IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF TEXAS
AMARILLO DIVISION

ALLIANCE FOR HIPPOCRATIC MEDICINE, *et al.*,	)	
Plaintiffs,	)	
v.	)	Case No. 2:22-cv-00223-z
U.S. FOOD AND DRUG ADMINISTRATION, *et al.*,	)	
Defendants.	)	

MOTION OF JUDICIAL WATCH, INC. FOR LEAVE TO FILE AN *AMICUS CURIAE* BRIEF IN SUPPORT OF PLAINTIFFS' COMPLAINT AND MOTION FOR TEMPORARY INJUNCTION

Pursuant to Fed. R. Civ. P. 7, proposed *amicus*, Judicial Watch, Inc., respectfully seeks this Court's leave to file the attached *amicus curiae* brief in support of Plaintiffs' Complaint (ECF. No. 1) and Plaintiffs' Motion for Preliminary Injunction (ECF. No. 6). *See* Local Rule 7.2(b). Counsel for Plaintiffs and Defendants have agreed to provide open consent to the filing of amicus curiae briefs in this case. *See* Local Rule 7.1(a).

In support of this motion, proposed amicus states as follows:

Proposed amicus, Judicial Watch, Inc. ("Judicial Watch") is a non-partisan, public interest organization headquartered in Washington, D.C. Founded in 1994, Judicial Watch seeks to promote accountability, transparency and integrity in government, and fidelity to the rule of law. Judicial Watch regularly files *amicus curiae* briefs and lawsuits related to these goals in both state and federal courts.

Proposed *amicus* should be granted leave to file the accompanying brief for two reasons. First, this case concerns a subject matter in which Judicial Watch has been involved for over two

decades: drugs approved by the federal government that intentionally end pregnancy. *See e.g.*, *Judicial Watch, Inc. v. FDA*, 449 F.3d 141 (D.C. Cir. 2006). Judicial Watch has used the Freedom of Information Act ("FOIA") law and subsequent lawsuits to obtain information vital to this case. *Id*. Second, the broader implication of this case extends beyond the specific subject matter into the larger concern of federal executive agency overreach. Judicial Watch has championed the constitutional principles of separation of powers and the balance of powers, and seeks to assist the Court in analyzing the implications of undue deference given a federal agency – particularly when there is evidence of improper political interference.

The Court has discretion regarding the filing of *amicus curiae* briefs as there is no controlling Federal Rules of Civil Procedure rule for motions for leave to appear as *amicus curiae* in federal district courts. "The Court has discretion to consider 'amicus' briefing where 'the proffered information is timely and useful or otherwise necessary to the administration of justice.'" *United States ex rel. Long v. GSD & M Idea City LLC*, 2014 U.S. Dist. LEXIS 185691, * 11 (N.D. Tex. Aug. 8, 2014) (*quoting Does 1-7 v. Round Rock Indep. Sch. Dist*., 540 F. Supp. 2d 735, 738 n.2 (W.D. Tex 2007); *see also Canamar v. McMillian Tex. Mgmt. Servs., LLC*, 2009 U.S. District LEXIS 108986, * (W. D. Tex. Nov. 20, 2009) (*citing Ryan v. Cmty. Futures Trading Comm'n,* 125 F.3d 1062, 1063 (7th Cir. 1997) (stating "amicus briefs should be allowed 'when the amicus has unique information or perspective that can help the court beyond that the lawyers for the parties are able to provide.'") (citation omitted).

Judicial Watch's *amicus* brief offers the Court timely and useful information from the unique perspective of an organization that has invested a great deal of time and analysis to the subject matter.

CONCLUSION

For these reasons, proposed amicus respectfully requests the Court grant the motion for leave to file the attached *amicus curiae* brief.

Dated: February 10, 2023

Respectfully submitted,

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CERTIFICATE OF CONFERENCE

Parties have agreed to permit the filing of *amicus curiae* briefs, thereby satisfying the requirements of Local Rule 7.1.

/s/ *Meredith Di Liberto*
Meredith Di Liberto

CERTIFICATE OF SERVICE

This is to certify that a true and correct copy of the foregoing was served, pursuant to the Federal Rules of Civil Procedure, on all counsel of record appearing herein via ECF on this 10th day of February, 2023 by the filing of this pleading with the Clerk of Court for the U.S. District Court for the Northern District of Texas using the Court's ECF system.

/s/ *Meredith Di Liberto*
Meredith Di Liberto

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***AMICUS CURIAE BRIEF* OF JUDICIAL WATCH, INC. IN SUPPORT OF PLAINTIFFS' COMPLAINT AND MOTION FOR TEMPORARY INJUNCTION**

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STATEMENT OF INTEREST OF *AMICUS CURIAE*

Judicial Watch, Inc. ("Judicial Watch") is a non-partisan, public interest organization headquartered in Washington, D.C. Founded in 1994, Judicial Watch seeks to promote accountability, transparency and integrity in government, and fidelity to the rule of law. Judicial Watch regularly files *amicus curiae* briefs and lawsuits related to these goals in both state and federal courts.

Judicial Watch seeks participation in this case for two reasons. First, this case concerns a subject matter in which Judicial Watch has been involved for over two decades: drugs approved by the federal government that intentionally end pregnancy. *See e.g.*, *Judicial Watch, Inc. v. FDA*, 449 F.3d 141 (D.C. Cir. 2006). Judicial Watch has used the Freedom of Information Act ("FOIA") law and subsequent lawsuits to obtain information vital to this case. *Id*. Second, the broader implication of this case extends beyond the specific subject matter into the larger concern of federal executive agency overreach. Throughout its existence, Judicial Watch has championed the constitutional principles of separation of powers, and the balance of powers, and seeks to assist the Court in analyzing the implications of undue deference given a federal agency – particularly when there is evidence of improper political interference.

SUMMARY OF THE ARGUMENT

The default position of bestowing undue deference on federal agencies has led to the rise of an unelected fourth branch of government that touches every aspect of our lives. These federal agencies wield budgets in the hundreds of billions of dollars with little to no oversight. When the agency is protected by the political party in power, it can act with extreme liberality and the American people are powerless to reign it in. The only hope of keeping federal agencies

from toppling the balance of powers is for the judiciary to perform its constitutional duty to keep them in check by way of judicial review.

The events described in Plaintiff's complaint are a prime example of the dire consequences of unchecked executive power employed by a federal agency, the Defendant, Food and Drug Administration ("FDA"). In 2000, the FDA harnessed the executive power from a political administration with a personal agenda bent on approving the drug mifepristone ("Mifeprex") which intentionally ends the life of a prenatal human.[1] In approving Mifeprex, the FDA violated its own unambiguous regulation and relied on pretext. In enacting subsequent major changes to Mifeprex safety restrictions in 2016 and 2021, the FDA laid bare the extent of the pretext used in its original approval by blatantly contradicting most of its previous rationalization. The FDA's actions in 2000, 2016, and 2021 violate the Administrative Procedures Act ("APA"). The Court should grant Plaintiffs motion for a temporary injunction and grant the relief requested in Plaintiffs' Complaint.

ARGUMENT

I. Legal Standards

The FDA's decision to approve the use of Mifeprex for the intentional ending of pregnancy and its subsequent decisions to significantly alter the safety restrictions are subject to the APA.[2] Under the APA, the FDA's decisions may be "set aside if found to be 'arbitrary,

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[1] For the purposes of this *amicus curiae* brief, Judicial Watch uses Danco's registered trademark name "Mifeprex" to refer to the abortion drug at issue.

[2] By reexamining its original decision to approve Mifeprex in both 2016 and 2021, the FDA reopened review of approval decision. *See Texas v. Biden*, 20 F.4th 928, 952 (5th Cir. 2021), *rev'd on other grounds*, *Biden v. Texas*, 142 S. Ct. 2528 (2022); *see also Nat'l Ass'n of Reversionary Prop. Owners v. Surface Transp. Bd*., 158 F.3d 135, 141 (D.C. Cir. 1998); *Public Citizen v. Nuclear Regulatory Com.,* 901 F.2d 147, 150-51 (D.C. Cir. 1990).

capricious, an abuse of discretion, or otherwise not in accordance with law." *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co*. ("*State Farm*"), 463 U.S. 29, 41 (1983) (*quoting* 5 U.S.C. § 706(2)(A)). Commonly referred to as the "arbitrary and capricious standard," courts "must 'hold unlawful and set aside agency action' that is 'arbitrary or capricious' when it fails to 'articulate a satisfactory explanation for its action including a rational connection between the facts found and the choices made.'" *Texas v. Becerra*, 575 F. Supp. 3d 701, 720 (N. D. Tex. 2021) (*quoting State Farm*, 463 U.S. at 43). In determining whether the FDA's decisions violated the arbitrary and capricious standard, courts consider several factors including: (1) whether the FDA's decisions were based on a consideration of the relevant factors at the time each decision was made; (2) whether the FDA made a clear error of judgment; (3) whether the FDA's offered explanation for each decision runs counter to the evidence; and (4) whether the FDA's proffered explanations for its decisions are so implausible that they cannot be explained by a difference of opinion or agency expertise.[3] *State Farm,* 463 U.S. at 43.

This Court's role in reviewing the FDA's decisions is clearly rooted in the APA's judicial review. *See* 5 U.S.C. § 706, *et seq*. Whether the FDA violated its own regulations and federal law are legal questions for which the Court, not the FDA, is the expert. The FDA is owed no special deference. Whether the FDA acted arbitrarily and on pretext alone for its decisions is a legal question for which the Court, not the FDA, is the expert. The FDA is owed no special deference. It is the Court that is granted the constitutional authority to determine whether the FDA violated the APA. Defendants' briefs are replete with references to the deference the FDA is supposedly owed, but they fail to acknowledge or understand the concept of the proper role of

[3] The U.S. Supreme Court articulated several other factors for consideration, but Judicial Watch is focusing on just a few for the purposes of this brief.

the Court. Judicial review is not the Court "second guessing" the science behind the FDA's decisions, as the Defendants' claim. Rather, it is the Court determining – based on the evidence before it – whether the FDA acted arbitrarily, capriciously, abused its discretion, or acted not in accordance with the law. This is quintessentially the role of the Court, and the Court is well equipped to make this determination.

II. The FDA's Approval of Mifeprex Was Arbitrary, Capricious, an Abuse of Discretion, and Not in Accordance with Law.

In reviewing the FDA's process for granting approval for Mifeprex as well as the contemporaneous evidence related to the decision, it is clear that the FDA's decision was arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law.[4] It is uncontested that the FDA approved Mifeprex pursuant to the accelerated approval procedure provided in 21 C.F.R. § 314.500. Referred to as Subpart H, the agency rule provides for the accelerated approval of new drugs for:

> [C]ertain new drug products that have been studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments (e.g., ability to treat patients unresponsive to, or intolerant of, available therapy, or improve patient response over available therapy).

21 C.F.R. § 314.500.

The summary of the final rule issued by the FDA clearly defines the purpose as providing an alternative and accelerated path to approval for certain drugs needed for serious or life-threatening illnesses. 57 FR 58942. This accelerated path to approval requires additional study and restrictions on use. *Id*. This requirement balances the potential for harm from the new drugs

[4] Defendants' APA violations are plentiful but Judicial Watch, Inc.'s focus is on two primary violations: (1) the violation of the FDA's own regulation; and (2) the FDA's reliance on pretext.

with the need for a drug that provides a "therapeutic benefit" to individuals suffering from a serious or life-threatening illness. *See id*. The FDA determined there were two situations in which this accelerated approval could be met. Mifeprex was approved under the second as a "drug, effective for the treatment of a disease, [that] can be used safely only if distribution or use is modified or restricted." *Id*.

For Subpart H to legally apply to the approval of Mifeprex, the FDA would have needed to demonstrate that, (1) pregnancy was a "serious or life-threatening illness" or a "disease," and (2) that the drug "provided a meaningful therapeutic benefit to patients over existing treatments." The FDA did neither. More to the point, the FDA *could* not. The plain language of the final rule shows that Subpart H was written for drugs that treat diseases. The scope of the final rule reads:

> The new procedures [accelerated approval] apply to certain new drugs, antibiotic, and biological products used in the treatment of serious or life-threatening ***diseases***, where the products provide a meaningful therapeutic advantage over existing treatment.

57 FR 58942 (emphasis added). In 2000, pregnancy was not classified as a "disease" by the FDA. The FDA's decision to apply Subpart H to pregnancy was arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law.

The FDA's historical usage of Subpart H solidifies the conclusion that Mifeprex did not qualify for Subpart H approval. Prior to the 2000 approval of Mifeprex, the FDA granted accelerated approval pursuant to Subpart H 37 times. *See* Appendix at 2-19.[5] Of these 37 accelerated approvals, 21 related to HIV drugs and 10 related to cancer drugs. *Id*. The remaining accelerated approvals were related to chronic low blood pressure, tuberculosis,

[5] This information is also available at: https://www.fda.gov/drugs/drug-and-biologic-approval-and-ind-activity-reports/accelerated-and-restricted-approvals-under-subpart-h-drugs-and-subpart-e-biologics.

leprosy, and bacterial infections. *Id.* Unlike pregnancy, each one of these drugs treats a condition widely considered a "disease" by both the medical community as well as the FDA. Since the 2000 approval of Mifeprex, the FDA has granted accelerated approval pursuant to Subpart H 26 times. *Id*. Of these 26 accelerated approvals, 9 related to HIV drugs, 10 related to cancer drugs, 3 related to hypertension, and 2 to blood disorders.[6] *Id*. The remaining accelerated approvals were related to hypogonadotropic hypogonadism (pituitary problem) and narcolepsy. *Id*. Unlike pregnancy, each one of these drugs treats a condition widely considered a "disease" by both the medical community as well as the FDA. In 64 instances of granting accelerated approval pursuant to Subpart H, there is exactly one drug that targets something non-disease related: Mifepristone. This shows the FDA's decision was arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law.

The plain language of Subpart H, as well as the unambiguous synopsis and scope of the final rule, run counter to the FDA's decision to approve Mifeprex pursuant to Subpart H. Subpart H was clearly designed to approve drugs for serious and life-threatening diseases. Referring to pregnancy as a disease is implausible based on the FDA's own understanding of pregnancy at the time of approval and the understanding of pregnancy by the wider medical community. *See e.g., State Farm*, 463 U.S. at 43 (an explanation counter to evidence is too implausible to accept). The FDA simply cannot demonstrate that pregnancy was a condition that fit the purpose or meaning of Subpart H. Similarly, the FDA's historical use of accelerated approval pursuant to Subpart H runs counter to the FDA's decision to approve Mifeprex pursuant to Subpart H. *See id*. (Evidence contrary to the agency decision is not a satisfactory explanation). Mifeprex is the exception to Subpart H regulation, and the FDA's decision is implausible. The FDA's decision

[6] *Ibid*. (The FDA's website states that it is current as of August 26, 2014.)

was arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law. *See State Farm*, 463 U.S. at 41.

The FDA's approval of mifepristone violates the APA for another reason: the FDA's reliance on pretext. While the FDA publicly asserted that the rationale for approving Mifeprex was for the health of American women, the evidence shows that the true motivation was political.

Former President Clinton was not shy about his personal interest in having mifepristone approved in the U.S. In fact, directing the approval of an abortion drug was his first official act as President of the United States. Appendix at 38. In his May 16, 1994 letter to the Chairman of Roussel Uclaf, the French pharmaceutical group which created and owned the abortion pill, President Clinton wrote that, "it is important for the health of women in the United States that they have access to the widest possible range of safe and effective medical treatments."[7] Appendix at 77. He then thanked the Chairman "on behalf of the government of the United States and for the women in America." *Id*. Roussel Uclaf would reply that same month to confirm that President Clinton's request was being granted and the abortion pill would be given the U.S. as an "unconditional gift" with "nothing in return." Appendix at 72. Only after the approval would it be discovered that President Clinton's very letter was a bargained-for part of a backroom deal between the President, the FDA, U.S. Department of Health and Human Services ("HHS"), and Population Council to approve Mifeprex in the U.S. for the express purpose of

[7] Neither the Clinton administration nor Defendants have ever rationally explained what therapeutic benefit to women's "health" was being addressed by the abortion pill. This relates back to Defendant FDA's arbitrary and capricious use of Subpart H – they utterly failed to articulate what "therapeutic benefit" Mifeprex provided that was not already available or addressed by the medical field. Even pretending that pregnancy can be legitimately categorized as a "serious or life-threatening illness," is of no avail. The maternal medical conditions that can give rise to serious or life-threatening situations like ectopic pregnancies or placenta previa cannot be treated with Mifeprex. In fact, using Mifeprex in those situations will most likely place the woman's life in immediate danger.

intentionally ending prenatal lives. *See* Appendix at 54. (Roussel demanded that President Clinton write the letter requesting the abortion drug "on behalf of women in America.")

The evidence uncovered of Defendants' true motivation for their decision to approve Mifeprex is eye-opening and shows the administration and FDA applying political pressure on not only international corporations, but on international governments – all for a drug to kill prenatal human beings. The evidence also shows the intricate political and corporate machinations spent in the service of promoting a drug that has nothing to do with women's health. Defendants pressured both Roussel, a French company, and Hoechst AG, the German pharmaceutical company and majority shareholder of Roussel, to bring the abortion pill to the U.S. *See* Appendix at Tab B, pp. 21-34. Hoechst was opposed to producing the drug for the U.S. and in fact, ordered Roussel to cease producing the abortion drug altogether.[8] The government of France exerted its legal and economic powers and forced Hoechst to continue producing the abortion drug.[9] This created a serious international rift for which Hoechst would respond by demanding complete indemnity for any future production of the abortion drug in the U.S. Hoechst would find an avenue to satisfy that indemnity desire – an American venture capitalist group, but Defendant-Intervenor Population Council refused to work with the group. *See* Appendix at 43.

Instead, the FDA became the deal-broker between Roussel and Population Council. This was not a simple negotiation, however, as Defendant admitted it needed to apply "pressure on Roussel Uclaf/Hoechst." Appendix at 43. In fact, Defendant wrote that political pressure was

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[8] *See* Melanie Israel, "Chemical Abortion: A Review," THE HERITAGE FOUNDATION, No. 3603, March 26, 2021 available at: https://www.heritage.org/life/report/chemical-abortion-review.

[9] *Ibid*; *see also* Appendix at 50.

the "only way to get RU-486 [Mifeprex] onto the U.S. market." Appendix at 50. In a November 15, 1993 letter from Donna Shalala, HHS Secretary to the White House, she states that "Dr. Kessler [FDA Commissioner] and I have taken steps to persuade Roussel Uclef and Hoechst to change their position." Appendix at 40. This same letter shows the FDA offering to discuss the possibility of offering Roussel federal legislative immunity as part of the deal despite that discussion "far exceed[ing] FDA's appropriate role." Appendix at 42.

Roussel's preference for satisfying its demand for federal legislative immunity was for the U.S. to exercise its eminent domain powers and take the patent for the abortion drug.[10] *Id.* However, neither the President, nor the FDA would agree to this proposal because it was a decision subject to congressional checks and balances and it put the President's personal quest for the abortion drug at risk of rejection. *See* Appendix at 44. The FDA did not want to incur the burden of having to convince Congress that the abortion drug was actually a medical benefit. It was absolutely necessary to close the deal between Roussel and Population Council, and Defendant was willing to pressure other governments to accomplish its goal.

This can be seen in a September 30, 1993 letter from the HHS Commissioner, Dr. Kessler, to the FDA Secretary Donna Shalala in which Secretary Shalala states:

> It may be that France and Germany would be unhappy to learn that their companies were not accommodating a request made by the United States Government. The U.S. Ambassadors to France and Germany will need to be consulted on these issues, and your counterparts in France and Germany may also need to be involved.

[10] It is significant to note that Roussel's primary liability concern related to women harmed by taking its abortion pill as well as the potential for delivery of a "deformed fetus." Appendix at 41. Roussel's concern about liability was so great that it offered to give Population Council the license royalty-free, foregoing all profits. It absolutely refused to manufacture the abortion drug for Population Council to distribute however, and demanded a new manufacturer be found. *Id*. at 48.

Appendix at 50-51.

The Administration and the FDA were willing to place political pressure on two foreign governments to accomplish the task of approving an abortion pill. This was not a life-saving medication or a drug that cured cancer. This was a drug which was being sought for one purpose and one purpose alone: the intentional death of prenatal humans. And for what reason? The ability to satisfy a financially and politically powerful group of abortion advocates.

In a May 11, 1994 memo from the HHS Chief of Staff to the White House, the true motivation of the FDA's decision is illuminated. The memo describes the political significance of closing the abortion pill deal:

> Because of the situation with the Health Security Act, the introduction of RU 486 [the abortion pill] will be of greater significance to the pro-choice and women's groups. If the Administration is viewed as closing the door or rejecting an apparently reasonable offer on RU 486, then the path toward reaching a non-confrontational agreement with the advocates on the Health Security Act could become much more difficult. ***It is, therefore, extremely important that the decision concerning RU 486 be placed in the context of promoting women's health and maintaining the close relationship of the Administration to these groups.***

Appendix at 64 (emphasis added).[11]

This extraordinary admission conclusively demonstrates that the Defendant's rationale for approving Mifeprex was nothing more than pretext. Defendant's pretextual rationale is "substantively invalid" and therefore, arbitrary and capricious. *Dep't of Commerce v. New York*, 139 S. Ct. 2551, 2575-76 (2019). "We are presented, in other words, with an explanation for agency action that is incongruent with what the record reveals about the agency's priorities and

[11] In fact, to this day, the rationalization of abortion as a woman's health matter has become a permanent justification and rallying cry of pro-abortion groups and their political and cultural allies.

decisionmaking process." *Id*. at 2575. Courts are not required to accept "contrived reasons" by an agency for its actions. *Id*. at 2576.

The FDA's decision to approve Mifeprex was arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law. The decision violated the unambiguous meaning of Subpart H and was based on nothing more than political manipulation. The dire consequences cannot be overstated: the very agency responsible for brokering the transfer of the drug at the personal request of the sitting President of the United States was then tasked with performing an unbiased review of the approval. Even the Secretary of the Defendant federal agency admitted in writing that their political interference was running the risk of bias and "compromising its [FDA's] role as objective reviewers of the safety and efficacy of the drug." Appendix at 50. Indeed, that role was fatally compromised and continues to be as the FDA permits Mifeprex to be recklessly distributed based on an arbitrary and capricious approval decision. *See State Farm*, 463 U.S. at 41.

III. The FDA's 2016 Changes to Mifeprex Safety Restrictions Were Arbitrary, Capricious, an Abuse of Discretion, and Not in Accordance with Law.

