively obstruct negotiation processes and/or availability of the MFP Such instances may include, but are not limited to, failure to make the MFP available to MFP-eligible individuals; failure to provide timely, complete, and accurate information that is necessary to execute the negotiation process or other administrative or monitoring functions of the Negotiation Program; repeated violations of the Agreement or other Negotiation Program requirements; or egregious and/or knowing violations of Negotiation Program requirements.

Broadly, CMS is establishing a structure for enforcement actions that:

1. Is within CMS' statutory authority,
2. Is not punitive in response to immaterial or other instances of noncompliance that are not substantive,
3. Can be applied consistently across applicable instances of Primary Manufacturer noncompliance, and
4. Facilitates the ability to successfully engage in all components of the negotiation process within the established statutory timeframes.

This revised guidance addresses violations by a Primary Manufacturer for failure to ensure access to a price for a selected drug less than or equal to the MFP, violation of terms of the Agreement, and provision of false information as related to the aggregation rule of the Small Biotech Exception and the Biosimilar Delay Rule. This revised guidance does not address failure to pay a rebate for a biological product pursuant to section 1192(f)(4) of the Act, as this topic will be addressed in future guidance. CMS provides details about the process for CMP imposition in section 100.4 of this revised guidance.

100.1 Failure of Manufacturer to Ensure Access to a Price Less than or Equal to the MFP
In accordance with section 1197(a) of the Act, CMS may impose a CMP on a Primary Manufacturer of a selected drug that has entered into an Agreement with CMS upon failure to provide access to a price that is less than or equal to the MFP to MFP-eligible individuals dispensed the selected drug and to pharmacies, mail order services, or other dispensers with respect to MFP-eligible individuals who are dispensed the selected drug, including the failure to do so in connection with sales of the selected drug by a Secondary Manufacturer. CMS will be monitoring the WAC in relation to other pricing metrics. Upon discovery and confirmation of a failure to make the MFP available, CMS will send the Primary Manufacturer a Notice of Potential Noncompliance that will include information on the potential violation and an opportunity for corrective action. CMS will establish an informal process in which the Primary Manufacturer will have 10 business days to respond to the Notice of Potential Noncompliance to provide additional context, evidence refuting the violation, proof of mitigation of noncompliance, and/or other factors for CMS' consideration. CMS will consider the materials

provided by the Primary Manufacturer when determining the Primary Manufacturer's CMP liability.

If the Primary Manufacturer fails to ensure access to a price less than or equal to the MFP, the statute provides for a CMP equal to 10 times the amount equal to the product of the number of units of such drug so dispensed (during such year) and the difference between the price for such drug made available (for such year by such manufacturer) to MFP-eligible individuals and the MFP for such drug for such year. For the purposes of calculating this CMP, CMS will use the amount that is equal to the required pass through of the MFP described in section 40.4 of this revised guidance. As described in section 40.5 of this revised guidance, CMS will monitor for compliance and audit, as needed, to ensure that the MFP or a price lower than the MFP is being made available for the selected drug.

100.2 Violations of the Agreement

Pursuant to section 1197(c) of the Act, any Primary Manufacturer of a selected drug that has entered into an Agreement with CMS under section 1193 of the Act that fails to comply with requirements determined by CMS to be necessary for the purposes of administering the Negotiation Program and monitoring compliance with the Negotiation Program pursuant to section 1193(a)(5) or fails to provide the information required under section 1193(a)(4) may be subject to a CMP of $1,000,000 for each day of such violation. In applying CMPs for Primary Manufacturer violations of the Agreement, CMS intends to use discretion such that CMPs are reserved for instances of substantive noncompliance. Examples of such violations are shown in the table below. Note that these examples are not an exhaustive list of violations that could warrant CMPs. CMS reserves the authority to issue CMPs for other violations as required to effectively administer and monitor the Negotiation Program.

Category	Example of Substantive Violations
Manufacturer Information Submission	• Failure to submit data required under section 1194(e)(1) of the Act, including failure to engage in requested corrective action to mitigate such failures. • Omissions or inaccuracies of manufacturer-submitted information that is critical to the negotiation processes (e.g., non-FAMP data from the Primary Manufacturer, including non-FAMP data for a selected drug sold by any Secondary Manufacturer(s), required for ceiling calculation) or other efforts to administer or monitor the Negotiation Program (e.g., information requested during an audit), including failure to engage in requested corrective action to mitigate such omissions or inaccuracies. • Submission of false information that interferes with the negotiation process (e.g., submission of false data on unit costs of production). • Knowing submission of false information under the procedures to apply the aggregation rule in section 1192(d)(2)(B) for the Small Biotech Exception. • Knowing provision of false information under procedures to apply the aggregation rule in section 1192(f)(1)(C) of the Biosimilar Delay.
MFP Availability	• Failure to make the MFP available to MFP-eligible individuals, and to pharmacies, mail order services, or other dispensers (see section 100.1 of this revised guidance) • Failure to process timely and complete reimbursement under a retrospective reimbursement structure as described in section 40.4 of this revised guidance.

As an example of when CMS would impose a CMP, consider the following. As described in section 40.2 of this revised guidance, information on non-FAMP for each applicable quarter (as described in section 50.1.1 of this revised guidance) for each NDC-11 of the selected drug for the applicable period will be due to CMS as part of the Negotiation Data Elements ICR no later than October 2, 2023 for initial price applicability year 2026. If the Primary Manufacturer fails to timely submit the required non-FAMP information, including the non-FAMP information for each NDC-11 of a selected drug for which there is a Secondary Manufacturer, CMS will determine the number of days in which the Primary Manufacturer is in violation of the Agreement by counting the day after the applicable submission deadline (e.g., October 3, 2023 for initial price applicability year 2026) as the first day of violation with each additional day of violation thereafter counted until the day the Primary Manufacturer provides the required information to CMS, the selected drug ceases to be a selected drug, or the Primary Manufacturer terminates the Agreement. In the event a manufacturer never provides the required information, the daily CMP will continue to accrue until the end of the negotiation period (i.e., the final deadline for reaching an agreed upon MFP). Upon reaching that deadline, the manufacturer may also be subject to a potential excise tax for failing to reach an agreed upon MFP pursuant to 26 U.S.C. § 5000D(b)(2).

CMS may require additional information to administer or monitor compliance with the Negotiation Program in accordance with section 1193(a)(5) of the Act. When applicable, CMS will provide a written request to the Primary Manufacturer with details for such requests, including a date by which any requested information must be submitted. CMS is committed to providing Primary Manufacturers with reasonable timeframes to accommodate these information requests. CMS will consider written requests for deadline extension submitted no later than three calendar days prior to the initial deadline. Extension requests must include a reasonable basis for requiring the extension as determined by CMS. Only one extension, if applicable, will be granted for each request. Manufacturers that fail to comply with requests for information required to administer or monitor compliance with the Negotiation Program on or before the due date may be subject to a CMP.

In the event the manufacturer does not meet the final established deadline to provide the requested information and CMS determines a CMP is warranted, the CMP will begin to accrue beginning on the day after the due date. For example, if CMS requests information for monitoring purposes by November 15, 2027, day one of the violation would be November 16, 2027. Each additional day of violation thereafter will be counted until the day the Primary Manufacturer provides the required information to CMS, the selected drug ceases to be a selected drug, or the Primary Manufacturer terminates the Agreement. The CMP will not include the day the information is submitted. Because the day of data submission is not included in CMP calculation, should a Primary Manufacturer submit the requested information on the day after the deadline, no CMP will be imposed.

To facilitate program operations and support manufacturer compliance, CMS will provide the Primary Manufacturer with: (1) written reminders of impending submission deadlines, including warning of potential liability for a CMP for submission violations; and (2) Notification of Potential Noncompliance, if applicable, and the applicable next steps (see, for example, sections

40.2.3 and 100.1 of this revised guidance). If CMS determines a violation warrants a CMP, CMS will follow the procedures outlined in section 100.4 of this revised guidance to notify the Primary Manufacturer and initiate the CMP process.

A Primary Manufacturer that submits false Information that is required under the Agreement and interferes with the administration of the Negotiation Program will be out of compliance with the requirement to submit information and may be subject to this CMP. In instances of a Primary Manufacturer submitting false information that is required under the Agreement, CMS will determine the number of days in which the Primary Manufacturer is in violation of the Agreement by counting the day after the established deadline for submission of information under the Agreement as the first day of violation with each additional day of violation thereafter counted until the day the Primary Manufacturer provides a complete and accurate submission of the required information to CMS, the selected drug ceases to be a selected drug, or the Primary Manufacturer terminates the Agreement.

100.3 Provision of False Information Related to the Small Biotech Exception and the Biosimilar Delay Rule

In accordance with section 1197(d) of the Act, if CMS determines that any manufacturer knowingly provides false information under the procedures to apply the aggregation rule in section 1192(d)(2)(B) for the Small Biotech Exception, such manufacturer shall be subject to a CMP equal to $100,000,000 for each item of such false information. Likewise, if CMS determines that any Biosimilar Manufacturer knowingly provides false information under the procedures to apply the aggregation rule in section 1192(f)(1)(C) of the Biosimilar Delay, such manufacturer shall be subject to a CMP equal to $100,000,000 for each item of such false information.

