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

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 (AP)
Lou Sepersky, Chair
Community Board 6

Sherman Hollander (AP)
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

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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, Triamcinolone Acetonide, Desmopressin and Aluminum/Magnesium Hydroxx, 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

March 3, 1993

Mrs. Donna Shalala
Secretary of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Dear Mrs. Shalala:

This letter is to advise you that _____ has expressed interest to Roussel-Uclaf of France in a license to develop and commercialize RU-486 in North America. Our firm is expert in the development of new chemical entity pharmaceuticals and is willing to pursue an agreement with Roussel-Uclaf providing us with exclusive rights.

Any assistance you can provide would be appreciated. We believe RU-486 will provide an additional therapeutic option for women considering abortion.

Background information about our firm is enclosed.

Very sincerely yours,

/S/

_____
President

cc: _____

Mr. E. Sakiz

Enclosure

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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 [redacted] 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/

cc: Mrs. Donna Shalala

April 20, 1993

Dr. David Kessler
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Dr. Kessler:

I have been following the story of the drug RU-486 from a distance for quite a while. I think there is an important place for this drug in medical practice, and I also think the anti-abortion activists have diverted proper attention from the drug.

RU-486 should be available in clinics and hospital emergency rooms for the prevention of pregnancy following rape. It could be treated as a Schedule II drug with all the limitations on access that that restriction puts on patent narcotics. This narrow indication and limited access would deny anti-abortion activists any logical complaint about widespread use of the drug as a "morning after pill". This approach would probably also reduce the market potential to the point where distribution by a recognized pharmaceutical company would not be feasible.

However, the factor that most limits the attractiveness of selling this drug by a reputable company is the current level of notoriety, which brings fear of a boycott of other products and even violence against company officials and employees.

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I would suggest the government use an innovative strategy to market this drug after FDA approval. The U.S. should set up a public-private alliance in which the alliance licenses the drug from Roussel-Uclaf, which would manufacture the drug - I assume that there are government facilities already in existence which meet DEA Schedule II requirements for vaults, etc. The private partner in the alliance would set pricing, bid the various hospitals and clinics, market the product to physicians and hospital pharmacies, and direct distribution from the warehouse, all for a fee/commission. The government would indemnify all the efforts of the alliance. Resultant profits to the government from the alliance could go to reducing the federal budget deficit, improving FDA drug reviews, or funding important programs such as prenatal clinics, family life education, pregnancy counseling or improved vaccination compliance.

Please give these ideas some thought. If you would like to meet to discuss them with my company and Roussel, I can very easily get to Rockville. Thank you.

Sincerely,

151

President

Physicians for RU-486

9033 Wilshire Blvd. #300
Beverly Hills, California 90211
310-364-4510

Organizing Committee: Cheryl L. Dunnett M.D. Susan J. Stein M.D. Daniel J. Stone M.D.

April 21, 1993

David Kessler, M.D.
Commissioner, The Food and Drug Administration
5600 Fishers Lane HF-1
Rockville, Maryland 20857

Dear Dr. Kessler:

I was very pleased to see that Roussel-Uclaf and Hoechst A.G. have agreed to release RU-486 to The Population Council, thereby opening the door to its availability for medical uses in which it can be shown to be safe and effective. The successful conclusion of this difficult negotiation is a tribute to the F.D.A. I hope that our press conference on April 2nd contributed to this positive development. I also hope that the Agency will able to expedite processing of the New Drug Application as was suggested last January.

I would appreciate it if you could keep us abreast of developments affecting the status of RU-486 so that we may inform our membership. Most of our members are practicing physicians, many of whom may be prescribing the drug or referring patients for its use in the future. Our new address is on the letterhead above. Thank you.

Sincerely:

Daniel J. Stone MD.

Daniel J. Stone, M.D.
Chair, Physicians for RU-486

cc. Grant Bagley, M.D.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

Chron

May 28, 1993

Daniel J. Stone, M.D.
Chair, Physicians for RU-486
9033 Wilshire Boulevard #300
Beverly Hills, California 90211

Dear Dr. Stone:

This is in response to your letter of April 21, 1993, to Dr. Kessler concerning the availability of mifepristone (RU-486) in the United States.

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 anyone else from pursuing the study and approval of RU-486.

Significant developments affecting the status of RU-486 in the United States will continue to be reported in the national press as they occur. Should you have any specific questions concerning any of these developments, please feel free to contact me.

Sincerely yours,

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[ ]

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Research Institute for Mindanao Culture
XAVIER UNIVERSITY
P.O. Box 24, 9000 Cagayan de Oro City, Philippines, Tel. 35-68

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,

ISI

Research Associate

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DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

June 23, 1993

Ms. Wendi Lehman
Education Director
The Right to Life League of Southern California
50 North Hill Avenue, Suite 306
Pasadena, California 91106

Dear Ms. Lehman:

This is in response to your letter of April 1, 1993, enclosing petitions signed by individuals opposed to abortion and to the use of RU-486 (mifepristone) as an abortifacient in the United States.

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 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.

FDA is responsible for ensuring the safety and effectiveness of drugs and, as part of the Public Health Service, for doing what it can to protect and promote the public health. Because abortion is legal in this country, FDA believes that if there is a safe and effective alternative to a surgical abortion, then American women should have the opportunity to access 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.

Recently, Roussel-Uclaf, the manufacturer of RU-486, agreed to license RU-486 to the Population Council, a non-profit organization, to permit the testing of RU-486 as an abortifacient in this country. Clinical testing of the drug in the United States will allow the collection of data on the drug, including information on how the drug could be used properly in this country; it will provide an opportunity to train doctors in the careful administration of the drug; and it will give American women who participate in the clinical trial access to the drug. You can be assured that the rights and welfare of these women will be protected in accord with FDA's regulations which require and set forth conditions for ensuring the protection of all human research subjects. The process that I have described is deliberative, scientific, and appropriately applied to this drug for this indication.

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The RIGHT TO Life LEAGUE OF SOUTHERN CALIFORNIA

April 1, 1993

Dr. David A. Kessler
Food And Drug Administration
Rockville, MD 20852

Dear Dr. Kessler:

The Right to Life League of Southern California has gathered the signatures of over 20,000 Americans who are opposed to the introduction of the abortion pill, RU-486, into the United States.

It has been reported that you have contacted Roussel-Uclaf President Dr. Edouard Sakis regarding bringing RU-486 into the country. This move causes us great concern.

We are distressed that the scientific community is moving away from the goals of improving and preserving life. Every abortion kills an unborn human being, and we do not want a drug released in the United States that facilitates the destruction of human life.

We are also concerned that RU-486 will be introduced hastily to appease the pro-abortion lobby at the expense of the safety of women. We do not want women used as guinea pigs for this human pesticide. This drug must be carefully monitored.

The Right to Life League does not oppose research on RU-486 as a treatment for diseases, which was its original purpose. We do ask that you continue to ban the use of RU-486 as an abortifacient. The lives of children and the health of women are at stake.

Sincerely,

Wendi Lehman

Wendi Lehman
Education Director

WL/dh

9302998

50 North Hill Avenue Suite 306 Pasadena, California 91106 (818) 449-8408 FAX (818) 449-4822

Please remember the Right to Life League in your Will.

Thank you for writing to let us know of your concerns.

Sincerely yours,

/S/

THE ASSOCIATION OF THE BAR
OF THE CITY OF NEW YORK
42 WEST 44TH STREET
NEW YORK, N.Y. 10036-6690

COMMITTEE ON MEDICINE AND LAW

EDWARD S. KORNREICH
CHAIR
1585 BROADWAY
NEW YORK, N.Y. 10036
(212) 969-3396
FAX # (212) 969-2900

PHILIP M. GASSEL
SECRETARY
250 PARK AVENUE
NEW YORK, N.Y. 10177
(212) 351-4781
FAX # (212) 661-0989

May 24, 1993

Honorable David A. Kessler
Commissioner of Food and Drugs (HF-1)
Food and Drug Administration
Room 14-71
5600 Fishers Lane
Rockville, MD 20857

Re: RU-486

Dear Dr. Kessler:

As chair of the Committee on Medicine and Law of the Association of the Bar of the City of New York, I write to request a report on the status of your agency's reconsideration of the Bush administration's prior decision to exclude the abortifacient prescription drug RU-486 from the FDA's exemption allowing individuals to import a three-months' supply of an unapproved new drug for a serious medical condition where the drug presents no significant health hazard.

As you know, President Clinton signed an executive order on January 22, 1993 directing the FDA to reconsider the decision not to allow RU-486 to qualify for the personal use exemption. We are not aware that this directive has been implemented to date.

Based on our committee's study of the underlying facts, we do not perceive a rational basis for the exclusion of RU-486 from this exemption (see the decision in Benton v. Kessler, No.

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CV-92-3161 (E.D.N.Y., July 14, 1992)). Moreover, the exclusion appears unwarranted in light of the principle that women should have equal access to justice.

We look forward to hearing from you.

Sincerely yours,

Edward S. Kornreich

ESK/vp
cc: Honorable Donna E. Shalala
Honorable Daniel P. Moynihan
Honorable Edward M. Kennedy
Honorable Henry A. Waxman
Honorable John A. Dingell

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

June 30, 1993

Edward S. Kornreich, Esq.
Chair, Committee on Medicine and Law
The Association of the Bar
of the City of New York
42 West 44th Street
New York, New York 10036-6690

Dear Mr. Kornreich:

This is in response to your letter of May 24, 1993, to Dr. Kessler concerning President Clinton's January 22, 1993, memorandum which directed Secretary Shalala to assess initiatives to promote the testing, licensing, and manufacturing in the United States of RU-486 (mifepristone) and to direct the Food and Drug Administration (FDA) to reassess whether RU-486 qualifies for importation under FDA's personal use importation policy. Specifically, you requested information about the status of the latter.

In accordance with the President's January 22 memorandum, FDA is reassessing whether RU-486 might qualify for importation under FDA's personal use importation policy and whether the import alert should be rescinded. The Agency plans to make a recommendation on this issue this summer. The lawsuit to which you referred, Benten v. Kessler, remains pending in federal district court.

Please be assured that we, too, firmly believe in the principle that women should have equal access to justice. The protections of the Federal Food, Drug, and Cosmetic Act apply to all women and men in this country.

Dr. Kessler has stated that because abortion is legal in the United States, if RU-486 is a safe and effective alternative to surgical abortion, women in this country should have access to that drug. We have encouraged the manufacturer of RU-486 to submit a new drug application to FDA so that we can assess its safety and efficacy. In accordance with the President's January 22 memorandum, we have continued to assess initiatives concerning licensing, testing, and manufacturing of RU-486 in this country.

As you may be aware, the manufacturer of RU-486 has agreed to license the drug to the Population Council, a non-profit scientific and technical organization, for testing and distribution in the United States and to transfer the technology

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necessary for producing the drug. The Population Council has stated its intention to begin a clinical trial to test the drug in the United States and to move as soon as possible to submit a new drug application to the Agency.

Thank you for expressing your organization's views on these important issues.

Sincerely yours,

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INSTITUTE OF MEDICINE
NATIONAL ACADEMY OF SCIENCES
2101 CONSTITUTION AVENUE WASHINGTON, D. C. 20418

KENNETH I. SHINE, M. D.

August 6, 1993

[redacted]

Office of the Commissioner
Food and Drug Administration
Department of Health and Human Services
5600 Fishers Lane, HF-1, Room 14-81
Rockville, MD 20857

Dear [redacted]

I am pleased to invite you to a dinner and briefing on the Institute of Medicine's forthcoming report, "Clinical Applications of Mifepristone (RU 486) and Other Antiprogestins: Assessing the Science and Recommending a Research Agenda" on Wednesday, September 8, 1993 at 6:30 pm.

The IOM report evaluates the current state of the science regarding clinical uses of antiprogestins and gives recommendations concerning future research on the potential clinical use of antiprogestins in the United States.

We expect the report to be released publicly on September 8, 1993, to coincide with this dinner and briefing. At the dinner the chairman of the committee, Leslie Z. Benet, along with several members of the committee will present a brief review of the committee's work and recommendations. The discussion following dinner will provide an opportunity for Administration officials, Members of Congress, agency representatives, foundation representatives, and private sector leaders to discuss aspects of the report with its authors. I hope you will join me on Wednesday evening, September 8, for a small reception at 6:30 p.m. in the Rotunda, with dinner following at 7:15 p.m. in the Members' Room of the National Academy of Sciences at 2101 Constitution Avenue, N.W. Please use the Constitution Avenue entrance.

We hope you will be able to attend this special event. Please RSVP to Kathi Hand at 202-334-1601 by August 27.

Yours sincerely,

Kenneth I. Shine, M.D.
President

cc: Kathi Hand

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INSTITUTE OF MEDICINE
NATIONAL ACADEMY OF SCIENCES
2101 CONSTITUTION AVENUE WASHINGTON, D. C. 20418

KENNETH I. SHINE, M. D.

August 6, 1993

David Kessler, M.D.
Commissioner
Food and Drug Administration
Department of Health and Human Services
Parklawn Building, Room 14-71
Rockville, MD 20857

Dear David:

I am pleased to invite you to a dinner and briefing on the Institute of Medicine's forthcoming report, "Clinical Applications of Mifepristone (RU 486) and Other Antiprogestins: Assessing the Science and Recommending a Research Agenda" on Wednesday, September 8, 1993 at 6:30 pm.

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We expect the report to be released publicly on September 8, 1993, to coincide with this dinner and briefing. At the dinner the chairman of the committee, Leslie Z. Benet, along with several members of the committee will present a brief review of the committee's work and recommendations. The discussion following dinner will provide an opportunity for Administration officials, Members of Congress, agency representatives, foundation representatives, and private sector leaders to discuss aspects of the report with its authors. I hope you will join me on Wednesday evening, September 8, for a small reception at 6:30 p.m. in the Rotunda, with dinner following at 7:15 p.m. in the Members' Room of the National Academy of Sciences at 2101 Constitution Avenue, N.W. Please use the Constitution Avenue entrance.

