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## Waiting for Mifepristone

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Physically, it is just a little white pill. But oh, what it could do: take abortion out of easily-identified clinics and disburse it to hospitals and doctor's offices, making what is so often called a "a private choice" actually private. And deprive pro-life activists of targets, publicity, and possibly support. For this potential to alter the current landscape, the New York Times Magazine has called it "The Little White Bombshell."<sup>1</sup> But at the moment, RU-486 is available at only a handful of clinics throughout the country, while everyone else is waiting for final approval of the drug from the FDA.

They have been waiting for about six years now, and that does not count the years spent hoping while the drug was available in Europe but could find no sponsor here. So the bombshell effect is, thus far, just a possibility. It looks as though the drug may finally be arriving soon, but it has looked that way before. Throughout the long wait, everyone has had their hands in the issue: governments, pharmaceutical companies, big name non-profits, grass-roots organizers, and pressure groups of all shades of opinion. A final history of this story is yet to come, after the drug is approved and the records of the FDA are investigated. But this is a brief history of who was where doing what with regard to this drug in the twenty years since it was first developed.

## Early Tests

RU-486, or mifepristone, is a steroid, and it was first synthesized for the French pharmaceutical firm Roussel Uclaf in 1980. (The name is an abbreviation of its internal designation, Roussel Uclaf 38486.) The drug is an antiprogestosterone, meaning that it blocks the action of progesterone, the hormone needed to maintain pregnancy and cease menstruation. It was developed by a small group of scientists led by Georges Teutsch,

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<sup>1</sup>Margaret Talbot, *The Little White Bombshell*, N.Y. TIMES MAGAZINE, July 11, 1999, at 39.

and their work was based on the similar work of Roussel consultant Dr. Etienne-Emile Baulieu. Based on Baulieu's long history of work on hormonal contraception, the company embarked on testing with the drug to determine its effects on the human reproductive cycle.<sup>2</sup> Although Baulieu did not actually first synthesize the drug, he has consistently been its most vocal supporter and the scientist most closely identified with it. Animal tests of course preceded those in humans, and those were not without problems. Baulieu himself admits that at extremely high levels, the drug caused adrenal failure in three out of six monkeys. Baulieu contends, however, that such a reaction was a sign of antiglucocorticosteroid activity of the drug, not toxicity. He managed to convince others of his point as well, in the face of some doubt.<sup>3</sup> The first human trials began only 17 months after of animal research, and it has been argued that this quick jump to humans reflected Roussel's desire to beat out other drug companies then researching similar compounds.<sup>4</sup>

The first human test was conducted in Geneva with 11 women participating. These women were given mifepristone alone, and it resulted in 9 abortions. The main side effect was hemorrhaging, which required curettage in one women and a blood transfusion and emergency surgery in another.<sup>5</sup> It was after this preliminary testing that Baulieu announced the existence of RU-486, as well as the results of the animal and Geneva studies, at his induction to the French Academy of Sciences in April 1982. At that point and for a few years afterward, the drug was proposed as a kind of birth control pill, taken only a few days a month, that would prevent any fertilized eggs from implanting in the uterus.<sup>6</sup> It was this speech that caused the first mention of mifepristone that I could find in a LEXIS search of major American newspapers, with both the New York Times and the Washington Post reporting on the new drug.

Moving on from the promising but mixed evidence from the Geneva study, larger human trials now began

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<sup>2</sup>See ETIENNE-EMILE BAULIEU, *THE ABORTION PILL* 83 – 84 (1991); JANICE G. RAYMOND ET AL., *RU 486: MISCONCEPTIONS, MYTHS AND MORALS* 9 (1991).

<sup>3</sup>See BAULIEU, *supra* note 2, at 84-85.

<sup>4</sup>See RAYMOND ET AL., *supra* note 2, at 9-10.

<sup>5</sup>See *id.* at 10.

<sup>6</sup>See Richard Eder, *Birth Control: 4-Day Pill is Promising in Early Test*, N.Y. TIMES, Apr. 20, 1982, § C, at 1.

in several countries. The FDA issued a testing permit for the drug to the Population Council, a non-profit research organization based in New York,<sup>7</sup> and the U.S. test was conducted in southern California.<sup>8</sup> These multi-national studies would eventually report greatly varying rates of success, with anywhere from 54% to 90% of pregnancies completely terminated by RU-486 alone. But the researchers in Sweden had hit upon a more effective combination: mifepristone and a prostaglandin, which had a success rate of 94% in the small Swedish study of 34 women.<sup>9</sup> Prostaglandins cause uterine contractions, thus obviously increasing the likelihood of terminating a pregnancy. However, prostaglandins can have serious adverse effects, and no laboratory research on the interaction of the two drugs was conducted before testing the combination in women.<sup>10</sup>

In December 1986, the French researchers published the results of a 100-woman trial of RU-486 in the *New England Journal of Medicine*. In that study, the drug had a success rate of about 85%, with bleeding as its major side effect. Other researchers who commented on the published results said that the success rate climbed to 95% when combined with prostaglandin and fell to 75% when given alone and two weeks after a missed period.<sup>11</sup> In the comments accompanying the published results as well as the comments with other test results published later, the “general tenor... [was] one of assured optimism.”<sup>12</sup> This is also the tenor I found in early newspapers articles about the drug, though this is hardly uncommon for new drugs. Already though, observers were discussing the difficulties in bringing the drug to the United States. Drug companies had two large disincentives to produce the new drug: opposition from abortion opponents and fear of liability.<sup>13</sup> Neither of these was an idle threat: the Dalkon Shield litigation and the pro-life boycott

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<sup>7</sup>See NARAL, *The Fight for Mifepristone (RU 486)* (last modified Jan. 6, 1999) <<http://www.naral.org/publications/facts/ruchrono.html>>.