CMS adopts a standard for "knowingly" that conforms with the Office of the Inspector General definition at 42 C.F.R. § 1003.110 in the application of other CMPs. Knowingly means that a manufacturer, for purposes of section 1197(d) of the Act for the Small Biotech Exception or a Biosimilar Manufacturer under section 1192(f)(1)(c) for the Biosimilar delay: (1) has actual knowledge of the information; (2) acts in deliberate ignorance of the truth or falsity of the information; or (3) acts in reckless disregard of the truth or falsity of the information. No proof of specific intent to defraud is required. Upon identifying instances of knowing submission of false information under either of these provisions, CMS will provide the Manufacturer with a CMP Notification detailing the final CMP amount and the basis for that amount, requesting payment, outlining the payment process, outlining the available appeals process, and establishing applicable deadlines for resolution.

100.4 Notice and Appeal Procedures

Where CMS makes a determination to impose a CMP, CMS will provide a written CMP Notification that the manufacturer has engaged in a substantive compliance violation and is subject to a CMP. As required by section 1128A of the Act, the CMP Notification will include the following:

- A description of the basis for the determination;
- The basis for the penalty;
- The Primary Manufacturer's right to a hearing (see below); and

- Information about where to file the request for a hearing.

In applicable cases (e.g., failure to provide required information), CMS will note the commencement date for a CMP accrual and alert the manufacturer that the daily CMP will continue to accrue until the period of noncompliance ends. CMS will send monthly noncompliance notices to the manufacturer during the noncompliance period to include the total amount of CMP accrued to date, the amount that will continue to accrue should the violation continue, and required actions on the part of the Primary Manufacturer to mitigate the noncompliance period (e.g., submission of required information), if applicable.

To operationalize the CMP appeal process in the Negotiation Program, CMS is adopting the existing procedures as codified in 42 C.F.R. section 423 subpart T: Appeal Procedures for Civil Money Penalties (see § 423.1000 through § 423.1094) that currently apply to Part D sponsors and to manufacturers under the Coverage Gap Discount Program. Pursuant to this appeals process, the manufacturer will have 60 calendar days from the date of receipt of the CMP Notification to request a hearing (§ 423.1020). The date of receipt is defined as the calendar day following the day on which the CMP Notification is issued. If the manufacturer requests a hearing, the procedures outlined in section 1128A of the Act and operationalized by 42 C.F.R. § 423 Subpart T will apply. As set forth in section 1128A(f), if the manufacturer does not pay the CMP timely, the CMP amount may be deducted from any sum then or later owing by the United States. CMP funds will be deposited in accordance with section 1128A(f).

The CMP amount will cease to accrue once the manufacturer has demonstrated compliance with the requirement(s) at issue in the relevant CMP Notification. Following the end of the noncompliance period, and at the conclusion of any appeals process initiated by the Primary Manufacturer within 60 days of the CMP Notification, CMS will issue the final CMP Notification. As required by section 1128A of the Act, the final notification will add the following to the information included in the initial CMP Notification and monthly noncompliance notices:

- The final amount of the penalty;
- The date the penalty is due; and
- Instructions for submitting the CMP payment.

110. Part D Formulary Inclusion of Selected Drugs

In accordance with section 1860D-4(b)(3)(I) of the Act, Medicare Part D plans shall include each covered Part D drug that is a selected drug under section 1192 of the Act on Part D formularies during contract year 2026 and all subsequent years for which the MFP of the selected drug is in effect during the price applicability period.[75] Because the selected drug includes all dosage forms and strengths to which the MFP applies for initial price applicability year 2026, the statute requires that all such dosage forms and strengths of the selected drug that constitute a covered Part D drug and for which the MFP is in effect be included on formulary. For contract year 2026, CMS will not implement explicit tier placement or utilization management requirements that

[75] As required by section 1860D-4(b)(3)(I)(ii) of the Act, nothing shall prohibit a Part D sponsor from removing a selected drug from a formulary if such removal would be permitted under 42 C.F.R. § 423.120(b)(5)(iv) (or any successor regulation).

apply uniformly across selected drugs in all formularies, but intends to apply the process described below.

While CMS understands that not all selected drugs and drug classes will present Part D sponsors and their Pharmacy & Therapeutics Committees with the same formulary considerations and might not warrant the same formulary placement in all situations, CMS is concerned that Part D sponsors may be incentivized in certain circumstances to disadvantage selected drugs by placing selected drugs on less favorable tiers compared to non-selected drugs, or by applying utilization management that is not based on medical appropriateness to steer Part D beneficiaries away from selected drugs in favor of non-selected drugs.

CMS reminds Part D sponsors of the existing statutory and regulatory restrictions on formulary design. Sections 1860D-2(b)(2)(B) and 1860D-4(c)(1)(A) of the Act permit Part D sponsors to use formularies and tiered cost sharing in their benefit design, subject to certain limitations, and requires them to have a cost-effective drug utilization management program that includes incentives to reduce costs when medically appropriate. Under section 1860D-11(e)(2)(D)(i) of the Act, CMS may approve a prescription drug plan only if the agency "does not find that the design of the plan and its benefits (including any formulary and tiered formulary structure) are likely to substantially discourage enrollment by certain part D eligible individuals under the plan." In addition, 42 C.F.R. § 423.272(b)(2)(i) states: "CMS does not approve a bid if it finds that the design of the plan and its benefits (including any formulary and tiered formulary structure) or its utilization management program are likely to substantially discourage enrollment by certain Part D eligible individuals under the plan." Furthermore, 42 C.F.R. § 423.120(b)(2)(iii) requires each Part D plan formulary to "include adequate coverage of the types of drugs most commonly needed by Part D enrollees, as recognized in national treatment guidelines." In addition, 42 C.F.R. § 423.120(b)(1)(v) requires that in making decisions about formulary design, the entity designing the formulary must "base clinical decisions on the strength of scientific evidence and standards of practice." CMS maintains a robust clinical formulary review process to ensure that all Medicare Part D plans meet these and other applicable requirements. CMS reviews all formularies annually to ensure that each formulary passes the agency's clinical review criteria, which includes comprehensive evaluation of tier placement and all utilization management restrictions and criteria.

Given CMS' statutory obligation to monitor Medicare Part D plans' compliance with all applicable formulary requirements, CMS will use its formulary review process to assess: (1) any instances where Part D sponsors place selected drugs on non-preferred tiers, (2) any instances where a selected drug is placed on a higher tier than non-selected drugs in the same class, (3) any instances where Part D sponsors require utilization of an alternative brand drug prior to a selected drug with an MFP (i.e., step therapy), or (4) any instances where Part D sponsors impose more restrictive utilization management (i.e., step therapy and/or prior authorization) for a selected drug compared to a non-selected drug in the same class.

For this review, CMS will consider class to mean the FDA Established Pharmacologic Class or other source that groups like drugs with similar mechanisms of action. Specifically, as part of the contract year 2026 Part D formulary review and approval process, CMS will expect Part D sponsors to provide a reasonable justification to support the submitted plan design that includes

any of the practices noted above during the annual bid review process. This justification should address applicable clinical factors, such as clinical superiority, non-inferiority, or equivalence of the selected and non-selected drugs, as well as the plan design's compliance with applicable statutory and regulatory requirements (e.g., the requirement to have a cost-effective drug utilization management program that bases decisions on the strength of the clinical evidence and standards of practice). CMS will evaluate these justifications for compliance with applicable statutory and regulatory requirements and will only approve a Part D plan bid submitted by a Part D sponsor if the plan benefit package complies with those requirements.

120. Application of Medicare Part B and Part D Prescription Drug Inflation Rebate Programs to Selected Drugs

This section of the guidance describes the application of Medicare Part B and Part D inflation rebates to selected drugs. As background, section 11101 of the IRA added a new section 1847A(i) to the Act to require that manufacturers of Part B rebatable drugs pay inflation rebates to Medicare for certain Part B rebatable drugs based on specific requirements and formulas. Likewise, section 11102 of the IRA added a new section 1860D-14B to the Act, which requires that manufacturers of Part D rebatable drugs pay inflation rebates to Medicare for certain Part D rebatable drugs based on specific requirements and formulas.[76]

Given that initial price applicability year 2026 is limited to drugs for which there is Part D utilization, this revised guidance describes the interaction between the Negotiation Program and the Part D inflation rebate program. CMS will address the application of Part B inflation rebates to selected drugs in future guidance for initial price applicability year 2028.

The Part D drug inflation rebate program is applicable to certain drugs that meet the definition of a Part D rebatable drug and are dispensed under Part D and covered and paid for by Part D plans for each 12-month applicable period, starting with the applicable period beginning October 1, 2022. These rebates are paid by manufacturers to the Medicare Prescription Drug Account in the Federal Supplementary Medical Insurance Trust Fund.

