APPEARS THIS WAY
ON ORIGINAL

SUMMARY OF OTHER EVENTS

1. Import Alert - In response to President Clinton's January 22, 1993, memorandum to you directing an assessment of the RU-486 import alert, FDA submitted a recommendation to the Assistant Secretary for Health on July 14, 1993, that the import alert be retained based on medical/safety reasons. The Agency's memorandum to _____ with its accompanying memorandum to you, are attached at Tab G. A decision on this issue is pending within the Department.

The Agency recommended [

]

2. Status of Benten v. Kessler - On August 1, 1992, the legality of the import alert was challenged by Ms. Benten who attempted to bring the drug into the U.S. (Benten v. Kessler, Civ. No. 92-3161, U.S. District Court for the Eastern District of New York.) The district court issued a preliminary injunction directing FDA to release the drug to Ms. Benten; but because that decision was stayed, Ms. Benten had a surgical abortion. In subsequent proceedings before the court last July, the government stated that FDA's recommendation on whether the import alert should be maintained had been forwarded to the Department; the government has also advised the court that it would inform the court when a decision was made by HHS on FDA's recommendation. Recently, the lawyers for Ms. Benten have indicated that they may attempt to reactivate the litigation, because HHS has failed to make a decision on the import alert.

3. Hearing on RU-486 - Mr. Ron Wyden, Chairman, Committee on Small Business, Subcommittee on Regulation, Business Opportunities, and Technology, has indicated his intention to hold a hearing on RU-486 on April 25. Mr. Wyden wants to ascertain where the parties are in the licensing negotiations, and to explore alternative solutions (e.g., taking the Roussel Uclaf patent) if the negotiations are not successful.

[

]

[redacted]

5. Women's Groups - Recently the FDA was contacted by an pro-choice group in Florida (Women's Information and Science Health Association) which intends to provide charter flights to an unspecified location in the Caribbean (possibly Haiti) where women could go and obtain abortions using RU-486 (or possibly a Venezuelan copy of the drug) beginning early next month. The group intends to publicize the fact that women in the United States have to go abroad in order to obtain medical abortions.

[redacted]

APPEARS THIS WAY
ON ORIGINAL

TAB F

APPEARS THIS WAY
ON ORIGINAL

INDEX
FDA/ES DOCUMENTS FOR FOI REQUEST ON RU-486
(FOI # 93-47009)

PRESIDENT CLINTON OR ANY REPRESENTATIVES OF

1. **Memorandum to Secretary, HHS, dated January 22, 1992, from President Clinton**

2. **Letter to President Clinton, dated January 23, 1993, from _____ Response dated March 24, 1993, also included.**
NOTE-Personal (patient) identifiers need to be dedacted

3. **Letter to President Clinton, dated January 19, 1993, from _____ Response dated May 11, 1993, also included.**
NOTE-Personal (patient) identifiers need to be dedacted

4. **Letters to President Clinton and Secretary Shalala, dated September 27, 1993, from _____ Response dated December 3, 1993, also included.**
NOTE-Personal (patient) identifier needs to be dedacted

U.S. REPRESENTATIVE RON WYDEN OR ANY REPRESENTATIVE OF

1. **Letters (10/6/93 from _____ and _____ response) to Wyden from _____**
NOTE-Personal identifiers need to be dedacted

2. **Letter to Secretary Shalala, dated December 22, 1993, from Wyden**
NOTE-Letter may also be provided by OLA

3. **Letter to Dr. Kessler, dated August 3, 1993, from Wyden Response dated August 19, 1993, also included.**
NOTE-Personal identifiers and handwritten notes need to be dedacted

4. **Letter to Secretary, HHS, dated December 5, 1990, from Wyden Response dated December 5, 1991, also included**

NOTE-This letter may also be provided by OLA

5. **Letter to Dr. Kessler, dated December 10, 1992, from Wyden Response letter, dated December 15, 1992, also included**
NOTE-These letters may also be provided by OLA

LAWRENCE LADER OF N.Y.C. OR ANY REPRESENTATIVES OF

1. Letter to Mr. Lader, dated May 11, 1993, from Acting ASH Incoming letter, dated March 31, 1993 also included

2. Letter to Secretary Shalala, dated February 25, 1993, from Mr. Costikyan (representing Mr. Lader)

* 3. Memorandum of Meeting (5/4/93) between several industry representatives (Mr. Lader) and FDA Staff * SHOULD NOT BE RELEASED 12/95

4. Letter to Secretary Shalala, dated May 12, 1993 from Mr. Costikyan (representing Mr. Lader)

5. Letter to Mr. Costikyan, dated May 7, 1993, from Secretary Shalala and incoming letters to the Secretary
NOTE-FDAFES has no enclosures for the 2/25/93 letter

HOECHST AG OF FRANKFURT, GERMANY OR ANY REPRESENTATIVES OF

1. Letter to Professor Hilger, dated February 3, 1993, from Dr. Kessler

2. Letter to Dr. Kessler, dated April 15, 1993, from Professor Hilger

3. Letter to Secretary Shalala, dated March 23, 1993, from Professor Hilger

N.Y.C., MAYOR DAVID N. DINKINS OR ANY REPRESENTATIVES OF

1. Letter to _____ dated February 16, 1993, from Lou Sepersky, Chair, N.Y.C. Community Board No. 6

2. Letter to David Dinkins, dated May 7, 1993, from Secretary Shalala. Incoming letter, dated January 22, 1993, from Dinkins also included.

PEOPLE'S REPUBLIC OF CHINA OR ANY REPRESENTATIVES OF

1. Letter to Francis C. Madigan, dated July 23, 1993, from _____. Incoming letter, dated May 20, 1993, also included.

ROUSSEL UCLAF OF PARIS, FRANCE OR ANY REPRESENTATIVES OF

1. Letter to Dr. Sakiz, dated January 22, 1993, from Dr. Kessler.
   NOTE-Entire enclosure may constitute commerical and/or trade secret information that is not releasable (check with CDER,(HFD-1))

2. Letter to _____ dated May 5, 1993 from Alain Deslauriers

3. Letter to Dr. Kessler, dated December 21, 1993, from Professor Hilger

4. Letter to Dr. Sakiz, dated December 14 1992, from Dr. Kessler

5. Letter to Dr. Ulmann, et al., dated January 22, 1993, from _____
   NOTE-Personal identifiers need to be deleted.

6. Record of Telephone Conversation (1/25/93) between Dr. Ulmann and _____
   NOTE-Personal (patient) identifier needs to be deleted

* 7. Letter to _____ dated February 26, 1993, from Catherine Euvard of Roussel-Uclaf * Should NOT be released 12/93

8. Letter to Secretary Shalala, dated March 18, 1993, from Mr. Sakiz
   NOTE-Handwritten notes should be deleted

9. Letter to Mr. Sakiz, dated March 4, 1993, from Dr. Vukovich
   NOTE-FDAVES does not have enclosure mentioned in letter

AMERICAN MEDICAL ASSOCIATION OR ANY REPRESENTATIVES OF

1. Letter to Dr. Kessler, dated May 15, 1992, from Dr. Todd

UNITED KINGDOM OR ANY REPRESENTATIVES OF

1. Letter to _____ dated July 31, 1992, from Mr. R.H. Forey, British Embassy

ROUSSEL UCLAF

Drug Regulatory Affairs
Health Care Division

AD/JA - n°307

May 5th, 1993

CDER will consider this for release.

Mifepristone (RU
mifepristone for te

Dear ——

Further to our letter of April 23, 1993, we are sending you by courrier a single copy of additional data intended to support our proposed training protocol for the use of mifepristone for termination of early pregnancy to be conducted in the United States.

The data enclosed includes :

1. The Index (n°9) dated May 1993, which has now been complemented with the listing of the clinical data and bibliographic data enclosed.

   This new version of the Index replaces and cancels the one sent to you April 23 and dated of April 1993.

102 et 111, Route de Noisy - B.P. N° 9 - 93230 Romainville
Tél. + 33 (1) 49 91 49 91 Tlx. ROUSS A 235 477 F
Fax. + 33 (1) 49 91 30 94 - 49 91 32 96 SIRET 542 008 081 00052 0004
CCP 3012 37 S
Adr. Télég. Roussel Uclaf Romainville
Société Anonyme à Directoire et Conseil de Surveillance

2. Human pharmacokinetics and bioavailability reports together with the reports on the clinical pharmacology and clinical trials sections.

3. Preclinical and clinical bibliographic data.

We trust this is to your satisfaction and please do not hesitate to let us know if you need any other information.

Sincerely,

[ ]

APPEARS THIS WAY
ON ORIGINAL

cc : Dr A. Ulmann

CONTENTS OF THE BOXES

BOX 1/3

Folder 08 : Index N°9 dated May 1993
Reports 9.1. / 9.2. / 9.6.

Folder 09 : Reports 9.7. to 9.11.

Folder 10 : Reports 9.12. to 9.14.

Folder 11 : Reports 9.15. to 9.22.

Folder 12 : Reports 10.1.1. to 10.1.5.

Folder 13 : Reports 10.2.1. to 10.2.5.

Folder 14 : Reports 10.2.6. to 10.2.9.

BOX 2/3

Folder 15 : Report 10.2.10.

Folder 16 : Reports 10.2.11. to 10.2.13.

Folder 17 : Reports 10.2.14. and 10.2.15.

Folder 18 : Reports 10.2.16. to 10.2.18.

Folder 19 : Report 10.2.19.

Folder 20 : Reports 10.2.20. to 10.2.24.

Folder 21 : Reports 10.2.25 to 10.2.27.(Books 1/5 & 2/5)

BOX 3/3

Folder 22 : Report 10.2.27.(Books 3/5, 4/5 & 5/5)

Folder 23 : Reports 10.2.28. to 10.2.30.

Folder 24 : Reports 10.3.1. to 10.3.3.

Folder 25 : Reports 10.4.1. and 10.4.2.

Folder 26 : Reports 10.5.1. to 10.5.5.

Folder 27 : Reports 10.6.1. and 10.6.2.
Bibliographic data listing + Bibliographic data (3 books)
April 1993

BOPP, COLESON & BOSTROM
ATTORNEYS AT LAW

JAMES BOPP, JR.

ASSOCIATES:
RICHARD E. COLESON
BARRY A. BOSTROM
JOHN K. ABBOG

2 FOULKES SQUARE
401 OHIO STREET
P.O. BOX 8100
TERRE HAUTE, INDIANA 47808-8100

TELEPHONE
812/232-2434
FAX
812/235-3685

93-477009

December 2, 1993

Freedom of Information Staff
(HFI-35)
Food & Drug Administration
Room 12A-16
5600 Fishers Lane
Rockville, MD 20857

Re: Information Request Under the Freedom of Information Act

Dear Madam/Sir:

This letter is written on behalf of our client National Right to Life Committee, Inc. Pursuant to the Freedom of Information Act (FOIA), 5 U.S.C. § 522 as amended, and 21 CFR § 20.40, we seek certain information.

Access is sought generally to any and all documents, including but not limited to correspondence, notes of conversations, and notes of meetings of any kind, relating to the pharmaceutical substance known as RU-486 ("mifepristone"), developed by the French pharmaceutical company Roussel-Uclaf SA, controlled by Hoechst AG, and commonly known as "the French abortion pill." The time frame of the documents requested is from January 1, 1992, to the present, i.e., present is the current date whenever the search is made for documents in compliance with this request.

The scope of the documents sought concerning RU-486 is any and all documents from the above-mentioned time period, including but not limited to correspondence to or from the following individuals and entities, notes of conversations with the following individuals and entities, and notes of meetings with the following individuals and entities.[1]

[1]Any references to geographical locations shall be understood to include the general geographical area surrounding a city listed in addition to the specific city boundaries of a location, e.g., Los Angeles includes the greater Los Angeles metropolitan area. Similarly, any identification information provided in the following list is intended as a general identification and is for assistance in locating the material requested; to the extent any identification is wholly or partially incorrect such

HFD-19
HFW-1

1. United States President Bill Clinton or his staff or any representative of himself or his staff;

COMPANIES

2. Roussel Uclaf of Paris, France, including corporate president Edouard Sakiz, Dr. Andre Ulmann, and any other corporate officer, employee, or representative;

3. Hoechst AG of Frankfurt, Germany, including corporate president Dr. Wolfgang Hilger, and any other corporate officer, employee, or representative;

4. Hoechst Celanese Corporation, of Somerville, New Jersey, including any corporate officer, employee, or representative;

5. Hoechst Roussel Pharmaceuticals of Somerville, New Jersey, including any corporate officer, employee, or representative;

6. Rhone-Poulenc of Paris, France, including any corporate officer, employee, or representative;

7. Rhone-Poulenc Rorer of Fort Washington, Pennsylvania, including any corporate officer, employee, or representative;

8. Schering AG of Berlin, Germany, including any corporate officer, employee, or representative;

9. G.D. Searle of Skokie, Illinois, including any corporate officer, employee, or representative;

10. Upjohn Company of Kalamazoo, Michigan, including any corporate officer, employee, or representative;

11. Gynopharma, Inc. of Somerville, New Jersey, including president Roderick MacKenzie and any corporate officer, employee, or representative;

12. Cabot Medical Corporation of Langhorne, Pennsylvania, including president and chief executive officer Warren G. Wood and any corporate officer, employee, or representative;

13. Adeza Biomedical Corporation of Sunnyvale, California, including president and chief executive officer Daniel O. Wilds and any corporate officer, employee, or representative;

14. Gynex Pharmaceuticals Inc. of Vernon Hills, Illinois, including president and chief executive officer Stephen M. Simes and any corporate officer, employee, or representative;

GOVERNMENTS

15. United Kingdom, including any governmental official or representative;

16. France, including any governmental official or representative;

---

inconsequential error should be disregarded and material produced as if the identifying information were wholly correct.

17. Sweden, including any governmental official or representative;
18. People's Republic of China, including any governmental official or representative;

UNITED STATES CONGRESS

19. U.S. Representative Ron Wyden of Oregon, including any member of his congressional staff member or representative of either himself or his staff and any staff member or representative of the Subcommittee on Regulation, Business Opportunities, and Energy of the Committee on Small Business, including Steve Jennings;
20. U.S. Representative Patricia Schroeder, including any member of her congressional staff or representative of either herself or her staff;
21. U.S. Representative John Porter, including any member of his congressional staff or representative of either himself or his staff;
22. U.S. Senator Paul Simon, including any member of his senatorial staff member or representative of either himself or his staff;

VARIOUS GROUPS AND INDIVIDUALS

23. Fund for the Feminist Majority, including Eleanor Smeal and any other employee, official, or representative;
24. Feminist Majority Foundation, including any employee, official, or representative;
25. National Abortion Rights Action League (NARAL) and/or its successor organization by any name whatsoever, including Kate Michelman and any employee, official, or representative;
26. National Abortion Federation of Washington, District of Columbia, including any employee, official, or representative;
27. Planned Parenthood Federation of America (PPFA) and/or any affiliates of PPFA, National Abortion Federation of Washington, District of Columbia, including any employee, official, or representative;
28. National Women's Health Network of Washington, District of Columbia, including any employee, official, or representative;
29. Reproductive Health Technologies Project, including Joanne Howes, Marie Bass, and any other employee, official, or representative;
30. City of New York, New York, Mayor David N. Dinkins, including any member of his staff member or representative of either himself or his staff;
31. City of New York, New York, Commissioner, Department of Consumer Affairs, including any staff member or representative of either himself or his staff;

32. Los Angeles Coalition for RU 486, including Dr. Carol R. Kurz, Carol Rowen, and any other employee, official, or representative;

33. Steven Heilig, M.D., of San Francisco, California, including any staff member or representative of either himself or his staff;

34. Marcus Conant, M.D., of San Francisco, California, including any staff member or representative of either himself or his staff;

35. "Every Child a Wanted Child" of San Francisco, California, including any employee, official, or representative;

36. Dr. E.E. Baulieu of Paris, France, including any staff member or representative of either himself or his staff;

37. Lawrance Lader of New York City, New York, including any staff member or representative of either himself or his staff;

38. The American Medical Association, including any employee, official, or representative;

39. Committee on Contraceptive Development of the National Academy of Sciences, including Luigi Mastroianni, M.D., Department of Obstetrics and Gyncecology, University of Pennsylvania, and any other employee, official, or representative;

40. American Society for Law and Medicine, including any employee, official, or representative;

41. Committee to Study Biomedical Decision Making of the Institute of Medicine of the National Academy of Science, including any employee, official, or representative.