<sup>8</sup>See Williams, *Women Sought for Birth Control Pill Evaluation*, SAN DIEGO UNION-TRIBUNE, Aug. 30, 1985, at D8.

<sup>9</sup>See RAYMOND ET AL., *supra* note 2, at 11.

<sup>10</sup>See *id.* at 11, ch. 4.

<sup>11</sup>See Phillip J. Hilts, *Success with Drug Reported; Product Developed in France; Obstacles Seen to U.S. Distribution*, WASHINGTON POST, Dec. 18, 1986, at A1.

<sup>12</sup>See RAYMOND ET AL., *supra* note 2, at 12.

<sup>13</sup>See, e.g., Hilts, *supra* note 11, at A1.

of Upjohn after it had worked on abortion-inducing drugs had both shown the industry the dangers of entering into the charged fields of contraception and abortion. And those fears were in addition to the major investment of time and money in securing FDA approval for the drug. It was clear that the drug would not be available in the U.S. for years, at least.

### **Approval in France, Accusations in the U.S.**

As RU-486 moved closer to approval in France, pressure on Roussel Uclaf to withdraw the drug increased. Dr. Edouard Sakiz, Roussel's chairman, had been an early advocate for the drug, but his doubts grew as the opposition to mifepristone, both inside and outside the company, became louder. By June of 1988, after the drug's application had already been submitted, the chairman was receiving up to 25 threatening letters a day and the company's headquarters was being regularly targeted by protestors.<sup>14</sup> The New York Times Magazine reported, however, that it was internal rather than external pressure that weighed more heavily upon the chairman. Roussel's parent company was the German chemical company Hoechst A.G., and Hoechst's CEO had publicly stated that RU-486 violated the company's principle of supporting life. In addition, three of the five members of Roussel's executive committee came to oppose the drug.<sup>15</sup> But this internal opposition was in fact at least partially caused by the external protests, including the threat of a boycott in America and comparisons of the drug to the cyanide gas manufactured for the Nazis by Hoechst's ancestor company, I.G. Farben.<sup>16</sup> So whatever the internal scruples of the companies may or may not have been, the organized opposition to the drug was having an effect.

Nevertheless, the French Minister of Health approved the use of mifepristone to end early pregnancies in September 1988, and China quickly followed suit. The regime approved by the French included taking

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<sup>14</sup> See Steven Greenhouse, *Abortion Pill: French Drug Ignites Public and Corporate Controversy*, ST. PETERSBURG TIMES [Reprinted from N.Y. TIMES MAGAZINE], Feb. 19, 1989, at 1D.

<sup>15</sup> See *id.*

<sup>16</sup> See *id.*

three RU-486 pills on three consecutive days, followed by an injection or suppository of prostaglandin. The approval was also limited to use in the first 49 days, or seven weeks, of pregnancy.<sup>17</sup> So whatever the promise of the drug to make abortion more private and individualized, it did not make the procedure easy.

After that, events quickly took a turn for the dramatic – and the farcical. Roussel announced on October 26 that it was suspending distribution of the drug in the face of a “polemic” of protests and boycott threats.<sup>18</sup> Roussel made explicit that its withdrawing of the drug was based on the negative public reaction and that it had not sought authorization to distribute the drug in the U.S. because of the opposition of anti-abortion groups.<sup>19</sup> On that same day, an international conference on gynecology and obstetrics was taking place in Rio de Janeiro. Once the conference goers heard of Roussel’s action, 3,000 of them signed a petition calling the move “dangerous.”<sup>20</sup> Dr. Baulieu likewise condemned the action of the company. Two days later, Minister of Health Claude Evin ordered the company to put the pill back on the market. The French government owned 36.25% of Roussel, but its real authority came from its power under French patent law to transfer the patent to RU-486 to another company.<sup>21</sup> It was also at this point that the French Minister coined the phrase “the moral property of women,” which went on to become a rallying cry for those trying to gain access to the drug. Thus RU-486 went back on the market in France, where it has stayed.

While the drug was gaining approval in France, its supporters in the U.S. were becoming louder in their questioning of why the drug was not available to them. By the time of its approval in France, the drug had been used by almost 7,000 women there,<sup>22</sup> and it looked safe and effective enough to gather wide support

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<sup>17</sup> See Gina Kolata, *France and China Allow Sale of Drug for Early Abortion*, N.Y. TIMES, Sept. 24, 1988, § 1, at 1.

<sup>18</sup> See Steven Greenhouse, *Drug Maker Stops All Distribution of Abortion Pill*, N.Y. TIMES, Oct. 27, 1988, § A, at 1.