The Part B and Part D inflation rebate programs apply to selected drugs, regardless of the status of the drug as a selected drug. Alternatively said, whether a drug is a selected drug will have no bearing as to whether the drug is also subject to the Part B and Part D inflation rebate program, as applicable. However, when a selected drug is no longer considered to be a selected drug, certain components of the applicable rebate amount formula are recalculated as discussed further below.

[76] CMS published initial guidance on both Part B and Part D inflation rebates on February 9, 2023, which includes more specific details on the operation of the Part B and Part D inflation rebate programs. See: https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf and https://www.cms.gov/files/document/medicare-part-b-inflation-rebate-program-initial-guidance.pdf.

The Part D inflation rebate calculation is based on changes in the AMP over time.[77] MFP is excluded from AMP and thus does not affect the rebate calculation.[78]

The statutory formula to determine the Part D drug inflation rebate amount owed by manufacturers for each Part D rebatable drug consists of various components, including the calculation of a benchmark period manufacturer price. This "benchmark period manufacturer price" is calculated based on a "payment amount benchmark period" for each Part D rebatable drug (established at section 1860D-14B(g)(3) of the Act for drugs first approved or licensed on or before October 1, 2021 and at section 1860D-14B(b)(5)(A) for drugs first approved or licensed after October 1, 2021), and a "benchmark period CPI-U"[79] for each Part D rebatable drug (established at section 1860D-14B(g)(4) of the Act for drugs first approved or licensed on or before October 1, 2021 and section 1860D-14B(b)(5)(A) for drugs first approved or licensed after October 1, 2021). The payment amount benchmark period is the basis for the calculation of the benchmark period manufacturer price. The benchmark period manufacturer price is based on a weighted AMP for the quarters in that period.

For the period of time before a Part D rebatable drug is a selected drug, and during the time it is a selected drug, CMS will calculate the Part D inflation rebate amount, if applicable, based on the Part D rebatable drug's applicable payment amount benchmark period and benchmark period CPI-U, which is determined based on when the drug is first approved or licensed, as noted above. However, the statute at section 1860D-14B(b)(5)(C) specifies a different "payment amount benchmark period" and "benchmark period CPI-U" for each Part D rebatable drug in the case such drug is no longer considered to be a selected drug under section 1192(c) of the Act, for each applicable period beginning after the price applicability period with respect to such drug. Accordingly, in such a case where a Part D rebatable drug is no longer a selected drug, the payment amount benchmark period will be reset as the last year that begins during such price applicability period for such selected drug, and the benchmark period CPI-U is established as the January of the last year beginning during such price applicability period.

[77] Section 1860D-14B(g)(6) of the Act defines AMP to have the meaning, with respect to a Part D rebatable drug of a manufacturer, given in section 1927(k)(1) with respect to a covered outpatient drug of a manufacturer for a rebate period under section 1927. Section 1927(k)(1) defines AMP, with respect to a covered outpatient drug of a manufacturer for a rebate period, to mean the average price paid to the manufacturer for the drug in the United States by (i) wholesalers for drugs distributed to retail community pharmacies, and (ii) retail community pharmacies that purchase directly from the manufacturer, subject to certain exclusions.

[78] Section 1927(k)(1)(B)(i)(VI), as amended by section 11001(b)(3) of the Inflation Reduction Act.

[79] CPI-U refers to the Consumer Price Index for all urban consumers (United States city average).

Appendix A: Email Template for Biosimilar Manufacturer to Indicate Intent to Submit an Initial Delay Request for Initial Price Applicability Year 2026

Email subject line:
Biosimilar Delay: Notice of Intent to Submit Initial Delay Request for Initial Price Applicability Year 2026

Body of email:
Dear CMS,

I, an authorized representative of [insert manufacturer name], am notifying CMS that my company is the manufacturer of a biosimilar biological product and we anticipate the reference product for our biosimilar biological product will be included in a negotiation-eligible drug with respect to initial price applicability year 2026 for the Medicare Drug Price Negotiation Program. My company reasonably believes the market entry of our biosimilar biological product meets the criteria for the special rule to delay selection and negotiation of the negotiation-eligible drug, described in section 1192(f) of the Social Security Act. Therefore, I am notifying CMS of my company's intent to request that CMS delay the inclusion of the negotiation-eligible drug that includes the reference product for our biosimilar biological product on the selected drug list for initial price applicability year 2026.

As part of this notification, I am providing the following information:

My job title:	[insert]
My email address:	[insert]
My phone number:	[insert]
My company's mailing address:	[insert]
My company's biosimilar biological product name:	[insert]
Product name of the reference product for my company's biosimilar biological product	[insert]

Signed,
[Insert name of authorized representative]

Appendix B: Template for the Initial Delay Request Form

Under the authority in sections 11001 and 11002 of the Inflation Reduction Act of 2022 (P.L. 117-169), the Centers for Medicare & Medicaid Services (CMS) is implementing the Medicare Drug Price Negotiation Program, codified in sections 1191 through 1198 of the Social Security Act (the Act), to negotiate maximum fair prices (MFPs)[80] for selected drugs. Under section 1192(f) of the Act (the "Biosimilar Delay"), the manufacturer of a biosimilar biological product ("Biosimilar Manufacturer" of a "Biosimilar") may submit a request, prior to the selected drug publication date, for CMS' consideration to delay the inclusion of a negotiation-eligible drug (as defined in section 1192(d) of the Act) that includes the reference product for the Biosimilar (such a negotiation-eligible drug is herein referred to as a "Reference Drug") on the selected drug list for a given initial price applicability year. The Biosimilar Manufacturer eligible to submit the request is the holder of the BLA for the Biosimilar or, if the Biosimilar has not yet been licensed, the sponsor of the BLA for the Biosimilar that has been submitted for review by FDA.

Please refer to the memo titled "Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments" (Initial Negotiation Program Guidance) for additional details regarding the implementation of the Biosimilar Delay for initial price applicability year 2026. This form serves as the template that a Biosimilar Manufacturer may complete to submit an Initial Delay Request with respect to initial price applicability year 2026.

Submission of the email described in that memo indicating the Biosimilar Manufacturer's intention to submit an Initial Delay Request for initial price applicability year 2026 and receipt of the fillable Initial Delay Request form template and request-specific Box folder should occur prior to completing this form.

Instructions

- Initial Delay Requests that are incomplete or not timely submitted will not be accepted. For an Initial Delay Request to be timely for initial price applicability year 2026, the Biosimilar Manufacturer must submit a complete Initial Delay Request to CMS no later than 11:59 pm PT on May 22, 2023. CMS will deem an Initial Delay Request to be complete if it includes a complete Initial Delay Request form using this fillable template and the following documentation:
    - All agreements related to the Biosimilar filed with the Federal Trade Commission or the Assistant Attorney General pursuant to subsections (a) and (c) of section 1112 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003;

[80] In accordance with section 1191(c)(3) of the Social Security Act ("the Act"), maximum fair price means, with respect to a year during a price applicability period and with respect to a selected drug (as defined in section 1192(c) of the Act) with respect to such period, the price negotiated pursuant to section 1194 of the Act, and updated pursuant to section 1195(b) of the Act, as applicable, for such drug and year.

  - The manufacturing schedule for the Biosimilar submitted to the FDA during its review of the application for licensure under section 351(k) of the PHS Act, to the extent available; and
  - Disclosures (in filings by the Biosimilar Manufacturer with the Securities and Exchange Commission required under section 12(b), 12(g), 13(a), or 15(d) of the Securities Exchange Act of 1934 about capital investment, revenue expectations, and actions taken by the manufacturer that are typical of the normal course of business in the year (or the 2 years, as applicable) before marketing of a biosimilar biological product) that pertain to the marketing of the Biosimilar, or comparable documentation that is distributed to the shareholders of privately held companies, to the extent available.
- The data entry component of this submission should be completed by an individual authorized by the Biosimilar Manufacturer.
- The certification of the Initial Delay Request should be executed by (1) the chief executive officer (CEO) of the Biosimilar Manufacturer, (2) the chief financial officer (CFO) of the Biosimilar Manufacturer, (3) an individual other than a CEO or CFO, who has authority equivalent to a CEO or a CFO, or (4) an individual with the directly delegated authority to perform the certification on behalf of one of the individuals mentioned in (1) through (3).

CMS is relying on the fullness, accuracy, and completeness of the Biosimilar Manufacturer's submission to determine whether to approve the Initial Delay Request for initial price applicability year 2026. If the Biosimilar Manufacturer submits an Initial Delay Request that is not timely, complete, and accurate, the submission may adversely affect the Negotiation Program, including the process for selecting drugs for negotiation for initial price applicability year 2026.

Section 1: Identifying information

Identifying information for Biosimilar Manufacturer

Q1. Complete the following table with identifying information for the Biosimilar Manufacturer.

Field	Response
Entity Type	☐ Biosimilar Manufacturer
Entity name	
Employer Identification Number (EIN(s))	
Address	
Unique Identifier Assigned by CMS (P-number)	
Labeler Code(s)	

Identifying information on Biosimilar

Q2. Complete the following table with identifying information for the Biosimilar.