42. R. Alta Charo, including any staff member or representative;

43. Center for Biomedical Ethics of the University of Minnesota, including Arthur Caplan and any other employee, official, or representative;

44. Karen Gervais, Ph.D., including any staff member or representative;

45. Steven Miles, M.D., including any staff member or representative;

46. Elizabeth Newhall, M.D., Medical Director of the Downtown Women's Clinic, Portland, Oregon, including any staff member or representative of herself or said clinic;

47. Kim Cross, M.D., President of the Oregon Medical Association, including any staff member or representative;

48. Kitty Piercy, Chair of Oregon RU 486 Task Force, including any staff member or representative;

49. Allie Stickney, Executive Director, Planned Parenthood of Columbia, Williamette, Portland, Oregon, including any staff member or representative;

50. Population Council, New York City, New York, including President Margaret Catley-Carlson, Vice President C. Wayne Bardin and any other employee, official, or representative;

51. Oregon Health Science University, Portland, Oregon, including E Paul Kirk, M.D., professor and chairman of Ob/Gyn Department; Lynn Loriaux, M.D., Ph.D., professor and head of endocrinology, Diabetes; Jeffrey Jensen, M.D., assistant professor, Department of Ob/Gyn; and any other employee, official, or representative;

52. David A. Grimes, M.D., University of Southern California School of Medicine, Los Angeles, including any staff or representative;

53. Daniel R. Mishell, M.D., chairman of the Department of Ob/Gyn, University of Southern California School of Medicine.

We request notice of available access to these documents for myself, my client, and/or an authorized representative of my client within ten (10) working days of the receipt of this letter. We stand ready, of course, to pay the standard fee for production of these materials.

In the event access is denied to any part of the requested records, please describe the deleted material in detail and specify the statutory basis for the denial as well as your reasons for believing the alleged statutory exception applies in this instance. Please separately state your reasons for not invoking your discretionary power to release the requested documents in the public interest. Such statements will be helpful to us in deciding whether to appeal an adverse determination and in formulating the arguments in case we do appeal. The Agency's written justifications might also help avoid possible unnecessary litigation.

We anticipate that you will make the requested material available to myself, my client, or an authorized representative within the statutorily prescribed time. We await your prompt reply. Thank you for your assistance.

Sincerely,

BOPP, COLESON & BOSTROM

James Bopp, Jr.
Richard E. Coleson

Certified Mail, # P 207 762 802
Return Receipt Requested
pc: Wanda Franz, Ph.D.
David O'Steen, Ph.D.
Richard Glasow, Ph.D.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

April 26, 1994

Mr. James Bopp, Jr.
Bopp, Coleson & Bostrom
Attorneys at Law
P.O. Box 8100
Terre Haute, Indiana 47808-8100

In reply refer to: 93-47009

Dear Mr. Bopp:

This is in response to your request (copy enclosed) for record(s) from the Food and Drug Administration pursuant to the Freedom of Information Act.

In order to help reduce processing time and costs, certain material has been deleted from the record(s) furnished to you because a preliminary review of the records indicated that the deleted information is not required to be publicly disclosed. If, however, you desire to review the deleted material, please make an additional request at the following address:

Food and Drug Administration
Freedom of Information Staff, HFI-35
5600 Fishers Lane
Rockville, MD 20857

Should the Agency then deny this information, you would have the right to appeal such denial. Any letter of denial will explain how to make this appeal.

The following charges may be included in a monthly invoice:

Reproduction	Search	Review	Total
$8.30	$208.00	$358.00	$574.30

The above total may not reflect final charges for this request. Please do not send payment unless you receive an invoice.

Sincerely yours,

/S/

FDA Executive Secretariat

Enclosures

MIF 003516

FOI REQUEST NO. 93-47009 -- RU-486

CALCULATION OF FEES

		SEARCH	REVIEW	REPRODUCTION
PAGES (.10/pg)	83			$ 8.30
~~ ($24/hr.)	6 hours	$146.00		
~~ ($24/hr.)	8 hours		$192.00	
~~ ($24/hr.)	2 hours		$ 48.00	
~~ ($24/hr.)	8 hours		$192.00	
~~ ($43/hr.)	4 hours		$ 92.00	
	28 hours	$146.00	+ $524.00	+ $ 8.30
			TOTAL COST =	$678.30

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

March 24, 1993

Dear _____

Your letter to President Clinton has been referred to the Food and Drug Administration (FDA) for response. We are sorry to hear that your daughter is suffering from Cushings Disease.

As you may know, the President has directed the Secretary of Health and Human Services to assess initiatives to promote the testing of RU-486 (mifepristone) and other antiprogestins in the United States. FDA is an active participant in this ongoing evaluation. Please be assured that we are prepared to review a marketing application for RU-486, if one is submitted, based on established legal and scientific criteria. On February 24, senior representatives of the FDA and Roussel-Uclaf, the manufacturer of RU-486, met to discuss clinical and manufacturing data on the drug that FDA would need in considering a new drug application for an abortifacient indication. At that meeting, FDA received a strong commitment from Roussel-Uclaf to continue to make the drug available for research on other potential uses, including Cushings Disease.

In order for your daughter to receive RU-486 for Cushings Disease, her physician would need to contact Roussel-Uclaf to receive the company's commitment to supply the drug for her treatment. We understand that the firm requires a brief, written, medical history in order to justify the request. Once your daughter's physician has received this commitment from the company, he or she should contact FDA's Division of Metabolism and Endocrine Drug Products. Generally, FDA may be expected to grant a single patient-use investigational new drug application if the company agrees to supply the drug.

The individual to contact at Roussel-Uclaf is:

André Ullman, M.D., Ph.D.
Head of Clinical Research
Roussel-Uclaf
102, Route de Noisy
93230 Romainville, France
Telephone: 33-1-49914821
Fax: 33-1-49915505

The individuals to contact in FDA's Division of Metabolism and Endocrine Drug Products are:

-FDA, HFD-510
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: 301-443-3520
Fax: 301-443-9282

I hope that this information is helpful to you and to your daughter.

Sincerely yours,

/S/

Senior Policy Analyst
Office of the Executive Secretariat

29 January 1993

President Clinton and Hillary Clinton
The White House
The United States of America

RE: RU486 -- AS A LIFESAVER NOT LIFETAKER

Dear Mr. President and Hillary Clinton.

First . . let me wish you wonderful years in the White House.

Second . . in regards to RU486. my daughter suffers from severe Cushings Disease. She is 26 years old. Cushings Disease is rare and can be fatal without successful treatment. Not only has RU486 been shown in European studies to greatly benefit women with breast cancer, persons with glaucoma and possibly other diseases - - it has proven to be an extremely effective medication for Cushings Disease without dangerous side effects. I ask you please, as my First Family, to seriously and quickly consider adding your efforts to secure RU486 for study and treatment in the United States, not only for my daughter but for the thousands of your citizens with various life threatening diseases it would give hope to.

To persons against this drug for abortion issues I say, I had my child and now she needs help.

Sincerely,

/s/

** TOTAL PAGE.001 **

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

May 11, 1993

Dear

This is a note to follow-up on our telephone conversation concerning your request to President Clinton for assistance in obtaining mifepristone (RU-486) for your father.

We are pleased to learn that your father has been able to obtain RU-486 for treatment of his meningioma. Please know that our thoughts are with you both. If you find that you need further assistance from the Food and Drug Administration, please feel free to contact me (301-443-1454).

Sincerely yours,

/S/

Senior Policy Analyst
Office of the Executive Secretariat

AP
HARDSHIP
HHS FDA

HHS

165286
590281

January 19, 1993

President Bill Clinton
The White House
Pennsylvania Avenue
Washington D.C.

Dear President Clinton:

Congratulations and welcome to the White House ! Please, I need your help. My father has a recurrent malignant meningioma of the brain. There seems to be some hope for patients with brain tumors with a pill called Mifepristone (RU-38486).

Mifepristone is not available in the United States, as you are aware of, but it is available in Europe, such as in France. This pill is manufactured in Paris by the company Roussel-Uclaf. The function of this pill is for abortions, but researchers believe it could help with brain tumors. Dr. André Ullman in Paris, from what I understand, is the person to get in contact with at Roussel-Uclaf. The phone number is 49.91.44.72.

My father has undergone four huge brain surgery operations, radiation and currently undergoing chemotherapy treatments. Doctors feel my father has to have brain surgery again in the future, but the dimensions of this operation would be so huge, we don't know if he could endure another one. In the meantime, doctors feel chemotherapy is the only way to go right now, but chemotherapy is taking it's toll on my father. He is going in every month for chemotherapy. It seems when he is almost recuperated from the session, he is back in for more.

As you may very well know, chemotherapy kills bad cells as well as good cells. How much chemotherapy can my father endure ?

Please, this pill is the only hope we have left to experiment with. Doctors have done and are doing all they can for my father but it is not enough. I know another patient that has been diagnosed with the same tumor as the one my father has. They need your help too.

We need your help. You are the only one that can get this medicine for us. This is our last hope to save my father. My father is fifty-one and has been battling with this for five years.

I am anxiously awaiting your response. Please feel free to write or call anytime, so I may supply any information you may need.

Sincerely,

151

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

December 3, 1993

Dear [redacted]

Your letters of September 27, 1993, to President Clinton and Secretary Shalala were recently referred to the Food and Drug Administration (FDA) for response.

As you may know, the President has directed the Secretary of Health and Human Services to assess initiatives to promote the testing of RU-486 (mifepristone) and other antiprogestins in the United States. FDA is an active participant in this ongoing evaluation and is prepared to review a marketing application for RU-486, if one is submitted, based on established legal and scientific criteria. Recently, senior representatives of the FDA and Roussel-Uclaf, the manufacturer of RU-486, met to discuss clinical and manufacturing data on the drug that FDA would need in considering a new drug application for an abortifacient indication. At that meeting, FDA received a strong commitment from Roussel-Uclaf to continue to make the drug available for research on other potential uses, including meningiomas.

In your letter, although you indicate you are a cancer patient, you did not mention the form of cancer. Because most of the inquiries that we have received for compassionate use of RU-486 for cancer relate to meningiomas, I will explain how you might be able to receive RU-486 for this indication. There are two possible ways for you to receive RU-486 for the treatment of meningioma. The first is as a participant in a research study involving the use of RU-486 for the treatment of meningioma; there is such a study ongoing in the United States which is sponsored by Dr. Grunberg. To determine whether you are eligible to participate in this study, your physician should contact:

Patricia Gutierrez
South-Western Oncology Group (SWOG) Operations Office
(210) 677-8808

If you are not eligible to participate in this study, it may be possible to obtain the drug through a single patient-use Investigational New Drug Application (IND). In order to proceed with a single patient-use IND, your physician would need to contact Roussel-Uclaf to receive the company's commitment to supply the drug for treatment of meningioma. We understand that

the firm requires a brief, written, medical history in order to justify the request and an explanation as to why you are not eligible to participate in the ongoing study. Once your physician has received a commitment from the company to supply the drug, he or she should contact FDA's Division of Oncology and Pulmonary Drug Products.

The individual to contact at Roussel-Uclaf is:

André Ullman, M.D., Ph.D.
Head of Clinical Research
Roussel-Uclaf
102, Route de Noisy
93230 Romainville, France
Telephone: 33-1-49914821
Fax: 33-1-49915505

The individuals to contact in FDA's Division of Oncology and Pulmonary Drug Products are:

FDA, HFD-150
1401 Rockville Pike, Suite 400S
Rockville, Maryland 20852-1448
Telephone: 301-594-2135
Fax: 301-594-1216

If you have questions about these general instructions, please feel free to contact me at 301-443-3900.

Sincerely yours,

/S/

Senior Policy Analyst
Office of the Executive Secretariat

93-9222

FDA

September 27, 1993

WILLIAM CLINTON, President of the United States
The White House
Washington, D. C., 20500

Dear Mr. President:

I am a cancer patient very much in need of assistance. My physicians have exhausted all the avenues of therapy available for my condition.

I have been advised of a new medication developed in France called RU-486 (Mifepristine). This drug has been tried and used successfully, after extensive clinical trials, as a therapy for certain cancers. It is my understanding that because of its use as a drug to induce abortion this drug has been severely restricted for import to the United States. There have been, however, cases where it has been imported for use on a "compassionate" basis.

I am a veteran of World War II who gave several yeasrs of my life to preserve our way of life, have always been a taxpayer and have never accepted any welfare, unemployment compensation, nor have I made any demands of our government and it distresses me that I cannot have access to a life saving drug because of political barricades.

I ask to have your thinking of assistance in this instance and enclose a self-addressed pre-stamped envelope for the convenience of your reply.

Very respectfully yours,

/S/

enc/1

cc:

FDA

September 27, 1993

The Honorable DONNA SHALALA, Secretary, Health & Human Services
200 Independance Avenue S. W.
Washington, D. C., 20201

Dear Madam:

I am a cancer patient very much in need of assistance. My physicians have exhausted all the avenues of therapy available for my condition.

I have been advised of a new medication developed in France called RU-486 (Mifepristine). This drug has been tried and used successfully, after extensive clinical trials, as a therapy for certain cancers. It is my understanding that because of its use as a drug to induce abortion this drug has been severely restricted for import to the United States. There have been, however, cases where it has been imported for use on a "compassionate" basis.

I am a veteran of World War II who gave several yeasrs of my life to preserve our way of life, have always been a taxpayer and have never accepted any welfare, unemployment compensation, nor have I made any demands of our government and it distresses me that I cannot have access to a life saving drug because of political barricades.

Your consideration or assistance in this matter will be most sincerely appreciated. May I Have the benefit of your thinking? I enclose a self-addressed pre-stamped envelope for the convenience of your reply.