<sup>19</sup> See *id.*

<sup>20</sup> See Edward Cody, *France Orders Sale of New Pill; Abortion Drug Had Been Shelved After Angry Protests*, WASHINGTON POST, Oct. 29, 1988, at A1.

<sup>21</sup> See Greenhouse, *supra* note 18, at ID.

<sup>22</sup> See *id.*

and attention in this county. The drug even earned tentative support from two groups often divided on questions of contraception: the big family planning non-profits, like Planned Parenthood and the Population Council, and grass-roots women's health groups, like the Boston Women's Health Book Collective.<sup>23</sup> But the women's groups at that point were no match for the potent power of the pro-life movement, which opposed the drug as strongly as it could. The National Right to Life Committee had sent a letter to Roussel saying that it would lead a boycott of all Roussel's products if RU-486 went on the market, in the U.S. or elsewhere. A high-ranking officer in the corporation made clear that it was that threat that stopped the company from selling the drug outside of France. And Roussel had good reason to be worried: its U.S. business was about \$170 million a year, or 10% of the firm's worldwide sale.<sup>24</sup> Hoechst-Roussel Pharmaceuticals of New Jersey, a subsidiary of Hoechst A.G., held the option rights to apply for FDA approval of the drug, but it had no plans to exercise that option.<sup>25</sup>

Given the intransigence of the pro-life movement and the fear it inspired in the pharmaceutical companies, supporters of mifepristone would have to turn to more unorthodox sources to get the drug produced here. Two family planning experts told the New York Times in 1988 that the American firm Gynopharma was in talks with Roussel and would likely apply to the FDA to market the drug. But the company would not confirm this report,<sup>26</sup> and it turned out to be just the first of many times that a possibility for the drug turned out to be elusive. Roussel was also reported to be in talks with non-profit groups in the U.S., Britain, and Germany to distribute the drug in their respective countries. If such non-profits distributed the drug, they would take the heat from pro-life groups.<sup>27</sup> Or, if no legitimate source could be found, women could turn to the black market. The president of Planned Parenthood predicted that women would if the drug

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<sup>23</sup> See Laura Fraser, *Pill Politics*, MOTHER JONES, June 1988, at 30, 32.

<sup>24</sup> See R.C. Longworth, *French Firm Sets Curbs on Abortion Pill Export*, CHICAGO TRIBUNE, Nov. 4, 1988, Zone C, at 1.

<sup>25</sup> See Gina Kolata, *Boycott Threat Blocking Sale of Abortion-Inducing Drug*, N.Y. TIMES, Feb. 22, 1988, § A, at 1.

<sup>26</sup> See Kolata, *supra* note 17, at 1.

<sup>27</sup> See Greenhouse, *supra* note 14, at 1D.

gained acceptance in other countries by not ours.<sup>28</sup> Perhaps she should not have said that publicly.

## The Import Alert

The Federal Food, Drug, and Cosmetic Act gives wide, broad, and flexible power to FDA, including the power to use its discretion to prohibit or allow the importation of unapproved drugs into this country.<sup>29</sup> Generally, the discretion to used to keep out unapproved drugs, which are untested by American standards and thus possibly dangerous. However, the Agency, in response to the AIDS crisis, issued guidelines in July 1988 to allow AIDS sufferers to bring unapproved foreign drugs into this country for their personal use. But the guidelines were sufficiently imprecise that it was not clear whether RU-486 would fall under the personal-use exception or not.<sup>30</sup>

In May 1989, three Congressmen wrote to the FDA Commissioner and demanded that the Agency formally confirm that RU-486 was specifically excluded from the personal-use exemption, as some other 40 drugs were. The letter cited concerns about both the promotion of abortion and the contraindications for mifeprisone, thus hitting both political and health notes. Further letters in the same vein from other legislators arrived in the next month.<sup>31</sup> On June 6, 1989, the FDA issues Import Alert 66-47, which declared that any amount of RU-486 brought into this country was subject to immediate detention. The given reasoning: “FDA has concluded that unapproved products of this kind would be inappropriate for release under the personal importation policy. The intended use of such drugs could pose a risk to the safety of the user.”<sup>32</sup>

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<sup>28</sup> See Fraser, *supra* note 23, at 44.

<sup>29</sup> See 21 U.S.C. § 381 (a) (3).

<sup>30</sup> See *Benten v. Kessler*, 799 F. Supp. 281, 285 (E.D.N.Y. 1992).

<sup>31</sup> See *id.* at 286.

<sup>32</sup> FDA, Import Alert 66-47 (June 6, 1989).



