HJR

58

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planned parenthood of alaska®

February 18, 1992

Representative Mark Boyer
State Capitol
Juneau, AK 99801-1182

Dear Representative Boyer,

Planned Parenthood of Alaska wholeheartedly endorses House Joint Resolution #58, which supports the introduction of RU 486 into the United States. We concur that this pharmaceutical agent should be available to physicians in the United States both for its properties as an abortifacient and as a potential treatment for cancer and other diseases. Women is this country deserve access to state-of-the-art medical treatment; the government has no role in preventing such access to its female citizens.

We commend your concern for women's health care and your introduction of this resolution. Planned Parenthood of Alaska would be more than happy to provide any support or assistance you may need to assure passage of this resolution. Please contact me or our Public Affairs Coordinator, Annalee McConnell, and let us know how we can assist you. We have recently received a grant to create a statewide pro-choice network of organizations in Alaska, and have received enthusiastic support from many groups. We will inform the network about your resolution, and hopefully they will also offer their support. I am enclosing a fact sheet from our national office regarding RU 486; please feel free to copy and distribute as needed.

Sincerely,

Donna Hurdle

Donna Hurdle, MSW
Executive Director

1008 West Northern Lights Blvd. • Anchorage, Alaska 99503 • (907) 561-8970

A United Way Agency

position papers.

ALASKA
CIVIL LIBERTIES UNION

POSITION PAPER

The Alaska Civil Liberties Union (AkCLU) supports passage of House Joint Resolution No. 58 (HJR 58).

The AkCLU supports the reproductive freedom of women. It also supports the health and welfare of women. The Union therefore seeks the introduction of RU 486 into the United States.

RU 486, approved for use in France in 1988 (in combination with a prostaglandin agent) and in Great Britain in 1991, has been placed under an import "alert" by the U. S. Food and Drug Administration. This alert has restricted the availability of RU 486 for scientific research in the U. S. In addition, in reaction to anti-abortion extremists, the French pharmaceutical company Roussel-Uclaf (RU), and its German parent company Hoescht A. G., have maintained tight controls on the release of RU 486 into the international medical community. As a result, to date, Rousell and Hoescht have not applied for a license to distribute the drug in the U. S.

Called a "contragestive" drug, derived from "contra-gestation," rather than a "contraceptive," derived from "contra-conception," RU 486 is a means of terminating **only** *very early pregnancies.* The action of RU 486, also known as mifepristone or mifegyne, closely mimics an early miscarriage and, for most women, resembles a heavy menstrual period. The body's natural hormone, progesterone, causes the maturation of the uterine lining which allows a fertilized egg to be implanted and then sustains its gestation. RU 486 appears to trick the uterine's progesterone receptors into reacting as if the hormone were present, thus blocking production of the true compound. Without progesterone, the lining of the uterus breaks down, as in normal menstruation, expelling the fertilized egg.

The effectiveness rate of RU 486 *drops sharply* after the first seven weeks of pregnancy, or up to three weeks after a woman has missed her period. After this time, the woman's own progesterone level is apparently too great to be affected by the drug.

The inventor of RU 486, Dr. Etiene Baulieu, stresses that the beginning of pregnancy is **not** a single moment in time, but rather a series of events. In the September 1989 issue of Science (vol. 245, p. 1356), he writes: "The continuum of the reproductive process includes meiosis before fertilization, implantation (a process taking several days), and several steps necessary for the proper development of the embryo." During this period, the female body naturally washes away an estimated 40% of fertilized eggs without the woman ever knowing. It is only when an embryo has fully implanted, and is on its way to becoming a fetus that full gestation -- or pregnancy -- has been established. RU 486 functions within this time period.

This process has granted women significant control over the termination of a potential pregnancy, particularly because it is non-invasive. The drug can be taken as soon as the woman discovers she has missed her period. She does not have to wait the seven weeks normally required of women seeking a surgical abortion. Nor does she have to risk the infections that sometime accompany vacuum aspiration, or suffer the local anesthesia commonly administered in the United States during aspiration.

In view of these facts, the American Medical Association (AMA) has endorsed introduction of RU 486 into this country. In addition, the AMA has recognized that the drug "may also be an important treatment for other indications, including treatment of breast cancer, gynecological malignancies, and labor induction." The list of other national and international organizations which support testing or clinical use of RU 486 is impressive.

What these organizations [along with the American Civil Liberties Union (ACLU) and its Alaska affiliate] have in common is a belief that it is unconscionable that a drug with so many significant benefits to women should be withheld from either use or testing in the United States by the ignorance or intolerance of others.

A concern of many is that this drug, while presently tightly controlled by its manufacturer, will eventually become the focus of black marketeers. It is only a matter of time before the drug is synthesized, duplicated, or smuggled out of France or England. Eventually RU 486 will be used in the United States, whether legal or not. Used improperly, or manufactured without the requisite tight controls, black market RU 486 could result in health problems for women forced to use the black market product.

It would be a travesty against women and their families if lives are lost when acceptance of this drug into the United States under normal research and development criteria would assure Americans of continued scientific progress and curtail the present inhibition of medical advancement in an area that promises far reaching results for a safer and healthier future for women.

Given that this drug works only at a very early stage of gestation, and in the face of overwhelming evidence to date from France of the safety and effectiveness of this drug, the AkCLU believes the current ban on its availability in the United States is deplorable and shocking. For these reasons, and others stated above, the AkCLU wholeheartedly endorses passage of HJR 58.

Dated: March 10, 1992

Sig: Randall P. Burns

Signed: Randall Executive Director

AMERICAN MEDICAL ASSOCIATION HOUSE OF DELEGATES

Resolution: 100
(A-90)

Introduced by: California Delegation

Subject: RU-486 Availability

Referred to: Reference Committee E
(Charles D. Sherman, Jr., M. D., Chairman)

Whereas, An antiprogesterone steroid, known as RU-486, has been developed and tested in Europe, and has been shown to be an efficacious and safe means of terminating early pregnancy when administered orally early in pregnancy by an appropriately trained physician; and

Whereas, The use of such a medication for terminating early pregancy constitutes a potentially significant medical and public health gain in terms of efficacy, safety, ease of use, cost and privacy of the physician-patient relationship; and

Whereas, RU-486 may also be an important treatment for other indications, including treatment of breast cancer, gynecological malignancies and labor induction; and

Whereas, Existing AMA policy holds that the early termination of pregnancy is a private medical matter to be decided between the patient and her physician, and AMA policy also does not prohibit abortion wherever legal and performed in accordance with good medical practice; and

Whereas, It is in keeping with basic medical standards to avoid surgical procedures whenever an equally effective non-invasive alternative is available; and

Whereas, The potential for a "black market" in RU 486 in this country is very real, with women's health activists already vowing to import the drug for use by American women, thus exposing them to the dangers of non-physician supervised use of the drug; therefore be it

RESOLVED, That the American Medical Association support the legal availability of RU-486 for appropriate research and, if indicated, clinical practice.

Fiscal Note: No significant fiscal impact

ORGANIZATIONS WHICH SUPPORT THE TESTING AND/OR CLINICAL USE OF RU 486 IN THE U.S.

(Partial list)

American Association for the Advancement of Science(AAAS)
American Association of Physicians for Human Rights
American Civil Liberties Union (ACLU)
American Institute of Biological Sciences
American Jewish Congress
American Medical Association (AMA)
American Pediatric Society
American Public Health Association (APHA)
Association of Reproductive Health Care Professionals
Earth Island Institute
Endocrine Society
Endometriosis Association
Feminist Majority Foundation
Fund for the Feminist Majority
International Planned Parenthood Federation (IPPF)
International Projects Assistance Services
International Women's Health Coalition
National Abortion Rights Action League (NARAL)
National Alliance of Breast Cancer Organizations (NABCO)
National Association of Nurse Practitioners in Reproductive Health
National Cushing's Association
National Organization for Women (NOW)
National Women's Health Network
National Women's Studies Association
Physicians for Choice, Los Angeles
Planned Parenthood Federation of America (PPFA)
Population Crisis Committee
Population-Environment Balance, Inc.
Society for Pediatric Research
Society for the Study of Reproduction
The Population Council
Women in Endocrinology
Zero Population Growth, Inc.

September 1991

Feminist Majority Foundation, 186 South Street, Boston, MA 02111 • (617) 695-9688, Fax (617) 695-9747

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Alaska State Legislature

Please enter into the record my testimony to the House HESS committee name

committee on HJR58: bill/subject, dated 3/11/92.

