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THE STORY OF RU-486 IN THE UNITED STATES

INTRODUCTION

On September 28, 2000, the Food and Drug Administration (the "FDA") approved mifepristone[1] as a safe and effective nonsurgical method for terminating early intrauterine pregnancy up to 49 days after the first day of a woman's last menstrual period.[2] From its initial development in France in 1980 to its official entry into the U.S. pharmaceutical market in September 2000, RU-486's 20-year journey has included numerous false starts and stops, a slow and politicized approval process, and enduring controversy. In a word, the story of RU-486 has been eventful. As each chapter in the story of RU-486 unfolded over the course of its 20-year odyssey, what started out as a mundane story about a scientific discovery in the laboratories of

[1] Mifepristone is the generic name of the first drug in the abortion pill combination that is commonly called RU-486. The term RU-486 is derived from the initials of Roussel-Uclaf, the French pharmaceutical company that developed the abortion pill, plus a serial number. *See* Philip J. Hilts, *Success with Abortion Drug Reported*, Wash. Post, Dec. 18, 1986, at C1, C19. In addition, RU-486 is known by its commercial name, Mifeprex, and by its brand name, Mifegyne. *See* Neal E. Boudette, *German Firm to Give Up Rights to Controversial Abortion Pill*, Wall St. J., Oct. 19, 2000, at A22.

[2] *See, e.g.*, Rachel Zimmerman, *FDA Gets Questions About Abortion Pill From Congressman*, Wall St. J., Oct. 20, 2000, at B2.

France quickly erupted into a controversial saga. This saga included allegations of fraud, a dozen lawsuits, a price tag of at least $50 million, political maneuvering both on a local and international level, and a delicate tension between the dictates of science, morality, the law, and public opinion.

In this paper, I will navigate you through the fascinating odyssey of RU-486 from its initial development in France to its official entry into the U.S. pharmaceutical market to the post-approval strife in which it is now embroiled. While many assumed that the FDA's approval of RU-486 on September 28, 2000 would mark the final chapter in the story of the drug's acceptance as an early pregnancy termination procedure, it actually marked the beginning of a new chapter, which ignited congressional efforts to stymie, or even abort, the growth of this chemical alternative to surgical abortion in the United States. As a result of these congressional efforts, the last chapter in the story of RU-486 remains to be written.

I. THE BIRTH OF A CONTROVERSY

A. Background: What is RU-486 and How Does It Work?

Mifepristone is an antiprogesterone agent that blocks progesterone from attaching to the wall of the uterus by binding to the progesterone receptors in the decidual lining of the uterus. It serves as a progesterone impostor, thereby preventing the real progesterone hormones from attaching to the uterine wall.[3] Progesterone is a hormone that conditions the endometrium, or mucous membrane lining the uterus, to accept and retain the fertilized egg.[4] The absence of progesterone in the uterus due to its competitive inhibition by mifepristone at the receptor site causes the uterine lining to break down and secrete prostaglandins,[5] which

[3] *See, e.g.,* Karen F. Richards, *RU-486: A Promising Birth Control Device Entangled in the Abortion Debate*, 6 J. Pharmacy & L. 117, 118 (1997).

[4] *See, e.g.,* Csilla Muhl, *RU-486: Legal and Policy Issues Confronting the Food and Drug Administration*, 14 J. Legal Med. 319, 327 (1993).

[5] A prostaglandin is an oxygenated unsaturated cyclic fatty acid that controls blood pressure or smoothes muscle contractions.

produce muscle contractions that dislodge the fertilized egg from the uterus.[6]

To more fully understand RU-486, it is important to understand how its treatment process works. Under the FDA-approved RU-486 treatment regimen, a woman who desires to undergo a nonsurgical early pregnancy termination must make three visits to a doctor's office or clinic over a two-week period. During her first visit, she takes 600 milligrams of mifepristone (three 200-milligram pills) by mouth. Two days later, she returns for 400 micrograms (two 200-microgram pills) of misoprostol, an FDA-approved oral prostaglandin that further induces uterine contractions, thereby helping to complete the process of expulsion of the fertilized egg. The reason behind the sequential administration of mifepristone and misoprostol is that the prostaglandin analogue, misoprostol, increases uterine muscle contractility beyond that which the progesterone-inhibiting action of mifepristone is able to accomplish.[7] The patient then returns for her third and final visit approximately 14 days after her first visit for a determination of whether the fertilized egg has been completely expelled from the uterus.[8] If the RU-486 regimen does not completely expel the products of conception, a supervising doctor advises the patient to undergo methods of surgical intervention such as suction, dilatation and curettage, or vacuum aspiration to complete the expulsion process.

See Merriam-Webster's Collegiate Dictionary 937 (10th ed. 1999).

[6] *See* Food and Drug Administration, Center for Drug Evaluation and Research, Division of Reproductive and Urologic Drug Products, Environmental Assessment and Finding of No Significant Impact for NDA 20-687, Mifepristone Tablets (July 9, 1996); Kari Hanson, *Approval of RU-486 as a Postcoital Contraceptive*, 17 U. Puget Sound L. Rev. 163, 169 (1993).

[7] *See, e.g.*, Remi Peyron, M.D., *et al., Early Termination of Pregnancy with Mifepristone (RU 486) and Oral or Vaginal Misoprostol,* 332 New Eng. J. Med. 984 (1995).

[8] HHS News, U.S. Department of Health and Human Services*, FDA Approves Mifepristone for the Termination of Early Pregnancy* (Sept. 28, 2000), *available at* <http://www.fda.gov/bbs/topics/news/new00737.html>.

B. The French Abortion Pill FuryThe origins of the RU-486 treatment regimen that I just described began in 1970 when French researchers discovered that antiprogestin receptors in the uterus interacting with the progesterone hormone could induce abortion.[9] A decade later, in 1980, a research team at the French pharmaceutical company, Roussel-Uclaf, which included Drs. Étienne-Émile Baulieu, Alain Belanger, Beatrice Couzinet, and Gilbert Schaison, as well as Roussel-Uclaf's chief chemist and director of endocrine research, George Teutsch, invented a synthetic drug labeled Roussel-Uclaf 38486 at the Hospital of Bicetre in Bicetre, France. They soon nicknamed the drug "RU-486."[10] The results of clinical trials conducted during the early and mid-1980's showed that the drug was safe and effective for use in early pregnancy termination. On September 23, 1988, after six years of clinical study, the French Ministry of Solidarity, Health, and Social Welfare approved RU-486 for distribution in France as an abortifacient.[11]

Only a month later, however, on October 25, 1988, threatened boycotts of all of its products and loud protests denouncing the banalization of abortion prompted Roussel-Uclaf to withdraw RU-486 from the French market and suspend plans to distribute the pill in France and elsewhere.[12] Despite Roussel-Uclaf's initial enthusiasm to market the drug, some key figures within the pharmaceutical company, particularly Dr. Edouard Sakiz, Roussel-Uclaf's chairman, began to reconsider the company's decision, especially in light of the fact that severe economic repercussions could befall the company if those threatened boycotts actually materialized.[13] Further, Roussel-Uclaf's German parent company, Hoechst AG, which owned a $6 billion-a-year American subsidiary, Hoechst Celanese, pressured Roussel-Uclaf to discontinue the marketing of RU-486 because it feared that burgeoning threats of boycotts, if actualized, could be ruinous to the business of its American subsidiary company.[14] Privately, Hoechst officials also expressed concern that the pro-life movement's statements that Hoechst and Roussel-Uclaf were responsible for exterminating fetuses in an act of "chemical warfare against the unborn" just as the Nazis had exterminated the Jews through the use of cyanide gas could impose irreversible

the late 1980's became increasingly adverse to abortion, which in turn had implications for the introduction of RU-486 in the United States. On July 3, 1989, the Supreme Court in Webster v. Reproductive Health Services[28] upheld a Missouri law that imposed restrictions on abortion, such as requiring doctors to perform tests for fetus viability at 20 weeks (and prohibiting abortion at the 20-week mark if the fetus were found to be viable), and barring the use of public hospitals or clinics for abortion services.[29] Most importantly, however,

[14]Id.

[15]Ellen Goodman, Politics, Technology a Volatile Mixture, Portland Oregonian, July 25, 1989.

[16]Steven Greenhouse, A New Pill, A Fierce Battle, N.Y. Times, Feb. 12, 1989.

[17]Steven Greenhouse, The Uphill Battle to Market the French Abortion Pill, S.F. Chron., Feb. 26, 1989.

[18]See Porter, supra note 9, at 195.

[19]See Étienne-Émile Baulieu & Mort Rosenblum, The Abortion Pill: RU-486, A Woman's Choice 13 (1990). The 1988 controversy surrounding the distribution of RU-486 in France was not the first time France had become embroiled in a vituperative debate over the abortion issue. Abortion has been legal in France since 1975. When abortion was legalized, a bitter debate arose between conservative Catholics and supporters of legalized abortion, including the Socialist Party. The controversy ignited again briefly in 1984 when the French public health system decided to reimburse abortion costs. See Edward Cody, France Orders Sale of New Pill: Abortion Drug Had Been Shelved After Angry Protests, Wash. Post, Oct. 29, 1988, at A1.

[20]The strict treatment protocol included four visits to a doctor's office or clinic with the first three visits occurring within the required seven-week gestation limit. During the first medical visit, the woman registered, underwent a pregnancy test and ultrasound to confirm the pregnancy, and signed a consent form. See Porter, supra note 9, at 193. The consent form contained a provision advising surgical intervention should the RU-486 regimen fail to result in complete expulsion of the fertilized egg or fail to terminate the pregnancy altogether. See id. During the second visit, which occurred after the one-week reflection period mandated by French law, the woman took 600 milligrams of RU-486 in the form of three pills. See id. Approximately 48 hours later, she returned to the facility to receive the prostaglandin and remained at the facility for an additional four to six hours for observation. See id. Seven to ten days later, the woman returned for her final visit in order to confirm the successful termination of the pregnancy. See id.

[21]See, e.g., Richards, supra note 3, at 126. Roussel-Uclaf especially wished to avoid marketing RU-486 in the United States. For one, given the intensity of the anti-abortion movement's sentiment in the United States and its vows to inflict economic reprisal on any pharmaceutical company that marketed the "abortion pill," Roussel-Uclaf could become the target of extensive boycotts of all of its products. Additionally, the privatization and decentralization of the U.S. health care system hindered the implementation and enforcement of stringent governmental controls over the treatment regimen, thereby raising significant safety and liability concerns for any company wishing to distribute the drug. See RU-486, Status Report on the U.S. Commercialization Project, Transfer of Anti-Progestin Technology to the United States: Hearing Before the Subcomm. on Regulation, Business Opportunities, and Technology of the House Comm. on Small Business, 103rd Cong. 1 (1994).

[22]410 U.S. 113 (1973).

[23]See, e.g., Muhl, supra note 4, at 337.

[24]Laura Fraser, The 'Abortion Pill': Why America Trails Europe, Newsday, July 5, 1988, at 49.

[25]See The Patent Term Restoration Review Procedure Act of 1999: Hearing on S. 1172 Before the Senate Committee on the Judiciary, 106th Cong. (1999) (statement of Peter Barton Hutt, Partner, Covington & Burling).

[26]Wells v. Ortho Pharmaceutical Corp., 615 F. Supp. 262 (N.D. Ga. 1985); see also Carl Djerassi, The Future of Birth Control: Our Present Methods Are Outdated and Unless We Act Now, They'll Never Be Better, Wash. Post, Sept. 10, 1989, at C1.

[27]See, e.g., Kociemba v. G.D. Searle & Co., 707 F. Supp. 1517 (D. Minn. 1989); see also Dolly M. Trompeter, Comment, Sex, Drugs, and the Restatement (Third) of Torts, Section 6(c): Why Comment E is the Answer to the Woman Question, 48 Am. U. L. Rev. 1139, 1164-65 (1999). Ironically, feminists and women's health collectives, the groups most actively involved in promoting RU-486, were responsible for encouraging and even funding litigation in the Dalkon Shield crisis, which had the unexpected effect of chilling RU-486 research and distribution in the United States.

[28]492 U.S. 490 (1989).

[29]*See* id. at 530 (O'Connor, J., concurring). A year after Webster, in a pair of cases, Hodgson v. Minnesota, 497 U.S. 417 (1990) and Ohio v. Akron Center for Reproductive Health, 497 U.S. 502 (1990), the Court further limited the strength of Roe in addressing the issue of parental notification in teenage abortion cases. In Hodgson, the Court ruled that a state may require

the Court's establishment of a new "undue burden" standard in Webster suggested that a majority of the Court did not consider abortion to be a fundamental constitutional right.[30] This new standard served as an invitation to state legislators to test just how far the Supreme Court would permit them to go.[31] As a result, between 1989 and 1992, more than 700 bills were introduced in various state legislatures to regulate access to abortion.

The undue burden analysis became the centerpiece of the Supreme Court's ruling in Planned Parenthood of Southeastern Penn Casey marked the first time since Roe that the Supreme Court allowed infringements on the right to choose that directly affect all women seeking abortion services.[33] In Casey, the Court reversed its decisions in Thornburgh v. American College of Obstetricians & Gynecologists[34] and City of Akron v. Akron Center for Reproductive H on the question of waiting periods, holding that important decisions will be more informed and deliberate if they follow some period of reflection... particularly where [a] statute directs that important information become part of the background of the decision.[36] In addition, the Court upheld its previous approval of statutory requirements that allowed certain informational material to be issued to a patient.[37] Consequently, in response to the Supreme Court's jurisprudence in these areas, state legislatures promulgated statutes that

a teenage girl to notify both parents before obtaining an abortion so long as the law also provides the alternative of a judicial hearing. *See* 497 U.S. at 422. A minor could, however, get a judicial bypass if at the judicial hearing the minor could convince the judge that she was mature and capable of giving informed consent. *See id.* Likewise, in Akron, the Court upheld a state law requiring notification of one parent because the statute also provided a judicial bypass procedure through which a minor could obtain a waiver of the notice provision if she presented clear and convincing evidence that she was mature enough to make the decision herself, that one of her parents had abused her, or that the notification was not in her best interest. *See* 497 U.S. at 507-08.