Very respectfully yours,

/S/

enc/1

cc:

93-9220

930930013

CONSULTING ENGINEER
REGISTERED LAND SURVEYOR
REGISTERED REAL ESTATE BROKER

FAX TRANSMISSION SHEET

TO: CONGRESSMAN RON WYDEN

RECEIVING FAX NUMBER: (202) 225-8914

TOTAL NUMBER OF PAGES, INCLUDING THIS PAGE: 2

DATE TRANSMITTED: 12/09/93 OPERATOR:

MESSAGE

CONGRESSMAN WYDEN, AS A RESULT OF YOUR FAX'ED LETTER TO ANDRE ULMANN, ROUSSEL-UCLAF, DATED OCTOBER 1, 1993, I RECEIVED A FAX'ED LETTER FROM HIM ON OCTOBER 6, 1993 GRANTING MY DAUGHTER USE OF RU-486 FOR HER MENINGIOMA TUMOR ON A "COMPASSIONATE BASIS."

SINCE THEN WE HAVE BEEN TRYING TO HAVE THE FDA RELEASE THIS MEDICATION TO HER --- TO NO AVAIL .... SEE CORRESPONDENCE TRANSMITTED HEREWITH ...

IF YOU DO NOT RECEIVE ALL PAGES, PLEASE CALL

AS SOON AS POSSIBLE

RESPOND TO FAX NUMBER

THANK YOU

ROUSSEL UCLAF
DOMAINE THERAPEUTIQUE ENDOCRINOLOGIE
Dr A. ULMANN
Fax 33 1 49 91 55 05
Tel. 33 1 49 91 48 21

TELECOPIE

ADRRSSRE A : ( )

TELECOPIE : ( )

COPIE A : R. WYDEN (1 202 225 8950)
E. SAKIZ
C. EUVRARD
J. SILVESTRE

REF. : 93-713

Date : October 6, 1993

Nbre de pages : 1 + /

Dear ( )

In reply to your request, I agree to provide your daughter with RU 486 for a compassionate treatment.

However, note that at present I cannot ensure you that the treatment will be beneficial to her.

In practical terms, I need that her oncologist or neurosurgeon contacts me so that I can explain him or her the protocol to be followed.

Also, note that because of various procedures, at least one month will be necessary before her doctor gets the tablets.

Sincerely yours,

André ULMANN, M.D., Ph.D.

CONSULTING ENGINEER
AND
LAND SURVEYOR

October 6, 1993

Andre Ulmann, M.D., Ph.D.
Roussel Uclaf
Domaine Therapeutique Endocrinologie
Paris, France

BY FAX TO: 011 33 1 49 91 55 05

Dear Dr. Ulmann:

I have received your telecopy message with the good news that you will furnish my Daughter, [redacted] with the medication, RU-486, on a compassionate basis for the treatment of her meningioma tumor.

I cannot thank you enough for this kind act on your, and your Company's part. I shall be ever grateful for your response to our need.

I have notified my Daughter of the receipt of your message. She has expressed her gratitude to me, but I am sure you will be receiving a message directly from her, expressing that gratitude to you.

Again, from a Father who had almost lost hope, I thank you from the bottom of my heart.

Sincerely

[redacted]

R-97X

RON WYDEN, OREGON
CHAIRMAN

103d Congress
United States House of Representatives
Committee on Small Business
Subcommittee on Regulation,
Business Opportunities, and Technology
B-363 Rayburn House Office Building
Washington, DC 20515-6318

December 22, 1993

The Honorable Donna E. Shalala
Secretary
U.S. Department of Health and
Human Services
Room 615F
Hubert H. Humphrey Building
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Madam Secretary:

I know we share an interest in improving both the health and healthcare choices of American women. I strongly endorse the significant initiatives you have launched in this regard. We will work hard to ensure your proposals get the attention and support they deserve during the remainder of the 103rd Congress.

I write to you, today, to urge your action on one element of the evolving healthcare agenda...the U.S. approval and distribution of the French drug RU 486. There have been substantial delays in the still-uncompleted licensing negotiations between the French manufacturer of this important drug, and the U.S.-based Population Council. This, in turn, defers the initiation of clinical trials needed for Food and Drug Administration approval and, ultimately, the drug's availability to American women.

A clear, personal admonition from you to the negotiating parties at this point, I believe, could do much to overcome final roadblocks to the completion of the licensing agreement.

I strongly urge you to contact executives of the drug manufacturing companies -- Roussel Uclaf of France, and Hoerchst AG Germany -- and request their cooperation.

As you know, RU 486 offers unique properties as an abortifacient and as a verifiable safe alternative to surgical pregnancy termination. And in testimony before this subcommittee, a number of medical researchers have testified that this anti-progestin also may be valuable in treating a number of other conditions and illnesses including endometriosis, Cushing's syndrome, meningioma and perhaps even

As one who has fought hard for nearly four years too get a fair and rapid assessment of this drug in the United States, I believe that our government should do all within its power to bring the current negotiations between the manufacturer and the Population Council to a swift and positive conclusion.

The potential benefits of this pharmaceutical...one which we could in the alternative replicate ourselves...are just too promising to ignore, or to be held hostage to the whims of a foreign manufacturer.

Thank you for your attention to this important matter, and for your continuing concern regarding woman's health issues. Should you have any questions regarding this request, please don't hesitate to contact me, or Steve Jenning of the subcommittee staff at (202) 225-7797.

Sincerely,

RON WYDEN
Chairman

APPEARS THIS WAY
ON ORIGINAL

RON WYDEN
Oregon
3d District

1111 Longworth Building
Washington, DC 20515-3703
(202) 225-4811

500 NE Multnomah, Suite 200
Portland, OR 97232
(503) 231-2300

Congress of the United States
House of Representatives

August 3, 1993

EXPORT TASK FORCE

The Honorable David A. Kessler, M.D.
Commissioner
U.S. Food and Drug Administration
5600 Fishers Lane, Room 14-90
Rockville, Maryland 20857

Dear Dr. Kessler:

I refer to you a letter from an Oregon constituent whose brother, apparently, is suffering from a highly aggressive brain tumor which may be treatable with the French drug RU 486.

For your information, I attach the constituent's letter. It includes details on the health problems of (————) the treatment he has had so far, and the reasoning and identity of doctors who suspect that RU 486 may be useful in his case.

This person and his doctors have had significant difficulty in obtaining from the manufacturer any quantity of this unapproved French drug, however, for compassionate use. All other therapies seem to have been exhausted in the case.

I write to you, today, to ascertain whether the Food and Drug Administration can use its good offices to assist (————) whose condition truly seems desperate and rapidly deteriorating at this point. I recall a similar instance two years ago involving a Georgia resident, (————) in which the FDA intervened on behalf of the patient. It is my understanding that in the interim, (————) who suffers from the same malady as (————), has experienced significant health improvement using the drug.

I wish to underscore that I am not suggesting or requesting that FDA exceed its usual practice, or circumvent any statutory authority or limitation in this matter. Should you have any questions regarding this request, please contact Steve Jenning of my staff at (202) 225-7797.

Sincerely,

RON WYDEN
Member of Congress

cc. ———— office of the commissioner

103d Congress

United States House of Representatives
Committee on Small Business

Subcommittee on Regulation, Business Opportunities, and Technology

2-363 Rayburn House Office Building
Washington, DC 20515-6318

TO: Steve Jenning / WYDEN

FROM: _____

SUBJECT: RU 486 Request.

2 PAGES INCLUDING COVER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

August 19, 1993

Dear

This is to follow-up on our telephone conversation earlier today concerning how to obtain RU-486 (mifepristone) for your brother,

As you may know, the President has directed the Secretary of Health and Human Services to assess initiatives to promote the testing of RU-486 (mifepristone) and other antiprogestins in the United States. The Food and Drug Administration (FDA) is an active participant in this ongoing evaluation and is prepared to review a marketing application for RU-486, if one is submitted, based on established legal and scientific criteria. Recently, senior representatives of the FDA and Roussel-Uclaf, the manufacturer of RU-486, met to discuss clinical and manufacturing data on the drug that FDA would need in considering a new drug application for an abortifacient indication. At that meeting, FDA received a strong commitment from Roussel-Uclaf to continue to make the drug available for research on other potential uses, including meningiomas.

There are two possible ways for you to receive RU-486 for the treatment of meningioma. The first way is as a participant in a research study involving the use of RU-486 for the treatment of meningioma; there is such a study ongoing in the United States which is sponsored by Dr. Grunberg. To determine whether you are eligible to participate in this study, your physician should contact:

Patricia Gutierrez
South Western Oncology Group (SWOG) Operations Office
(512) 677-8808

If you are not eligible to participate in this study, it may be possible to obtain the drug through a single patient-use Investigational New Drug Application (IND). In order to proceed with a single patient-use IND, your physician would need to contact Roussel-Uclaf to receive the company's commitment to supply the drug for treatment of meningioma. We understand that the firm requires a brief, written, medical history in order to justify the request. Once your physician has received this commitment from the company, he or she should contact FDA's

Division of Oncology and Pulmonary Drug Products. Generally, FDA applies similar criteria for issuing a single patient-use IND.

As I stressed in our telephone conversation, you must decide who will serve as your brother's physician for the purpose of administering a single patient-use IND. Thus far, [ ] in our oncology review division, has described the process for obtaining RU-486 to two different physicians--[ ] We have now received a letter from a third physician, [ ] In order to best serve the needs of your brother, [ ] needs to have the physician you choose call her and indicate that he has been designated by your brother to serve as his physician for this purpose. Ms. [ ] will then be able to work with this physician on behalf of [ ]

The individual to contact at Roussel-Uclaf is:

André Ullman, M.D., Ph.D.
Head of Clinical Research
Roussel-Uclaf
102, Route de Noisy
93230 Romainville, France
Telephone: 33-1-49914821
Fax: 33-1-49915505

The individuals to contact in FDA's Division of Oncology and Pulmonary Drug Products are:

[ ]
FDA, HFD-150
1401 Rockville Pike, Suite 400S
Rockville, Maryland 20852-1448
Telephone: 301-594-2135
Fax: 301-594-1216

I hope that this information is helpful to you and your brother. Please know that our thoughts are with you. If you have any questions, please call me at (301) 443-3900.

Sincerely yours,

/S/

Senior Policy Analyst
Office of the Executive Secretariat

MAJORITY MEMBERS
RON WYDEN, OREGON
CHAIRMAN

ELIOT L. ENGEL, NEW YORK
JIM OLIN, VIRGINIA
MICHAEL R. McNULTY, NEW YORK

101st Congress

United States House of Representatives
Committee on Small Business
Subcommittee on Regulation, Business Opportunities, and Energy
B-363 Rayburn House Office Building
Washington, DC 20515

MINORITY MEMBERS
WM. S. BROOMFIELD, MICHIGAN
MILTON G. HANCOCK, MISSOURI
JOEL HEFLEY, COLORADO

STEVE JENNINGS
SUBCOMMITTEE STAFF DIRECTOR
202-225-7757

PAUL RUSHOFF
MINORITY SUBCOMMITTEE PROFESSIONAL
STAFF MEMBER
202-225-6176

December 5, 1990

The Honorable Louis W. Sullivan
Secretary
U.S. Department of Health and Human Services
H.H. Humphrey Building
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Mr. Secretary:

I know we share a deep interest in the public health concerns facing this nation, and in the fundamental role played by the federal government in creating a healthier society.

You may be aware of important medical research that has been undertaken in this country using the French anti-progesterone RU 486. Medical researchers testifying before my subcommittee have termed this drug a breakthrough invention which could have great -- perhaps unique -- utility in treating a variety of debilitating and deadly disease, from cancer to Cushing's Syndrome.

However, as I have related to you in previous communications, it is apparent that a combination of anti-abortion fervor in this country and an arbitrary import ban imposed by the Food and Drug Administration has discouraged the drug's manufacturer, Roussel UCLAF, from continuing existing clinical trials with this drug or providing the drug for new research projects.

This is tragic. Sick and dying Americans could be helped with this drug. And today I urge you to take several actions which I believe could help remedy this unnecessary and embarrassing problem which has stained our nation's reputation as a leader in health care policy and research.

Mr. Secretary, I urge you to act as quickly as possible on the following proposals:

-1- Lift the ban on personal importation of RU 486. It is unnecessary and appears to have been ordered solely to assuage anti-abortion groups. Our review of FDA files found that (1) there was no record of surreptitious importation of this drug in any form, (2) that there was no indication that a black market in RU 486 existed, and (3) that the FDA failed to consult

with either the medical community or other public health officials prior to the issuance of the June 1989 ban.

Moreover, it appears that while this ban does not specifically restrict medical research with the unapproved drug, since the imposition of the alert no new RU 486-related clinical trials in this country have been initiated. Earlier trials with the drug have been concluded, or are winding down, in some cases because the drug's manufacturer has declined to make available new quantities of RU 486. I believe that the company's decision is in part a response to the FDA's import alert.

-2- Short supplies of the drug in this country have closed highly successful therapeutic programs for treatment of Cushing's Syndrome -- a sometimes fatal auto-immune disease. It is my understanding that RU 486 is the only known drug treatment for this illness.

New clinical trials of this treatment at the National Institutes of Health have been placed on hold because the company will not guarantee that new quantities of the RU 486 will be made available for Cushing's Syndrome patients. This will mean more suffering for some, and perhaps an early death for others.

Therefore, I ask you to use the good offices of your position and request that the company give quantities of RU 486 to NIH to expand this important clinical trial.

-3- Your department and the FDA must make affirmative statements that (1) this Administration without qualification supports medical research in the United States using RU 486, and (2) that Roussel UCLAF, related companies, its subsidiaries or its licensees will receive a fair and politically unbiased hearing when and if a new drug approval application for RU 486 is submitted.

On this question, perhaps you could initiate these important statements by responding to me, in writing, the views of your department and the Administration regarding for research with, and licensing of RU 486 in this country.

My subcommittee has a clear jurisdiction to investigate, assess and recommend changes in federal regulation as it impacts the competitiveness of American enterprise. I believe that the FDA's decision in this area has created a significant roadblock for U.S. drug research and development efforts insofar as they are dependent on investigations with RU 486, its companion drugs, or new drugs which may be developed on similar chemical models.

I also believe that the FDA has clearly abused its discretionary regulatory authority in the case of RU 486, and that its blatantly insufficient arguments before this subcommittee demonstrate an obvious disregard of the agency's congressional mandate.

If I may quote from a Monday, December 3, 1990, editorial on this subject in the Los Angeles Times: "The FDA is a partner in medicine, certifying scientists' claims for their new drugs. As such, it shares the responsibility of physicians to provide help. In this case, the agency is hiding, not providing, and the White House must set it straight."

As the nation's chief health officer, you, I believe, are in a unique position to begin setting this issue straight. Should you have any questions regarding this request, please don't hesitate to call on me or Steve Jenning of the subcommittee staff at (202) 225-7797.

Sincerely,

Ron Wyden

RON WYDEN
Chairman

cc. David Kessler, Commissioner, Food and Drug Administration

APPEARS THIS WAY
ON ORIGINAL

The Honorable Ron Wyden
Chairman, Subcommittee on Regulation,
Business Opportunities, and Energy
Committee on Small Business
House of Representatives
Washington, D.C. 20515

Dear Mr. Wyden:

This is in response to your letter regarding issues related to the unapproved new drug, RU-486. As you may remember you raised this issue during our October 29 meeting. I sincerely apologize for the lengthy delay in responding.