Field	Response
Product Name	

Active Ingredient	
NDC-9(s) (if applicable)	[optional, only if available]

Q3. List all applications for licensure for the Biosimilar under 351(k) of the Public Health Service (PHS) Act regardless of status (i.e., including applications that are approved, accepted for review, and submitted but not yet accepted for review). Leave approval date blank if license has not been approved.

Add additional rows for each application

Application Number	Submission Number	Application status	Approval Date [if licensed]	Indication	Dosage Form and Strength	Licensure planned before September 1, 2025?	Marketing planned before September 1, 2025?
nnnnnn	nnn	[Approved, Accepted for Review, Submitted]	MM/DD/ YYYY	Text	Text	[Yes/No]	[Yes/No]

Identifying information on Reference Product

Q4. Complete the following table with identifying information for the reference product for the Biosimilar.

Field	**Response**
Product Name	
Active Ingredient	
NDC-9(s)	

Q5. List the Biologic License Application (BLA) approved by the Food and Drug Administration (FDA) under section 351(a) of the PHS Act for the reference product for the Biosimilar.

Application Number	Submission Number	Approval Date	Indication	Dosage Form and Strength	Sponsor
nnnnnn	nnn	MM/DD/ YYYY	Text	Text	Text

Identifying information on Reference Manufacturer

Q6. Complete the following table with identifying information for the Reference Manufacturer.

Field	**Response**
Entity Type	☐ Reference Manufacturer
Entity name	

Employer Identification Number (EIN)	*[Optional, only if known]*
Address	*[Optional, only if known]*
Unique Identifier Assigned by CMS (P-number)	*[Optional, only if known]*
Labeler Code(s)	*[Optional, only if known]*

Section 2: Attestations to Requirements for Granting an Initial Delay Request

In accordance with section 1192(f)(2)(D)(iv) of the Act, CMS will not delay inclusion of a biological product on the list of selected drugs if the Biosimilar Manufacturer meets any of the statutory criteria for an excluded manufacturer. Questions 7 through 9 address whether the Biosimilar Manufacturer is an excluded manufacturer.

Q7. Relationship between Biosimilar Manufacturer and Reference Manufacturer: In accordance with section 1192(f)(2)(D)(iv) of the Act, CMS will not approve an Initial Delay Request if the Biosimilar Manufacturer is the same as the Reference Manufacturer or is treated as being the same as the Reference Manufacturer based on the aggregation rule in section 1192(f)(1)(C) of the Act. This aggregation rule provides, "all persons treated as a single employer under subsection (a) or (b) of section 52 of the Internal Revenue Code of 1986, or in a partnership, shall be treated as one manufacturer" for purposes of the Biosimilar Delay. Further, section 1192(f)(1)(C) of the Act establishes that "the term 'partnership' means a syndicate, group, pool, joint venture, or other organization through or by means of which any business, financial operation, or venture is carried on" by two or more parties for the purposes of the Biosimilar Delay.

Read the following statement and check the box if accurate:

I confirm consistent with sections 1192(f)(1)(C) and 1192(f)(2)(D)(iv) of the Act that the Biosimilar Manufacturer submitting this request is not the same or is not treated as being the same as the Reference Manufacturer.	☐

Q8. Incentives: In accordance with section 1192(f)(2)(D)(iv)(II)(aa) of the Act, CMS will not approve any Initial Delay Request submitted by a Biosimilar Manufacturer that has entered into an agreement with the Reference Manufacturer that requires or incentivizes the Biosimilar Manufacturer to submit an Initial Delay Request.

Read the following statement and check the box if accurate:

I confirm consistent with section 1192(f)(2)(D)(iv)(II)(aa) of the Act that the Biosimilar Manufacturer submitting this request has not entered into an agreement with the Reference Manufacturer named in this request that requires or incentivizes the Biosimilar Manufacturer to submit this or any other Initial Delay Request.	☐

Q9. Quantity Restriction: In accordance with section 1192(f)(2)(D)(iv)(II)(bb) of the Act, CMS will not approve any Initial Delay Request submitted by a Biosimilar Manufacturer that has entered into an agreement with the Reference Manufacturer that restricts the quantity, either directly or indirectly, of the Biosimilar that may be sold in the United States over a specified period of time.

Read the following statement and check the box if accurate:

I confirm consistent with section 1192(f)(2)(D)(iv)(II)(bb) of the Act that the Biosimilar Manufacturer submitting this request has not entered into an agreement with the Reference Manufacturer named in this request that restricts the quantity, either directly or indirectly, of the Biosimilar that may be sold in the United States over a specified period of time.	☐

In accordance with section 1192(f)(1)(A) of the Act, CMS will only approve an Initial Delay Request for initial price applicability year 2026 if CMS determines there is a high likelihood that the Biosimilar will be licensed and marketed before September 1, 2025. Questions 10 and 11 are relevant for this determination.

Q10. Licensure: In accordance with section 1192(f)(1)(A) of the Act, CMS will only approve an Initial Delay Request for initial price applicability year 2026 if CMS determines there is a high likelihood that the Biosimilar will be licensed before September 1, 2025. For the purposes of this Initial Delay Request, 'licensed' means approved by the FDA under section 351(k) of the PHS Act.

Select the following option that best describes the current licensure status of the Biosimilar as of the submission of this Initial Delay Request:

(A) I confirm consistent with section 1192(f)(1)(A) of the Act that the Biosimilar Manufacturer has submitted an application for licensure of the Biosimilar under section 351(k) of the PHS Act and the Biosimilar has been licensed.	☐
(B) I confirm consistent with section 1192(f)(1)(A) of the Act that the Biosimilar Manufacturer has submitted an application for licensure of the Biosimilar under section 351(k) of the PHS Act and the FDA has accepted such application for review.	☐
(C) I confirm consistent with section 1192(f)(1)(A) of the Act that the Biosimilar Manufacturer has submitted an application for licensure of the Biosimilar under section 351(k) of the PHS Act and has not received a determination from FDA that such application has been accepted for review.	☐
(D) I confirm consistent with section 1192(f)(1)(A) of the Act that the Biosimilar Manufacturer has not submitted an application for licensure of the Biosimilar under section 351(k) of the PHS Act.	☐

Q11. Marketing: In accordance with section 1192(f)(1)(A) of the Act, CMS will only approve an Initial Delay Request for initial price applicability year 2026 if CMS determines there is a high likelihood that the Biosimilar will be marketed before September 1, 2025.
Select the following option that best describes the current marketing status of the Biosimilar as of the submission of this Initial Delay Request:

(A) I confirm consistent with section 1192(f)(1)(A) of the Act that the Biosimilar is currently marketed.	☐
(B) I confirm consistent with section 1192(f)(1)(A) of the Act that the Biosimilar has not yet been marketed but the Biosimilar Manufacturer expects it to be marketed by September 1, 2025.	☐

(C) I confirm consistent with section 1192(f)(1)(A) of the Act that the Biosimilar has not yet been marketed and the Biosimilar Manufacturer does not expect it to be marketed by September 1, 2025.	☐

Section 3: Supporting Documentation

Q12. Manufacturing schedule: In accordance with section 1192(f)(1)(B)(ii)(I) of the Act, an Initial Delay Request must include, to the extent available, the manufacturing schedule for the Biosimilar submitted to the FDA during its review of the Biosimilar's application for licensure. Further, in accordance with section 1192(f)(3)(B) of the Act, CMS will consider such information in determining whether there is clear and convincing evidence that the Biosimilar will be marketed.

Using the 'Supporting Documentation - Manufacturing schedule' subfolder within the Box folder that CMS shared for the purposes of this Initial Delay Request, upload the manufacturing schedule(s) for the Biosimilar submitted to the FDA for each application listed in Q3.

Read the following statements and check the boxes if accurate:

I confirm consistent with section 1192(f)(1)(B)(ii)(I) of the Act that the manufacturing schedule(s) for the Biosimilar submitted to the FDA during its review of the Biosimilar's application for licensure is available for submission.	☐
I confirm consistent with section 1192(f)(1)(B)(ii)(I) of the Act that I have submitted to CMS the manufacturing schedule(s) for the Biosimilar submitted to the FDA during its review of the Biosimilar's application for licensure.	☐

Q13. Disclosures: In accordance with section 1192(f)(1)(B)(ii)(I) of the Act, an Initial Delay Request must include, to the extent available, disclosures (in filings by the Biosimilar Manufacturer with the Securities and Exchange Commission required under section12(b), 12(g), 13(a), or 15(d) of the Securities Exchange Act of 1934 about capital investment, revenue expectations, and actions taken by the Biosimilar Manufacturer that are typical of the normal course of business before marketing of a biosimilar biological product) that pertain to the marketing of the Biosimilar, or comparable documentation that is distributed to the shareholders of privately held companies. Further, in accordance with section 1192(f)(3)(B) of the Act, CMS will consider such information in determining whether there is clear and convincing evidence that the Biosimilar will be marketed.