[30] A.J. Stone, III, *Consti-Tortion: Tort Law as an End-Run Around Abortion Right After* Planned Parenthood v. Casey, 8 Am. U.J. Gender Soc. Pol'y & L. 471, 476 (2000).

[31] Marcy J. Wilder, *The Rule of Law, The Rise of Violence, and the Role of Morality: Reframing America's Abortion Debate in* Abortion Wars: A Half Century of Struggle 85 (Rickie Solinger ed., 1998).

[32] 505 U.S. 833 (1992).

[33] Kathryn Kolbert & Andrea Miller, *Legal Strategies for Abortion Rights in the Twenty-First Century, in* Abortion Wars: A Half Century of Struggle 98 (Rickie Solinger ed., 1998).

[34] 476 U.S. 747 (1986).

[35] 462 U.S. 416 (1983).

[36] 505 U.S. at 885.

[37] *See* 505 U.S. at 882 (finding that the distribution of factual literature relating to abortion is permissible, overruling Thornburgh v. American College of Obstetricians & Gynecologists, 476 U.S. 747 (1986) and affirming Planned Parenthood of Cent. Mo. v. Danforth, 428 U.S. 52, 67 n.8 (1976) (allowing mandatory informed consent provisions of statute because such information tells the patient just what would be done and... its consequences).

mandated waiting periods for patients and required patients to receive informational material before obtaining an abortion.[38] While the Court in Casey stated that [n]o development of constitutional law... has implicitly or explicitly left Roe behind, the Court's new "undue burden" standard limited the applicability of the fundamental right/strict-scrutiny approach in Roe in place of a less definite standard that allowed more restrictions on abortions.[39]

Thus, the Supreme Court's jurisprudence had two significant implications for the future of RU-486 in the United States. On the one hand, these decisions heightened concerns within the abortion rights community that the Supreme Court's erosion of the Roe framework exhibited its inclination to not only restrict access to current methods of abortion but also to impede the introduction of any new methods of abortion in the United States. On the other hand, the Supreme Court's jurisprudence raised significant questions about whether the RU-486 treatment regimen would even be subject to the same statutory requirements as surgical abortion. In light of this uncertainty, the abortion rights advocates' need for a more private, nonsurgical alternative to abortion took on new immediacy, especially if the RU-486 treatment regimen had even a remote possibility of eschewing statutory regulation.

D. Abortion Politics Goes Conservative

Meanwhile, the executive branch of the federal government, which was enjoying significant success and popularity throughout the 1980's, vigorously opposed the introduction of RU-486 into the United States on the grounds that it morally diluted the act of abortion. In addition to opposing RU-486, the Reagan and Bush Administrations overturned many federally financed abortion programs that abortion advocates viewed as fundamental. For example, they outlawed some federal support for fertility research, discontinued

[38] *See* Stone, *supra* note 30, at 477-78.
[39] 505 U.S. at 857; *see also* Stone, *supra* note 30, at 476-77.

the financing of leading international family planning organizations, and forbade the counseling of women in federally financed clinics about the possibility of abortion. Given both Presidents' opposition to surgical and nonsurgical abortion and abortion-related services, they stood as major roadblocks in RU-486's path toward approval in the United States, especially since they had the authority to control the direction of FDA policy by appointing Commissioners who shared their attitudes toward abortion.

E. Regulatory Restrictions on Abortion

Finally, on the regulatory front, the FDA implemented severe pre-approval restrictions on RU-486. By way of background, Section 381 of the Food, Drug, and Cosmetic Act, which was enacted in 1938, prohibits the importation of unapproved new drugs into the United States.[40] By July 1988, however, the FDA, out of a concern for persons with AIDS and cancer who needed potentially life-saving unapproved new drugs, launched a pilot program called Pilot Guidance. Pilot Guidance allowed the importation of some unapproved new drugs so long as they were imported in small quantities for personal use and did not present unreasonable safety risks or evidence of fraud.[41] On September 26, 1988, Burton Love, director of the Division of Field Investigations for the FDA, issued an import bulletin, which excluded RU-486 from the Pilot Guidance program.

Soon after its initial implementation, on February 1, 1989, Pilot Guidance was expanded through revision

[40] *See* 21 U.S.C. § 381 (1999).

[41] Debora C. Fliegelman, *The FDA and RU486: Are Politics Compatible With the FDA's Mandate of Protecting Public Health and Safety?*, 66 Temp. L. Rev. 143, 149 (1993). The personal use exemption, as it is commonly called, allows the FDA to exercise its discretion in allowing the importation of drugs not covered under an approved New Drug Application ("NDA") so long as the imported articles satisfy certain conditions. *See* Peter Barton Hutt & Richard A. Merrill, Food and Drug Law: Cases and Materials 562 (2d ed. 1991). While such products are presumptively subject to refusal, the FDA may allow their importation without sampling or detention if: (1) the product was purchased for personal use; (2) the product is not for commercial distribution; (3) the amount of the product is not excessive; (4) the intended use of the product is appropriately identified; (4) the patient affirms in writing that the product is for her own personal use and provides the name and address of the doctor licensed in the United States responsible for her treatment with the product; and (5) the product presents no unreasonable safety risks or evidence of fraud. *See id.* Products that are not identified, are not accompanied by appropriate documentation of intended use, are imported in large quantities inconsistent with the personal use requirement, have been fraudulently promoted or misrepresented, or present an unreasonable health risk due to toxicity or contamination should be detained under FDA guidelines. *See id.*

of the Regulatory Procedures Manual[42] to cover drugs for life-threatening or serious conditions whether or not AIDS or cancer-related.[43] This expansion of the program briefly left open the possibility that RU-486 could be imported into the United States under the personal use exemption before obtaining FDA approval. On June 6, 1989, however, about a month after 11 members of Congress lobbied the FDA Commissioner for an even more explicit exclusion of RU-486 from the personal use exemption list, the FDA implemented Import Alert 66-47, which barred RU-486's entry into the United States and excluded it from the FDA's personal use exemption list because of RU-486's purported health and safety implications.[44] Import Alert 66-47 directed field workers to immediately detain any imported abortifacient drugs.[45] Amidst increasing concern that RU-486 could not be imported even for research purposes, the FDA, in a hearing before the House Small Business Subcommittee, clarified that its import ban targeted individuals who either carried the drug into the country personally or received it in the mail and that the ban did not cover importation of the drug for research purposes.[46]

Predictably, in light of the seemingly interminable trials and tribulations in the story of RU-486, the FDA's import ban did not go unchallenged. On July 1, 1992, in an organized act of defiance, Leona Benten, a social worker from California who was six-weeks pregnant, arrived at New York's Kennedy International Airport from London with 12 RU-486 pills.[47] The group that had organized Ms. Benten's act of defiance alerted customs officials the morning of her arrival that Ms. Benten was carrying the banned drugs into the country, and upon her arrival at the airport, the customs officials seized her pills.[48] Ms. Benten immediately moved for an injunction requiring the FDA and the customs officials to return her pills.[49]

[42] *See* Food & Drug Administration, FDA/ORA Regulatory Procedures Manual, ch. 9, Subchapter on Coverage of Personal Importations (rev. May 12, 1998), *available at* <http://www.fda.gov/ora/compliance_ref/rpm_ new2/ch9pers.html>.
[43] *See, e.g.,* Muhl, *supra* note 4, at 335.
[44] Ron Wyden, *Let the Pill into the U.S.*, N.Y. Times, Apr. 10, 1991, at A25.
[45] Fliegelman, *supra* note 41, at 149.
[46] Philip J. Hilts, *FDA Says It Allows Study of Abortion Drug*, N.Y. Times, Nov. 20, 1990, at C9.
[47] Philip J. Hilts, *Abortion Pills Are Confiscated By U.S.*, N.Y. Times, July 2, 1992, at A12.
[48] Philip J. Hilts, *U.S. Is Sued Over Ban on Importing Abortion Pill*, N.Y. Times, July 8, 1992, at A16.
[49] *See* Benten v. Kessler, 799 F. Supp. 281, 287 (E.D.N.Y. 1992).

On July 14, 1992, nearly two weeks after the initial confrontation and with precious time in the drug's time limitations for effective use slipping away, a U.S. District Court Judge for the Eastern District of New York, Charles P. Sifton, refused to order the government to lift its import ban, but granted Ms. Benten's request for an injunction.[50] The court found that the FDA's import ban was a substantive rule under the Administrative Procedure Act (the "APA") and was therefore subject to the notice and comment requirements of the APA.[51] Given this procedural impropriety, the court held that the FDA could not legitimately seize Ms. Benten's pills without having implemented the import ban through the notice and comment procedures required for the enactment of substantive rules.[52] Alternatively, the Benten court held that even if the import ban was not a substantive rule under the APA, the FDA's own rules required notice and comment whenever any departure from standard agency practice occurred.[53] Before the confiscated pills could be returned to Ms. Benten, however, the U.S. Court of Appeals for the Second Circuit stayed the lower court's order.[54] The final word on the status of Ms. Benten's imported pills came from the highest court in the land. On July 17, 1992, the Supreme Court, in a 7-to-2 vote, with Justices Stevens and Blackmun dissenting, held that Ms. Benten failed to show a substantial likelihood of success on the merits of her claim that Import Alert 66-47 was promulgated without the proper notice and comment procedures required by the APA or FDA regulations and thereby upheld the Court of Appeals' stay.[55] As a result of the Supreme Court's ruling, the government did not return Ms. Benten's pills, the FDA's import ban continued, and perhaps most

[50] *See* id. at 291.

[51] *See* id. at 290-91. The court also stated that the FDA's importation ban was likely based not from any bona fide concern for the safety of users of the drug, but on political considerations having no place in FDA decisions on health and safety. Id. at 286.

[52] *See* id. at 291.

[53] *See* id. at 290.

[54] 505 U.S. 1084, 1084 (1992); *see also* Philip J. Hilts, *Justices Uphold Federal Seizure of Abortion Pill*, N.Y. Times, July 18, 1992, at A1. In the increasingly political battle over RU-486, the battle lines had been drawn along predictable political party lines. The decision favoring Leona Benten came from U.S. District Judge, Charles P. Sifton, a President Carter appointee, while the stay was enacted by a panel of three judges, John M. Walker, President Bush's cousin and a Bush appointee, and Frank X. Altimari and Daniel J. Mahoney, both President Reagan appointees. *See* Philip J. Hilts, *Judge Overturns Federal Seizure of Abortion Pill*, N.Y. Times, July 15, 1992, at A1.

[55] *See* 505 U.S. 1084, 1085 (1992).

significantly, the abortion pill remained bottled up in France.[56]

III. THE ABORTION TIDE BEGINS TO TURN

A. A New Administration

After more than a decade of anti-abortion executive administrations and an FDA unreceptive to the possibility of RU-486's entrance into the U.S. pharmaceutical market, a change in political administrations in 1993 signaled a sea change in U.S. abortion policy. In one of his first acts as President, and on the 20^{th} anniversary of Roe v. Wade, President William J. Clinton directed the FDA to determine whether sufficient evidence existed to warrant exclusion of RU-486 from the list of drugs that qualify for the personal use importation exemption. Under President Clinton's directive, if the FDA concluded that RU-486 satisfied the criteria for the personal use exemption, it was instructed to immediately rescind Import Alert 66-47.[57] Moreover, he directed the FDA to assess initiatives to promote the testing of RU-486 and other antiprogestins and to investigate possible licensing and manufacturing arrangements for the drug in the United States. [58] In attempting to reverse a decade of Republican anti-abortion decrees, President Clinton also repealed the ban on abortion counseling at federally funded clinics, lifted restrictions on fetal tissue research, reversed a Reagan Administration prohibition on aid to international family planning programs that provide abortion-related services, and eliminated a ban on all abortions in U.S. military hospitals.[59]

[56]Despite the import ban, a cancer patient, J. David Grow, who had inoperable meningioma and who testified before a Congressional subcommittee on July 28, 1992 that the unapproved abortion pill might prolong his life, received government permission to obtain the drug from its French manufacturer. *See* Claire L. Ahern, *Drug Approval in the United States and England: A Question of Medical Safety or Moral Persuasion? – The RU-486 Example*, 17 Suffolk Transnat'l L. Rev. 93, 104 n.62 (1994); Gina Kolata*, Cancer Patient Can Get Unapproved Abortion Pill*, N.Y. Times, July 30, 1992, at A22.

[57]Memorandum for the Secretary of Health and Human Services, Importation of RU-486, 58 Fed. Reg. 7459 (1993).

[58]Notice, Department of Health and Human Services, Office of the Secretary, Actions Regarding Family Planning Service Projects, Transplantation of Human Fetal Tissue, and Importation of the Drug Mifepristone, 58 Fed. Reg. 7468 (1993).

[59]Robin Toner, *Settling In: Easing Abortion Policy; Clinton Orders Reversal of Abortion Restrictions Left by Reagan and Bush*, N.Y. Times, Jan. 23, 1993, at A1.

Although the political landscape was becoming increasingly favorable toward the introduction of RU-486 in the United States, the pill's French manufacturer, and in particular the French manufacturer's German parent company, remained hesitant to introduce the drug in the United States or even to license it to a pharmaceutical company in the United States, for fear of the lurking economic and political ramifications. Responding to Roussel-Uclaf's and Hoechst's reticence, the Clinton Administration, along with FDA Commissioner at the time, Dr. David A. Kessler, initiated proactive efforts to change both Roussel-Uclaf's and Hoechst's minds.[60] In fact, on February 24, 1993, pharmaceutical executive, Dr. Edouard Sakiz of Roussel-Uclaf, met with Dr. Kessler at FDA headquarters in Rockville, Maryland at the FDA's request to discuss bringing RU-486 to the American market.[61] While Dr. Sakiz conceded the importance of bringing the drug to market in the United States, he also continued to stress the company's unwillingness to be directly involved in the process.[62]

B. The Involvement of the Population Council

Even as Roussel-Uclaf persisted in its refusal to market RU-486 in the United States, all hopes to bring the drug to the U.S. pharmaceutical market were not lost. In fact, the Population Council, an American non-profit contraceptive research group that was created in 1952 by John D. Rockefeller, III, had expressed

[60] Even before President Clinton and Dr. Kessler joined the effort to bring RU-486 to the United States, longtime feminist activists Peg Yorkin, a Hollywood producer, and Eleanor Smeal, a former president of the National Organization for Women, took 700,000 petitions to France in 1989 to persuade Roussel-Uclaf to sell the drug in the United States. *See* Sharon Bernstein, *Persistence Brought Abortion Pill to U.S.: Two Feminist Activists Culled Nonprofit Organizations and Dedicated Individuals To Do The Work That No Pharmaceutical Company Was Willing to Tackle*, L.A. Times, Nov. 5, 2000, at A1.