First, let me emphasize the strong commitment of the Food and Drug Administration (FDA) both to appropriate implementation of the law and to making important therapies available to those who need them. We firmly believe that it is the pre-eminent responsibility of the FDA to protect the public health.

You expressed concern about the current import alert on RU-486, and especially about a potential adverse impact on research. It was public health reasons that led FDA to restrict the importation of RU-486 for personal use. The rationale for that decision, discussed by FDA witnesses at a November 19, 1991 hearing before your Subcommittee, included concerns about the potential risk of serious adverse effects such as excessive uterine bleeding to patients who, because of the intended use of the product, might not be under the care of a physician. In addition, as Mr. Chesemore stated at that time, RU-486 does not fit current criteria for allowing for personal importation of an unapproved drug; that is, as an abortifacient, RU-486 is not proposed for treatment of a serious condition for which no alternative therapy exists, a primary consideration in the development and implementation of our personal importation policy.

It is my understanding that the import alert in no way restricts the importation of this drug for research purposes. FDA also has provided clarification to its field offices relative to the importations of unapproved drugs for non-clinical research, stating that such importation will be allowed if certain regulatory requirements are met. A copy of that guidance is enclosed for your information.

FDA's drug review authority under the Federal Food, Drug, and Cosmetic Act is limited to determinations based on the data and information requirements mandated by the statute. Our regulations governing the conduct of clinical investigations require a person who wishes to conduct a clinical investigation on an unapproved drug to submit to FDA an Investigational New Drug Application (IND) and to comply with all applicable regulatory requirements governing the conduct of clinical investigations. Studies using RU-486 have been allowed by FDA under INDs for a number of years and have in some cases been supported by the National Institutes of Health. An IND becomes effective within thirty days unless FDA notifies the sponsor of the investigation that the proposed clinical trial should not proceed. The grounds for taking such action are that (1) the sponsor has not provided sufficient information to evaluate the risks of the drug, (2) the risks to the subject are unreasonable, (3) the investigators are not qualified, or (4) the information provided to the investigator is misleading.

Finally, your letter raises the issue of a fair and unbiased review of any application received by FDA. Let me emphasize that we are committed to maintaining the scientific integrity of FDA's new drug testing and approval process carried out under existing law. I can assure you that any protocol submitted to FDA will be given a fair review based on the scientific issues involved.

I appreciate your perspective on this complex issue and your commitment to improving the public health of all Americans

Sincerely yours,

Carol R. Scheman
Deputy Commissioner
for External Affairs

Enclosure

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

December 15, 1992

Representative Ron Wyden
Chairman
Subcommittee on Regulation,
Business Opportunities, and Energy
House of Representatives
B-363 Rayburn House Office Building
Washington, D.C. 20515-6318

Dear Mr. Wyden:

This is in response to your letter of December 10, 1992, regarding the drug mifepristone (RU-486) manufactured by Roussel-Uclaf, in which you ask several questions.

You asked first whether the Food and Drug Administration would consider clinical trials in Europe as adequate evidence of the drug's safety and efficacy for purposes of approval in the United States for interruption of early pregnancy and whether additional human testing might be necessary to fulfill United States requirements. As with any other drug, the FDA is willing to consider foreign clinical trials as evidence of safety and efficacy, although we always reserve the right to audit the data according to our usual procedures. We recently approved an oral contraceptive (Desogen) based entirely on clinical studies conducted in the United Kingdom. Other drugs have also been approved on the basis of foreign trials alone. Agency staff who will be responsible for reviewing any mifepristone application report that, based on publicly available information and literature reports, the available data may well be sufficient to permit an adequate review. Therefore, further clinical trials may not be required. However, without an application submitted to the Agency for review, we cannot give a definitive answer on this question.

You also ask for an estimate of the length of time and the costs involved for a company seeking to obtain approval of mifepristone in the United States. While we are not experts on cost issues, the costs of preparing a new drug application for this product should not be excessive because much of the necessary information is already available. The Pharmaceutical Manufacturers Association, or its member companies, may be able to be more helpful on this issue. Based on our current knowledge regarding the data on the drug's safety and effectiveness, we estimate that the review process at the FDA would take approximately four to six months, which would include the involvement of a public advisory committee.

Representative Ron Wyden

In response to your last question, an unresolved issue would be obtaining access in this country to a prostaglandin which, as you know, under the terms of the foreign approvals, must be taken in conjunction with mifepristone. In addition, as you are aware, distribution of mifepristone is closely controlled under the terms of the foreign approvals. The appropriate distribution system for mifepristone in this country would also need to be resolved.

Sincerely yours,

Carol R. Scheman

Carol R. Scheman
Deputy Commissioner
for External Affairs

APPEARS THIS WAY
ON ORIGINAL

102d Congress

United States House of Representatives
Committee on Small Business

Subcommittee on Regulation, Business Opportunities, and Energy

2-363 Rayburn House Office Building
Washington, DC 20515-6315

December 10, 1992

Dr. David A. Kessler
Commissioner
U.S. Food and Drug Administration
Room 14-71
5600 Fishers Lane
Rockville, Maryland 20857

Via Fax: (301) 443-3100

Dear Dr. Kessler,

This subcommittee is investigating several issues relating to the U.S. regulation of, and marketplace opportunities for the French drug RU 486, manufactured by Roussel Uclaf. Key to this inquiry is the current view of the U.S. Food and Drug Administration regarding the safety and efficacy proofs which will be required should the manufacturer decide to market this drug in the United States, and the time burden likely to face the company should it seek a new drug approval from your agency.

While the agency should not -- and does not -- intend to in any way lessen the normal burden of proof required for any new drug, in the case (prospectively) of RU 486, we are interested in whether scientists within the FDA's new drug approval section have any views regarding the breadth and quality of experience with this drug in France, and in other foreign markets.

In this context, I have several questions for the agency:

-- To what extent does the agency deem European experience with this drug, including more than 100,000 clinical medical cases in France since 1988, as evidence of the drug's safety and efficacy for purposes of approval in the United States?

-- If European experience with RU 486 is directly applicable to requirements demanded within the FDA standard drug approval process, is it possible to attach some comparative value to that which is already known about the drug?

Specifically, can you give a rough estimate as to the percentage or portion of the usual U.S. drug approval process, including demands for extensive human testing, which may already be satisfied by the European experience?

-- Similarly, can you provide any estimate as to how long a U.S. drug approval process would take in light of the extensive evidence of safety and effectiveness already available for RU 486? Perhaps the agency can point to the case of another foreign drug used extensively, and safely, overseas prior to the manufacturer's application for a U.S. drug approval?

-- Subcommittee staff have spoken with a number of U.S. pharmaceutical companies which have an interest in licensing and distributing RU 486, or a similar drug, in the U.S. These companies have suggested that U.S. approval of this drug, for the reasons mentioned above, would be relatively swift and inexpensive.

The representative of one firm interviewed by subcommittee staff estimated that the total cost would be well under $5 million -- a marked difference from the average cost of a full-scale, full-phase, drug approval process estimated by Tufts University at more than $200 million.

While this estimate of the possible cost of taking RU 486 through the U.S. drug approval process obviously is very speculative, would you say that this forecast still could be in the ballpark given what we know of the European experience with RU 486 in terms of safety and effectiveness, and whatever additional proofs may be demanded by the agency?

-- Finally, are you aware of any unusual or unique circumstances involving this drug which could delay, jeopardize or otherwise seriously impede its review in the FDA's drug approval process, should the company come forward with an application?

Thank you for your attention to these questions. I would very much appreciate your earliest possible response. Should you have any questions, please don't hesitate to contact me, or Steve Jenning of the subcommittee staff at (202) 225-7797.

Sincerely,

RON WYDEN
Chairman

cc. Congressional Affairs, FDA.

APPEARS THIS WAY
ON ORIGINAL

1285 AVENUE OF THE AMERICAS
NEW YORK, NEW YORK 10019-6064

TELEPHONE (212) 373-3000
FACSIMILE (212) 757-3990
TELEX WUI 666-843

1615 L STREET, NW
WASHINGTON, DC 20036-5694
TELEPHONE (202) 223-7300
FACSIMILE (202) 223-7420

199, BOULEVARD SAINT-GERMAIN
75007 PARIS, FRANCE
TELEPHONE (33-1) 45.49.33.85
FACSIMILE (33-1) 42.22.64.38

AKASAKA TWIN TOWER
17-22, AKASAKA 2-CHOME
MINATO-KU, TOKYO 107, JAPAN
TELEPHONE (81-3) 3505-0291
FACSIMILE (81-3) 3505-4540

WRITER'S DIRECT DIAL NUMBER
(212) 373-3332

May 12, 1993

Honorable Donna E. Shalala
Secretary
U.S. Department of Health
and Human Services
200 Independence Avenue, S.W.
Room 615F
Washington, D.C. 20201

Dear Donna:

Thank you for your letter of May 7. I have passed it on to Larry Lader.

While no final decision has been reached, I believe that an effort will be made to secure approval of either the Chinese version of mifepristone or of a domestically produced product, if only to provide an alternative if the Roussel Population Council effort is not productive.

Keep up the good work!

Kindest personal regards.

Sincerely,

Ed

Edward N. Costikyan

ENC:cd

T5672[illegible]
TRACER

9305170018

MIF 003547

Office of the Assistant Secretary
for Health
Washington DC 20201

MAY 11 1993

Mr. Lawrence Lader
President
Abortion Rights Mobilization
175 Fifth Avenue, Suite 814
New York, New York 10010

Dear Mr. Lader:

This is in response to your recent letter to Secretary Shalala concerning the availability of mifepristone (RU-486) in the United States.

We appreciate you sharing your research plans with us and for offering to share your expertise in manufacturing RU-486. As you may be aware, in an April 20 meeting with senior representatives of the Food and Drug Administration (FDA), Roussel Uclaf agreed to license the drug RU-486 to the Population Council, a non-profit scientific and technical organization, for distribution in the United States, and to transfer the technology necessary for producing the drug. The Population Council will identify a manufacturer for RU-486 in the United States market, will begin a clinical trial to test the drug in the United States, and will move as soon as possible to submit a New Drug Application to FDA.

These actions do not, of course, preclude you from pursuing the

be interested in pursuing FDA approval for your product, you may wish to contact the FDA before submission of an Investigational New Drug Application (IND) to arrange for a pre-IND meeting.

Again, we appreciate your offer of assistance.

Sincerely yours,

/s/

APPEARS THIS WAY
ON ORIGINAL

ABORTION RIGHTS MOBILIZATION
175 Fifth Avenue (Suite 814)
New York, N.Y. 10010
212/673-2040

March 31, 1993

Hon. Donna E. Shalala
Secretary Of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Shalala:

Abortion Rights Mobilization, Inc., has been actively seeking to make RU 486 available to the women of this country. ARM organized last summer's court test of the FDA's import ban and earlier this year announced our intention to start testing the drug manufactured in China. We are announcing tomorrow that ARM's research scientists have manufactured RU 486 at a laboratory here in the United States and that ARM will be applying to the Food and Drug Administration for permission to test our version of the pill.

ARM's efforts in this area demonstrate that sufficient quantities of RU 486 can be readily obtained, either by importation from China or by domestic manufacture, for the drug to be made generally available to American women, once the FDA approval process has been completed. To date, the stumbling block to achieving this end has been the obstinate refusal of Roussel Uclaf, the holder of the patent, to sell or license others to produce RU 486 in the United States. Roussel's intractability need not penalize American women any longer.

As you know, on January 22, 1993, President Clinton directed 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." There is a simple and cost-free initiative you can take to satisfy this goal and make RU 486 widely available in this country.

Section 1498(a) of Title 28 of the United States Code authorizes the government, without the consent of a patent holder, to use or manufacture a private company's patented invention with the

T55524
TRACER

compensation for the government's use to be determined by the United States Claims Court. This statute gives the government a power akin to eminent domain -- the right to impose a license agreement upon a patent holder for a public purpose -- and forbids the patent owner from enjoining the government's (or the government's contractor's) use of its patent.

Under this section, your Department can contract with a drug company in this country or elsewhere to manufacture and distribute RU 486 to American women at cost. Obtaining the medical and social benefits of RU 486, particularly when compared to the cost, trauma, and in many areas, unavailability, of surgical abortions, the only FDA approved alternative, is a clear and compelling public purpose justifying the invocation of the compulsory license provisions of 28 U.S.C. § 1498(a).

ARM urges you to implement President Clinton's January 22nd directive by informing Roussel that if it does not apply for a new drug application immediately, then your Department will contract with a drug company here to test, manufacture and distribute the drug to American women. Your Department should immediately solicit proposals from drug companies for the production of RU 486 so that there will be no further delay in getting this important drug to the people who have been so cruelly denied it.

Towards this end, ARM will gladly turn over to the drug company chosen by you, free of charge, ARM's considerable learning and expertise in the manufacture of RU 486. This will save the new company months of work and shorten the time needed to start the full-scale production of the drug.

Very truly yours,

Lawrence Lader

Lawrence Lader, President

960120112

PAUL, WEISS, RIFKIND, WHARTON & GARRISON
1285 AVENUE OF THE AMERICAS
NEW YORK, NEW YORK 10019-6064

WRITER'S DIRECT DIAL NUMBER
(212) 373-3332

February 25, 1993

Honorable Donna E. Shalala
Secretary
U.S. Department of Health
and Human Services
200 Independence Avenue, S.W.
Room 615F
Washington, DC 20201

Dear Donna:

Thank you for responding to my letter about [redacted] The building of your staff after the record of the last 12 years must be a challenging task.

I am writing about a matter that falls within your jurisdiction and in which I think you might have an interest. For some years I have represented Larry Lader of the Abortion Rights Mobilization in connection with his efforts to get RU486, the French abortifacient, available for women in the United States. You may remember that some months ago Lader arranged to have a RU486 pill brought into the country as a basis for challenging the regulations of the FDA that prohibited its importation.

In the course of his exploration of the problem, he learned that the Chinese have produced a pill which appears to be the functional equivalent of the French pill and he has arranged with the supervisor of the Chinese program, the Peking Union Medical College, to obtain a supply of that pill for testing purposes in the United States. It is his intention in due course to submit the results of those tests to the FDA and to go through the FDA procedures to secure approval of the importation and use of the pill in this country. I enclose a copy of the

T54262
TRACER

statement that Larry made some weeks ago which is self-explanatory, along with a copy of a statement by Dr. Louise Tyrer, who is well-known in the field and is the medical consultant to Abortion Rights Mobilization.

I also understand that a representative of the French company will be visiting or has visited the FDA in the last week or so. Obviously, if Roussel were prepared to import their pill, a lot of problems would be avoided, including possible patent litigation between Roussel and the Chinese.

I bring this to your attention in the hope that it may be helpful in whatever discussions may take place with the French manufacturer and also so that you will be aware that there is an alternative route to accomplishing the objective if Roussel continues its present position.

I see you on television with regularity and you look like you are enjoying it all, as you should.