We hope you will be able to attend this special event. Please RSVP to Kathi Hand at 202-334-1601 by August 27.

Yours sincerely,

Kenneth I. Shine, M.D.
President

cc: Kathi Hand

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DISCIPLE RENEWAL
Founded: 1988

P.O. Box 109 • Lovington, Illinois 61937 • Phone (217) 873-5128 • FAX (217) 873-5127

ECFA Member
The symbol of trust

August 2, 1993

Mr. David Kessler, Director
U.S. Food and Drug Administration
U.S. Dept. of Health and Human Services
1555 Parklawn Building
5600 Fishers Lane
Rockville MD 20857

Dear Mr. Kessler:

I write on behalf of the leadership of Disciple Renewal, a renewal group within the Christian Church (Disciples of Christ). On July 20 the General Assembly of the Christian Church (Disciples of Christ) adopted a resolution concerning the experimental drug RU-486. The resolution states that you will be contacted and urged to "take immediate steps to establish the safety and effectiveness of RU-486 and other anti-progesterone drugs so that they may become readily accessible to the citizens of the U.S..."

We have serious reservations about RU-486 and wish to register our concerns as you consider whether or not the drug should be made available. First of all, RU-486 is primarily known as an "abortion pill." Much reliable scientific data indicates that its only proven use is as an abortifacent and often with serious side affects. The ramifications of a drug which could be used to cause abortion in the form of a pill creates a whole new set of problems for the regulation of the abortion industry. If RU-486 is legalized, abortion could well become a primary means of birth-control in this country. For many of us, this would be a tragedy.

Mr. Kessler, you need to know that our General Assemblies and denominational leadership are not representative of our church as a whole. Do not believe that our General Assembly reflects the sentiments of the people of this church, it does not. Many Disciples are very much opposed to the drug RU-486 and do not want to see it made "readily accessible."

I appreciate your hearing us on this matter.

Sincerely,

Kevin D. Ray
Executive Director

cc: Richard L. Hamm

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"Renewing Disciples for Christ"

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TV12 WPEC
A CBS AFFILIATE

Fairfield Drive P O Box 24612 West Palm Beach, FL 33416 4612 407 844 1212 Fax 407 881 0741

August 11, 1993

[redacted]

Food and Drug Administration
Room 14-81
5600 Fishers Lane (HF-1)
Rockville, MD 20857

Dear [redacted]

Thank you so much for the interview on Friday, July 29 about RU-486. We appreciate your time and assistance in putting together our series. We are working hard to bring the story of this drug to our viewers and viewers around the country through our network of satellite stations. As you know, we'll be traveling to Paris in September. We'd like to contact you by phone to check up on the status of the process when we return. Thanks again for your assistance.

Sincerely,

Cheryl Snedeker

Holly Hadley, M.D.

93-4035

INSTITUTE OF MEDICINE
NATIONAL ACADEMY OF SCIENCES
2101 Constitution Avenue, Washington, D.C. 20418

Division of Health Promotion and Disease Prevention
Committee on Antiprogestins: Assessing the Science
Molla S. Donaldson
Study Director

TEL (202) 334-2145
FAX (202) 334-3862
INTERNET: MDONALDS@NAS.EDU

September 14, 1993

David Kessler, M.D.
Commissioner
Food and Drug Administration
Department of Health and Human Services
Parklawn Building, Room 14-71
Rockville, MD 20857

Dear Commissioner Kessler:

I am pleased to enclose a copy of the Institute of Medicine's report, *Clinical Applications of Mifepristone (RU 486) and Other Antiprogestins: Assessing the Science and Recommending a Research Agenda.*

The IOM report evaluates the current state of the science regarding clinical uses of antiprogestins and gives recommendations concerning future research on the potential clinical use of antiprogestins in the United States. We do have a small number of additional copies available on request. Separately published summaries of the report and multiple copies of the report itself are available from the National Academy Press. Their toll free number is 1-800-624-6242.

Sincerely,

Molla S. Donaldson

Molla S. Donaldson
Study Director

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Group
486
PO Box 7974
Berkeley, CA 94707

September 15, 1993

David Kessler
Executive Director
Food And Drug Administration
5600 Fishers Lane
Rockville, Md 20857

Dear Dr. Kessler,

Group 486 was established to expedite the introduction of RU-486 to the American market. The foundation of our business is the belief that an ever-increasing population degrades the quality of life for all. In a world with resource and social limits, every child should be wanted and cared for. Our dedicated focus is to promote social and market viability and overcome opposition to this important product by mobilizing the support of financial, manufacturing and political entities.

Roussel-Uclaf, manufacturer of RU 486, has been quoted as having reluctance to sell their patented pharmaceuticals for use in abortions. This is unfortunate because it would be fairly easy to demonstrate the safety of these formulations. Our question to you is: Can a generic form of RU 486 manufactured under the Population Council's US patent expect to be given as swift an approval by the FDA as the Roussel form could expect?

After all, both drugs would be chemically identical. Only the manufacturing site would differ. Since there are only 7 years remaining on the original patent, this is obviously an important consideration for anyone in the business of selling Mifepristone-based abortifacient. And according to the National Academy of Sciences recent analysis of European data, RU 486 is safe and effective.

Your prompt reply is appreciated. It would also be appreciated if you could send a copy of any pertinent materials FDA has regarding RU 486.

Sincerely,

Group 486
Jay Moritz
Geoffrey Dalander

93-4671

GROUP
486

November 9, 1993

[ ]
Food and Drug Administration
5600 Fisher's Lane, HF-1
Rockville, Maryland 20857

Dear ———

It was good to meet you at the APHA meetings in San Francisco last week. Unfortunately, we had to rush to another presentation before we could talk to you at length. The major question we have regards the New Drug Application process. Is it possible for a potential manufacturer to submit an NDA before they have won production rights from the holder of a patent?

We are specifically interested in RU 486. Right now, the Population Council is negotiating with Roussel Uclaf over the introduction of RU 486 to America. The question is whether Population Council, or any manufacturer for that matter, can start an NDA without Roussel's approval? Perhaps you could supply us with some literature or the legal citations regarding patents and production.

One of the possible avenues for RU 486 allies to take is to wait until the patent for RU 486 goes off patent. At that time, a generic manufacturer could start producing the drug. However, they would still have to go through the NDA, if we're not mistaken. Is this correct? Or is there other information we haven't considered? And could you please provide us information on off-label use of drugs. Searle has called use of misoprostol a misuse of their product. But all recent clinical trials of RU 486 have used Cytotec (Searle's misoprostol) for the prostaglandin portion of the therapy

This information will all be part of our educational campaign. We have a monthly newsletter which we intend to share with RU 486 supporters. Enclosed is a copy for your interest.

Sincerely,

Jay Moritz
Geoffrey Dalander

PO Box 7974 Berkeley, CA 94707

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

January 21, 1994

Mr. Jay Moritz
Mr. Geoffrey Dalander
Group 486
P. O. Box 7974
Berkeley, California 94707

Dear Mr. Moritz and Mr. Dalander:

This is in response to your letters of September 14, 1993, to Dr. Kessler, September 15, 1993, to Secretary Shalala, and November 9, 1993, to [redacted] concerning RU-486. In your letter to Dr. Kessler you asked whether a generic form of RU-486 could be expected to be given as swift an approval as the Roussel Uclaf form of RU-486.

I believe that you may have misunderstood the nature of the agreement between Roussel Uclaf and the Population Council. Roussel Uclaf has announced that it has agreed to license RU-486 to the Population Council for testing and distribution in the United States and to transfer the technology necessary for producing the drug. The Population Council has stated its intention to begin a clinical trial to test the drug in the United States and to move as soon as possible to submit a new drug application (NDA) to the Agency.

It is our understanding that under this agreement, Roussel Uclaf would retain its patent on RU-486, but provide a license under that patent to the Population Council. Thus, any drug produced under that license would not be considered an off-patent "generic" drug. FDA is committed to reviewing any NDA for RU-486 expeditiously once it is submitted to the Agency.

You also requested a copy of any information FDA had on RU-486. Information submitted to the Agency concerning a new drug is considered confidential. A great deal of information, however, is available in the Institute of Medicine's report, "Clinical Applications of Mifepristone (RU 486) and Other Antiprogestins: Assessing the Science and Recommending a Research." Copies of this report are available from the National Academy Press (toll free number: 1-800-624-6242).

In your letter to Secretary Shalala, you expressed concern regarding Searle's willingness to allow Cytotec to be used in clinical trials with RU-486. Because Cytotec is a legally marketed product in this country, we do not anticipate that there

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will be a significant problem in obtaining Cytotec for use in clinical trials.

Thank you for expressing your organization's views on these important issues.

Sincerely yours,

/S/

[ ]

September 11, 1993.

Re: September 9, 1993.
Article regarding Sales of RU486.

Please

I am very interested in marketing the drug called RU486 in the U.S.

Please contact me immediately regarding the needs to purchase it from you; and send me what you term an application.

If approved, I will incorporate under the name _____.
It will be a subsidiary corporation.

I believe very strongly in the use of this pill if you can send me the documentation proving that it does what you say.

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I really know that I could build an organization effectively.

You don't need a drug company, you need a sales force. I have that at my disposal.

Please contact me at your earliest convenience; relaying to me all the necessary information to begin working with you.

Best Regards,

[redacted]

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

October 12, 1993

[redacted]

Dear [redacted]

This is in response to your letter of September 11, 1993, expressing your interest in marketing RU-486 in the United States.

In order for a drug to be lawfully marketed in the United States, a sponsor, usually the drug's manufacturer, must submit and the Food and Drug Administration (FDA) must approve a new drug application (NDA). For RU-486, as with other drugs, the NDA would contain the results of well-controlled clinical studies which document the claim that RU-486 is both safe and effective as an abortifacient and information on the manufacturing procedures and controls used in producing the drug. FDA's responsibility is to review the manufacturer's data and to make a determination on the product's safety and efficacy. If FDA approves the NDA, the drug may be marketed in the United States. FDA does not test drugs, nor does it provide documentation concerning a product's safety or efficacy to a sponsor; both of these responsibilities reside with the sponsor of the drug product.

Therefore, while your views concerning the marketing of RU-486 are novel, a sponsor is, in fact, needed in order to supply the evidence to FDA to support the safety and efficacy of RU-486 before it can be lawfully marketed in the United States.

I appreciate your writing to let me know of your interest in marketing RU-486.

Sincerely yours,

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SUR LES
COMMUNICATIONS HORMONALES.

INSTITUT NATIONAL DE LA SANTE
ET DE LA RECHERCHE MEDICALE
INSERM U 33

Professeur Etienne-Emile Baulieu

FACULTE DE MEDECINE DE BICETRE
80, RUE DU GENERAL LECLERC
F. 94276 LE KREMLIN-BICETRE CEDEX

Le December 3, 1993

CL

Dear —

I deliver this paper at the Ciba Foundation discussion meeting on "The role of the media in science communication" in Stockholm, on December 7-8, 1993.

I am pleased to send you a copy of the manuscript which may interest you.

Sincerely,

tell me your opinion about it.

Etienne Baulieu

APPEARS THIS WAY
ON ORIGINAL

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TEL: (33) (1) 49 59 18 84/18 82
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The presentation of RU486 in the media

Etienne-Emile Baulieu

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I am not a journalist and nor am I a (mass) media specialist. I therefore believe that when the Ciba Foundation asked me to report on "the presentation of RU486 in the media", they were seeking the specific reactions of a scientist who had initiated the work on a compound which became controversial, and who persists in helping it make its way to women and patients in need, in spite of obstacles of various kinds.

This is not the first time that the media have intervened in the modern history of birth control. Since the beginning of the 19th century, the press, particularly in Britain and the USA, has published many articles defending or attacking puritanic principles: around 1850 it headlined "female monthly pills", such as those of Madam Restell, and paid a great deal of attention to the physicians grouped in the then conservative American Medical Association; it reported the activity of Leagues such as that in New York "For the Suppression of Vice", publicised Margaret Sanger's arrest in 1916 and continues to comment on the contrast between the ban on birth control by the Catholic Church and the views of the Orthodox and Reformed Churches and Islamic and Jewish religions. The press is also responsible for the general acknowledgement of the gap between the teaching of the Vatican and the practice of most catholic women.

Something new did appear about 30 years ago, principally because of Pincus's contraceptive pill, and that was the major *involvement of science* in the debate. Within a few years, the *concept of contraception*, previously controversial (Pincus was initially treated as being a "sterilizer of women"), was definitely and definitively accepted. It is my conviction that, when a scientific discovery and a humane demand go together, the trend is irresistible, and in the delicate field of human reproduction this occurred for the first time with "*the pill*". Indeed, we first saw the discovery of oral contraceptives in the fifties, next the legalization and implementation of contraceptive practices came in the sixties, and then the legalization of

abortion in many countries followed in the seventies, *before* a new medical, scientifically based, means of interrupting pregnancy became available (even if the instrumental technique, suction, is safe). In the same way as the pill is symbolic (and in fact is only taken by approximately 5% of the women in the world who could use it), when we published the first paper (Herrmann *et al.* 1982) RU486 was received as a potentially revolutionary product of scientific research.

Media welcome RU486

On April 19, 1982, the report on the "Effects of an antiprogesterone in woman: interruption of the menstrual cycle and of early pregnancy", was presented before the French Académie des Sciences. A reporter for the Agence France-Presse was present and wrote a dispatch which headed the front page of many newspapers all over the world, while reporters rushed to interview me for French, American and many other foreign TV channels and radios. Since, in addition to several thousands of scientific papers and communications, RU486 has generated a continuous stream of articles, comments and editorials in almost all newspapers or magazines throughout the world, with periods of great enthusiasm and some days of severe criticism.