In a congressional hearing after the 2000 approval of Mifeprex, the FDA asserted that it chose to approve mifepristone pursuant to Subpart H to maintain more stringent safety restrictions on the drug. Appendix at 87.[12] This included the requirement that the drug be administered "by or under the supervision of a physician" who met several qualifications. Among these qualifications were: (1) the ability to assess the duration of the pregnancy accurately and diagnose ectopic pregnancies; (2) "the ability to provide surgical intervention in

[12] A transcript of the U.S. House of Representatives Subcommittee on Criminal Justice, Drug Policy, and Human Resources May 17, 2006 Hearing on RU-486 [Mifeprex] is available in its entirety at: https://www.govinfo.gov/content/pkg/CHRG-109hhrg31397/html/CHRG-109hhrg31397.htm

cases of incomplete abortion or severe bleeding, or have made plans to provide such care through other qualified physicians, and are able to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary"; (3) the requirement to provide each patient with the Medication Guide, provide the patient with the chance to ask questions, and obtain a patient signature; and (4) the requirement to notify the sponsor of drug failure (an ongoing pregnancy after use of the drug) and to report any hospitalization, transfusion or other serious events to the sponsor. Appendix at 89-91.

Additionally, the FDA approval was for a specific regimen (600 mg of mifepristone, followed by 400 mg of misoprostol) and for a specific duration: through 49 days' pregnancy. Appendix at 93-103. The FDA approval also included a specific number of doctor visits: one visit for the mifepristone, another for the misoprostol, and a final follow-up visit 14 days after taking the drugs to be certain the abortion was complete. *Id*. In 2004, the FDA increased the black box safety warnings on Mifeprex to include risk of serious bacterial infections, sepsis, bleeding, and death as possible effects of the drug use.[13] And in 2011, the FDA issued a new risk evaluation and mitigation strategy ("REMS") and included the requirement for a medication guide as well as three elements to assure safe use ("ETASU").[14] Appendix at 105-107. This history shows that in the first decade of post-approval use, the FDA *increased* Mifeprex safety requirements.

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[13] *See e.g.*, https://scrip.pharmaintelligence.informa.com/PS062593/Mifeprex-Black-Box-Warning-Revised-On-Reports-Of-Sepsis-Deaths

[14] Due to the FDA's Amendments Act of 2007, all drugs approved pursuant to Subpart H, including those previously approved, would fall under the risk evaluation and mitigation strategy ("REMS"). Mifeprex was required to participate in REMS and establish elements to assure safe use ("ETASU").

The FDA was very clear about the need for Mifeprex safety restrictions and its approval criterion. *See e.g.*, Appendix at 87. Yet, despite these very public safety concerns, the FDA significantly revised the Mifeprex labeling and REMS in 2016 and *reduced* the safety requirements. These changes included significantly altered dosage, removal of the follow-up medical visit, removal of the requirement to take the drug in a doctor's office, and expansion of the use through 70 days gestation.[15] Also of significance and concern, the FDA modified the REMS to require reporting of only deaths attributable to the drug. No longer would hospitalizations, transfusions, or other serious adverse events need to be reported.[16]

The FDA's asserted rationalization for these significant changes was that it was "following the science." The FDA has not, however, provided the science it followed that could reasonably explain the changes. For example, the expansion in use from 49 days to 70 days gestation. It was very clearly established that expanding the use of Mifeprex past 49 days decreased the effectiveness – meaning, the pregnancy was not ended – and increased the adverse events such as hospitalization.[17] Thus, according to the science, by increasing the gestational period of use, the FDA decreased the effectiveness of the drug while increasing the danger. This obvious fact makes the FDA's rationalization implausible as it runs counter to the evidence. *See State Farm*, 463 U.S. at 43.

The change to in-person medical visits is another example of evidence contrary to the FDA's 2016 decision. Mifeprex was originally approved with three in-person medical visits –

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15 *See supra* note 8.

16 *Ibid.*

17 Irving Spitz, "Early Pregnancy Termination with Mifepristone and Misoprostol in the United States," NEW ENGLAND JOURNAL of MEDICINE, 1998, 338 (18) 1241-47.

the first two to watch for immediate side effects of the drugs following ingestion, and the third, to be certain the abortion was complete. The third visit was absolutely necessary because the delivery of the dead baby most often occurred outside a medical setting, with no one to confirm whether the abortion was medically complete. The potential for a failed or incomplete abortion would run a huge risk for infection, sepsis, a need for surgical intervention and hospitalization. Indeed, "retained products of conception" was the most common cause of maternal morbidity after Mifeprex use.[18] And, as described above, by decreasing the effectiveness of the drug with longer gestational usage, the likelihood of incomplete abortions increased, thereby making the follow-up visit even more significant to protect the health of the woman. But rather than "follow the science," the FDA removed the follow-up visit requirement, leaving women more vulnerable to serious adverse events with no medical supervision. The FDA's 2016 Mifeprex changes are arbitrary, capricious, an abuse of discretion, and not in accordance with law.

As with the original approval in 2000, the 2016 changes are steeped in political manipulation. First, by removing critical safety restrictions from the original approval and the subsequent REMS update without rational evidence supporting the decision, the FDA shows its motivation to assuage abortion advocates. Abortion proponents and lobbying groups had a history of challenging safety restrictions in the use and distribution of Mifeprex. Accessibility was key to increasing abortion numbers which had fallen since the 1990's and the abortion lobby needed Mifeprex expanded to accomplish this goal.[19] Increasing the gestational age of use,

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[18] Kathi Aultman, Christina Cirucci, *et al*., "Deaths and Severe Adverse Events after the use of Mifepristone as an Abortifacient from September 2000 to February 2019," ISSUES IN LAW AND MEDICINE, Volume 36, No. 1, 2021 report to South Carolina General Assembly State Medical Affairs Committee.

[19] *See e.g*., https://www.guttmacher.org/article/2016/06/public-health-implications-fda-update-medication-abortion-label

decreasing doctor involvement and decreasing the dosage all helped to meet the abortion lobby's goal.

Second, the FDA's partnership with another abortion-minded administration, who, like the Clinton administration, sought the political and financial support of the abortion lobby, benefitted greatly from the FDA changes. Facing a critical election, Former President Obama was able to take the credit for increasing the use of Mifeprex, despite that very increase being scientifically unsound.[20] The increased usage would, of course, increase profits for Danco, the manufacturer of Mifeprex.[21] By increasing the gestational age of use to 70 days, the FDA effectively ***doubled*** the number of eligible pregnancies.[22] The FDA's decision certainly improved the market for Mifeprex and Danco, though at the expense of exposing women to increased health risks.

The lack of a rational connection between the evidence (or lack thereof) and the FDA's 2016 decision to change the Mifeprex safety and labeling, and the suggestion of pretext, lead to the conclusion that the decision was arbitrary and capricious. *See State Farm*, 463 U.S. at 41; *see also Dep't of Commerce*, 139 S. Ct. at 2575-2576.

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[20] *See e.g.*, https://www.nytimes.com/2016/03/31/health/abortion-pill-mifeprex-ru-486-fda.html

[21] Danco is a private company which has refused to disclose its investors but evidence suggests Danco is financially backed by very wealthy, politically connected individuals and foundations that supported abortion rights. *See* https://www.liveaction.org/news/abortion-industry-financial-conflicts-interest-politicians-media/; *see also* https://www.latimes.com/archives/la-xpm-2000-nov-05-mn-47330-story.html (detailing the secretive and questionable business dealings of Danco)

[22] *See supra* note 20

IV. The FDA's 2021 Changes to Mifeprex Restrictions Were Arbitrary, Capricious, an Abuse of Discretion, and Not in Accordance with Law.

In 2021, using the COVID-19 pandemic as a tool, abortion proponents, led by the American College of Obstetricians and Gynecologists "(ACOG"), sued the FDA to dispense with the REMS in-person medical visit as a prerequisite for obtaining Mifeprex and permit the drug to be mailed.[23] ACOG and the other abortion lobbying groups asserted that the in-patient visit put women at risk of COVID-19 or delayed their abortion decision too long to make Mifeprex an option. The FDA accepted ACOG's request and temporarily suspended the in-person medical visit based solely on the COVID-19 pandemic.[24] COVID-19 was, however, just pretext for the FDA's decision.[25] With the pandemic declared over by President Biden on September 18, 2022, the foundation of concern for in-person medical visits should have ended.[26] Instead, the FDA maintained its temporary suspension and continued permitting Mifeprex to be mailed. Then, on December 16, 2022, the FDA permanently removed the REMS requirement for any in-person medical visits.[27]

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[23] *See* https://www.acog.org/news/news-articles/2020/07/courts-order-lifting-burdensome-fda-restriction-what-you-need-to-know.

[24] *See supra* note 17

[25] Indeed, COVID-19 was just pretext for ACOG as well. ACOG has a long history of fighting for the removal of Mifeprex REMS, including in-person visits. COVID-19 had nothing to do with ACOG's motivations. *See* https://www.acog.org/news/news-releases/2016/03/acog-statement-on-medication-abortion; *see also* https://www.acog.org/clinical-information/policy-and-position-statements/position-statements/2018/improving-access-to-mifepristone-for-reproductive-health-indications

[26] *See e.g.*, https://www.cnn.com/2022/09/19/politics/biden-covid-pandemic-over-what-matters/index.html

[27] *See e.g.*, https://abcnews.go.com/Politics/fda-women-obtain-abortion-pill-mail/story?id=81798959

Removing any in-person medical visit and permitting Mifeprex to be mailed do not allow the prescriber to ascertain the gestational age of the baby or determine whether there is an ectopic pregnancy – two essential pieces of information in the Mifeprex safety approval.[28] The FDA's rationalization for permanently removing in-person medical visits was:

> [T]he FDA analyzed postmarketing data to determine if there was a difference in adverse events between periods when in-person dispensing was and was not enforced. Based on this review, the agency concluded that there did not appear to be a difference in adverse events between periods when in-person dispensing was and was not enforced.[29]

The FDA made this public assertion despite the FDA Commissioner acknowledging that the study designs it relied on were "limited" and "do not appear to show increases in serious safety concerns." Appendix at 109-110. And critically missing from this rationalization is the admission that the FDA's 2016 REMS changes dispensed of the reporting requirement for any nonfatal adverse events.[30] The "serious safety concerns" the Commissioner was "reviewing" had not been routinely reported in nearly ***five years***. What reporting data was the FDA comparing? Pre-2016 data, which required ***all*** adverse events as well as failed abortions compared to post-2016 data, which required

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[28] Ectopic pregnancies occur in approximately 1-2% of pregnancies, though that percentage can rise significantly due to certain factors like smoking, IVF treatments, or IUD usage. https://www.aafp.org/pubs/afp/issues/2020/0515/p599.html. Fatal ectopic pregnancies account for roughly 2.7% of maternal deaths. *Id*. ACOG's own website states that ectopic pregnancies can be life-threatening and recommends the involvement of a health care professional. https://www.acog.org/womens-health/faqs/ectopic-pregnancy; *see also* https://www.dailysignal.com/2023/01/18/fda-has-made-abortion-wild-west-rule-change-drugs-ob-gyn-says

[29] https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-mifepristone-medical-termination-pregnancy-through-ten-weeks-gestation

[30] *See supra* note 8.

only reports of death? This defies all logic and reason and demonstrates that the 2021 decision was not rationally related to the facts, but rather, was arbitrary, and capricious. *See State Farm*, 463 U.S. at 41.

Bolstering this assessment is more evidence of political manipulation. President Biden's affinity for the abortion lobby is widely known and acknowledged.[31] The Acting FDA Commissioner, Robert Califf, was the FDA Commissioner during the 2016 Mifeprex changes.[32] The FDA's decision to permanently dispense with in-person medical visits occurred just days after Califf's Senate hearing. Lobbying by ACOG and other abortion lobbyists is at an all-time high, emboldened by an administration bent on forcing states to accept the President's abortion agenda.[33] It is reported that lobbying spending by these abortion lobbyists increased by 107% in the first few months of 2021 – prompted by the possibility of *Roe v. Wade* being overtured.[34] In fact, the President issued a response to the U.S. Supreme Court's *Dobbs v. Jackson Women's Health Organization* decision which clearly supported mail-order Mifeprex and made no mention of the COVID-19 pretext.[35] Appendix at 112-113. The FDA desired to alter the Mifeprex REMS and used COVID-19 to do so. Evidence shows this was pretext and the decision was arbitrary, capricious, an abuse of discretion, and not in accordance with law. S*ee Dep't of Commerce*, 138 S. Ct. at 2575-2576.

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31 *See* https://www.politico.com/news/2021/04/12/abortion-pills-481092

32 As FDA Commissioner in 2016, Dr. Califf refused to respond to a congressional inquiry into the 2016 REMS changes for Mifeprex. https://www.lankford.senate.gov/news/press-releases/lankford-opposes-controversial-pro-abortion-fda-nominee;

33 *See e.g.*, *supra* note 32

34 *See* https://www.opensecrets.org/news/2021/05/abortion-rights-up-lobbying-with-roe-threatened

35 142 S. Ct. 2228 (2022)

CONCLUSION

The evidence is clear. The FDA had one goal: approval of an abortion drug. The FDA's arbitrary and capricious decisions in 2000, 2016, and 2021 demonstrate that the "how" was unimportant. Each of these decisions violate the APA and should be set aside.

Dated: February 10, 2023

Respectfully submitted,

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CERTIFICATE OF SERVICE

This is to certify that a true and correct copy of the foregoing was served, pursuant to the Federal Rules of Civil Procedure, on all counsel of record appearing herein via ECF on this 10th day of February, 2023 by the filing of this pleading with the Clerk of Court for the U.S. District Court for the Northern District of Texas using the Court's ECF system.

/s/ *Meredith Di Liberto*
Meredith Di Liberto

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF TEXAS
AMARILLO DIVISION

ALLIANCE FOR HIPPOCRATIC MEDICINE, *et al.*,	)	
Plaintiffs,	)	
v.	)	Case No. 2:22-cv-00223-z
U.S. FOOD AND DRUG ADMINISTRATION, *et al.*,	)	
Defendants.	)	

APPENDIX TO *AMICUS CURIAE* BRIEF OF JUDICIAL WATCH, INC.

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TAB A

Accelerated and Restricted Approvals Under Subpart H (drugs) and Subpart E (biologics)

- NDAs
- NDA Supplements
- BLAs
- BLA Supplements

NDA's

NDA Number	Proprietary Name	Established Name	Receipt Date	Approval Date	Total Approval Time	Approval Basis	Indication
22187	Intelence	etravirine	18-Jul-07	18-Jan-08	6.0	S	Provides for the treatment in combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-experienced adult patients who have evidence of viral replication and HIV-1 strains resistant to a non-nucleoside reverse transcriptase inhibitor (NNRTI) and other antiretroviral agents.

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22145	Isentress	raltegravir	13-Apr-07	12-Oct-07	6.0	S	Provides for the treatment in combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-experienced adult patients who have evidence of viral replication and HIV-1 strains resistant to multiple antiretroviral agents.
22068	Tasigna	nilotinib hydrochloride monohydrate	29-Sep-06	29-Oct-07	13.0	S	Provides for chronic phase (CP) and accelerated phase (AP) Philadelphia chromosome positive chronic myelogenous leukemia (CML) in adult patient resistant to or intolerant to prior therapy that included Gleeves (imatinib).
22128	Selzentry	maraviroc	20-Dec-06	6-Aug-07	6.0	S	Provides for the treatment of patients infected with CCR5-tropic HIV-1.

21986	Sprycel	dasatinib	28-Dec-05	28-Jun-06	6.0	S	Provides for the use of Sprycel (dasatinib) Tablets for the treatment of adults with chronic myeloid leukemia with resistance or intolerance to prior therapy including imatinib.
21976	Prezista	darunavir	23-Dec-05	23-Jun-06	6.0	S	Provides for the use of Prezista (darunavir) tablets, coadministered with 100 mg of ritonavir, for the treatment of human immunodeficiency virus (HIV) infection in antiretroviral treatment-experienced adult patients, such as those with HIV-1 strains resistant to more than one protease inhibitor.
22081	Letairis	ambrisentan	18-Dec-06	15-Jun-07	5.9	R	Provides for the treatment of pulmonary arterial hypertension (WHO Group 1) in patients with WHO class II or III symptoms to improve exercise capacity and delay clinical worsening.

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21880	Revlimid	lenalidomide	7-Apr-05	27-Dec-05	8.7	R	Provides for the treatment of patients with transfusion-dependent anemia due to Low- or Intermediate-1-risk myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.
21882	Exjade	deferasirox	2-May-05	2-Nov-05	6.0	S	Provides for the use of Exjade® (deferasirox) Tablets for Oral Suspension for the treatment of chronic iron overload due to blood transfusions (transfusional hemosiderosis) in patients 2 years of age and older.

Top ()

21877	Arranon	nelarabine	29-Apr-05	28-Oct-05	6.0	S	Provides for the use of Arranon (nelarabine) Injection for the treatment of patients with T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens.
21814	Aptivus	tipranavir	22-Dec-04	22-Jun-05	6.0	S	Provides for the use of Aptivus® (tipranavir) capsules, 250 mg, coadministered with 200 mg of ritonavir, for combination antiretroviral treatment of HIV-1 infected adult patients with evidence of viral replication, who are highly treatment-experienced or have HIV-1 strains resistant to multiple protease inhibitors.

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21673	Clolar	clofarabine	30-Mar-04	28-Dec-04	8.9	S	Provides for the use of Clolar (clofarabine) intravenous infusion for the treatment of pediatric patients 1 to 21 years old with relapsed or refractory acute lymphoblastic leukemia after at least two prior regimens
21322	Luveris	lutropin alfa	1-May-01	8-Oct-04	41.3	S	Provides for the use of Luveris® 75IU (lutropin alfa for injection), concomitantly administered with Gonal-f ® (follitropin alfa for injection) for stimulation of follicular development in infertile hypogonadotropic hypogonadal women with profound LH deficiency (LH

Top ()

21752	Truvada	emtricitabine; tenofovir	12-Mar-04	2-Aug-04	4.7	S	Provides for the use of Truvada™ (emtricitabine (200 mg) and tenofovir disoproxil fumarate (300 mg)) tablets in combination with other antiretroviral agents (such as nonnucleoside reverse transcriptase inhibitors or protease inhibitors) for the treatment of HIV-1 infection in adults

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21320	Plenaxis	abarelix	12-Dec-00	25-Nov-03	35.4	R	Provides for the use of Plenaxis (abarelix for injectable suspension, 100 mg) for the palliative treatment of men with advanced symptomatic prostate cancer, in whom LHRH agonist therapy is not appropriate and who refuse surgical castration, and have one or more of the following: (1) risk of neurological compromise due to metastases, (2) ureteral or bladder outlet obstruction due to local encroachment or metastatic disease, or (3) severe bone pain from skeletal metastases persisting on narcotic analgesia
21602	Velcade	bortezomib	21-Jan-03	13-May-03	3.7	S	Provides for the use of Velcade (bortezomib) for Injection for the treatment of multiple myeloma patients who have received at least two prior therapies and have demonstrated disease progression on the last therapy

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21399	Iressa	gefitinib	5-Aug-02	5-May-03	9.0	S	Provides for the use of IRESSA (gefitinib tablets) as monotherapy for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of both platinum-based and docetaxel chemotherapies
21588	Gleevec	imatinib mesylate	16-Dec-02	18-Apr-03	4.0	S	Provides for the use of Gleevec (imatinib mesylate) 100 mg and 400 mg tablets for the treatment of patients with chronic myeloid leukemia (CML) in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alfa therapy
21481	Fuzeon	enfuvirtide	16-Sep-02	13-Mar-03	5.9	S	Provides for the use of Fuzeon (enfuvirtide) for injection, in combination with other antiretroviral agents, for the treatment of HIV-1 infection in treatment experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy

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21492	Eloxatin	oxaliplatin	24-Jun-02	9-Aug-02	1.5	S	Provides for the use of Eloxatin (oxaliplatin) for Injection in combination with infusional 5-FU/LV for the treatment of patients with metastatic carcinoma of the colon or rectum whose disease has recurred or progressed during or within 6 months of completion of first line therapy with the combination of bolus 5-FU/LV and irinotecan
21196	Xyrem	sodium oxybate	2-Oct-00	17-Jul-02	21.5	R	Provides for the use of Xyrem Oral Solution for the treatment of cataplexy associated with narcolepsy
21272	Remodulin	treprostinil sodium	16-Oct-00	21-May-02	19.1	S	Provides for the use of Remodulin (treprostinil sodium) Injection 1.0, 2.5, 5.0, and 10.0 mg/ml for the treatment of pulmonary arterial hypertension (PAH)
21290	Tracleer	bosentan	17-Nov-00	20-Nov-01	12.1	R	Treatment of pulmonary arterial hypertension

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21356	Viread	tenofovir disoproxil fumarate	1-May-01	26-Oct-01	5.9	S	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults
21335	Gleevec	imatinib mesylate	27-Feb-01	10-May-01	2.4	S	Provides for the use of Gleevec (imatinib mesylate) 50 and 100 mg capsules for the treatment of patients with chronic myeloid leukemia (CML) in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy
21205	Trizivir	abacavir sulfate, lamivudine, and zidovudine	17-Dec-99	14-Nov-00	10.9	S	Provides for the use of Trizivir either alone or in combination with other antiretroviral agents for the treatment of HIV-1 infection
20687	Mifeprex	mifepristone	18-Mar-96	28-Sep-00	18.0e	R	For medical termination of intrauterine pregnancy through 49 days' pregnancy
21226	Kaletra	lopinavir/ritonavir	1-Jun-00	15-Sep-00	3.5	S	Kaletra in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients age six months and older

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21251	Kaletra	lopinavir/ritonavir	1-Jun-00	15-Sep-00	3.5	S	Kaletra in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients age six months and older
21174	Mylotarg	gemtuzumab ozogamicin	29-Oct-99	17-May-00	6.6	S	Treatment of patients with CD33 positive acute myeloid leukemia in first relapse who are 60 years of age or older and who are not considered candidates for cytotoxic chemotherapy
50747	Synercid	quinupristin/dalfopristin	5-Sep-97	21-Sep-99	7.8d	S	Treatment of vancomycin resistant Enterococcus faecium
21029	Temodar	temozolomide	13-Aug-98	11-Aug-99	11.9	S	Treatment of adult patients with refractory anaplastic astrocytoma, i.e., patients at first relapse who have experienced disease progression on a drug regimen containing a nitrosourea and procarbazine

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21007	Agenerase	amprenavir	16-Oct-98	15-Apr-99	6	S	Provides for the use of Agenerase (amprenavir), in combination with other antiretroviral agents, for the treatment of HIV-1 infection
21039	Agenerase	amprenavir	8-Dec-98	15-Apr-99	4.2	S	Provides for the use of Agenerase (amprenavir), in combination with other antiretroviral agents, for the treatment of HIV-1 infection
21041	DepoCyt	cytarabine	5-Oct-98	1-Apr-99	5.9	S	Depocyt is indicated for the intrathecal treatment of lymphomatous meningitis
20977	Ziagen	abacavir sulfate	24-Jun-98	17-Dec-98	5.8	S	Provides for the use of Ziagen (abacavir sulfate), in combination with other antiretroviral agents, for the treatment of HIV-1 infection
20978	Ziagen	abacavir sulfate	24-Jun-98	17-Dec-98	5.8	S	Provides for the use of Ziagen (abacavir sulfate), in combination with other antiretroviral agents, for the treatment of HIV-1 infection