Kindest personal regards,

Sincerely,

Ed Costikyan

Edward N. Costikyan

Enclosures

APPEARS THIS WAY
ON ORIGINAL

ABORTION RIGHTS MOBILIZATION
175 Fifth Avenue (Suite 814)
New York, N.Y. 10010
212/673-2040

STATEMENT BY LAWRENCE LADER
PRESIDENT, ARM

THIS PILL IN MY HAND IS CHINA'S VERSION OF RU486, THE FRENCH ABORTIFACIENT. IT MAY PRODUCE A BREAKTHROUGH IN OUR CEASELESS CAMPAIGN TO MAKE AN ABORTION PILL AVAILABLE TO AMERICAN WOMEN.

IN ORDER TO CONDUCT THE FIRST RESEARCH TESTS IN THE U.S. ON THE CHINESE PILL PEKING UNION MEDICAL COLLEGE, WHICH SUPERVISES THE CHINESE PROGRAM, HAS GIVEN US PERMISSION FOR TESTING. IT HAS ALSO SUPPLIED US WITH BOTH PILLS AND ITS RESEARCH STUDIES.

OUR GROUP HAS MADE CONTACTWITH THE FOOD AND DRUG ADMINISTRATION (FDA), WHICH HAS TO APPROVE A NEW DRUG. WE WERE ENCOURAGED TO START PRE_CLINICAL TESTING ON THE CHINESE PILL.

THE FIRST CRITICAL RESEARCH STEP IS TO COMPARE RU 486 WITH THE CHINESE PILL. ONE OF OUR SCIENTISTS HAS COMPLETED AN ORGANIC CHEMICAL ANALYSIS OF THE TWO PILLS, AND HAS REPORTED THAT THE ACTIVE, CHEMICAL INGREDIENT IN BOTH IS INDISTINGUISHABLE.

ANOTHER SCIENTIST IS CONDUCTING A BLOOD PROFILE STUDY IN PRIMATES TO COMPARE THE PHARMOCOLOGIC AND METABOLIC CHARACTER OF BOTH PILLS. IT SHOULD BE COMPLETED SHORTLY, AND MAY GIVE US FURTHER CORROBORATION THAT BOTH

arm
ABORTION RIGHTS MOBILIZATION
175 Fifth Avenue (Suite 814)
New York, N.Y. 10010
212/673-8040

PILLS ARE EFFECTIVELY THE SAME.

THESE STUDIES WILL BE SUBMITTED TO THE FDA IN OUR IND OR NEW DRUG APPLICATION. IF THE FDA DECIDES THAT THE CHINESE PILL AND RU486 ARE INDISTINGUISHABLE, ...IF CHINESE RESEARCH STUDIES AND EXPERIENCE IN THOUSANDS OF PATIENTS IS COMPARABLE IN SAFETY AND EFFICACY TO THE 150,000 CASES IN FRANCE, SWEDEN AND BRITAIN, FURTHER TESTING REQUIRED BY THE FDA WILL BE CONSIDERABLY SHORTENED.

AS TO THE PATENT ON RU486 HELD BY THE ROUSSEL COMPANY OF FRANCE, OUR LEGAL TEAM HAS ASSURED US THAT UNDER THE LAW OF 35 U.S.CODE 271 (e) (1) RESEARCH TESTING ON THE CHINESE PILL MAY BE CARRIED OUT AS LONG AS NO COMMERCIAL PRODUCTION AND SALE ARE INVOLVED

WE FORTUNATELY NOW HAVE A PRESIDENT SUPPORTING SUCH TESTING. ON JANUARY 22, PRESIDENT CLINTON ORDERED THE SECRETARY OF HEALTH AND HUMAN SERVICES TO "PROMOTE THE TESTING, LICENSING AND MANUFACTURING IN THE UNITED STATES OF RU486 OR OTHER ANTI-PROGESTINS."

TO ENSURE OUR TESTING MEETS THE HIGHEST STANDARDS, WE HAVE ENLISTED DR. LOUISE TYRER, FOR 16 YEARS MEDICAL DIRECTOR OF PLANNED PARENTHOOD FEDERATION OF AMERICA, NOW RETIRED, TO SUPERVISE THE MEDICAL PROGRAM.

ABORTION RIGHTS MOBILIZATION
175 Fifth Avenue (Suite 814)
New York, N.Y. 10010
212/673-2040

WHAT EFFECT WILL THE CHINESE PILL HAVE ON THE APPROVAL OF AN ABORTION PILL FOR THE U.S.? PRESIDENT CLINTON WANTS IT. EVERY WOMEN'S GROUP WANTS IT. WE EXPECT THAT OUR TESTING WILL PROVE TO THE ROUSSEL COMPANY THAT IT CAN NO LONGER DENY AMERICAN WOMEN ONE OF THE MOST EFFICIENT AND SAFEST METHODS OF EARLY ABORTION. WE EXPECT TO SPUR ROUSSEL TO MAKE IMMEDIATE APPLICATION TO THE FDA TO BRING RU486 INTO THE U.S., OR TO WORK OUT AN ARRANGEMENT WITH THE CHINESE OFFICIALS OR AN AMERICAN DRUG MANUFACTURER FOR COMMERCIAL PRODUCTION HERE.

WE WILL ACCEPT NO MORE EVASIONS OR DELAYS. THE TIME HAS COME FOR AMERICA TO HAVE THE BEST ABORTION PILL AVAILABLE.

---LAWRENCE LADER; AUTHOR OF THE BOOK ABORTION, IN 1966, CITED MANY TIMES IN THE SUPREME COURT'S ROE V. WADE, AND OF THE RECENTLY PUBLISHED RU486, LADER WAS FOUNDING CHAIR OF NATIONAL ABORTION RIGHTS ACTION LEAGUE (NARAL) FROM 1969 TO 1975. SINCE THEN HE HAS BEEN PRESIDENT OF ABORTION RIGHTS MOBILIZATION (ARM), AND THE RECIPIENT OF MANY AWARDS INCLUDING NOW'S CERTIFICATE OF DISTINCTION AND THE FEMINIST MAJORITY'S "FEMINIST OF THE YEAR" AWARD IN 1994.

To Implement and Guarantee A Woman's Right To Legal Abortion as Defined by the U.S. Supreme Court Decisions under Sec. 501(c)3

ABORTION RIGHTS MOBILIZATION
175 Fifth Avenue (Suite 814)
New York, N.Y. 10010
212/673-2040

STATEMENT OF DR.LOUISE TYRER
MEDICAL CONSULTANT TO ARM

MY COMMITMENT TO WOMEN'S REPRODUCTIVE HEALTH STARTED DURING THE FIRST 16 YEARS OF MY LIFE WHICH WERE SPENT IN OLD CHINA WHERE I SAW CHINESE WOMEN

DIE NEEDLESSLY FROM UNCONTROLLABLE CHILD BEARING AND BOTCHED ABORTIONS. I FOLLOWED THE CALLING OF THE HEART TO BECOME AN OB/GYN SPECIALIST, AND HAVE DEDICATED MY LIFE TO FURTHER THE AVAILABILITY OF BIRTH CONTROL SERVICES TO WOMEN OF THE WORLD. AND MOST PARTICULARLY FOR DISADVANTAGED WOMEN.

FROM 1970 TO 1975 I DIRECTED THE DIVISION OF FAMILY PLANNING OF THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS AS THE FIRST WOMEN STAFF PHYSICIAN OF THAT PRESTIGIOUS ORGANIZATION. I THEN SERVED FOR 16 YEARS IN THE POSITION OF VICE PRESIDENT FOR MEDICAL AFFAIRS OF PLANNED PARENTHOOD FEDERATION OF AMERICA, AN ORGANIZATION THAT YEARLY PROVIDES REPRODUCTIVE HEALTH SERVICES TO NEARLY 3 MILLION INDIVIDUALS IN THE U.S. I HAVE ALWAYS INSISTED THAT ACCESS TO BIRTH CONTROL MUST BE ACCOMPANIED BY HIGH QUALITY SERVICE, AND THAT ONLY SCIENTIFICALLY PROVEN SAFE AND EFFECTIVE METHODS BE PROVIDED.

ABORTION RIGHTS MOBILIZATION
175 Fifth Avenue (Suite 814)
New York, N.Y. 10010
212/673-2040

IN THIS RESEARCH PROJECT ON THE CHINESE PILL, WE RECOGNIZE THAT THE HEALTH OF THE AMERICAN WOMEN IS AT STAKE. WE HAVE ENLISTED THE MOST HIGHLY REGARDED SCIENTISTS, AS WELL AS THOSE MOST EXPERIENCED IN THIS FIELD OF RESEARCH. IN ACCORDNACE WITH SCIENTIFIC STANDARDS, THEIR NAMES WILL BECOME PUBLIC RECORD WHEN THEIR STUDIES ARE SUBMITTED IN A FORMAL IND APPLICATION TO THE FDA.

OUR FIRST SCIENTIFIC RESOURCE WAS THE STUDIES CARRIED OUT UNDER THE SUPERVISION OF DR.YU-MING WU OF BEIJING MEDICAL COLLEGE, WHO IS THE LEADING CHINESE RESEARCHER IN THIS FIELD. SOME RESULTS OF THESE STUDIES HAVE BEEN PUBLISHED BY INTERNATIONAL JOURNALS SUCH AS THE JOURNAL OF REPRODUCTIVE MEDECINE. (V.1 NO.2, 1982).

HOWEVER, THE MAIN OBJECTIVE IN PRE-CLINICAL TESTING IS TO COMPARE THE CHINESE PILL TO RU486, WHICH HAS ALREADY BEEN PROVEN TO BE SAFE AND EFFICACIOUS IN SOME 150,000 CASES IN FRANCE, BRITAIN AND SWEDEN. IF THE ACTIVE INGREDIENT IN BOTH PILLS ARE INDISTINGUISHABLE (AS HAS BEEN SHOWN IN THE FIRST ANALYSIS AND MAY BE CORROBORATED IN THE SECOND STUDY TO BE COMPLETED IN THE NEAR FUTURE), WE WILL ASK THE FDA TO APPROVE THE START OF HUMAN TESTING IN THE U.S.

SINCE I WILL BE THE PHYSICIAN IN CHARGE OF THE HUMAN TESTING, I WILL INSIST UPON A CAREFULLY DRAWN UP RESEARCH PROTOCOL THAT ADHERES TO THE HIGHEST

ABORTION RIGHTS MOBILIZATION
175 Fifth Avenue (Suite 814)
New York, N.Y. 10010
212/673-2040

STANDARDS OF CARE, ALONG WITH DATA COLLECTION AND ANALYSIS. WOMEN TAKING THE PILL WILL BE FULLY INFORMED AND CAREFULLY EVALUATED VOLUNTEERS. THEY WILL BE SCREENED TO ENSURE THAT THEY MATCH THE CRITERIA DETAILED IN OUR RESEARCH PROTOCOL AND DO NOT HAVE ANY MEDICAL CONTRA-INDICATIONS SUCH AS HIGH BLOOD PRESSURE, CORONARY HEART DISEASE, HEAVY SMOKING, AND THAT THEIR PREGNANCY IS WITHIN THE TIME LIMITS FOR ITS MOST EFFECTIVE USE. ABOVE ALL, I WILL BE IN ATTENDANCE TO THE WOMEN VOLUNTEERS. THE PILL CAUSES BLEEDING WHICH IS USUALLY LITTLE MORE THAN NORMAL MENSTRUAL FLOW. THE CYTOTEC OR OTHER PROSTAGLANDIN TAKEN TWO DAYS LATER WILL ASSIST WITH COMPLETE EMPTYING OF THE UTERUS. I WILL ENSURE THAT IN THE EVENT OF A RARE CASE OF HEAVY BLEEDING, PROMPT AND APPROPRIATE TREATMENT IS INSTITUTED TO RESOLVE THE SITUATION. THE WOMAN WILL BE CHECKED SUBSEQUENTLY TO BE CERTAIN THAT THE PREGNANCY HAS BEEN TERMINATED.

IN THIS PROJECT WE WANT TO BE SURE THAT THE CHINESE PILL IS AS SAFE AND EFFECTIVE AS RU486 AND THEN TO FIND WAYS TO ENSURE U.S. WOMEN ACCESS TO THE SAME ADVANCED TECHNOLOGY FOR TERMINATING AN EARLY PREGNANCY AS IS AVAILABLE TO WOMEN IN FRANCE, BRITAIN, SWEDEN AND CHINA.

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

MAY - 7 1993

Mr. Edward N. Costikyan
Paul, Weiss, Rifkind, Wharton & Garrison
1285 Avenue of the Americas
New York, New York 10019-6064

Dear Ed:

This is in response to your letters regarding the drug RU-486 (mifepristone). I appreciate your sharing the information on Larry Lader's efforts related to the Chinese version of RU-486 and of his concerns regarding the continued availability of Cytotec.

As you may know, President Clinton has directed me to study the issues surrounding the availability of RU-486 in the country, including initiatives that can be undertaken to promote the drug's testing and licensing in this country. In addition, the President directed an assessment of whether there is sufficient evidence to exclude qualification of RU-486 for importation under the Food and Drug Administration's (FDA) personal use importation policy. If the assessment shows that the drug qualifies for importation, the import alert would be rescinded. The FDA is an active participant in this ongoing evaluation.

On February 24, senior representatives from FDA and Roussel-Uclaf met to discuss the scientific and medical issues involved in the submission of a marketing application. Although Roussel-Uclaf asserted at the meeting that RU-486 should be made available in the United States, the firm emphasized the importance of finding a way to achieve that goal without its direct involvement.

FDA is fully prepared to review an investigational new drug or marketing application for mifepristone (as with any other drug), if one is submitted, based on established legal and scientific criteria. Thus, if your client wishes to submit an investigational new drug application for testing the Chinese version of mifepristone in the United States, FDA is prepared to review the application and to provide advice on the extent of testing that would be required for marketing approval.

Thank you again for writing. I also appreciate your kind words of encouragement.

Sincerely,

Donna E. Shalala

APPEARS THIS WAY
ON ORIGINAL

PAUL, WEISS, RIFKIND, WHARTON & GARRISON

1285 AVENUE OF THE AMERICAS NEW YORK, NEW YORK 10019-6064

TELEPHONE [illegible]
FACSIMILE [illegible]
TELEX [illegible]

1615 L STREET, NW
WASHINGTON, DC [illegible]
TELEPHONE [illegible]
FACSIMILE [illegible]

199, BOULEVARD SAINT-GERMAIN
75007 PARIS, FRANCE
TELEPHONE [illegible]
FACSIMILE [illegible]

AKASAKA TWIN TOWER
17-22, AKASAKA 2-CHOME
MINATO-KU, TOKYO 107, JAPAN
TELEPHONE [illegible]
FACSIMILE [illegible]

WRITER'S DIRECT DIAL NUMBER

(212) 373-3332

March 12, 1993

Honorable Donna E. Shalala
Secretary
U.S. Department of Health
and Human Services
200 Independence Avenue, S.W.
Room 615F
Washington, D.C. 20201

Dear Donna:

A piece of information has come to my attention which I think I should bring to yours. The RU 486 treatment requires the use of a drug called Cytotec as part of the treatment. It is an essential part. Cytotec is manufactured by Searle, which is a subsidiary of Monsanto.

Larry Lader has been advised that Monsanto has decided to remove Cytotec from the market. The result of that would be to make RU 486 unusable.