I most strongly support the effort to bring RU486 legally into the U.S. As a scientist, I feel we must get to the facts of this issue, not keep our heads in the sand.

If the drug is safe and effective it must be made legally and safely available to all. The potential of this new drug to treat a full range of ailments deserves to be explored.

Please move this bill, HJR58, on with recommendation to Do Pass -

Signed: _____
Testifier

Robert Jellis

_____
Representing (Optional)

Box 2966

_____
Address

Sitka AK 99835

_____
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the HESS committee name

committee on House Joint Resolution 55 bill/subject dated 3/11/92.

I feel this drug (mifepristone) should be Available to Anyone who needs it without the cost of traveling to France.

This would solve all questions regarding abortion, making it truly a private matter between a woman and her physician.

Since the drug is also useful For other purposes, it should be made available, even if only for these other uses, which are very significant.

Signed: Irene Shuler
Testifier

Representing (Optional)

Box 438
Address

Sitka, AK. 747-8615
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the House HESS
committee name

committee on HJR 58 . dated 3/11/92 .
bill/subject

please support the HJR-58 Resolution, making RU 486 available to any woman who wishes to use it. Please help end the tragedy of unwanted children. No choice makes sense. The legal status of all humans needs to be based on actually having been born - it's unreasonable for the rights of women to be lower than even those who are unborn - those people who believe in such fanciful theorys - should not be allowed to force their views on others who do not agree.

sincerely,
Joan Kilcup
Jerry Virchow

Signed: Joan Kilcup & Jerry Virchow
Testifier

Representing (Optional)
4251 H.P.R. Sitka
Address
747 6221
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the House Joint Resolution N.O 58
committee name

committee on HESS , dated ~~1-14-92~~ 3-11-92.
bill/subject

I support HJR 58. The drug mifepristone should be available to woman who choose it as it is an effective method of terminating a pregnancy during the earliest part of the term when termination can be done most safely.

In addition the potential for mifepristone being a promising treatment for breast cancer and other diseases is reason enough to pass this bill.

Signed: Theresa Heyburn
Testifier

Representing (Optional)

BOX 6310
Address

747-4808
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the HESS
committee name

committee on H.J.R. 58, dated 1-14-92.
bill/subject

I strongly urge the passage of this joint resolution - because of its significant medical value. Our thoughts should not be clouded by the abortion possibility in as much as it is a promising treatment for breast cancer. Remember our great loss of women's lives to breast cancer in this country.

Thank you,

Signed: Clothilde Bakewell
Testifier

Representing (Optional)

623 Oe Street Sitka
Address

747-8195
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the House HESS
committee name

committee on HJR58 , dated 3/11/92 .
bill/subject

I support HJR 58, to bring RU 486 into The United States.

Sincerely
Nancy Gustavson
1716 Edgecumbe Dr
Sitka, Ak. 99835

Signed: _____
Testifier

_____
Representing (Optional)

_____
Address

_____
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the House H.E.S.S.
committee name

committee on HJR 58, dated 3-11-92.
bill/subject

Please see attached (2) two-pages testimony.

Signed: Mary J. McNally
Testifier

Representing (Optional)

608 Sawmill Creek Rd, Sitka
Address

747-3877
Phone No.

I urge you to vote NO on Joint House Resolution No. 58. RU486 is a dangerous drug, which when used alone, has a "success" rate of only 80-85%. "Success" meaning a complete abortion. Not the 97-99% "success" rate of surgical abortions. Though this drug is touted as being one that women can take on their own, without the need of medical assistance, these figures would indicate that 15-20 women out of 100 would be required to seek additional medical attention to finish the incomplete abortion.

RU486 is not to be used alone and must be followed by an injection of a prostaglandin in order to achieve the desired "success" rate. There is presently no appropriate prostaglandin available in the United States and none is likely to be available in the near future. Those that are available are presently used for second and third trimester abortions and must be used by a licensed physician under stringent circumstances.

There are documented deaths of women who have taken RU486 and we must not allow women to take a drug that is potentially dangerous and even life threatening. Let us not rush into what seems to be the "answer" if legal abortions are outlawed in this nation. People are at a panic stage and are seemingly willing to ignore a real threat of harm just to keep abortion options available.

STOP! LOOK AT ALL THE FACTS! The evidence is not yet in on this drug and the drugs that must be administered with it to accomplish complete abortions. I believe we have been sold a "bill of goods" on the benefits, success and safety of RU486. Much additional research is needed to determine if this drug is safe

enough to allow women to use. There are no studies on the long-term effects on women, their ability to have children at a later time, nor on any children they may have in the future.

Please vote NO on this Resolution.

Submitted by,

Mary Jo McNally

Mary Jo McNally
608 Sawmill Creek Road
Sitka, Alaska 99835
747-3877

Alaska State Legislature

Please enter into the record my testimony to the H. H.E.S.S.
committee name

committee on HJR 58 , dated 3-11-92 .
bill/subject

March 11, 1992

Reference HJR58

I fully support the availability of RU486 and urge my legislators to take a stand in supporting RU486 for the State of Alaska.

Nancy E. Britton
721 A St.
Sitka, AK 99835
747-3568

Signed: Nancy E. Britton
Testifier

721 A St.
Representing (Optional)

Sitka AK 99835
Address

747-3568
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the H. H.E.S.S.
committee name

committee on HJR 58, dated 3-11-92.
bill/subject

I strongly oppose legislation that would allow testing of the Abortion Pill under HJR 58. I feel this is more detrimental to the mother than abortion. I am also strongly opposed to federal/state sanction of abortion in any way.

Signed: Beverly J. Fokke
Testifier

~~Date~~

Representing (Optional)

631 DeGroff Sitka, AK 99835
Address

907-966-2570
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the House HESS
committee name

committee on HJR 58 , dated 3/11/92 .
bill/subject

House Health, Education & Social Services
Juneau, Alaska

Greetings:

Sitkans for Choice strongly supports passage of House Joint Resolution No. 58, relating to the drug mifepristone (RU 486). The goals of Sitkans for Choice are to keep abortion safe, legal and accessible to all women regardless of age, marital status, or ability to pay. RU 486 would not only make terminations more accessible to all women but would be safer, less expensive, and certainly more confidential than aspiration abortions.

Sitkans for Choice would like to take this opportunity to thank Representatives Boyer, Brown, Finkelstein, and Ulmer for sponsoring this resolution.

Sincerely,

Ruth McKenzie

Ruth McKenzie
Sitkans for Choice
Box 2966
Sitka, Alaska 99835

Signed: _____
Testifier

_____
Representing (Optional)

_____
Address

_____
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the HESS
committee name

committee on HJR-58 , dated March 11, 1992 .
bill/subject

I am writing in support of HJR No 58 which supports the use of RU 486. I reject the opposition of this drug based on religious and political grounds The decision as to the use of this drug to abort pregnancy is the decision of the woman involved, regardless of age when administered by trained physicians.

Signed: William J. Brooks
Testifier

Representing (Optional)

1805 Sawmill Creek Road, Sitka, Alaska 99835
Address

(907) 747-3956
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the Hess committee name

committee on HJR-58 bill/subject, dated March 11, 1992.

I support Resolution No. 58 and the testing of RU486 in the U.S. The issuance of an import alert/ban against any drug ~~due~~ to political and or moral rationale is inappropriate and should not be part of our political process.

Signed: Jeanine Brooks (Jeanine Brooks)
Testifier

Representing (Optional)

1805 Sawmill Creek Rd. Sitka 99835
Address

907 - 747- 3956
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the Hess
committee name

committee on HJR-58 , dated March 11, 1992.
bill/subject

I support Resolution No. 58 and the testing of RU 486 in the U.S. I feel that it is a medically safe procedure for those women who need to use it to protect their lives and that this is useful medically for other medical purposes. If this ban is against the moral issue of abortion, then it is inappropriate.

Signed: Shirley Brooks
Testifier

Representing (Optional)

1805 Sawmill Creek Road Sitka 99835
Address

907-747-3956
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the H.H.E.S.S.
committee name

committee on HJR 58, dated 3-11-92.
bill/subject

Please See Attached Testimony.

Signed: Carol A. Lyskey
Testifier

Representing (Optional)

220 Lakeview Dr. Sitka AK 99835
Address

907-747-5923.
Phone No.