Using the 'Supporting Documentation – Disclosures' subfolder within the Box folder that CMS shared for the purposes of this Initial Delay Request, upload all such disclosures.
Read the following statements and check the boxes if accurate:

I confirm consistent with section 1192(f)(1)(B)(ii)(I) of the Act that disclosures (in filings by the Biosimilar Manufacturer with the Securities and Exchange Commission required under section12(b), 12(g), 13(a), or 15(d) of the Securities Exchange Act of 1934 about capital investment, revenue expectations, and actions taken by the Biosimilar Manufacturer that are typical of the normal course of business before marketing of a biosimilar biological product) that pertain to the marketing of the	☐

Biosimilar, or comparable documentation that is distributed to the shareholders of privately held companies, are available for submission.	
I confirm consistent with section 1192(f)(1)(B)(ii)(I) of the Act that I have submitted to CMS all such disclosures.	☐

Q14. Agreements:
In accordance with section 1192(f)(1)(B)(ii)(I) of the Act, an Initial Delay Request must include all agreements related to the Biosimilar filed with the Federal Trade Commission or the Assistant Attorney General pursuant to subsections (a) and (c) of section 1112 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. Further, in accordance with section 1192(f)(3)(B) of the Act, CMS will consider such information in determining whether there is clear and convincing evidence that the Biosimilar will be marketed.

Using the 'Supporting Documentation – Agreements' subfolder within the Box folder that CMS shared for the purposes of this Initial Delay Request, upload all such agreements.

Read the following statement and check the box if accurate:

I confirm consistent with section 1192(f)(1)(B)(ii)(I) of the Act that I have submitted to CMS all agreements related to the Biosimilar filed with the Federal Trade Commission or the Assistant Attorney General pursuant to subsections (a) and (c) of section 1112 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003.	☐

Section 4: Certification

I hereby certify, to the best of my knowledge, that the information being sent to CMS in this submission is complete and accurate, and the submission was prepared in good faith and after reasonable efforts. I reviewed the submission and made a reasonable inquiry regarding its content. I understand the information contained in this submission is being provided to and will be relied upon by CMS for Medicare reimbursement purposes, including to determine whether CMS should delay the selection of a biological product that would, absent this request, be included on the selected drug list for initial price applicability year 2026, as described in section 1192(f) of the Social Security Act. I also certify that I will timely notify CMS if I become aware that any of the information submitted in this form has changed. I also understand that any misrepresentations may also give rise to liability, including under the False Claims Act.

Yes []
No []

Contact Information

Field	Response
Name of the Person Responsible for the Submission	
Title	
Telephone	
Email	
Signature	
Date	

Appendix C: Definitions for Purposes of Collecting Manufacturer-Specific Data

For the purposes of describing the data at sections 1194(e)(1), 1194(e)(2), and 1193(a)(4)(A) of the Act to be collected for use in the Negotiation Program, as described in sections 40.2, 50.1, and 50.2 of this revised guidance and the Negotiation Data Elements Information Collection Request (ICR), CMS adopts the following definitions and standards.

General

- When calculating monetary values, assume at most an 8.1 percent annual cost of capital for purposes of applying an adjustment. If a Primary Manufacturer uses a cost of capital below 8.1 percent, that amount should be used.

Non-FAMP

- Non-FAMP: Section 1194(c)(6) of the Act defines "average non-Federal average manufacturer price" as the average of the non-FAMP (as defined in section 8126(h)(5) of title 38 of the U.S. Code) for the four calendar quarters of the year involved.[81] For initial price applicability year 2026, these are the quarters of 2021. When there are less than 30 days of commercial sales data for all NDC-11s of the selected drug in calendar year 2021, the applicable year will be the first full calendar year following market entry of such drug. When there are at least 30 days of commercial sales data but less than a calendar quarter of data to calculate the non-FAMP in calendar year 2021 (or the first full year following market entry of such drug, when applicable) for a given NDC-11 of such drug, the non-FAMP reported by the manufacturer to CMS should reflect the temporary non-FAMP predicated upon the first 30 days of commercial sales data. The temporary non-FAMP should be calculated following the same methodology used to calculate the temporary non-FAMP amount used to determine the Temporary Federal Ceiling Price, as described in the Department of Veterans Affairs (VA) 2023 Updated Guidance for Calculation of Federal Ceiling Prices (FCPs) for New Drugs subject to Public Law 102-585. Any restatements of the non-FAMP made in any manufacturer non-FAMP submissions to the VA must be reflected in the non-FAMP submitted to CMS.
- Non-FAMP unit: Non-FAMP unit is the package unit as described in 38 U.S.C. § 8126(h)(6).
- Non-FAMP dosage form unit: The non-FAMP dosage form unit is the dosage form of the NDC that is reported in the "Dose form" field of the Excel workbook used by the Office of Pharmacy Benefits Management Services at the VA to collect non-FAMP information.

Research and Development (R&D) Costs

R&D costs mean a combination of costs incurred by the Primary Manufacturer for all FDA-approved indications of a drug falling into the five categories below, and excluding (a) prior Federal financial support, (b) costs associated with applying for and receiving foreign approvals,

[81] The term "non-Federal average manufacturer price" means, with respect to a covered drug and a period of time (as determined by the Secretary), the weighted average price of a single form and dosage unit of the drug that is paid by wholesalers in the United States to the manufacturer, taking into account any cash discounts or similar price reductions during that period, but not taking into account— (A) any prices paid by the Federal Government; or (B) any prices found by the Secretary to be merely nominal in amount. 38 U.S.C. § 8126(h)(5).

and (c) costs associated with *ongoing* basic pre-clinical research, clinical trials, and pending approvals:

1. R&D: Acquisition Costs
2. R&D: Basic Pre-Clinical Research Costs
3. R&D: Post-Investigational New Drug (IND) Application Costs
4. R&D: Abandoned and Failed Drug Costs
5. R&D: All Other R&D Direct Costs

CMS is calculating recoupment of R&D costs using both the global and U.S. total lifetime net revenue for the selected drug:

6. Recoupment: Global and U.S. Total Lifetime Net Revenue for the Selected Drug

The definitions and associated time periods for these terms are included below.

Definitions for 1. R&D: Acquisition Costs

- For the sole purpose of data collection under section 1194(e)(1)(A) of the Act, acquisition costs are defined as costs associated with the Primary Manufacturer's purchase from another entity of the rights to hold previously approved or future NDA(s) / BLA(s) of the selected drug.

Definitions for 2. R&D: Basic Pre-Clinical Research Costs

- Basic pre-clinical research costs are defined as all discovery and pre-clinical developmental costs incurred by the Primary Manufacturer with respect to the selected drug during the basic pre-clinical research period and are the sum of (1) direct research expenses and (2) the appropriate proportion of indirect research expenses (defined below).
- For each indication of the selected drug, the basic pre-clinical research period is defined as the date of initial discovery *or* the date the Primary Manufacturer acquired the right to hold the potential NDA(s) / BLA(s) or NDA(s) / BLA(s) of the selected drug (whichever is later) to the day before the last IND application for that indication of the selected drug went into effect.[82, 83] The basic pre-clinical research period may include both the initial research on the discovery of the selected drug and basic pre-clinical research related to new applications of the selected drug. If the length of the basic pre-clinical research period for the selected drug cannot be calculated, use 52 months ending the day before the first IND application went into effect. For example, if the selected drug had five IND applications that went into effect, use the date of the first IND application that went into effect as the end date for the 52-month period.[84]

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[82] CMS acknowledges that the exact date of initial discovery might not be known, but manufacturers should use their best estimate.

[83] For the purposes of identifying the date the Primary Manufacturer acquired the right to hold the potential NDA(s) / BLA(s) or NDA(s) / BLA(s) of the selected drug, use the earliest date of acquisition for any NDA / BLA of the selected drug.

[84] CMS believes that 52 months represents a solid average across studies. For example, one study reported that the pre-clinical phase takes 52 months on average. See DiMasi, J, Hansen, R, Grabowski, H. The price of innovation: new estimates of drug development costs. *Journal of Health Economics*, 2003, https://fds.duke.edu/db?attachment-

- Direct basic pre-clinical research costs are costs that can be specifically attributed to the discovery and pre-clinical development of the selected drug. Direct research expenses could include personnel (compensation for investigators and staff) researching the selected drug, materials for conducting basic pre-clinical research, and the costs of in vivo and in vitro studies on the selected drug before an IND application went into effect.
- Indirect basic pre-clinical research costs and relevant general and administrative costs are operating costs for basic pre-clinical research beyond the basic pre-clinical research costs for the selected drug, including administrative personnel and overhead costs (expenses for clinical facilities and equipment) that are shared across multiple potential drugs or biologics. To calculate the proportion of indirect costs, the Primary Manufacturer must use proportional allocation, whereby the same proportion of spending allocated for direct research on the selected drug is used to estimate the proportional spending for indirect research.[85, 86] For example, if the *direct* pre-clinical research costs spent on the selected drug were approximately 10 percent of a Primary Manufacturer's total *direct* basic pre-clinical research costs, then *indirect* costs should be allocated proportionally, thus for the selected drug they should be 10 percent of the total spending on *indirect* pre-clinical research costs during that time period.