I understand there is legislation which bars removal from the market of a drug which is important for public health purposes. I suggest that Cytotec is such a drug and, if it is, that the government should be interested in whether or not the report of its withdrawal from the market is accurate and take some steps to prevent it from happening.

Certainly, the report is worth inquiry.

T54798

TRACER

MIF 003561

Kindest personal regards.

Sincerely,

Edward N. Costikyan

ENC:cd

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

February 3, 1993

Professor Wolfgang Hilger
President of the Board
Hoechst AG
D-6230 Frankfurt-am-Main 80
GERMANY

Dear Professor Hilger:

The Food and Drug Administration contacted Dr. Edouard Sakiz of Roussel-Uclaf in December 1992 to discuss the availability of mifepristone in the United States for research and marketing.

The purpose of this letter is to inform you directly of our interest in this important matter. The Food and Drug Administration wants the opportunity to review a New Drug Application for RU-486 for termination of early pregnancy. To that end, we think that Roussel-Uclaf should submit an application as soon as possible. If Roussel-Uclaf thinks that additional research on RU-486 is required, Dr. Sakiz should advise us as to what research he thinks is necessary and provide us with a time frame for conducting such research. We would appreciate it if you would expedite progress in this regard.

At our February 24, 1993 meeting with Dr. Sakiz we plan to discuss the status of knowledge concerning the safety and efficacy of the drug, the readiness for a New Drug Application for this indication, the suitability of a treatment IND as an interim undertaking, and the identity of the applicant.

We would appreciate hearing your views on this matter. I can be reached at (301) 443-2410 and my mailing address is: Room 14-71 Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857.

Sincerely yours,

David A. Kessler, M.D.
Commissioner of Food and Drugs

cc: Dr. Edouard Sakiz

PROF. DR. WOLFGANG HILGER
[illegible]
[illegible]

[illegible]
[illegible]
[illegible]

Dr. David Kessler
Commissioner of the
Food and Drug Administration
5600 Fishers Lane, HF-40
Rockville, Maryland 20857
U.S.A.

April 15, 1993

Fax: 001-301-443-1863

Dear Dr. Kessler,

Thank you for your letter of April 14 concerning the meeting you propose on the Roussel Uclaf compound RU 486.

We are both aware that the development of RU 486 in the field of abortion has confronted us with an extremely complex social issue which is almost impossible to resolve in a way that would be acceptable to all concerned.

In spite of our position to not be involved in the marketing or production of RU 486 for the American market, we are making a considerable effort to respect your intention to make the compound available to the medical profession in the United States.

I am aware that substantial progress has been made since your last meeting with Dr. Sakiz on February 24 in Washington D.C.

If the FDA considers a clinical trial to be necessary, you know that it can be carried out by the Population Council, with whom Roussel Uclaf has a long-standing agreement on this compound.

Concerning the eventual distribution in the United States, this can only be done through third parties, as we have always indicated and as I have reiterated in my press conference on March 23.

The question of production can be resolved as indicated in the Roussel Uclaf agreement with the Population Council, which permits a transfer of their production technology to a third party.

I know that Dr. Sakiz will be meeting with you on April 20 to determine the next steps to be taken to make RU 486 available in the United States. He is the most knowledgable individual on this issue within the Hoechst organisation and is fully aware of all the problems concerning RU 486. We are entirely confident that he is the best representative we could send for the meeting you have proposed. I believe that sending another representative of Hoechst would serve no useful purpose.

Be assured that I am following this matter very closely and am confident that a satisfactory solution for all parties can be found.

Sincerely yours,

W. Hilger.

PROF. DR. WOLFGANG HILGER
VORSITZENDER DES VORSTANDES
HOECHST AKTIENGESELLSCHAFT

6230 FRANKFURT AM MAIN 80
POSTFACH 80 03 20
TELEFON (0 69) 3 05-71 20

March 23, 1993

The Secretary of Health and Human Services
Mrs. Donna E. Shalala
Washington, D.C. 30201

U.S.A.

Dear Mrs. Shalala:

Many thanks for your letter of March 12, 1993, which I have received by fax.

I would like to describe the present situation in the USA as follows:

On the request of the Food and Drugs Administration, a meeting with Dr. Edouard Sakiz, President of Roussel Uclaf has taken place to discuss relevant question on the drug RU 486.

In their wide-ranging discussions both sides recognized the complexities of the issue, involved in any decision to make the drug available in the United States.

The FDA has clearly pointed out that you are very much willing to see RU 486 made available in the USA. However, the FDA accepts that Roussel Uclaf has no intention to approach the FDA to obtain marketing licence for the drug. The FDA has undertaken to approach third parties who are competant and might be interested to sponsor clinical studies and to market the drug in the USA. Because the drug is currently available only under very restricted distribution (France, the United Kingdom and Sweden) it will become necessary that the FDA will issue new regulation to control the use and distribution.

Both sides will continue their consultations to clarify the many open questions on the issue. At a later stage a common decision on how to proceed in the USA will be taken.

Yours sincerely,

Wolfgang Hilger.

93-1820

155370 PHS

CITY OF NEW YORK
COMMUNITY BOARD NO. 6 MANHATTAN

330 East 26th Street, New York, N.Y. 10010-1997 (212) 679-0907 Fax 683-3749

FEB 24 '93

RECEIVED
93 FEB 22 PM 1:25
CONTROL CENTER

February 16, 1993

Dr. Billy E. Jones, MD.
President
Health and Hospitals Corporation
125 Worth Street
New York, NY 10013

Dear Dr. Jones:

Enclosed please find a resolution passed at the Community Board Six Manhattan Full Board Meeting of February 10, 1993 concerning a moratorium on Roussell-UCLAF pharmaceutical products and petition to Roussell-UCLAF to begin testing of RU-486 by the Federal Food and Drug Administration ("FDA").

If there are any questions pertaining to this resolution, please contact the Board office at (212)679-0907.

Sincerely,

Lou Sepersky (CAP) Sherman Hollander (CAP)

Lou Sepersky, Chair
Community Board 6

Sherman Hollander, Chair
Health, Seniors & Human
Services Committee

cc: Hon. Daniel P. Moynihan
Hon. Alfonse M. D'Amato
Hon. Carolyn Maloney, U.S. Congress
Hon. Charles B. Rangel, U.S. Congress
Louis W. Sullivan, M.D., Secretary of Health
Margaret A. Hamburg, M.D. NYC Dept. of Health
Peter Kelly, Beth Israel Hospital
Pam Brier, Bellevue Hospital
Martin Begun, NYU Medical Center
Mr. Jeffrey Frerichs, Cabrini Medical Center
Mr. James Romer, Hospital for Joint Diseases
Community Boards Citywide

CITY OF NEW YORK
COMMUNITY BOARD NO. 6 MANHATTAN
330 East 26 Street, New York, N.Y. 10010-1997 (212) 679-0907

FEBRUARY 1993

RE - MORATORIUM ON ROUSSELL-UCLAF PHARMARCEUTICAL PRODUCTS AND PETITION TO ROUSSELL-UCLAF TO BEGIN TESTING OF RU-486 BY THE FEDERAL FOOD AND DRUG ADMINISTRATION ("FDA")

WHEREAS, RU-486 is a drug that can be used to terminate an unwanted pregnancy without a surgical procedure and further shows great promise in the treatment of breast cancer, which kills 46,000 women each year in the United States, including 4,100 in New York State and 1,600 in New York City; and

WHEREAS, some physicians believe that RU-486 can also be useful in treating meningioma, brain tumors, endometrioses and Cushing's syndrome and in assisting in difficult childbirth; and

WHEREAS, the sole owner and holder of the manufacturing rights to RU-486 is Roussel-Uclaf ("Roussel"), a French Company; and

WHEREAS, Roussel has refused to apply for Food and Drug Administration ("FDA") approval to market or conduct substantial testing and research on RU-486 in the United States; and

WHEREAS, the New York City Health and Hospitals Corporation ("HHC") is a major purchaser of drugs from two U.S. companies that are affiliates of companies that own a total of 89% of Roussel; and

WHEREAS, HHC will purchase from one of these two companies, Hoechst-Roussel, Pharmaceutical of New Jersey, over $1.26 milion in drugs, including Claforan, DiaBeta, Trental, Lasix, Streptase, and Topicort, over a one-year period; and

WHEREAS, HHC will purchase from the other company, Rhone-Poulenc Rorer of Pennsylvania, over $450,000 in drugs, including - Maalox, Theophylline Anhydrous, Calcitontin, Triamcincolene Acetonide, Desmopressin and Aluminum/Magnesium Hydrox, over a one-year period; and

WHEREAS, RU-486 is currently available to women in France, England and Sweden and clinical trials of RU-486 are reportedly being conducted in approximately ten other countries, including Hungary, Italy, India and Chile; now

THEREFORE BE IT

RESOLVED, that Community Board 6 Manhattan condemns the continued refusal of Roussel to apply to apply to the FDA for approval to market or conduct substantial testing of RU-486 in the U.S. as an unwarranted and outrageous denial of access to women of this important product and a dangerous limitation on medical professionals in their ability to find new treatment for a range of life threatening diseases; and be it further

RESOLVED, that Community Board 6 Manhattan adds its voice to those of prominent medical and health organizations in the U.S., including the American Medical Association, the American College of Obstetricians and Gynecologists, and American Women's Medical Association and the National Alliance of Breast Cancer Organizations, in supporting the testing of RU-486 in the U.S.; and be it further

RESOLVED, that Community Board 6 Manhattan calls upon the New York City Health and Hospitals Corporation and the NYC voluntary hospitals to refuse to purchase any and all drugs from Roussel and Roussel affiliates, for which adequate substitutes are available, until Roussel takes the steps necessary to petition the Food and Drug Administration for the full marketing and testing of RU-486 in the U.S. and advises HHC and the NYC voluntary hospitals that it has done so; and be it further

RESOLVED, that Community Board 6 Manhattan calls for the support and comment from the 59 other Community Boards in adopting a similar resolution that would encourage both public and voluntary hospitals within their borders to institute a similar moratorium.

PASSED: 22 IN FAVOR, 0 OPPOSED, 0 ABSTENTIONS, 0 ABSTENTIONS FOR CAUSE, 1 PRESENT AND NOT VOTING

THE CITY OF NEW YORK
OFFICE OF THE MAYOR
NEW YORK, N.Y. 10007

January 22, 1993

The Honorable Donna Shalala
Secretary of Health and Human Services
1120 Vermont Avenue N.W.
Room 1088
Washington, D.C. 20270

Dear Madam Secretary: Donna

I am writing you today, the 20th anniversary of the Supreme Court's decision in the Roe v. Wade case, to ask that you remove the Roussel Uclaf product RU 486 from the "import alert" list and eliminate undue regulatory impediments to its approval.

This drug, which is an alternative to early abortion, is currently available to women in Europe and has been used by more than 100,000 of them. Yet it remains unavailable to women in our nation, despite indications that it may also prove useful in combatting other serious illnesses, including brain tumors, breast cancer, endometriosis and uterine fibroids.

In large measure, its unavailability can be traced to the unwillingness of the parent company of Roussel Uclaf, Hoechst AG of Germany, to challenge what it considers the daunting hurdle of U.S. anti-choice forces. I have written to the chairman of the company, Dr. Wolfgang Hilger, suggesting that he re-appraise the political climate in our country and noting President Clinton's election last November as one measure of the change in spirit and in policy that is occurring here.

But given that Hoechst's and Roussel Uclaf's reluctance appears to be based on political rather than strictly medical or commercial considerations, I believe that federal action that indicates our wish to make this drug available to American women would have a dramatic impact upon the thinking of Dr. Hilger.

T53269
TRACER

MIF 003569

Therefore, I request that you reverse the current posture with respect to RU 486 of the federal agencies that fall under your jurisdiction and assist in making the drug available here in the U.S.

American women deserve and need to have access to this drug. I am hopeful that you will be able to help make it available to them.

Be well and God bless.

Sincerely,

David N. Dinkins
MAYOR

APPEARS THIS WAY
ON ORIGINAL

9301270169

9300445

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

MAY 7 1993

The Honorable David N. Dinkins
Mayor of the City of New York
Office of the Mayor
New York, New York 10007

Dear David:

This is in response to your letter regarding the drug RU-486 (mifepristone). I appreciate your writing to let me know of your concerns related to women in this country not having access to RU-486 as an alternative to surgical abortions and for other medical indications currently under study.

As you may know, President Clinton has directed me to study the issues surrounding making RU-486 available in the United States, including initiatives which can be undertaken to promote the drug's testing and licensing in this country. In addition, the President directed this Department to assess whether there is sufficient evidence to exclude qualification of RU-486 for importation under the Food and Drug Administration's (FDA) personal use importation policy. If the assessment shows that the drug qualifies for importation, FDA would rescind the import alert. The FDA is an active participant in this ongoing evaluation.

I want to assure you that the FDA's import alert provision is not designed or intended to thwart appropriate research or clinical trials on a drug. The import restrictions do not prevent importation of RU-486 or other drugs for research for any therapeutic use if an approved Investigational New Drug Application (IND) exists. For example, the National Institutes of Health has active INDs in which RU-486 is currently being studied for use in Cushing's disease and certain psychiatric conditions.

As you may be aware, in an April 20 meeting with senior representatives of the FDA, Roussel Uclaf agreed to license the drug RU-486 for the Population Council, a non-profit scientific and technical organization, for distribution in the United States and to transfer the technology necessary for producing the drug. The Population Council will identify a manufacturer for RU-486 in the United States market, will begin a clinical trial to test the drug in this country, and will move as soon as possible to submit a New Drug Application to FDA. FDA is fully prepared to review a

marketing application for RU-486, if one is submitted, based on established legal and scientific criteria.

I appreciate hearing your concerns. Thank you for taking the time to write and to express your views on this important issue.

Sincerely,

Donna E. Shalala

Donna E. Shalala

APPEARS THIS WAY
ON ORIGINAL

Research Institute for Mindanao Culture
XAVIER UNIVERSITY
P.O. Box 24, 9000 Cagayan de Oro City, Philippines, Tel. 35-88

May 20, 1993

Commissioner David Kessler
Food and Drug Administration
Washington, D.C.

Dear Commissioner Kessler:

I was surprised and chagrined at your advocacy of abortion, quoted in the press for April 16, 1993 (Jackman, Washington News Bureau), in which you stated: "Abortion is legal in this country" and thus the drug RU 486 should be made available to the American public.

I believe that your office of its nature demands that the FDA, and especially its Commissioner, take an objective and scientific stance at all times in regard to the licensing of drugs in the U.S. Your advocacy of a radical, pro-abortion stance has severely shaken my confidence in the FDA's objectivity and dispassionate testing.

I believe you should resign your position in view of the loss of confidence you have brought upon the whole Food and Drug Administration by this unfortunate lack of discretion upon your part. I shall certainly use my own vote as an American citizen, in future elections to turn out from office Democratic party incumbents in our government, and shall exhort all those I influence to do the same.

Sincerely yours,

151

Research Associate

RECEIVED
JUN 3 3 33 PM '93
FDA
EXECUTIVE SECRETARIAT

9302755

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Rockville MD 20857

July 23 ,1993

Research Associate
Mindanao Center for Population Studies
Research Institute for Mindanao Culture
Xavier University
Post Office Box 24
9000 Cagayan de Oro City, Philippines

Dear _____

This is in response to your letter of May 20, 1993, concerning a statement by Dr. Kessler quoted in the press on the drug RU-486 (mifepristone). The complete quote was "Abortion is legal in this country and if there is a safe medical alternative to a surgical procedure, then it should be available to the American public."