RU486, as we often read, is a "second generation" pill. The "Pincus pill", which has been available for more than 30 years, embodied the knowledge of *hormone physiology* at that time (Pincus 1965): the pill's progestagen blocks the pituitary hormones in charge of ovulation, as progesterone does during pregnancy. While the media have efficiently promoted the concept of "scientific" contraception, they have always been relatively reluctant to applaud the use of hormones, even in countries such as France where more than half the women take some sort of Pincus pill. Maybe it is the unfounded fear of hormones: the theoretical danger of breast cancer is frequently evoked, even though the interpretation of the data is somewhat controversial. Anyhow, *molecular endocrinology* was only born after 1965 with, in the case discussed here, the discovery of the progesterone receptor in the mammalian uterus (Milgrom *et al.* 1970). A receptor is, in target cells, a molecule which transforms the arrival of the hormone into a response by the cellular machinery. Therefore, discoveries concerning receptors lay the ground for developing corresponding antihormonal compounds which work at this level. Specifically, I

suggested to Roussel-Uclaf that they develop a compound with anticortisone (antiglucocorticosteroid) activity since there are a number of possible medical applications, and for structural reasons, an anticorticosteroid compound might also be active as a antiprogesterone. I was also impressed by the structure of the so-called triphenyl ethylene antiestrogen molecules (see pp.75-77 in Baulieu & Rosenblum 1991 and Baulieu 1993), and the Roussel-Uclaf chemists produced RU486, whose global structure is consistent with the concept of analogous mechanisms for several antihormones at the receptor level. RU486 was found to be an antiglucocorticosteroid (Philibert *et al.* 1981), and displayed antiprogestin activity (Herrmann *et al.* 1982). Abortion was the first application of RU486, since the work of Csapo and others (Csapo & Erdos 1976) had indicated that pregnancy can be terminated after a relatively brief interruption of progesterone action, and there was the century-old demand by women for a safe, non aggressive mean of abortion and an imperative need to save the lives and health of hundreds of thousands of women in developing countries. While the problem of the efficacy of an antiprogesterone for interrupting pregnancy was relatively rapidly solved scientifically, for the media and most people it was just the beginning since women had (and at present still have) to wait for it in most countries.

As far as the use of RU486 as an *abortifacient* is concerned, the press has always been very supportive. Full reports of the actual results were published rapidly in refereed scientific/medical journals and thus made freely available. After the 80% efficacy published by Herrmann et al. (1982) had been confirmed, the complementary effect of a small dose of prostaglandin administered two days after RU486, first tested by M. Bygdeman (Bygdeman & Swahn 1985), was largely publicised: it brought the success rate up to 95%. In France, in several tens of thousands of cases, we used the same injected prostaglandin as in Sweden (sulprostone): this was responsible for a few cardiovascular incidents and for one death (it was a medical mistake to administer such a prostaglandin to a woman, reportedly 31 years old, a heavy smoker, and having previously had thirteen pregnancies). The accident was clearly associated with the method - not even attributable to RU486 but to the intramuscularly injected sulprostone (which has since been removed from the market for this indication). As it happened, just at the same time, we published the use of an orally active prostaglandin,

misoprostol, which is much safer, and also more convenient and cheaper (Aubény & Baulieu 1991). At first, the media were highly attentive to the accident, and this influenced the use of RU486 negatively in French centres. However, even though submission for registration of misoprostol by the Ministry of Health had not been yet been made, soon after the scientific presentation of the activity of misoprostol was mentioned in the press, physicians performing voluntary pregnancy termination switched to the oral prostaglandin and the use of RU486 increased again. Further successful trials were confirmatory (Peyron *et al.* 1993), and misoprostol was officially registered by the Ministry of Health. Searle, which sells the prostaglandin, accepted its use in conjunction to RU486 in France. The medical and social significance of the RU486 plus misoprostol method for the USA, as for the developing world, was underlined in Time Magazine (Time 1993) which based its cover story on the paper (Peyron *et al.* 1993) and the Editorial (Rosenfield 1993) published by the New England Journal of Medicine.

The reaction of the press to *newer clinical applications* of RU486 differ interestingly according to the case. When, on the basis of medical trials, we speak of RU486 for helping a suffering mother and/or child to start labor in *delayed deliveries*, there is not too much enthusiasm, even though the data are very neat. However, when there are some very preliminary results, far from being firmly confirmed, with *breast cancers* or *meningiomas*, there is a lot of press coverage: I certainly understand how important the treatment of tumours can be, but I am often forced to moderate the enthusiasm of journalists. At the very moment of writing this contribution to the Ciba meeting we are, in a multicentre effort, working on two new domains: a new approach to female *contraception* with *very low* doses of RU486 and a paper reporting effects of RU486 on *sperm* function, which will be soon published (Yang *et al.* 1994). I am waiting with interest to see what the reaction of the lay press will be - I cannot predict it. What is certain is that the abortion issue and the other medical applications of RU486 are interwoven. As defined originally, RU486 is an antisteroid hormone molecule, and not just an abortifacient. The "*political chemistry*" (Hodgen 1991) of the molecule slows down its use in medicine, but conversely the publicity related to the abortifacient property of RU486

has made it known to all physicians very rapidly and therefore helped to understand what its uses could be outside the field of abortion.

From time to time, the lay press has tried to attract the attention of readers to controversial issues such as, for example, an unfair lack of recognition of the merit of my colleagues, particularly the chemists of Roussel-Uclaf who synthetised the compound, as if I had to be a chemist myself (to be both a physician and a biologist is enough, for me): this allegation which, interestingly, was mostly propagated by the "pro-lifers" has dissipated rapidly (see pp. 83-84 in Baulieu & Rosenblum 1991 and p. 98 in Baulieu 1990). There have also been over-emphatic descriptions of the threatening letters or telephone calls I receive, or of physical threats and protection by bodyguards. Some journalists would probably like to make me more "interesting" for the public, who would then follow the story of the compound more closely and understand better what it can do, as also suggested by the offers of TV producers who wanted to make a "docu-drama" about my life. However, I believe that the private life or the personality traits of a scientist will not modify the validity of his work, nor influence the use of a compound such as RU486, which will ultimately remain the personal and responsible choice of each woman.

Politics of RU486

Hoechst holds 54% of the shares of of Roussel-Uclaf. It has clearly exerted its power negatively in the RU486 story, but only since 1988. This means that the initial studies on antihormones over several years, which I announced and described at yearly internal Roussel-Uclaf meetings attended by Hoechst representatives, apparently did not attract much attention... The media explosion after the publications of 1982 and in 1985 on the RU486 plus prostaglandin association was *not* enough to alert the Hoechst directors. Was it a collective "acte manqué" which made these men, who later demonstrated their opposition to RU486, deaf? Alternatively, they might have approved this research, but later on had to obey their President, Dr Hilger, when he learned of it and was strongly opposed to the use of an antiprogesterone compound for abortion. I understand that, in financial terms, RU486 is small compared to Hoechst big business. Maybe, but the "noise" that occurred afterwards made

Hoechst-Roussel very unhappy, even though they got more publicity than ever. Whether they like the outcome of the RU486 story or not, Roussel-Uclaf and Hoechst are highly beneficiary, now being internationally designated as very competent companies in innovative fine chemistry.

In France, the media played a very important role when RU486 was about to be registered. In September 1987, RU486 was submitted to the French Ministry of Health in order to be used for voluntary interruption of early pregnancy. The decision-making committee was about to decide when the media gave echo to the prostaglandin story, which paradoxically stopped the whole process. At the Academy I had announced the French tests, and Lancet had published those by David Baird which extended the positive results obtained by the combined use of RU486 and prostaglandin. The committee had not yet received the corresponding documents, and postponed approval. This delay was an unhoped-for gift to the pro-lifers: thanks to the media, they knew about the new timing and sent the Ministry threatening messages, raised petitions in America and held meetings against the registration of RU486.

Five days before the expected decision, I was told that the Chinese authorities had approved RU486. It would be used by one quarter of humanity! I decided to keep this information for myself, fearing that headlines just before the French Ministry's decision would seem like more pressure. Finally, on September 23, 1988, the exploitation permit was given and the media announced: "the morning after pill is for today" (France-Soir headlines), thus baptising RU486 in a colloquial but incorrect formula to describe what has been tested. Simultaneously, the wave of protests increased, and the Cardinal, Archibishop of Paris used the radio to accuse us of experimenting on "little Chinamen". At the end of November, all of sudden, Roussel unexpectedly announced they were giving up and would not make RU486 available for abortions although they had so been authorised a few weeks before.

I went to Rio de Janeiro to participate in the World Congress of the International Federation of Obstetrics and Gynaecology, chairing a symposium on RU486, ... sponsored by Roussel-Uclaf! I was touched by the flood of support, so different from the more typical quiet processes of science. Inadvertently, the retreat had launched a huge publicity campaign *for* RU486 and the Roussel-Uclaf directors, instead of escaping criticism, were pilloried on the

front page of the New York Times. In Paris, influential doctors such as Michele Barzach and Léon Schwartzenberg had the opportunity to protest through the media and, two days later, Claude Evin, the Minister of Health, declared: "From the moment governmental approval for the drug was granted, RU486 came to be the moral property of women, not just the property of a drug company". This was an extraordinarily publicised declaration, and RU486 became available to French women. In fact, in registered centres, its use had never stopped since trials began Good science and the political power had won, helped by the media.

The media by themselves are not always sufficient: Dr Hilger has never conceded to the press or the other media, whether the influential German 'Spiegel' or the Italian 'Expresso', or the most reknowned scientific magazines such as the American 'Science', who printed a long cover story, or JAMA (Journal of the American Medical Association) which published my Lasker Award lecture. He and his colleagues directors at Hoechst behaved as if they were more sensitive to the noisy pro-lifers than to the quasi-unanimous press, whether medical, scientific or for the general public. In contrast, the Food and Drug Administration (FDA) of the USA was highly responsive to the attitude of the press: for many years, the FDA has been accused of being the "limiting factor" which prevented the entry of RU486 into the USA. Even when I repeatedly stated that this was not accurate and that Roussel-Uclaf, or anyone else having a licence, had not presented the administration with a request for registration of the compound, the press did not believe it, and wanted the "baddy" to be in the USA. If there was a "baddy", it was the political situation in the country and, after Bill Clinton's election, it was a real revenge for the FDA to be able to demonstrate its support publicly, calling the Hoechst-Roussel people to Washington and asking them to do something to make RU486 available for American women. The Population Council, a non-profit-making institution based in New York and very active in the field of human fertility control, was the candidate agreed upon by both the FDA and Hoechst-Roussel for initiating the process. This first step towards the entry of RU486 into the USA has been acclaimed by the media. Indeed, registration of RU486 in the USA will be a critical step for the world-wide distribution of RU486, including in the developing countries.

This is, on theoretical grounds at least, the most important part of this presentation. Beyond the scientific achievement, beyond the real, though yet insufficient, progress towards making RU486 available where needed, there is a more fundamental issue. It concerns all human beings.

Contraception means contra-conception. If conception specifically means fertilization, and if fertilization is considered as the beginning of pregnancy (as the Roman Catholic Church thinks, while physicians wait for a positive pregnancy test to indicate implantation with passage of the chorionic hormone hCG into the woman), then only sterilization, barrier methods and blockade of ovulation or spermatogenesis are contraceptive methods. These differ from methods acting post-ovulatorily, when there is a preembryo or an embryo, such as progestins (used as pills, injected in a form with prolonged action, or as implants such as Norplant), IUDs and antiprogestins (the latter being efficacious also when taken before the date of expected menses). But, in turn, these methods differ radically from "abortion", if we refer to women's attitudes, and the century-long use of the word.

Abortion means, to lay people, interruption of a proven, established pregnancy and the later it is, the more and more difficult it becomes (physically and psychologically). Everyone feels the difference between stopping a process from starting and interrupting its evolution after it has begun. It is difficult to "draw the line" (McLaren 1984) for oneself. The word abortion carries a traditional connotation of instrumental aggression, with the usual entourage of operating theatre, gynaecological table, hospital ward and so on, even in developed countries where the tragedies of perforations, infections, etc. are now avoided (this is not the case in most developing countries). Need we add that the pressure exerted by the pro-life-sponsored production of posters and movies (i.e. 'The Silent Scream') aimed at unduly frightening and penalising women, do not help women already in trouble. More subtly, there is also a current trend in the media to popularise a large number of documentary films about the presupposed sensitivity, emotions, not to say thinking or decision-making capability attributed to the foetus and even to the embryo. The newest techniques are commentated with outdated declarations having little scientific substrate, and thus we are manipulated emotionally,

projecting our adult perception of life instead of making the appropriate differenciations between the concepts of living substance, human biological life, human individual and person.

Contragestion, whose use I proposed, is neither contraception nor abortion. It openly designates "contra-gestation", thereby not hiding that it precludes the development of pregnancy, and thus respecting, as scientific ethics command, "what is" (Primo Levi). The word contragestion corresponds to several techniques applicable after ovulation which, temporally, are somewhat superimposed (Fig.). Indeed, the word contraception is not longer correct when applied to progestins and IUDs, as we have seen above; however, these methods are not considered as abortion, particularly because, working permanently, almost automatically, their activity does not need the conscious decision of the woman on each occasion. Even though biologically, the action of RU486 may be similar, there is a *decision* involved in taking it.

I have mismanaged the launching of the definition of contragestion, and thus blurred the image of RU486 as a contragestive agent, distinct from a "simple" abortion pill. When RU486 was discovered, I tried to explain its use as a contragestive, but I did not use the term soon enough, and so, for the public, it became a "morning-after pill", a "post-coital pill". This was confusing because, as indicated above, RU486 became available *after* we had abortion laws. In France, we had (and still have) one law for contraception and another for abortion, defined as termination after a positive pregnancy test (in addition, women have to respect a delay of one week before undertaking the abortive manoeuvre). Between conventional contraception and classical abortion, there is a period of time which is not covered by any legal instruction. Therefore, the only way to have RU486 used was by testing and registering it in the context of the abortion law and by necessity it became "*the abortion pill*" for the media and the public. This connotation was especially popular in the USA, where abortion is also a political issue and where a vast public is waiting for a solution to the abortion debate. The media indicated that it was a medical technique precisely substitutive for a surgical manoeuvre. For registration in France we just placed ourselves in the legal framework previously edicted for surgical termination.