Definitions for 3. R&D: Post-Investigational New Drug (IND) Application Costs

- Post-IND costs are defined as all direct costs associated with dosing and preparing the selected drug for clinical trials and the selected drug's Phase I, Phase II, and Phase III clinical trials for each FDA-approved indication. Post-IND costs also include all direct costs associated with completed FDA-required, post-marketing trials that are conducted after the FDA has approved a product. Post-IND costs exclude FDA-required, post-marketing trials that were not completed.
- Direct post-IND costs are defined as Institutional Review Board (IRB) review and amendment costs, user fees, patient recruitment, per-patient costs, research and data collection costs, personnel, and facility costs that are directly related to conducting the dosing and Phase I, Phase II, and Phase III clinical trials during the post-IND period. Direct post-IND costs also include patient recruitment, per-patient costs, research and data collection costs, personnel, and facility costs that are directly related to conducting the completed FDA-required, post-marketing trial.

25--1301-view-168. Another study estimated that the pre-clinical phase can take 31 months on average. See DiMasi, J, Grabowski, H, Hansen, R. Innovation in the pharmaceutical industry: New estimates of R&D costs, *Journal of Health Economics*, 2016, as cited by the Congressional Budget Office (CBO) in Research and Development in the Pharmaceutical Industry, April 2021, https://www.cbo.gov/publication/57126. Other estimates have found that the pre-clinical phase ranges from three to six years. See PhRMA, "Biopharmaceutical Research & Development: The Process Behind New Medicines," 2015, http://phrma-docs.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf.

[85] Wouters OJ, McKee M, Luyten J. Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018. *JAMA*. 2020;323(9):844–853. doi:10.1001/jama.2020.1166

[86] Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. *Methods for the Economic Evaluation of Health Care Programme*. 3rd ed. Oxford, UK: Oxford University Press; 2005, https://pure.york.ac.uk/portal/en/publications/methods-for-the-economic-evaluation-of-health-care-programme-third-edition(e43f24cd-099a-4d56-97e6-6524afaa37d1)/export.html.

- The post-IND period begins on the day the IND went into effect for the first FDA-approved indication for the selected drug through the date when the last FDA-required post-marketing trial was completed for the selected drug.

Definitions for 4. R&D: Abandoned and Failed Drug Costs

- Failed or abandoned product costs include a sum of the portion of direct *basic pre-clinical research* costs on drugs with the same active moiety / active ingredient or mechanism of action as the selected drug that did not make it to clinical trials and a portion of direct *post-IND costs* for drugs in the same therapeutic class as the selected drug that did not achieve FDA approval.
- Failed or abandoned product costs include a portion of direct *basic pre-clinical research* costs on drugs with the same active moiety / active ingredient or mechanism of action as the selected drug that did not make it to clinical trials.
    - Direct research expenses are costs that can specifically be attributed to the discovery and pre-clinical development of the drug.
    - Direct research expenses include personnel (compensation for investigators and staff) researching the drug, materials for conducting basic pre-clinical research, and in vivo and in vitro studies on the drug.
- Failed or abandoned product costs include a portion of direct *post-IND costs* for drugs in the same therapeutic class as the selected drug that did not achieve FDA approval.
    - Direct post-IND costs are costs that can specifically be attributed to the dosing and clinical trials for the drug.
    - Direct post-IND costs include IRB review and amendment costs, user fees, patient recruitment, per-patient costs, research and data collection costs, personnel, and facility costs that are directly related to conducting dosing and clinical trials for the drug.

Definitions for 5. R&D: All Other R&D Direct Costs

- All other R&D direct costs are any other allowable costs that do not align with R&D definitions 1-4. For example, other R&D direct costs may include direct costs associated with conducting FDA-required post-marketing trials that were not completed. No additional definitions adopted.

Definitions for 6. Global and U.S. Total Lifetime Net Revenue for the Selected Drug

CMS will use both the Primary Manufacturer's global and U.S. total lifetime net revenue for the selected drug to determine the extent to which the Primary Manufacturer has recouped R&D costs for the selected drug.

Definitions for 6a. Global, including U.S., Total Lifetime Net Revenue for the Selected Drug

- Global, total lifetime net revenue for the selected drug is defined as the direct sales and payments from all other entities, minus the discounts, chargebacks, rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, other price concessions or similar benefits offered to any purchasers or any royalty payments or percentage payments in purchase contracts.

- Global, total lifetime net revenue period is defined as the date the drug or biologic was first sold anywhere globally through the date of the publication of the selected drug list that includes the drug as a selected drug for an initial price applicability year.
- If global, total lifetime net revenue for the selected drug is not available through the date of the publication of the selected drug list that includes the drug as a selected drug for an initial price applicability year, calculate net revenue through the most recent quarter for which such data are available.

Definitions for 6b. U.S. Lifetime Net Revenue for the Selected Drug

- U.S. lifetime net revenue for the selected drug is defined as the direct sales and payments from U.S. entities, minus the discounts, chargebacks, rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, other price concessions or similar benefits offered to any purchasers or any royalty payments or percentage payments in purchase contracts.
- U.S. lifetime net revenue period is defined as the date the drug or biologic was first sold in the U.S. through the date of the publication of the selected drug list that includes the drug as a selected drug for an initial price applicability year.
- If U.S. lifetime net revenue for the selected drug is not available through the date of the publication of the selected drug list that includes the drug as a selected drug for an initial price applicability year, calculate net revenue through the most recent quarter for which such data are available.

Current Unit Costs of Production and Distribution

- In accordance with section 1191(c)(6) of the Act, the term "unit" means, with respect to a drug or biological product, the lowest identifiable amount (such as a capsule or tablet, milligram of molecules, or grams) of the drug or biological product that is dispensed or furnished.
- Units must be reported in one of the three National Council for Prescription Drug Programs (NCPDP) Billing Unit Standards (BUS)[87]: each (EA), milliliter (ML), or gram (GM). The unit reported must be specified for each of the NDC-11s of the selected drug. Selections of EA, ML or GM must be made as follows:
    - "EA" is used when the product is dispensed in discrete units. These products are not measured by volume or weight. The Billing Unit of "EA" is also used to address exceptions where "GM" and "ML" are not applicable. Examples of products defined as "EA" include, but are not limited to:
        - Tablets;
        - Capsules;
        - Suppositories;
        - Transdermal patches;
        - Non-filled syringes;
        - Tapes;
        - Devices/Digital Therapies;

[87] See: https://standards.ncpdp.org/Billing-Unit-Request.aspx#:~:text=Billing%20Unit%20Requests,grams%22%20or%20%22milliliters.%22.

- Blister packs;
- Oral powder packets;
- Powder filled vials for injection;
- Kits;[88] and
- Unit-of-use packages of products other than injectables with a quantity less than one milliliter or gram should be billed as "one each," for example, ointment in packets of less than 1 gram or eye drops in dropperettes that contain less than 1 ML.

- "ML" is used when a product is measured by its liquid volume. Examples of products defined as "ML" include, but are not limited to:
  - Liquid non-injectable products of 1 ML or greater;
  - Liquid injectable products in vials/ampules/syringes;
  - Reconstitutable non-injectable products at the final volume after reconstitution except when they are in powder packets; and
  - Inhalers (when labeled as milliliters on the product).
- "GM" is used when a product is measured by its weight. Examples of products defined as "GM" include, but are not limited to:
  - Creams (of 1 GM or greater);
  - Ointments (of 1 GM or greater); and
  - Inhalers (when labeled as GM on the product).[89]

- Costs of production are defined as all (direct and allocation of indirect) costs related to:
  - Purchase of raw ingredients, including intermediates, active pharmaceutical ingredients, excipients, and other bulk chemicals;
  - Formulation and preparation of the finished drug product;
  - Quality control and testing of the drug; and
  - Operating costs for personnel, facilities, transportation, importation (if any), and other expenses related to the preparation of the finished drug product for the selected drug.
- Costs of distribution are defined as all (direct and allocation of indirect) costs related to:
  - Packaging and packaging materials;
  - Labeling (e.g., the mechanical aspects of printing and affixing the approved label);
  - Shipping to any entity (e.g., distributor, wholesaler, retail or specialty pharmacy, physician office or hospital, etc.) that acquires the drug from the Primary Manufacturer or any Secondary Manufacturer; and
  - Operating costs for facilities, transportation, and other expenses related to packaging, labeling, and shipping to any entity that acquires the drug from the Primary Manufacturer or any Secondary Manufacturer.
- Current unit costs of production and distribution of the selected drug are defined to include:

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[88] Kits are defined as products that contain one of the following: (1) at least two distinct items with different billing units; (2) one product packaged with medicated or unmedicated swabs, wipes and/or cotton swabs/balls; or (3) meters packaged with test strips.