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20747	Actiq	fentanyl citrate	13-Nov-96	4-Nov-98	23.7	R	For the management of breakthrough cancer pain in patients with malignancies who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain
20972	Sustiva	efavirenz	11-Jun-98	17-Sep-98	3.2	S	Provides for the use of efavirenz in combination with other antiretroviral agents for the treatment of HIV-1 infection
20933	Viramune	nevirapine	20-Apr-98	11-Sep-98	4.7	S	Provides for an oral suspension, which is indicated for use in combination therapy with other antiretroviral agents for the treatment of HIV-1 infection
20785	Thalomid	thalidomide	20-Dec-96	16-Jul-98	18.8	R	Thalomid is indicated for the acute treatment of the cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL) and as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence

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21024	Priftin	rifapentine	22-Dec-97	22-Jun-98	6	S	Priftin is indicated for the treatment of pulmonary tuberculosis (TB)
19832	Sulfamylon	mafenide acetate	31-Mar-97	5-Jun-98	14.2 c	S	Indicated for use as an adjunctive topical antimicrobial agent to control bacterial infection when used under moist dressings over meshed autografts on excised burn wounds
20896	Xeloda	capecitabine	31-Oct-97	30-Apr-98	6	S	Treatment of patients with metastatic breast cancer resistant to both paclitaxel and an anthracycline-containing chemotherapy regimen or resistant to paclitaxel and for whom further anthracycline therapy may be contraindicated
20705	Rescriptor	delavirdine mesylate	15-Jul-96	4-Apr-97	8.7	S	Treatment of HIV infection in combination with appropriate antiretroviral agents when therapy is warranted
20778	Viracept	nelfinavir mesylate	26-Dec-96	14-Mar-97	2.6	S	Treatment of HIV infection when therapy is warranted

Top ()

20779	Viracept	nelfinavir mesylate	26-Dec-96	14-Mar-97	2.6	S	Treatment of HIV infection when therapy is warranted
19815	ProAmatine	midodrine hydrochloride	25-Sep-95	6-Sep-96	11.4 b	S	Treatment of symptomatic orthostatic hypotension
20604	Serostim	somatropin	11-Sep-95	23-Aug-96	11.4	S	Treatment of AIDS wasting associated with catabolism loss or cachexia
20636	Viramune	nevirapine	23-Feb-96	21-Jun-96	3.9	S	Combination with nucleoside analogues for the treatment of HIV-1 infected adults who have experienced clinical and/or immunologic deterioration
20571	Camptosar	irinotecan hydrochloride	28-Dec-95	14-Jun-96	5.6	S	Treatment of refractory colorectal cancer
20449	Taxotere	docetaxel	27-Jul-94	14-May-96	21.6	S	Treatment of patients with locally advanced or metastatic breast cancer who have progressed or relapsed during anthracycline based therapy
20685	Crixivan	indinavir sulfate	31-Jan-96	13-Mar-96	1.4	S	Treatment of HIV infection in adults
20659	Norvir	ritonavir	21-Dec-95	1-Mar-96	2.3	S	In combination with nucleoside analogues or as monotherapy for the treatment of HIV infection

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20680	Norvir	ritonavir	21-Dec-95	1-Mar-96	2.3	S	In combination with nucleoside analogues or as monotherapy for the treatment of HIV infection
20628	Invirase	saquinavir mesylate	31-Aug-95	6-Dec-95	3.2	S	Treatment of advanced HIV infection in selected patients in combination with nucleoside analogues
20564	Epivir	lamivudine	7-Jul-95	17-Nov-95	4.4	S	Treatment of HIV infection in selected patients
20596	Epivir	lamivudine	7-Jul-95	17-Nov-95	4.4	S	Treatment of HIV infection in selected patients
50718	Doxil	doxorubicin hydrochloride	2-Sep-94	17-Nov-95	14.3	S	Treatment of AIDS-related Kaposi's sarcoma in patients with disease that has progressed on prior combination chemotherapy or in patients who are intolerant to such therapy
20498	Casodex	bicalutamide	14-Sep-94	4-Oct-95	12.7	S	Use in combination therapy with a Luteinizing-Hormone Releasing Hormone (LHRH) analogue for the treatment of advanced prostate cancer

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20212	Zinecard	dexrazoxane	5-Aug-94	26-May-95	9.7 a	S	To reduce the incidence and severity of cardiomyopathy associated with doxorubicin administration in certain breast cancer patients
20412	Zerit	stavudine	28-Dec-93	24-Jun-94	5.9	S	Treatment of adults with advanced HIV infection - alternative therapy
50698	Biaxin	clarithromycin	2-Nov-92	23-Dec-93	13.7	S	Treatment of disseminated mycobacterial infections due to Mycobacterium avium and Mycobacterium intracellular
20199	Hivid	zalcitabine	31-Oct-91	19-Jun-92	7.6	S	Combination therapy with zidovudine in advanced HIV infection

NDA Supplements Approved Under Subpart H

NDA Number	NDA Supp Number	Proprietary Name	Established Name	Receipt Date	Approval Date	Total Approval Time	Approval Basis	Indication
50718	SE7 033	Doxil	doxorubicin hydrochloride liposome	10-Aug-07	10-Jun-08	10.0	S	Provides for the treatment of AIDS-related Kaposi's Sarcoma after failure of prior systemic chemotherapy or intolerance to such therapy.

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TAB B

A Judicial Watch Special Report:

The Clinton RU-486 Files

♦

The Clinton Administration's Radical Drive to Force an Abortion Drug on America

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Introduction

This Judicial Watch Special Report analyzes newly uncovered documents from the National Archives at the Clinton Presidential Library in Little Rock, Arkansas, describing the Clinton administration's radical drive to introduce the abortion drug RU-486 (mifepristone) into the American marketplace.

The records include the Clinton administration's legal, political and press strategies for rushing RU-486 through the Food and Drug Administration (FDA) processes, despite the manufacturer's historical refusal to permit marketing the drug here. The legal, political and press memos articulate the Clinton administration's views regarding various players in the drug approval and marketing process -- women's groups, members of Congress, public interest groups and the media.

Judicial Watch has engaged in a five-year legal battle with the FDA for release of records under the provisions of the Freedom of Information Act (FOIA), 5 U.S.C. §552, concerning RU-486. We uncovered over 9,300 pages of documents and 840 Adverse Event Reports pertaining to the abortion drug. To date, the deaths of at least six women have been attributed to RU-486. The FDA scheduled a scientific conference for May 11, 2006 in order to study the controversial abortion drug and the circumstances leading to the deaths.

Judicial Watch promotes transparency, integrity and accountability in government, politics and the law. We make aggressive use of open records and open meetings laws as a means to obtain documents with which to educate the American public on the operations of their government and to hold public officials accountable. Judicial Watch also provides technical, research and litigation assistance to public interest groups interested in obtaining information about government activity which may not have the necessary resources or experience to pursue information on their own as part of the Judicial Watch Open Records Project.

Thomas Fitton
President
Judicial Watch, Inc.

April 26, 2006

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The Clinton RU-486 Files:
The Clinton Administration's Radical Drive to Force an Abortion Drug on America

Executive Summary

During a February 2006 research trip to the National Archives at the Clinton Presidential Library, Judicial Watch uncovered new records detailing the Clinton administration's rush to market the abortion drug RU-486 (mifepristone) to American women. The documents include political, legal and press strategy memoranda from Health and Human Services (HHS) Secretary Donna Shalala, FDA Commissioner, Dr. David Kessler, and HHS Chief of Staff Kevin Thurm. Some of the memoranda are addressed to the White House -- in particular, Carol Rasco, the Clinton administration Director of Domestic Policy.

Analysis of the records shows:

- President Clinton ordered HHS and FDA to coordinate and promote the marketing of RU-486 as his first official act in office.
- Within one month, the FDA Commissioner had met with the RU-486 manufacturer and their parent company.
- Official U.S. Government political, economic and diplomatic pressure was brought to bear to strong-arm the companies into changing their policies in order to make the drug available in the United States.
- The FDA was compromised in its role as objective reviewers of the safety and efficacy of the drug.
- The five standard requirements for certifying a drug "safe and effective" were circumvented to rush RU-486 to market.
- Radical, pro-abortion extremists dominated the Clinton administration's "women's health care" agenda and their reckless drive to bring RU-486 to America ultimately cost at least six women their lives and the lives of over 560,000 unborn children.

The Clinton RU-486 Files:
The Clinton Administration's Radical Drive to Force an Abortion Drug on America

* * *

"Hoechst has historically refused to permit Roussel Uclaf to seek marketing approval for RU-486 as an abortifacient in the United States. Both Dr. Kessler [FDA Commissioner] *and I have taken steps to persuade Roussel Uclaf and Hoechst to change their position."*

Donna Shalala
Health & Human Services Secretary
Clinton Administration
November 15, 1993
Confidential Memo to White House

* * *

In February 2006, Judicial Watch uncovered previously confidential files and working papers from the holdings of the National Archives at the Clinton Presidential Library in Little Rock, Arkansas that provide remarkable insight into the Clinton administration's relentless drive to market RU-486 (mifepristone), a drug used to cause abortion, to American women. The documents offer a window into the political strategy, legal theories and media "spin" on the Clinton administration's abortion program.

RU-486 was first developed in France in 1981. It is a manmade steroid designed to work against the hormone progesterone, which is required to promote a baby's proper growth and development. RU-486 works to chemically destroy the unborn child's environment, cutting off nourishment and starving the baby to death in the mother's womb. A second chemical, misoprostol, is then used to create cramping and contractions to expel the dead baby from the mother's womb. The "procedure" must begin within 49 days of conception. The Clinton administration considered this method of abortion part of "women's health care." President Clinton thanked the maker of RU-486 in writing, "On behalf of the government of the United States and for the women of America. . ."[i]

On January 22, 1993, in his first official act, President Clinton issued a memorandum directing HHS Secretary Donna Shalala to promote the testing and licensing of RU-486 in the United States. (See Tab A)

Abortion was a key domestic policy item for President Clinton. RU-486 was just one part of the overall strategy for his administration's agenda. For example, in a

National Archives document entitled, "President William J. Clinton -- Eight Years of Peace, Prosperity and Progress," the first "accomplishment" listed reads:

> **Abolished Restrictions on Medical Research and the Right to Choose** As his first executive actions, President Clinton revoked the Gag Rule, which prohibited abortion counseling in clinics that receive federal funding to serve low-income patients. He also revoked restrictions on a woman's legal right to privately funded abortion services in military hospitals, restrictions on the import of RU-486, and restrictions on the award of international family planning grants (the "Mexico City Policy"). The President also lifted the moratorium on federal funding for research involving fetal tissue, allowing progress on research into treatments for Parkinson's disease, Alzheimer's, diabetes and leukemia. (Executive Memoranda, 1/22/93)[ii]

The tone was set for the Clinton administration's drive towards promoting abortion as "health care." Shalala and FDA Commissioner, Dr. David Kessler, engaged in a political, legal and economic campaign to force the French pharmaceutical firm, Roussel Uclaf, and their German parent corporation, Hoechst, A.G., to file a "new drug application" (NDA) with the FDA, and begin marketing RU-486 to American women.[iii]

In April 1993, the FDA brokered a meeting between Roussel Uclaf and the Clinton administration's anointed abortion proponent, the Population Council, a non-profit organization that conducts research on so-called "reproductive health issues." Roussel Uclaf and the Population Council already had an existing contractual relationship concerning provision of abortifacients (substances that induce abortion) for various clinical trials.[iv] It is difficult to understand the FDA's role in bringing the parties together, other than to continue to bring official U.S. government pressure on Roussel Uclaf and to designate the Population Council as the Clinton administration's abortion drug development and marketing proxy.

The Population Council claims to be " . . . an international, nonprofit, nongovernmental organization, seeks to improve the well-being and reproductive health of current and future generations around the world and to help achieve a humane, equitable, and sustainable balance between people and resources."[v] The organization was founded by John D. Rockefeller III in 1952. In 2005, they projected spending over $71 million in 70 countries around the world. Their work is funded by governments, foundations, individuals and "multilateral organizations."[vi]

According to the Clinton RU-486 files, Roussel Uclaf made the decision to use the Population Council as the administration's surrogate for forcing RU-486 on America.

There is no mention in the memoranda of Planned Parenthood or the National Abortion and Reproductive Rights Action League (NARAL). There is no mention of public disclosure, discussion, competition or bidding. One might imagine a selection process or staff discussion of the relative pros and cons for selection of another abortion group, but there is no evidence of any such discussion or consideration. In a memo by HHS Chief of Staff Kevin Thurm (discussed in detail below), the Clinton administration seems to have been predisposed to using the Population Council to carry out their abortion plans based on an existing relationship of the abortion non-profit with the maker of RU-486.

Roussel Uclaf repeatedly sought total U.S. government-sponsored indemnification from any damages it might incur by bringing RU-486 to the U.S. marketplace. Roussel Uclaf President, Dr. Edouard Sakiz, specifically expressed concerns over liability actions against his firm "if a woman had an incomplete abortion and delivered a deformed fetus." Dr. Sakiz was also particularly concerned about "consequential damages," such as the economic costs from boycotts. The Clinton administration's fervent commitment to making RU-486 part of the American abortion industry is demonstrated through Dr. Sakiz's reservations concerning legal and economic exposure. The Clinton administration's near-obsession with introducing a "safe and effective" abortion drug is revealed in Shalala's confidential memo to the White House of November 15, 1993:

> "Dr. Sakiz's view was that if the United States Government wanted RU-486 to be marketed in the United States, it should compensate Roussel Uclaf for any damages that the company might suffer from complying with the United States Government's request."

(See Tab B)

Dr. Sakiz was saying, in other words, "If <u>you</u> want it so badly, <u>you</u> pay the consequences." The Clinton administration was attempting to trump a business decision of the pharmaceutical company while exposing the corporation to risk for abiding by a U.S. government request.

Even Clinton FDA Commissioner Kessler understood and memorialized the controversy over the administration's aggressive efforts to introduce RU-486 when he wrote in a September 30, 1993 memorandum to Shalala:

> " . . . other Congressional members have written to Hoechst expressing their strong opposition to the marketing of RU-486 in this country. This, and the well-publicized activities of anti-abortion groups, have provided Hoechst and Roussel Ucalf with evidence that the U.S. population

> lacks cohesiveness on this issue and that the abortion debate continues."

(See Tab C)

The Clinton administration realized that attempting to enact blanket indemnification by the U.S government of a foreign corporation for an abortion drug was politically and practically impossible. According to the Clinton RU-486 files, Dr. Sakiz still went ahead and committed to negotiating with the Clinton administration surrogates – the Population Council – agreeing:

- To license RU-486 to the Population Council which would conduct a clinical trial involving 2000 women pursuant to an investigational new drug application;
- The Population Council would ultimately submit an NDA to the FDA based on the results of the clinical trial and on other studies conducted by Roussel Uclaf; and
- The Population Council, with the concurrence of Roussel Uclaf, would chose a new manufacturer for the drug, and that Roussel Uclaf would transfer its technology for making the drug to that manufacturer because Roussel Uclaf did not want to manufacture the drug for sale in this country. [Emphasis added.]

(See Tab B)

According to the Clinton RU-486 files, over the next few months Roussel Uclaf reiterated its desire for protective federal legislation providing blanket indemnification from the use of RU-486. Roussel Uclaf did not anticipate any profit from selling RU-486 in the United States; and was only entering the American market at the insistence of the Clinton administration. FDA representatives told Roussel Uclaf that such protection was extremely unlikely.

In a September 30, 1993 memorandum to Shalala, FDA Commissioner Kessler recounts a conversation he had with Jim Boynton, legal counsel for the Population Council, concerning the Roussel Uclaf indemnification legislation. Kessler pointed out the recent passage of the Hyde Amendment (restricting federal funds for abortion), and that with one exception (swine flu event), the United States had never agreed to indemnify any drug manufacturer. Apparently sensing that it might be perceived as inappropriate for the FDA commissioner to be discussing indemnification with a drug company representative for a supposedly safe drug, Kessler tried to cover his tracks. Kessler wrote that he, ". . . further explained that it would go far beyond FDA'S

appropriate role to seek such protection for a drug company." [Emphasis added.] Nonetheless, the FDA offered to advance the idea within HHS.

Not satisfied with the denials of indemnification from the FDA and HHS, in September 1993 Roussel Uclaf hired legal counsel (reportedly, Lester Hyman and John Hoff of the firm Swidler & Berlin) to lobby the federal government for indemnification "at levels higher than the FDA" – presumably from President Clinton and other pro-abortion advocates in the Congress, such as Rep. Ron Wyden and Rep. Henry Waxman. Concerned with these moves, HHS Chief of Staff Kevin Thurm and HHS General Counsel Harriet Rabb initiated a meeting with attorneys from Swidler & Berlin. During that meeting Roussel Uclaf's lawyer suggested that the United States could exercise its statutory powers of eminent domain and seize the patent for RU-486 for the abortifacient uses of the drug.[vii]

Meanwhile, the Population Council and Roussel Uclaf pressed forward with licensing details, and simultaneously made plans to sway the leadership of Hoechst to allow their subsidiary to enter into an agreement with the Population Council. Shalala's confidential memo to the White House warns, ". . . we do not think the negotiations will be successfully concluded without pressure on Roussel Uclaf/Hoechst."[viii]

Shalala suggested the Clinton administration bring the force of the United States Government to bear on the Hoechst and Roussel Uclaf corporations. She also went on to suggest that the United States exercise its international diplomatic and economic pressure on the German and French governments, as a means of further "influence" against the corporations. In a November 15 confidential memo to the White House, Shalala wrote: "The French and German governments might be displeased to learn that their companies are not accommodating a request made by the United States Government."

While the Clinton administration pondered exercising the full economic and diplomatic weight of the United States Government to advance its abortion agenda, it is important to note that Roussel Uclaf was willing to give a royalty-free license to any major U.S. pharmaceutical company – but no U.S. company would take the license.

The Clinton RU-486 files show specualtion among administration officials concerning delays in the negotiations between Roussel Uclaf and the Population Council. The pending retirement of the chief executive officer of Hoechst, Professor Wolfgang Hilger, was discussed in Kessler's September memo, noting that Prof. Hilger was "very staunchly Catholic." There was also a discussion of the likelihood of an international foundation being created by the drug's inventor, Dr. Etiene Balieu, for broader marketing opportunities. Apparently the Clinton administration was concerned about competition from an abortion drug "insider."[ix]

Just as the name of the Population Council "appeared" in the Clinton administration's confidential memos without a trace of how it became the administration's surrogate, so too does the recommendation for Felix Rohatyn to serve as an "expert advisor."[x]

After a review of the economic, political and diplomatic issues involved in strong-arming Hoechst and Roussel Uclaf, Dr. Kessler advanced Mr. Rohatyn's name by concluding with a political point: "We think that someone familiar to these circles would advance the Administration's goal to bring a safe and effective abortifacient to the U.S. market." Again, there is no discussion, alternatives or explanation offered for this appointment. The question of appointment of an "expert advisor" for the U.S. government is raised and answered in the space of one paragraph.

In a remarkable admission that the FDA had been thoroughly politicized in the Clinton administration's radical drive for RU-486, the agency's commissioner, Dr. Kessler, wrote in his September memo, " . . . the FDA cannot take this issue too far without compromising its role as objective reviewers of the safety and efficacy of the drug."

The Clinton RU-486 file offering the most comprehensive treatment of the administration's strategic campaign to introduce RU-486 to the American market is a memorandum dated May 11, 1994 from HHS Chief of Staff Kevin Thurm to the White House – in particular, Carol Rasco, Director of the Clinton administration Domestic Policy Council. (See Tab D)

Thurm's memo details three issues submitted for decision by the President:

- Whether the President is willing to write a letter to the maker of RU-486, asking that the U.S. patents for the drug be assigned to a non-profit entity in this country [Population Council].

- If the negotiations between Roussel Uclaf and the Population Council fail, and the "only" available option is the "gift offer," is the U.S. Government willing to accept the RU-486 patent rights, and under what conditions?

- If the government is not willing to accept the patent rights, what will be the basis for that decision, and how will it be communicated to the American public?

Thurm develops and discusses each of the factors bearing on the subject in a series of tabs and exhibits to his memo. He provides a history and background tab recounting the Clinton administration's position on RU-486; a tab discussing legal issues;

a brief marketing study addressing timing, administration, and abortion proxies; political considerations; and finally, a discussion of press strategies and concerns.

Thurm explains that on April 26, 1994, the Board of Roussel Uclaf passed a resolution authorizing the assignment of RU-486 patent rights to either the U.S. Government or to a non-profit organization. If the rights were to go to a non-profit organization [Population Council], then Roussel Uclaf demanded a letter from the President of the United States requesting RU-486 on behalf of the women of the United States. President Clinton signed exactly such a letter on May 16, 1994. (See Tab E)

President Clinton's extraordinary letter is direct documentary evidence of his personal intervention as a politician, and clear evidence that the RU-486 patent rights would never have been assigned to the Population Council without his compliance with Roussel Uclaf's demands.

President Clinton's RU-486 request letter to Dr. Edouard Sakiz of Roussel Uclaf claims that it is important for the women of the United States to have "safe and effective medical treatments." Under that rubric, President Clinton writes that he "understands" Roussel Uclaf has been in negotiations with the Population Council. Of course, the Population Council had been serving as a Clinton administration abortion "front" for several months. President Clinton closes his RU-486 request letter by stating: "On behalf of the government of the United States and for the women of America, I thank you for your work."

Thurm's memo specifically addresses the requirements for RU-486 clinical trials and the Population Council's requirements for marketing application for the FDA. The significance of speedy approval and abbreviation of various timelines is a theme throughout his analysis. Not surprisingly, the Clinton administration's radical drive to bring RU-486 to the American market manifested itself in other ways, once the patent rights were obtained by the Population Council. For example, the five standard requirements for certifying a drug "safe and effective" were circumvented to rush RU-486 to market.[xi] Probably the most reckless act by the FDA was the waiver of the normal requirement for random, double-blind, control tests for new drugs. The FDA's expedition in this process was justified with language reserved for drugs developed to cure life-threatening conditions. Certainly, pregnancy is not a disease, nor is it likely to be life threatening – so how could they have twisted the rules so dramatically? What political pressure was brought to bear?

The "political issue discussion" tab to Thurm's memo offers a glimpse into the Clinton administration's abortion politics techniques. The Clinton administration steadfastly continues the manipulation of language that seeks to forever separate the words "kill," "baby" and "abortion." Thurm states: "It is, therefore, extremely important that the decision concerning RU-486 be placed in the context of promoting women's

health and maintaining the close relationship of the administration to these ["pro-choice" and women's groups] groups."

The Clinton administration wanted a quick victory on RU-486 and was deeply concerned that RU-486 might remain a "front burner" issue through the 1996 presidential election. They were particularly sensitive to the prospect of prolonged, intense, public attention and debate on RU-486. Thurm advised political caution concerning unintended consequences, allowing " . . . Republicans and others opposed to the administration to focus attention on this decision and its aftermath."