To: House and Health Social Services Committee Members.
RE: House Joint Resolution No 58.

I am strongly opposed to the legalization of the drug RU 486. There has been no long term testing for short and long term biological consequences for woman or future children. The FDA has not endorsed this drug. It is imperative that this dangerous drug is not introduced to the American public. In order to safegaurd our nations health.

Sincerely,

Carol A Hughey

Carol A Hughey.

Alaska State Legislature

Please enter into the record my testimony to the House HESS
committee name

committee on HJR 58 , dated March 11, 1992.
bill/subject

I do not support the use of the RU 486 drug. I do not agree with those who support abortion and especially through a dangerous drug like RU 486. I hope you will see others do not support this bill.

Signed: John T Morrison
Testifier

Representing (Optional)

114 B Darrin Sitka AK 99835
Address

747-5433
Phone No.

TO: House H.E.S.S. Committee

FROM: Robin Smith
Abortion Rights Project

We need to have RU 486 available in the United States. This drug has multiple health potentials, but what impedes this drug is its link to abortion.

As a society, we in America are sexually distressed. This can be seen in how we either obsess or ignore sexuality. As a result, we are sexually irresponsible. RU 486 offers a birth control option less wrenching than surgical abortion.

Until men as well as women become sexually responsible and until we can offer all children and their mothers social and economic security, we must offer alternatives. RU 486 is an option.

Just as men would not like government telling them to have vasectomies or compulsory castrations, we women do not want the government telling us what we can or cannot do to our bodies. Banning RU 486 is another way of restricting our freedom of choice and privacy.

Supporting the introduction of RU 486 is a progressive decision. We should join other world communities and make this promising drug available to the people of America. Don't deny this drug to those who can medically benefit from its many uses.

Thank you for considering my opinion.

14100 Jarvi
Anchorage, AK 99515

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Alaska State Legislature

Please enter into the record my testimony to the House HESS
committee name

committee on HJR58 , dated March 11, 1992.
bill/subject

Please attached

Testimony

Signed: Cathy Hazel
Testifier

Representing (Optional)

Box 1876, Sitka 99835
Address

Phone No.

3-11-92

To: House Rules Committee

From: Cathy L Hazel
Box 1836
Sitka, AK 99835

Re: RU486 / 92 hr pill

Committee:

This is to inform you of my opposition of any bill that would allow the 72 hour pill to be legally available in the United States.

There are several reasons why this drug should not be legalized in the U.S.

1. With the current controversy regarding abortion and the acknowledgement that this pill aborts approximately 72 hours after ingestion, this pill will be known as a contraceptive. Even though it is being advocated for victims of incest and rape, it is fairly certain to ascertain that the average female can and will use it as a means of birth control.

1 of 4

2. This drug should be subject to the standard testings and regulations before it is even considered for release to the American public. The FDA has the format & responsibility to do this. Would this step be eliminated? If so, why? It's availability should not be based on political pressure or special interest groups that want to leap frog the established system.

3. Morally, our constitution and government are founded and based on Godly principles. In the past our government has violated and ignored many of these principles. But not acknowledging them does not change these principles. Abortion is morally wrong and goes against the initial intent of our laws that govern the U.S. History has proved that men & women of integrity won't standing for what's morally right.

I appreciate your consideration of my argument. I sincerely challenge you to not allow this drug to

become legalized in the United States of America

Sincerely,

Cathy Hoseth

Alaska State Legislature

Please enter into the record my testimony to the House Health & Social Service committee
committee name

committee on House Jt. Resolution #58, dated 3-11-92.
bill/subject

TO: House Health & Social Service Committee Members
House Joint Resolution #58

I Am Strongly opposed to legalizing the drug RU 486 in the U.S. There have been no long term testing to determine the biological consequences on women. Evidence is showing that this is a very dangerous drug. "It's not nice to fool with Mother Nature."

Signed: Stephanie D. Viera
Testifier

Representing (Optional)

611 Broadway
Address

7473698
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the House HESS
committee name

committee on HJR 58, dated March 11, 1992.
bill/subject

LIO OFFICE TO: House Health & Social Services Committee Members

OPPOSE - HOUSE JOINT RESOLUTION No. 58
I understand the drug RU486 would cause an abortion at the woman's home. There has been no long-term testing for short and long term biological consquences for the woman or future children. Our Federal Food and Drug Administration opposes it. Evidence is accumulating that it is a dangerous drug.

Thank you.
Alene Henning

Alene Henning
Box 993
Sitka, AK
99835

Signed: _____
Testifier

_____
Representing (Optional)

_____
Address

_____
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the HESS (House)
committee name

committee on HJR 58, dated 3/11/92.
bill/subject

My name is Jeannette Chavez & strongly support House Joint Resolution #58, supporting the introduction of RU 486 into the United States.

The safety and effectiveness of RU 486 in terminating early pregnancy has been well documented, and the medical community has recognized its value and supports further research for other medical applications as well.

In the interest of public health, it is important that the medical and scientific communities be allowed to research the benefits of RU 486, free of political pressures from special interest groups.

Signed: Jeannette Chavez
Testifier

Representing (Optional)

Box 2722, Sitka, AK 99835
Address

747 6127
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the ~~House~~ HESS committee name

committee on ~~House Bill No. 58~~ bill/subject dated March 11, 1992.

I oppose the use of the drug RU486 due to the fact that I feel the full effects of this drug is unknown. I object to the American women being used for experimentation. I also oppose abortion and would ask that you ban the use of this drug.

Signed: Christine Horan
Testifier

Representing (Optional)

P.O. Box 2003 Sitka Alaska 99835
Address

747-6471
Phone No.

1.21

Alaska State Legislature

Please enter into the record my testimony to the House HESS
committee name

committee on HJR 58, HB28, dated 3/11/92.
bill/subject

I speak as a woman + registered nurse RU486 is a pandoras box to a womans body. It blocks the action of progesterone, but it is not limited to the womb. It also acts on the hypothalmic-pituitary-adrenal system, the respiratory system, + has unknown long range effects on metabolism. Death has occurred where the drug is legal!

Infants have been born with teratogenic anomalies incompatible with life. Should these infants survive, the "cost" to the state would be enormous. I mention "cost" not because it is an issue to me, but because it is the "main" issue to many pro abortionists.

Do you want AK women and children to become guinea pigs? Pro abortion women have strongly criticized RU486. FDA has not approved this drug. Please. Take no part in victimizing innocent women and children with a deadly poison, by telling us its safe, or legal, or effective!

Many of us did not get to testify today. Most of the speakers time was pro RU486. Many of us against RU486 were not heard. Please let us speak.

Signed: Mary A. Soltis
Testifier

Representing (Optional)
615 DeGroff

Address
747-5624

Phone No.

Alaska State Legislature

Please enter into the record my testimony to the House HESS committee name

committee on HJR 58 - R4486 bill/subject, dated 3/11/92.

The use of R4486 is dangerous, not only for the the unborn child but also for the women taking the drug. The absence of long-term data on the effects of this drug are alarming. Documentation of serious side effects such as nausea, vomiting, extensive bleeding, and life-threatening heart attacks are also alarming. Legislators who are truly concerned with the emotional, mental & physical health of the women of Alaska will not support the introduction of this dangerous drug into our country.

Signed: Shirley Demmert
Testifier

Representing (Optional)

316 Wortman Loop Sitka, Ak
Address

907-747-3196
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the H. H. & S. S.
committee name

committee on HJR 58 , dated 3-11-92 .
bill/subject

Please See Attached

Testimony

Signed: Charles Horan
Testifier

CHARLES HORAN
Representing (Optional)

BOX 2003, SITKA, AK
Address

747-6666
Phone No.

March 11, 1992

Testimony of Charles Horan
PO Box 2003
Sitka, Ak 99835
747-6666 or 747-6471

Abortion Pill Hearing HESS Committee

House Joint Resolution No.58 resolves that the Alaska State Legislature supports introduction of RU 486 into the United States. This drug is promoted as an easy safe alternative to surgical abortion. The Food and Drug Administration has not allowed it in the U. S. because it is not./ Their are two important factual reasons this pill should not be supported by our legislature.

The pill causes the destruction of a unique human life. This child within the womb has the same right to live a happy prosperous life just like you and I. The legislative endorsement of this destruction of human life devalues all human life. It lulls people involved in crises pregnancies into considering this life taking choice. The government's primary function is to preserve liberty and freedom. Without life there is no liberty no choice for this most innocent helpless member of society.