[89] See: https://standards.ncpdp.org/Standards/media/pdf/BUS_fact_sheet.pdf. *Permission is hereby granted to any organization to copy and distribute this material as long as this copyright statement is included, the contents are not changed, and the copies are not sold.*

- Units (and associated costs) marketed by the Primary Manufacturer and any Secondary Manufacturer(s);
- Average unit costs during the 12-month period ending May 31, 2023 (for selected drugs for initial price applicability year);
- Only units (and associated costs) produced and distributed for U.S. sales; costs incurred outside of the U.S. are included, provided that they are incurred for the production or distribution of units produced and distributed for use in the U.S.;
- Only costs incurred by the Primary Manufacturer and any Secondary Manufacturers; such costs may include payments to third parties (e.g., contractors) performing activities that qualify as production or distribution, as specified above; and
- Allocated shared operating and other indirect costs (such as capitalized production facility costs, benefits, generalized and administrative costs, and overhead expenses) specific to each NDC-11 based on unit volume.

- Current unit costs of production and distribution of the selected drug are defined not to include:
  - R&D costs; and
  - Marketing costs.
- "Marketing costs" are defined as expenditures incurred in the introduction or delivery for introduction into interstate commerce of a drug product, specifically including media advertisements, direct-to-consumer promotional incentives including patient assistance programs, promotion of the drug to health professionals, and other paid promotion.

Prior Federal Financial Support

For the purposes of describing prior federal financial support for novel therapeutic discovery and development to be collected for use in the Negotiation Program with respect to the selected drug, as described in section 1194(e)(1) of the Act and section 50.1 of this revised guidance, CMS adopts the definitions described in this subsection.

- "Federal financial support for novel therapeutic discovery and development" refers to tax credits, direct financial support, grants or contracts, and any other funds provided by the federal government that support discovery, research, and/or development related to the selected drug.
- "*Prior* Federal financial support" refers to Federal financial support for novel therapeutic discovery and development (as defined above) issued during the time period from when initial research began (as defined above in the R&D Costs subsection), or when the drug was acquired by the Primary Manufacturer, whichever is later, to the day through the date the most recent NDA / BLA was approved for the selected drug.

Patents, Exclusivities, and Approvals

- CMS considers relevant patents, both expired and unexpired, and relevant patent applications to include:
  - All patents issued by the United States Patent and Trademark Office (USPTO), as of September 1, 2023, both expired and unexpired, for which a claim of patent infringement could reasonably be, or has been, asserted against a person or manufacturer engaged in the unlicensed manufacture, use, or sale of the selected

drug in any form or any person or manufacturer seeking FDA approval of a product that references the selected drug.
    - All patents related to the selected drug, both expired and unexpired, where the Primary Manufacturer is not listed as the assignee/applicant (for example, for a joint venture product or if any patents related to the selected drug are held by a federal agency).
    - All patent applications related to the selected drug that are pending issuance by the USPTO.
    - Patents and patent applications related to the selected drug include, but are not limited to, any patents that are, have been, or may be listed for the selected drug in the FDA Orange Book or Purple Book[90]; utility patents that claim the drug product (formulation or composition), drug substance (active ingredient), metabolites or intermediaries of a selected drug, method(s) of using the drug, or method(s) of manufacturing the drug; and design patents that, for example, claim a design on the packaging of the selected drug.
- Exclusivity periods under the FD&C Act or the PHS Act refer to certain delays and prohibitions on the approval of competitor drug products. An NDA or BLA holder is eligible for exclusivity if statutory requirements are met. Exclusivities include:
    - Orphan Drug Exclusivity (ODE);[91]
    - New Chemical Entity Exclusivity (NCE);[92]
    - Generating Antibiotic Incentives Now (GAIN) Exclusivity for Qualified Infectious Disease Products (QIDP);[93]
    - New Clinical Investigation Exclusivity (NCI);[94]
    - Pediatric Exclusivity (PED);[95] and
    - Reference Product Exclusivity for Biological Products.[96]
- Active and pending FDA applications and approvals includes all applications for approval under section 505(c) of the FD&C Act or sections 351(a) of the PHS Act, including those not yet decided.

Market Data and Revenue and Sales Volume Data

- Wholesale Acquisition Cost (WAC) unit price: The manufacturer's list price for the drug or biological product to wholesalers or direct purchasers in the United States, not including prompt pay or other discounts, rebates or reductions in price, for the most recent month for which the information is available, as reported in wholesale price guides or other publications of drug or biological product pricing data (as defined in section 1847A(c)(6)(B) of the Act). The WAC unit price is reported at the NDC-11 level.

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[90] FDA serves a ministerial role with regard to the listing of patent information in the Orange Book and Purple Book.
[91] Section 527 of the Federal Food, Drug and Cosmetic (FD&C) Act.
[92] Section 505(c)(3)(E)(ii) and Section 505(j)(5)(F)(ii) of the FD&C Act.
[93] Section 505E(a) of the FD&C Act.
[94] Section 505(c)(3)(E)(iii) & (iv) and Section 505(j)(5)(F)(iii) & (iv) of the FD&C Act.
[95] Section 505A(b) & (c) of the FD&C Act.
[96] Section 351(k)(7) of the PHS Act.

- National Council of Prescription Drug Programs (NCPDP) Billing Unit Standards: The three NCPDP Billing Unit Standards (BUS)[97] are: each (EA), milliliter (ML), and gram (GM). For certain volume data of the selected drug, CMS is requesting units be reported using the NCPDP BUS to facilitate comparison with the amounts in the quantity dispensed field found in PDE data, which also uses the NCPDP BUS.
- Medicaid best price: The Medicaid best price is defined in 42 C.F.R. § 447.505(a). The Medicaid best price is reported at the NDC-9 level.
- Average manufacturer price (AMP) unit: The unit type used by the manufacturer to calculate AMP (42 C.F.R. § 447.504) and best price (42 C.F.R. § 447.505) for purposes of the Medicaid Drug Rebate Program (MDRP): injectable anti-hemophilic factor, capsule, suppository, gram, milliliter, tablet, transdermal patch, each, millicurie, microcurie. Such units are reported by the manufacturer on a monthly basis at the NDC-9 level.
- Federal supply schedule (FSS) price: The price offered by the VA in its FSS program, by delegated authority of the General Services Administration.[98] The FSS price is reported at the NDC-11 level.
- Big Four price: The Big Four price is described in 38 U.S.C. § 8126. The Big Four price is reported at the NDC-11 level.
- U.S. commercial average net unit price: For the sole purpose of data collection under section 1194(e)(1)(E) of the Act, the average net unit price of the selected drug for group or individual commercial plans on- and off-Exchange, excluding Medicare fee-for-service (Parts A and B), Medicare Advantage, Medicare Part D, Medicaid fee-for-service, and Medicaid managed care. The average net unit price must be net of discounts, chargebacks or rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, or other price concessions or similar benefits offered by the Primary Manufacturer and any Secondary Manufacturer(s) to any purchasers. The U.S. commercial average net unit price is reported at the NDC-11 level.
- U.S. commercial average net unit price— without patient assistance program: For the sole purpose of data collection under section 1194(e)(1)(E) of the Act, the U.S. commercial average net unit price net of manufacturer-run patient assistance programs that provide financial assistance such as coupons and co-payment assistance or free drug products to patients offered by the Primary Manufacturer and any Secondary Manufacturer(s). The U.S. commercial average net unit price— without patient assistance program is reported at the NDC-11 level.
- U.S. commercial average net unit price— best: For the sole purpose of data collection under section 1194(e)(1)(E) of the Act, the lowest U.S. commercial average net unit price offered by the Primary Manufacturer and any Secondary Manufacturer(s) to any commercial payer in the U.S. The average net unit price must be net of discounts, chargebacks or rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, or other price concessions or similar benefits offered by the Primary Manufacturer or any

[97] See: https://standards.ncpdp.org/Billing-Unit-Request.aspx#:~:text=Billing%20Unit%20Requests,grams%22%20or%20%22milliliters.%22.
[98] See: https://www.fss.va.gov/index.asp.

Secondary Manufacturer(s) to any purchasers. The U.S. commercial average net unit price— best is reported at the NDC-11 level.