So thus was the importation of RU-486 banned. Of course, this ban only applied to personal use of the drug and not to any of the clinical research then being conducted in this country under INDs. But what was the motivation of FDA? Was it truly for the safety of American women, or were political considerations involved? FDA surely hears from legislators frequently, so the mere fact of correspondence to it does not signal a political motive. Nevertheless, it is true that the atmosphere surrounding abortion was even more poisonous in the late 1980s than it is today, and the Bush administration took a hard line in opposing abortion. All federal spending having anything to do with abortion was prohibited, as was government funding for fetal tissue research. Certainly, the press, Democrats in Congress, and advocates of the drug cried foul at the FDA's action. For example, the National Abortion Rights Action League's chronology of the RU-486 story includes this entry for 1989: "In response to pressure from the Bush Administration and anti-choice members of Congress, the FDA bans the importation of mifepristone. . . ." <sup>33</sup> Outside of the circle of those advocating the drug, the ban did not seem to generate too much attention until the Washington Post editorialized on the subject in February 1990: "This looks to us more like a political decision than a scientific one." <sup>34</sup>

The ban proved to be an inviting target for the House Subcommittee on Regulation, Business Opportunities, and Energy. Then chaired by Rep. Ron Wyden, Democrat of Oregon, the Subcommittee used this issue to hold the first of four hearings on RU-486. Rep Wyden, a supporter of RU-486, accused FDA of banning the personal import of the drug for no reason other than political pressure. He claimed to have found no evidence of a black market, no evidence of any attempts to bring the drug into the country, and no evidence at all about the safety, or lack thereof, of the drug in FDA's files. <sup>35</sup> Ronald Cheesemore, then FDA's Associate Commissioner for Regulatory Affairs, was its representative at the hearing. He did not so much deny the

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<sup>33</sup> See NARAL, *supra* note 7.

<sup>34</sup> See Opinion Editorial, *Politics and RU-486*, WASHINGTON POST, Feb. 17, 1990, at A28.

<sup>35</sup> See *RU 486: The Import Ban and its Effects on Medical Research: Hearing Before the Subcomm. On Regulation, Bus. Opportunities, and Energy of the House Comm. on Small Bus*, 102st Cong. 1-2 (1990) (statement of Rep. Wyden).

Representative's charges as try to fill them in with more facts. Cheesemore emphasized that the norm for drugs was to be denied importation without domestic approval, and only in special cases was that norm waived. In addition to the imported dosage being only a personal one, the drug in question had to treat a serious condition, have no other commercially available treatment, not be promoted here, and pose no unreasonable safety risks.<sup>36</sup> Regarding RU- 486, pregnancy is not usually defined as a serious disease, and surgical abortion is a safe and effective procedure already available in this country. The great amount of publicity the drug received worried FDA that a black market for it might arise, although it had no evidence of one in late 1990. Additionally, the Agency emphasized the unknown dangers from the combination of mifepristone and prostaglandins, and the known dangers from prostaglandins alone. Users might also take the drugs without the supervision of a physician, thus rendering them more vulnerable to side effects.<sup>37</sup> It was a long and contentious hearing, with all the traditional congressional theatrics and hostile questions.<sup>38</sup> Despite the suspicious timing and the tricky political climate, I would argue that FDA did act appropriately in this case. The American Medical Association argued the same thing. At the very least, even if political considerations played a role in the agency's decision, it had the discretion and authority to ban the importation of RU-486. But the very hearing on the ban itself showed that that issue was just a side-show to the real game of the testing and approval of the drug. In Europe, the drug was very tightly controlled, so it would not be easy to create a black market. And Rep. Wyden's biggest coup was the charge that the import ban was having a chilling effect on legitimate research with RU-486 under several INDs then in existence for it.<sup>39</sup> The drug has the potential to treat several diseases, including Cushing's disease and some brain tumors, but I am discussing only its abortifacient use because the scope of this essay is limited and the problems using RU-486 for treatment all stem from its main use.

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<sup>36</sup> See *id.* at 35 (statement of Ronald Cheesemore).

<sup>37</sup> See *id.* at 36 (statement of Ronald Cheesemore).

<sup>38</sup> See Curt Suplee, *Hill Holds Heated Hearing on RU 486; FDA Denies Antiabortion Bias in Banning Drug with Several Uses*, WASHINGTON POST, Nov. 20, 1990, at A21.

<sup>39</sup> See *RU 486: The Import Ban*, *supra* note 35, at 2 (statement of Rep. Wyden).

## **The Push to Bring Mifepristone to the U.S.**

While the issue of the import ban was being fought out, the U.S. supporters of the drug organized their efforts and gained momentum. They realized that the biggest barrier to use here in the U.S. was the refusal of Roussel to license or sell the drug here. They were helped along in their task by Dr. Baulieu's receipt of the top U.S. Medical award, the Albert Lasker Clinical Medical Research Award. Baulieu predictably used his acceptance speech to urge wider use of his drug. Pro-life groups were outraged, saying that Baulieu's achievement was to kill people.<sup>40</sup> Women's group took the news in stride as they organized: The National Organization for Women (NOW) and the Feminist Majority Foundation (FMF) announced a formal campaign to bring mifepristone to the U.S. in June 1989.<sup>41</sup> The FMF's campaign took to it directly to Roussel: the group eventually sent three delegations to France to talk with the company, the second of which met for five hours with the chairman, Edouard Sakiz, and included the presentation of 115,000 signatures on a petition supporting the drug.<sup>42</sup> Several women's health and feminist groups joined forces to create the lobbying group Reproductive Health Technologies Project to promote education about and the distribution of RU-486.<sup>43</sup> Efforts for the drug were also growing at the grass-roots: a former San Francisco supervisor announced that she had formed a small company to acquire, market, and distribute the drug, and claimed she had investors offering her \$400,000.<sup>44</sup> The idea of small, specialty company to produce RU-486 had been floated before, but this effort was bound to end for naught, as so often happens in the work of start-up corporations. Public opinion also supported introduction of the pill, with 59% and 51% of respondents favoring legalization in two surveys by the Associated Press in 1989.<sup>45</sup>

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<sup>40</sup> See Michael Specter, *French Researcher Wins Top U.S. Medical Award, Angering Abortion Foes*, Washington Post, Sept. 28, 1989, at A12.