The Clinton press strategy documents discuss the ramifications of accepting or rejecting the gift of the RU-486 patents. Acceptance of the patent gifts was relegated to Secretary Shalala "on behalf of American women," but specifically as a means of "insulating the White House." While seeking insulation, the press memo stresses the need to credit President Clinton for keeping his campaign promises and giving a major "reproductive rights victory" to American women. The memo also contains a disturbing directive:

> " . . . there should also be a concerted effort on the part of HHS Public affairs team to place stories that outline the hurdles that must be overcome to shield the Administration against fallout from our allies in the event efforts to get RU-486 to the market become stalled in bureaucratic process, in Congress or for other reasons."[xii]

If the Clinton administration's RU-486 strategy failed all together, it appears the press response included a calculated scenario for resorting to lying to the American public. Working through the various scenarios, the author of the memo offers an "alternative":

> " . . . another potential argument we could embrace is the position that we wanted more than the rights they were willing to grant because our interest in this drug goes beyond the issue of abortion, the need for which we are committed to making as rare as possible."[xiii]

Still worried about potential fallout and damage with abortion proponents and allied political groups, the press memo ends stating:

> "Without a doubt, a 'no' will subject the Administration to a firestorm of protest by pro-choice and women's groups; and there will be few natural political allies vocally defending this decision, particularly in light of the relative difficulty of explanation."[xiv]

Beyond the Clinton Files -- RU-486 in 2006

As Judicial Watch reviewed the Clinton RU-486 files, documenting the extraordinary lengths the administration went to rush the abortion drug to U.S. markets, the earliest correspondence on file at the Archives caught our attention and, in hindsight, provided some perspective for examining RU-486 matters in 2006. (See Tab F)

The file contained a handwritten letterhead note from Betsey Wright, President Clinton's former Chief of Staff, and the White House staff member charged with covering-up "bimbo eruptions." The note reads: "To Carol Rasco. This just got forwarded to me. Please handle. BW 3/9/93." There is an additional notation that reads: "cc for Shalala on Tues. MK," with the name Shalala circled and a line drawn to the words "To handle."[xv]

Betsey Wright's note was attached to a letter dated January 6, 1992, from Ron Weddington, an attorney that served as co-counsel in the infamous *Roe v. Wade* lawsuit. Weddington attached an "open letter" to President-elect Clinton. Weddington's letter recommends that the new president should, " . . . start immediately to eliminate the barely educated, unhealthy and poor segment of the country . . ." and that the " . . . government is going to have to provide vasectomies, tubal ligations and abortions . . . RU-486 and conventional abortions."[xvi]

Weddington states: "Condoms won't do it. Depo-Provera, Norplant and the new birth control injection being developed in India are not a complete answer, although the savings that could be effected by widespread government distribution and encouragement of birth control would amount to billions of dollars."

The full text of Weddington's letter is a breathtakingly arrogant exegesis on the abortion lobby's culture of death. As disturbing as the Weddington letter is to read, what is more disturbing is the fact that Betsey Wright, one of President Clinton's closest confidantes, tasked Donna Shalala to "handle" it along with the Director of the White House Domestic Policy Council, Carol Rasco. Weddington's ravings were not relegated to a file for unsolicited constituent correspondence. On the contrary, the Weddington letter is, chronologically and philosophically, the foundation document for the Clinton RU-486 files.

Today we are faced with the horrible results of the political and "health care" campaign to put RU-486 on the market. Since RU-486 was approved for use in the United States in September 2000, at least six women have died after taking the abortion drug. Only after the death of 18 year old Holly Patterson, on September 17, 2003, did the media and the FDA begin to pay attention to the dangers of RU-486.

In November 2004, following the third woman's death, the FDA elected to "strengthen the warning notice," a step that may have provided some sort of "informational" or disclaimer insulation for the FDA, but a tactic that certainly did not make RU-486 any safer for women.

Planned Parenthood, which had ignored the FDA's warnings concerning how to administer the drug regimen, played a role in the deaths of four women as the "procedure" provider. The FDA has determined that the four California women who died after taking RU-486 all suffered from a highly lethal bacterial infection -- Clostridium sordellii. The bacterium flourishes in the uterus and then enters the bloodstream, eventually leading to toxic shock.

It is quite likely that more women have died from RU-486 and their deaths have gone unreported because doctors, medical examiners and coroners are not obligated to forward reports dealing with RU-486 side effects to the FDA. This is particularly true in cases where local health officials may not associate a death with an RU-486 abortion, especially if the woman's death occurs several days or even weeks later.

Even abortion providers now have low regard for the safety of RU-486. Dr. Warren Hern, an abortionist in Denver, Colorado has stated: "I think surgery should be the procedure of choice." Pills, he said, "are a lousy way to perform an abortion." He is not alone. Dr. Damon Stutes, an abortionist from Reno, Nevada reluctantly agrees with Pro-Life critics of RU-486, stating, "the truth is the truth," and that, "The complications from RU-486 far exceed the complications of surgical abortion." [xvii]

It seems that the federal government has finally come to grips with the growing number of deaths attributed to the use of RU-486 and is prepared to take some action, however late. The government will convene a scientific conference at the Center for Disease Control in Atlanta, Georgia on May 11, 2006. More than two dozen scientists and doctors will make presentations concerning the deadly bacterial infections that killed the California women mentioned above.

Conclusion

Judicial Watch hopes that this special report on the Clinton RU-486 files has provided the reader with sufficient documentary evidence from primary sources to illuminate the Clinton administration's rush to achieve part of its abortion agenda through bringing RU-486 to America. Armed with the long-delayed facts from Clinton insider memoranda, the reader is now equipped to evaluate policy and hold public officials accountable.

On September 28, 2000, the day RU-486 was approved for U.S. markets, the FDA Commissioner, Dr. Jane E. Henney, said in an interview, "Politics had no role in this

decision."[xviii] The public now has copies of the the Clinton RU-486 files that unequivocally say otherwise.

Endnotes

[i] See Tab E: Letter from President William J. Clinton to Dr. Edouard Sakiz, Chaiman of Roussel Uclaf, dated May 16, 1994.

[ii] See: http://clinton5.nara.gov/media/pdf/eightyears.pdf

[iii] Hoechst had a historical reason for wanting to keep a low profile concerning RU-486. Hoechst was part of a cartel connected to the infamous I.G. Farben Chemical Company, the makers of Zyklon-B -- the cyanide gas used in Nazi death camps. In 1999, Hoechst merged with another European pharmaceutical company to form Aventis.

[iv] Copies of the Roussel Uclaf – Population Council contract were not available from the Archives.

[v] See: http://www.popcouncil.org/about/index.html

[vi] See: http://www.popcouncil.org/mediacenter/PC_Key_Facts.html

[vii] See Tab C: FDA Commissioner Kessler's Memorandum to HHS Secretary Shalala, dated September 30, 1993.

[viii] See Tab B: HHS Secretary Shalala's Confidential Memorandum to White House Director of Domestic Policy Carol Rasco, dated November 15, 1993.

[ix] See Tab C, pages 4-5.

[x] Felix Rohatyn is a Wall Street investment banker and served as President Clinton's Ambassador to France from 1997 to 2000.

[xi] Donna J. Harrison, M.D., "Dangerous Medicine," *The New York Times*, November 19, 2004.

[xii] See Tab D: HHS Chief of Staff Kevin Thurm's Memorandum to White House Director of Domestic Policy Carol Rasco, Subject: RU-486, dated May 11, 1994; Tab 5: Press Strategies and Concerns.

[xiii] *Ibid.*

[xiv] *Ibid.*

[xv] See Tab F: Clinton Transition Team Director of Public Outreach Betsey Wright's correspondence file Re: RU-486 from Mr. Ron Weddington, dated 3/9/93.

[xvi] *Ibid.*

[xvii] Gardiner Harris, "Some Doctors Voice Worry Over Abortion Pill's Safety," *The New York Times*, April 1, 2006.

[xviii] Gina Kolata, "U.S. Approves Abortion Pill; Drug Offers More Privacy, and Could Reshape Debate, *The New York Times*, September 29, 2000.

Tab A

THE WHITE HOUSE

WASHINGTON

January 22, 1993

MEMORANDUM FOR THE SECRETARY OF HEALTH AND HUMAN SERVICES

SUBJECT: Importation of RU-486

In Import Alert 66-47, the Food and Drug Administration ("FDA") excluded the drug Mifepristine -- commonly known as RU-486 -- from the list of drugs that individuals can import into the United States for their "personal use," although the drugs have not yet been approved for distribution by the FDA. (See FDA Regulatory Procedures Manual, Chapter 9-71.) Import Alert 66-47 effectively bans the importation into this Nation of a drug that is used in other nations as a nonsurgical means of abortion.

I am informed that in excluding RU-486 from the personal use importation exemption, the FDA appears to have based its decision on factors other than an assessment of the possible health and safety risks of the drug. Accordingly, I hereby direct that you promptly instruct the FDA to determine whether there is sufficient evidence to warrant exclusion of RU-486 from the list of drugs that qualify for the personal use importation exemption. Furthermore, if the FDA concludes that RU-486 meets the criteria for the personal use importation exemption, I direct that you immediately take steps to rescind Import Alert 66-47.

In addition, I direct that you promptly assess initiatives by which the Department of Health and Human Services can promote the testing, licensing, and manufacturing in the United States of RU-486 or other antiprogestins.

You are hereby authorized and directed to publish this memorandum in the Federal Register.

William J. Clinton

Tab B

THE SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

NOV 15 1993

~~CONFIDENTIAL~~

file

DATE: 4/14/04

MEMORANDUM FOR CAROL RASCO

The purposes of this memorandum are: (1) to inform you of the Department's progress in implementing the President's directive of January 22, 1993, to "assess initiatives by which the Department of Health and Human Services can promote the testing, licensing, and manufacturing in the United States of RU-486 or other antiprogestins;" and (2) to outline the necessary next steps to accomplish the President's directive.

Background: You may recall that RU-486 is manufactured by the French firm Roussel Uclaf and is approved to induce abortions in France, the United Kingdom, and Sweden. Roussel Uclaf has stated that it can act in the United States only with the approval of its parent company, Hoechst AG, a German firm. Hoechst has historically refused to permit Roussel Uclaf to seek marketing approval for RU-486 as an abortifacient in the United States.

Both Dr. Kessler and I have taken steps to persuade Roussel Uclaf and Hoechst to change their position. In February Dr. Kessler met with Dr. Edouard Sakiz, the President of Roussel Uclaf, to discuss the availability of RU-486 in the United States for research and marketing. In March I wrote to Professor Wolfgang Hilger, President of the Board of Hoechst, to ask him to permit Roussel Uclaf to begin any necessary testing of RU-486 in the United States in preparation for filing a new drug application with the FDA. Later in March there were press reports that Roussel Uclaf would respond to the requests of the Clinton Administration to make RU-486 available in this country and that testing of the drug would begin approximately two months later (i.e., in May).

In April 1993, FDA arranged a meeting between Roussel Uclaf and the Population Council, a non-profit corporation that conducts research on reproductive health issues. The meeting's purpose was to facilitate an agreement between those parties to work together to test RU-486 and file a new drug application for the drug. The Population Council was identified as the most likely group to work with Roussel Uclaf because of an existing contract between these two parties that required Roussel Uclaf to give the Population Council sufficient amounts of the drug for the Population Council to conduct clinical trials. The contract also appeared to require Roussel Uclaf to license the drug to the Population Council if Roussel Uclaf were unwilling to sell the drug in the United States.

At the April meeting, Dr. Edouard Sakiz, President of Roussel Uclaf, raised the issue of federal legislation to indemnify

Roussel Uclaf from any damages it might incur by permitting RU-486 to be marketed in the United States. Dr. Sakiz was worried about product liability actions against Roussel Uclaf if a woman had an incomplete abortion and delivered a deformed fetus. Dr. Sakiz was also concerned about consequential damages, such as the economic costs from boycotts of other Roussel Uclaf or Hoechst products, or bombings of Roussel Uclaf/Hoechst facilities by right-to-life groups. Dr. Sakiz's view was that if the United States Government wanted RU-486 to be marketed in the United States, it should compensate Roussel Uclaf for any damages that the company might suffer from complying with the United States Government's request.

Dr. Sakiz was clearly informed at the April meeting that such legislation would never be enacted and that the FDA would not support Roussel Uclaf in seeking it.

Despite being told that there was no possibility of obtaining federal legislation to protect Roussel Uclaf from consequential damages or product liability suits, Dr. Sakiz committed Roussel Uclaf to negotiate with the Population Council to bring RU-486 onto the United States market. Specifically, at the April meeting Roussel Uclaf and the Population Council agreed:

- That Roussel Uclaf would license RU-486 to the Population Council, which would conduct a clinical trial involving 2000 women pursuant to an investigational new drug (IND) application;

- That the Population Council would ultimately submit a new drug application (NDA) to FDA, based on the results of the clinical trial and on other studies that have been conducted by Roussel Uclaf; and

- That the Population Council, with the concurrence of Roussel Uclaf, would choose a new manufacturer for the drug, and that Roussel Uclaf would transfer its technology for making the drug to that manufacturer because Roussel Uclaf does not want to manufacture the drug for sale in this country.

It was then left for the Population Council and Roussel Uclaf to revise the terms of their contract, while Roussel Uclaf began sending scientific information to FDA and the Population Council. A tentative goal of September 15 was established for concluding the contract negotiations. As of late July 1993, the Population Council thought that the negotiations were proceeding smoothly, though slowly.

CURRENT STATUS

On August 2, 1993, the Population Council's lawyer notified FDA that **Roussel Uclaf had recently reasserted its demand for protective federal legislation.** Roussel Uclaf insisted that the Population Council obtain a commitment from the United States Government that: 1) legislation would be enacted making it a crime for any person to hurt or harass any doctor administering RU-486, their patients, or the drug's manufacturers, distributors, and salespersons; 2) the Department of Justice publicly commit to enforce this law, if enacted; 3) legislation would be enacted indemnifying Roussel Uclaf for any product liability exposure resulting from the use of RU-486 in this country, or, as an alternative, a prohibition of any product liability actions against Roussel Uclaf for RU-486; 4) as part of any legislation, indemnification for consequential damages.

In exchange Roussel Uclaf would give the Population Council a royalty-free license because it has decided to forego any profit from entering the United States market. **In short, Roussel Uclaf's position is that it should not incur any liability exposure as a result of making RU-486 available in this country** as an abortifacient because it does not anticipate any profit from selling RU-486 for that use in the United States and is entering the American market only at the request of the United States Government. Roussel Uclaf remains willing to exploit its patent for non-abortifacient uses of RU-486, should any other use be found to be safe and effective.

FDA advised the Population Council's lawyer that it could not make a commitment to seek such legislation and that its enactment was extremely unlikely, both for political reasons and because the United States had never agreed to indemnify any drug manufacturer, with the exception of the swine flu precedent. The FDA also communicated that seeking such protection for a drug company far exceeded FDA's appropriate role, but that the agency would discuss the situation with the Department.

In mid-September Roussel Uclaf hired legal counsel, Swidler and Berlin, to lobby the federal government at levels above FDA to obtain the legislation described above. On October 5, Kevin Thurm, the Department's Chief of Staff, and Harriet Rabb, the Department's General Counsel, met with lawyers from Swidler and Berlin to discuss the situation. The Department initiated the meeting to assess how the United States Government might facilitate successful completion of the negotiations between Roussel Uclaf and the Population Council. At that meeting, the company reiterated its concerns about obtaining indemnification for potential losses and was again told emphatically that the Department would not support its efforts to obtain federal legislation. Roussel Uclaf's lawyer then suggested that the

United States could exercise its statutory powers of eminent domain and take over the patent for RU-486 insofar as it covers abortifacient uses of the drug.

The Population Council appears to be attempting to meet those demands of Roussel Uclaf that do not require the enactment of federal legislation. We have been advised by the Population Council that they sent a proposed licensing agreement to Roussel Uclaf on October 11, although we do not know whether Roussel Uclaf and Hoechst will find this proposal acceptable. In addition, the Population Council's President recently met with the President of Roussel Uclaf, and is planning to send a delegation to Germany during the first few weeks of November in the hope that if Hoechst understands that the Population Council is a serious, credible organization, Hoechst will withdraw its objections and permit Roussel Uclaf to enter into an agreement with the Population Council. Despite these moderately positive developments, we do not think that the negotiations will be successfully concluded without pressure on Roussel Uclaf/Hoechst.

Moreover, we have learned that Hoechst is interested in using an American venture capitalist group as a partner for the Population Council; this group is thought to be able to secure funds sufficient to indemnify Hoechst at the level it desires. However, it is our understanding that the Population Council appears unwilling to work with this group. This issue has further complicated the negotiations.

AVAILABLE OPTIONS TO MOVE FORWARD NEGOTIATIONS

The negotiations between Roussel Uclaf and the Population Council have not been successfully concluded because of the insistence of Roussel Uclaf and Hoechst that they be protected from all economic harm if they permit RU-486 to be marketed in this country. There are two options for moving forward the stalled negotiations:

One option is to enlist the aid of Felix Rohatyn, or someone of comparable stature, to negotiate with Roussel Uclaf and Hoechst on behalf of the United States Government. The negotiations require a person with extensive experience in the international business community, especially France and Germany. In addition the person must understand the pharmaceutical industry and have the standing to participate in high-level discussions that might involve appropriate ambassadors, as well as the Health Ministers in France and Germany.

A second option is for the United States to exercise its statutory powers of eminent domain and take over the patent for RU-486, insofar as it covers the abortifacient use of the drug. The Government could then contract with a company to manufacture

and distribute the drug. As noted above, this option was suggested by Roussel Uclaf's lawyers in their October 5 meeting with the Department's Chief of Staff and is clearly the company's preferred approach. While the United States government has the legal authority to take over the patent, such an approach is rare and in this case is politically complex. Although legal, there are particular concerns about the political viability of this approach and the willingness of Congress to permit such an action to stand. We note that Roussel Uclaf did not demand that the governments of France, England, or Sweden take such steps.

NEXT STEPS

Unless you object, the Department plans to engage the services of Felix Rohatyn or someone comparable as a negotiator. This negotiator would require the State Department's support in making appropriate diplomatic contacts, both with the United States Ambassadors to France and Germany, the French and German Ambassadors to this country, and other high-level officials in France and Germany, such as the respective Health Ministers. The purpose of such contacts would be to assess the situation and determine what measures the United States could take to persuade Roussel Uclaf and Hoechst to make RU-486 available in the United States. The French and German governments might be displeased to learn that their companies are not accommodating a request made by the United States Government. In addition, a negotiator of Felix Rohatyn's caliber might identify means other than federal legislation to satisfy Roussel Uclaf's and Hoechst's concerns.

In order for the negotiator to succeed, the Department and the Administration must be unequivocal in the position that taking over the patent for RU-486 is not an option. To avoid any ambiguity on this point, the negotiator should have a letter signed by the Secretary of Health and Human Services making clear on behalf of herself and the Administration that the United States government will not take over the patent. In addition the letter should request on behalf of the Administration that Hoechst and Roussel Uclaf conclude negotiations for the entry of RU-486 onto the U.S. market expeditiously. Roussel Uclaf will have every incentive to delay the negotiations if it thinks that the United States will ultimately take over the patent. It is the Department's position that this option should be unambiguously rejected, not only because it is controversial, but because its continued existence will make it impossible for the negotiator to obtain any other agreement.

Donna E. Shalala

Tab C

Food and Drug Administration
Rockville MD 20857

September 30, 1993

NOTE TO: The Secretary

FROM: The Commissioner of Food and Drugs

SUBJECT: RU-486

On January 22, 1993, President Clinton issued a memorandum directing you to assess initiatives to promote the testing, licensing, and manufacturing in the United States of RU-486 (mifepristone).[1] The Agency has had ongoing dialogue with Roussel Uclaf to get a marketing application submitted to FDA for the drug. Both you and the FDA are on record as stating that if RU-486 is a safe and effective alternative to surgical abortion, then women in the U.S. should have access to that drug. The President also directed you to reassess whether RU-486 qualifies for importation under FDA's personal use importation policy.[2]

I. Current Marketing of the Drug

RU-486 is manufactured by the French firm Roussel Uclaf and it is approved to induce abortions in France, the United Kingdom, and Sweden. Roussel Uclaf has stated that it can act in the United States only with the approval of its parent company, Hoechst AG. Hoechst has historically refused to permit Roussel Uclaf to seek marketing approval for RU-486 as an abortifacient in the United States. Both you and I have asked Hoechst to permit Roussel Uclaf to file a new drug application (NDA) for the drug. Hoechst remains adamant in its refusal. While some members of Congress have written to Hoechst urging the company to

[1] Although there are several investigational new drug applications (INDs) on file with FDA for RU-486 for other uses, including Cushing's syndrome, diabetes, meningioma, and breast cancer, Roussel Uclaf will not pursue marketing applications for these indications until the abortion issue is resolved. FDA representatives have met with representatives from the National Institutes of Health (NIH) to discuss initiatives to promote the testing in the United States of RU-486 and other antiprogestins. NIH is limited in what it can do by the restrictions placed on its appropriation by the Hyde Amendment.

[2] In accordance with the President's January 22 memorandum, FDA has reassessed whether RU-486 might qualify for importation under FDA's personal use importation policy and whether the import alert should be rescinded. There are significant public health implications associated with rescinding the import alert, especially related to whether the drug could be safely used under these circumstances; the availability of counterfeit RU-486 on the world market for which the Agency cannot attest to purity, quality, or safety; and the fact that Roussel Uclaf's RU-486 is so tightly controlled as to be unavailable for personal importation even if the import alert were to be rescinded. The Agency submitted its recommendation on this issue to PHS on July 14, 1993. Because the import alert has been challenged by a woman who attempted to bring a small quantity of RU-486 into the country, the Agency is working with the Department on an appropriate response to this ongoing litigation.

submit a marketing application for RU-486, other Congressional members have written to Hoechst expressing their strong opposition to the marketing of RU-486 in this country. This, and the well-publicized activities of anti-abortion groups, have provided Hoechst and Roussel Uclaf with evidence that the U.S. population lacks cohesiveness on this issue and that the abortion debate continues.

II. Summary of Discussions with Roussel Uclaf Regarding Testing of the Drug

In April 1993, FDA arranged a meeting between Roussel Uclaf and the Population Council to attempt to get those parties to agree to work together to test RU-486 and file a new drug application for the drug. The Population Council was identified as the most likely group to work with Roussel Uclaf because the Population Council had a contract with Roussel Uclaf which required Roussel Uclaf to give the Population Council sufficient amounts of the drug so that the Population Council could conduct clinical trials. The contract also appeared to require Roussel Uclaf to license the drug to the Population Council if Roussel Uclaf was unwilling to sell the drug in the United States. A copy of that contract, which must remain confidential, is attached.