[61] Philip J. Hilts, *Door May Be Open For Abortion Pill To Be Sold In U.S.*, N.Y. Times, Feb. 25, 1993, at A1.

[62] *See Roussel-Uclaf Discusses Possible RU-486 Launch with FDA*, Pharmaceutical Bus. News, Mar. 5, 1993, at 5. In spite of the changing political landscape in the United States, a fear of boycotts, protests, and liability exposure prevented RU-486's French manufacturer from marketing the drug in the United States or licensing it to another company in the United States. In an effort designed to signal to RU-486's French manufacturer that there was competition in the marketplace, a pro-choice group, Abortion Rights Mobilization, launched a campaign seeking FDA approval for distribution of the Chinese equivalent of the French abortion pill. American Political Network, Spotlight Story, Story RU-486: Chinese Pill To Be Tested in U.S., 4 Abortion Rep. No. 139, Feb. 17, 1993, *available in* WL APN-AB File. Abortion Rights Mobilization secured an agreement from the Beijing Union Medical College to use the abortion pills it had developed and planned to begin safety testing on animals. *See* Philip J. Hilts, *Abortion Rights Group Uses Chinese Pill To Goad French*, N.Y. Times, Feb. 18, 1993, at B9. Members of Abortion Rights Mobilization stated that they had already recruited a team of scientists at an unidentified New York laboratory to make about 100 doses of the pill to begin clinical testing if Roussel-Uclaf persisted in its refusal to market the drug in the United States. *See* Philip J. Hilts, *Group to Copy French Abortion Pill in Bid to Speed Its Sale in U.S.*, N.Y. Times, Apr. 2, 1993, at A16.

an interest in the drug since its discovery in France in the early 1980's.[63] The Population Council's interest in RU-486 derived from its belief that unsafe abortions were a significant public health risk to women in developing countries and its concern that the unavailability of RU-486 would deprive women in all countries of a safe and effective method for early medical termination of pregnancy.[64] Its involvement with RU-486 and Roussel-Uclaf officially began in 1982 when the Council entered into an agreement with Roussel-Uclaf concerning the possibility of running pre-clinical and clinical studies on RU-486 in the United States in an effort to secure FDA approval.[65] After the Population Council had obtained an Investigational New Drug Application (IND) from the FDA for clinical testing of the safety and efficacy of RU-486, the only FDA-approved study of RU-486 was undertaken from 1983 to 1989 at the University of Southern California.[66] Fearing similar repercussions to the French upheaval in 1988, *see supra* section I, part B, however, Roussel-Uclaf's parent company, Hoechst, ordered the discontinuation of testing at the University of Southern California.[67] About four years after the termination of this cooperative enterprise between the Population Council and Roussel-Uclaf, Roussel-Uclaf finally agreed to license RU-486 in the United States to the Population Council on April 21, 1993.[68] Under the licensing agreement, the Population Council planned to sponsor a clinical trial in the United States involving at least 2,000 women, while Roussel-Uclaf agreed to provide the FDA with the toxicology and chemistry data from its own French clinical trial.[69]

[63] Diane L. Slifer, *Growing Environmental Concerns: Is Population Control the Answer?*, 11 Vill. Envtl. L.J. 111, 127 n.107 (2000).

[64] *See RU-486, Status Report on The U.S. Commercialization Project, Transfer of Anti-Progestin Technology to the United States Before the Subcomm. on Regulation, Business Opportunities, and Technology of the House Comm. on Small Business*, 103rd Cong. 80 (1994)[hereinafter *Transfer Hearings*] (statement of James S. Boynton, Counsel to The Population Council, Inc.).

[65] *See* Étienne-Émile Baulieu & Mort Rosenblum, The Abortion Pill: RU-486, A Woman's Choice 30 (1990).

[66] *See* Sylvia A. Law, *Tort Liability and the Availability of Contraceptive Drugs and Devices in the United States*, 23 N.Y.U. Rev. L. & Soc. Change 339, 391 (1997); *see also Transfer Hearings, supra* note 64, at 80.

[67] *See* Law, *supra* note 66, at 390-91.

[68] *See* Warren E. Leary, *Maker of Abortion Pill Reached Licensing Pact With U.S. Group*, N.Y. Times, Apr. 21, 1993, at A18. It should be noted that Roussel-Uclaf's German parent company, Hoechst, under the chairmanship of Wolfgang Hilger, bore the brunt of the criticism for encumbering RU-486's entry into the U.S. market. Hilger had publicly pronounced his pro-life beliefs and had further expressed wariness over potential boycotts of the company's products and the volatility of the company's financial status in a characteristically litigious American society. *See* Fliegelman, *supra* note 41, at 148 n.43.

[69] *See* Warren E. Leary, *Maker of Abortion Pill Reaches Licensing Pact With U.S. Group*, N.Y. Times, Apr. 21, 1993, at A8.

In spite of the promising start to the 1993 agreement between the Population Council and Roussel-Uclaf, plans for testing and marketing in the United States stalled. Six months after the initial licensing agreement, Roussel-Uclaf had not yet signed a contract with the Population Council authorizing it to proceed with testing.[70] As the two entities remained mired in negotiations, in a move prompted by both pressure politics and practical considerations, the Marie Stopes Health Clinic in London began offering RU-486 to American women.[71] Moreover, on May 15, 1994, after more than a year of quagmired negotiations, some members of Congress threatened to rescind Roussel-Uclaf's U.S. patent if it did not expeditiously reach an agreement with the Population Council. Expended from all the negotiations and political maneuvering, Roussel-Uclaf finally decided to simply cede its patent rights without remuneration to the Population Council.[72] The agreement between the two entities arranged for the transfer of Roussel-Uclaf's patent rights and all of its technology to the Population Council. The Council, in turn, planned to secure an American manufacturer to produce the pill. In exchange for the donation of patent rights, RU-486's French manufacturer insulated itself from product liability claims and anti-abortion boycotts and protests.[73]

C. Concern From the Pro-Life Movement

[70] Tamar Lewin, *Plans for Abortion Pill Stalled in U.S.*, N.Y. Times, Oct. 13, 1993 at A17. Before signing the licensing agreement, Roussel-Uclaf had publicly announced that five conditions had to be met before it would introduce RU-486 into a new country. Those conditions were: (1) abortion must be legal in the country; (2) the political climate must be accepting of abortion; (3) a suitable prostaglandin must be available; (4) the health care system must be equipped to monitor patients and the drug supply; and (5) informed consent procedures must be followed. *See* Porter, *supra* note 9, at 191. Many believed that Roussel-Uclaf hesitated to introduce the drug into the United States because the second condition remained to be achieved.

[71] Tamar Lewin, *British Offering Abortion Drug To U.S. Women*, N.Y. Times, Feb. 18, 1994, at A1. The British treatment regimen was similar to the French procedure. The first step involved a physical and ultrasound examination to verify the pregnancy and confirm that it fell within the permitted British nine-week gestation limit. At the first session, the patient also received counseling. After the counseling session, two doctors' approvals were required to proceed with the treatment regimen. Once the patient had secured the appropriate approval, she returned for a second visit, where she received three RU-486 tablets and waited for about two hours to ensure that there were no unanticipated complications. In some cases, the woman fully expelled the fertilized egg or fetus before the second visit. Because that was not usually the case, most women returned for a third visit approximately 48 hours later, where they received a prostaglandin in suppository form, which induced further contractions, thereby helping to complete the expulsion process. Under the rules in effect at the time, the patient remained at the clinic overnight for observation and returned a week later to verify that the pregnancy had been terminated. *See* Nina Darnton, *Surprising Journey For Abortion Drug*, N.Y. Times, Mar. 23, 1994, at C12. The British procedure cost $500, not including the airfare, hotel accommodations, and food for the week patients were required to remain in Britain for follow-up care. *See* Lawrence Lader, *RU-486, Made in America*, N.Y. Times, Mar. 17, 1994, at A23.

[72] *See Editorial*, *RU-486 – Here at Last*, N.Y. Times, May 17, 1994, at A18.

[73] *See* Katharine Q. Seelye, *Accord Opens Way for Abortion Pill in U.S. in Two Years*, N.Y. Times, May 17, 1994, at A1.

With the conclusion of negotiations between Roussel-Uclaf and the Population Council, the arrival date of the drug in the United States now seemed imminent. Once again, the polemic surrounding the abortion debate intensified. Marcy Wilder, legal director of the National Abortion Rights Action League, stated that [t]he Clinton Administration has helped end the tyranny of anti-choice extremists who for too long have held science hostage to their religious and ideological views.[74] Susan Hill, an abortion provider and president of the National Women's Health Organization, asserted, "... mifepristone could stop this ghettoization of abortion providers. Women [could] finally have the option of privacy in their choice. Staff and physicians would no longer be targets but once again medical professionals providing medical services."[75] In contrast, opponents of abortion called RU-486 a human pesticide.[76] Critics also charged the Clinton Administration with inappropriately attempting to hasten the FDA approval process before the 1996 presidential election to avoid what he considered to be negative changes that could occur under a new executive administration. Privately, opponents of abortion feared that their worst nightmare had come true. They recoiled at the trivialization and the dilution of the moral significance of the act of abortion that would result if an abortion could be accomplished simply by swallowing some pills. In particular, they worried that the seeming simplicity of the procedure might encourage women to use RU-486 as a means of birth control or that the drug might condone a mentality of sexual irresponsibility, teen pregnancy, and infidelity.[77]

According to opponents of abortion, the drug, if approved, could irrevocably alter the national abortion debate in a number of ways. First, in the minds of abortion opponents, the availability of RU-486 could increase the dwindling corps of OB-GYNs willing to offer abortion services, thereby increasing the geographic availability of abortion. This perception on the part of abortion opponents was confirmed in a 1998 study

[74] *See id.*

[75] *New Drug Application for the Use of Mifepristone for Interruption of Early Pregnancy Before the Food and Drug Administration's Reproductive Health Drugs Advisory Committee, Center for Drug Evaluation and Research* (July 19, 1996) [hereinafter *New Drug Application*].

[76] *See* Katharine Q. Seelye, *Accord Opens Way for Abortion Pill in U.S. in Two Years*, N.Y. Times, May 17, 1994, at A1.

[77] *See* Mindy J. Lees, *I Want a New Drug: RU-486 and the Right to Choose*, 63 S. Cal. L. Rev. 1113, 1125 (1990).

by the Henry J. Kaiser Family Foundation which found that 45% of the family practitioners polled said they were either very or somewhat likely to offer abortion services once RU-486 received FDA approval, partly because of the anonymity associated with the prescription of a pill.[78] Second, abortion opponents believed that the distribution of an abortion pill could enhance the privacy of the abortion decision by reducing the need for special surgical abortion clinics. This decentralization and privatization of abortion, which would remove it from the public specter of infamous abortion clinics to unidentified, scattered doctors' offices, ordinary medical clinics, or even the home, could have the effect of making protests outside of a specific physical location difficult because no one would ever know where a woman was taking the pills. Third, abortion opponents feared that the availability of an early pregnancy termination treatment regimen could make abortions more politically tenable. For example, a 1998 New York Times/CBS News poll found that Americans tend to favor legal abortion in the early stages of pregnancy and that support for abortion drops precipitously as pregnancy develops.[79] This theory has been supported by legal scholar Ronald Dworkin who wrote, "[i]t is an almost universal conviction that abortion becomes steadily more problematic morally as a fetus develops toward infanthood."[80] According to Dworkin's theory, if fetal life is a progressing continuum, then the more infant-like an aborted fetus, the greater the insult to the sanctity of human life. Dworkin's theory was further buttressed by the contention of Douglas Johnson, the present legislative director of the National Right to Life Committee, that technological developments have created "a window to the womb, which makes people more cognizant of the humanity of the unborn child."[81] This cognizance, in turn, has made early abortion much more palatable to Americans than later surgical abortions when the humanity of the aborted fetus is much more pronounced. Lastly, abortion opponents worried that the availability of an early pregnancy termination option would marginalize the visual images that are typical in the surgical

[78] *See* Margaret Talbot, *The Little White Bombshell*, N.Y. Times, July 11, 1999, § 6 (Magazine), at 39.
[79] *See id.*
[80] *See id.*
[81] *See* Robin Toner, *The Abortion Debate: Stuck in Time*, N.Y. Times, Jan. 21, 2001, § 3, at 1.

abortion context of three to six-month old fetuses with human characteristics being discarded into garbage bags. This is because RU-486 pills are advised for women who are less than 49 days pregnant – a time when the fetus does not have physical human characteristics. In a visually oriented society, abortion opponents fretted that the absence of those images, and their concomitant emotional impact, in addition to the increasing geographic availability and privatization of abortion, could very well reconfigure the politics and perception of abortion in the United States.[82]

IV. THE TIDE TURNS AGAIN – The Political Pendulum Swings to the Right

A. The Politics of Abortion Run Into The Contract With America

Despite the enduring controversy, the Population Council began its U.S. clinical trial of RU-486 in the fall of 1994 with the enrollment of 2,121 women.[83] Meanwhile, until the Population Council submitted a New Drug Application ("NDA") and had it approved by the FDA, RU-486 remained illegal in the United States.[84] In

[82]Even though Roussel-Uclaf had removed itself from the U.S. process, a coalition of anti-abortion groups identified products of Hoechst's U.S. affiliates such as Hoechst Celanese Corp., Hoechst-Roussel Pharmaceuticals Inc., and Copley Pharmaceutical and started a boycott of these entities' products in an effort to pressure Roussel-Uclaf and its parent company to rescind the license it had granted to the Population Council and to dissuade American manufacturers from becoming involved in what, in their opinion, promised to be an economically disastrous enterprise. *See* Elyse Tanouye, *U.S. Companies Targeted in Protest of Abortion Pill*, Wall St. J., July 8, 1994, at B3.

[83]*New Drug Application, supra* note 75.