<sup>41</sup> See *Now Leaders Open Campaign to Bring Abortion Pill to the U.S.*, LOS ANGELES TIMES, Jun. 1, 1989, at A2.

<sup>42</sup> See *The Fight to Make RU 486 Available to U.S. Women* (visited on Jan. 30, 2000), <<http://www.feminist.org/gateway/ru486two.html>>.

<sup>43</sup> See RAYMOND ET AL., *supra* note 2, at 3.

<sup>44</sup> See Nanette Asimov, *Ex-Supervisor's Goal A Move to Import French Abortion Pill*, SAN FRANCISCO CHRONICLE, Oct. 14, 1989, at A2.

<sup>45</sup> See R. Alto Charo, *A Political History of RU-486*, in *Bio-Medical Politics* 43,71-72 (Kathi E. Hanna, ed., 1991).

Meanwhile, Roussel's absolutism decreased and medical approval of the drug increased. In March 1990, the *New England Journal of Medicine* published the largest study at that point on RU-486, involving over 2000 women in France. The drug was found to be 96% effective and to have no worse side effects than conventional surgical abortion. This finding was hailed as the most definitive evidence yet of the safety and efficacy of RU-486.<sup>46</sup> Roussel then announced that it would henceforth proceed with sale of the drug in Britain and Scandinavia, a reversal of its earlier position.<sup>47</sup> Scientific organizations also began to throw their weight behind American testing and possible use of the drug. Examples include the American Medical Association in 1990<sup>48</sup> and the American Association for the Advancement of Science in 1991.<sup>49</sup>

The issue was becoming directly political. The testing of the drug became an issue in the California gubernatorial election because drugs without FDA approval may be tested in California. Supporters continued with their campaign of education and pressure.<sup>50</sup> In 1991, New Hampshire became the first of several states whose legislatures passed resolutions urging the beginning of clinical trials of RU-486 in the U.S.<sup>51</sup> But by 1991, clinical trials still had not begun in the U.S., meaning that any potential approval of the drug was still years away.

Then a woman in France died after using the drug. The woman was a heavy smoker, and died after treatment with mifepristone and a form of prostaglandin called sulprostone. The French government convened an inquiry, and reminded doctors that the drug was not recommended for women who were smokers, or had heart problems, high cholesterol, or diabetes.<sup>52</sup> A couple weeks later the French Health Ministry announced that RU-486 could not longer be given to women over 35 or smokers, and that the amount of prostaglandin

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<sup>46</sup> See *Abortion Pill Found to be Safe, Effective in Largest Study Yet*, LOS ANGELES TIMES, Mar. 8, 1990, at A23.

<sup>47</sup> See Susan Okie, *French Abortion Pill to be Sold Abroad; Use of RU 486 Planned in Britain and Scandinavia Fists*, Washington Post, May 22, 1990, § Health, at 27.

<sup>48</sup> See *Health: AMA OKs French Abortion Pill*, CHICAGO TRIBUNE, Jun. 28, 1990, part P, at 2.

<sup>49</sup> See *The Fight to Make RU 486 Available*, *supra* note 42.

<sup>50</sup> See Martha Shirk, *Abortion Pill: French Firms Urged to Make the Drug in U.S.*, ST. LOUIS POST-DISPATCH, Mar. 26, 1990, at 1B.

<sup>51</sup> See *The Right to Make RU 486 Available*, *supra* note 42.

<sup>52</sup> See Alan Riding, *Frenchwoman's Death is Linked to Abortion Pill and a Hormone*, N.Y. TIMES, Apr. 10, 1991, at A10.

used must be reduced. The woman had died as result of the prostaglandin she had received.<sup>53</sup>

Nevertheless, it appeared that the tide had turned in favor of the drug, and its steady increase in support continued. Representative Ron Wyden introduced a bill that would rescind FDA's import alert, and New York Mayor David Dinkins launched a letter writing campaign in favor of the drug.<sup>54</sup> However, it remained the fact that Roussel held the patent to the drug, and it could not be tested here unless Roussel agreed. But RU-486 was approved for use in Britain and Sweden, and Roussel began distribution in those countries. There was hope, but it was still distant.

For at least one activist, the hope was too distant. To Lawrence Lader, veteran abortion activist, the pace of the RU-486 campaign was far too slow. So Lader set up a court challenge to the import alert, more for symbolic and publicity value than for its effects. He arranged to travel with a pregnant California activist to England, obtain the drug, fax U.S. Customs his plans, and then return to the States with the RU-486 pills.<sup>55</sup> That much of his plan went smoothly, and the woman then filed suit for an injunction to get the pills back. The judge who heard the case actually ruled in favor of the woman, finding that the import alert and personal use guidelines of the FDA were issued without the required notice-and-comment procedures and so was not enforceable.<sup>56</sup> However, the case was appealed all the way to the U.S. Supreme Court, which upheld the staying of the injunction by the Court of Appeals.<sup>57</sup> But the case did succeed in its goal of further publicizing both RU-486 and the import alert.