As you may know, the President has directed the Secretary of Health and Human Services to assess initiatives to promote the testing of RU-486 (mifepristone) and other antiprogestins in the United States. The Food and Drug Administration (FDA) is an active participant in this ongoing evaluation and is prepared to review a marketing application for RU-486, if one is submitted, based on established legal and scientific criteria. Recently, senior representatives of the FDA and Roussel-Uclaf, the manufacturer of RU-486, met to discuss clinical and manufacturing data on the drug that FDA would need in considering a new drug application for an abortifacient indication. At that meeting, FDA received a strong commitment from Roussel-Uclaf to continue to make the drug available for research on other potential uses, such as Cushings Disease and meningioma.

FDA believes that if there is a safe and effective alternative to a surgical abortion, then American women should have the opportunity for that safe and effective medical procedure. To that end, FDA has urged the submission of a new drug application for RU-486 in order to have the opportunity to determine whether or not the drug is safe and effective for use in the United States. Until the Agency fully evaluates the scientific data, it cannot say how much further testing would be required to permit a scientific determination of whether RU-486 is safe and effective for marketing in the United States as an abortifacient. The process that I have described is a scientific one which, because abortion is legal in this country, is appropriately applied to

this drug for this indication. Dr. Kessler was saying the same thing when he was quoted in the press.

Sincerely yours,

/s/

Food and Drug Administration
Rockville MD 20857

January 22, 1993

Edouard Sakiz, M.D.
President, Roussel-Uclaf
102 route de Noisy
F-93230 Romainville

Dear Dr. Sakiz:

This letter is pursuant to my letter to you of December 15, 1992, and confirms my meeting with you and Dr. Andre Ulmann to take place as soon as possible. I understand that sometime during the first 3 days of February may be possible.

The purpose of the meeting is to discuss possible therapeutic uses of anti-progestational drugs and, in particular, our interest in receiving a New Drug Application for approval of mifepristone for interruption of early pregnancy. Several of my colleagues will also attend the meeting.

I am pleased that you and Dr. Ulmann are able to respond to my invitation to discuss these important issues. My office will work with yours in establishing when we shall meet.

Sincerely yours,

David A. Kessler, M.D.
Commissioner of Food and Drugs

APPEARS THIS WAY
ON ORIGINAL

ROUSSEL UCLAF

Paris, December 17, 1992

DEC 17 11 55 AM '92

Docteur Edouard Sakiz
Président du Directoire

Doctor David A. Kessler
Commissioner of Food and Drugs
Department of Health & Human Services
Food and Drug Administration
Rockville, MD 20857
USA

Dear Doctor Kessler,

Thank you very much for your recent letter concerning RU 486.

Indeed, we are perfectly aware that the change in the opinion of the Americ
administration will modify considerably the status of the drug in the United Stat

I am also fully confident that in light of the considerable number of clinical t
on voluntary termination of pregnancy which were initiated many years ag
should probably be possible for us to ask for an NDA.

Like me, you are, no doubt, aware of the numerous violent reactions which
been launched against RU 486 by pro-lifers. As a matter of fact, althou
received thousands of signatures and petitions from these people, we receive
more letters of support from pro-choice people.

Under these circumstances, it has appeared to me that it would be better
clinical trials in the United States. There are many possibilities: thro
Population Council, Family Planning organizations, by licensing-out
parties... This, in order to give American scientists and clinicians the opp
to experiment the drug and get a chance to make public statements on
applications.

We are presently in the process of reviewing our strategy in this directi
should be able to come up with some proposals by the end of January
then, be delighted to meet you in order to discuss the RU 486 issue in yo

Yours sincerely,

92-8252

35, Boulevard des Invalides - 75007 Paris

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

December 14, 1992

Edouard Sakiz, M.D.
President, Roussel-Uclaf
102 Route de Noisy
F-93230 Romainville
France

Dear Dr. Sakiz:

In a December 7, 1992, article by William Drozdiak, a Paris reporter for the Washington Post, concerning the likelihood of RU-486 becoming available in this country for interruption of pregnancy, you are quoted as saying that "we [Roussel-Uclaf] are preparing to see how we can have a clinical trial start in the U.S." The same article also quotes me as saying that the Food and Drug Administration "would welcome an application" for your company's product.

There may be a misunderstanding regarding Federal Food, Drug, and Cosmetic Act requirements for drug approval. We accept foreign clinical trials, so long as we are able to audit the data, according to our normal procedures. Agency staff who will be responsible for reviewing the application report that based on publicly available information and literature, the available data may well be sufficient to permit an adequate review. In light of existing data, further clinical trials may not be required.

My colleagues and I would be pleased to discuss this issue with you further if that would be of help.

Sincerely yours,

David A. Kessler, M.D.
Commissioner of Food and Drugs

AF
9209093

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

January 22, 1993

Andre Ulmann, M.D., Ph.D.
Louise Silvestre, M.D.
Roussel Sante R. et D.
Domaine Therapeutique Endocrinologie
Roussel Uclaf
Romainville, France

Dear Drs. Ulmann and Silvestre:

The Food and Drug Administration has received a request for assistance in obtaining a "compassionate IND" for the use of mifepristone (RU-486) in the treatment of [redacted] a patient with recurrent meningioma. I have spoken to her physician, [redacted] and have informed him that we would be willing to approve a single patient IND for [redacted] if you agree to provide the drug. Although [redacted] may be eligible for the [redacted] study, she is unwilling to be randomized to placebo and is unable to travel to one of the study centers. In her letter she hints that she may commit suicide if her disease continues to progress. Because of her psychological state, we ask that you give her request serious consideration. In addition, if she does not receive the drug she plans to make her case to the media. The media coverage is likely to generate even more requests for the drug. Someone from the Commissioner's office is scheduled to be interviewed about the request on CNN on Tuesday, January 26, 1993.

We understand that you are concerned about the number of requests that you have received for the drug for single patient INDs for unresectable meningioma. We share your concern and agree that whenever possible patients should be encouraged to participate in the ongoing Phase III study. However, for a variety of reasons, some patients are unwilling or unable to participate in a study. As long as accrual to the Phase III study is not significantly compromised, it is our policy to consider individual patient IND's in situations where there is sufficient reason to expect benefit and there is no satisfactory alternative therapy. It would be preferable to enter these patients on a single open Phase II study so that data could be collected on response and toxicity.

We would be happy to discuss your concerns with you and how best to handle this situation. My telephone number is

[redacted] and fax numbers are [redacted] or [redacted].

We look forward to your response.

Sincerely,

/S/

[redacted]

Division of Oncology and
Pulmonary Drug Products
Center for Drug Evaluation and
Research
Food and Drug Administration

APPEARS THIS WAY
ON ORIGINAL

RECORD OF TELEPHONE CONVERSATION

With: Andre Ulmann, M.D., Ph.D.
Firm: Roussel Uclaf
Date: January 25, 1993
Drug: mifepristone (RU-486)
Telephone#: 011-33-1-49-91-48-21

Dr. Ulmann called regarding my letter of January 22, 1993. He asked what we should do regarding (————) request for a compassionate IND for the use of mifepristone in the treatment of her meningioma. I told him that I was in general agreement with their policy of encouraging all eligible patients to enroll in the (——) phase III study. However, since (————) is unwilling and is hinting at suicide, I recommended that we approve the request. He agreed to supply the drug for (————) and also for another patient, (————)

We then discussed how the many compassionate requests should be handled. We agreed that patients should be strongly encouraged to enroll in the —— study. However, patients who were not eligible for the study or who could not participate for a very good reason would be considered for individual INDs. Dr. Ulmann emphasized that physicians would have to document the reasons that an eligible patient could not participate. Belief that the drug is effective and unwillingness to be randomized to placebo would not be sufficient since patients randomized to placebo could cross over to mifepristone at progression.

Dr. Ulmann also expressed concern about the quality of the data received on the compassionate IND patients. He was especially concerned about adverse reaction data. We discussed the possibility of an open phase II study. He stated that they send a protocol with information on the drug and case report forms to investigators but don't always receive completed forms. I told him that we would ask investigators to send us copies of the forms and could help if any investigators were delinquent. We agreed to call if there were any problems.

/S/

FYI
CCC has no record of stated (S)

ROUSSEL UCLAF

Docteur Edouard Sakiz
Président du Directoire

Paris, March 18, 1993

Mrs. Donna E. Shalala
Secretary of the Department of Health
& Human Services
H.H.H. Building - Room 615 F
Washington, D.C. 20201
U.S.A.

Dear Mrs. Shalala,

It was very thoughtful of you to send me a copy of your March 12 letter to Professor Wolfgang Hilger, for which I thank you very much.

The Roussel Uclaf Group and I appreciate your commitment to the expansion of safe and effective healthcare choices for American women for the termination of unwanted pregnancy. The comments contained in your letter also reflect President Clinton's determination to keep the promises he made throughout his campaign.

The message delivered to Professor Hilger will greatly contribute to progress further in order to sort out the complexities of the issues involved in any decision to make the drug available in the United States.

The meeting held last month with Dr. Kessler is already proving very rewarding as new steps are going to be considered with the help of Margaret Catley-Carlson, the President of the Population Council, who has also assured us of her support wi regard to getting clinical trials started in the United States.

In view of the clinical studies and the training program which are to be undertaken because French and US regulations concerning early termination of pregnancy are not the same, it will still take some time before RU 486 is made available to American women.

I will be pleased to keep you informed of any further development.

Yours sincerely,

9301600

35, Boulevard des Invalides 75007 Pari
Tel. + 33 (1) 40 62 44 28 Fax. + 33 (1)

March 4, 1993

Via Fax

Mr. Edouard Sakiz
President
Laboratories Roussel-Uclaf SA
35 bvd. des Invalides
BP 12007, 75323 Paris
Cedex 07
France

Dear Mr. Sakiz:

During the past two years I have been in touch with several members of your company, our FDA, and responsible members of the medical community indicating the willingness of _____ _____ to develop and commercialize RU 486 in North America.

Please accept this letter as a firm indication of our interest in RU 486 and willingness to enter into exclusive licensing discussions for rights to this drug in our home markets.

For your background and information I enclose materials describing our firm. I am at your disposal regarding a meeting to commence discussions with Roussel-Uclaf.

Very sincerely yours,

/S/

_____

President

cc: Mrs. Donna Shalala

American Medical Association
Physicians dedicated to the health of America

James S. Todd, MD
Executive Vice President

515 North State Street
Chicago, Illinois 60610

312 464-5000
312 464-4184 Fax

May 15, 1992

David A. Kessler, MD, Commissioner
Food and Drug Administration
1500 Fishers Lane
Rockville, Maryland 20857

RE: The Development and Approval of New Contraceptives

Dear Dr. Kessler:

The availability of safe and effective contraceptives that are acceptable to individuals throughout their childbearing years is an important health care issue. Today U.S. residents have fewer contraceptive options than their peers elsewhere in the world and most experts do not expect that any major innovation in contraception method will be available in the U.S. in this century.

Many of the available contraceptive methods are not sufficiently effective, are associated with undesirable side effects, or are undesirable to users. As a result, there are many potential contraceptive users who find these options unacceptable or inadequate. These individuals include women who do not want to be sterilized and (because they are at high risk of heart disease or stroke) cannot safely use the oral contraceptive pill; insulin-dependent diabetics; breast feeding women; and women with chronic diseases that preclude the use of existing contraceptives. Men who wish to assume a more active role in contraception also have few options.

The American Medical Association (AMA) urges the FDA to consider the special health care needs of Americans who are not adequately served by existing contraceptive products when considering the safety, effectiveness, risk and benefits of new contraception drugs and devices.

Sincerely,

James S. Todd MD

James S. Todd, MD

JST/ajz

6598p

9204460

MIF 003584

UNCLASSIFIED FAX MESSAGE FROM:

ROY FORNY

SCIENCE AND TECHNOLOGY SECTION
BRITISH EMBASSY
3100 MASSACHUSETTS AVENUE NW
WASHINGTON DC 20008-3600 USA

OUR FAX NUMBER: 202-898-4224

TELEPHONE NUMBER FOR ENQUIRIES: 202-898-4588

MESSAGE SENT ON: 31 July 1992

TO: [redacted]
FDA Office of Health Affairs

FAX NO: (301) 443 1309

REF NO: 4J8 NO OF PAGES: 2

RU-486

You asked about the residency requirement in England in order to get an abortion using RU-486.

Treatment under the NHS is available to anyone with permanent residency in the UK. This includes both out-patient and in-patient hospital treatment. GPs have discretion to make people wait up to a year to be registered. However non-residents who have sufficient means to pay can obtain private medical or surgical treatment in the UK and that includes, subject to compliance with the requirements of the 1967 Act, termination of pregnancy.

It is a requirement of the Abortion Act (which applies to England, Scotland and Wales but not Northern Ireland) that treatment for the termination of pregnancy must be carried out in a National Health Service hospital/NHS Trust hospital or a place approved by the Secretary of State for Health. Termination of pregnancy can only take place if two registered medical practitioners are of the opinion formed in good faith that the termination is justified under one or more of the grounds specified in the Act.

Use of RU-486 (Mifegyne) is subject to the provisions of the 1967 Act to the same extent as abortions performed by any of the methods currently in use. This means that both stages of this new treatment (anti-progesterone tablets followed by prostaglandin pessary 36-48 hours later) may take place only in an NHS hospital/NHS Trust hospital, or one of the places approved by the Secretary of State under the 1967 Act, and additionally authorised to use this method. The use of Mifegyne in the UK is normally on a day-care basis, ie the woman can return home after each stage after staying for the set times. In the case of medical termination using Mifegyne a woman should not have to travel more than one hour to reach home or the address at which she will spend the night after each part of the treatment. She must return to the care of a doctor near her home who has agreed to provide cover following the treatment. Because of this it is a Department requirement that the use of RU-486 in the private sector should be restricted to resident women (ie those with permanent residency).

I appreciate this is a complicated answer to what seems on the surface a simple question, but these are the facts as they stand. Should you need further clarification please contact me again.

Yours Sincerely

Roy Forey

R H FOREY
Science & Technology Officer

APPEARS THIS WAY
ON ORIGINAL

THE WHITE HOUSE

WASHINGTON

January 22, 1993

MEMORANDUM FOR THE SECRETARY OF HEALTH AND HUMAN SERVICES

SUBJECT: Importation of RU-486

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

I am informed that in excluding RU-486 from the personal use importation exemption, the FDA appears to have based its decision on factors other than an assessment of the possible health and safety risks of the drug. Accordingly, I hereby direct that you promptly instruct the FDA to determine whether there is sufficient evidance 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

9300432

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

April 22, 1994

James S. Boynton, Esq.
Christy & Viener
620 Fifth Avenue
New York New York 10020-2402

Lester S. Hyman, Esq.
Swidler & Berlin, Chartered
3000 K Street, N.W., Suite 300
Washington, D.C. 20007-5116

Dear Mr. Boynton and Mr. Hyman:

As you requested, enclosed are the Agency's preliminary comments on the April 11, 1994, proposed distribution scheme for mifepristone in the United States. As I have mentioned to you, the question as to whether any residency requirement can be imposed needs further examination. Moreover, any final comments on the distribution scheme must follow the Food and Drug Administration's review of the scientific, medical, and other data and information contained in a new drug application for the drug.