Abortion by itself, unfortunately, will long remain as a solution for many women because contraception will never be 100% perfect and nor will 100% of women use it. RU486 as an abortion pill, both for women's dignity and health, will remain essential.

But this is not all it will be. In my opinion it is only a backup to contragestive and, even better, contraceptive methods. The earlier a medical method is used, the better it is, and prevention is preferable to treatment: these rules are followed by all physicians when possible.

In summary, because there is a medical problem with abortion, because there was an opportunity to test the efficiency of RU486 in women "easily", and because it was necessary to register the compound, we had to start with abortion and up to now the concept of contragestion has not been widely taken up by the media. It would have been preferable to start differently, that is firstly to present RU486 as a menstrual regulator, as suction is in Bangladesh where it is accepted by the Islamic and the governmental authorities.

The use of the RU486 compound and the contragestion concept may be proposed jointly, as a new approach to a difficult problem. This has not yet been possible, for practical and legal reasons. Even if we currently insist on "contragestion", we are conducting research with RU486, to find out classically defined contraceptive methods, which, *in fine*, I prefer to contragestion.

I would also like to recall that an antiprogestin compound interferes in reproductive processes, as can be predicted from the knowledge of the activities of progesterone, in several different manners that are difficult to present to the public at large. Notwithstanding this difficulty, the overall role of the media has been positive.

Each generation has to re-learn the most important principles of life and society. I hope that the media will take the scientific data more and more into consideration so that they can continuously promote the beneficial use of biomedical discoveries.

Acknowledgments

I would like to thank Dr Krzysztof Rajkowski for editorial assistance and Corinne Legris and Jean-Claude Lambert for their help with the manuscript.

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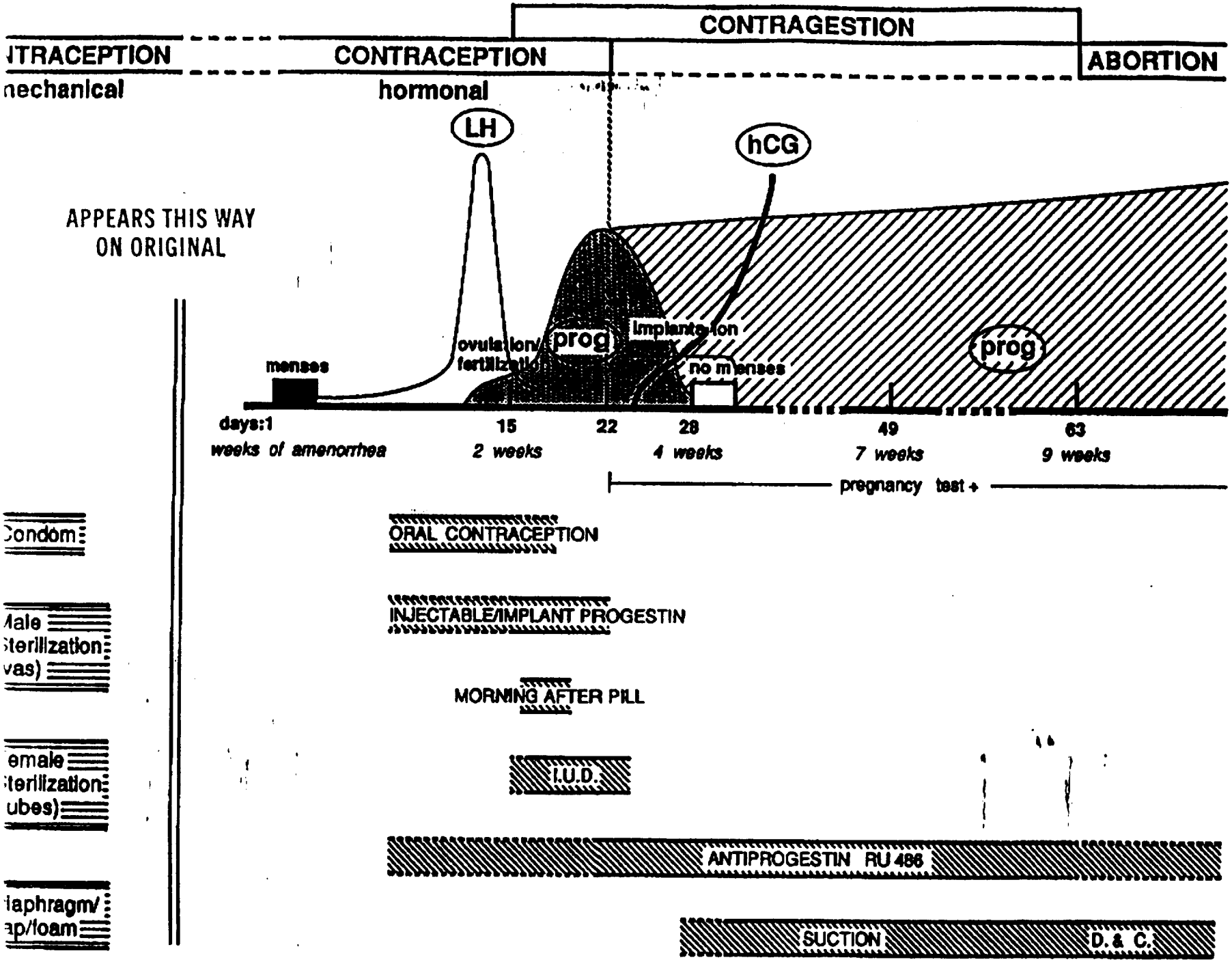
Figure Legend

FIG. 1. Birth control techniques range in time from methods preventing fertilization to the interruption of pregnancy at various stages. This chart shows the overlapping categories of several methods-classified as contraception, contragestion, and abortion-and their periods of efficacy, measured from the last menses.

Common terms are ambiguous. *Contraception* is usually understood to mean preventing fertilization, but specialists also refer to it until implantation is complete. To many biologists and theologians, *abortion* might mean any maneuver after fertilization; to practitioners, it is only after implantation. Most techniques can work in several ways. Even some oral contraceptives do not always block ovulation, for example; they can alter the endometrium and may prevent implantation, which is a post-ovulatory effect.

The diagram also shows *contragestion* from day 15, when fertilization takes place, and it spans the time of other post-ovulatory methods.

Techniques are shown in shaded bars. Solid lines indicate the time when a method is most efficient; for mechanical conception not time-dependency in indicated. Dotted lines show when the method might also have some effect.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January 11, 1994

[redacted]

Food and Drug Administration
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Dear [redacted]

Tom Barba and Richard Willard of Steptoe & Johnson and I extend our thanks and the deep appreciation of the [redacted] family for your efforts in expediting FDA's approval for the importation of RU 486 for Mr. [redacted], an extremely ill cancer patient.

We also wish to acknowledge the meritorious actions of four other FDA officials who were responsible for FDA granting approval within 24 hours after my initial call to your office. They are: [redacted]

We realize that significant burdens are placed on FDA employees who work through the holidays, and we very much appreciate the fact that FDA staff were able to take the time to guide us through the process and make the appropriate evaluation of Mr. [redacted]'s case so close to the onset of the

APPEARS THIS WAY ON ORIGINAL

JAN 14 1994

94-565

MIF 003845

Christmas Holidays. Please extend our thanks to the FDA employees who were so helpful to us, and who demonstrated what public service means.

Sincerely,

John R. Fleder

JRF:svg

cc: The Honorable David A. Kessler, M.D.
Commissioner of Food and Drugs

American Life League, Inc.

National Headquarters: P.O. Box 1350, Stafford, VA 22555
(703) 659-4171 • Metro D.C. 690-2049 • Fax (703) 659-2586

15th Anniversary

June 3, 1994

RECEIVED
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FDA
EXECUTIVE SECRETARIAT

Commissioner David A. Kessler, M.D.
U. S. Food and Drug Administration
5600 Fishers Lane, Room 1471
Rockville, MD 20857

Dear Dr. Kessler:

We at American Life League have read with interest of the aggressive role the Clinton administration and you have played in pressuring Roussel-Uclaf to reach an agreement with the Population Council to bring the abortion drug RU-486 to the United States. The history of the Population Council (see below) has made clear that they have a political agenda that places the human rights and health of women at a lesser premium than the goal of curbing reproduction among the poor.

We are deeply concerned about the potential impact of this agenda on the approval process for RU-486, and we are similarly concerned that the aggressive stance of yours and of the the Clinton administration will compromise the ethical and medical standards that should apply in the conduct of RU-486 trials. The Food and Drug Administration's own record in approving the Pill and IUD as initially safe for women who were subsequently harmed by these drugs and devices is hardly reassuring. Moreover, it is troubling in this context that the FDA has a history of relying upon advisors who have a population control agenda.

Because of this, we are asking that you immediately release to the public the following:

* The names and curricula vitae of all FDA advisors of all current members of the FDA's obstetric and gynecological committee;
* The names of the principal investigators conducting the trials for the Population Council or its agent;
* Copies of the informed consent form(s) and related materials to be distributed and/or signed by the women who participate in the RU-486 experiments;
* Information regarding the procedures and oversight the FDA will insist upon to ensure that the group or groups selected for RU-486 trials and experiments will not be lost to follow-up, as happened in the original oral contraceptive trials in Puerto Rico;
* A description of the economic/social characteristics of the women who will participate in the RU-486 trials;

94-5321

* Information regarding whether any woman under the age of 18 will participate in the RU-486 trials and, if so, whether her parents or guardians will be required to give consent for her participation;
* The medical warnings, if any, that will be given to women in these trials, as well as information regarding any waivers required for participation in RU-486 trials;
* Information regarding U.S. policy with respect to medical coverage of injuries suffered by any women as a result of participation in RU-486 trials;
* A statement as to whether you made any representation or promise to any official or representative of Roussel-Uclaf or other party interested in marketing RU-486 regarding the availability of prostaglandin drugs from Searle, or any other company, to be used in conjunction with RU-486.

Our concerns regarding these issues are based on bitter experience.

It is obvious that prototypical health standards--specifically the injunction against intentional or negligent infliction of physical harm upon an individual--have regularly been overridden where the collective values of the population control community are enthroned as policy guidelines. For example, Planned Parenthood's Dr. Elizabeth Connell, who later became a consultant to an FDA Drug Advisory Committee, stated: "It would be unreasonable to expect those attempting to deal with the exigencies of the population crisis and the agonies caused by unwanted pregnancies to view the pill precisely the same way as medical traditionalists demanding a preparation proved 100 percent effective, safe and devoid of all side effects."[1]

The Population Council's disregard for the health and rights of women has an even older pedigree. I call your attention to a remark by Dr. J. Robert Willson at a 1962 conference sponsored by the Population Council, which was promoting the now discredited IUD. Dr. Willson said: "... suppose one [patient] does develop an intrauterine infection and suppose she does end up with a hysterectomy ... How serious is that for the particular patient and for the population of the world in general? Not very. Perhaps we have to stop thinking in terms of individual patients ... perhaps the individual patient is expendable in the general scheme of things, particularly if the infection she acquires is sterilizing but not lethal."[2]

Dr. Mary Calderone, Planned Parenthood's Medical Director at that time, said: "It thrilled me to hear a clinician like Dr. Willson talk in terms of public health applications as I, a public health person, would not have dared to talk, particularly in this assembly."[3]

Dr. Jack Lippes, inventor of the FDA-approved Lippes Loop, said: "As you know, I have no reservations about ascending infection. This is not one of the things I worry about."[4]

To put it rather mildly, ascending infection associated with intrauterine devices gave tens of thousands of American women a great deal to worry about. That sorry experience, a result of the indifference of population-control activist physicians, and of the rush to judgment of a sympathetic FDA, should never be repeated. That is why it is of surpassing importance that the FDA insure that the processes, personnel, and protocols involved in the examination of the safety of RU-486 be conspicuous and contemporaneously released to the public now for examination.

For the health and safety of American women, we strongly urge you to proceed forthrightly and in the open, and make a full disclosure of all material relating to the review and potential for approval of RU-486.

Sincerely yours in the Lord of Life,

Judie Brown

(Mrs.) Judie Brown, President
American Life League, Inc.

1 *Family Planning Perspectives*, January 1970.
2 Intrauterine Contraceptive Devices, Proceedings of the Conference. Excerpta Medica Foundation, April-May, 1962, p. 124, 125.
3 Ibid.
4 Ibid.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

June 13, 1994

Mrs. Judie Brown
President
American Life League, Inc.
Post Office Box 1350
Stafford, Virginia 22555

Dear Mrs. Brown:

This is in response to your letter of June 3, 1994, to Dr. David Kessler, requesting information concerning RU-486 (mifepristone).

I have enclosed those documents that you requested that the Agency has in its possession. These are limited to the names and curricula vitae of current voting members of the Center for Drug Evaluation and Research's Fertility and Maternal Health Drugs Advisory Committee and the Center for Devices and Radiological Health's Medical Devices Advisory Committee's Obstetrics-Gynecology Devices Panel. The Agency is not in possession of the other documents that you requested.

This drug, like any other drug, will be studied pursuant to Food and Drug Administration (FDA) regulations, 21 CFR Part 312, and any new drug application for the drug will not be approved unless the drug meets all FDA requirements, 21 U.S.C. §355 and 21 CFR Part 314. We cannot comment on the specific questions you have raised, because the details of any investigational new drug application that have not been disclosed by the sponsor are confidential, in accordance with FDA's regulations.

You also requested information regarding United States policy with respect to medical coverage for injuries incurred by patients who participate in clinical trials. FDA's informed consent regulations require, for research involving more than minimal risk, that each research subject be provided an explanation as to whether any compensation is available and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained (21 CFR 50.25(a)(6)). We are not aware of any U.S. policy that would require either the clinical investigator or the study sponsor to provide medical coverage for injuries incurred as a result of participation in this type of clinical study. Clearly, a clinical investigator or sponsor may choose to do so, but there is no federal requirement.

9405321

Under Agency policy, this drug, as well as any other drug, is to be studied consistent with appropriate ethical, legal, and scientific standards.