[84]However, an alternative drug treatment became available in New York. Dr. Richard Hausknecht, an obstetrician at the Mount Sinai School of Medicine in New York and abortion rights crusader, had performed 126 abortions by using two drugs that were already on the market, though approved for other purposes. *See* John Tierney, *A Lone Doctor Adapts Drugs For Abortions*, N.Y. Times, Oct. 10, 1994, at A1. Although neither drug had been approved by the FDA for use in abortions, once a drug is on the market for other purposes, physicians have discretion to use it for off-label purposes. Under Dr. Hausknecht's pregnancy termination regimen, the woman could be no more than eight weeks pregnant. At her first visit, the patient received an injection of methotrexate, a drug that inhibits tissue growth and has been used for many years to treat cancer tumors, psoriasis, arthritis, and ectopic pregnancies. *See id.* Four days later, the woman returned for tablets of misoprostol to be inserted into the vagina. The patient then went home and usually expelled the fertilized egg or fetus within three days. Dr. Hausknecht stated that 121 of his procedures had been successful, while five required surgery to complete the procedure. *See id.* A few years after Dr. Hausknecht's experiment, Planned Parenthood of New York obtained FDA approval to begin a nationwide clinical trial of the methotrexate-misoprostol combination to gain on-label approval of methotrexate for use as an abortifacient. *See Planned Parenthood to Test Nonsurgical Method for Abortions*, Wall St. J., Sept. 12, 1996, at B10.

November 1994, however, following the political realignment of Congress, it appeared that RU-486 might be stopped dead in its tracks even before the approval process ever got underway. Eighty-four freshmen GOP members, 68 of whom described themselves as staunchly pro-life, joined the ranks of Congress. In the House of Representatives, abortion opponents outnumbered supporters by a margin of 225 to 162. The Senate was equally divided between abortion supporters and opponents, perhaps with a slight margin in favor of abortion opponents.[85] Hoping to redefine government's role, the new conservative members of Congress and their veteran conservative counterparts made a "Contract With America" to reduce the role of government in American life. In keeping with this promise to shrink the size and role of the federal government, Newt Gingrich, the new Speaker of the House of Representatives, called for a total restructuring of the FDA, which conservatives had denounced as a symbol of regulatory excess that needed to be shrunk down to size. The House of Representatives also instituted a moratorium on new regulations that would stay in effect until Congress had a chance to revise or repeal the statutes under which the regulations were promulgated.[86] This had the effect of stopping the FDA from moving forward with many of its initiatives.

Furthermore, to uphold its "Contract With America," the new conservative movement in Congress, including then House Commerce Committee Chairman, Thomas Bliley of Virginia, sought to ease regulatory restrictions on businesses. As the Republican members of Congress were pursuing these initiatives, however, more than a dozen of them, including Representative Bliley, also signed an Americans United for Life petition, calling upon the FDA to apply the most stringent standards in reviewing RU-486, once an NDA was submitted by the Population Council, and urging the FDA not to accept data from foreign clinical studies.[87] While

[85] *See* Jennifer Lenhart, *Poor Timing: Abortion Pill RU-486 Starts U.S. Tests Just as Conservatives Capture Congress*, Houston Chron., Dec. 13, 1994, at 1.

[86] *See* John Schwartz, *Conservative Foes of Government Regulation Focus on the FDA*, Wash. Post, Jan. 21, 1995, at A7. While the House passed the moratorium in the Regulatory Transition Act of 1995, H.R. 450, 104th Cong., 1st Sess. (Feb. 24, 1995), in 141 Cong. Rec. H2209-10 (Feb. 24, 1995), the Senate passed a much more scaled back version in S. 219, 104th Cong., 1st Sess. (Mar. 16, 1995). *See* Timothy Noah, *Senate to Consider Less Sweeping Bill on Regulatory Moratorium Than House*, Wall St. J., Mar. 22, 1995, at A2.

[87] *See* American Political Network, Spotlight Story, Story RU-486: Group Files Petition To Block Fast-Track Approval, 6 Abortion Rep. No. 149, Mar. 1, 1995, *available in* WL APN-AB File.

conservatives sought to eliminate many regulatory restrictions on businesses, their politics on abortion prevented them from pursuing the same agenda with respect to RU-486, which in turn, critics charged exhibited the inconsistency and politicization of Republican regulatory policy. These obviously conflicting initiatives to, on the one hand, erect regulatory restrictions on the RU-486 approval process, and to, on the other hand, ease regulatory burdens on businesses, demonstrated that the politics of abortion was experiencing a head-on collision with the "Contract With America."

B. Conservative Congressional Legislation

By June 1995, over a dozen abortion-related bills were pending in Congress, signaling that the political pendulum was swinging back in favor of the anti-abortion movement. For example, under consideration were bills to reinstate a ban on abortions at American military hospitals overseas, ban and criminalize partial-birth abortion, repeal or modify Title X of the Public Health Service Act (which provided abortion-related services to low-income women), and curtail federal funds to family planning programs that provide abortions with private money.[88] Congress also considered measures to lift a ban against the use of foreign aid money for abortion counseling, limit the use of federal Medicaid money for abortions to only those cases where the pregnancy threatened the life of the mother, end Medicaid financing of abortions in the case of pregnancies that result from rape or incest, and discontinue fetal tissue research.[89] The intensity of the anti-abortion sentiment within congressional ranks was further evidenced by measures to prohibit abortion counseling at federally funded family planning clinics, restore the ban on the use of federal money for abortions in federal prisons, prohibit the District of Columbia from using tax revenue to fund abortions, prohibit insurance coverage for abortion of federal employees, and end clinical testing of RU-486.

[88] *See* Nadine Strossen, *Women's Rights Under Siege,* 73 N.D. L. Rev. 207, 226-27 (1997).
[89] *See id.*

Although congressional Republicans engaged in these efforts, with House Democrats vigorously opposing these measures and with a Democrat in the White House, the Republicans were mostly unsuccessful in effectuating any change in domestic abortion policy.[90] On March 14, 1996, after years of political maneuvering and in spite of the continued polarizing debate between the combatants on both sides of the abortion issue, the FDA approval process officially began when the Population Council submitted an NDA to the FDA under section 505(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 505(b) (1999), for the approval of RU-486.[91]

V. THE FDA APPROVAL PROCESS GETS UNDERWAY

A. Background on the Evolution of the FDA Approval Process

Passed in 1906, the Food and Drugs Act established standards of purity and labeling requirements for drugs.[92] In 1937, however, due to minimal requirements and lack of enforcement of the purity and labeling standards, 100 children died from an untested toxic liquid sulfa drug, Elixir of Sulfanilamide.[93] This tragedy caused the repeal of the Food and Drugs Act and the enactment in 1938 of the Federal Food, Drug, and Cosmetic Act.[94] This new Act established requirements for any drug proposed for sale in interstate commerce. To secure FDA approval, the Act required that in an NDA the manufacturer describe the uses of the new drug and prove that the drug was safe for its intended uses.[95] Although the Act did not contain a specific efficacy

[90] *See* Jill Zuckman, *GOP Bill Targets Rare, Late-Term Type of Abortion*, Boston Globe, Nov. 1, 1995, at A12.

[91] On March 31, 1996, the Population Council transferred the exclusive legal right to organize the manufacture and distribution of the pill in the United States to a newly formed private company called Advances in Health Technology. *See* Tamar Levin, *FDA Approval Sought for French Abortion Pill*, N.Y. Times, Apr. 1, 1996, at A12.

[92] Food and Drugs Act, Pub. L. No. 59-384, 34 Stat. 768 (1906) (codified at 21 U.S.C. §§ 1-15 (1934)) (repealed in 1938 by 21 U.S.C. § 392(a)); *see also* Richards, *supra* note 3, at 121.

[93] *See* Richards, *supra* note 3, at 121.

[94] Federal Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301-92 (1994)); *see also* Muhl, *supra* note 4, at 331.

[95] *See* Muhl, *supra* note 4, at 331.

requirement, the FDA nevertheless considered the efficacy of a drug when the drug was known to have serious side effects or was used to treat life-threatening illnesses.[96] Under the statute, the FDA had to grant automatic approval to the application within 60 days, unless the drug had not been proven to be sufficiently safe.[97] In 1962, Congress amended the Food, Drug, and Cosmetic Act to eliminate the 60-day automatic approval requirement and to add a specific efficacy requirement.[98]

The first step in the modern FDA drug approval process requires a drug's sponsor to submit an IND which contains information on the uses of the drug, its pharmacological and toxicological effects based on animal toxicity studies, and a plan for the clinical phases of human testing.[99] If the FDA approves the IND application, several phases of human testing may begin.[100] Phase One testing is conducted on patients or healthy volunteers and is used to establish the metabolism of the drug to determine an optimal dosage level. Phase One testing also assesses the effects of the drug on the human body, its side effects, and its effectiveness for its intended uses.[101] Phase Two testing involves controlled clinical studies to evaluate the drug's effectiveness in patients with the disease or condition for which the drug is indicated.[102] Finally, Phase Three testing consists of expanded controlled and uncontrolled studies designed to gather additional safety and efficacy data.[103]

Assuming the drug performs satisfactorily during the clinical phase, the sponsor may then submit an NDA to the FDA, requesting approval to market the drug based on the results of clinical testing. In addition to the results of the clinical tests, the NDA must contain information about the drug's composition, toxicology,

[96] *See* Richards, *supra* note 3, at 122.
[97] *See* Muhl, *supra* note 4, at 331.
[98] Act of October 10, 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962); *see* 21 U.S.C. § 408 and accompanying regulations. A new drug must also undergo a series of tests and trials to prove that the drug is safe and accomplishes what it claims. *See* 21 U.S.C § 355 (1992); *see also* Muhl, *supra* note 4, at 331.
[99] *See* Richards, *supra* note 3, at 122.
[100] *See* Hanson, *supra* note 6, at 172.
[101] *See* Hanson, *supra* note 6, at 172; Muhl, *supra* note 4, at 333.
[102] *See* Richards, *supra* note 3, at 122.
[103] *See* Hanson, *supra* note 6, at 172.

manufacturing, processing, packaging, and behavior in the human body.[104] Once the NDA is filed, the FDA determines its review priority based on the drug's chemical composition and its potential benefits. In other words, if the drug features an active ingredient never before marketed in the United States or, if it represents an important therapeutic gain over existing drugs on the market, the FDA can grant the drug the highest priority review, which means that the approval process will be expedited.[105] In some cases, if foreign clinical tests have already been completed and if those tests have generated ample data, the long approval process can also be somewhat circumvented. When, in the FDA's judgment, a foreign clinical study was well-designed and conducted in accordance with ethical principles, the FDA will accept the foreign data in support of an NDA.[106] Once the NDA has been submitted, the FDA must, within 60 days, decide whether or not to file the application.[107] If the FDA files the application, it then conducts its own clinical, pharmacology, toxicology, chemistry, manufacturing, statistical, biopharmaceutics, and pharmacokinetics reviews.[108] In the end, the standards that must be satisfied in order to secure FDA approval of a new drug are safety for its indicated use and substantial evidence of efficacy.[109]

B. The Results of RU-486's French Clinical Trial

1. The Methodology and Procedures of the French Clinical Trial

The French clinical trials of RU-486, upon which most of the Population Council's NDA was based, con-

[104] *See* Hanson, *supra* note 6, at 172.
[105] *See* Richards, *supra* note 3, at 122.
[106] *See* Muhl, *supra* note 4, at 334.
[107] *New Drug Application, supra* note 75.
[108] *New Drug Application, supra* note 75.
[109] *See* 21 U.S.C. §355(d) (1994) (setting efficacy standards); *see also* 21 C.F.R. §§ 312.20-212.130 (1999); Sarah Ricks, *The New French Abortion Pill: The Moral Property of Women*, 75 Yale J. L. & Feminism 75, 77 (1989).

sisted of two multicenter (24 centers) studies.[110] Study One contained 1,286 women, 1,089 of whom had a gestational duration of 49 days or less calculated from the date of the first day of the woman's last menstrual period.[111] Study Two included 1,194 women, 492 of whom had a duration of gestation of 49 days or less and 702 of whom had a duration of gestation of 50 days or more.[112] The first French study excluded women over the age of 35, while the second French study excluded women over the age of 35 who smoked more than ten cigarettes a day, had cardiovascular disease, asthma, diabetes, glaucoma or high intraocular pressure, hyperlipidemia, or a history of renal, adrenal, or hepatic insufficiency.[113] The second French clinical trial also excluded women who had been treated with corticosteroids during the previous six months, were anemic, were using anticoagulants, had a hemostatic abnormality, or lived more than one hour away from the clinic where they would receive treatment.[114]

In both studies, the treatment protocol involved the ingestation of 600 milligrams of mifepristone in the form of three 200-milligram tablets during the first visit.[115] During the second visit, the participants received a 400-microgram dose of misoprostol and then remained in the clinic for observation for approximately four hours.[116] In Study Two, those women who had not had a medical termination within three hours of the

[110] Department of Health and Human Services, Public Health Service, Food and Drug Administration, Center for Drug Evaluation and Research, Application Number 20-687: Statistical Review(s) (Feb. 14, 2000) [hereinafter Statistical Review].
[111] *New Drug Application, supra* note 75.
[112] *See id.*
[113] *See id.*
[114] *See id.*
[115] *See id.*
[116] *See id.* Misoprostol is not the only oral prostaglandin which has been used in clinical studies of the RU-486 treatment regimen. In fact, there have been three types of prostaglandins which have been used. First, studies have been conducted using sulprostone, a PGE2, which stands for prostaglandin E of the 2 series, analogue, which is an expensive preparation, given parenterally, and requiring refrigeration. *See id.* Second, studies have used gemeprost, a PGE1, which stands for prostaglandin E of the 1 series, analogue, which is an expensive compound, given as a vaginal suppository, and requiring refrigeration. *See id.* Third and most commonly, studies have employed misoprostol, also a PGE1 analogue, which is administered orally, does not require refrigeration, and is relatively inexpensive. *See id.* In studies involving the use of sulprostone, the success rate for medical abortion was 95.7%. Similarly, in studies involving gemeprost, the success rate was 95.5%. *See id.* Success in these studies, or the primary efficacy parameter, was the proportion of patients who experienced a complete expulsion without the need for surgical intervention. *See id.* In 1 out of 20,000 women, however, the use of sulprostone was associated with adverse carotid effects. As a result, the use of sulprostone as a prostaglandin analogue has been discontinued, leaving gemeprost and particularly misoprostol as the most commonly used prostaglandins. *See id.* Both the French and the U.S. clinical trials used the mifepristone-misoprostol combination.