We are heartened by the fact that you, Roussel Uclaf, and Hoechst AG are close to agreeing on a distribution plan. As the Secretary noted, however, we expect all issues, not just the distribution issue, to be concluded by May 15, 1994.

As Commissioner Kessler promised in our recent meeting, the Food and Drug Administration stands ready to assist all parties in any scientific, medical, or labeling issues that may arise.

Sincerely yours,

/S/

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

September 14, 1994

Note to: Secretary Donna Shalala

We thought you would be interested in the status of RU-486. We have been told by the Population Council that its pilot studies on mifepristone (RU-486) will begin this week in Texas and California. The larger studies (involving 2,100 women) will begin in 12 to 16 clinics after the investigators from those clinics meet at the Population Council on October 3-4, 1994, to review the protocol, informed consent procedures, and other study issues.

The Population Council's efforts to obtain information from Roussel Uclaf and to manufacture mifepristone are [redacted] I have asked Roussel Uclaf to provide the necessary safety, effectiveness, and manufacturing data to the Population Council. We have also let the Population Council know the importance of resolving the chemistry and manufacturing issues early. We will continue working with Roussel Uclaf and the Population Council in an effort to resolve these outstanding concerns.

/S/

[redacted]

cc: [redacted]

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

Food and Drug Administration
Rockville MD 20857

October 25, 1994

NOTE TO: [redacted]
Executive Secretary

FROM: [redacted]

SUBJECT: RU-486 Update

As we discussed, in response to the Population Council's notification that it plans to announce on Thursday the start of the clinical trials of RU-486 as an abortifacient, we have prepared a summary that explains these studies and the fact that they are unrelated to the methotrexate/misoprostol studies recently publicized by Dr. Hausknecht (attached at Tab A). I have also attached at Tab B the press package that we have received from the Population Council. Later today we will be sending you a memorandum for the Chief of Staff's signature to inform [redacted] at the White House, and an information memorandum for the Secretary that will include the fact sheet, talking points, and Q's and A's. That package should be delivered to you this afternoon.

Please feel free to call me at (301)443-4094 if you have any questions.

/S/

Attachments

Tab A - Summary
Tab B - Population Council Press Package

APPEARS THIS WAY
ON ORIGINAL

94-9520

MIF 003590

APPEARS THIS WAY
ON ORIGINAL

Update on Medical Abortion

On Thursday, October 27, 1994, in New York City, the Population Council will hold a news conference to announce that clinical trials of the abortifacient mifepristone (known in Europe as RU-486) have begun in the United States. The clinical trials became possible after the Department of Health and Human Services earlier this year helped arrange a transfer of the drug's patent rights to the Population Council, a nonprofit research organization involved in reproductive health and population issues. The clinical trials will be conducted under a protocol which has been reviewed and approved by the FDA.

The clinical trials are designed to determine the safety, effectiveness, acceptability, and feasibility of using mifepristone and prostaglandin to induce a medical abortion. Mifepristone works to interrupt an early pregnancy, and the prostaglandin -- which is administered 48 hours later -- causes the uterus to contract and expels the fertilized egg.

The combination of mifepristone and prostaglandin will be tested in 2100 American women over the age of 18 at more than a dozen sites around the United States. Clinics were selected on the basis of their ability to provide experienced scientific investigators and high quality abortion services. Trial locations include hospital-based clinics, Planned Parenthood and feminist health center facilities, and free-standing abortion clinics.

The Population Council does not intend to identify the trial sites, but individual clinics and women may choose to identify themselves.

Mifepristone in combination with a prostaglandin is approved for use in France, the United Kingdom, and Sweden. It has been used in more than 150,000 women in those countries.

As part of an agreement reached last year with Roussel-Uclaf, the Population Council is conducting the U.S. clinical trials of mifepristone and has agreed to find a manufacturer for the drug. The Population Council has also announced its intention to seek marketing approval from the FDA for mifepristone.

Other Medical Treatments

In a related matter, there has been considerable publicity recently of another method of medical abortion. The anti-metabolite drug methotrexate is being clinically tested, in combination with a prostaglandin, as an abortifacient by Dr. Mitchell Creinin and his colleagues under FDA-approved protocols at three sites around the U.S. Last week Dr. Creinin published the results of his most recent study of this drug in the Journal of the American Medical Association.

Although the preliminary results are somewhat promising, this combination has only been studied in approximately 40 women. The very limited data to date suggest that this regimen is significantly less effective than the mifepristone-prostaglandin combination that is being tested in the Population Council clinical trials. Dr. Creinin and his colleagues have urged physicians not to use this experimental treatment outside of clinical trials.

In the meantime, Dr. Richard Hausknecht, a New York City obstetrician-gynecologist, has been promoting and using the methotrexate-prostaglandin combination in his own private practice. Dr. Hausknecht has granted extensive interviews with major national newspapers and television programs, and he has distributed detailed information about his use of these drugs to thirty or forty physicians around the U.S.

Although the FDA encourages research into medical alternatives to surgical abortion, the agency has told Dr. Hausknecht of its regulatory requirement that his study be carried out only under FDA-approved clinical trials. The FDA regards the methotrexate-prostaglandin combination as experimental and has urged women not to allow this combination to be used for pregnancy termination unless the research is being carried out in an FDA-approved clinical trial.

FDA is concerned that women understand that this drug regimen is experimental -- not a proven treatment. FDA also believes that women deserve the assurance that any clinical research on this drug combination has been scrutinized by an Institutional Review Board, which concerns itself with ethical issues in clinical trials.

The FDA and the Department of Health and Human Services will continue to support research into medical alternatives to surgical abortion. The study of mifepristone and prostaglandin being carried out by the Population Council has been properly designed, and the FDA is confident that women participating in it will understand that they are undergoing an experimental procedure. FDA can offer no such assurances about Dr. Hausknecht's treatment regimen using methotrexate and prostaglandin.

APPEARS THIS WAY
ON ORIGINAL

Briefing Invitation
Revised Draft for Approval -- October 17, 1994

This is media invitation to go out Monday afternoon.

********** Media Invitation **********

Who: The Population Council

What: Media Briefing on Mifepristone Trials
(Formerly known as RU 486)

When: Thursday, October 27, 1994

8:00 to 8:30 am -- continental breakfast
8:30 to 10:00 am -- briefing

Where: Le Parker Meridien Hotel
118 West 57th Street
Salon Vendome -- 3rd Floor

********** BY INVITATION ONLY **********

RSVP required

Only media presenting press credentials and this invitation will be admitted to the October 27 briefing

****

Please note that a separate telephone conference call will also be arranged on October 27 for reporters upon request

****

RSVP to Alicia Cimbora at Burns McClellan for either the press briefing or the conference call
phone: 212-505-1919
fax: 212-505-1085

The Population Council

One Dag Hammarskjold Plaza, New York, New York 10017

Statement of Margaret Catley-Carlson, President of the Population Council
Media Briefing -- Mifepristone Clinical Trials*
October 27, 1994

The Population Council announces today that clinical trials of mifepristone--formerly called RU 486--are under way in the United States. The trials will involve 2100 women at over a dozen sites around the country. Enrollment of women volunteers has already started. The goal is to test the safety, efficacy, acceptability, and accessibility of nonsurgical medical abortion, leading to an application for FDA approval for marketing. We are making this announcement--which is unusual for a clinical trial and not something the Council routinely does--because of the enormous amount of media interest in all aspects of this project and because we want the method to be described in a balanced and scientific manner.

We will not identify the locations of the studies, to protect the security of the clinics and the confidentiality of the women who will volunteer for these trials. Individual clinics and women may choose to identify themselves and talk about their experiences. In selecting the clinics, the Population Council looked for institutions that could provide scientific investigators with experience in conducting clinical trials or the ability to work under trial conditions and staff experienced in providing high quality abortion services. Each potential clinic was inspected by Council monitors. We also attempted to vary the type of facility, geographic location, and clientele. We made our selection from a large group of outstanding clinics.

At the recent population conference in Cairo, the international community strongly affirmed that unsafe abortion is a major public health concern and that unwanted pregnancies should be prevented through expanded and improved family planning services. This is the Population Council's position as well. We are a research organization. We do not promote the use of abortion; we promote the use of contraception. We do not lobby for specific legislation and we are not abortion advocates. Our program supports: prevention of unwanted pregnancy through development and promotion of new safe, effective contraceptives; prevention of unsafe abortion, which is responsible for thousands of maternal deaths and illnesses, particularly in developing countries; and, because abortion exists and is legal, development of alternative safe methods.

We believe mifepristone is an important scientific advance in women's reproductive health care. Mifepristone has been shown in numerous studies to be safe and effective for early medical abortion. Over 150,000 women have used the drug safely in Europe; over 52,000 French women have used the same combination of mifepristone and prostaglandin that is being used in the U.S. We believe this will provide an equally safe alternative to surgical abortion that women can use in the earliest weeks of a pregnancy. Women who have used this regimen report it is similar to a natural miscarriage.

Medical abortion eventually will increase women's access to abortion services and give them

Telephone: (212) 339-0500 Telex: 9102900660 POPCO Facsimile: (212) 755-6052 Cable: POPCOUNCIL NEW YORK

privacy in making their reproductive health decisions. Women will be able to obtain medical abortion at doctors' offices, free of anti-choice violence and harassment. We believe mifepristone will not lead to an increased number of abortions--it hasn't in France, where it has been available since 1989--but it will expand women's options.

American women urgently need better access to effective contraceptive methods to prevent unintended pregnancy. But when a woman does face a crisis pregnancy, she must have access to all medically safe options. The Population Council believes mifepristone can significantly expand women's reproductive choices.

*Mrs. Catley-Carlson is out of the country. The statement was read for her by Sandra Arnold, Vice President for Corporate Affairs of the Population Council.

Mifepristone Chronology

1970 By this date, researchers in many countries have discovered the receptors within the uterine cells that interact with the hormone progesterone.

1980 Research team at Roussel Uclaf synthesizes an antiglucocorticoid and shows that it also is a drug that fits into progesterone receptors, thus blocking the hormone needed to sustain pregnancy. The drug, mifepristone, is named Roussel Uclaf 38486, shortened to RU 486.

1982 Roussel Uclaf reports a successful initial trial of mifepristone to induce abortion, begins years of trials in several countries to test the drug in women less than seven weeks pregnant.

1983 The Population Council gets FDA approval to test mifepristone in the US; during the next six years, over 300 women receive mifepristone at the University of Southern California.

1984 A WHO-sponsored study in Sweden shows efficacy of a combination of mifepristone and a prostaglandin.

1985 NIH begins to support research on other potential medical uses of mifepristone.

1988 French Health Ministry announces approval of mifepristone combined with a prostaglandin for early medical abortion. Responding to months of protests from anti-abortion groups, Roussel Uclaf decides to suspend marketing mifepristone, but the French Minister of Health orders the drug back on the market two days later, calling it the "moral property of women." Mifepristone is approved in China, but Roussel suspends plan for distribution there and in other countries.

1989 Mifepristone becomes available in France. In the US, the FDA places mifepristone on its "import alert" list.

1991 Mifepristone is approved for use in the United Kingdom.

1992 Mifepristone is approved for use in Sweden. An oral prostaglandin is approved for use with mifepristone in France.

1993 Jan. 22: President Clinton directs HHS to "promote the testing, licensing, and manufacturing in the US of mifepristone and other antiprogestins." April 20: In a joint announcement by the Population Council and Roussel Uclaf at the FDA, the company says it will license the Council to conduct a clinical trial, file NDA, select manufacturer and distributor. May 27: Studies in *New England Journal of Medicine* show effectiveness of mifepristone plus an oral prostaglandin. Sept. 8: Institute of Medicine report gives hope that mifepristone can be helpful in fighting diseases ranging from breast cancer to brain tumors. Contract talks between the Population Council and Roussel Uclaf stall.

-more-

1994 Feb. 17: Marie Stopes Clinics announce that American women may be treated with mifepristone/prostaglandin in England. April 20: Congressional briefing on mifepristone. April 26: Abortion Rights Mobilization announces it has signed agreement with overseas manufacturer to produce a clone of mifepristone. May: Administration officials pressure Roussel Uclaf to conclude contract with the Council. May 16: The Council and Roussel Uclaf announce that Roussel Uclaf will turn over to the Council without compensation US rights for all identified medical uses of mifepristone. Announcement is made at a hearing called by Rep. Ron Wyden. October: Clinical trials of mifepristone to begin in the US.

Source: The Case for Antiprogestins: A Report of the Reproductive Health Technologies Project, 1992; The Population Council

APPEARS THIS WAY
ON ORIGINAL

October 1994

One Dag Hammarskjold Plaza, New York, New York 10017

Other Potential Uses of Mifepristone

The antiprogestin, mifepristone, has the potential for use in treating a wide range of hormone disorders and problems associated with pregnancy. According to a report published in 1993 by the Institute of Medicine, potential areas where mifepristone use might be very important are difficulties in labor, infertility, endometriosis, uterine fibroids, breast cancer, and certain other types of tumors. Mifepristone has not been approved by the Food and Drug Administration for any of these uses.

Postcoital Contraception

The World Health Organization is currently conducting a 14-center clinical trials using mifepristone for emergency or postcoital contraception. One of these trials is at the University of California at San Francisco. –

Earlier randomized clinical trials in Scotland showed that mifepristone can be used effectively as an emergency contraceptive when used within 72 hours of unprotected intercourse. These studies compared the standard "morning after pill" (a high dose of oral contraceptives) to 600 mg of mifepristone. None of the 597 women who took mifepristone became pregnant, whereas nine of the 589 women who used the standard method became pregnant.

Contraception

Mifepristone has been shown to delay endometrial development or block ovulation, depending on when during the menstrual cycle it is administered. However, female contraceptive research with this drug is still in an early stage. Researchers are also investigating the possibility of using mifepristone as a male oral contraceptive. The drug is expected to slow the motility of sperm; however, it may be years before this drug is studied for this use in humans.

Cervical Dilation

Mifepristone may be valuable in preparing women for surgical abortions, in part, by dilating the cervix. Studies indicate that it is as effective for this use as prostaglandins, but causes fewer side effects.

Induction of Labor

Mifepristone has been used to induce labor after an intrauterine death of a fetus. It has been suggested that mifepristone could also be useful in inducing labor at the end of the third trimester. A randomized trial showed that 50 percent of women receiving mifepristone went into spontaneous labor, as compared with 25 percent who received a placebo.

Breast Cancer

Because some tumors in the breast have progesterone receptors, researchers have begun to explore the effect of mifepristone on this type of cancer. Early studies suggest that some women with breast cancer may respond to mifepristone. In some animal trials, mifepristone was used in combination with an antiestrogen, or a gonadotropin-releasing-hormone agonist.

Telephone: (212) 339-0500 Telex: 9102900660 POPCO Facsimile: (212) 755-6052 Cable: POPCOUNCIL NEW YORK