

Tab C



September 30, 1993

NOTE TO: The Secretary
FROM: The Commissioner of Food and Drugs
SUBJECT: RU-486

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

I. Current Marketing of the Drug

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

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

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RU-486 might qualify for importation under FDA's personal use importation policy and whether the import alert should be rescinded.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

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

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

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

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

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

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

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

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- o That the Population Council would ultimately submit an NDA to FDA, based on the results of the clinical trial and on other studies that have been conducted by Roussel Uclaf; and
- o That the Population council, with the concurrence of Roussel Uclaf, would choose a new manufacturer for the drug, and that Roussel Uclaf would transfer its technology for making the drug to that manufacturer, because Roussel Uclaf does not want to manufacture the drug for sale in this country.

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

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

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

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

III. Analysis

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

- o It would create an unacceptable precedent for any manufacturer of a significant vaccine or drug to seek indemnification as a condition for bringing the product to market. There is little basis to distinguish RU-486 from a breakthrough AIDS drug or unique vaccine. The swine flu indemnification plan proved very problematic for the United States Government.
- o If public health problems were to occur post-approval, the interest of the United States as an indemnifying party would be to disprove that problems had occurred, while FDA's obligation would be to objectively investigate and take appropriate actions to protect the public health. This would be an untenable conflict for the United States Government.

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

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

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

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

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

IV. Recommendation for Expert Advisor

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

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

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

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

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

Attachment: Contract

cc: Dr. Philip Lee
Mr. Kevin Thurm

THE WHITE HOUSE
WASHINGTON

January 22, 1993

MEMORANDUM FOR THE SECRETARY OF HEALTH AND HUMAN SERVICES

SUBJECT: Importation of RU-486

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

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

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

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

William J. Clinton