Despite the death in France and the court side-show, the campaign to finally bring RU-486 to this country only stepped up. The Feminist Majority Foundation's effort expanded its focus to include the American subsidiary of Hoechst A.G.,<sup>58</sup> and Representative Pat Schroeder introduced legislation the would legalize

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<sup>53</sup> See *France, After a Death, Restricts Abortion Pill*, N.Y. TIMES, Apr. 21, 1991, § 1, at 3.

<sup>54</sup> See *Opinion, Why a French firm is Scared by America; Abortion Politics Locks Promising Medicine Out of the U.S.*, LOS ANGELES TIMES, Apr. 21, 1991, part M, at 4.

<sup>55</sup> See *Putting a New Focus on Abortion Pill*, ORLANDO SENTINEL TRIBUNE, Jul. 20, 1992, at A1.

<sup>56</sup> See *Benten v. Kessler*, 799 F. Supp. 281 (E.D.N.Y. 1992).

<sup>57</sup> See *Benton v. Kessler*, 505 U.S. 1084 (1992).

<sup>58</sup> See *Campaign for Drug Is Intensifying*, N.Y. TIMES, Jan. 23, 1992, at A17.

the importation of the pill.<sup>59</sup> Rep. Ron Wyden held another hearing on the subject, which featured the testimony of a man stricken with cancer who said he could not convince Roussel to give him the drug on a compassionate use basis. After the publicity of the hearing, Roussel changed its mind, and the patient did receive the drug.<sup>60</sup> But in the most momentous sign yet, Candidate Bill Clinton strongly favored more reproductive choice for women and specifically promised to allow the importation of RU-486.<sup>61</sup>

## The FDA's Push

Official action to encourage the submission of RU-486 to the FDA began almost as soon as the election was over. FDA had never refused to allow trials of the drug, as opposed to its private importation, but the political climate and the opposition of Roussel meant that FDA had never received a New Drug Application for RU-486 as an abortifacient. Additionally, In October 1992, the *New England Journal of Medicine* reported again on the drug's safety and effectiveness, this time as an emergency contraceptive taken within 72 of unprotected sex.<sup>62</sup> In December 1992, FDA said in a letter to Congressional advocates of RU-486 that the drug could probably receive quick approval in the U.S. without further testing, based on the large number of European trials.<sup>63</sup> Thirty-four newly elected members of Congress also appealed directly to Hoechst A.G. to allow clinical trials in the U.S.<sup>64</sup>

On January 22, 1993, just the second day of his presidency, Bill Clinton signed a sweeping Presidential

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<sup>59</sup> See Rep. Schroeder Plans Bill on Abortion Pill, CHICAGO TRIBUNE, Jul. 21, 1992, at 6.

<sup>60</sup> See Cancer Patient Can Get Unapproved Abortion Pill, N.Y. TIMES, Jul. 30, 1992, at A22.

<sup>61</sup> See Richard Saltus, Congressman Says Abortion Pill Firm is Stalling U.S. Entry, BOSTON GLOBE, Nov. 4, 1992, at 6.

<sup>62</sup> See Anna Glazier, et al., Mifepristone (RU 486) Compared with High-Dose Estrogen and Progesterone for Emergency Postcoital Contraception, 327 NEW ENG. J. MED. 1041 (1992).

<sup>63</sup> See FDA Clearing Way for French Abortion Pill, SAN FRANCISCO CHRONICLE, Dec. 17, 1992, at A9.

<sup>64</sup> See Abortion Pill Maker Urged to Apply for U.S. Trials, JOURNAL OF COMMERCE, Dec. 18, 1992, at 9A.

Memorandum to Secretary of Health and Human Services Donna Shalala. The Memorandum's declared purpose was to "free science and medicine from the grasp of politics" and to "separate our national health and medical policy from the divisive conflict over abortion."<sup>65</sup> The Memorandum ended all of the policies of the Reagan and Bush administrations that dealt with abortion, including the prohibition of federal funds for fetal tissue research. It also instructed Secretary Shalala to instruct FDA to reevaluate its import ban on RU-486 and to explore the promotion of testing of the drug.<sup>66</sup>

Immediately after the Presidential Memorandum, David Kessler wrote to Dr. Sakiz at Roussel requesting a meeting on RU-486, and he also let Hoechst A.G. know of FDA's interest in the drug. The first such meeting between FDA and Roussel Uclaf took place in February 1993 and more continued throughout that spring. By April, Roussel was indicating it would work with the Population Council, a research non-profit based in New York, to ensure testing and distribution in the U.S.<sup>67</sup> At the same time, Kessler was publicly blasting Roussel for "dragging its feet" in submitting a New Drug Application.<sup>68</sup> Later in April, it was announced that Roussel would license the drug to the Population Council, and it was anticipated that the drug could be available in two years' time.<sup>69</sup> This was just one in a string of deadlines and hopes not met as the transfer and eventually manufacture of the drug stumbled.