administration of misoprostol were given an additional 200 micrograms of misoprostol and were required to remain in the clinic for an additional two hours of observation.[117] At the end of two weeks, the women in both studies returned for an assessment of their pregnancy status. The percentage of women who had a medical termination of pregnancy within three hours in both groups was 36%.[118] Among the women with a duration of gestation of 49 days or less, there was complete medical termination of pregnancy in 95.5% percent of them.[119] 1.3% of these women had a continuing pregnancy which was then terminated by a dilatation and curettage or a vacuum aspiration, 2.9% of them had an incomplete abortion, and 0.3% of them required dilatation and curettage or vacuum aspiration to stop excessive bleeding.[120] The results of the clinical studies indicated that there is a statistically significant inverse relationship between success rate and gestational age and between success rate and the chronological age of the patient.[121] For instance, while the predicted probability of complete medical termination in a woman of 35 days duration of pregnancy is 97%, it is only 92% for a woman with a duration of gestation of 49 days.[122] Moreover, a 19-year-old woman at 49 days duration has a 97% predictive probability of complete termination of pregnancy, whereas her 35-year-old counterpart at the same gestational age has a 92% predictive probability of complete termination.[123]

2. Adverse Reactions Found in French Clinical Trial

In spite of the seeming simplicity of the procedure, which involves swallowing a series of pills and returning to a clinic or doctor's office for follow-up care, many adverse events were found to accompany the RU-486

[117] *See id.*
[118] *See id.*
[119] *See id*
[120] *See id.*
[121] Statistical Review, *supra* note 110..
[122] *New Drug Application, supra* note 75.
[123] *See id.*

treatment regimen. For example, the most commonly recorded adverse event during the French clinical trial was painful uterine contractions, occurring in 82% of the patients.[124] Nausea occurred in 45% of the patients, vomiting in 20%, diarrhea in 15%, headaches in 3%, fainting, dizziness, and metrorrhagia (an abnormal hemorrhage of the uterus) in 2%, anemia, asthenia (loss or lack of bodily strength), chills, and fever in 1%, hot flashes in slightly more than 0.5%, and skin conditions, anxiety, and breast conditions such as itching and discharge in less than 0.5%.[125] Much less commonly, the study subjects experienced palpitations (5 patients), tachycardia (excessively rapid heartbeat in 5 patients), hypotension (7 patients), syncope (brief loss of consciousness caused by transient anemia in 2 patients), and thoracic pain (1 patient).[126] Furthermore, 21 women out of the 2,480 clinical study population had a severe bleeding episode.[127] Two of those women received surgical intervention to stop the bleeding, and four received transfusions.[128] Finally, the mean duration of bleeding as a result of the treatment regimen was 9.1 days, with the longest duration of bleeding being 69 days.

3. Summary of French Study's Findings

In summary, 2,480 subjects enrolled in the two French studies. Study One, which included mostly women with a pregnancy duration of no more than 49 days, had an overall success rate of 95.5%. Study Two, which included women with a pregnancy duration up to 63 days, had an overall success rate of 92.8%.

4. Results of Animal Testing

[124] *See id.*
[125] *See id.*
[126] *See id.*
[127] *See id.*
[128] *See id.*

In addition to the human phase of clinical testing, tests were run on laboratory animals to assess the effects of RU-486 on different organ systems. In general, there were either no or mild effects in the nervous, cardiovascular, respiratory, and gastrointestinal systems.[129] The genitourinary studies, however, revealed a decreased excretion of sodium and potassium in some of the laboratory animals after the administration of the drug.[130] In addition, the animal toxicity studies indicated that a dose of 1,000 milligrams per kilogram of mifepristone caused some toxicity in the rodents in the form of ambulatory difficulties and distension of the stomach.[131]

Out of a concern that the use of RU-486 could cause future fertility difficulties in women who have used the drug or could cause birth defects in children who are born after the unsuccessful completion of the treatment regimen, reproductive toxicology studies were conducted on the laboratory animals to assess the effects of RU-486 on the reproductive system. In one study, rats received two doses of the drug, up to three milligrams per kilogram each, which resulted in the disruption of the estrous cycles of these rats during the course of a 21-day treatment.[132] After the drug was withdrawn, the rats gradually resumed their estrous cycles.[133] When they later mated with normal males, gestation, parturition, litter size, and the morphology, body weight, and survival rate of the offspring were not affected by the treatment, leading to the conclusion that RU-486 does not negatively affect fertility.[134] Additionally, to assess the potential for birth defects after the administration of RU-486, mice, rats, and rabbits received a dose of the drug at the time of implantation and at various other points during their pregnancies.[135] These tests indicated that there were no teratogenic effects in the animals. Finally, the animal genetic toxicology studies demonstrated that mifepristone does not cause mutations or chromosomal aberrations.[136]

[129] *See id.*
[130] *See id.*
[131] *See id.*
[132] *See id.*
[133] *See id.*
[134] *See id.*
[135] *See id.*
[136] *See id.*

C. The Results of the U.S. Clinical Trial

1. The Methodology and Procedures of U.S. Clinical Trials

From September 13, 1994 to September 12, 1995, the efficacy and safety of mifepristone were evaluated in two multicenter studies in the United States according to two identical protocols at 17 centers in 15 states.[137] Only centers that could perform abortions either by vacuum aspiration or dilatation and curettage and had ready access to facilities that provided blood transfusions and performed emergency resuscitation procedures were allowed to serve as treatment sites.[138] The participants were divided into three groups according to gestational age. The first group contained patients with a gestation of 49 days or less; the second group consisted of patients with a gestation of 50-56 days; and the third group contained patients with a gestation of 57-63 days.[139] A total of 2,121 women enrolled in the study, with 859 patients in the first group, 722 patients in the second group, and 540 patients in the third group.[140] Most of the participants were Caucasian (71%), 20-29 years of age (61%) with a mean age of 26.9 years, of normal body mass index (71%), nulliparous (55%), and had a previous elective abortion (51%).[141]

To be considered for inclusion in the U.S. clinical trial, a woman had to be at least 18 years of age and needed to meet some minimum health requirements. In addition, each participant had to request a voluntary termination of pregnancy, had to have a positive urine pregnancy test and an intrauterine pregnancy with a

[137] Department of Health and Human Services, Public Health Service, Food and Drug Administration, Center for Drug Evaluation and Research, Application Number: 20-687, Medical Review(s), Medical Officer's Review of Amendments 024 and 033 [hereinafter Review of Amendments]. Because the data gathered from the U.S. clinical trial was still being audited at the time of the submission of the Population Council's NDA, the results of the French trial formed the basis of the Council's NDA. Nevertheless, the U.S. clinical trial was necessary in order to assess how the regimen would operate within the American health care system and to assure that the results of the French trials were not haphazard or unreliable.

[138] Review of Amendments, *supra* note 137.

[139] *Id.*

[140] *Id.* The treatment regimen was the same as in France. It consisted of the administration of 600 milligrams of mifepristone followed two days later by 400 micrograms of misoprostol. Clinical observation for four hours followed misoprostol administration. The participant returned to the site approximately two weeks later to confirm pregnancy termination. *See* Beverly Winikoff, *et al.*, *Acceptability and Feasibility of Early Pregnancy Termination by Mifepristone-Misoprostol: Results of a Large Multicenter Trial in the United States*, 7 Archives of Fam. Med. 360 (1998).

[141] *See* Review of Amendments, *supra* note 137.

duration of gestation of 63 days or less that was confirmed by uterine size on a pelvic examination and by a vaginal ultrasound evaluation, and had to agree to undergo surgical intervention if the study procedures failed to terminate her pregnancy. Finally, the study only included U.S. residents who had proffered informed written consent to a supervising physician.[142]

On the other hand, exclusion criteria included the existence of any disorder which represented a contraindication to the use of mifepristone or misoprostol, a history of severe liver disease, respiratory problems, renal disease, thromboembolism, cardiovascular disease, chronic hypertension, anemia, clotting defects, or pelvic inflammatory disease.[143] Women who had an intrauterine device *in situ*, were breastfeeding, or had an ectopic pregnancy were also excluded.[144] Furthermore, women who were unlikely to understand or comply with the requirements of the study or who lived more than one hour from the emergency care facility which provided surgical or resuscitation procedures for the abortion center were not allowed to participate in the trial.[145] Lastly, any woman who was over 35 years old and smoked more than 10 cigarettes a day, and who had additional risk factors for cardiovascular disease such as diabetes or hyperlipidemia could not participate in the U.S. clinical trial.[146]

2. Adverse Reactions Found in U.S. Clinical Trial

The results of the U.S. trial were similar to the results of the French clinical trial. Overall, a total of 259 patients, out of the 2,121 patient population, had failed medical abortions. Of these failed abortions, 79 (27%) had ongoing pregnancies, 126 (43%) had incomplete abortions, 30 (10%) requested surgical terminations,

[142] *See id.*
[143] *See id.*
[144] *See id*
[145] *See id.*
[146] *See id.*

and 60 (20%) had surgical terminations because of medical indications related to the medical procedure.[147] As in the French clinical trial, many adverse episodes were found to accompany the RU-486 treatment regimen. 99% of the patients in each gestational cohort reported adverse events, and most patients reported even more than one adverse event.[148] While 23% of the adverse events were judged to be severe, the majority of such events were of mild or moderate severity.[149] The most commonly reported adverse episodes were abdominal pain and uterine cramping followed by nausea, vomiting, headache, dizziness, and diarrhea.[150] Additionally, the first, second, and third cohorts experienced median bleeding durations of 14 days, 15 days, and 15 days respectively, which were considerably longer than the bleeding durations found in the French clinical trial.[151] Although there were no deaths, 14 (0.7%) patients were hospitalized for an adverse event.[152] In particular, of these 14 patients, two of four from the 49 gestational days or less group, three of five from the 50-56 gestational days group, and three of five from the 57-63 gestational days group endured a drug-related adverse event, most commonly excessive bleeding.[153] The remaining six patients were hospitalized for reasons unrelated to the treatment regimen such as pneumonia, meningitis, automobile accident, depression, shooting injury, and endometritis.[154] Nineteen patients (0.9%) had emergency room visits that did not result in hospitalization. Of those 19 patients, 16 experienced excessive bleeding (two from the 49 days or less group, seven from the 50-56 days group, and seven from the 57-63 days group), while the other three had chest pain, nausea and vomiting, and cramping.[155]

Moreover, four patients received blood transfusions (one from the 49 gestational days or less group, two from the 50-56 gestational days group, and one from the 57-63 gestational days group). IV fluids were

[147] *See id.*
[148] *See id.*
[149] *See id.*
[150] *See id.*
[151] *See id.*
[152] *See id.*
[153] *See id.*
[154] *See id.*
[155] *See id.*

administered to nine patients in the 49 days or less group, 19 patients in the 50-56 days group, and 18 patients in the 57-63 days group.[156] The proportion of patients with a decrease in hemoglobin or hematocrit of more than 20% from their pre-mifepristone levels increased significantly with gestational age, from 3.1% in the 49 gestational days or less cohort to 8% in the 57-63 gestational days cohort.[157] Hypotension after mifepristone administration occurred in 0.3% - 1.4% of the treatment population, and hypertension after mifepristone administration occurred in 1.5% - 1.7% of all treated patients.[158] Finally, 18.2% - 21.3% of all patients experienced a decrease in heart rate by over 20% after the administration of misoprostol, while, on the other hand, 11.8% - 14.1% of all patients experienced an increase in heart rate by over 20% after the administration of misoprostol.[159]

Even in light of all of these recorded adverse episodes, the Population Council determined, based on an acceptability and feasibility study it had conducted, that the treatment regimen of oral mifepristone and misoprostol was both acceptable to women and health care providers in the United States and feasible for continued clinical practice. Nearly all of the participants in the U.S. clinical trial (95.7%) recommended the procedure to others, 91.2% claimed they would choose it again, and 87.6% considered the procedure either very or moderately satisfactory.[160] Surprisingly, even among those women for whom the method had failed, 69.6% said they would try it again, 84.9% would recommend it to others, and 51.9% considered it either very or moderately satisfactory.[161] The Population Council's acceptability and feasibility study found that the most commonly cited positive attributes of the RU-486 treatment regimen were the lack of surgery, the

[156] *See id.*
[157] *See id.*
[158] *See id.*
[159] *See id.*
[160] *See* Beverly Winikoff, *et al.*, *Acceptability and Feasibility of Early Pregnancy Termination by Mifepristone-Misoprostol: Results of a Large Multicenter Trial in the United States*, 7 Archives of Fam. Med. 360 (1998).
[161] *See* Beverly Winikoff, *et al.*, *Acceptability and Feasibility of Early Pregnancy Termination by Mifepristone-Misoprostol: Results of a Large Multicenter Trial in the United States*, 7 Archives of Fam. Med. 360 (1998).

noninvasiveness of the procedure, and its simplicity.[162] On the other hand, the most commonly cited worst features related to the fear of side effects and uncertainty over the newness of the procedure.[163] Overall, two-thirds of the patient population expressed that the experience was better than expected.[164] On the feasibility front, the study data suggested that a significant proportion of women found it cumbersome to manage the three visits required by the trial regimen, citing professional obligations, child care needs, and transportation.[165] As a result of the cumbersome nature of the treatment regimen, these women and some health care providers endorsed the feasibility of home administration of mifepristone and misoprostol.[166]

D. RU-486 Receives Conditional Approval

On July 19, 1996, only four months after the Population Council's submission of its NDA, the Reproductive Health Drugs Advisory Committee of the FDA assembled at the FDA's Technical Center in Gaithersburg, Maryland to examine the safety and efficacy data presented by the Population Council and to advise the FDA on whether to approve RU-486 for use as an abortifacient.[167] In keeping with the continuous twists and turns of RU-486's saga, the Advisory Committee's meeting presented yet another illustration of RU-486's eventful path toward approval. Given the controversial nature of the subject at issue and the passion that animated both sides of the abortion debate, the FDA took unusual security precautions for its all-day meeting. Based on the extraordinary security measures taken by the FDA, the meeting could have been mistaken for an unveiling of CIA secrets. For example, uniformed police officers patrolled the entrances to