At the April meeting, Dr. Edouard Sakiz, president of Roussel Uclaf, raised the issue of federal legislation to indemnify Roussel Uclaf from any damages it might suffer from permitting RU-486 to go onto the United States market. Dr. Sakiz was worried about product liability actions against Roussel Uclaf if a woman had an incomplete abortion and a deformed fetus. Dr. Sakiz was also concerned about consequential damages, such as the economic costs from boycotts of Roussel Uclaf (or Hoechst) products, bombings of Roussel Uclaf/Hoechst facilities, etc. by right-to-life groups. Dr. Sakiz's view was that if the United States Government wanted RU-486 on the U.S. market, then the United States Government should make Roussel Uclaf whole for any damages Roussel Uclaf might suffer because it had agreed to the United States Government's request.

Dr. Sakiz was told quite clearly at the April meeting that such legislation would never be enacted and the FDA would not support Roussel Uclaf in its advancement of that idea.

Despite being told that there was no possibility of obtaining favorable legislation, Dr. Sakiz committed Roussel Uclaf to go forward with the Population Council to bring RU-486 onto the United States market. Specifically, at the April meeting Roussel Uclaf and the Population Council agreed:

- That Roussel Uclaf would license RU-486 to the Population Council, which would conduct a clinical trial involving 2000 women pursuant to an investigational new drug (IND) application;

- That the Population Council would ultimately submit an NDA to FDA, based on the results of the clinical trial and on other studies that have been conducted by Roussel Uclaf; and

- That the Population council, with the concurrence of Roussel Uclaf, would choose a new manufacturer for the drug, and that Roussel Uclaf would transfer its technology for making the drug to that manufacturer, because Roussel Uclaf does not want to manufacture the drug for sale in this country.

It was then left for the Population Council and Roussel Uclaf to revise the terms of their contract, while Roussel Uclaf began sending scientific information to FDA and the Population Council. The contract negotiations continued from sometime after the April meeting until recently. As of late July 1993, the Population Council thought the contract negotiations were proceeding smoothly, though slowly. In those negotiations the Population Council was represented by Jim Boynton of Christy and Viener and Roussel Uclaf was represented by Joe Orsini, its corporate council in Paris.

On August 2, 1993, Jim Boynton, the Population Council's lawyer, notified FDA that Roussel Uclaf had recently demanded that the Population Council obtain a commitment from the U.S. Government that the U.S. would enact legislation that would protect all persons who had anything to do with RU-486. This was described as similar to "right-to-access" legislation that would make it a crime for any person to hurt or harass any doctor administering RU-486, their patients, and the manufacturers, distributors, and salespersons for the drug. Roussel Uclaf also demanded that the Department of Justice promise to expend its resources to enforce this law, if enacted. Roussel Uclaf also asked for legislation that would indemnify Roussel Uclaf against any product liability exposure as a result of the use of RU-486 in this country or, as an alternative, that would ban any product liability actions against Roussel Uclaf for RU-486. Finally, Roussel Uclaf asked for legislation that would indemnify Roussel Uclaf against consequential damages. Roussel Uclaf's principal assertion is that it is willing to give the Population Council a royalty-free license, because it has decided (given a push by Hoechst), that it will forego any monetary gain from entering the U.S. market. In short, because Roussel Uclaf does not expect to make any money off of RU-486 in the U.S. market, and sees itself as permitting RU-486 to enter the U.S. market only because asked to do so by the United States Government, then it should not incur any liability exposure on account of the drug.

FDA advised Mr. Boynton that the FDA could not make a commitment to seek such legislation, pointing out that Congress had recently reenacted the Hyde Amendment and that other than the swine flu situation, the United States had never agreed to indemnify any drug manufacturer. The FDA further explained that it would go far beyond FDA's appropriate role to seek such protection for a drug company. The FDA offered to advance the idea within the Department, but was advised by Mr. Boynton that the answer given was sufficient.

In mid-September, Roussel Uclaf hired legal counsel (allegedly, Lester Hyman and John Hoff of Swindler and Berlin) to lobby the federal government at levels above FDA to obtain legislation protecting the company from potential losses, as described above.

III. Analysis

The FDA's principle objection to Roussel Uclaf's request for indemnification and related relief has been pragmatic--we did not (and do not) think Congress would ever pass such legislation. Having said that, we also think that there are other policy reasons for refusing to seek indemnification of a drug manufacturer, for example:

- It would create an unacceptable precedent for any manufacturer of a significant vaccine or drug to seek indemnification as a condition for bringing the product to market. There is little basis to distinguish RU-486 from a breakthrough AIDS drug or unique vaccine. The swine flu indemnification plan proved very problematic for the United States Government.

- If public health problems were to occur post-approval, the interest of the United States as an indemnifying party would be to disprove that problems had occurred, while FDA's obligation would be to objectively investigate and take appropriate actions to protect the public health. This would be an untenable conflict for the United States Government.

Roussel Uclaf's liability and boycott concerns should not be underestimated. Because Roussel Uclaf is willing to give the Population Council a royalty-free license, it wants to eliminate any potential for expenses due to the drug's introduction into the United States market. Roussel Uclaf has also expressed its willingness to give a royalty-free license to any other major U.S. pharmaceutical company, but has found no company willing to take the license. Roussel Uclaf could, possibly, sell the drug to the Population Council (or to others) but it appears unwilling to do so, perhaps because the drug may have important other therapeutic benefits in the future, and it may want to maintain the right to sell to those markets. However, Hoechst may be willing to simply abandon the patent or give it to the United States.

There are some that suggest that Roussel Uclaf is simply playing a delaying game--waiting until the very staunchly Catholic Hoechst CEO (Prof. Wolfgang Hilger) retires in April 1994--so that then Roussel Uclaf would be free to exploit the drug in the United States and elsewhere for all uses. Others suggest that Roussel Uclaf does not want to reach agreement with the Population Council, but is merely stalling until an international foundation is created by Dr. Etienne Balieu, the inventor of the drug and a former Roussel Uclaf employee, to which Roussel Uclaf could then sell the rights to the drug.

The speculation is fueled by the essentially unanswered question--as to why Roussel Uclaf is willing to manufacture and sell RU-486 to some markets (England, France, and Sweden) but not to others (e.g., the United States). The common thinking is that Hoechst is only willing to permit Roussel Uclaf to sell RU-486 in a country when Hoechst is forced to do so politically, and, therefore, the only way to get RU-486 onto the U.S. market is to exercise political pressure on Roussel Uclaf and on Hoechst.

This thinking appears borne out by the circumstances here--Roussel Uclaf was willing to come to the table (at FDA) when it had received pressure from President Clinton (the January 23, 1993, Executive Order), you (your March 12, 1993, letter to Prof. Hilger at Hoechst), and FDA, but that since that pressure has waned the incentive to come to an agreement has also waned.

Another possibility is that the Population Council is simply attempting to reach an agreement that leaves Roussel Uclaf with too little, and that if the Population Council were willing to settle for less (e.g., the ability to study, but not to market the drug or to indemnify Roussel Uclaf) then a deal could be reached.

IV. Recommendation for Expert Advisor

This situation calls for someone of Felix Rohatyan's caliber for several reasons. At the outset, we must make it clear that the FDA cannot take this issue too far without compromising its role as objective reviewers of the safety and efficacy of the drug. But equally as important is the fact that this is an issue where business and politics intersect quite dramatically. Because of the abortion debate, Roussel Uclaf is left alone to promote its drug. Other major U.S. drug manufacturers have, to date, refused to join forces with Roussel Uclaf--either by agreeing to go forward with their own abortifacient drug products, or by agreeing to be the manufacturer or distributor of RU-486. Therefore, Roussel Uclaf feels isolated (and vulnerable) by the U.S. demands. It will take an experienced person, familiar with the drug industry, to sort out these issues.

Second, there are pragmatic, economic concerns to be faced. Roussel Uclaf's concerns about indemnification are realistic concerns that need to be satisfied. Someone with extensive experience in the business community (in France and Germany as well as in the United States) will have a better understanding of the various ways this concern can be overcome.

Finally, there are diplomatic issues that may need to be addressed. It may be that France and Germany would be unhappy to learn that their companies were not accommodating a request made by the United States Government. The U.S. Ambassadors to France and Germany will

need to be consulted on these issues, and your counterparts in France and Germany may also need to be involved. We think that someone familiar to these circles would advance the Administration's goal to bring a safe and effective abortifacient to the U.S. market.

Mary Pendergast
for David A. Kessler, M.D.

Attachment: Contract

cc: Dr. Philip Lee
Mr. Kevin Thurm

THE WHITE HOUSE

WASHINGTON

January 22, 1993

MEMORANDUM FOR THE SECRETARY OF HEALTH AND HUMAN SERVICES

SUBJECT: Importation of RU-486

In Import Alert 66-47, the Food and Drug Administration ("FDA") excluded the drug Mifepristine -- commonly known as RU-486 -- from the list of drugs that individuals can import into the United States for their "personal use," although the drugs have not yet been approved for distribution by the FDA. (See FDA Regulatory Procedures Manual, Chapter 9-71.) Import Alert 66-47 effectively bans the importation into this Nation of a drug that is used in other nations as a nonsurgical means of abortion.

I am informed that in excluding RU-486 from the personal use importation exemption, the FDA appears to have based its decision on factors other than an assessment of the possible health and safety risks of the drug. Accordingly, I hereby direct that you promptly instruct the FDA to determine whether there is sufficient evidence to warrant exclusion of RU-486 from the list of drugs that qualify for the personal use importation exemption. Furthermore, if the FDA concludes that RU-486 meets the criteria for the personal use importation exemption, I direct that you immediately take steps to rescind Import Alert 66-47.

In addition, I direct that you promptly assess initiatives by which the Department of Health and Human Services can promote the testing, licensing, and manufacturing in the United States of RU-486 or other antiprogestins.

You are hereby authorized and directed to publish this memorandum in the Federal Register.

William J. Clinton

Tab D

MAY 11 1994

TO: Carol Rasco

FROM: Kevin Thurm

SUBJECT: RU 486

Background

Roussel Uclaf, a French subsidiary of the German company, Hoechst, holds two United States patents for its product, RU 486, which has abortifacient and potentially scores of other medical uses. The French company has engaged the Population Council, a not-for-profit organization, in over 14 months of negotiations designed to transfer Roussel Uclaf's United States patent rights to the Population Council which would then take steps to bring RU 486 to market in this country. Those negotiations are on-going.

On May 9, 1994, Roussel Uclaf wrote a letter to Secretary Shalala stating the company's wish, instead, to offer the RU 486 United States patent rights to the American government insofar as the abortifacient and other gynecological uses are concerned. The company proposes voluntarily to assign its patent rights, as so limited, to the government free of charge, asking nothing in return.

Were the government willing to accept the "gift" offer, negotiations with the Population Council would be discontinued, and the patents, as so delimited, would be made available for assignment to the United States.

Alternatively, Roussel Uclaf has advised that should its bilateral negotiations with the not-for-profit be resolved, the deal cannot be finally closed unless and until the President of the United States writes a letter to the French company asking, on behalf of the women in America, that the patents be assigned to a non-profit entity in this country.

Roussel Uclaf strongly favors the gift to the government arrangement. Your advisors strongly favor the bilateral arrangement and have taken steps consistently and firmly to so insist.

Issues for Decision

One: Whether the President is willing to write a letter to the manufacturer of RU 486 asking that the United States patents for that product be assigned to a not-for-profit entity in this country. A suitable letter might read as follows:

> It is important for the health of women in the United States that they have access to the widest possible range of safe and effective medical treatments. In support of

> that goal, in January 1993, I asked the Secretary of Health and Human Services to promote the testing and licensing of mifepristone [RU 486] and other antiprogestins in the United States.
>
> To permit the appropriate testing, development and distribution of RU 486 in the United States, I ask that your company give its mifepristone patent rights in the United States to a non-profit organization that would take all necessary steps to file a new drug application with the Food and Drug Administration [FDA], so that the FDA can determine whether the drug is safe and effective for use in the United States.

Two: If the bilateral negotiations between Roussel Uclaf and the not-for-profit entity fail, and the only option then currently on the table is the gift offer, is the government of the United States willing, and if so, under what conditions, to accept the offer of the patent rights for RU 486?

Three: If the government is not willing to accept the offer of the patent rights, on what is that decision to decline based, and how will it be communicated to the American people?

* * * * * * * * * * * * * * *

The following tabs set forth discussion of the various factors that may be brought to bear on the decision-making:

Tab 1:	History and background of RU 486 in this Administration
Tab 2:	Legal issues
Tab 3:	Bringing RU 486 to market [timing, available entities, administrative hurdles]
Tab 4:	Political considerations
Tab 5:	Press strategies and concerns

The following documents are attached for your reference;

Exhibit 1:	The President's Memorandum of January 22, 1993
Exhibit 2:	Roussel Uclaf's May 9, 1994 letter to Secretary Shalala attaching a draft offer of the gift
Exhibit 3:	Roussel Uclaf's draft letter to the President
Exhibit 4:	Minutes in French and translation of the April 26, 1994 Roussel Uclaf board meeting setting out the need for a letter from the President

BACKGROUND

Roussel Uclaf, a French subsidiary of the German company, Hoechst, holds two United States patents for its product RU 486, which has abortifacient and various other medical uses. The patents will expire in the years 2000 and 2001. Hoechst, the parent company, is co-owned by the Celanese Corporation, whose direct or indirect product lines include Nike sneakers and seat belts; the company does about $8 billion worth of business per year in the United States.

On January 22, 1993, the President directed the Secretary to "assess initiatives by which the Department of Health and Human Services can promote the testing, licensing, and manufacturing in the United States of RU 486 or other antiprogestine" (Exhibit 1). Within the month, the FDA, through Commissioner David Kessler, requested both Roussel Uclaf and Hoechst to expedite the process and met with representatives of Roussel to discuss issues. In March 1993, Secretary Shalala wrote to the president of Hoechst urging him to eliminate all corporate barriers to introduction of RU 486 in the United States.

Roussel Uclaf identified the Population Council, a non-profit organization based in New York, as the most likely vehicle through which to produce, distribute and test RU 486; the two parties have a 1982 contract which gives the Population Council some limited rights to license Roussel Uclaf product in this country.

Over the past fourteen months, the two parties have conducted on-again/off-again negotiations over a distribution scheme, liability insurance (product and damage to property), and insurance for lost profits due to economic boycotts of non-related products. During these talks, Roussel, in addition to the three main issues, occasionally raised subsidiary matters; these bumps in the road served to delay the negotiations (some believe that Roussel was in a holding pattern in anticipation of corporate leadership changes in January and April of this year). In several newspaper stories on this issue during this period, representatives of the two parties have been quoted saying they expected a deal shortly. Obviously this has yet to materialize.

Last fall, lawyers representing Roussel Uclaf met with HHS officials to discuss ways the federal government might help the negotiations. Over a series of meetings, the corporation's lawyers presented a variety of requests, including whether the Administration would seek legislation indemnifying Roussel for all potential damages or would seize the patents. HHS officials repeatedly told Roussel's lawyers that neither was a possibility, and that the deal should be done through the private parties.

On April 14, 1994, the Secretary, along with other HHS officials, met with representatives of the two parties, including Professor

Ernst Afting (current CEO of Roussel), Dr. Edouard Sakiz (past CEO and current Board Chair of Roussel), and Margaret Carlson (head of the Population Council). The Secretary stated that the U.S. government would neither seek legislation indemnifying Roussel nor seize the patents. She made clear to the parties the importance she attached to the introduction of the product in the U.S. through an agreement between them. She ended the meeting by imposing a May 15, 1994 deadline for successful completion of their negotiations.

In light of this deadline and hearings scheduled by Congressman Ron Wyden for 10:00 a.m. on May 16 to obtain a status report, the parties have continued their negotiations. Although many issues have been resolved, some remain: the extent of insurance coverage for product liability and damage to property, and a "pull the plug" option which would give Roussel the authority to require the Population Council to withdraw the product from the market if the potential liability from all lawsuits exceeded a specified amount.

On April 26, 1994, the Board of Roussel Uclaf passed a resolution authorizing under certain circumstances the assignment of patent rights to either the United States government or to a non-profit organization (Exhibit 4). If the rights are to be given to a non-profit, the President of the United States must so request by letter on behalf of the women of the country (see draft letter in cover memo).

By letter of May 9, 1994, Roussel notified the Secretary that it was prepared to assign the patent rights (for abortifacient and other gynecological uses) to the government and attached a draft letter to the President from Professor Afting, the president and CEO of Roussel (Exhibits 2 and 3). This draft letter closely mirrored an earlier informal draft discussed with Kevin Thurm, Harriet Rabb and David Kessler during the prior week.

Discussions between the parties are scheduled to continue through the end of the week. If the private arrangement is not concluded, we must be prepared to have an answer to Roussel's letter which we believe the company would send (or at least publicize). There is some "buzz" among pro-choice and women's groups about this issue so there is a chance developments will leak before the deal is finished or the letter is formally sent.

LEGAL ISSUES DISCUSSION

I. **Gift Acceptance.** The first question is whether the government should insist that any gift be for all known medical uses, not just abortifacient and gynecological [including, perhaps, "morning after"] uses. On the one hand, the broader rights may make the patent more attractive to potential licensees. On the other hand, some potential licensees may be appropriate repositories of the government's patent rights for the designated uses, but not the full range of known medical uses. Finally, the burden of testing and bringing forward the product for abortifacient and gynecological uses may be more than enough obligation. The responsibility of pursuing research and testing on all the known medical uses to bring the promising ones to fruition may be more than the government and any licensee want to assume.

The Secretary has statutory authority to accept a gift, such as a patent, on behalf of HHS's Public Health Service. Alternatively, the directors of the national research institutes at HHS's National Institutes of Health (NIH) have statutory authority to accept gifts to support the activities of their institutes. Each option has pluses and minuses.

A. Secretarial gift acceptance. Because patents are intangible property, by statutory directive, the evidence of the gift (in this case, the original patent assignments), must be lodged with the Department of the Treasury. Treasury has the discretion to hold the property or liquidate it at HHS's request. There is unlikely to be a problem raised by Treasury, but, to date, that Department has had no part in the RU 486 issue and must be consulted should this route be chosen.

B. NIH gift acceptance. No involvement of Treasury is required. Gifts to NIH institutes must be made to support the activities of the receiving institute - so a showing of such purpose would have to be made. This is not likely to pose a problem, but no work has been done to identify a likely institute recipient or to prepare the gift justification.

Finally, with regard to gift acceptance, since Roussel Uclaf is an entity doing business with HHS, including specifically the Public Health Service and its components, the government will have to be sure that accepting the gift does not give rise to a public perception concern. There is no ethical impediment to accepting gifts from entities so positioned, but care must be taken to weigh the benefits and consequences so that the public can be assured that no favor has been curried or promised. In fact, it has not.

II. **Transfer of the Gift.** Roussel Uclaf has offered to assign its rights to the abortifacient and gynecological patent uses to the government. Were the United States to accept the assignment

from Roussel Uclaf, the government would in turn find a licensee or licensees willing and able to take responsibility for obtaining FDA approval and bringing the product to market. Although it is conceivable that the government could perform these tasks itself, only the Department of Defense now manufactures drugs on a large scale.

Since, by law, federal agencies are authorized to grant licenses in federally owned patents, were the government to have the patents by assignment, subsequent licensing arrangements are possible. Additionally, patent law provides the patent owner (or, in this case, the patent assignee) with the right to sue for patent infringement. Such capacity to bring suit could be consequential if counterfeit product began to appear in the United States.

III. **Licensing the United States Patent Rights.** Government agencies are authorized by law to grant non-exclusive, exclusive or partially exclusive licenses under federally-owned patents. Licenses to PHS-owned inventions are negotiated by the NIH Office of Technology Transfer in accordance with government-wide regulations.

Under the regulations, non-exclusive licenses can be given by the government relatively easily and directly to any applicants, generally speaking, whose capacity to act responsibly regarding the license has been demonstrated.

Exclusive or partially exclusive licenses are subject to a different, but not much more difficult process. Notice of the patent's availability must be published in the Federal Register, and a sixty day period for filing written objections must be allowed. No less than three months after the date of publication, and after consideration of any objections received, an exclusive or partially exclusive license may be granted. In that event, the agency must make determinations regarding the necessity for an exclusive license, rather than a nonexclusive one, the effect of the license on competition, and whether small business firms have been given first preference in accordance with the statute and regulations.

If and once the United States accepts the gift, it will be critically important that some bidder(s) come forward seeking a license to bring the product to market. Roussel Uclaf's efforts to shop this product around to United States pharmaceutical companies to get one or more to take up the responsibility of bringing RU 486 to market have been unsuccessful. Roussel Uclaf reports that the reluctance reflects other companies' unwillingness to bear (i) the product liability risks associated with the abortifacient or (ii) the political pressure from anti-abortion forces.

IV. **Possible United States Tort Liability.** The likelihood of United States tort liability depends, in large measure, on the

government's role in bringing RU 486 to market. Through sovereign immunity, the United States government is not subject to liability except to the extent that it consents to be sued. The Federal Tort Claims Act (FTCA) is a statutory limited waiver of sovereign immunity and, thus, acts as consent to being sued. Under the FTCA, the government is liable for personal injury caused by the negligent or wrongful act or omission of a Federal employee under circumstances where the government, if a private party, would be liable to the plaintiff. It would be unlikely for a court to allow a suit to go forward against the government under the FTCA if the government merely performed the "discretionary functions" of accepting a gift, licensing the patents, and acting on an application for FDA to approve a drug.

However, were the government to become enmeshed in facilitating or playing a direct role in the transfer of the technical background information that makes it possible actually to make RU 486, for example, the government risks being drawn into liability. An approach which limits the government's role in bringing RU 486 to market, while solving the lion's share of the potential government liability risk, creates other problems. Without the backup technical "know how," it would be years before any government licensee could create the product. Since it is unlikely that a licensee would bid for these patent rights without the actual prospect of bringing the product into existence, the United States could be left holding the patents with no licensee willing to step up and take them.

Alternatively, if a European or other off-shore manufacturer made the product in a fashion that meets FDA standards, the product is potentially importable by a government licensee. One wrinkle on this process results from the technology transfer regulations referenced above which note that normally, licensees of United States patents have to agree that the product will be produced substantially in the United States.

In short, to the extent the government refuses to become involved in actually transferring the technology, tort liability is kept at bay. But licensees may be kept at bay as well, leaving the government holding the patents with no prospect of bringing RU 486 to the women in America.

BRINGING RU 486 TO MARKET

A. Direct Patent Transfer to Population Council

If Roussel Uclaf agrees to license its patent rights in RU 486 to the Population Council, the Population Council would then have to take the following steps:

o Locate a drug manufacturer that would be willing to manufacture RU 486 for the United States market (we are advised that such a manufacturer has been identified by the Population Council).

o Obtain information from Roussel Uclaf on how Roussel Uclaf manufactures RU 486 and on its testing of the drug, so that the new manufacturer could follow parallel processes and the Population Council could refer to Roussel Uclaf's animal and human testing of RU 486 in any submission to the Food and Drug Administration. If Roussel Uclaf provides this information and technology transfer, it will significantly shorten the amount of time it will take to bring the drug to the United States market (assuming the drug is found to be safe and effective by FDA). With Roussel Uclaf's information, it might take six to twelve months for the Population Council's manufacturer to begin production of the drug, and for the Population Council to file its marketing application with the FDA. If Roussel Uclaf refuses to provide such information, it will take the Population Council eighteen months to two years to begin production, and up to five years to repeat the animal and human tests that show whether the drug is safe and effective.