In the meantime, the drug regime got easier to use, by substituting the oral prostaglandin-like drug misoprostol for the hormone prostaglandin.<sup>70</sup> But still, the parties struggled through negotiations to transfer the drug to the U.S. This was because Roussel and the Population Council were negotiating over the transfer of the U.S. patent to the drug, not just licensing. After a year of negotiation and no visible progress, Secretary

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<sup>65</sup>Remarks by the President During Signing of Presidential Memoranda (January 22, 1993).

<sup>66</sup>*See id.*

<sup>67</sup>*See RU-486: Status Report on the U.S. Commercialization Project, Transfer of Antiprogestin Technology to the United States: Hearing Before the Subcomm. On Regulation, Bus. Opportunities, and Technology of the House Comm. on Small Bus.*, 103d Cong. 6-7 (1994) (statement of Commissioner Kessler).

<sup>68</sup>*See* Larry Lipman, *FDA Blasts Abortion Pill's Maker*, HOUSTON CHRONICLE, Apr. 16, 1993.

<sup>69</sup>*See* Warren E. Leary, *Inching Toward America; Maker of Abortion Pill Agree to Let Others Make It*, N.Y. TIMES, Apr. 25, 1993, § 4, at 2.

<sup>70</sup>*See Easier Way Found For Abortion Pill*, N.Y. TIMES, May 27, 1993, § B, at 9.

Shalala and Commissioner Kessler met with representatives of both Roussel and the Population Council in April 1994. The Secretary then set a deadline of May 15, 1994 for the talks to conclude.<sup>71</sup> It was only after this intervention by the U.S. government that the two groups came to an agreement. On May 16, an agreement was announced: Roussel was donating its U.S. patent rights to the drug to the Population Council without remuneration. The Population Council would develop the abortifacient use of RU-486 itself, and allow other uses of the drug to be developed separately.<sup>72</sup> With this deal, Roussel washed its hands of the drug, at least in the U.S. And although the government stepped in to facilitate the transfer of the rights, the government could not develop the drug itself. Though a significant roadblock to RU-486 had now been eliminated, the problems and delays in the process were not nearly over.

But again, this pace of progress was too slow for Lawrence Lader. Lader's group, Abortion Rights Mobilization, brought the drug to the U.S. on its own. It got the Chinese to allow the group to test the Chinese clone to mifepristone.<sup>73</sup> At the time of the Roussel/Population Council announcement, Lader was announcing that his group was making arrangements with a laboratory to produce the drug and would begin its own clinical tests.<sup>74</sup> Lader's promise has come true, and the substitute-mifepristone his organization is dispensing is now the only medical abortion that can be obtained in this country.

## The Home Stretch?

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<sup>71</sup>See *RU-486: Status Report*, *supra* note 67, at 7 (statement of Commissioner Kessler).

<sup>72</sup>See Population Council, *The Population Council Announces Receipt of Mifepristone (RU 486) Rights from Roussel Uclaf for the United States* (May 19, 1994).

<sup>73</sup>See *The Fight to Make RU-486 Available*, *supra* note 42.

<sup>74</sup>See Lawrence Lader, Editorial, *RU-486, Made in America*, N.Y. TIMES, Mar. 17, 1994, at A23.



The Population Council conducted its own clinical trial of mifepristone (as it should now be known because Roussel has withdrawn from the picture) in the winter of 1994 – 95. The test involved 2,121 women of various ethnic and economic backgrounds at 17 sites throughout the U.S. The success rate of the drug was 92% (with a very generous definition of failure) and a large majority of women who used it said they would recommend it to others.<sup>75</sup> At the same time, the Council was preparing a New Drug Application with the data from several foreign studies of mifepristone. On March 31, 1996, the Population Council filed its NDA with FDA. Simultaneously, the Council also announced that it was giving its legal rights to mifepristone to a newly-formed company, Advances in Health Technology. The former move translated into progress on the availability of the drug, but the latter move did not.

An FDA Advisory Committee met to review mifepristone in July 1996. The meeting took place amid unusual security measures given the volatile nature of the topic. But the eight physician on the panel tried to stick to the medical merits of the drugs, raising points about is inconvenient four visits to the doctor and its failure level.<sup>76</sup> It was the Reproductive Health Drugs committee that was involved, and it listened to presentations from the Population Council as well as about 35 individuals.<sup>77</sup> The panel did recommend approval, with three different votes that each had 6 or 7 physicians in favor of the drug.<sup>78</sup> As is its usual practice, FDA followed the Committee's recommendation and issued an approvable letter for mifepristone on September 18, 1996. The letter states that FDA was satisfied as to the drug's safety and efficacy, but the manufacturing process and label for the drug must also be submitted before the drug could be finally approved.<sup>79</sup>

And that has been the last official word on the drug. Final approval is still pending, as of the end of

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<sup>75</sup> See Population Council, Frequently Asked Questions: Medical Abortion (last modified Dec. 22, 1999) <<http://www.popcouncil.org/faqs.abortion.html>>.

<sup>76</sup> See Gina Kolata, *Panel Advises FDA to Allow Abortion Pill*, N.Y. TIMES, Jul. 20, 1996, § 1, at 1.

<sup>77</sup> See FDA Talk Papers, FDA Advisory Committee Reviews Mifepristone (July 19, 1996) <<http://www.fda.gov/bbs/topics/ANSWERS/ANS00748.html>>.

<sup>78</sup> See Kolata, *supra* note 76, at 1.