[162] *See* Press Release, Population Council, Early Medical Abortion with Mifepristone and Misoprostol Is Highly Acceptable to American Women and Feasible Within the U.S. Health Care System (July 14, 1998), *available at* http://www.popcouncil.org/news_views/earlymed.html.
[163] *See id.*
[164] *See id.*
[165] *See id.*
[166] *See id.*
[167] *See* Gina Kolata, *Abortion Pill Reaches New U.S. Juncture*, N.Y. Times, July 19, 1996 at A10. The FDA chose to begin its review process so soon after the submission of the NDA because it had classified the application as a priority application on the grounds that it was the first drug proposed for its indication. *See New Drug Application, supra* note 75. Under the goals delineated in the Prescription Drug User Fee Act of 1992, Pub. L. No. 102-571, 106 Stat. 4491 (1992) (codified as amended at 21 U.S.C. §§ 379g-h (1994 & Supp. III 1997)), the FDA is to act on priority applications within six months.

the FDA's Technical Center; attendees assembled at a motel in Washington, D.C. and were surreptitiously transported to the meeting site by special vans;[168] and upon arriving at the meeting, participants had to pass a blockade of local and federal police before being ushered in through metal detectors. As the attendees quickly filtered into the meeting, a small assembly of people protested outside the building but were kept away from the meeting and the participants by a security blockade.[169] In a letter dated before the date of the Advisory Committee meeting, members of pro-life groups criticized the Clinton Administration for politicizing the drug approval process and called upon Dr. Kessler to recuse himself from the proceedings of the Advisory Committee meeting on the grounds that his proactive efforts with the Clinton Administration to bring the drug to the American market had created impermissible conflicts of interest.[170]

Even in the face of all of this controversy and drama, the meeting went forward as planned. By a vote of 6 to 2, the Committee ruled that the French data indicated the efficacy of the RU-486 regimen in terminating early pregnancy.[171] A unanimous Committee, however, did express reservations about final efficacy questions in the current absence of final audited U.S. data and recommended that the FDA review the U.S. data when completed to assess if it was consistent with the French clinical data.[172] With seven in favor and one abstention, the Committee also found that the French data and the preliminary U.S. data adequately demonstrated the safety of the regimen for use in the United States under its proposed indication.[173] Taking into consideration the overall safety and efficacy data, in a 6-0 vote with two abstentions, the Committee further determined that the French studies revealed that the benefits of a mifepristone and misoprostol regimen outweighed its risks.[174] The Committee then reserved the right to reexamine the data if information from the U.S. clinical trial contradicted the French data.[175]

[168] *See RU-486: FDA Receives Some Good Advice,* Star-Tribune (Minneapolis-St. Paul), July 24, 1996, at 12A.
[169] *See* Sheryl Stolberg, *FDA Panel Calls for OK of Abortion Pill*, L.A. Times, July 20, 1996, at A1.
[170] *See* Cal Thomas, *The Silver Bullet of Abortion*, Fort Worth Star-Telegram, July 23, 1996, at 11.
[171] *See New Drug Application, supra* note 75.
[172] *See id.*
[173] *See id.*
[174] *See* Review of Amendments, *supra* note 137.
[175] *See* Gina Kolata, *Panel Advises FDA to Allow Abortion Pill*, N.Y. Times, July 20, 1996, at A1.

Two months after the Advisory Committee meeting, and after a then seven-year battle to introduce RU-486 into the United States, the FDA granted conditional approval to RU-486 on September 18, 1996. However, the FDA did subject the Population Council to the following Phase Four commitments: (1) to monitor the adequacy of the drug's distribution and credentialing system; (2) to follow up on the outcome of a representative sample of mifepristone-treated women who have surgical abortions after method failure; (3) to evaluate the long-term effects of multiple uses of the treatment regimen; (4) to assess whether women adhere to the complete regimen; (5) to study the safety and efficacy of the drug in women under the age of 18, women over the age of 35, and women who smoke; and (6) to ascertain the effect of the drug on children born after the RU-486 treatment had failed and the pregnancy had not been terminated by methods of surgical intervention.[176] Furthermore, in its approvable letter, the FDA requested additional information on the drug's labeling and manufacturing processes.[177]

VI. ON THE CUSP OF APPROVAL: THE ABORTION PILL'S UNITED STATES DEBUT IS POSTPONED

A.

[176]Department of Health and Human Services, Public Health Service, Food and Drug Administration, Center for Drug Evaluation and Research, Application Number 20-687: Approval Letter (Sept. 18, 1996).

[177]*See* Gina Kolata, *Pill for Abortion Clears Big Hurdle To Its Sale In U.S.*, N.Y. Times, Sept. 19, 1996, at A1. The announcement by the Population Council that it had secured conditional FDA approval not surprisingly came on the eve of a hotly contested abortion vote in the House of Representatives. The Population Council was attempting to declare victory over its anti-abortion opponents and to signal to these opponents that any anti-abortion legislative activity on the horizon could not encumber RU-486's imminent entry into the United States, especially in light of its recent receipt of conditional approval from the FDA. The House vote the following day involved the legalization of a form of late-term abortion called partial-birth abortion, which had been outlawed by Congress in the Partial-Birth Abortion Act of 1995, H.R. 1833, 104th Cong. (1995); S. 939, 104th Cong. (1995). Having been vetoed by President Clinton, the House voted to override the veto 285-137. *See* Gina Kolata, *Pill for Abortion Clears Big Hurdle To Its Sale In U.S.*, N.Y. Times, Sept. 19, 1996, at A1. Anti-abortion forces were stung, however, when the Senate voted to sustain President Clinton's veto. Despite subsequent congressional attempts, the partial-birth abortion ban has not been enacted into law.

For a brief moment, the RU-486 approval process was running smoothly. After the Population Council had secured conditional approval from the FDA, it appeared that the French abortion pill would soon debut on the U.S. pharmaceutical market. Of course, RU-486's brief moment of calm would not last for long. Indeed, its attainment of conditional FDA approval was the period of calm before the storm. Soon after winning conditional approval, the story of RU-486 took another interesting turn, which ensnared it in the most controversy it had seen to date and served to snag its trajectory toward the U.S. pharmaceutical market.

By way of background to this controversy, the Population Council had licensed another nonprofit organization, Advances in Health Technology, *see supra* note 91, to manufacture and distribute RU-486 in the United States.[178] Advances in Health Technology subsequently sub-licensed the manufacturing and distribution rights to NeoGen Industries, a corporation controlled by a lawyer and businessman named Joseph Pike. Pike had earlier worked with the Population Council on the development of an intrauterine contraceptive device.[179] In an effort to raise money from investors to finance the RU-486 project, Pike established a series of limited partnerships and some other companies that were incorporated in the Cayman Islands.[180] One investor, the Giant Group of Beverly Hills, paid $6 million to Pike for a 26% interest in Pike's companies and allegedly secured as part of the agreement a restrictive covenant that barred Pike from selling a significant portion of his entities to other prospective investors.[181] When Pike allegedly violated this agreement by attempting to sell a substantial share of his entities to various other purchasers, the Giant Group filed suit in Los Angeles Superior Court, accusing Pike of fraud, breach of fiduciary duty, fraudulent concealment, breach of contract, and unfair business practices.[182] In keeping with RU-486's fascinating and controversial odyssey was the lawsuit's further contention that Mr. Pike was a disbarred lawyer who had been convicted of forgery

[178] *See Editorial, The Troubles of RU-486*, N.Y. Times, Nov. 8, 1996, at A32.
[179] *See* Tamar Lewin, *Abortion Pill's Legal Woe May Be Nearing an End*, N.Y. Times, Jan. 25, 1997, at A7.
[180] *See* Gina Kolata, *Business Dispute May Delay Introduction of Abortion Pill*, N.Y. Times, Nov. 1, 1996, at A20. The Cayman Islands entities were not required to disclose the names of officers and partners. *See id.*
[181] *See id.*
[182] *See id.*

in North Carolina and, as a result, received a suspended two-year sentence and 18 months probation.[183] Information about Pike's alleged notorious dealings and shady past soon ignited a flurry of lawsuits against him that hindered RU-486's entry into the U.S. consumer market. KCC Delaware, one of the investors in Pike's entities, sued Pike and accused him of concealing his past and mishandling the investment deal.[184] In a separate suit filed on November 4, 1996 in New York State Supreme Court, the Population Council and Advances in Health Technology charged Pike with fraud.[185] The lawsuit alleged that Pike had not properly accounted for the money that was invested in his entities and had ciphoned off money into some dubious off-shore entities.[186] While the Population Council and Advances in Health Technology did not seek to rescind the sublicenses Pike had issued to Danco Laboratories and other companies to manufacture and distribute the drug, they did seek to wrest control of the company from him by having his interest in the entities transferred to a court-appointed receiver.[187] The Population Council strongly believed that Pike's past legal troubles and his efforts to conceal them disqualified him from serving as a fiduciary and the lead business entrepreneur in the RU-486 enterprise – a politically sensitive and controversial venture that needed a person of irrefutable integrity at its helm.

After months of legal jostling, the stalemate finally came to an end on February 12, 1997 when the Population Council announced that it had settled the lawsuit surrounding control of RU-486 and had arranged for a new privately held company, Advances for Choice, to handle the drug.[188] Under the settlement, Pike agreed to sell most of his equity interest in the RU-486 enterprise, keeping only a modest passive investment, and to

[183] *See id.*

[184] *See* Sharon Bernstein, *Persistence Brought Abortion Pill to U.S.: Two Feminist Activists Culled Nonprofit Organizations and Dedicated Individuals To Do The Work That No Pharmaceutical Company Was Willing to Tackle*, L.A Times, Nov. 5, 2000, at A1.

[185] *See* Tamar Lewin, *Dispute May Delay Abortion in the U.S.*, N.Y. Times, Nov. 6, 1996, at A16

[186] *See id.*

[187] *See* Caryle Murphy & Kathleen Day, *Abortion Pill's U.S. Debut Snagged by Business Dispute: Sponsor Seeks to Oust Associate For Not Disclosing Disbarment*, Wash. Post., Jan. 12, 1997, at A1.

[188] *See* Tamar Lewin, *Legal Bout Over Abortion Pill Ends*: *Group Will Apply For FDA Approval*, L.A. Daily News, Feb. 13, 1997, at N19. The Population Council had previously intended to distribute RU-486 through Advances for Health Technology, which was subsumed into the new company. *See* FDC Reports*, Mifepristone (RU-486) Distribution Given to a New Company Headed by Former Generic Exec Van Hulst*, The Pink Sheet, Feb. 17, 1997.

relinquish any role in the management of the newly formed company.[189] Jack Van Hulst, a Dutch attorney and Population Council consultant, became the president and chief executive of Advances for Choice and forecasted that the drug would be available to doctors and clinics by December 1997.[190]

B.

[189] American Political Network, Spotlight Story, Story RU-486: Suit Settled; Sales May Begin in '97, 7 Abortion Rep. No. 137, Feb. 13, 1997, *available in* WL APN-AB File.

[190] *See* Tamar Lewin, *Legal Hurdle Cleared in Sale of French Abortion Pill in U.S.*, N.Y. Times, Feb. 13, 1997, at A28.

Predictably, Mr. Van Hulst's prediction did not come to fruition as yet another twist in the long and convoluted battle to bring the French abortion pill to the U.S. market arose. Just two weeks after the smoke had cleared in the Pike conflagration, the Population Council's European manufacturer, Budapest-based Chemical Works of Gedeon Richter, Ltd., announced that it was terminating its five-year bulk mifepristone manufacturing agreement.[191] This shocking announcement caused Danco Laboratories Ltd., the domestic marketer and distributor of the drug, to file suit against Gedeon Richter for breach of contract in New York State Supreme Court in Manhattan.[192] Under the manufacturing and supply agreement, Gedeon Richter had agreed to replace Roussel-Uclaf as manufacturer and produce all of Danco's requirements for bulk mifepristone, while an unnamed manufacturer had agreed to put mifepristone into tablet form.[193] Danco's law suit contended that Gedeon Richter's decision could be "a major and potentially ruinous setback."[194] Danco further asserted that the manufacturing delays could jeopardize Danco's RU-486 U.S. patent rights, which were scheduled to expire on January 8, 2002, and could cause Danco to lose sales and marketing opportunities well in excess of $200 million.[195]

C.

[191]See Aaron Zitner, What Ever Happened to the Saga of RU-486?, Boston Globe, Nov. 23, 1997, (Magazine), at 18. At approximately the same time, Roussel-Uclaf and its parent company, Hoechst, transferred without remuneration the patent rights for RU-486 to a newly formed small company called Excelgyn, headed by former chief executive of Roussel-Uclaf, Edouard Sakiz. See Pill for Abortion Ends Production, N.Y. Times, Apr. 9, 1997, at D2. Roussel-Uclaf admitted that boycotts of the company's products, particularly the boycott of Hoechst's new allergy drug, Allegra, which was expected to exceed $3 million in sales within the next three years and be much more profitable than RU-486, along with general pressure from the pro-life movement, influenced its decision. See American Political Network, Story, RU-486: Pharmaceutical Company Gives Up Rights, 7 Abortion Rep. No. 174, Apr. 9, 1997, available in WL APN-AB File. Roussel-Uclaf expected that Sakiz's smaller company would be less vulnerable to consumer pressure. The transaction between the two companies did not affect the American situation or the availability of RU-486 in the United States since Roussel-Uclaf had transferred the American rights to the drug years earlier.

[192]See FDC Reports, Richter Exit From RU-486 Bulk Supply Agreement Could Jeopardize Danco Patent Rights, The Pink Sheet, June 16, 1997.

[193]See id. The Population Council had submitted its NDA for RU-486 with Roussel-Uclaf as the "stand-in active substance manufacturer" until Gedeon Richter provided the Population Council with internal stability tests and demonstrated the comparability of its manufacturing processes to those of Roussel-Uclaf. See id.

[194]See American Political Network, Health & Reproduction, Story, RU-486: Delay Seen To Be Inevitable, 7 Abortion Rep. No. 212, June 13, 1997, available in WL APN-AB.