If the legislature chooses to abdicate its responsibility to preserve the child's life it should not endorse this method of abortion for the sake of the mother's health. The pill is not a simple procedure. It is usually administered by a doctor, it causes premature birth and it occasionally fails. If the child survives she or he has a high risk of sever deformities. Complications to the mother include nausea, vomiting, extensive bleeding, and life threatening heart attacks. To increase the effectiveness of the drug to abort the child the drug prostaglandin is often taken later. This drug causes further complications. The book RU 486: Misconceptions, Myths and Morals by three self proclaimed abortion advocates has criticized the "cocktail drug" for its harmful effects on women urging that it be removed from the market immediately.

If you are concerned about the safety of our smallest Alaskans and the welfare of their mothers please withdraw your support for this resolution.

9.f3

Alaska State Legislature

Please enter into the record my testimony to the House HESS
committee name

committee on HJR 58/ RU 468 , dated 3/11/92
bill/subject

As a medical professional and a woman I urge this committee and the legislature to pass HJR 58. RU 468 is a drug of significant medical value as attested to by its use in France as well as the U.S medical professionals and scientists supporting its use in this country. The FDA is not a scientific body but a bureaucratic body that is swayed by the current President's views as well as those of a small minority of the population. I thank the sponsors for having the foresight to introduce this legislation

Signed: Ruth E McKegie
Testifier

Representing (Optional)

Box 1922, Sitka, Alaska 99835
Address

747-6819
Phone No.

9/86 Legislative Information Office

1 of 1

Alaska State Legislature

Please enter into the record my testimony to the House HESS
committee name

committee on HJR 58 / RU486, dated March 11, 1992.
bill/subject

I wish to testify in favor of HJR 58, concerning RU 486.

Most discussion I have heard at this teleconference has focused on the polemics regarding the abortion issue. Some support a woman's right to choose, and others oppose it.

Although related to the abortion issue, the research on and approval of RU486 is really a medical issue. Abortion is still legal in Alaska and the US, and women therefore have the right to medical alternatives to the current abortion technology. In addition, RU486 has potential medical benefits beyond its abortifacient use which merit research. Please pass HJR 58.

Signed: Kathleen Wrabetz
Testifier

Representing (Optional)

Box 2891, Sitka, AK 99835
Address

747-3654
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the Health & Social Services
committee name

committee on House Joint Resolution #58 dated March 11, 1992.
bill/subject

I am testifying not from my own expertise but from the report, "RU 486: Misconceptions, Myths and Morals," by Janice G. Raymond, Renate Klein and Lynette J. Dumble published by the Institute on Women and Technology at the Massachusetts Institute of Technology.

This report is too extensive for me to quote completely but it is noteworthy that #1 they consider themselves feminists and are actively pro-abortion and #2 it offers documentation that there is clear evidence of severe adverse complications upon using RU 486 - specifically- its action is not limited to the womb but also acts on the hypothalmic-pituitary-adrenal system and the respiratory system.

If the position that RU 486 is not acceptable in the State of Alaska for the sake of unborn children then I hope you'd seriously consider the liability and ramifications on the women of our state, many who are already in tenuous health care situations

Signed: Carolyn Ohmer
Testifier

Representing (Optional)

2414 HPR, Sitka, AK 99835
Address

747-6732
Phone No.

TELECOPY COVER SHEET
Ketchikan Legislative Information Office
Office - (907) 225-9675 Fax - (907) 225-8546

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FROM: Susan Gass R.N. - 719 Grant St. Ketchikan PHONE: _____

INSTRUCTIONS: testimony & magazine article on HJR 58 (T/c 92-03-042)

SENT: Date 3/11/92 Time 10:25 am

DISPOSAL OF ORIGINAL: Discard _____ Hold for Pickup _____

NUMBER OF PAGES: 3 (NOT counting cover sheet)

TRANSMITTED BY: Rae

the trouble with RU 486

The new French pill is supposed to make abortion easier and safer, cure a host of diseases, *and* make protesters shut up and go home. But as SUSAN INCE reports, there's a lot wrong with this picture

THE NEW REPUBLIC HEADLINED ITS STORY "DRUG OF Choice." The *National NOW Times*'s read "RU 486 Spurs Global Feminist Solidarity." *The Boston Globe*'s was "A Pill Whose Time Has Come."

The headlines are typical of the yearlong media blitz on RU 486. Abortion in France, we're told, has become as easy as taking a pill—safe, quick, and private. American women would have this option, too, if only the drug's French manufacturer and the U.S. Food and Drug Administration could be persuaded to ignore this country's vehement antiabortion protesters.

Thousands have rallied to bring RU 486 to the United States. Touting the drug for a dizzying range of possible uses—as a treatment for everything from breast cancer to AIDS—the American Association for the Advancement of Science adopted a pro–RU 486 resolution at its February meeting. The Feminist Majority Foundation has dumped hundreds of pounds of petitions on the pharmaceutical company, Roussel Uclaf. New York City's mayor, David Dinkins, has appealed directly to President Bush. *People* magazine and *Vanity Fair* have profiled RU 486's beleaguered inventor, Etienne-Emile Baulieu.

For many of the drug's enthusiasts, RU 486 provides a way to end the wrangling over abortion once and for all *and* make abortion more accessible. "How could a state control swallowing?" asked syndicated columnist Ellen Goodman. Eleanor Smeal, past president of the National Organization for Women and founder and president of the Feminist Majority Foundation, says that RU 486 profoundly changes the nature of the abortion debate. The drug would make picketing abortion clinics "meaningless," she says. "RU 486 works so early that it is much closer to a contraceptive than to traditional abortion. And the American people overwhelmingly support contraception."

To be pro-choice, it seems, means embracing RU 486. But not every pro-choice advocate is buying it. This month the Institute on Women and Technology, based at the Massachusetts Institute of Technology, will issue a one-hundred-page review of the scientific literature on RU 486. The report suggests that much of what is commonly believed about the French pill is simply wishful thinking.

"Claims that RU 486 abortion is private and demedicalized are belied by the number of medical visits and the whole drug cocktail a woman may be exposed to," says Janice Raymond, associate director of the Institute on Women and Technology and the report's coauthor.

In France, abortion with RU 486 is neither easy nor private. It's a tightly structured four-step regimen, and the pill's maker says it won't export the drug to countries that do not control the drug's use in a similar way. Here's how it works:

Visit 1: After a pregnancy test and dating of conception (the cutoff for use of the drug is forty-nine days after the last menstrual period), the woman undergoes a blood test, a pelvic exam, and often an ultrasound exam via a probe inserted into the vagina.

Visit 2: After a one-week waiting period required by French law, three RU 486 tablets are registered under the woman's name; she takes them in the specially licensed clinic and then leaves. The drug begins to block the action of progesterone, a hormone essential to the maintenance of the uterine lining.

Visit 3: Thirty-six to forty-eight hours later, a second drug, a synthetic prostaglandin, is injected to induce uterine contractions and shedding of the uterine lining. The woman stays in the clinic for about four hours so that doctors can monitor and treat any side effects (most commonly pain, nausea, vomiting, and diarrhea). Pain medications are often required, as are antibiotics to fend off possible infections. Three out of four women abort while still in the clinic; others return home to wait.

Visit 4: Seven days later, the woman visits the clinic again to be certain that the abortion is complete and to have her bleeding monitored (bleeding can last from three to forty-four days). If the drugs have failed, a surgical abortion is scheduled; this happens about once every twenty times. (In vacuum aspiration abortion in the

United States, fewer than one in two hundred women require a repeat procedure.)

Total cost? With all the clinic visits added to pill costs, slightly *higher* than surgical abortion—although in France, both methods are largely subsidized through the national health service.

Roussel Laboratories' own data support the view that RU 486 abortion isn't as simple as most people think. Last September the company applied for drug approval in the United Kingdom, submitting a dossier that included these findings: out of 950 women followed, 907 had complete abortions, most of them in the clinic in the three to four hours after prostaglandin was administered. Two hundred seventy suffered pain so intense that narcotics were required; another 280 used less-powerful painkillers. Two hundred seventy-six women suffered vomiting; 106 had diarrhea. Forty-three failed to abort and had to start over with a traditional abortion. Seven lost so much blood a transfusion was needed.

Using RU 486 in France is neither easy nor private. And it costs more than surgical abortion

In March the post–RU 486 prostaglandin injection sent a thirty-one-year-old French woman, a one-pack-a-day smoker, into cardiovascular shock. She was dead within an hour.