<sup>79</sup> See FDA Talk Papers, FDA Issued Approvable Letter for Mifepristone (Sept. 18, 1996) <<http://www.fda.gov/bbs/topics/ANSWERS/ANS00758.html>>.

January 2000. The reason why is the enormous trouble that the Population Council has had in securing a manufacturer for the product. Large pharmaceutical companies are still scared away from the drug by the ongoing threat of boycott. That left the Council to seek out smaller players, with all the problems small, unknown, and not always legitimate players entail. The Council has also striven to keep the names of its manufacturers private, but they leaked out after the deals went bad.

The manufacturing troubles are a tangled story, but here is what is widely known to have happened. As mentioned above, the Council created a company called Advances in Health Technology to market the drug, but sought to keep the manufacturer secret. The first manufacturer was Joseph D. Pike, but he turned out to a forger who has been disbarred in North Carolina. The Population Council and Advances in Health Technology sued him for fraud in 1996.<sup>80</sup> The parties settled the litigation the next year, and the Population Council said that new a company, Advances for Choice, would now market and distribute the drug.<sup>81</sup> Meanwhile, in Europe, Hoechst G.A. gave the patent rights to former Roussel CEO Edouard Sakiz, saying that it wanted out of the controversy surrounding the drug.<sup>82</sup> Somewhere along the way, the marketer of the drug in the U.S. became Danco Laboratories. I am not sure if that is the just a new name for Advances for Choice, or rather the company of the same name that Pike had set up. Either way, by June 1997 the Council had Danco as its marketer but no manufacturer: the latest candidate, Gedeon Richter of Budapest, withdraw at that point. This dispute also wound up in litigation.<sup>83</sup> At that point, estimates for eventual release on the U.S. market were estimated to be three to five years.<sup>84</sup> It was only in November 1997 that the Population Council settled the last lawsuit resulting from the Pike fiasco, brought by a company who had invested with Pike.<sup>85</sup> At long last, the Council looked poised to finally bring the pill to market.

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<sup>80</sup> See Tamar Levin, *Dispute May Delay Abortion Drug in the U.S.*, N.Y. TIMES, Nov. 16, 1996, at A16.

<sup>81</sup> See Tamar Levin, *Legal Hurdles Cleared in Sale of French Abortion Pill*, N.Y. TIMES, Feb. 17, 1997, at A28.

<sup>82</sup> See *Pill for Abortion Ends Production*, N.Y. TIMES, Apr. 9, 1997, at D2.n.

<sup>83</sup> See John Sullivan, *Another Delay in Store for French Abortion Pill on U.S. Market*, N.Y. TIMES, Jan. 13, 1997, at A16.

<sup>84</sup> See *id.*

<sup>85</sup> See Tamar Levin, *Lawsuits' s Settlement Bring New Hope for Abortion Pill*, N.Y. TIMES, Nov. 13, 1997, at A14.

As of early 1999, Danco claimed to have found a manufacturer but would not release the name for fear of negative publicity.<sup>86</sup> For the past year, the media has been saying that the drug is finally nearing final approval. A Danco spokeswoman said in March 1999 that the company expected the drug to be approved by the end of 1999.<sup>87</sup> But that did not happen. Now the company will say only that it has submitted all the required data to FDA and hopes to get approval by the end March 2000.<sup>88</sup> Beyond that, the company is mum, as is FDA. It looks like mifepristone may finally be with us, but with this drug, it's not over until FDA sings.

The suspense over FDA approval is not the only potential roadblock still in the drug's way. For the last two years, Rep. Tom Coburn, Republican of Oklahoma, has tacked onto federal agriculture spending bills a prohibition for mifepristone. Both years it has died in conference committees on the bill,<sup>89</sup> but that it does mean that the bill might not have a greater chance after the next election. The next president might also have a large say in what happens to the drug. Recall how President Clinton's Memorandum gave FDA the impetus to nudge mifepristone along. A pro-life president could do just the opposite. Indeed, George W. Bush declares that he would likely not accept an FDA ruling that approved the drug.<sup>90</sup>

So given the uncertain status of mifepristone at this point, a definitive history of the drug is yet to be written. But thus far, the long wait for the drug seems to be a potent expression of the power of grass-roots activism of all persuasions and unremitting polarization of the abortion battles. Pro-life activists kept Roussel too scared to introduce the drug here for years, then pro-choice activists pressured the group into a compromise. Though admittedly, governments helped the cause either way. This story is not yet done, but I will keep paying attention until it is.

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<sup>86</sup> See Laura Fraser, *The Abortion Pill's Grim Progress*, MOTHER JONES, January 1999.

<sup>87</sup> See Marc Kaufman, *Abortion Pill Inches Closer to Production*, WASHINGTON POST, Mar. 23, 1999.

<sup>88</sup> See Laurel Campbell, *Abortion Pill Nears Approval by FDA*, CINCINNATI POST, Jan. 10, 2000.

<sup>89</sup> See David E. Rosenblum, *Senate Approves \$8.7 Billion for Emergency Aid to Farmers*, N.Y. TIMES, Oct. 14, 1999, at A22.

<sup>90</sup> See *Bush Backed into a Corner*, CHICAGO TRIBUNE, Jan. 21, 2000.