[195]See Danco Lab., Ltd. v. Chemical Works of Gedeon Richter, Ltd., 274 A.D.2d 1, 6-7, 711 N.Y.S.2d 419 (1st Dep't 2000); see also FDC Reports, Richter Exit From RU-486 Bulk Supply Agreement Could Jeopardize Danco Patent Rights, The Pink Sheet, June 16, 1997. With plans to market RU-486 in the United States in complete upheaval, a New York abortion-rights organization, Abortion Rights Mobilization, under the presidency of Lawrence Lader, began offering the drug to as many as 10,000 women in New York. See Tamar Lewin, Group Is Intensifying Its Campaign To Distribute Abortion Pill, N.Y. Times, July 2, 1997, at A21. In 1996, Abortion Rights Mobilization had secured FDA approval to use its version of the RU-486 drug in research trials in New York, Nebraska, Vermont, Montana, California, and Washington. See id. Although the Population Council holds the U.S. patent rights to RU-486, others are permitted to copy patented drugs for research use so long as the drugs are not sold commercially. See id.

For over a year, the fate of RU-486 remained uncertain; in fact, RU-486's future seemed rather bleak. The drug's sponsors experienced colossal difficulties in locating a new manufacturer after Gedeon Richter's withdrawal. Moreover, with Republicans in the majority on Capitol Hill, RU-486's path toward approval, already mired in a manufacturing and litigation mess, became further quagmired. On June 25, 1998, the House of Representatives voted 223 to 202 to block the FDA from approving RU-486.[196] **While the House's conservative position on the drug was unsurprising, advocates of RU-486 became concerned that RU-486 might encounter some problems from an unexpected source. In September 1998, the White House officially announced the nomination of Jane Henney, M.D., a 51-year old Indiana native and former vice president for health sciences at the University of New Mexico, as the next FDA Commissioner.**[197] **Not surprisingly, questions about Henney's position on RU-486 abounded at her confirmation proceedings. In particular, congressional leaders expressed interest in whether she would pursue the same policy activism of her predecessor. To win Senate approval, Dr. Henney reiterated to the Senate Labor and Human Resources Committee that, in her prior tenure as Deputy Commissioner for Operations, she had not actively solicited an application for approval of RU-486. Dr. Henney's transparent, though subdued, support for the drug, prompted some Republicans to stall her confirmation; however, in the end, as a result of her political adroitness in dealing with such a politically potent issue, she was able to gain Senate confirmation.**[198]

After failing to block Dr. Henney's confirmation, some Republicans made another effort to keep RU-486 bottled up and out of the U.S. pharmaceutical market. On June 8, 1999, House Republicans, led by Representative Tom Coburn of Oklahoma passed an amendment to the FY2000 Agriculture Appropriations bill that barred the FDA from using government funds to approve abortifacient drugs, including mifepristone.[199] Ultimately, however, this measure proved unsuccessful as the Senate approved $1.18 billion in spending for the FDA in the Agriculture/FDA appropriations bill passed on October 13, 1999, H.R. 2684, 106th Cong., 1st Session.[200] Representative Coburn's language barring the FDA from approving RU-486 or any other

[196] See Katharine Q. Seelye, House Votes to Block FDA on Approval of Abortion Pill, N.Y. Times, June 25, 1998, at A20.
[197] See New Commissioner, New Challenges, BioPharm, Sept. 1, 1998, at 12.
[198] See FDC Reports, FDA Commissioner Negotiations Focus on Non-FDA Abortion Issues, The Pink Sheet, Oct. 19, 1998.
[199] *See* Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Act, 2000, H.R. 3780-03, 106th Cong. (1999); *see also* Press Release, NARAL, Congress Blocks FDA Approval of RU-486 (June 8, 1999), *available at* http://www.naral.org/mediaresources/press/pr060899_congress.html.
[200] *See* FDC Reports, *FDA Appropriations*, The Pink Sheet, Oct. 18, 1999.

abortifacient drug was removed from the bill during conference.[201]

VII. READY, SET, NO GO

A. The FDA's Second Approvable Letter

By the end of 1999, Danco Laboratories, the Population Council's sublicensee responsible for the marketing of RU-486 in the United States, announced that it had finally obtained a replacement for Gedeon Richter. However, out of a concern for potential extremist violence, Danco chose to withhold the name of the new manufacturer.[202] On February 18, 2000, following the resolution of the manufacturing crisis, the FDA issued another approvable letter, expressing that RU-486 would receive approval, but only pending resolution of certain specified marketing and labeling issues.[203] In particular, the approvable letter reminded the Population Council of its Phase Four commitments, as delineated in the September 1996 approvable letter, and expressed concern that the FDA had not received adequate information demonstrating that the drug, when marketed in accordance with the terms of the proposed distribution system, is safe and effective for its indicated use.[204] The FDA further demanded that only abortion practitioners prescribe RU-486, that all prescribing doctors be trained in the drug's use and in reading ultrasound scans to confirm the duration of pregnancy, and that prescribing doctors maintain admitting privileges at an emergency care facility no more than one hour away from their offices.[205] Following receipt of this second approvable letter from the

[201] *See id.*

[202] *See* FDC Reports*, Mifepristone Ancillary Trial Costs Are Being Covered By Seattle-Area Insurers*, The Pink Sheet, Oct. 11, 1999.

[203] *See* FDC Reports, *Mifepristone*, The Pink Sheet, Feb. 21, 2000.

[204] February 18, 2000 Approvable Letter (FDA letter to Population Council regarding NDA 20-687).

[205] Similar requirements have been imposed on other drugs, including thalidomide and some narcotics used to relieve pain in cancer patients. *See* Sheryl Gay Stolberg, *FDA Adds Hurdles in Approval of Abortion Pill*, N.Y. Times, June 8, 2000, at A21. After learning of these new requirements, abortion advocates feared that the FDA's demands could lead to the creation of a national registry of RU-486 providers and that such a registry, which would give abortion opponents the opportunity to single out and potentially harass such providers, would discourage doctors from becoming abortion providers, thereby limiting access to abortion services.

FDA, the Population Council and Danco Laboratories promptly addressed the FDA's concerns by the end of March 2000.[206] The FDA then proceeded to set September 30, 2000 as the action date upon which a decision on RU-486's status in the United States would finally be made.[207] This action date indicated that the Population Council's and Danco's submission in response to the February 18, 2000 approvable letter was regarded as a "Class 2" submission requiring substantial review time, which under the Prescription Drug User Fee Act guidelines, is usually six months.[208]

B. G.D. Searle Distances Itself from RU-486

As the crucial September 30, 2000 federal deadline neared, RU-486's compelling saga took another interesting turn, which had the potential of encumbering the drug's entrance into the U.S. market altogether. Only a month before FDA action on the pending NDA for RU-486 was expected, Pharmacia Corp.'s G.D. Searle & Co., the manufacturer of a gastric ulcer treatment called Cytotec, the brand name for misoprostol, issued a statement indicating that its gastric ulcer treatment was contraindicated for use in pregnant women.[209] In this statement, the company distanced itself from Cytotec's use in combination with mifepristone in early pregnancy termination and noted that although "the uterotonic effect of Cytotec is an inherent property" of the prostaglandin product, "Cytotec is not approved for the induction of labor or abortion."[210] In a move criticized for its partiality on the part of abortion opponents, the FDA inserted itself into the controversy by attempting to negotiate with Searle. The FDA suggested a change to Cytotec's label to include pregnancy termination as an indicated use of misoprostol.[211] Abortion advocates, on the other hand, applauded the

[206] *See* FDC Reports, *RU-486 Action Date Is September 30: Allen Named Reproductive Division Director*, The Pink Sheet, June 12, 2000.
[207] *See id.*
[208] *See* The Prescription Drug User Fee Act of 1992, Pub. L. No. 102-571, 106 Stat. 4491 (1992) (codified as amended at 21 U.S.C. §§ 379g-h (1994 & Supp. III 1997)).
[209] *See* FDC Reports, *Searle Cytotec Pregnancy Reminder Issued as RU-486 Action Nears*, The Pink Sheet, Aug. 28, 2000.
[210] *See id.*
[211] *See* FDC Reports, *Searle/FDA Cytotec Labeling Negotiations Continue Ahead of Mifeprex Launch*, The Pink Sheet, Oct. 9, 2000. Outraged by the FDA's tactics, Representative Coburn contended that "a precedent has been set because we now have the FDA asking a manufacturer to allow a drug to be used off label by their implicit approval of another two-drug combination, when in fact the manufacturer doesn't want any part of it and doesn't want the liability associated with it." *See id.*

FDA's proactive, though unsuccessful efforts in this regard, while also decrying Searle's action as a deliberate attempt to hinder mifepristone's entrance into the U.S. pharmaceutical market.

VIII. RU-486 FINALLY DEBUTS

A. At Last, FDA Approval

On September 28, 2000, in spite of Searle's actions, and after a 12-year intense journey with numerous false starts and stops, RU-486 finally secured FDA approval under 21 C.F.R. § 314.520 (Subpart H).[212] The timing of the FDA's approval deadline was acute: by ensuring completion of its review before the end of 2000, the FDA avoided confronting the potentiality of a new adverse executive administration, as well as a possible appropriations rider that would deny funding for review in fiscal year 2001.[213]

The approval letter, however, delineated several restrictions for the distribution of RU-486 in the United States. First, under 21 C.F.R. § 314.520, RU-486 must be provided by or under the supervision of a physician who must be qualified: (1) to assess the duration of pregnancy, leaving ultrasound evaluation to the professional judgment of the treating physician; (2) to diagnose ectopic pregnancies; and (3) to provide surgical intervention in situations of incomplete expulsion or excessive bleeding, or a plan to provide such emergency care through other qualified physicians. In addition, the physician must read and understand the provisions of the prescriber's agreement, provide each patient with a medication guide and patient agreement form, fully explain both, and obtain the patient's signature on the patient agreement form, notify the sponsor

[212]FDA Approval Letter, September 28, 2000, NDA 20-687. Subpart H grants accelerated approval to certain new drugs that have been studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefits to patients over already existing treatments. Because the FDA determined that the termination of an unwanted pregnancy is a serious condition within the scope of Subpart H and because it resolved that the meaningful therapeutic benefit over existing treatments was the avoidance of a surgical procedure, the FDA granted RU-486 approval under Subpart H. Subpart H allows for restrictions on use or distribution if the FDA concludes that a drug shown to be effective can only be used safely if restrictions on use or distribution are implemented. *See* 21 C.F.R. § 314.520 (2000). The rules grant the FDA special authority to restrict the distribution of the newly licensed drug and delineate a procedure for quick removal from the market should problems arise.

[213]*See* FDC Reports, *Searle Cytotec Abortion Use Clears FDA – In Another Sponsor's Label*, The Pink Sheet, Oct. 2, 2000.

or its designate in writing of any instances of ongoing pregnancy which are not terminated subsequent to the conclusion of the treatment procedure, report all hospitalizations, transfusions, or other serious events to the sponsor or its designate, and record the drug package's serial number in each patient's record.[214] Second, with respect to the aspects of distribution other than physician qualifications, the FDA mandated certain procedures for storage, dosage tracking, and damaged product returns to ensure the integrity of the product.[215] In particular, the FDA required secure manufacturing, receiving, and holding areas for the drug, secure shipping procedures, including tamper-proof seals, controlled returns procedures, a tracking system that can trace individual packages to a patient while maintaining patient confidentiality, use of authorized distributors and agents with the necessary expertise to handle distribution requirements, and a direct, confidential distribution system that allows only qualified physicians to receive the drug for the purpose of patient dispensation.[216]

Third, as permitted under 21 CFR § 201.57(e), the FDA imposed a black box warning requirement whereby the package would include information regarding the desirability of surgical intervention and access to these services either through the prescriber or by referral should the treatment procedure fail.[217] Fourth, some of the Phase Four commitments that were specified in both the September 1996 and February 2000 approvable letters were integrated into a cohort-based study of the safety outcomes of patients having medical abortion under the care of physicians with surgical intervention skills as compared to the safety outcomes of those patients whose physicians must refer them to other physicians for surgical procedures.[218] Finally, the FDA requested the completion of a surveillance study on the outcomes of ongoing pregnancies on children born after the unsuccessful completion of the RU-486 treatment regimen.[219]

[214] FDA Approval Letter, September 28, 2000, NDA 20-687.
[215] *See* Memorandum, Department of Health and Human Services, Public Health Service, Food and Drug Administration, Center for Drug Evaluation and Research, September 28, 2000.
[216] *See id.*
[217] *See* 21 C.F.R. § 201.57(e)(2000).
[218] *See* Memorandum, Department of Health and Human Services, Public Health Service, Food and Drug Administration, Center for Drug Evaluation and Research, September 28, 2000.
[219] FDA Approval Letter, September 28, 2000, NDA 20-687. Although the FDA had expressed an interest in conducting studies

IX. THE ABORTION PILL IS HARD TO SWALLOW

A.

As expected, the FDA's approval of RU-486 incited a "political tempest"[220] with abortion rights advocates celebrating the drug's FDA approval as the most remarkable triumph of abortion rights since Roe v. Wade. On the other hand, anti-abortion activists decried the pill as an "easily wielded tool of infanticide."[221] Abortion rights advocates nonetheless acknowledged that their victory was an exceedingly fragile one. For one, the FDA decision came just over a month before the 2000 presidential election. Given this political backdrop, RU-486's future probably depended on the next occupant of the White House, especially because the politicized nature of the drug could factor heavily into the new President's selection of an FDA Commissioner. While both candidates stated opinions on the FDA's decision to approve RU-486, neither was willing to expend political capital on the abortion issue and risk alienating moderate, independent voters.[222] Bush called the decision "wrong," warning, "I fear this abortion pill... will make abortions more common. As president, I will work to build a culture that respects life."[223] However, when asked specifically if he would overturn

on the long-term effects of multiple use of the regimen, privacy concerns militated against the implementation of such a study. *See* FDC Reports, *Mifeprex Label Allows Use by Physicians Not Trained in Surgical Abortion*, The Pink Sheet, Oct. 2, 2000.

[220] American Political Network, American Health Line, Campaign 2000, RU-486: FDA Approval Evokes Political 'Tempest', 6 Abortion Rep. No. 9, Sept. 29, 2000, *available in* WL APN-AB File.