Sincerely yours,

/S/

[redacted]

Enclosures

A PROPOSED FUNCTION STUDY OF RU486 vs. ARSENIC POISONING vs. NEMBUTAL TREATMENT (re.: CELL DEATH SIGNAL THEORY). -

An Outline by E.A.Greenhalgh to Coincide with a Request to the National Institute of Health(NIH) for an Investigation into Scientific Misconduct in Reproductive Endocrinology.

10 June 1994

FROM :

E.A.Greenhalgh
265-7 Regina St.N.,
Waterloo,Ontario, N2J 3B9
Canada
ph. (519)-884-3318

TO :

Dr. Samuel Marrow, the National Institute of Health (NIH)
Ms.Cindy Peirson, Program Director, National Women's Health Network
Mr.David Kessoler, Commissioner, the Food & Drug Administration
Rep. Christopher Smith (D-NJ), RU486 Review,
Rep. John D. Dingell (D), the Oversight Committee.

Enclosed is a scientific argument with support material. The request to Dr.Samuel Harrow of NIH will follow at a later date due to the time-consuming requirements of accuracy and cross-referencing. And human testing of RU486 will begin in the fall. The material can be examined as you desire. A long standing academic dispute (threatening to some major researchers) based on ethics and safety has been ongoing since 1987. The major surprise has been the appalling lack of safety standards and agencies to investigate problems in Canada. To highlight this point, Canada has had to invite the FDA to provide safety standards concerning blood products for the Canadian Red Cross.

Note my 3 publications : Toxicology (1986)v.42 ; a histological study/comparison of pesticides, and the two Journal of Endocrinology (UK) papers,v.125 (1990); regression studies of luteal cells, mentioning the Cell Death Signal theory. Please note the 1986 letter from a Dr.Pace-Asciak of Toronto's Sick Children's Hospital :"work could be of clinical value." Similarly, Dr.G.L. Nicolson of the M.D.Anderson Cancer Center and his incredibly kind support noting that the theory should be followed up on. Also , Dr.Peddie of Princess Anne Hospital (UK) original kind reply about my work being in accord with their own research.The concerns about blacklisting and suppression are in the copy of the letter sent to the Ontario Human Rights Commission and government agencies. Note replies.

The above stresses that my work is credible being published in divergent disciplines , and the theory has a basis in reality. The work had been started but blocked. Why? I do not know, but theories must be tested , and blacklisting prevents same. Suppression should be a concern to the reader suggesting something important. That concept/theory follows (in very simplified form).

RU486 vs. Arsenic/Nembutal or Other Poisoning

In spontaneous and/or induced abortion there is :

1. A prostaglandin surge affecting the pituitary initiating the "resetting" of the menstrual cycle. This over-rides the positive hormonal signal from the fetus. In induced abortions this is the prostaglandin injection.

2. The fetus must be harmed/killed to over-ride the positive signal of the fetal hormones that are maintaining the pregnancy. RU486 harms/kills the fetus.

Point : Harmful side-effects (mutagenic/carcinogenic/other) by RU486 to the adult female are unknown.

Let us examine concepts suppressed by the University of Waterloo, Canada. Why is not known, but a directly comparable model is available. In examination of luteal regression, Greenhalgh called regression a form of induced cell death (hence, Cell Death Signal theory). Experiments were begun to compare the effects of sodium pentabarbitol (aka Nembutal) on the ovary/luteal cells (see enclosed photocopied pages of suppressed thesis). Here is the point, sodium pentabarbitol caused the same effects of regression (decreased progesterone) as had the prostaglandin injections. Consider the effect as induced cell death, then using my toxicology experience I considered, "what kills cells?" Combining toxicology and endocrinology, I looked for similar experiments. Two papers I reviewed before my work was stopped were :

1. "Changes in Steroidogenic Activity of PreOvulatory Rat Follicles after Blockage of Ovulation with Nembutal," in the Dynamics of Ovarian Function (1981).

2. "Impaired Ovarian Functions in Arsenic-treated Freshwater Fish, Colisa Fasciatus(BL & SCH.)"Toxicology Letters,20(1984).

These two papers are noted because of corelations to results my work found and the following hypothesis/model.

RU486's side-effects are not known. However, a chemical is required to harm/kill the fetus causing a chain/cascade of events to reset the female's reproductive cycle. Two points :

1. Women who have used RU486 report being very ill and nauseous etc. Not To Say it is, but these symptons are similar to arsenic poisoning. Why not test a MODEL using arsenic/prostaglandin regimen as done with RU486? The effect would be :
   (a) using prostaglandin to reset the female reproductive cycle.
   (b) killing the fetus.

2. Arsenic has a long studied human medical history.
   (a) Arsenic at a sublethal , non-chronic dose may not cause long term harm or genetic mutations as other pharmaceuticals can, or other long term side-effects (i.e., the intergeneration carcinogenic relationship of DES for example).

   (b) Arsenic is cheap. All major health care initiatives/pharmaceutical claims for the use of drug therapy(over surgery) is to reduce the cost of medical care.

Sublethal doses of an arsenic compound should cost much less than one RU486 pill. Generic companies can be involved making prescription costs much cheaper and more widely available. Further, prescriptions can be specifically tailored to match the individual. Therefore, a cost effective medicine.

Medicine? Arsenic is a poison. So are many cancer drugs and other prescriptions. Anything that can be of therapeutic value, carefully controlled and prescribed is a medicine /drug. Drugs, even long used ones are continuously retested, some removed, others added. How can the theory using arsenic / RU486 be tested cheaply and safely? Compare them using the sodium pentabarbitol model noted from the suppressed thesis, adding histological examinations. The costs are minimal with large amounts of data accumulated quickly.

Why bother? RU486's side-effects, especially long term, are unknown. IF it can damage the ovary, i.e., pre-mature ageing, (whether or not the fetus is aborted and removed, the ovary remains in the body) this information is critical because the ovary (and its hormones) is vital to a female's well being. To a female being a female. Other organs may be affected, but this model centers on the ovary. Many problems will follow a woman if she loses her ovaries (or their functioning). Further, treating a woman for the rest of her life will increase medical costs(and the possiblility of cancer with hormone treatments), therefore, any short term gains will be more than lost later. By testing models NOW we can avoid harm. Questions will be answered. DES and thalidomide tragedies need not be repeated. Models are available (and cheap!).

Model Outline :

To compare the effects of RU486 vs. arsenic compounds on the ovary and its functioning. Proposed Model : pseudo-pregnant rats as described in J. Endocrinology v.125 (1990), and the suppressed sodium pentabarbitol study. Other studies using ovine, porcine, bovine and even primate ovaries may be considered. Further, human ovaries donated from accident victims or surgerical procedures could later verify results (perfusion in vitro techniques). The study will compare :

1. Cell culture hormone secretions
2. Histological examination of treated ovaries.

Points to Note :

1. Paper # 1 can be directly compared to my sodium pentabarbitol studies wherein regression effects were induced. They found MORPHOLOGICAL changes to the ovary/ovarian follicles. I quote p. 46, " In summary, blockage of ovulation by Nembutal results in degeneration of large preovulatory follicles." Both our studies found physiological changes.

2. Paper # 2 (arsenic pollution on fish ovaries) found, "After 15 days of exposure to a sublethal concentration of arsenic(III)oxide (14.0 mg/L) there were no appreciable histological alterations in the ovary, but 30 days of exposure resulted in marked degenerative changes during the mature phase. These changes included prominent follicular spaces, reduction in the development of IInd and IIIrd stage oocyte, reduced number and diameter of nucleoli and increased atretic follicles ."...atretic follicles N.B.

The common link my hypothesis found was the degeneration of follicles or atresia. Increased atretic follicles is part of the normal ageing of the ovary until a woman becomes menopausic. The question then becomes that if you have any agent that increases atresia , are you speeding up the onset of menopause? Would such an agent be harming the functioning of the ovary? Is RU486 such an agent? How serious a question is it? Is the answer worth discovering, especially if the costs are minimal?

We have a model; common measurable parameters , decreased progesterone secretion, and histological tissues to examine for artefacts (i.e., the percentage of atretic follicles) caused by prostaglandin, sodium pentabarbitol and arsenic. Ru486 can now be measured against these parameters on a model. The immediate concern for everyone , but especially women, is, will RU486 cause a lasting /permanent harm to the ovary's functioning, or is it a very minor effect? Would arsenic? Questions can be answered immediately if you want to.

Is abortion right or wrong? Whether chemical or other , you are killing the fetus. The pharmaceutical companies are not creating the problem, merely providing a means to an end. The dilemma resides in society : can every child be loved and nurtured to grow to be positive, or be mistreated to become a danger? Society has to make that decision, but it comes down to choices. Who decides. One question that can be answered , will RU486 cause premature ageing of the ovary and subsequent hardship to the older female (with higher health costs later)? This question can be answered.

Final Point : Why were Greenhalgh's theories and work suppressed? Greenhalgh does not know, there may be many reasons. What is more important , would repeating the work

(anywhere, by anyone, even in FDA labs)in the above context benefit women's health and safety? The public? Such is my belief otherwise I wouldn't have prepared this outline , nor taken any of my very costly past stands concernning ethics and safety.

Please review the enclosed material . Answers are available if you choose to examine and investigate. Remember DES, thalidomide and the Poisson cancer study. The choice is yours.

Thank you.

Yours truly,

Edward A. Greenhalgh

Edward A. Greenhalgh.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

July 11, 1994

Mr. Edward Greenhalgh
265-7 Regina Street, North
Waterloo, Ontario, N2J 3B9
Canada

Dear Mr. Greenhalgh:

Thank you for your letter of June 10, 1994, and accompanying materials referring, in part, to RU486 and arsenic. I have shared these materials with our Division of Metabolism and Endocrine Drug Products in the Food and Drug Administration's (FDA) Center for Drug Evaluation and Research.

FDA is committed to approving safe and effective products, and we work with sponsors to ensure that the necessary steps to secure approval are taken. Approval of a drug is not a quick process, due to the need for a drug's sponsor to conduct clinical studies demonstrating that a product is safe and effective in humans. These requirements are specified in the Food, Drug, and Cosmetic Act and the implementing regulations. In general, clinical studies are sponsored by drug manufacturers, conducted by clinical investigators, and monitored by FDA.

FDA approves a drug for use in the United States after it has reviewed the results of the manufacturer's/sponsor's New Drug Application, containing data (results of human, animal, and laboratory testing, and manufacturing information) which demonstrate the product's safety and efficacy. Investigational drugs may not be distributed or imported for trial on humans unless the sponsor has filed an Investigational New Drug (IND) application as specified in FDA's regulations.

I hope this information has been helpful, and once again thank you for taking the time to write.

Sincerely yours,

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Clinton

May 21, 1994

OR ORIGINAL

Dear Mrs. Clinton:

I have had brain surgery for benign meningiomas three times (1982, 1987 and 1992), a record only a handful of people in the United States can match. I have been left with a residual (remaining) tumor which was impossible for the surgeon to remove. It is presently wrapped around both of my optic nerves and rests above the pituitary gland, a most dangerous location indeed.

My neurosurgeon (Dr.) recommends Radiation but the possible side effects because of its location could be extremely detrimental in my case, according to radiologist Dr. My neurologist Dr. agrees. All would favor treatment with RU-486 if I could gain access to the drug in the near future.

You are the most influential person in the area of Health Reform and I need your help. The drug RU-486 retards my type of meningioma and ideally could cause it to shrink.

I know this because my close friend, Mr. David Grow of Atlanta, Georgia last year appeared before Representative Ron Wyden's Subcommittee on Health and Environment in Washington and was given permission to take the drug. David took RU-486 for six months when the brain scan (MRI) proved his meningioma had ceased to grow, and mine is the same general type (non-malignant meningioma) as David's. My non-malignant tumor may shrink within six months if I take RU-486.

I am sixty-three years old and the abortion effects of RU-486 are irrelevant, but I am prohibited from taking this drug under current law.

Please help me obtain RU-486 on a compassionate use basis. I need the medication soon so that no damage such as blindness or to the pituitary gland will take place due to further growth of my tumor.

I am presently a tenured professor with a Ph.D. who teaches at Florida A. & M. University, an historically Black university in Tallahassee, Florida. My husband is and we have full State Medical Insurance coverage. I will be happy to furnish complete medical records to whomever you suggest.

Will you please help me gain approval to take this medication? What steps do you recommend I take? I do know of Representative Ron Wyden's Committee before which David appeared. Perhaps you could arrange for me to appear before them in order to accomplish release of the drug to me on a compassionate use basis? Is there a way for me to be included in a clinical study?

Thank you for any help you can give me. I am asking for my sight and very possibly my life. Think of all the students who can gain from my ability to teach in the years to come.

Yours sincerely,

APPEARS THIS WAY
ON ORIGINAL

MIF 003860

March 16, 1995

David Kessler, M.D., Commissioner
Food and Drug Administration
Rockville, Maryland 20857

Dear Dr. Kessler:

I am very concerned about the introduction of RU 486 into this country for use as an abortifacient. My specific concern is this: although I am firmly pro-choice, my personal religious convictions do not permit my participation in the act of abortion. As a small percentage of RU 486 patients need surgical completion of their abortions, it is inevitable that these women will begin to appear in emergency rooms. What am I to do in these circumstances? I don't do abortions-- not the beginning, not the middle, and not the finishing up.

I believe, in the interest of fairness, the FDA should insist that the distribution of this drug is limited to physicians with surgical privileges, those able to do dilation and curettage procedures. Otherwise, physicians like me will face a terrible moral dilemma when the midwives, nurse practitioners, physician assistants, and family practitioners begin to prescribe this drug.

Please understand that I support the availability of the drug and that I am pro-choice, but I must have the right not to participate. Most community hospitals extract emergency room coverage from their staff as a condition of obtaining privileges. Under these circumstances, what happens to people like me?

Please, give this issue your immediate attention. I understand that Family Planning is beginning to test the drug in their clinics, and in this area of the country, those clinics are staffed by residents, nurse midwives, nurse practitioners, etc. This should be considered immediately.