Roussel Uclaf has stated that they will transfer the technology to the Population Council, but we do not consider this a strong assurance.

o Begin some clinical testing of the drug in the United States. Clinical trials, though not absolutely necessary for FDA approval, would permit women in the United States to have access to the drug, and for United States physicians to become familiar with the drug, while the Population Council prepared its marketing application for the FDA.

If Roussel Uclaf were to provide French-made RU 486 to the Population Council for the clinical trials, such trials could begin in the United States in approximately six months (five months for the Population Council to design its trials and find physicians willing to do the trials, and one month for FDA approval). If Roussel Uclaf were not willing to provide the drug for clinical trials, such trials would have to wait until (1) the Population Council's manufacturer could begin production of the drug, and (2) either Roussel Uclaf gave the Population Council its animal studies or the Population Council did its own animal studies.

Roussel Uclaf has stated that it would provide the French-made RU 486 to the Population Council for the clinical trials, but again we do not consider this a strong assurance.

o File a marketing application with the FDA. As indicated above, if Roussel Uclaf provides information and transfers its technology to the Population Council, a marketing application could be filed with the FDA within six to twelve months. FDA review would take no longer than six months. Many of the scientific decisions on the proper use and distribution of the drug have already been considered by the FDA, based on information already provided to FDA by Roussel Uclaf and the Population Council. Roussel Uclaf would not need to finish its United States clinical trials before filing a marketing application with FDA; such trials could be used to refine the use of the drug at a later time.

B. Patent Transfer to the United States

If Roussel Uclaf gives its patents to the United States, the United States would have to take the following steps:

o The United States would have to determine the scope of the rights given to the United States -- are the rights only in the abortifacient and other gynecological uses of the drug, or in all uses of the drug (e.g., gynecological uses, Cushing's disease, breast cancer).

o The United States would then need to transfer its rights in the patents to a third party. This process is discussed at Tab 2, and would take at least six months.

o The license holder would then need to take all of the steps outlined above, i.e., find a manufacturer, conduct the necessary tests, and file a marketing application with the FDA. The length of time these steps will take depends on whether Roussel Uclaf is willing to transfer its information, technology, and the drugs necessary for clinical trials to the license holder. Roussel Uclaf has advised the government that it would provide the information and French-made RU 486 for clinical trials to the United States' licensee, but it could change its mind.

It is difficult to determine whether the United States's license holder would take appreciably longer to bring RU 486 to market than the Population Council would need if the Population Council received a direct transfer of rights from Roussel Uclaf. Obviously, if the United States licensee is the Population Council, little time will be lost above that associated with the transfer of the patent rights from the United States to the Population Council. If another group becomes the United States's

licensee, that group might be able to bring the drug to the United States market slightly faster than the Population Council (if the group chosen was very familiar with the drug, had a good manufacturing facility, the cooperation of Roussel Uclaf, experience in FDA marketing applications, and excellent contacts with United States physicians) or much slower (if the group falls short on any factor).

We anticipate that if Roussel Uclaf gives its patent to the United States, it will add at least six months, and quite possibly twelve to eighteen months, onto the time needed to bring the drug to the United States market. This estimate excludes any additional time generated by litigation (see Tab 2).

POLITICAL ISSUE DISCUSSION

In viewing the various options, it is important to place them in a broader political context, particularly as they relate to health care reform, given the likelihood that Congress will narrow the current Health Security Act provisions that provide for abortions under pregnancy-related services.

Because of this situation with the Health Security Act, the introduction of RU 486 will be of greater significance to the pro-choice and women's groups. If the Administration is viewed as closing the door or rejecting an apparently reasonable offer on RU 486, then the path toward reaching a non-confrontational agreement with the advocates on the Health Security Act could become much more difficult. It is, therefore, extremely important that the decision concerning RU 486 be placed in the context of promoting women's health and maintaining the close relationship of the Administration to these groups.

With regard to other political considerations, the acceptance of RU 486 by the federal government, as opposed to by a private non-profit organization, would most certainly lead to a floor amendment on the Labor, HHS appropriations bill, or other legislative vehicle to prohibit federal funds from being used in conjunction with RU 486. It is difficult to predict the exact nature of the amendment. However, in the last Congress, Representatives Dornan, Dannemeyer, Lent, Bartlett, Bunning and Hunter co-sponsored a bill to prohibit federal funds from being used for clinical studies of RU 486 as an abortifacient. Given the likelihood of another Hyde-type amendment on the House and Senate floors this year, as well as the expected abortion-related amendments on health care reform, the members of the House and Senate will be frustrated at having to face another abortion-related vote (on RU 486 appropriation limits). The outcome of such a vote is difficult to predict.

To date, we have worked very cooperatively with Congressman Ron Wyden, the chief Congressional advocate in providing access to RU 486 to women in this country. We expect to be able to continue this close working relationship through the upcoming hearing on May 16. Because Congressman Wyden has postponed past hearings, and is very frustrated by the fourteen months of negotiations, it is unlikely that he would be willing to postpone the May 16 hearing. He is convinced that Roussel Uclaf and Hoechst have been stalling for time, and that it is important to remain firm on the hearing date in order to force agreement or to make it clear to the American public that the companies have no intention of providing RU 486 to the American market.

Finally, regardless of the precise wording of the President's January 22, 1993 memorandum, the expectation it created among the pro-choice and women's groups is that the federal government will do everything possible to get RU 486 introduced in this country. Leaders of these groups will be concerned with Administration action on health care reform and other issues, including the choice to replace Justice Blackmun. Saying "no" to a facially reasonable offer by Roussel Uclaf weakens our political base and may subject the President to criticism that he is not sticking to his original position.

Given the expression of Presidential support for RU 486 in January 1993, a "yes" adds marginal political cost (separate from issues like health care reform). For 1996 purposes, we probably lose few friends and anger few voters not already positioned on this or related issues.

A "yes", however, also means the Administration will have this issue on its front burner for a significant period of time. Anticipated floor amendments in Congress, rallying at HHS or other government buildings by pro-life groups, and the necessarily public process to secure licensees will provide ample opportunity for Republicans and others opposed to the Administration to focus attention on this decision and on its aftermath.

LIST OF MEMBERS INTERESTED IN THE RU-486 ISSUE

HOUSE

Ron Wyden
Henry Waxman
Michael McNulty (D-NY)
Jim Bunning (R-KY)
Robert Dornan (R-CA)
Duncan Hunter (R-CA)

SENATE

Carol Moseley Braun (D-IL)
Paul Simon (D-IL) (wrote on behalf of constituent)
John Breaux (D-LA) (wrote on behalf of constituent)

BACKGROUND

For five years Wyden has been by far the most active and vocal Member on RU-486. He has held numerous hearings and cosponsored a bill with Waxman in the last Congress to overturn the FDA import ban. Also in the last Congress, 6 Republicans (Dornan, Dannemeyer, Lent, Bartlett, Bunning, and Hunter) cosponsored a bill to prohibit federal funds from being used for clinical studies of RU-486 as an abortifacient. No one in the Senate is consistently active on this issue.

Obviously, the womens' caucus will be interested in any actions taken on Ru-486 as will the pro-life caucus (especially Hyde, Helms, and C. Smith). However, in the last four years the Department has not received RU-486 letters from either group.

Very little mail has been received by the Clinton Administration on RU-486. A typical letter is the attached C. Moseley-Braun letter inquiring as to the status of the President's Directives.

In the Bush Administration a typical letter is the attached California delegation letter on RU-486 as an important option for American women. Also, letters often stressed the importance of allowing research on RU-486 to go forward in areas of breast cancer, glaucoma, Cushing's disease, etc.

Please let me know if I can get additional information for you.

PRESS ISSUES DISCUSSION

If negotiations with the Population Council collapse, the Clinton Administration will be left with two possible courses of action. The following is an examination of the public relations ramifications of both choices:

If the Administration decides to accept the gift of the patent from Roussel Uclaf, for purposes of insulating the White House, it should be accepted by Secretary Donna Shalala at the direction of the President of the United States and on behalf of the women in America. This could be done in a press conference on Friday, May 13, 1994, with up to four principals: Secretary Shalala, Roussel Uclaf President, Population Council (if they would agree to run the clinical trials) and possibly Congressman Ron Wyden (who has been pushing this issue on Capitol Hill).

It would be made very clear that this step is the result of the process that was set in motion by President Clinton's memorandum of January 22, 1993, and that it is being taken because it was impossible for Roussel Uclaf to come to closure with a private sector entity. Because a non-surgical (and sometimes safer) abortion alternative would thus be available to women in the United States (as it is to many women in Europe), accepting the patent gift should be touted as a reproductive rights victory for American women and another example of the Clinton Administration's commitment to deliver on its promises. However, Secretary Shalala's remarks would be tempered by caution about the long and difficult road ahead and the potential roadblocks to bringing RU 486 to the marketplace.

While it should not be a part of the formal press conference, there should be a concerted effort on the part of the HHS Public Affairs team to place stories that outline the hurdles that must be overcome to shield the Administration against the fallout from our allies in the event efforts to get RU 486 to market become stalled in bureaucratic process, in Congress or for other reasons.

Because the Clinton Administration would actually be in possession of the RU 468 patent for a period of time while the licensing process moves foreward, during that time, the Administration may well be the focus of protest by conservative organizations that have become increasingly vocal and militant. These groups have suffered recent setbacks in court (e.g. a ruling that has imposed massive fines and barred them from physically blocking access to abortion facilities). They would welcome an extremely high visibility focal point for their activities. Protest marches in front of the White House and HHS are imaginable, and the conservative talkshow circuit would help to sustain the furor. This could go on while other abortion-related issues are before Congress, including debate on the Health Security Act and the FY 1995 enactment of the Hyde

Amendment. In the worst case, it could put the abortion issue centerstage, with the Clinton Administration as a high-profile player right up through the kick-off of the 1996 re-election campaign.

It would also be necessary to recruit a cadre of lawmakers, pro-choice and women's advocates willing and able to speak up for the Administration over the course of this heated debate. That is critically important for holding our own on the conservative talkshow circuit.

If the Administration decides to reject the gift of the patent from Roussel Uclaf, news of that decision should be disclosed in a press conference on Friday, May 13, 1994, by Secretary Shalala and FDA Commissioner David Kessler. It will be necessary to construct a rationale for why that course of action is better than the alternative one for American women. The argument will have to be that giving the patent to the United States government does not speed the drug to the American marketplace. In fact, it does just the opposite. Administrative regulatory process and the potential for legislative stonewalling could be very time consuming and could ultimately prevent the women in America from gaining access to
RU 486.

We should also highlight in the Secretary's statement the unprecedented nature of what Roussel Uclaf was attempting to position the United States to do. Never before has a patent been accepted by the government. The novelty of the situation makes the issue potentially more likely to be tied up in litigation or legislative maneuvering. One of the speakers would provide details of the formidable obstacles that may delay or even prevent the United States from moving the drug onto the market.

If Roussel Uclaf is willing to grant the United States patent rights for using RU 486 only for abortifacient and other gynecological purposes, another potential argument we could embrace is the position that we wanted more than the rights they were willing to grant because our interest in this drug goes beyond the issue of abortion, the need for which we are committed to making as rare as possible.

We would stress that a private sector deal is the only viable option for getting RU 486 quickly through clinical trials and into the market place. We should outline in detail all that the Population Council did to try and close the deal during the 14-month negotiations with Roussel Uclaf. The message, either implicitly or explicitly, is that Roussel Uclaf does not really want to close a deal with an entity that clearly has the potential to bring RU 486 to the marketplace because the company fears pressure from American conservatives.

Our position should be publicly to challenge Roussel Uclaf to go back to the bargaining table with the Population Council or to open negotiations with another entity; to stop playing games; and to get serious about responding to the request that President Clinton made of them almost a year and a half ago.

Without a doubt, a "no" will subject the Administration to a firestorm of protest by pro-choice and women's groups; and there will be few natural political allies vocally defending this decision, particularly in light of the relative difficulty of explanation.

* * * * * * *

It should be noted that Roussel Uclaf has already begun, informally, to circulate word of its potential offer to the United States. Many representatives of the pro-choice community already know about the potential gift offer. We may be forced to confront a news account of the issue prior to the Congressional hearings on May 16, 1994. Such a story will, undoubtedly, be presented from the Roussel Uclaf perspective as opposed to the Administration's point of view.

THE WHITE HOUSE

WASHINGTON

January 22, 1993

MEMORANDUM FOR THE SECRETARY OF HEALTH AND HUMAN SERVICES

SUBJECT: Importation of RU-486

In Import Alert 66-47, the Food and Drug Administration ("FDA") excluded the drug Mifepristine -- commonly known as RU-486 -- from the list of drugs that individuals can import into the United States for their "personal use," although the drugs have not yet been approved for distribution by the FDA. (See FDA Regulatory Procedures Manual, Chapter 9-71.) Import Alert 66-47 effectively bans the importation into this Nation of a drug that is used in other nations as a nonsurgical means of abortion.

I am informed that in excluding RU-486 from the personal use importation exemption, the FDA appears to have based its decision on factors other than an assessment of the possible health and safety risks of the drug. Accordingly, I hereby direct that you promptly instruct the FDA to determine whether there is sufficient evidence to warrant exclusion of RU-486 from the list of drugs that qualify for the personal use importation exemption. Furthermore, if the FDA concludes that RU-486 meets the criteria for the personal use importation exemption, I direct that you immediately take steps to rescind Import Alert 66-47.

In addition, I direct that you promptly assess initiatives by which the Department of Health and Human Services can promote the testing, licensing, and manufacturing in the United States of RU-486 or other antiprogestins.

You are hereby authorized and directed to publish this memorandum in the Federal Register.

William J. Clinton

ROUSSEL UCLAF

Professeur Edouard Sakiz / Henri-Gérard Afting
Président du Directoire

Paris, May 9, 1994

Honorable Donna SHALALA
Secretary of Health and Human Services
Room 615 F
Hubert Humphrey Building
200 Independence Avenue SW
WASHINGTON, D.C. 20201
USA

Attention : Mr. Kevin THURM

Dear Secretary Shalala,

Following various meetings with your Staff and with FDA officers, the latest on May 6, 1994 with Dr. Kessler, we would like to confirm that we are ready to assign our US patent rights on RU 486 in accordance with the attached draft letter from us to the President of the United States of America.

This document is substantially similar to the draft that was given to Mr. Kevin Thurm, on April 29, 1994, by our counsel Lester Hyman, to allow a review of the situation by your Administration.

Of course we will continue to work with you and all relevant people in a constructive spirit and we look forward to meet you personally by the end of this week, as planned.

Sincerely,

Pr. R-G. AFTING
President & CEO

cc. Dr. KESSLER

35, Boulevard des Invalides 75323 Paris Cedex 07
[illegible]

ROUSSEL UCLAF

DRAFT

Paris, May ..., 1994

Honorable William J. CLINTON
President of the United States
The White House
1600 Pennsylvania Avenue NW
WASHINGTON, D.C. 20500
USA

Attention : Ms. Nancy HERNREICH

Dear Mr. President,

You have requested that ROUSSEL UCLAF allow the RU 486 compound to be used in your country.

We have been working to react to that request in a responsible manner.

I now am pleased to inform you that we have decided to contribute mifepristone (RU 486) for abortifacient purposes (and other gynecological uses) to the people of the United States of America, completely free of charge, by voluntarily assigning our relevant patent rights to the US Government.

This an unconditional gift, we ask for nothing in return.

Sincerely,

Pr. E-G. AFTING
President & CEO

35, Boulevard des Invalides 75323 Paris Cedex 07

PROJET 09.05.94

ROUSSEL UCLAF
Société anonyme à Directoire et Conseil de Surveillance
au capital de 544.749.300 F.
Siège social : 35, Boulevard des Invalides 75007 PARIS
R.C.S. Paris B 542 000 021

Extrait du Projet de Procès-Verbal
de la séance du Conseil de Surveillance du 4 Mai 1994
à 17 h 30

Présents

Membres du Conseil de Surveillance :

Dr. E. SARIZ, Président,
Dr. M. FRUEHAUF, Vice-Président,
MM. F. BOISSON, C. de CROISSET, le Pr. J. DAUSSET, E. ERAMBERT,
le Pr. G. MILHAUD, H. MONOD, E. de ROYERE, le Dr. K.G. SEIFERT.

Sans voix délibérative :

Pr. R.G. APTING, Président du Directoire,
M. G. JACQUINSON, Directeur Général, Membre du Directoire,
M. D. CAMUS, Membre du Directoire,
M. B. WINICKI, Membre du Directoire.

M. J.F. CHAVANCE et Mme D. PIERRON, Délégués du Comité Central d'Entreprise.

M. F. DESCOURS, Secrétaire du Conseil.

Absents excusés

M. le Dr. G. METZ, Membre du Conseil de Surveillance,
M. J. MISCHE, Membre du Conseil de Surveillance.
MM. F. BRECHARD et D. GAILLET, Délégués du Comité Central d'Entreprise.

.....

.../...

MIFEPRISTONE - ÉTATS-UNIS

Le Docteur E. SAKIZ informe le Conseil de Surveillance que son assentiment est demandé sur les décisions que le Directoire va être amené à prendre à propos de la mifépristone aux États-Unis d'Amérique, compte tenu des exigences pressantes formulées au plus haut niveau par les autorités gouvernementales fédérales de ce pays.

Étant donné les caractères très particuliers du système médical des États-Unis par comparaison à celui des pays d'Europe où la mifépristone est actuellement utilisée, et considérant également le climat hautement conflictuel créé autour de ce produit aux États-Unis, le Directoire estime que ROUSSEL UCLAF ne saurait en aucune façon s'impliquer elle-même dans la production ou la diffusion de la mifépristone aux États-Unis.

Toutefois, prenant acte de la volonté du gouvernement américain de procurer aux citoyennes des États-Unis cette alternative médicale à l'interruption chirurgicale de la grossesse, le Directoire s'est résolu à offrir au gouvernement des États-Unis de lui céder, sans rémunération, les deux brevets référencés "U.S. Patents Nos. 4,386,085 and 4,447,424".

Au cas où ce gouvernement déclinerait cette offre pour lui-même tout en la jugeant recevable par une institution qu'il désignerait à cet effet, ROUSSEL UCLAF accepterait de poursuivre dans cette voie et de passer les accords nécessaires, à condition d'en être formellement requise par une lettre officielle, portant la signature du Président des États-Unis, et d'obtenir un certain nombre de garanties contractuelles.

Le Conseil de Surveillance prend acte de cette position qui n'appelle de sa part aucune objection, et manifeste ainsi au Directoire l'assentiment de principe sollicité.

.....

[Translation of Fax from Dr. Sakiz to Mary Pendergast of draft minutes of the Supervisory Board Meeting of May 4, 1994]

MIFEPRISTONE - UNITED STATES

Dr. E. SAKIZ informed the Supervisory Board ("Conseil de Surveillance") that its assent is requested concerning decisions that the Director ["le Directoire"] is being led to take a propos mifepristone in the United States of America, taking account of pressing exigencies formulated at the highest level by authorities of the federal government of that nation.

Given the very particular characteristics of the U.S. medical system, in comparison to that of the European countries where mifepristone is currently used, and considering equally the highly conflicted climate created around this product in the U.S., the Director deems that ROUSSEL UCLAF would be in no way implicated itself in the production or distribution of mifepristone in the United States.

Nevertheless, considering the wish of the American government to procure for U.S. citizens this medical alternative to the surgical termination of pregnancy, the Director has resolved to offer to cede to the government of the United States, without remuneration, the two patents referred to as "U.S. Patents Nos. 4,386,085 and 4,447,424."

In the event that the government should decline this offer for itself and at the same time judging it receivable by an institution that it would designate to this end, ROUSSEL UCLAF would accept this path and would adopt the necessary agreements, on the condition of being formally required by an official letter, bearing the signature of the President of the United States, and of obtaining a certain number of contractual guarantees.

The Supervisory Council acknowledged this position, which generated no objections, and manifested to the Director its assent to the principle being offered.

[translated by L. Bachorik, 5/10/94]

Tab E

THE WHITE HOUSE

WASHINGTON

May 16, 1994

Dr. Edouard Sakiz
Chairman, Supervisory Board
Roussel Uclaf
35, boulevard des Invalides
75323 Paris Cedex 07
FRANCE

Dear Dr. Sakiz:

It is important for the health of women in the United States that they have access to the widest possible range of safe and effective medical treatments. In support of that goal, in January 1993, I asked the Secretary of Health and Human Services to promote the testing and licensing of mifepristone (RU 486) and other antiprogestins in the United States.

I understand that since at least that time, your company has been in negotiations with The Population Council, Inc., a nonprofit organization with whom you have had dealings on mifepristone since early in the last decade. Those discussions, I understand, have been directed toward the purpose on which I charged the Secretary. I am grateful for the effort those negotiations represent.

In order to permit the appropriate testing, development, and distribution of your product, I urge, at the conclusion of your negotiations, that you bring your plans to fruition. I understand that your company will assign without remuneration your United States patent rights on mifepristone to The Population Council, Inc. which has been studying this product since 1982 and which would take all necessary steps to file a new drug application with the Food and Drug Administration, so that the agency can determine whether the drug is safe and effective for use in the United States.

On behalf of the government of the United States and for the women in America, I thank you for your work.

Sincerely,

Bill Clinton

Tab F

BETSEY WRIGHT

Jeffrey M. Friedman
James R. (Ron) Weddington

Shari L. Nichols
Kirk W. Tate

F&W

Friedman & Weddington, Attorneys, L.L.P.

502 W. 13th Street
Austin, Texas 78701
(512) 477-9641
Fax: (512) 320-8312

file

January 6, 1992

Betsey Wright
Director for Public Outreach
Transition Team
P. O. Box 615
Little Rock, AR 72203

Dear Betsey,

Enclosed is a "letter" to your boss, which I am going to try to get published. If I am unsuccessful, I may try to raise the money to print it as an ad in The N. Y. Times and other places.

Sarah and I have been discussing the notion of our setting up a non-profit corporation to license and distribute R U 486. Being non-profit would eliminate the need for products liability insurance, which is a major hang-up for a company thinking about marketing a new drug.

It's possible that such an endeavor could be the vehicle for a number of birth control efforts. Something's got to be done very quickly. 26 million food stamp recipients is more than the economy can stand.

Congratulations on your work for Clinton. It's good to see a UTYD doing good. I hope the new President can find the time to deal with the issues I raise in my letter. Please give it to him if you get a chance.

Sincerely,

Ron

Ron Weddington

Jeffrey M. Friedman
James R. (Ron) Weddington

Shari L. Nichols
Kirk W. Tate

F&W

Friedman & Weddington, Attorneys, L.L.P.

502 W. 13th Street
Austin, Texas 78701
(512) 477-9641
Fax: (512) 320-8312

Dear President-To-Be Clinton,

Some years ago another Southern Governor, when asked about the possibilities for prison reform, supposedly said something to the effect of, "Well, I don't think we're going to get very far until we get a better class of prisoner."