Evidence About Alternative Treatments

- Therapeutic Alternative: A therapeutic alternative must be a pharmaceutical product that is clinically comparable to the selected drug. CMS will consider different therapeutic alternatives for each indication, as applicable. Therapeutic alternatives may be a brand name drug or biological product, generic drug, or biosimilar and may be on-label or off-label to treat a given indication. CMS will begin by identifying therapeutic alternatives within the same drug class as the selected drug based on properties such as chemical class, therapeutic class, or mechanism of action before considering therapeutic alternatives in other drug classes. In cases where there are many potential therapeutic alternatives for a given indication of the selected drug, CMS may focus on the subset of therapeutic alternatives that are most clinically comparable to the selected drug.
- Outcomes: Outcomes may be clinical or related to the functioning, symptoms, quality of life, or other aspects of a patient's life. Outcomes such as cure, survival, progression-free survival, or improved morbidity could be considered when comparing the selected drug to its therapeutic alternative(s). Outcomes such as changes in symptoms or other factors that are of importance to patients, and patient-reported outcomes will also be identified and considered in determining clinical benefit, if available. Additional outcomes such as changes to productivity, independence, and quality of life will also be considered, including patient-centered outcomes when available, to the extent that these outcomes correspond with a direct impact on individuals taking the drug. The caregiver perspective will be considered when there is a direct impact on the individuals taking the selected drug or therapeutic alternative.
- Patient-centered outcome: An outcome that is important to patients' survival, functioning, or feelings as identified or affirmed by patients themselves, or judged to be in patients' best interest by providers and/or caregivers when patients cannot report for themselves.[99]
- Specific populations: Specific populations include individuals with disabilities, the elderly, individuals who are terminally ill, children, and other patient populations among Medicare beneficiaries including those that may experience disparities in access to care, health outcomes, or other factors when taking the selected drug that impact health equity.
- Health equity: The attainment of the highest level of health for all people, where everyone has a fair and just opportunity to attain their optimal health regardless of race, ethnicity, disability, sexual orientation, gender identity, socioeconomic status, geography, preferred language, or other factors that affect access to care and health outcomes.[100]
- Unmet medical need: A drug or biological product may be considered to meet an unmet medical need if the drug or biological product treats a disease or condition in cases where no other treatment options exist or existing treatments do not adequately address the

[99] Source: ISPOR Plenary, Patrick (2013) via FDA's "Patient-Focused Drug Development: Collecting Comprehensive and Representative Input – Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders" (June 2020). See: https://www.fda.gov/media/139088/download.
[100] See: https://www.cms.gov/pillar/health-equity.

disease or condition.[101] Unmet medical need is determined at the time of submission of this information.

[101] CMS will consider the nonbinding recommendations in the FDA "Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics" (May 2014) when considering if a drug addresses an unmet medical need for the purpose of the Negotiation Program.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTRAZENECA PHARMACEUTICALS LP, *et al.* v. XAVIER BECERRA, in his official capacity as SECRETARY OF HEALTH AND HUMAN SERVICES, *et al.*	Civ. No. 1:23-cv-931-CFC

DECLARATION OF CHERI RICE

I, Cheri Rice, pursuant to 28 U.S.C. § 1746, and based upon my personal knowledge and information made known to me in the course of my employment, hereby make the following declaration with respect to the above-captioned matter:

1. I currently serve as the Deputy Director of the Center for Medicare at the Centers for Medicare & Medicaid Services ("CMS"). In my role as Deputy Director, I oversee implementation of the Medicare Drug Price Negotiation Program including the process by which CMS selected the first 10 drugs for negotiation.

2. The Inflation Reduction Act ("IRA") (Pub. L. 117-169) established the Medicare Drug Price Negotiation Program to enable Medicare to negotiate maximum fair prices with willing manufacturers for certain high expenditure, single source drugs and biological products. Under section 1192(a)(1) of the Social Security Act ("Act"), for the first year of the Negotiation Program (the "initial price applicability year 2026"), the Secretary is required to select and publish a list of the 10 negotiation-eligible drugs

with the highest "Total Expenditures" under Medicare Part D. The Secretary has delegated this authority to CMS. Under Section 1192(d) of the Act, to be a negotiation-eligible drug, a drug must be, among other things, a "Qualifying Single Source Drug." In accordance with section 1192(e)(1) of the Act, a drug or biological product is not a Qualifying Single Source Drug if it is the listed drug for any drug approved and marketed under an Abbreviated New Drug Application ("ANDA") under section 505(j) of the Food, Drug & Cosmetic Act or the referenced biological product for any biological product that is licensed and marketed under section 351(k) of the Public Health Service Act. Drugs approved and marketed under section 505(j) of the FD&C Act are colloquially referred to as generic drugs.

3. Section 1192(d)(3)(B) of the Act states that CMS shall use data that are aggregated across dosage forms and strengths of the drug, including new formulations of the drug, such as an extended release formulation, and not based on the specific formulation, package size, or package type of the drug for purposes of determining whether a Qualifying Single Source Drug is a negotiation-eligible drug under section 1192(d)(1) of the Act and applying the exception for small biotech drugs under section 1192(d)(2) of the Act. Similarly, section 1196(a)(2) of the Act directs CMS to establish procedures "to compute and apply the maximum fair price across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug."

4. On March 15, 2023, CMS published an initial memorandum to provide interested parties with information regarding CMS' implementation of the first year of the Negotiation Program, including CMS' process for identifying selected drugs. On June 30, 2023, CMS published revised guidance for initial price applicability year 2026, which addressed public comments received in response to the initial memorandum and set forth CMS' final policies on the topics discussed for initial price applicability year 2026.

5. The Revised Guidance provided, among other things, that for the purposes of identifying the 10 selected drugs for initial price applicability year 2026, CMS would identify potential Qualifying Single Source Drugs, in accordance with sections 1192(d)(3)(B) and 1196(a)(2) of the Act, by using all dosage forms and strengths of the drug with the same active moiety and the same holder of a New Drug Application (NDA), inclusive of products that are marketed pursuant to different NDAs. *See* Revised Guidance at 99. The Revised Guidance also provided that in determining whether a drug is the listed drug for any [generic] drug that is approved and marketed under section 505(j) of such Act, CMS will consider a generic drug to be marketed when the totality of the circumstances and data reveals that the manufacturer of that drug is engaging in bona fide marketing of that drug. *See id.* at 102.

6. On August 29, 2023, CMS announced the 10 drugs for which it would seek to negotiate prices during the Negotiation Program's first year. One of those 10 selected drugs is Farxiga (dapagliflozin), which is manufactured by AstraZeneca AB.

7. I understand that Plaintiffs in this action challenge CMS's interpretation of the IRA in two respects. According to Plaintiffs, the statute prohibits CMS from (a) treating all dosage forms and strengths of the drug with the same active moiety as part of the same Qualifying Single Source Drug if those different forms of the drug are approved and marketed under different NDAs, or (b) considering whether a generic drug is being marketed on a bona fide basis.

8. Adopting either of Plaintiffs' interpretations of the statute, however, would have had no effect on Farxiga's selection by the Secretary as one of the 10 selected drugs for initial price applicability year 2026.

9. First, Farxiga is approved and marketed under a single NDA (NDA #202293). Thus, the "Total Expenditures" for Farxiga under Medicare Part D would be the same whether CMS aggregated expenditures by active moiety across multiple NDAs or not. Moreover, the aggregation of expenditures by active moiety of other drugs did not affect Farxiga's inclusion on the list of top 10 drugs by "Total Expenditures" for initial price applicability year 2026. Indeed, in this case, applying Plaintiffs' approach of disaggregating expenditures for different drug formulations with the same active moiety if those formulations are approved and marketed under different NDAs could only ever have the effect of causing Farxiga to rise in the "Total Expenditure" rankings (by, for example, causing a drug above Farxiga in the rankings to fall below it after disaggregating expenditures of multiple formulations of the other drug). Accordingly, the Revised Guidance interpretation of "Qualified Single Source

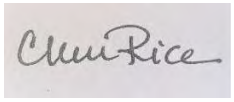
Drug" as requiring aggregation of expenditures by active moiety had no effect on Farxiga's selection for initial price applicability year 2026.

10. Second, there are no approved ANDAs for a generic version of Farxiga. Thus, Farxiga "is not the listed drug for any drug that is approved and marketed under section 505(j)" of the Food, Drug & Cosmetic Act and thus is a Qualifying Single Source Drug under section 1192(e)(1) of the Act. Accordingly, CMS' bona fide marketing interpretation had no effect on Farxiga's selection for initial price applicability year 2026. Because there are no approved generic versions of Farxiga, CMS' interpretation of the "marketed" requirement as requiring bona fide marketing is irrelevant.

11. In sum, even if CMS had applied either or both of the interpretations of the statute I understand Plaintiffs have advanced in this lawsuit, it would have had no effect on Farxiga's selection for initial price applicability year 2026.

12. As the Revised Guidance itself makes clear, CMS's Revised Guidance applies only for initial price applicability year 2026. *See* Revised Guidance at 2. In the future, CMS will issue new guidance to govern future price applicability years.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.



Executed on November 1, 2023

Cheri Rice
Deputy Director
Center for Medicare
Centers for Medicare & Medicaid Services

CERTIFICATE OF SERVICE

I certify that the foregoing Joint Appendix was filed with the Clerk using the appellate CM/ECF system on July 15, 2024. All counsel of record are registered CM/ECF users, and service will be accomplished by the CM/ECF system. I also hereby certify that pursuant to Third Circuit Local Appellate Rule 30.1, four paper copies of the foregoing Joint Appendix were sent on today's date via overnight Federal Express to the Clerk of this Court.

July 15, 2024

/s/ Catherine E. Stetson
Catherine E. Stetson
HOGAN LOVELLS US LLP
555 Thirteenth Street, N.W.
Washington, D.C. 20004
(202) 637-5600
cate.stetson@hoganlovells.com

Counsel for Plaintiffs-Appellants