Thank you.

Sincerely,

151

95-2698

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

April 6, 1995

[redacted]

Dear [redacted]

This is in response to your March 16, 1995, letter to Dr. Kessler about your concerns, as a physician who chooses not to conduct abortions, should a woman be admitted to the emergency room in need of medical care following an incomplete abortion, after the administration of RU 486 (mifepristone).

While I understand your moral dilemma, you should know that, in general, clinical trials are strictly controlled and designed to minimize risk to patients. However, I have forwarded your letter to FDA's Center for Drug Evaluation and Research for their consideration should a New Drug Application for mifepristone ever be submitted to FDA for use as an abortifacient.

I appreciate you writing to express your concerns.

Sincerely yours,

151

[redacted]

April 11, 1995

Department of Health and Human Services
Food and Drug Administration
Rockville, Maryland 20887

Dear _____

Thank you very much for your reply to my letter. Unfortunately, you completely missed my point. I am not worried about the clinical trials of RU 486. I am worried about what will happen when it is released for general use.

If there are no restrictions on who can prescribe it, then any non-surgical physician (i.e., psychiatrists, pediatricians, family practitioners, dermatologists, etc.) can prescribe it-- without regard to their ability to handle the complications. And then their patients will begin appearing in emergency rooms where non-abortion-performing physicians like myself will be expected to care for them.

And this will be a violation of my civil rights and religious freedom.

The solution is simple: restrict the distribution of RU 486 to hospital pharmacies and restrict the hospitals from dispensing RU 486 except over the prescription of a surgeon/gynecologist who has surgical privileges at the hospital.

This simple solution keeps the drug out of the hands of doctors who cannot do a dilation and curettage. It saves me the anguish of seeing a suffering woman whom I cannot help.

This is an important concept. Please, bring it to the attention of the appropriate committees. Thank you for your help.

Sincerely,

/S/

95-3751

July 24, 2000

Jane Henney, M.D., Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Henney:

Enclosed please find the American College of Obstetricians & Gynecologists' Analysis of Possible FDA Mifepristone Restrictions.

I have also sent a letter with E. Ratcliffe Anderson, Jr., MD of the American Medical Association that touches our joint concerns with the proposed restrictions and requests a meeting with you.

Thank you for your interest in this important issue.

Sincerely,

Ralph W. Hale MD

Ralph Hale, MD
Executive Vice President
The American College of Obstetricians and Gynecologists

00-4973

American College of Obstetricians and Gynecologists

Analysis of the Possible FDA Mifepristone Restrictions

July 27, 2000

FDA Proposal 1: Distribution and use of the drug would be limited to only licensed physicians.

a. Prohibiting the prescription, dispensing, or use of the medication by anyone other than licensed physicians interferes with state medical, pharmacy, and nursing scope of practice laws. These laws, not the FDA, determine which professionals are allowed to prescribe and dispense medications within each state. There is no reason to treat this drug as a controlled substance. There are many other medications, some of which are abortifacients, that are available through prescription to a pharmacy.

b. Marketing mifepristone directly to physicians or facilities rather than through pharmacies may be a reasonable way that the company would choose to begin marketing this drug. However, a requirement to do so by the FDA will be difficult to change and may restrict wider distribution in the future.

c. Any information about physician offices, pharmacies, hospitals, or any other facilities that receive the drug must remain strictly confidential in order to protect those who use the drug from anti-abortion violence. Any government requirement that would result in a list would immediately place those who provide the drug in jeopardy.

FDA Proposal 2: The physician must be "trained and authorized by law" to provide surgical abortion.

Requiring that a physician be trained as a provider of surgical abortion is not necessary to administer mifepristone correctly and safely. Nor is such training necessary to treat spontaneous abortion. Requiring certification of this training does not reflect current medical practice. In fact, there is no method to certify physicians as surgical abortion providers or for any other type of surgery. Responsibility for certification of medical

professionals in this case rests with state licensing boards and the American Board of Obstetrics and Gynecology, a professional body established for this purpose.

FDA Proposal 3: The physician must have "certification" for ultrasound dating of pregnancy and detecting ectopic pregnancy.

a. Requiring ultrasound to date a pregnancy or determine if there is an ectopic pregnancy is not required to administer the drug safely and correctly. Physicians and patients can quite accurately date a woman's pregnancy.[1]

b. Currently the American Institute of Ultrasound in Medicine (AIUM) and the American College of Radiology, which are the only certifying bodies for ultra-sound in the United States, do not certify physicians to provide specific ultrasound procedures, including dating pregnancies and detecting ectopic pregnancies. Furthermore, ultrasound certification is controversial, with implications for third party reimbursement issues, and is not related to prescribing this drug.

FDA Proposal 4: Distributing physicians must be certified to provide mifepristone through a curriculum approved by the FDA.

Requiring special training is also not necessary to safely administer mifepristone. Evidence from the clinical trials is unequivocal in demonstrating the drug's safety and efficacy as the FDA approvable letter states. Further, the FDA is not an educational institution and has no mechanism in place to develop medical curricula.

[1] Ellertson, Charlotte, et al. "Accuracy of assessment of pregnancy duration by women seeking early abortions." *THE LANCET* March 11, 2000: 355: 877-881.

FDA Proposal 5: Prescribing physicians must have admitting privileges at a hospital within an hour of the offices where the drug is dispensed or administered.

Privileges at a hospital are not necessary for prescribing mifepristone safely. The complication rates for mifepristone are very low, with a small number of patients requiring emergency room care or hospitalization. The April 30th, 1998, New England Journal of Medicine article, "Early Pregnancy Termination with Mifepristone and Misoprostal in the United States," states that only 2% of women using these drugs required hospitalization, underwent surgical intervention, or received intravenous fluid.[2] Another New England Journal of Medicine article states, "This regimen appears to be as safe as surgical abortion performed under the safest conditions."[3]

The prescribing physician does not need to be in the emergency room or to be the admitting physician if a patient requires follow-up emergency care. Women experiencing miscarriages and spontaneous abortions frequently require the same services and care and appropriately receive this care at their physicians' offices.

The FDA has imposed no similar requirements on drugs that are far more likely to cause complications requiring emergency care. This requirement discriminates against physicians in rural areas, and creates a significant barrier to access for women in these areas.

[2] Spitz, I.M. et al. "Medical termination of pregnancy." *New England Journal of Medicine* 1998: 338: 1241-1247.
[3] Spitz, I.M., Bardin, C.W. "Mifepristone (RU486): a modulator of progestin and glucocorticoid action. *New England Journal of Medicine* 1993: 329: 404-412.

00-4973

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

August 7, 2000

Ralph Hale, M.D.
The American College of Obstretricians
and Gynecologists
P. O. Box 96920
Washington, DC 20090-6920

Dear Dr. Hale:

This is in response to your letter of July 24, 2000, to Dr. Henney, Commissioner of Food and Drugs, regarding mifepristone. Your letter was forwarded to the Center for Drug Evaluation and Research for a response.

Thank you for sharing the results of your organization's analysis on the possible restrictions of mifepristone. These comments are being sent to the staff responsible for the review of this product for their information.

If we can provide future assistance please do not hesitate to contact us.

Sincerely.

/S/

Executive Operations Staff (HFD-6)
Center for Drug Evaluation and Research

Log No. 2000-1662

FDA No. 00-4973

cc: HF-40
HFD-103 –
HFD-580 –

Drafted
Concur:

July 24, 2000

Jane Henney, M.D., Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Henney:

The undersigned organizations, representing 340,000 physicians, are very concerned about restrictions we understand the Food and Drug Administration (FDA) has proposed for distribution and administration of the drug mifepristone.

We understand that the FDA has proposed at least five restrictions on access to the drug. These requirements are not based upon scientific facts, do not follow current medical practice, and impose inappropriate conditions on the practice of medicine.

We would like the opportunity to meet with you and your staff to discuss this important issue. It's imperative that the FDA fully understands the effect that these proposals would have on the quality of health care. It's equally imperative that the FDA's work be based solely on evidence from the drug's clinical trials, and be entirely free from any political influence.

Thank you for your interest in this important issue. We look forward to meeting with you and your staff at your earliest opportunity to discuss our concerns in greater detail.

Sincerely,

Ralph W. Hale MD

Ralph Hale, MD
Executive Vice President
The American College of Obstetricians and Gynecologists

E. Ratcliffe Anderson, Jr., MD
Executive Vice President
American Medical Association

00-4974

MIF 003871

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

August 11, 2000

Ralph Hale, M.D.
Executive Vice President
The American College of Obstetricians
and Gynecologists
409 12th Street, S.W.
Washington, D.C. 20024-2188

E. Ratcliffe Anderson, Jr., M.D.
Executive Vice President, CEO
American Medical Association
515 North State Street
Chicago, IL 60610

Dear Drs. Hale and Anderson:

Thank you for your letter of July 24 expressing concerns about proposed restrictions for the distribution and administration of mifepristone and requesting a meeting with me and my staff to discuss these issues. We also appreciate receiving the copy of your analysis of possible mifepristone restrictions, and have provided a copy of it to staff in the Center for Drug Evaluation and Research.

At my request, [redacted], tried to contact you to respond to your request to meet. Her office routinely answers requests of this nature. Unfortunately, she was unable to reach Dr. Hale by phone, but in an effort to make contact expeditiously, did send an e-mail, which we hope has been received.

Since your request was to meet with me, I want to be clear that I frequently meet with officials from health organizations as well as advocacy groups in various forums to discuss broad scientific and policy issues that affect the Agency. However, I have made it a practice not to meet with outside organizations or their representatives to discuss a product that is actively under review by the Agency. I believe this approach safeguards the integrity of the product review process the FDA is mandated to conduct and all who are subsequently affected by the final decision on a product undergoing review.

We recognize that you believe strongly that a meeting is appropriate to present your views. As [redacted] mentioned in her e-mail, she and representatives from FDA's Office of Women's Health, are willing to meet and listen to your concerns since they are not in the product review division. They will not be able to discuss with you any

specifics under consideration about mifepristone. These discussions are appropriately taking place between the FDA and the sponsor of the new drug application.

We can assure you that the Agency's decisions on this application, as on all others, will be made based on sound science and on whether the products are safe and effective for the patients who will use them.

Thank you for sharing your concerns. I look forward to working with ACOG and AMA in the future on important public health issues of mutual interest.

Sincerely,

Jane E. Henney, M.D.
Commissioner of Food and Drugs

Trac #00 4974

Drafted

Edited:

Doc name: G:\wp\

Bcc: HF-1 (2)
HF-10
HF-224
HFD-006
HF-12
HF-24
GCF-1
HFD-005
HF-40

FEMINIST MAJORITY FOUNDATION

Working for Women's Equality

Eleanor Smeal
President

Peg Yorkin
Chair of the Board

Katherine Spillar
National Coordinator

■ Washington D.C. Office
1600 Wilson Boulevard
Suite 801
Arlington, VA 22209
703 522 2214
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□ West Coast Office
8105 West Third Street
Los Angeles, CA 90048
323 651 0495
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Web Site:
http://www.feminist.org

E-mail:
femmaj@feminist.org

September 11, 2000

Commissioner Jane Henney
Food and Drug Administration
Parklawn Building
5600 Fishers Lane
Rockville, MD 20857

Dear Commissioner Henney,

As a part of our campaign to educate the public about mifepristone and to urge its approval in the United States, the Feminist Majority Foundation has collected hundreds of thousands of petitions from concerned citizens who believe that American women should have access to this medical breakthrough. We would like to share with you two boxes of 5938 petitions urging immediate approval of mifepristone without unnecessary restrictions to give you a sense of the breadth of support for mifepristone in the American public. These representative petitions have been gathered by mail, by volunteers, and on the internet.

Public support for mifepristone has remained very strong for the past 12 years. Women and men believe that mifepristone provides women with a safe, effective, private and early medical method of abortion. They also believe that medication has the capacity to expand abortion access and curtail the ability of anti-abortion extremists to target abortion providers. And the public is very excited about mifepristone's promising indications as a possible treatment for fibroid tumors, meningioma, ovarian cancer and a number of other diseases and conditions that primarily affect women. Support for expanding clinical trials on mifepristone's non-abortion uses is extremely strong.

We hope that these petitions convey the urgency of public support for mifepristone. We ask the Food and Drug Administration to immediately approve mifepristone, which the agency already has found to be safe and effective. Thank you for your consideration.

Sincerely,

Eleanor Smeal

Eleanor Smeal
President

00-5697

FEMINIST MAJORITY FOUNDATION
Working for Women's Equality

September 11, 2000

Commissioner Jane Henney
Food and Drug Administration
Parklawn Building
5600 Fishers Lane
Rockville, MD 20857

Dear Commissioner Henney,

■ Washington D.C. Office
1600 Wilson Boulevard
Suite 801
Arlington, VA 22209
703 522 2214
703 522 2219 fx

West Coast Office
8105 West Third Street
Los Angeles, CA 90048
323 651 0495
323 653 2689 fx

Web Site:
http://www.feminist.org

E-mail:
femmaj@feminist.org

For the past 12 years, the Feminist Majority Foundation has been leading a public education campaign to help bring mifepristone to the United States. This campaign has garnered support from almost every major scientific, medical, and women's rights organization. Both women's rights and scientific communities are elated that this long-awaited medical breakthrough may soon be approved in the United States, but we are very concerned about the restrictions that the United States Food and Drug Administration (FDA) is considering putting on mifepristone distribution.

We know that you already have received letters from the American Medical Association, the American Association of Obstetricians and Gynecologists, National Alliance of Breast Cancer Organizations, American Brain Tumor Association, and the National Brain Tumor Foundation expressing opposition to these unprecedented restrictions. We have enclosed a list of 56 additional scientific, medical, and women's rights organizations such as the American Nurses Association, Endometriosis Association, National Organization for Women, Planned Parenthood Federation of America, American Women's Medical Association, and the National Women's Health Network who have signed the enclosed resolution expressing grave concerns about these debilitating restrictions.