"That death was tragic," says MIT report coauthor Lynette Dumble, "but it shouldn't have come as a surprise. Prostaglandins were at one time used alone to induce abortion, but the pain and the number of deaths were considered intolerable. They've just added a new drug to a failed drug and told us how lucky we are."

Prostaglandin plus RU 486 had already caused life-threatening heart trouble in two other women in France, and after the recent death, the health ministry barred smokers and women over thirty-four from taking the drug. Women with circulation problems, bronchial asthma, high blood pressure, fibroids, glaucoma, ulcers, colitis, anemia, or gynecologic infections, and women who have had a recent cesarean section, are also advised to avoid RU 486. "That's a hell of a long list, and some of these conditions are fairly common, even in young women," says Merceth Turshen, associate professor of public health at Rutgers University in New Brunswick, New Jersey. "What's certain is that this is not a benign pill that can be taken in the privacy of your own home."

The same week that the RU 486/prostaglandin death made the international news, Baulieu told the French Academy of Science that he was already testing an alternative prostaglandin. In early studies, a prostaglandin pill called misoprostol (sold under the commercial name Cytotec) seemed just as effective as the original combination and less likely to cause side effects.

But Dumble, director of transplantation research at the University of Melbourne, Australia, isn't comforted. She has used Cytotec to suppress the immune system in transplant patients. The abortion dosage is many times higher, and she worries that even one-time use could result in long-lasting immune-system and fertility problems that may not be obvious in short-term studies.

RU 486 itself may have a greater impact throughout the body than has been discussed. Besides blocking action of the hormone progesterone, it blocks receptors for cortisone—a hormone produced by the adrenal glands that regulates sugar and protein metabolism, helps maintain blood pressure, and protects the body from physical stress. Raymond suspects that some of the quirkier RU 486 side effects that show up in the medical literature—extreme thirst, fainting, mood changes, fatigue—may be related to RU 486's effect on the adrenal and pituitary glands.

The drug would certainly have to work far beyond the uterus in order to deliver on even a fraction of the potential uses that proponents are talking about. When RU 486 promoters testified before a House subcommittee last November, the list of potential uses was as long as that for Lydia Pinkham's tonic: the drug, it was claimed, could save lives by halting the growth of hormone-dependent tumors in the breast and the brain; treat AIDS, Cushing's disease, diabetes, glaucoma, hypertension, and prostate problems. Don't want pregnancy? RU 486 could be more than an early abortion pill: it could be a contraceptive or an adjunct to traditional suction abortion. Want to have a baby? It might reverse infertility and endometriosis, induce or hasten stalled labor, prevent the need for cesarean sections, and boost milk production after delivery. Not concerned about pregnancy? How about relief from irregular periods, PMS, or postmenopausal complaints? Or stress-related illness, obesity—even the symptoms of aging?

Chances are good that RU 486, like other hormone blockers, *will* prove to have significant medical value. Roussel Uclaf is now finishing designs for large studies to test RU 486 as a breast cancer or brain cancer treatment. But we're a long way from knowing much about the drug's other effects.

"To anyone familiar with the history of DES and estrogen replacement therapy," says MIT's Janice Raymond, "the claims have the all-too-wondrous ring of promise later turned peril. How many times have we been told that this or that drug will save us?"

Until supplies ran out in February 1990, David Grimes, a professor of obstetrics and gynecolo- ▶ 90

gy and preventive medicine at the University of Southern California, conducted trials on RU 486 (unlike most other researchers, without using prostaglandin). He looks forward to the day when abortion drugs will be available over the counter—perhaps even packaged along with early-pregnancy tests. Grimes loves old movies, and he likes to recount an old Groucho Marx exchange whenever doubts are raised about RU 486:

"Say, Groucho, how's your wife?"

"Compared to what?"

Says Grimes, "Sure, I'd love to have a medication with no side effects, but we never will. Let's assume that you're in remote Bangladesh. If RU 486 carries a 1 percent incidence of serious bleeding, I'm concerned about that—but the incidence might be 20 or 30 percent for women trying to abort using a stick. You have to look at the alternatives."

Abortion with RU 486 is a tightly structured four-step regimen

How realistic an alternative is RU 486 in underdeveloped areas? The safest current method in Bangladesh, to use Grimes's example, is menstrual regulation, a suction technique performed by local paramedics. "If a woman hasn't been able to get to these existing local services, will RU 486 really be able to reach her?" asks Joan Dunlop, president of the International Women's Health Coalition, a group involved with eighty third-world reproductive health programs. "It's a fantasy to think that a woman will be able to make four trips to a clinic, walking five or ten miles each trip."

And RU 486 can't make abortion legal. According to Paul Van Look of the World Health Organization, most deaths from abortion occur in countries where it is illegal. He thinks RU 486 holds promise in only a handful of developing countries (notably the two largest, China and India) where surgical abortion facilities do exist but suffer from overcrowding. RU 486 could be used to handle the demand; when the drug failed, abortion clinics could provide the necessary backup.

Applying the "compared to what" test may help explain the allure of RU 486 in Western Europe. In France, for instance, *contraception* has only been legal since the seventies, and abortions are done under very different circumstances than in the United States. "French women are comparing RU 486 with the experience of undergoing general anesthesia and surgery," says Judy Norsigian, codirector of the Boston Women's Health Book Collective. "They talk about the benefits of being conscious, which don't really apply in the United States."

In the United Kingdom, bureaucratic gridlock at the National Health Service means that it's not unusual for women to wait five weeks for an abortion. As in France, abortions are usually performed in hospital operating rooms, using general anesthesia; more than 40 percent of women spend at least one night in the hospital. RU 486 would not only save the NHS an estimated ten to fifteen million pounds a year, it could prod it into giving better service to everyone. Jane Roe, coordinator of Britain's Pro-Choice Alliance, also hopes that RU 486 will make a big difference in the campaign for abortion on request. British law now requires two doctors to certify that an abortion is needed for health reasons.

In the United States, RU 486 has come on the scene at the same time that political pressures are threatening all kinds of scientific research. The government has already halted fetal tissue research. In 1989 the FDA issued an RU 486 import alert, which doesn't prohibit research but is said to have stalled many U.S. scientists. This spring Congressman Robert K. Doman of California introduced legislation that would ban the drug outright.

"Where will it stop?" asks Eleanor Smeal. "If we can't do research on any medication that could damage a fetus, that's the end of research on cancer in women."

The promise of RU 486 has also emerged just as abortions have become harder to obtain in this country—because of Medicaid restrictions, the Supreme Court's *Webster* decision, and state laws demanding that women notify their parents or spouses before having an abortion. Since 1977 the number of physicians performing abortions in rural areas has dropped by half.

But would RU 486 really improve access to abortion for women in the United States? "Let's face it—how many women don't get a Pap smear every year?" asks Naima Major, acting executive director of the National Black Women's Health Project in Atlanta. "Could they really see a doctor just after they miss a period, and arrange work and child care to make four clinic visits? Women who would have the least access would be women of color, women who rely on public funding, and women in rural areas."

Janice Raymond has this recommendation for people who want to ensure safe and accessible abortions for every woman who needs one: "Don't focus on an unproven drug," she says. "Push for less medical control over the whole abortion procedure." Vermont and Montana, she points out, allow physician's assistants to perform first-trimester suction abortions. In Vermont these practitioners are already performing one-third of the state's abortions.

How does this compare with the alternatives? Very well indeed. A study in Vermont showed that the practioners' safety records beat not only that of RU 486—they beat the national standard for abortion performed by doctors. ●

10 March 1992

House HESS Committee
Georgiana Lincoln, Chair
Alaska State Legislature

Re: House Joint Resolution 58 - RU 486

I strongly support this resolution to bring RU 486 into the United States. Then it can be tested and treated as any other drug. I believe the issue is: will we have the drug tested and administered under FDA regulations and with the full participation of the medical and scientific community, or will we have women self-dosing with questionable drugs obtained on the streets?

Enclosed is a copy of an article on RU 486 from the journal SCIENCE, the journal of the American Association for the Advancement of Science.

Stating that RU 486 is the moral property of women, the French Health Minister told Roussel, the pharmaceutical company that developed RU 486, that he "could not permit the abortion debate to deprive women of a product that represents medical progress".