Well, I don't think you are going to get very far in reforming the country until we have a better educated, healthier, wealthier population.

Face it, you know that anything that even resembles the programs of Democratic Presidents in the past is going to make you a one term President. Reagan spent all our money on bombs and even if there were money for programs such as pre-natal health care, job training and day care centers it would be years before we would see any dramatic results. And, as anyone who follows education can see, more money doesn't necessarily translate into better educated kids.

But you can start immediately to eliminate the barely educated, unhealthy and poor segment of our country. No, I'm not advocating some sort of mass extinction of these unfortunate people. Crime, drugs and disease are already doing that. The problem is that their numbers are not only replaced but increased by the birth of millions of babies to people who can't afford to have babies.

There, I've said it. It's what we all know is true, but we only whisper it, because as liberals who believe in individual rights, we view any program which might treat the disadvantaged differently as discriminatory, mean-spirited and...well...so Republican.

In 1989, 27 percent of all births were to unmarried mothers, a huge percentage of whom were teenagers. If current trends continue, soon a majority of the babies born will be born into poverty and one half of the country cannot support the other half, no matter how good our intentions.

I am not proposing that you send federal agents armed with Depo-Provera dart guns to the ghetto. You should use persuasion rather than coercion. You and Hillary are a perfect example. Could either of you have gone to law school and achieved anything close to what you have if you had three or four or more children before you were 20? No! You waited until you were established and in your 30's to have one child. That is what sensible people do. For every Jesse Jackson who has fought his way out of the poverty of a large family there are millions mired in poverty, drugs and crime.

If Ronald Reagan could use the media to convince the American public that a trillion dollars of borrowed money needed to be spent to combat the "Evil Empire," then you ought to be able to persuade people to only have children when they are able to afford them. Point out that only people like George Bush who inherit money can pay for more than one or two kids in today's economy. (And even then, some of the kids grow up to do embarassing things like loot savings and loans.)

You made a good start when you appointed Dr. Elders, but she will need a lot of help. You will have to enlist the aid of sports and entertainment stars to counteract the propaganda spread by church officials seeking parishioners, generals seeking cannon fodder and businessmen seeking cheap labor that, throughout the ages, has convinced the poor that children are necessary to fulfillment as a person.

It wouldn't hurt to point out that while only 11.1 percent of three person families are below the poverty level, 20.2 percent of six person families and 28.6 percent of families of seven or more are poor. (1992 Statistical Abstract of the United States, p. 459)

And, having convinced the poor that they can't get out of poverty when they have all those extra mouths to feed, you will have to provide the means to prevent the extra mouths, because abstinence doesn't work. The religious right has had 12 years to preach their message. It's time to officially recognize that people are going to have sex and what we need to do as a nation is prevent as much disease and as many poor babies as possible.

Condoms alone won't do it. Depo-Provera, Norplant and the new birth control injection being developed in India are not a complete answer, although the savings that could be effected by widespread government distribution and encouragement of birth control would amount to billions of dollars.

No, government is also going to have to provide vasectomies, tubal ligations and abortions...RU 486 and conventional abortions. Even if we make birth control as ubiquitous as sneakers and junk food, there will still be unplanned pregnancies. There have been about 30 million abortions in this country since Roe v. Wade. Think of all the poverty, crime and misery ...and then add 30 million unwanted babies to the scenario. We lost a lot of ground during the Reagan-Bush religious orgy. We don't have a lot of time left.

You could do it, Mr. President-To-Be. You are articulate and you've already alienated the religious right with your positions on abortion and homosexuals. The middle-class taxpayer will go along with this plan because it will mean fewer dollars for welfare. The retirees will also go along because because poor people contribute very little to Social Security.

And the poor? Well, maybe if we didn't have to spend so much on problems like low birth weight babies and trying to educate children who come to school hungry, we might have some money to help lift the ones already born, out of their plight.

The biblical exhortation to "Be fruitful and multiply," was directed toward a small tribe, surrounded by enemies. We are long past that. Our survival depends upon our developing a population where everyone contributes. We don't need more cannon fodder. We don't need more parishioners. We don't need more cheap labor. We don't need more poor babies

Very truly yours,

Ron Weddington

P.S. I was co-counsel in Roe V. Wade, have sired zero children and one fetus, the abortion of which was recently recounted by my ex-wife in her book, A Question Of Choice. (Grosset/Putnam, 1992) I had a vasectomy in 1969 and have never had one moment of regret.

TAB C

RU–486: DEMONSTRATING A LOW STANDARD FOR WOMEN'S HEALTH?

HEARING

BEFORE THE

SUBCOMMITTEE ON CRIMINAL JUSTICE, DRUG POLICY, AND HUMAN RESOURCES

OF THE

COMMITTEE ON GOVERNMENT REFORM

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In order to assure that Mifeprex was used by qualified specialists, FDA and the sponsor agreed that the drug would be approved under 21 CFR 314.520. This section of Subpart H concerns safety, not effectiveness. This infrequently used regulatory provision allows approval of a drug with restrictions to assure safe use. In this case, distribution of Mifeprex is restricted to physicians qualified to supervise medical abortion and its complications and who have agreed to fully inform patients and obtain their written agreement to provide an FDA-approved patient information sheet and agreed to report serious adverse events to the sponsor.

This product met the requirements of all applicable laws and regulations, including Subpart H. As FDA made clear in the preamble to the final rule, the Subpart H regulations were intended to apply to serious or life-threatening conditions, such as depression, not only to diseases. Approval of Mifeprex under restricted distribution had nothing to do with accelerated approval based on a surrogate end point, which is a separate provision of the regulations.

FDA has monitored reports of Mifeprex-related adverse events very carefully after marketing. As of March 31, 2006, 950 cases related to the approved use were submitted to FDA. Consistent with the clinical trials' experience and the drug label, heavy vaginal bleeding was the most frequently reported adverse event, with 422 cases, followed by incomplete abortion, with approximately 400 cases. Other serious events included 88 instances of infection, with 18 of them considered severe, and 27 ectopic pregnancies. This adverse event profile was consistent with prior experience with medical termination of pregnancy.

Since approval, FDA has evaluated nine reports of death in the United States potentially associated with the approved indication. Three of these have either been found or appear to be unrelated to medical abortion. An additional death was due to a ruptured ectopic pregnancy. The use of Mifeprex is contraindicated in ectopic pregnancy. Five deaths were due to a rapidly fatal toxin mediated shock syndrome. One of these was caused by infection with Clostridium Perfringens. The four additional deaths, all in California, were caused by infection with a rare anaerobic bacterium, Clostridium Sordellii. An additional Clostridium Sordellii fatality previously occurred in a clinical trial in Canada.

This rapidly fatal toxin mediated shock syndrome was not anticipated to be a complication of medical abortion. It has not been reported in the extensive European experience to date, estimated over 1.5 million uses of the drug. Eight previous U.S. cases of fatal shock due to C. Sordellii, primarily after vaginal delivery or Caesarian delivery, have been reported in the obstetrical literature.

FDA responded aggressively to the reports, with extensive follow-up and expert consultation. Last week, NIH, CDC, and FDA cosponsored a scientific workshop on potential emerging Clostridium infections. CDC researchers identified three additional C. Sordellii cases, two fatal, that occurred after spontaneous abortion. CDC has also instituted an investigation in California looking into 321 unexplained pregnancy-associated deaths between 2000 and 2003. They have excluded 303 cases from being related to toxic shock-related syndrome and are further investigating 18 more.

TAB D

SEP 28 2000

NDA 20-687

Population Council
Attention: Sandra P. Arnold
Vice President, Corporate Affairs
1230 York Avenue
New York, NY 10021

Dear Ms. Arnold:

Please refer to your new drug application (NDA) dated March 14, 1996, received March 18, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for MIFEPREX™ (mifepristone) Tablets, 200 mg.

We acknowledge receipt of your submissions dated April 19, June 20, July 25, August 15 and September 16 and 26, 1996; January 30, March 31, July 28, August 5, September 24, November 26, 1997; January 30 (2), February 19, April 27, June 25, October 26, December 8, 1998; February 8 and 22, March 31, April 28, May 10 and 20, June 3 (2), 15, 23, 25, and 30, July 14 (2) and 22, August 3, 13, 18 and 30, September 3, 8, 13 and 30, October 5, 26 and 28, November 16 and 29 (2), December 6, 7 and 23, 1999; and January 11, 21 and 28 (2), February 16 and 24, March 3, 6, 9, 10, 30 and 31 (2), April 20, May 3, 11 and 17, June 22 and 23, July 11, 13, 25 and 27, August 18, 21 and 24, September 8, 12, 15 (2), 19 (2), 20, 21, 22, 26 (2), and 27 (2), 2000. Your submission of March 30, 2000 constituted a complete response to our February 18, 2000 action letter.

This new drug application provides for the use of Mifeprex™ for the medical termination of intrauterine pregnancy through 49 days' pregnancy.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to approve Mifeprex™ (mifepristone) Tablets, 200 mg, for use as recommended in the agreed upon labeling text. The application is approved under 21 CFR 314 Subpart H. Approval is effective on the date of this letter. Marketing of this drug product and related activities are to be in accordance with the substance and procedures of the referenced regulations.

The final printed labeling (FPL) [including the professional labeling (Package Insert), the Medication Guide required for this product under 21 CFR Part 208, the Patient Agreement Form, and the Prescriber's Agreement Form] must be identical to the submitted draft labeling (Package Insert, Medication Guide, Patient Agreement Form, and the Prescriber's Agreement Form submitted September 27, 2000; and the immediate container and carton labels submitted July 25, 2000). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative

purposes, this submission should be designated "FPL for approved NDA 20-687." Approval of this submission by FDA is not required before the labeling is used.

Under 21 CFR 314.520, distribution of the drug is restricted as follows:

Mifeprex™ must be provided by or under the supervision of a physician who meets the following qualifications:

- Ability to assess the duration of pregnancy accurately.
- Ability to diagnose ectopic pregnancies.
- Ability to provide surgical intervention in cases of incomplete abortion or severe bleeding, or have made plans to provide such care through other qualified physicians, and are able to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.
- Has read and understood the prescribing information of Mifeprex™.
- Must provide each patient with a Medication Guide and must fully explain the procedure to each patient, provide her with a copy of the Medication Guide and Patient Agreement, give her an opportunity to read and discuss both the Medication Guide and the Patient Agreement, obtain her signature on the Patient Agreement and must sign it as well.
- Must notify the sponsor or its designate in writing as discussed in the Package Insert under the heading DOSAGE AND ADMINISTRATION in the event of an ongoing pregnancy, which is not terminated subsequent to the conclusion of the treatment procedure.
- Must report any hospitalization, transfusion or other serious events to the sponsor or its designate.
- Must record the Mifeprex™ package serial number in each patient's record.

With respect to the aspects of distribution other than physician qualifications described above, the following applies:

- Distribution will be in accordance with the system described in the March 30, 2000 submission. This plan assures the physical security of the drug product and provides specific requirements imposed by and on the distributor including procedures for storage, dosage tracking, damaged product returns, and other matters.

We also note the following Phase 4 commitments, specified in your submission dated September 15, 2000. These commitments replace all previous commitments cited in the September 18, 1996 and the February 18, 2000 approvable letters. These Phase 4 commitments are:

1. A cohort-based study of safety outcomes of patients having medical abortion under the care of physicians with surgical intervention skills compared to physicians who refer their patients for surgical intervention. Previous study questions related to age, smoking, and follow-up on day 14 (compliance with return visit) will be incorporated into this cohort study, as well as an audit of signed Patient Agreement forms.

2. A surveillance study on outcomes of ongoing pregnancies.

You have agreed to provide the final Phase 4 protocols for these studies within six months.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

We also remind you that, under 21 CFR 314.550, after the initial 120 day period following this approval, you must submit all promotional materials, including promotional labeling as well as advertisements, at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We are waiving the pediatric study requirement for this action on this application.

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call [redacted]

Sincerely,

/S/

Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

TAB E

If Mifeprex* results in incomplete abortion, surgical intervention may be necessary. Prescribers should determine in advance whether they will provide such care themselves or through other providers. Prescribers should also give patients clear instructions on whom to call and what to do in the event of an emergency following administration of Mifeprex.

Prescribers should make sure that patients receive and have an opportunity to discuss the Medication Guide and the PATIENT AGREEMENT.

DESCRIPTION

Mifeprex tablets each contain 200 mg of mifepristone, a synthetic steroid with antiprogestational effects. The tablets are light yellow in color, cylindrical and biconvex, and are intended for oral administration only. The tablets include the inactive ingredients colloidal silica anhydrous, corn starch, povidone, microcrystalline cellulose, and magnesium stearate.

Mifepristone is a substituted 19-nor steroid compound chemically designated as 11ß-[*p*-(Dimethylamino)phenyl]-17ß-hydroxy-17-(1-propynyl)estra-4,9-dien-3-one. Its empirical formula is $C_{29}H_{35}NO_2$. Its structural formula is:

The compound is a yellow powder with a molecular weight of 429.6 and a melting point of 191-196°C. It is very soluble in methanol, chloroform and acetone and poorly soluble in water, hexane and isopropyl ether.

* Mifeprex is a trademark of Danco Laboratories, LLC.

CLINICAL PHARMACOLOGY

Pharmacodynamic Activity

The anti-progestational activity of mifepristone results from competitive interaction with progesterone at progesterone-receptor sites. Based on studies with various oral doses in several animal species (mouse, rat, rabbit and monkey), the compound inhibits the activity of endogenous or exogenous progesterone. The termination of pregnancy results.

Doses of 1 mg/kg or greater of mifepristone have been shown to antagonize the endometrial and myometrial effects of progesterone in women. During pregnancy, the compound sensitizes the myometrium to the contraction-inducing activity of prostaglandins.

Mifepristone also exhibits antiglucocorticoid and weak antiandrogenic activity. The activity of the glucocorticoid dexamethasone in rats was inhibited following doses of 10 to 25 mg/kg of mifepristone. Doses of 4.5 mg/kg or greater in human beings resulted in a compensatory elevation of adrenocorticotropic hormone (ACTH) and cortisol. Antiandrogenic activity was observed in rats following repeated administration of doses from 10 to 100 mg/kg.

Pharmacokinetics and Metabolism

Absorption

Following oral administration of a single dose of 600 mg, mifepristone is rapidly absorbed, with a peak plasma concentration of 1.98 mg/l occurring approximately 90 minutes after ingestion. The absolute bioavailability of a 20 mg oral dose is 69%.

Distribution

Mifepristone is 98% bound to plasma proteins, albumin and α_1-acid glycoprotein. Binding to the latter protein is saturable, and the drug displays nonlinear kinetics with respect to plasma concentration and clearance. Following a distribution phase, elimination of mifepristone is slow at first (50% eliminated between 12 and 72 hours) and then becomes more rapid with a terminal elimination half-life of 18 hours.

Metabolism

Metabolism of mifepristone is primarily via pathways involving N-demethylation and terminal hydroxylation of the 17-propynyl chain. *In vitro* studies have shown that CYP450 3A4 is primarily responsible for the metabolism. The three major metabolites identified in humans are: (1) RU 42 633, the most widely found in plasma, is the N-monodemethylated metabolite; (2) RU 42 848, which results from the loss of two methyl groups from the 4-dimethylaminophenyl in position 11ß; and (3) RU 42 698, which results from terminal hydroxylation of the 17-propynyl chain.

Excretion

By 11 days after a 600 mg dose of tritiated compound, 83% of the drug has been accounted for by the feces and 9% by the urine. Serum levels are undetectable by 11 days.

Special Populations

The effects of age, hepatic disease and renal disease on the safety, efficacy and pharmacokinetics of mifepristone have not been investigated.

Clinical Studies

Safety and efficacy data from the U.S. clinical trials and from two French trials of mifepristone are reported below. The U.S. trials provide safety data on 859 women and efficacy data on 827 women with gestation durations of 49 days or less (dated from the first day of the last menstrual period). In the two French clinical trials, safety evaluable data are available for 1800 women, while efficacy information is available for 1681 of these women. Success was defined as the complete expulsion of the products of conception without the need for surgical intervention. The overall rates of success and failure, shown by reason for failure, for the U.S. and French studies appear in Table 1.

In the U.S. trials, 92.1% of the 827 subjects had a complete medical abortion, as shown in Table 1. In 52 women (6.3%) expulsion occurred within two days, and resulted from the action of mifepristone (600 mg) alone, unaided by misoprostol, an analog of prostaglandin E_2. All other women without an apparent expulsion took a 400 µg dose of misoprostol two days after taking mifepristone. Many women (44.1%) in the U.S. trials expelled the products of conception within four hours after taking misoprostol and 62.8% experienced expulsion within 24 hours after the misoprostol administration. There were 65 women (7.9%) who received surgical interventions: 13 (1.6%) were medically indicated interventions during the study period, mostly for excessive bleeding; five (0.6%) interventions occurred at the patient's request; 39 women (4.7%) had incomplete abortions at the end of the study protocol; and eight (1.0%) had ongoing pregnancies at the end of the study protocol.

Women who participated in the U.S. trials reflect the racial and ethnic composition of American women. The majority of women (71.4%) were Caucasian, while 11.3% were African American, 10.9% were East Asian, and 4.7% were Hispanic. A small percentage (1.7%) belonged to other racial or ethnic groups. Women aged 18 to 45 were enrolled in the trials. Nearly two-thirds (66.0%) of the women were under 30 years old with a mean age of 27 years.

In the French trials, complete medical abortion occurred in 95.5% of the 1681 subjects, as shown in Table 1. In 89 women (5.3%), complete abortion occurred within two days of taking mifepristone (600 mg). About half of the women (50.3%) in the French trials expelled the products of conception during the first four hours immediately following administration of misoprostol and 72.3% experienced expulsion within 24 hours after taking misoprostol. In total, 4.5% of women in the French trials ultimately received surgical intervention for excessive bleeding, incomplete abortions, or ongoing pregnancies at the end of the protocol.

Table 1

Outcome Following

Treatment with Mifepristone and Misoprostol in the U.S. and French Trials

	U.S. Trials		French Trials	
	N	%	N	%
Complete medical abortion	**762**	**92.1**	**1605**	**95.5**
Timing of expulsion				
Before second visit	52	(6.3)	89	(5.3)
During second visit				
• less than 4 hrs after misoprostol	365	(44.1)	846	(50.3)
After second visit				
• greater than 4 hrs but less than 24 hrs after misoprostol	155	(18.7)	370	(22.0)
• greater than 24 hrs after misoprostol	68	(8.2)	145	(8.6)
Time of expulsion unknown	122	(14.8)	155	(9.2)
Surgical intervention	**65**	**7.9**	**76**	**4.5**
Reason for surgery				
Medically necessary interventions during the study period	13	(1.6)	NA	(NA)
Patient request	5	(0.6)	NA	(NA)
Treatment of bleeding during study	NA	(NA)	6	(0.3)
Incomplete expulsion at study end	39	(4.7)	48	(2.9)
Ongoing pregnancy at study end	8	(1.0)	22	(1.3)

Total	**827**	**100**	**1681**	**100**

Note: Mifepristone 600 mg oral was administered on Day 1, misoprostol 400 µg oral was given on Day 3 (second visit).

INDICATION AND USAGE

Mifeprex is indicated for the medical termination of intrauterine pregnancy through 49 days' pregnancy. For purposes of this treatment, pregnancy is dated from the first day of the last menstrual period in a presumed 28 day cycle with ovulation occurring at mid-cycle. The duration of pregnancy may be determined from menstrual history and by clinical examination. Ultrasonographic scan should be used if the duration of pregnancy is uncertain, or if ectopic pregnancy is suspected.

Any intrauterine device ("IUD") should be removed before treatment with Mifeprex begins.

Patients taking Mifeprex must take 400 µg of misoprostol two days after taking mifepristone unless a complete abortion has already been confirmed before that time (see DOSAGE AND ADMINISTRATION).

Pregnancy termination by surgery is recommended in cases when Mifeprex and misoprostol fail to cause termination of intrauterine pregnancy (see PRECAUTIONS).

CONTRAINDICATIONS

Administration of Mifeprex and misoprostol for the termination of pregnancy (the "treatment procedure") is contraindicated in patients with any one of the following conditions:

- Confirmed or suspected ectopic pregnancy or undiagnosed adnexal mass (the treatment procedure will not be effective to terminate an ectopic pregnancy);

- IUD in place (see INDICATION AND USAGE);

- Chronic adrenal failure;

- Concurrent long-term corticosteroid therapy;

- History of allergy to mifepristone, misoprostol or other prostaglandin;

- Hemorrhagic disorders or concurrent anticoagulant therapy;
- Inherited porphyrias.

Because it is important to have access to appropriate medical care if an emergency develops, the treatment procedure is contraindicated if a patient does not have adequate access to medical facilities equipped to provide emergency treatment of incomplete abortion, blood transfusions, and emergency resuscitation during the period from the first visit until discharged by the administering physician.

Mifeprex also should not be used by any patient who may be unable to understand the effects of the treatment procedure or to comply with its regimen. Patients should be instructed to review the Medication Guide and the PATIENT AGREEMENT provided with Mifeprex carefully and should be given a copy of the product label for their review. Patients should discuss their understanding of these materials with their health care providers, and retain the Medication Guide for later reference (see PRECAUTIONS).

WARNINGS

(see CONTRAINDICATIONS)

1. Bleeding

Vaginal bleeding occurs in almost all patients during the treatment procedure. According to data from the U.S. and French trials, women should expect to experience bleeding or spotting for an average of nine to 16 days, while up to 8% of all subjects may experience some type of bleeding for 30 days or more. Bleeding was reported to last for 69 days in one patient in the French trials. In general the duration of bleeding and spotting increased as the duration of the pregnancy increased.

In some cases, excessive bleeding may require treatment by vasoconstrictor drugs, curettage, administration of saline infusions, and/or blood transfusions. In the U.S. trials, 4.8% of subjects received administration of uterotonic medications and nine women (1.0%) received intravenous fluids. Vasoconstrictor drugs were used in 4.3% of all subjects in the French trials, and in 5.5% of women there was a decrease in hemoglobin of more than 2 g/dL. Blood transfusions were administered in one of 859 subjects in the U.S. trials and in two of 1800 subjects in the French trials. Since heavy bleeding requiring curettage occurs in about 1% of patients, special care should be given to patients with hemostatic disorders, hypocoagulability, or severe anemia.

2. Confirmation of Pregnancy Termination

Patients should be scheduled for and return for a follow-up visit at approximately 14 days after administration of mifepristone to confirm that the pregnancy is completely terminated and to assess the degree of bleeding. Vaginal bleeding is not evidence of the termination of pregnancy. Termination can be confirmed by clinical examination or ultrasonographic scan. Lack of bleeding following treatment, however, usually indicates failure. Medical abortion failures should be managed with surgical termination.

PRECAUTIONS

General

Mifeprex is available only in single dose packaging. Administration must be under the supervision of a qualified physician (see DOSAGE AND ADMINISTRATION).