[221] *See* Raja Mishra, *New Option Marks a Turning Point*, Boston Globe, Sept. 29, 2000, at A12.

[222] On paper, the candidates offered two diametrically opposed perspectives on abortion. While Al Gore is a supporter of abortion rights, George Bush is on record supporting a constitutional amendment that would outlaw abortion except in cases of rape, incest, or when the life of the mother is in danger. *See* Robin Toner, *The 2000 Campaign: Focus On The Issues, Both Sides on Abortion Issue Step Up Fight*, N.Y. Times, Oct. 27, 2000, at A29. George Bush's political adroitness, however, allowed him to give these reassurances to the pro-life movement, while nevertheless occasioning speculation on how fervently he would pursue this agenda. For example, he said that in making appointments to the Supreme Court he would look for strict constructionists like Justices Scalia and Thomas but painstakingly avoided saying that he would appoint only Justices who would seek to overturn Roe v. Wade. *See* Robin Toner, *The 2000 Campaign: Focus On The Issues, Both Sides on Abortion Issue Step Up Fight*, N.Y. Times, Oct. 27, 2000, at A29.

[223] *See* American Political Network, American Health Line, Campaign 2000, RU-486: FDA Approval Evokes Political 'Tempest', 6 Abortion Rep. No. 9, Sept. 29, 2000, *available in* WL APN-AB File.

the FDA's decision, Bush's campaign spokesperson, Scott McClellan, stated [i]t appears the president does not have the authority to order drugs off the market. As president, he would order a careful review to ensure that the FDA considered all the risks and did not do this as a result of political pressure from the White House."[224] Al Gore, on the other hand, contended that "[t]he FDA's decision is not about politics, but the health and safety of American women and a woman's fundamental right to choose."[225] Thus, it was evident that if Gore was elected president, the status quo on the FDA's decision to approve RU-486 would remain in place.

B. The House and Senate Get Involved Again

Furthermore, on the legislative front, the fragility of the abortion victory was readily apparent. With RU-486 now having approved status, anti-abortion members of Congress realized that rollback of the FDA's decision would not be easy. In theory, however, Congress could pursue a number of different avenues in an effort to accomplish this goal. First, Congress could instruct the Drug Enforcement Administration to classify RU-486 as a dangerous substance having adverse consequences to a woman's health. This could be accomplished by reinterpreting the existing safety data and by emphasizing the fact that most women experience bleeding and uterine pain.[226] Second, Congress could encourage the Secretary of Health and Human Services to declare the drug an "imminent hazard to health" on the grounds that it ends the life of an unborn child.[227] Third and finally, the Department of Health and Human Services could seek to withdraw the drug from the market if the government's restrictions on distribution are not followed.[228]

Because such efforts have been unsuccessful in the past and because the FDA generally reconsiders drug approvals only when new evidence arises that places into doubt the drug's safety or effectiveness, the pro-life

[224] *See* Robin Toner, *Joy and Outrage*, N.Y. Times, Sept. 29, 2000, at A1.
[225] *See* American Political Network, American Health Line, Campaign 2000, RU-486: FDA Approval Evokes Political 'Tempest', 6 Abortion Rep. No. 9, Sept. 29, 2000, *available in* WL APN-AB File.
[226] *See* Sarah Lueck, *Abortion Foes Face Tough Battle Against RU-486 Drug*, Wall St. J., Feb. 12, 2001, at A28.
[227] *Society: The Abortion Pill*, Newsweek Int'l, Oct. 9, 2000.
[228] *See* Sarah Lueck, *Abortion Foes Face Tough Battle Against RU-486 Drug*, Wall St. J., Feb. 12, 2001, at A28.

members of Congress decided instead to focus their legislative activity on restricting the availability of the drug. For instance, on October 4, 2000, in the 106^{th} Congress, Representative Tom Coburn of Oklahoma and Senator Tim Hutchinson of Arkansas introduced the RU-486 Patient Health and Safety Act.[229] This Act would require administering physicians to complete an FDA-approved program before becoming RU-486 abortion providers. The proposed bill also required licensed physicians to be qualified to handle complications resulting from an incomplete or ectopic pregnancy; to be trained to perform surgical abortions; to be certified for ultrasound dating and detection of ectopic pregnancies; and to be able to admit patients at emergency care facilities no more than one hour away from their treatment sites.[230]

C. Chinese Manufacturer Creates Public Image Problems

In addition to the anti-abortion legislative activity that sprung up in the wake of RU-486's approval, another controversy erupted which tarnished the drug's public image and threatened the drug's acceptance within the medical community and the general public. When news leaked out that the previously undisclosed manufacturer of the drug is Shanghai Hua Lian Pharmaceutical Co. Ltd., an entity owned by the Chinese government, anti-abortion passions were inflamed. Senator Hutchinson's remarks immediately following this disclosure evidenced the intensity of anti-abortion passions:

[229] *See* To Require the Food and Drug Administration to Establish Restrictions Regarding the Qualifications of Physicians to Prescribe the Abortion Drug Commonly Known as RU-486, S. 3157, 106th Cong., 2d Sess. and H.R. 5385 106th Cong., 2d Sess.; *see also* FDC Reports, *Searle/FDA Cytotec Labeling Negotiations Continue Ahead of Mifeprex Launch*, The Pink Sheet, Oct. 9, 2000. After this legislation was not enacted in the 106th Congess, Senator Hutchinson and Representative David Vitter, a Republican from Louisiana, reintroduced it in the 107^{th} Congress on February 6, 2001. *See* FDC Reports, *RU-486 Lower Dose, Home-Administered Misoprostol Being Evaluated*, The Pink Sheet, Feb. 12, 2001. Presently, the legislation is still pending.

[230] *See* FDC Reports, *Searle/FDA Cytotec Labeling Negotiations Continue Ahead of Mifeprex Launch*, The Pink Sheet, Oct. 9, 2000. All of these requirements had been seriously considered by the FDA before it granted its approval to RU-486 and were ultimately rejected.

> China is well known as the leading proliferator of weapons of mass destruction. China has given new meaning to the term with the confirmation that a Chinese government firm will be the manufacturer of the recently approved RU-486 drug. China will add death and destruction to its list of exports. It is telling that no U.S. firm would manufacture the drug and that the FDA had to look to the home of forced abortion and the notorious one-child policy to find a manufacturer for the U.S. market.[231]

On another front, another abortion opponent, Douglas Johnson of the National Right to Life Committee, stated that the FDA could not adequately monitor the manufacturing processes of the Chinese factory given the factory's remote location.[232] This concern was further magnified when the House of Representatives began investigating allegations that in the recent past China had shipped tainted and mislabeled drugs into the United States.[233] Conservative members of the House and Senate bolstered their claims by citing to numerous examples of problems involving the manufacturing of drugs by the Chinese.[234] Needless to say, this interlude did not cause RU-486 to garner popularity from the general public.

D. Bush Elected President

Finally, the election of George W. Bush to the Presidency of the United States signaled perhaps the single most important factor in a potential change in domestic abortion policy and the legal status of RU-486. Although during the campaign President Bush had expressed his belief that he could not reverse the FDA's prior decision, his actions after securing the presidential victory caused abortion advocates to fret. For example, on January 23, 2001 (the 28th anniversary of Roe v. Wade), he addressed a crowd gathered for the annual March for Life,

[232] *See id.*

[233] *See id.*

[234] According to House investigators, betamethasone phosphate, a drug produced by Hua Lian for use in skin creams and asthma drugs, had been detained in Cincinnati by FDA officials earlier in the year because of false labeling. *See* Aaron Zitner, *RU-486 Firm Linked to Drug Impurities Investigation: Chinese Company That Produces Abortion Pill for U.S. Market Was Cited for Violation of Federal Laws*, L.A. Times, Oct. 20, 2000, at A29. In addition, a study conducted by the California Department of Health Services in 1998 found that high levels of contamination were present in an herbal remedy called composite tegafuri capsules and hundreds of similar products, all of which had been produced at the Hua Lian plant in China. *See id.* To further support allegations of plant integrity problems, Representative Thomas J. Bliley alerted the FDA to a report by one of its own officials who had inspected the Shanghai plant in October 1999, which found the existence of data integrity problems at the plant. *See id.*

via Representative Christopher H. Smith, a Republican from New Jersey, who transmitted the President's statement to the assembly:

> We share a great goal: to work toward a day when every child is welcomed in life and protected in law. We know that this will not come easily or all at once, but the goal leads us onward, to build a culture of life, affirming that every person and every stage and season of life, is created equally in God's image.[235]

On that same day, in a symbolic move, reversing what President Clinton had done eight years earlier, President Bush reinstated a ban on federal assistance to international organizations that "actively promote abortion as a method of family planning."[236]

Furthermore, the new President's disinclination to maintain RU-486's legal status was evidenced by his appointment of former Wisconsin Governor, Tommy G. Thompson, a conservative opponent of abortion, Secretary of the Department of Health and Human Services, the department which oversees the FDA.[237] At his confirmation hearing before the Senate Committee on Health, Education, Labor, and Pensions, Mr. Thompson assured the Committee that he would not roll back the FDA's decision unless RU-486 was proven to be unsafe.[238] He also added, however, that significant evidence of safety concerns existed that justified a fresh review of the FDA's approval process.[239] Thompson's stated position at his confirmation hearing allowed him wide latitude to either maintain the status quo on RU-486 or order his agency to conduct a new evaluation of the FDA's decision to approve RU-486. Regardless of what was said at his confirmation hearings, it did not take long for Thompson to come to a decision on RU-486. On January 20, 2001,

[236] *See id.*

[237] *See* David E. Sanger, *The 43rd President: The Transition; New Picks Firm up Conservative Cast of Bush's Cabinet*, N. Y. Times, Dec. 30, 2000, at A1.

[238] *See* Robert Pear, *Transition in Washington: Health and Human Services; Thompson Says He Will Order A New Review Of Abortion Drug*, N.Y. Times, Jan. 20, 2001, at A17.

[239] *See id.*

Thompson announced that he would conduct a new review of the safety of the abortion pill.[240]

CONCLUSION

It is clear that the final chapter in the RU-486 saga remains to be written. How that final chapter will be written remains to be seen. While the FDA's approval of RU-486 as a treatment regimen in the United States would seemingly end the debate over the drug's future, if there has been one constant throughout this drug's 20-year history, it is that whenever a resolution appears to have been reached, another significant issue or controversy develops soon thereafter. The question is what will cause the next significant issue or controversy. Will scientific and technological advances in the 21st century offer a treatment regimen that far surpasses the benefits of RU-486, and, as a result, moot this whole issue? Will the pro-life movement in the United States focus its efforts on staging a boycott of the drug companies associated with RU-486 – like the pro-life movement in France did in 1988 – thereby forcing drug companies to disassociate themselves from the drug? Will RU-486 cause some presently unknown health ailment and subject the companies associated with it to the same huge liability costs that befell the entities responsible for other contraceptive and reproductive products such as Ortho-Gynol, Dalkon Shield, and Copper-7 in the 1980's? Will abortion rights groups unite, like they have done in the past, to prevent the imposition of any restrictions on the accessibility of RU-486 and transform RU-486 into a battleground issue? Will the U.S. Supreme Court become much more conservative on abortion issues over the next few years, especially with a Republican president making all future nomination decisions, overturn Casey and Roe, and roll back abortion rights, effectively eliminating the use of RU-486? Will the distributors and manufacturers of RU-486 self-destruct and become embroiled in lawsuits against one another (*e.g.*, what resulted from the drug's association with Joseph Pike and Gedeon

[240] *See id.*

Richter)? Will the new political composition in Washington, with the Republican Party holding majorities in both legislative branches, become more proactive on issues involving RU-486 and enact similar legislative initiatives to the bills sponsored in the past by Rep. Coburn and Sen. Hutchinson? Will the HHS, under the leadership of Tommy Thompson, conduct a new review of the safety and efficacy of RU-486 and attempt to cause the reversal of the FDA's prior decision to approve the drug?

Based on this Paper's chronology of RU-486's prior history, each one of the aforementioned scenarios is possibly in the future for RU-486. My own prediction is that RU-486 will remain on the U.S. market, despite some of the inclinations of the new executive administration. Undoubtedly, the normative debate over the morality of abortion will persist as it should given that the termination of human life or potential human life, however one sees it, is an issue of the utmost gravity. In the end, however, I predict that the conclusion will be reached that Roe v. Wade is settled law. This, in turn, will leave the abortion landscape virtually unaltered, with one significant modification, the addition of a new method of abortion in the United States in the form of RU-486. Yet, as shown throughout this Paper, any assumptions regarding the last chapter of the RU-486 story is foolhardy.

Even with these looming questions and possibilities in mind, the chapters of RU-486's story delineated in this Paper have illuminated at least one certainty: RU-486 is not merely a story about the scientific merits of a new drug. If that had been the case, the FDA approval process would have taken far less time than it did because the evidence from both the French and U.S. clinical trials overwhelmingly mitigated in favor of RU-486's approval as a safe and effective drug for its indicated uses. Instead, the RU-486 story has really been a symbolic fight over a most controversial and delicate subject that reached the forefront of our political landscape 28 years ago in one of the Supreme Court's most momentous opinions, Roe v. Wade. The fight over the morality of abortion has pitted two warring ideologies against one another, one which advocates the need to preserve a woman's reproductive autonomy, the other which espouses the moral imperative to

preserve the sanctity of all human life, including fetal human life.

In the end, in spite of these political, ideological, and moral disagreements and the various plot twists during the drug's history, I believe that the FDA fulfilled its congressional mandate. The FDA followed the dictates of science and the law and was not held hostage to political, moral, or ideological pressure. As a matter of pure science and law then, which should be the FDA's paramount concern, the RU-486 approval decision was appropriate because the scientific evidence available demonstrated that RU-486 satisfied the statutory requirements of "safety" and "efficacy" for its intended uses. As a moral matter, however, a province wholly outside the FDA's jurisdiction, the question surrounding RU-486's approval is much more complex. It involves a plethora of considerations, most importantly the cultural and moral implications of living in a society where the termination of either human life or potential human life is legally permitted. This grave complexity explains why RU-486's entrance into the U.S. pharmaceutical market took over a decade and created the basis for a most interesting and convoluted tale.

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