We must let women make the choice. We must let doctors and pharmaceutical companies use their resources and skills to help them. We must NOT allow a strident minority of zealots to prevent the testing and possible use of a drug that has promise not only as an inducer of early abortion without surgery, but also for the treatment of a number of other human medical problems, including Cushing's Syndrome, glaucoma, breast cancer, meningiomas, inducing labor, and a contraceptive which prevents ovulation.

Thank you for your attention. Please move HJR 58 with a DO PASS recommendation.

Sincerely,

Natasha I. Calvin

Natasha I. Calvin
P.O. Box 2966
Sitka, Alaska 99835
747-8950

encl.

The Pill of Choice?

RU 486 is sweeping France, replacing surgery for abortion. But protests are restricting its use, a particular hardship for developing countries where the drug could save lives

FOR A DRUG not yet a decade old that most people have never heard of, RU 486 is causing quite a ruckus. In scores of research laboratories, molecular biologists are arguing about how it binds to steroid receptors; in government health ministries, bureaucrats are debating whether to license it for use; in the boardrooms of a number of powerful corporations, executives are arguing over whether to risk marketing it. But there is one thing no one argues about: RU 486 taken in conjunction with prostaglandins is an extremely effective method of terminating pregnancy within the first 9 weeks of gestation. And that means that RU 486 could change the context of the debate over abortion and birth control.

The development of RU 486 is a case study in how the forces of biomedical research and public policy occasionally collide. From the start, groups opposed to abortion under any circumstances were calling RU 486 the "death pill," and they have been largely responsible not only for keeping the drug out of this country, but also for intimidating researchers interested in exploring the myriad potential medical uses for the drug.

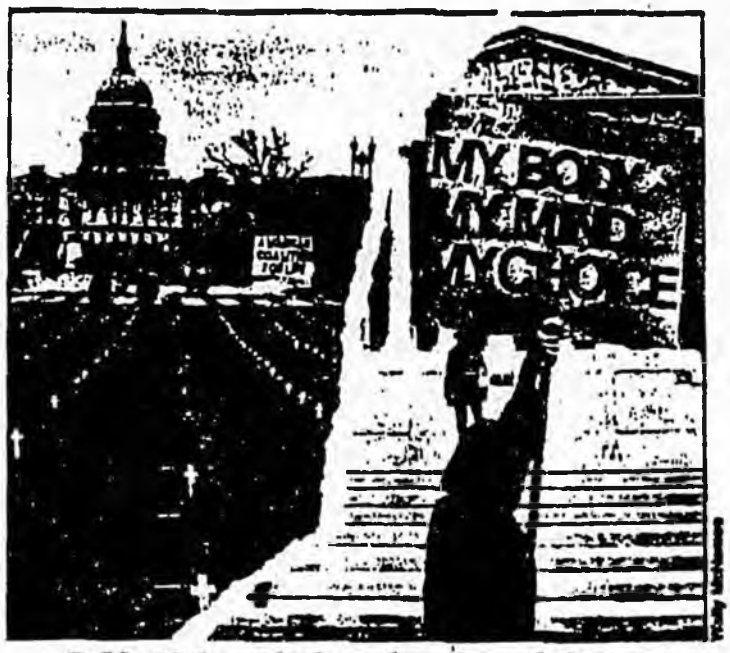
Why should anyone care about an abortion pill, at least in industrialized nations where abortions have become quick, safe, and relatively inexpensive procedures?

The significance of RU 486 for developed countries is not that it is measurably safer or more effective than up-to-date surgical methods but that it can be used in relative privacy. Women seeking early abortions could be treated by their regular doctors and not be forced to visit abortion clinics where protestors may be demonstrating outside.

It is not surprising, then, that RU 486 is viewed with alarm by antiabortion groups. They have good reason to worry: In France, approximately 25,000 have chosen RU 486 over surgery for abortion in the past 11 months since the government decreed that it be made available on an experimental basis.

So far, however, France is the only country in which RU 486 is widely available. The company that manufactures it has been unwilling to permit the drug to be sold anywhere else. And this is threatening to touch off a counterattack from "pro-choice" advocates frustrated at being denied what they see as a prizewinning breakthrough in the technology of reproductive medicine.

The sluggishness with which RU 486 is being brought to the market around the world is also a source of immense frustration to its chief developer, Etienne-Emile Baulieu, one of France's leading scientists (see p. 1323). Baulieu developed RU 486 in the late 1970s while retained as a consultant by the French pharmaceutical company Roussel-Uclaf, a subsidiary of the giant German company Hoechst AG. He has been one of the most outspoken crusaders for the drug, pointing out at every opportunity that it could save thousands of lives. He's not just hyping his own work: Mahmoud Fathalla of the World Health Organization (WHO) says, "the figures are alarming. Possibly 200,000 die every year. In some countries almost 50% of the maternal mortality is due to unsafe abortion."



RU 486 and the abortion debate: "It creates a whole new playing field."

The French experience. Although the French government has agreed with Baulieu that women should have access to his drug, RU 486's road to market has been anything but smooth. Health officials gave Roussel permission to begin sending RU 486 out to registered abortion clinics on 23 September 1988. But just 1 month later Roussel decided to suspend distribution of the drug for reasons that even today are not completely clear. In France the abortion debate has not been as vociferous as in the United States, but it has not been without passion. Roussel executives say that the company had received threats of bomb attacks for its plans to market the drug. But Roussel medical director André Ulmann says threats weren't the main reason Roussel withdrew the drug: "At the maximum we received 400 letters, which is nothing."

Profits may have been more important than personal intimidation in Roussel's decision. Some within the company have suggested that boycott threats were influential. Antiabortionists and Catholic hospitals served notice that they would stop buying any product made by Hoechst or its international subsidiaries if the company continued

The Story of RU 486

The article that begins on this page describes clinical experience with RU 486 in France and the debate over its use.

- How the drug works: page 1320.
- Research on medical uses other than abortion: page 1322.
- How it was discovered: page 1323.
- The scientific issues—an article by Etienne-Emile Baulieu: page 1351.

Stopping the Process of Pregnancy

RU 486 works by blocking the normal action of the hormone progesterone during pregnancy. In the first half of a woman's ovulatory cycle, estrogens secreted by the ripening egg follicle (prompted by hormones from the brain) cause the wall of the uterus to start thickening. Near the middle of the cycle, when estrogens are at their peak, a surge of the hormone called luteinizing hormone cues the follicle to release its egg. The cells left behind form the corpus luteum, which secretes progesterone. Progesterone prepares the womb for pregnancy.

In the preparation process, known as decidualization, the lining of the womb becomes thicker and the blood supply to it increases. An embryo will typically attach to the uterine wall about 2 weeks after the egg has been fertilized. After 14 days, unless a fertilized egg implants in the womb, the corpus luteum disintegrates, the level of progesterone drops, and the lining of the womb is expelled.

If there is an embryo, cells around it secrete a hormone called human chorionic gonadotropin, which rescues the corpus luteum, keeping it active and secreting progesterone. As a result the cells lining the uterus, called the endometrium, stay in place and accept the implantation of the embryo. After about 9 weeks the placenta takes over the manufacture of progesterone from the corpus luteum and keeps the level of the hormone high. High levels of progesterone, among other effects, suppress the brain hormones responsible for triggering a new cycle of ovulation, one reason why no further eggs are produced during pregnancy.

Progesterone causes decidualization of the endometrium by directly affecting the transcription of specific genes in the nucleus. Etienne-Emile Baulieu has investigated two of the most important links in the chain of communications between the hormone and the genes. One is the receptor itself. The other is a so-called heat shock protein. (Cells react to being heated to 40° or 41°C, instead of the normal 37°C, by shutting down protein synthesis. A few anomalous proteins, the heat shock proteins, increase instead of decrease when the cell is stressed, and one of these heat shock proteins is an essential component of the progesterone receptor system.)

In normal activation, progesterone (P) changes shape of receptor, releases heat shock protein (HSP), begins DNA transcription.

RU 486 blocks entry of progesterone; heat shock protein remains in place.

According to the presently accepted model, the heat shock protein binds to the receptor and blocks off a region of the receptor that would otherwise connect with areas on a cell's DNA called hormone response elements. When progesterone enters the cell, it also binds to the receptor and, in the process, it changes the shape of the receptor in a way that frees the heat shock protein. This allows the receptor-hormone complex to bind to the hormone response elements on the DNA. That step, in turn, alters the DNA so that the genes controlled by progesterone can be transcribed.