The use of Mifeprex is assumed to require the same preventive measures as those taken prior to and during surgical abortion to prevent rhesus immunization.

There are no data on the safety and efficacy of mifepristone in women with chronic medical conditions such as cardiovascular, hypertensive, hepatic, respiratory or renal disease; insulin-dependent diabetes mellitus; severe anemia or heavy smoking. Women who are more than 35 years of age and who also smoke 10 or more cigarettes per day should be treated with caution because such patients were generally excluded from clinical trials of mifepristone.

Although there is no clinical evidence, the effectiveness of Mifeprex may be lower if misoprostol is administered more than two days after mifepristone administration.

Information for Patients

Patients should be fully advised of the treatment procedure and its effects. Patients should be given a copy of the Medication Guide and the PATIENT AGREEMENT. (Additional copies of the Medication Guide and the PATIENT AGREEMENT are available by contacting Danco Laboratories at 1-877-4 Early Option) (1-877-432-7596). Patients should be advised to review both the Medication Guide and the PATIENT AGREEMENT, and should be given the opportunity to discuss them and obtain answers to any questions they may have. Each patient must understand:

- the necessity of completing the treatment schedule, including a follow-up visit approximately 14 days after taking Mifeprex;

- that vaginal bleeding and uterine cramping probably will occur;

- that prolonged or heavy vaginal bleeding is not proof of a complete expulsion;

- that if the treatment fails, there is a risk of fetal malformation;

- that medical abortion treatment failures are managed by surgical termination; and

- the steps to take in an emergency situation, including precise instructions and a telephone number that she can call if she has any problems or concerns.

Another pregnancy can occur following termination of pregnancy and before resumption of normal menses. Contraception can be initiated as soon as the termination of the pregnancy has been confirmed, or before the woman resumes sexual intercourse.

Patient information is included with each package of Mifeprex (see Medication Guide).

Laboratory Tests

Clinical examination is necessary to confirm the complete termination of pregnancy after the treatment procedure. Changes in quantitative human Chorionic Gonadotropin (hCG) levels will not be decisive until at least 10 days after the administration of Mifeprex. A continuing pregnancy can be confirmed by ultrasonographic scan.

The existence of debris in the uterus following the treatment procedure will not necessarily require surgery for its removal.

Decreases in hemoglobin concentration, hematocrit and red blood cell count occur in some women who bleed heavily. Hemoglobin decreases of more than 2 g/dL occurred in 5.5% of subjects during the French clinical trials of mifepristone and misoprostol.

Clinically significant changes in serum enzyme (serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase, gamma-glutamyltransferase (GT)) activities were rarely reported.

Drug Interactions

Although specific drug or food interactions with mifepristone have not been studied, on the basis of this drug's metabolism by CYP 3A4, it is possible that ketoconazole, itraconazole, erythromycin, and grapefruit juice may inhibit its metabolism (increasing serum levels of mifepristone). Furthermore, rifampin, dexamethasone, St. John's Wort, and certain anticonvulsants (phenytoin, phenobarbital, carbamazepine) may induce mifepristone metabolism (lowering serum levels of mifepristone).

Based on in vitro inhibition information, coadministration of mifepristone may lead to an increase in serum levels of drugs that are CYP 3A4 substrates. Due to the slow elimination of mifepristone from the body, such interaction may be observed for a prolonged period after its administration. Therefore, caution should be exercised when mifepristone is administered with drugs that are CYP 3A4 substrates and have narrow therapeutic range, including some agents used during general anesthesia.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term studies to evaluate the carcinogenic potential of mifepristone have been performed. Results from studies conducted *in vitro* and in animals have revealed no genotoxic potential for mifepristone. Among the tests carried out were: Ames test with and without metabolic activation; gene conversion test in *Saccharomyces cerevisiae* D4 cells; forward mutation in *Schizosaccharomyces pompe* P1 cells; induction of unscheduled DNA synthesis in cultured HeLa cells; induction of chromosome aberrations in CHO cells; i*n vitro* test for gene mutation in V79 Chinese hamster lung cells; and micronucleus test in mice.

The pharmacological activity of mifepristone disrupts the estrus cycle of animals, precluding studies designed to assess effects on fertility during drug administration. Three studies have been performed in rats to determine whether there were residual effects on reproductive function after termination of the drug exposure.

In rats, administration of the lowest oral dose of 0.3 mg/kg/day caused severe disruption of the estrus cycles for the three weeks of the treatment period. Following resumption of the estrus cycle, animals were mated and no effect on reproductive performance was observed. In a neonatal exposure study in rats, the administration of a subcutaneous dose of mifepristone up to 100 mg/kg on the first day after birth had no adverse effect on future reproductive function in males or females. The onset of puberty was observed to be slightly premature in female rats neonatally exposed to mifepristone. In a separate study in rats, oviduct and ovary malformations in female rats, delayed male puberty, deficient

male sexual behavior, reduced testicular size, and lowered ejaculation frequency were noted after exposure to mifepristone (1 mg every other day) as neonates.

Pregnancy

Mifepristone is indicated for use in the termination of pregnancy (through 49 days' pregnancy) and has no other approved indication for use during pregnancy.

Teratogenic Effects

Human Data

Over 620,000 women in Europe have taken mifepristone in combination with a prostaglandin to terminate pregnancy. Among these 620,000 women, about 415,000 have received mifepristone together with misoprostol. As of May 2000 a total of 82 cases have been reported in which women with on-going pregnancies after using mifepristone alone or mifepristone followed by misoprostol declined to have a surgical procedure at that time. These cases are summarized in Table 2.

Table 2

Reported Cases (as of May 2000) of On-going Pregnancies Not Terminated by Surgical Abortion at the End of Treatment with Mifepristone Alone or with Mifepristone-Misoprostol

	Mifepristone Alone	**Mifepristone Misoprostol**	Total
Subsequently had surgical abortion	3	7	10
No abnormalities detected	2	7	9
Abnormalities detected (sirenomelia, cleft palate)	1	0	1
Subsequently resulted in live birth	13	13	26
No abnormalities detected at birth	13	13	26
Abnormalities detected at birth	0	0	0
Other/Unknown	26	20	46
Total	42	40	82

Several reports in the literature indicate that prostaglandins, including misoprostol, may have teratogenic effects in human beings. Skull defects, cranial nerve palsies, delayed growth and psychomotor development, facial malformation and limb defects have all been reported after exposure during the first trimester.

Animal Data

Teratology studies in mice, rats and rabbits at doses of 0.25 to 4.0 mg/kg (less than 1/100 to approximately 1/3 the human exposure level based on body surface area) were carried out. Because of the antiprogestational activity of mifepristone, fetal losses were much higher than in control animals. Skull deformities were detected in rabbit studies at approximately 1/6 the human exposure, although no teratogenic effects of mifepristone have been observed to date in rats or mice. These deformities were most likely due to the mechanical effects of uterine contractions resulting from decreased progesterone levels.

Nonteratogenic Effects

The indication for use of Mifeprex in conjunction with misoprostol is for the termination of pregnancy through 49 days' duration of pregnancy (as dated from the first day of the last menstrual period). These drugs together

disrupt pregnancy by causing decidual necrosis, myometrial contractions and cervical softening, leading to the expulsion of the products of conception.

Nursing Mothers

It is not known whether mifepristone is excreted in human milk. Many hormones with a similar chemical structure, however, are excreted in breast milk. Since the effects of mifepristone on infants are unknown, breast-feeding women should consult with their health care provider to decide if they should discard their breast milk for a few days following administration of the medications.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

The treatment procedure is designed to induce the vaginal bleeding and uterine cramping necessary to produce an abortion. Nearly all of the women who receive Mifeprex and misoprostol will report adverse reactions, and many can be expected to report more than one such reaction. About 90% of patients report adverse reactions following administration of misoprostol on day three of the treatment procedure. Those adverse events that occurred with a frequency greater than 1% in the U.S. and French trials are shown in Table 3.

Bleeding and cramping are expected consequences of the action of Mifeprex as used in the treatment procedure. Following administration of mifepristone and misoprostol in the French clinical studies, 80 to 90% of women reported bleeding more heavily than they do during a heavy menstrual period (see WARNINGS, Bleeding for additional information). Women also typically experience abdominal pain, including uterine cramping. Other commonly reported side effects were nausea, vomiting and diarrhea. Pelvic pain, fainting, headache, dizziness, and asthenia occurred rarely. Some adverse reactions reported during the four hours following administration of misoprostol were judged by women as being more severe than others: the percentage of women who considered any particular adverse event as severe ranged from 2 to 35% in the U.S. and French trials. After the third day of the treatment procedure, the number of reports of adverse reactions declined progressively in the French trials, so that by day 14, reports were rare except for reports of bleeding and spotting.

Table 3

Type of Reported Adverse Events Following Administration of

Mifepristone and Misoprostol in the U.S. and French Trials* (percentages)

	U.S. Trials	French Trials
Abdominal Pain (cramping)	96	NA
Uterine cramping	NA	83
Nausea	61	43
Headache	31	2
Vomiting	26	18
Diarrhea	20	12

Dizziness	12	1
Fatigue	10	NA
Back pain	9	NA
Uterine hemorrhage	5	NA
Fever	4	NA
Viral infections	4	NA
Vaginitis	3	NA
Rigors (chills/shaking)	3	NA
Dyspepsia	3	NA
Insomnia	3	NA
Asthenia	2	1
Leg pain	2	NA
Anxiety	2	NA
Anemia	2	NA
Leukorrhea	2	NA
Sinusitis	2	NA
Syncope	1	NA
Decrease in hemoglobin greater than 2 g/dL	NA	6
Pelvic pain	NA	2
Fainting	NA	2

* Only adverse reactions with incidence >1% are included.

OVERDOSAGE

No serious adverse reactions were reported in tolerance studies in healthy non-pregnant female and healthy male subjects where mifepristone was administered in single doses greater than threefold that recommended for termination of pregnancy. If a patient ingests a massive overdose, she should be observed closely for signs of adrenal failure.

The oral acute lethal dose of mifepristone in the mouse, rat and dog is greater than 1000 mg/kg (about 100 times the human dose recommended for termination of pregnancy).

DOSAGE AND ADMINISTRATION

Treatment with Mifeprex and misoprostol for the termination of pregnancy requires three office visits by the patient. Mifeprex should be prescribed only by physicians who have read and understood the prescribing information. Mifeprex may be administered only in a clinic, medical office, or hospital, by or under the supervision of a physician, able to assess the gestational age of an embryo and to diagnose ectopic pregnancies. Physicians must also be able to provide surgical intervention in cases of incomplete abortion or severe bleeding, or have made plans to provide such care through others, and be able to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.

Day One: Mifeprex Administration

Patients must read the Medication Guide and read and sign the PATIENT AGREEMENT before Mifeprex is administered.

Three 200 mg tablets (600 mg) of Mifeprex are taken in a single oral dose.

Day Three: Misoprostol Administration

The patient returns to the healthcare provider two days after ingesting Mifeprex. Unless abortion has occurred and has been confirmed by clinical examination or ultrasonographic scan, the patient takes two 200 µg tablets (400 µg) of misoprostol orally.

During the period immediately following the administration of misoprostol, the patient may need medication for cramps or gastrointestinal symptoms (see ADVERSE REACTIONS). The patient should be given instructions on what to do if significant discomfort, excessive bleeding or other adverse reactions occur and should be given a phone number to call if she has questions following the administration of the misoprostol. In addition, the name and phone number of the physician who will be handling emergencies should be provided to the patient.

Day 14: Post-Treatment Examination

Patients will return for a follow-up visit approximately 14 days after the administration of Mifeprex. This visit is very important to confirm by clinical examination or ultrasonographic scan that a complete termination of pregnancy has occurred.

According to data from the U.S. and French studies, women should expect to experience bleeding or spotting for an average of nine to 16 days. Up to 8% of women may experience some type of bleeding for more than 30 days. Persistence of heavy or moderate vaginal bleeding at this visit, however, could indicate an incomplete abortion.

Patients who have an ongoing pregnancy at this visit have a risk of fetal malformation resulting from the treatment. Surgical termination is recommended to manage medical abortion treatment failures (see PRECAUTIONS, Pregnancy).

Adverse events, such as hospitalization, blood transfusion, ongoing pregnancy, or other major complications following the use of Mifeprex and misoprostol must be reported to Danco Laboratories. Please provide a brief clinical and administrative synopsis of any such adverse events in writing to:

Medical Director
Danco Laboratories, LLC
P.O. Box 4816
New York, NY 10185
1-877-4-Early Option (1-877-432-7596)

For immediate consultation 24 hours a day, 7 days a week with an expert in mifepristone, call Danco Laboratories at 1-877-4 Early Option (1-877-432-7596).

HOW SUPPLIED

Mifeprex will be supplied only to licensed physicians who sign and return a Prescriber's Agreement. Distribution of Mifeprex will be subject to specific requirements imposed by the distributor, including procedures for storage, dosage tracking, damaged product returns and other matters. Mifeprex is a prescription drug, although it will not be available to the public through licensed pharmacies.

Mifeprex is supplied as light yellow, cylindrical, bi-convex tablets imprinted on one side with "MF." Each tablet contains 200 mg of mifepristone. Tablets are packaged in single dose blister packets containing three tablets and are supplied in individual cartons (National Drug Code 6487500103).

Store at 25^{0}C (77^{0}F); excursions permitted to 15-30^{0}C (59-86^{0}F) [see USP Controlled Room Temperature].

Manufactured for:

Danco Laboratories, LLC
P.O. Box 4816
New York, NY 10185
1-877-4 Early Option (1-877-432-7596)

www.earlyoptionpill.com

TAB F

NDA 20-687 MIFEPREX (mifepristone) Tablets, 200 mg

Danco Laboratories, LLC
PO Box 4816
New York, NY 10185

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS

A. To provide information to patients about the benefits and risks of MIFEPREX before they make a decision whether to take the drug.

B. To minimize the risk of serious complications by requiring prescribers to certify that they are qualified to prescribe MIFEPREX and are able to assure patient access to appropriate medical facilities to manage any complications.

II. REMS ELEMENTS

A. Medication Guide

1. A Medication Guide will be dispensed with each MIFEPREX prescription in accordance with 21 CFR 208.24.

2. Please see the appended Medication Guide.

B. Elements to Assure Safe Use

1. Healthcare providers who prescribe MIFEPREX will be specially certified.

   Danco will ensure that healthcare providers who prescribe MIFEPREX are specially certified.

   a. To become specially certified, each prescriber must complete and fax to the MIFEPREX distributor the one-time Prescriber's Agreement, agreeing that they meet the qualifications and will follow the guidelines outlined in the Prescriber's Agreement.

   b. The following materials are part of the REMS and are appended:

      i. Prescriber's Agreement.

      ii. Patient Agreement.

2. MIFEPREX will be dispensed only in certain health care settings, specifically clinics, medical offices, and hospitals.

   Danco will ensure that MIFEPREX will only be available to be dispensed in a clinic, medical office, or hospital, by or under the supervision of a specially certified prescriber. MIFEPREX will not be distributed to or dispensed through retail pharmacies.

3. MIFEPREX will only be dispensed to patients with documentation of safe use conditions.

   Danco will ensure that MIFEPREX will only be dispensed to patients with documentation of the following safe use conditions:

   a. The patient has completed and signed the Patient Agreement, and the Patient Agreement has been placed in the patient's medical record.

   b. The patient has been provided copies of the signed Patient Agreement and the Medication Guide.

C. Implementation System

The Implementation System will include the following:

1. Distributors who distribute MIFEPREX will be certified. To become certified, distributors must agree to:

   a. Ship drug only to site locations identified by specially certified prescribers in signed Prescriber's Agreements, and maintain secure and confidential records of shipments.

   b. Follow all distribution guidelines, including those for storage, tracking package serial numbers, proof of delivery, and controlled returns.

2. Danco will assess the performance of the certified distributors with regard to the following:

   a. Whether a secure, confidential and controlled distribution system is being maintained with regard to storage, handling, shipping, and return of MIFEPREX.

   b. Whether MIFEPREX is being shipped only to site locations identified by specially certified prescribers in the signed Prescriber's Agreement and only available to be dispensed to patients in a clinic, medical office, or hospital by or under the supervision of a specially certified prescriber.

3. If Danco determines the distributors are not complying with these requirements, Danco will take steps to improve their compliance.

D. Timetable for Submission of Assessments

Danco will submit REMS assessments to the FDA one year from the date of the approval of the REMS and every three years thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the assessment reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Danco will submit each assessment so that it will be received by the FDA on or before the due date.

TAB G

April 12, 2021

Maureen G. Phipps, MD, MPH, FACOG
Chief Executive Officer
American College of Obstetricians and Gynecologists
c/o Rachel Tetlow, Federal Affairs Director
rtetlow@acog.org

Skye Perryman, General Counsel
sperryman@acog.org

William Grobman, MD, MBA
President
Society for Maternal-Fetal Medicine
w-grobman@northwestern.edu

Dear Drs. Phipps and Grobman,

In your letter of April 20, 2020, to former Commissioner Stephen Hahn, you expressed concerns about the in-person dispensing requirements for certain prescription drugs during the current public health emergency. In my letter to you of March 19, 2021, I indicated that staff in the Food and Drug Administration's (FDA) Center for Drug Evaluation and Research (CDER) were evaluating the issues you raised.

Following up on my March 19, 2021, letter I am writing to report the results of CDER's review and analysis.

CDER conducted a literature search for studies pertinent to the in-person dispensing requirement in the Mifepristone REMS Program during the COVID-19 pandemic. Based on this literature search, CDER identified four publications that included relevant clinical outcome data.[1] CDER

[1] Chong E, et al. Expansion of a Direct-to-Patient Telemedicine Abortion Service in the United States and Experience during the COVID-19 Pandemic. Contraception 2021 (accepted manuscript). https://www.sciencedirect.com/science/article/pii/S0010782421000913; Kerestes C, et al. Provision of medication abortion in Hawai'i during COVID-19: Practical experience with multiple care delivery models. Contraception 2021 (accepted manuscript). https://doi.org/10.1016/j.contraception.2021.03.025; Aiken A et al. Effectiveness, Safety and Acceptability of No-test Medical Abortion Provided Via Telemedicine: a National Cohort Study. British J Obstet Gynecol 2021. https://obgyn.onlinelibrary.wiley.com/doi/10.1111/1471-0528.16668; Reynolds-Wright JJ et al. Telemedicine medical abortion at home under 12 weeks' gestation: a prospective observational cohort study during the COVID-19 pandemic. BMJ Sex Reprod Health 2021. https://srh.bmj.com/content/early/2021/02/04/bmjsrh-2020-200976

found that although there are limitations to the study designs, the overall findings from these studies do not appear to show increases in serious safety concerns (such as hemorrhage, ectopic pregnancy, or surgical interventions) occurring with medical abortion as a result of modifying the in-person dispensing requirement during the COVID-19 pandemic.

CDER also reviewed postmarketing adverse events that reportedly occurred from January 27, 2020 - January 12, 2021, with mifepristone use for medical termination of early pregnancy, along with available information about deviations or noncompliance events associated with the Mifepristone REMS Program.[2] CDER found that the small number of adverse events reported to FDA during the COVID-19 public health emergency (PHE) provide no indication that any program deviation or noncompliance with the Mifepristone REMS Program contributed to the reported adverse events.

In summary, provided the other requirements of the Mifepristone REMS Program are met, and given that the in-person dispensing of mifepristone for medical termination of early pregnancy may present additional COVID-related risks to patients and healthcare personnel because it may involve a clinic visit solely for this purpose, CDER intends to exercise enforcement discretion during the COVID-19 PHE with respect to the in-person dispensing requirement of the Mifepristone REMS Program, including any in-person requirements that may be related to the Patient Agreement Form. Further, to the extent all of the other requirements of the Mifepristone REMS Program are met, CDER intends to exercise enforcement discretion during the COVID-19 PHE with respect to the dispensing of mifepristone through the mail either by or under the supervision of a certified prescriber, or through a mail-order pharmacy when such dispensing is done under the supervision of a certified prescriber.

CDER is communicating this decision to the approved application holders subject to the Mifepristone REMS Program.

Sincerely yours,

Janet Woodcock, M.D.
Acting Commissioner of Food and Drugs

[2] See Mifepristone REMS Program at https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=390. CDER's analysis covers both products that are subject to the Mifepristone REMS Program (Mifeprex and the approved generic, Mifepristone Tablets, 200 mg).

TAB H

JUNE 24, 2022

FACT SHEET: President Biden Announces Actions In Light of Today's Supreme Court Decision on Dobbs v. Jackson Women's Health Organization

Today, President Biden announced actions that his Administration is taking to protect women who will face the grave consequences of today's Supreme Court decision. This decision expressly took away a Constitutional right from the American people that it had recognized for nearly 50 years – a woman's right to choose, free from government interference.

This decision will have devastating consequences in the lives of women around the country.

The President made clear that the only way to secure a woman's right to choose is for Congress to restore the protections of *Roe* as federal law. Until then, he has announced two actions the Administration is taking to protect women.

Protecting the Right to Seek Medical Care

As the Attorney General made clear, women must remain free to travel safely to another state to seek the care they need.

A person has the right to travel between states for whatever reason they want – it is no one else's business – especially the government's. If a woman lives in a state that restricts abortion, the Supreme Court's decision does not prevent her from traveling from her home to a state that allows it.

If any state or local official tries to interfere with women exercising this basic right, the Biden Administration will fight that deeply un-American attack.

Protecting Access to Medication

The President directed the Secretary of Health and Human Services to protect women's access to critical medications for reproductive health care that are approved by the Food and Drug Administration—including essential preventive health care like contraception and medication abortion.

More than 20 years ago, the FDA approved mifepristone to safely end an early pregnancy; this drug is also commonly used to treat miscarriages. The American Medical Association and the American College of Obstetricians and Gynecologists wrote to President Biden and Vice President Harris, asking the federal government to protect access to this care. In the face of threats from state officials saying they will try to ban or severely restrict access to medication for reproductive health care, the President directed the Secretary of Health and Human Services to identify all ways to ensure that mifepristone is as widely accessible as possible in light of the FDA's determination that the drug is safe and effective—including when prescribed through telehealth and sent by mail.

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IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF TEXAS
AMARILLO DIVISION

ALLIANCE FOR HIPPOCRATIC MEDICINE, *et al.*,	)	
Plaintiffs,	)	
v.	)	Case No. 2:22-cv-00223-z
U.S. FOOD AND DRUG ADMINISTRATION, *et al.*,	)	
Defendants.	)	

[PROPOSED] ORDER

Upon consideration of Proposed Amicus, Judicial Watch, Inc.'s, Motion of Judicial Watch, Inc. for Leave to File an Amicus Curiae Brief in Support of Plaintiffs' Complaint and Motion for Temporary Injunction, it is hereby ORDERED that:

1. Proposed Amicus, Judicial Watch, Inc.'s motion is GRANTED.

SO ORDERED this ___ day of _____, 2023.

_____
The Honorable Matthew J. Kacsmaryk
U.S. District Court Judge, ND Texas