We believe that unprecedented restrictions limiting which medical providers can administer mifepristone, putting in place excessive training and certification mandates, and requiring unnecessary hospital admitting privileges interfere with the practice of medicine, scientific research, and women's health care. Allowing only physicians who currently provide abortion to administer mifepristone will serve only to limit the number of abortion providers in an era where fear of anti-abortion violence and a steady decline in the number of residents trained in abortion procedures has created a shortage of abortion providers nationwide.

Requirements of special certification and training for physicians administering mifepristone could potentially result in a listing of physicians providing medical abortion, ~~which~~ could in turn expose these providers to anti-abortion violence. Moreover, the certification requirements under consideration are far more burdensome than for other medications.

Abortion providers, like other physicians, generally have collaborative arrangements with physicians who have privileges at nearby hospitals, thereby eliminating the need for a requirement that any physician administering mifepristone have admitting privileges at a hospital within one hour of his or her practice. We fear that the enormous expense of malpractice insurance for hospital treatment and the control of many hospitals by the Catholic Church will make obtaining hospital privileges extremely difficult for abortion providers, thereby exacerbating the current shortage of providers.

Finally, we are concerned that such restrictions on mifepristone will have a chilling effect on the development of the drug's non-abortion indications. A newly released study

found that mifepristone may demonstrate efficacy as a treatment for some types of ovarian cancer. Other trials have found that mifepristone is effective in the treatment of endometriosis, fibroid tumors, and meningioma, as well as in labor induction. In very low doses, mifepristone is an effective form of emergency contraception. Furthermore, mifepristone's glucocorticoid action may have implications for the treatment of depression, HIV/AIDS, Alzheimer's disease and conditions related to elevated cortisol levels. Also, mifepristone is effective in treating Cushing's syndrome.

The data on these non-abortion uses are still preliminary, but the potential is enormous and demonstrates the compelling need for more and larger mifepristone trials on its many promising uses. If these debilitating restrictions are imposed, they will serve to jeopardize further research on the medication's other potential uses because it could be financially prohibitive for any company to supply the medication.

We ask that the FDA not place unnecessary restrictions on mifepristone. American women have already been forced to wait far too long for access to this medical breakthrough. Placing additional obstacles on its availability would be tragic. Thank you for your consideration.

Sincerely,

Eleanor Smeal

Eleanor Smeal
President

SIGNERS OF FEMINIST MAJORITY FOUNDATION
ORGANIZATIONAL APPEAL TO PRESIDENT CLINTON
AND FDA COMISSIONER HENNEY
URGING APPROVAL OF MIFEPRISTONE WITHOUT UNNECESSARY RESTRICTIONS

American Medical Women's Association
American Medical Student Association
American Nurses Association
American College of Nurse-Midwives
Planned Parenthood Federation of America
National Abortion Rights Action League
National Organization for Women
Business & Professional Women, USA
Association of Reproductive Health Professionals
Coalition of Labor Union of Women
Center for Reproductive Law and Policy
Endometriosis Association
National Uterine Fibroids Foundation
National Council of Women's Organizations
National Political Congress of Black Women
Religious Coalition for Reproductive Choice
National Family Planning and Reproductive Health Association
National Women's Health Network
Medical Students for Choice
Association for Women in Psychology
Older Women's League
Pro-Choice Resource Center
Sexual Assault/Domestic Abuse Advocacy Program
Women Organized Against Rape
RAINBO
Domestic Abuse Awareness
The Empowerment Program
Choice USA
Abortion Rights Mobilization
Catholics for a Free Choice
Americans for Religious Liberty
Equal Partners in Faith
Rainbow Light: Center for Women's Spirituality and Social Change
Women's Alliance for Theology Ethics and Ritual
Genders Journal
Americans for Democratic Action
American Humanist Association
Women's International Network
American Humanist Association
Buffalo Womenservices
Boston Women's Health Book Collective
California Abortion Rights Action League
Civil Liberties & Public Policy Program/Hampshire College
Georgians for Choice
Hawaii State Coalition Against Domestic Violence

Iowa Coalition Against Domestic Violence
Louisiana Coalition Against Domestic Violence
Pacific Institute for Women's Health
Pensacola Medical Services, Inc.
Pro-Choice Network of CUNY
Quad Cities Rape/Sexual Assault Counseling Program
Rhode Island Coalition Against Domestic Violence
Syracuse Cultural Workers
Women's Law Center of Maryland
YWCA of Lancaster, PA
Illinois Coalition Against Sexual Assault

ORGANIZATIONAL APPEAL

TO PRESIDENT CLINTON AND FDA COMMISSIONER HENNEY

ON MIFEPRISTONE

WHEREAS ... Millions of women will benefit from the development and dissemination of mifepristone, which is a safe, effective method of early pregnancy termination and shows promise as a possible treatment for ovarian cancer, endometriosis, fibroid tumors, meningioma, and some types of breast cancer, and in assisting labor induction.

WHEREAS ... Mifepristone's availabilty in the U.S. will make a very early and private abortion option available to women, increase access to abortion services, reframe the abortion debate, and ultimately, curb the targeting of physicians and clinics by anti-abortion extremists; and

WHEREAS ... Anti-abortion politics has already brought research on mifepristone to a standstill, and only when mifepristone wins approval as a method of early abortion will adequate supplies of the medication be available for development of the drug's other indications.

WHEREAS ... The FDA is reportedly discussing burdensome restrictions that are unprecedented and medically unnecessary. Not only would unnecessary restrictions on mifepristone limit access to a safe and very early form of medical abortion, but it also would mean that mifepristone would remain largely unavailable for research on its other very important possible uses because it would be almost financially impossible for a company to continue to supply the medication.

THEREFORE BE IT RESOLVED ... _____ appeals to you to do everything in your power to make sure that mifepristone, which the Clinton Administration has strongly supported and which has already been deemed safe and effective by the FDA, is expeditiously approved without unnecessarily limiting restrictions that interfere with women's health care, the practice of medicine, and life-saving scientific research.

Officer/Director _____ Title _____

Organization _____

Street _____

City/State/Zip _____

Telephone _____ Fax _____ E-mail _____

Date _____

PLEASE RETURN THIS APPEAL TO:

EMERGENCY MIFEPRISTONE CAMPAIGN
FEMINIST MAJORITY FOUNDATION
1600 WILSON BLVD., SUITE 801
ARLINGTON, VA 22302
www.feminist.org

AMERICAN CIVIL LIBERTIES UNION

WASHINGTON NATIONAL OFFICE
Laura W. Murphy
Director

122 Maryland Avenue, NE Washington, D.C. 20002

Tel (202) 544-1681 Fax (202) 546-0738

September 22, 2000

Jane Henney, M.D.
Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Henney:

We understand that the Food and Drug Administration ("FDA") is considering a variety of restrictions on the distribution and administration of the drug mifepristone. As an organization committed to women's health and reproductive freedom, we write to urge you to consider the serious health consequences of any restrictions that would curtail access to this drug.

A primary promise of mifepristone is its ability to provide access to earlier abortion options for women who live far from a surgical abortion provider. Restrictions on the drug -- particularly any limitation on who can administer it -- would rob women of mifepristone's promise of access to earlier, and therefore in many cases safer, abortions. Moreover, such restrictions are not necessary, where the FDA has already found mifepristone to be safe and efficacious.[1] Considered in the broader context of the provision of reproductive health care in this country, restrictions that limit who can provide the drug and that thereby reduce access will disserve, not further, women's health. Because the FDA's mandate is to further public health, it should approve mifepristone without the considered restrictions.

Restrictions on mifepristone that unjustifiably limit the number of licensed providers will serve to delay abortions to the detriment of women's health. Mifepristone is available for procedures used between the earliest point at which a pregnancy can be confirmed and 49 days (or 7 weeks) of pregnancy, whereas many facilities do not perform surgical abortions until 6 to 8 weeks. In addition, many women experience further delay in their attempts to obtain a surgical abortion. A primary cause of this delay is lack of access to an abortion provider.

The problem of access is pervasive. In 86% of counties in the country, there is no abortion provider.[2] South Dakota, for example, has only one abortion provider, leaving women

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1 *See* Letter from FDA to Population Council (Sept. 18, 1996).

2 Stanley K. Henshaw, *Abortion Incidence and Services in the United States, 1995-1996*, 30 Fam. Plan. Persp. 263, 266 (1998).

60-5925

to travel hundreds of miles for care.[3] Women who live far from a provider often have difficulty arranging the procedure: They face difficulties scheduling an absence from home or work for the several days such procedures can take, including travel time. They also often have trouble raising funds for the trip, adding to the delay.[4] The problems are, of course, greatest for poor women and women for whom confidentiality is crucial, such as battered women.

Any delay in obtaining an abortion is significant because gestational age is an important determinant of medical risk. While surgical abortions are extremely safe, the risk of death from abortion increases approximately 30 percent with each week of gestation from 8 weeks of pregnancy measured from the woman's last menstrual period (lmp) to 20 weeks lmp.[5] The risk of major medical complications increases approximately 20 percent with each week of gestation from 7 weeks onward.[6]

Thus, for example, without mifepristone, a woman located several hundred miles away from the nearest surgical abortion provider might be unable to obtain an abortion until the 10th week of pregnancy. If mifepristone were available in her community, she could obtain an earlier non-surgical abortion that would possibly be safer.

Mifepristone can serve women's health by increasing the number of abortion providers and making the procedure available outside the traditional surgical abortion setting. In a recent survey, 31% of gynecologists who have never performed surgical abortions or have not performed them in the past five years stated that they were "very likely" or "somewhat likely" to prescribe mifepristone if it were available.[7] The promise is even greater when other physicians are considered. Thirty-one percent of family practice physicians, 98% of whom do not perform

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[3] *Id.* at 267 (Table 5). Not all providers of surgical abortions are obstetrician/gynecologists. Moreover, the legality of any effort to impose such a requirement, or to otherwise limit the physicians who can provide abortions, is dubious at best. *See Pro-Choice Mississippi v. Thompson*, No. 3:96CV596BN, slip op. at 18 (S.D. Miss. Sept. 28, 1996) (preliminarily enjoining regulations requiring physicians providing abortions to have completed an American Medical Association-approved residency in obstetrical/gynecology). The United States Supreme Court has held that a physician licensed by the state possesses sufficient qualifications to perform an abortion. *See Doe v. Bolton*, 410 U.S. 179, 199-200 (1973); *Word v. Poelker*, 495 F.2d 1349, 1352 (8th Cir. 1974) ("We are referred to no other single surgical procedure where doctors are required to 'prove up' their overall fitness as they are here."); *Mahoning Women's Ctr. v. Hunter*, 610 F.2d 456, 460 (6th Cir. 1979) (holding that the city may not define the term "physician" to mean more than "a physician currently licensed by the State") (quoting *Roe v. Wade*, 410 U.S. 113, 165 (1973))), *vacated and remanded on other grounds*, 447 U.S. 918 (1980).

[4] *See* Ada Torres & Jaqueline Darroch Forrest, *Why Do Women Have Abortions*, 20 Fam. Plan. Persp. 169, 174 (1988).

[5] *See* Herschel W. Lawson et al., *Abortion Mortality, United States, 1972 through 1987*, 171 Am. J. Obstet. & Gynecol. 1365, 1367 (Table II) (1994).

[6] Christopher Tietze & Stanley K. Henshaw, *Induced Abortion: A World Review 1986*, at 103 (The Alan Guttmacher Institute, 6th ed. 1986).

[7] The Henry J. Kaiser Family Foundation, *A National Survey, Views of Women's Health Care Providers on Abortion: An Update on Mifepristone* 2 (2000) <<http://www.kff.org/content/2000/20000613a/Toplines.PDF>.

surgical abortions, similarly indicated that they were "very" or "somewhat" likely to prescribe mifepristone.[8]

Moreover, some women may prefer a non-surgical abortion and may be motivated to seek care earlier if such an option were available. The fact that mifepristone is available only in the first few weeks of pregnancy is part of the publicity surrounding the drug. In contrast, many women are unaware of the fact that surgical abortions are safer if performed earlier in pregnancy. Thus, wide access to mifepristone may steer women away from later, and potentially riskier surgical abortion procedures.

In approving mifepristone, the FDA should not focus narrowly on what may, in a perfect world, be the ideal conditions for a single administration of the drug. Rather, as an agency dedicated to protecting public health, the FDA should also consider the health advantages of increased access to earlier and safer abortion options. Any restrictions by the FDA limiting those who may prescribe mifepristone would dramatically decrease its availability and would thus rob women of one of the drug's major health benefits. We urge you to consider the broad health implications of any such restrictions.

Sincerely,

Laura Murphy
Director, Washington National Office

Catherine Weiss
Director, Reproductive Freedom Project

[8] *Id.* at 2-3.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

October 4, 2000

Ms. Laura Murphy
Ms. Catherine Weiss
Washington National Office
American Civil Liberties Union
122 Maryland Avenue, NE
Washington, D.C. 20002

Dear Ms. Murphy and Ms. Weiss:

This is in response to your letter of September 22, in which you voice support for the approval of mifepristone without unnecessary restrictions. As I am sure you are aware, FDA approved this non-surgical alternative on September 28. I am enclosing a copy of a press release announcing the approval. For more detailed information on the approval, please review our website, which may be found online at:
http://www.fda.gov/cder/drug/infopage/mifepristone/

Sincerely,

Jane E. Henney, M.D.
Commissioner of Food and Drugs

Enclosure

trac# 00 5966

cc:
HF-1 (2 copies)
HF-2
HF-8
HF-10
HFA-224

RD: [redacted] :HF-40:9/29/2000
cleared/revised: [redacted] :HF-40:10/02/00
cleared/revised: [redacted] HF-40:10/03/00
Revised: [redacted] :HF-1:10/4/00
F/T: [redacted] .HF-40:10/4/00

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HHS NEWS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

P00-19
September 28, 2000
FOR IMMEDIATE RELEASE

FOOD AND DRUG ADMINISTRATION
Print Media: 301-827-6250
Broadcast Media: 301-827-3434
Consumer Inquiries: 888-INFO-FDA

FDA APPROVES MIFEPRISTONE FOR THE TERMINATION OF EARLY PREGNANCY

The Food and Drug Administration today approved mifepristone (trade name Mifeprex) for the termination of early pregnancy, defined as 49 days or less, counting from the beginning of the last menstrual period.