RU 486, like progesterone, binds to the receptor but does not release the heat shock protein. Indeed, the heat shock protein may become even more tightly bound to the receptor. As a result, the receptor is unable to bind to the hormone response elements, and no transcription of the DNA takes place. RU 486 occupies the receptors, preventing progesterone from binding to them, and any processes that depend on progesterone, such as the maintenance of pregnancy, fail. —J.C.

to market RU 486. But others say the company was anxious to appear as the unwilling debutante, being forced by its government to go forward with a controversial product.

In any case, forces favoring the drug mounted an economic threat of their own. Doctors at the World Congress of Obstetrics and Gynecology meeting that month in Rio de Janiero also threatened to boycott Hoechst products if the company did not make the drug available. Baulieu himself harshly condemned Roussel's decision at the congress and in numerous press interviews.

In the end, it fell to French health minister Claude Evin to change Roussel's corporate mind. Using the French government's 36% stake in Roussel-Uclaf as leverage, Evin threatened to transfer Roussel's patent to another company, something French law allows. He told Roussel that he "could not permit the abortion debate to deprive women of a product that represents medical progress. From the moment government approval for the drug was granted, RU 486 became the moral property of women, not just the property of the drug company."

On 28 October Evin announced that the company had agreed to start supplying the drug once again. The results have been impressive. Roussel has distributed about 150 to 200 treatments per day. RU 486 is being used for between a quarter and a third of all pregnancy terminations in France.

The treatment consists of three 200-milligram pills of RU 486, followed 48 hours later by a small amount of prostaglandin, either as an injection or a pessary. RU 486 blocks the normal action of progesterone on the cells lining the uterus to accept and sustain an embryo through development (see box, left) and the prostaglandin helps encourage the womb to contract and expel its contents. Approximately 96% of women receiving the two drugs within the first 9 weeks of conception have a complete abortion within a day of receiving the prostaglandin. In about one case in a thousand bleeding is sufficient to require a transfusion. Minor pain, cramps, and nausea are the reported side effects, but these are indistinguishable from heavy menstruation.

These results are mirrored in numerous small trials around the world. Other countries have completed the tests necessary for licensing RU 486, but Roussel's parent Hoechst has been unwilling to market the drug outside France. In Britain David Baird, professor of reproductive endocrinology at Edinburgh University, coordinated a multicenter trial involving more than 1000 women at 13 hospitals and clinics and handed the results to Roussel in November 1988. He says Roussel has been dragging its heels

over applying for a product safety license in the United Kingdom. Roussel has also withdrawn an application for a license in Holland.

Illegal markets? Will the success of RU 486 in France prompt a black market in countries where the drug isn't available? Clearly Roussel is concerned about this possibility.

"If the drug becomes available for England," says Ulmann, "and not for the U.S., it is clear that one way or another there will be a black market." Illegally obtained pills used improperly—but nevertheless bearing Roussel's trademark—could become a corporate nightmare if they caused injury or death.

But can Roussel keep control of the drug's destinations to prevent a black market developing? At present RU 486 goes directly from Roussel to the clinics where it is made available to physicians free of charge. But in a matter of weeks Roussel plans simply to make RU 486 available through its normal wholesalers. The company is currently negotiating with health officials in France over the price.

A black market might be supplied by doctors receiving the treatment from Roussel. Or it could come from other sources. "You can find Korean or Hungarian chemists who can synthesize [RU 486] very well and put it on the market," Ulmann points out.

"There will be a black market eventually," agrees Marie Bass, a Washington lobbyist on reproductive rights issues. "I can't imagine that there wouldn't be. And then we have to worry that [RU 486] will be misused."

The potential for misuse will not be limited just to pills obtained on the black market, however. If the drug does become legally available by prescription from pharmacies it is probably inevitable that it will be improperly used. "The problem that I foresee with . . . home use is the adolescent who is, in her own mind, still a virgin until she is 4 months [pregnant] and can no longer fit into her blue jeans," says Sharon Kamp of the Population Crisis Committee. "If [adolescents] were to get their hands on this and try to use it at 4 months' pregnant, it might have some serious consequences."

The U.S. debate. But for the present, there is no chance that RU 486 will be available legally in the United States. Both RU 486 and the prostaglandin that must be taken with it lack approval from the Food and Drug Administration. "A U.S. protocol in my estimate would take 3 years to complete if it started today," says Sheldon J. Segal, director for population sciences at the Rockefeller Foundation.

Jeremy Charles

"If the drug becomes available for England and not for the U.S., it is clear that one way or another there will be a black market."

—André Ulmann

There have, however, been clinical trials of RU 486 as an abortifacient in the United States. The University of Southern California (USC) has given the drug to some 400 women in a variety of doses at different stages of pregnancy. But Segal says drug registration trials would require testing a particular dose at a particular regimen, so the USC experience may not be directly applicable to licensing the drug in this country.

Because surgical abortion has been legal and widely available in the United States, there has been little grass-roots pressure to get RU 486 approved here. But this year's Supreme Court decision in the case of *Webster v. Reproductive Health Services* may dramatically increase interest in the drug. By signaling that it was prepared to place legal limits on the rights to an abortion granted in the landmark *Roe v. Wade* case, many "pro-choice" groups fear the Supreme Court may go further in subsequent cases.

"There was fairly strong support for the drug as a technological advance even before *Webster*, and I think that people are seeing it as even more important now," says David J. Andrews, executive vice president of the Planned Parenthood Federation of America. If states start to restrict abortion services—as some of them are likely to do in the aftermath of *Webster*—that would enhance the need for easy alternatives to surgical abortion, according to Andrews.

Pro-choice supporters feel RU 486 will change the very nature of the abortion debate. "I think it creates a whole new playing field and it is likely to undermine to a very great degree the strength of the antiabortion movement," says Kamp. "If you were able to make abortion something that is entirely private . . . the tactics of the antiabortion movement would have to change. Who are they going to picket?"

To stop what they call "chemical war against babies," organizations like the American Life League and the National Right to Life Coalition have enlisted the support of sympathetic congressmen in making access to the drug as difficult as possible. It is currently illegal for the National Institutes of Health to support any research on abortifacients such as RU 486, although NIH has studied the drug for other medical uses. But normally voluble scientists at NIH are uncharacteristically cautious when talking about research on RU 486. "They've suffered a kind of chilling effect," says Rockefeller's Segal. "They're scared to death of the threats against anybody who does anything with this drug."

NIH isn't the only institution that's nervous. Marcia Lacarra, a nurse and family planning counselor at USC's Women's Hospital where RU 486 is being tested, absolutely refuses to discuss what USC is doing with the drug. "We're tired of getting threatening letters," says Lacarra.

The Bush Administration, like the Reagan Administration before it, has gone along with the restrictions on the drug sought by conservative legislators. As recently as 9 June this year, FDA Commissioner Frank E. Young wrote to Representative Robert K. Dornan (R–CA) assuring him that FDA would not permit RU 486 to be imported into the United States for personal use, something the FDA has allowed for certain other unapproved drugs.

The developing world's needs. The United States has also used its political clout to try to slow testing of the drug by the WHO. The United States does not give financial support to WHO's special program on human reproduction, and observers say the WHO's Director General Hiroshi Nakajima fears that they will stop supporting other WHO programs if WHO continues its research on RU 486.

But WHO is continuing its research program, expanding it to include ZK98734, a drug that acts in the same way as RU 486, made by Schering AG. WHO program officer Paul Van Look says the agency's goal is to find abortion protocols that would not require a second visit to the clinic. RU 486

Hormone Antagonist with Broad Potential

Although medical research has focused primarily on RU 486's usefulness as an abortifacient, researchers at scores of labs around the world are quietly investigating other potential applications of the drug.

At the U.S. National Institutes of Health, George Chrousos has been using RU 486 to treat patients with Cushing's syndrome, a condition resulting from excess production of cortisone. Since RU 486 blocks not only the progesterone receptor but also glucocorticoid receptors, it counteracts the effects of the excess cortisone. Chrousos says that Cushing's syndrome, which effects about 500 people each year, can be caused by a tumor in the adrenal cortex that can't be detected when it first arises. RU 486 can be used to keep patients alive until the tumor becomes large enough to be isolated and surgically removed.

RU 486 also has a role in basic research on how the glucocorticoid receptor works because it binds to the receptor with such high affinity. Using RU 486, researchers can block receptor activation at different stages: from when it first binds to the hormone to when it turns on genes in the cell nucleus.