Under the approved treatment regimen, a woman first takes 600 milligrams of mifepristone (three 200 milligram pills) by mouth. Two days later, she takes 400 micrograms (two 200-microgram pills) of misoprostol, a prostaglandin. Women will return for a follow-up visit approximately 14 days after taking mifepristone to determine whether the pregnancy has been terminated.

Because of the importance of adhering to this treatment regimen, each woman receiving mifepristone will be given a Medication Guide that clearly explains how to take the drug, who should avoid taking it, and what side

-More-

effects can occur.

"The approval of mifepristone is the result of the FDA's careful evaluation of the scientific evidence related to the safe and effective use of this drug," said Jane E. Henney, M.D., Commissioner of Food and Drugs. "The FDA's review and approval of this drug has adhered strictly to our legal mandate and mission as a science-based public health regulatory agency."

FDA based its approval of mifepristone on data from clinical trials in the United States and France.

The labeling for mifepristone emphasizes that most women using the product will experience some side effects, primarily cramping and bleeding. Bleeding and spotting typically last for between 9 and 16 days. In about one of 100 women, bleeding can be so heavy that a surgical procedure will be required to stop the bleeding.

The drug's labeling also warns that it should not be used in women with the following conditions:

- Confirmed or suspected ectopic ("tubal") pregnancies
- Intrauterine device (IUD) in place
- Chronic failure of the adrenal glands

- Current long-term therapy with corticosteroids
- History of allergy to mifepristone, misoprostol or other prostaglandins
- Bleeding disorders or current anticoagulant (blood-thinning) therapy.

Under the terms of the approval, mifepristone will be distributed to physicians who can accurately determine the duration of a patient's pregnancy and detect an ectopic (or tubal) pregnancy. Physicians who prescribe mifepristone must also be able to provide surgical intervention in cases of incomplete abortion or severe bleeding -- or they must have made plans in advance to provide such care through others.

To gather additional data about the use of mifepristone, the Population Council (sponsor of the product) has made a commitment to conduct postmarketing studies. These include a study comparing patient outcomes among physicians who refer their patients needing surgical intervention compared to those who perform surgical procedures themselves; an audit of prescribers that will examine whether patients and their physicians are signing the patient agreement and placing it in the patient's

medical record, as required; and a system for surveillance, reporting and tracking rare ongoing pregnancies after treatment with mifepristone in the U.S.

Mifepristone, which was developed by a French pharmaceutical firm, was first approved for use in France in 1988. Since then, more than 620,000 European women have taken mifepristone in combination with a prostaglandin to terminate pregnancy. The drug has also been approved in the United Kingdom, Sweden, and other countries.

Mifepristone will be distributed in the U.S. by Danco Laboratories, LLC, New York, N.Y.

More detailed information about this product is available on FDA's website at http://www.fda.gov/cder/drug/infopage/mifepristone/

####

American Academy of Family Physicians
2021 Massachusetts Avenue, N.W., Washington, DC 20036-1011

September 25, 2000

Jane Henney, MD
Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Henney,

On behalf of the 89,400 member American Academy of Family Physicians, I am writing to express our concern about proposed restrictions we understand the agency is considering for the drug mifepristone.

In particular, we are concerned that the proposed limits around distribution and administration of the drug may affect not only access to the medication for patients, but negatively impact family physicians' ability to prescribe the drug. Specifically, we are concerned about any restrictions that would limit the scope of practice of family physicians, which is regulated by each state. For example, we understand that the agency may propose restricting the distribution of mifepristone to physicians trained and authorized by law to provide surgical abortion. We believe that any attempt by the agency to regulate medical practice in this area would be inappropriate.

The Academy would appreciate the opportunity to meet with you to discuss the proposed restrictions. Thank you in advance for your attention to this important issue. We look forward to hearing from you.

Sincerely,

Lanny R. Copeland, MD

Lanny R. Copeland, MD
Board Chair

CC-5923

(888) 794-7481
(202) 232-9033
Fax: (202) 232-9044
E-mail: capitol@aafp.
http://www.aafp.org

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

October 12, 2000

Lanny R. Copeland, M.D.
Chairman
American Academy of Family Physicians
2021 Massachusetts Avenue, NW
Washington, D.C. 20036-1011

Dear Dr. Copeland:

This is in response to your letter of September 25, which expressed your concerns about restrictions for mifepristone. As you are aware, FDA approved this product on September 28. In addition, I understand that the American Academy of Family Physicians (AAFP) was faxed information on this approval at the time it was publicly announced.

Your letter also included a request to meet and discuss the terms of the mifepristone approval. Please understand that I have made it a practice to not meet with outside organizations or their representatives to discuss specific products. I believe that this approach safeguards the integrity of the review process and all who may subsequently be affected by the final review decision. I do, however, frequently meet with officials from health organizations and advocacy groups to discuss broad scientific and public health issues.

I assure you that the Agency's decision on this application, as on all others, was based on sound science and the best available medical judgement. I look forward to working with AAFP in the future on important issues of mutual interest.

Sincerely,

Jane E. Henney

Jane E. Henney, M.D.
Commissioner of Food and Drugs

trac# 00 5923

bcc:
HF-1 (2 copies)
HF-8
HF-40
HFD-1
HFD-6
HFA-224

RD: [redacted] HF-40:10/04/2000
cleared/revised: [redacted] HF-40:10/05/00
cleared/revised: [redacted] HF-40:10/06/00
revised: [redacted] HF-40:10/16/00 (based on comments received)
revised/cleared: [redacted] HF-40:10/16/00
edited p [redacted] HF-40:10/20/00

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PUBLIC ADVOCATE FOR THE CITY OF NEW YORK

MARK GREEN
Public Advocate

September 22, 2000

Jane Henney, M.D.
Commissioner of Food and Drugs
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: RU-486

Dear Dr. Henney:

Earlier this week Planned Parenthood of New York City, NARAL-New York, the Access Project and Physicians for Reproductive Health and Choice joined me in convening a public hearing in New York City on pending action by the Food and Drug Administration on mifepristone, also known as RU-486.

Allowing New York women access to this safe and effective drug has been a priority of mine for a nearly a decade. As NYC Consumer Affairs Commissioner in the early 1990s, I worked closely with then Mayor David N. Dinkins to bring RU-486 to the United States. We convened roundtable discussions with reproductive and medical experts and religious leaders. We created a coalition of two dozen pro-choice mayors from around the country who together urged the president of the French company that controlled the patent on the drug to allow it to be exported here for testing. The coalition also wrote to then President George Bush urging him to take the drug off the import black list. We were unsuccessful until the first month of President Clinton's presidency, when he persuaded the French manufacturer to transfer its patent so clinical trials in the U.S. could begin.

So I was pleased this summer to hear that this non-surgical option might soon be available to American women considering having an abortion – and also concerned about the restrictions on access to RU-486 that the FDA is said to be considering. We called the hearing to explore whether these restrictions were medically necessary and whether they would have unintended effects that could hurt rather than help women. We heard

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mgreen@pubadvocate.nyc.gov TTY: (212) 669-7438

that the restrictions are not necessary, go far beyond the restrictions that apply to other drugs, and seriously undercut the main benefits of RU-486: wide accessibility of abortion and privacy.

As you approach the deadline for final action, I hope you will consider the enclosed summary and full testimony from our hearing on RU-486. I am pleased to submit it on behalf of the hearing panel made up of Jo Ivey Boufford, M.D., Dean of the Robert F. Wagner School of Public Service at New York University; Allan Rosenfield, M.D., Dean of the Mailman School of Public Health at Columbia University; Victor W. Sidel, M..D., President of the Public Health Association of New York City; and me.

Given that the FDA deemed RU-486 "safe and effective" four years ago and it has been used widely abroad, it is past time for the FDA to approve RU-486. RU-486 should be treated like any other drug. Once it's approved for use, any physician should be able to prescribe it when he or she judges it medically appropriate. Afterall, doctors are not required to be heart surgeons in order to prescribe cholesterol-reducing medication.

RU-486 can help put reproductive choice where it belongs – in the hands of women and their doctors. Please do not allow ideology to supplant science.

Sincerely,

Mark Green

cc: Donna E. Shalala
Sarah Kovner

Public Hearing Report

RU-486: The Impact of Proposed Restrictions on Its Use and Distribution

Mark Green
Public Advocate for the City of New York

September 19, 2000

Public Hearing Summary:

The Impact of Possible FDA Restrictions On the Distribution and Use of RU-486

Convened by Mark Green Public Advocate for New York City

September 19, 2000
City Hall, New York City

Introduction

On September 19, 2000, New York City Public Advocate Mark Green convened a public hearing on the current status and future of the abortion pill mifepristone, more commonly known as RU-486.

Press and other reports suggest that RU-486 is on the verge of approval for use in the United States with potentially onerous, unprecedented restrictions imposed on its availability. The hearing was called to allow the leading medical and legal experts in the City and State of New York to go on the record regarding the safety, efficacy and availability of RU-486.

The testimony from the hearing demonstrates that: RU-486 is safe and effective; the need for RU-486 has not diminished since a decade ago when public health officials and abortion providers began trying to secure its approval and marketing rights in the U.S; a variety of health care professionals are qualified to provide medical abortion; and

increased anti-abortion activity and clinic violence make this not just a safe and early option for women, but vital to ensuring women's constitutional right to abortion.

Twelve medical and legal experts testified before a hearing panel made up of NYC Public Advocate Mark Green; Jo Ivey Boufford, M.D., Dean of the Robert F. Wagner Graduate School of Public Service at New York University; Allan Rosenfield, M.D., Dean of the Mailman School of Public Health at Columbia University; and Victor Sidel, M.D. Distinguished University Professor of Social Medicine at Montefiore Medical Center and Albert Einstein College of Medicine and President of the Public Health Association of New York City.

This document summarizes the testimony presented at the hearing.

Safety Issues: the Safety and Efficacy of RU-486

Eric Schaff, M.D., University of Rochester's Mifepristone Trials

Linda Prine, M.D., Family Practitioner and Planned Parenthood Abortion Provider

Carolyn Westhoff, M.D., Columbia College of Physicians and Surgeons, and the Mailman School of Public Health

Laura MacIsaac, M.D., Albert Einstein College of Medicine

The medical experts on the panel testified that there is vast and compelling evidence that RU-486 is both safe and effective as an abortifacient and that New York women who have used mifepristone are very satisfied with the experience and results. In addition to the half a million European women who have used the drug, rigorous clinical trials have been conducted in the U.S. These trials led the FDA to pronounce mifepristone safe and effective in March of 1996 and again in February of 2000.

Dr. Eric Schaff testified that since 1996 he has participated in six multi-center U.S. clinical trials of the mifepristone-misoprostal drug combination to terminate the pregnancies of more than 6,600 women. The trials found the two-drug intervention to be effective approximately 95% of the time when administered early in the pregnancy. Over 90% of the women in the trials found the procedure acceptable and would choose this method again if they were pregnant. Side effects from the drugs were common, but were acceptable to women.

New York women's experience tracks national statistics: 96% of women who were part of the U.S. clinical trials said they would recommend it to others and more than 90% said they would choose it again if necessary (Archives of Family Medicine, 1998).

Dr. Linda Prine addressed the proposed FDA restriction that would require that only doctors trained to perform surgical abortions be allowed to provide medical abortions for reasons of "safety." Dr. Prine is a family physician and also a surgical

abortion provider at Planned Parenthood of New York City, and spoke from experience. Family practitioners often initiate treatment for patients who in the end may need more specialized care. For example, a family physician may prescribe medication for a patient with heart pain. If more extensive treatment, such as surgery is needed later, the family practitioner refers the patient to a cardiac surgeon. Family practitioners deliver babies but may not be trained to perform caesarean sections; if a caesarian is necessary, the doctor would make a referral to an obstetrician/gynecologist. Knowing when to refer a patient to a specialist is a standard part of a family practitioner's medical training and routine. Medical abortion would be no different. Said Dr. Prine: "If the proposed requirement that medical abortion providers be trained in surgical abortion were applied to other areas of medicine, a primary care doctor would not be able to treat a patient for heart pain with medication or deliver a baby."

Dr. Carolyn Westhoff, Medical Director of New York Presbyterian Hospitals family planning and abortion services , has worked closely with Dr. Schaff throughout the clinical trials and agreed with his testimony. She rarely encounters emergencies with either medical or surgical abortion patients and believes that the rate of complications is very similar with either method of abortion. An additional study at her clinic of patient satisfaction with both surgical and medical abortion investigated how patients felt physically, emotionally and psychologically both before they underwent the abortion and several weeks to a month following. The results were similar for both abortion techniques. Medical and surgical abortion patients showed equal improvement immediately after and a month after abortions. "Therefore", said Dr. Westhoff, "I think

it is very important that we should all accept mifepristone as a great option for women to have as soon as possible."

Dr. Laura MacIsaac, an obstetrician/gynecologist in private practice, director of family planning and abortion services at Albert Einstein College of Medicine and former medical director at Planned Parenthood of New York City, gave her perspective as a busy clinician performing the full range of obstetrician/gynecologist services but being particularly well educated and skilled in the provision of abortion services.

One of Dr. MacIsaac's main concerns is that if the restrictions on mifepristone become unwieldy the entire benefit of giving her female patients the chance to make abortion choices early will be removed, at the risk of patient safety. The longer a woman waits to obtain an abortion, the higher the morbidity associated with the procedure. Dr. MacIsaac concluded: "The availability of mifepristone will change the whole dialogue about fertility awareness for the general obstetrician/gynecologist physician and her patients by encouraging women to make their pregnancy decisions early and by that virtue in itself, far safer than anything we do now."

Access Issues: Scientific Evidence Regarding Restrictions on Early Non-Surgical Abortion