At Tufts University Health Sciences Center in Boston, ophthalmology chairman Bernard Schwartz has experimented with RU 486 in eyedrops as a treatment for glaucoma, a condition characterized by increased pressure within the eyeball that can cause blindness. Schwartz says glaucoma patients have increased levels of cortisone in their blood which seem to cause the increased pressure. The idea was to use RU 486 locally to block its effect on the eye. But results on rabbits so far have been disappointing, and it has proven difficult to limit the effect of the drug only to receptors in the eye.

Further in the future, RU 486's antiglucocorticoid activity may find a use in the local treatment of skin wounds such as burns and abrasions. Corticosteroids delay healing, so RU 486's developer Etienne-Emile Baulieu believes that anticorticosteroids will accelerate healing.

Other potential medical applications derive from RU 486's effects on the progesterone receptor. Meningiomas, for example, are primary tumors of the membranes that surround the brain. For unknown reasons the cells of the tumor have an abundance of progesterone receptors and few, if any, estrogen receptors. Generally these tumors are benign, but they can become large enough to cause neurological disorders and can be difficult to remove surgically. Teams in Holland, France, and the United States are looking at the effect of RU 486 on these tumors, but no clear-cut results are in yet.

In breast cancer, too, there may be a role for RU 486. Some tumors require a combination of estrogen and progesterone to keep growing. Antiestrogens such as Tamoxifen can halt these tumors, but studies in Montpellier in the south of France indicate that RU 486 can make the antiestrogens more effective. A group at the Lombardi Center of Georgetown University in Washington, D.C., is examining the value of RU 486 in breast cancers that have become resistant to antiestrogens.

RU 486 should also find uses in the management of pregnancy beyond contraception and abortion. Because it effectively removes progesterone, it can mimic the onset of labor, including changes such as the softening and dilation of the cervix that accompany a normal delivery. At present a complex cocktail of drugs is needed to induce labor, but the hope is that RU 486 will be able to do the job more simply in the future. This will be enormously helpful in cases where the fetus has died in utero, and it may also reduce the number of cesarean sections performed.

Baulieu is also enthusiastic about RU 486 as a potential birth control method. He sees three different ways in which the drug could be used for this purpose.

First is what Baulieu calls a "menses inducer." If a woman takes RU 486 in the second half of her cycle, there is an 80% chance that she will begin to bleed. Although a 20% failure rate may seem high, even women with active sex lives conceive on only one in five cycles, so the actual failure rate is 4%.

A second approach is to use very small amounts of RU 486 during the second, luteal, phase of the cycle. This can be tricky, because although the luteal phase always lasts 14 days, the first part of the cycle is variable, making it difficult to know when to start taking RU 486. The idea is not to provoke bleeding but to act solely on the endometrium, preventing the implantation of the embryo. The woman would have to take small doses of RU 486 every day for 10 to 12 days.

The final, and perhaps most promising, potential use of RU 486 is as a contraceptive in the conventional sense. In the first, follicular phase of the cycle there is a small amount of progesterone that seems to be very important for ovulation. Blocking that could block release of the egg. A Finnish team has shown in a small-scale trial that RU 486 can prevent ovulation without the need for estrogens. ■ J.C. AND J.F.

and the Schering drug have an unacceptably low success rate—in some studies as low as 60%—when taken without prostaglandins. The ideal situation would be a combination drug where the prostaglandin wouldn't go to work until after the RU 486 had done its job of starting the shedding of the uterine wall and sensitizing the womb to the prostaglandin.

Opponents of RU 486 worry that the drug will be used indiscriminately in developing countries. Bob Marshall of the American Life League says that, in their rush to terminate pregnancy, supporters of RU 486 are ignoring the health of the mother. "What that tells me is 'get them unpregnant at any cost,' and if a few die in the process, or a number die, the hell with it," he says. "If you start hemorrhaging out in the bush in Kenya, well, goodbye."

But Van Look says that's just not how the drug will be used. "Any medical approach to termination of early pregnancy—like an approach involving one of these antiprogestins—will always require backup from surgical facilities," he says. "What it could offer developing countries is that where existing facilities are overstretched you can now have an outpatient treatment which will be successful in 95% of cases, so you only need facilities and skilled personnel for the remaining 5%."

WHO says Roussel has promised to deliver the drug to any WHO member country that requests it for the purpose of further study, but according to Van Look no other country has made a formal request. The Peoples Republic of China, a participant in WHO-sponsored trials of RU 486, is the only country besides France to approve the drug for use as an abortifacient. It is currently Roussel's policy not to supply the drug outside France, but many believe the Chinese have the capability to manufacture the drug on their own. And since China does

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not presently subscribe to international patent conventions, there is no legal roadblock to their doing so.

RU 486's future. If Roussel can be persuaded to begin selling RU 486 outside France—and some believe that despite the company's public reticence, that is exactly what it plans to do—marketing it in the United States will still be a problem. A spokeswoman for Roussel's U.S. affiliate, Hoechst-Roussel Pharmaceuticals, Inc., says that the company has no plans to sell the drug. Product liability and the adverse political climate may scare off other large, established pharmaceutical companies. Kamp thinks a more likely scenario is a small company backed by venture capital that would market only RU 486. Boycotts of such a company would be fruitless, since there would be no other products to boycott, and liability suits would find little reward since the company would be designed to have few assets. Another possibility for marketing would be a nonprofit organization, such as the Planned Parenthood Federation.

RU 486 may also have a role as a drug not for abortion but for contraception. That raises the issue of what exactly RU 486 is. Although widely thought of as an abortion pill, its discoverer Baulieu questions that terminology. He calls it a contragestive, derived from contra-gestation just as contraceptives are contra-conception. Baulieu's neologism goes beyond newspeak. It is a genuine attempt to point out that popular attitudes about when life begins were formed at a time when not much was known about the process. He sees gestation as a continuum, from the meiosis that generates the eggs and sperm, to the birth of a baby. All steps are essential, and none is sufficient by itself. But "for society's sake" it has become vitally necessary to find better ways to control gestation. "My aim is to get rid of the word abortion," Baulieu says, because the word "is almost as traumatic as the fact itself." As far as he is concerned his research is not aimed at gaining women abortions. It is aimed at helping them control gestation.

However it may ultimately be used, RU 486 has forced participants in the debate over the moral issues of human reproduction to reconsider their points of view. But it seems likely that legal prohibitions will not be able to stop a drug with the promise of RU 486.

Jose Barzelatto, formerly at WHO and now at the Ford Foundation, puts it succinctly: "The antiprogestins will come into the market one way or another. There's no question about it. They're too important to be stopped." ■ JOSEPH PALCA

With reporting by Jeremy Cherfas in Paris.

Etienne-Emile Baulieu: In the Eye of the Storm

Paris

FOR THE PAST FEW YEARS, Etienne-Emile Baulieu has been on a crusade. Ever since the drug he helped create, popularly known as RU 486, was shown to be highly effective in putting an end to pregnancy without surgery, he has been arguing in every forum he can for its widespread medical use. In the process, he has drawn the wrath of opponents of abortion, heard his discovery condemned by the cardinal of Paris, and even seen the company that manufactures the drug, Roussel-Uclaf, temporarily abandon the first large-scale trials in France in the face of protests.

It is an unusual position for a world-class medical researcher, and Baulieu, an authority on steroid hormones, is certainly that.

RU 486 was only one of Baulieu's important breakthroughs. In the 1950s, he was the first to discover that the adrenal glands secrete a steroid that is soluble in water—a feature that was entirely unexpected and had implications for the hormone's transport in the blood. He followed that discovery with pioneering work on the estrogen and progesterone receptors, the molecules within the cell that are responsible for detecting and passing on the hormonal message. He built on his knowledge of these receptors to create RU 486. And recently he has shown that there are cells in the brain that make steroids, though as yet he has no idea what the hormones are doing there.

Baulieu, 62, made these discoveries while working for INSERM, the French government's medical research organization, which has funded his research for nearly three decades. He currently works at INSERM labs within the Kremlin-Bicêtre hospital in the south of Paris. Baulieu has also been a consultant to Roussel—"independent and exclusive," as he puts it—for more than 25 years.

© Ken Regan/Camera 5

Practical physician. *Baulieu says he is "a medical doctor who does science."*

The attempt to marry pure science to practical medicine is characteristic of all Baulieu's work. "I am a medical doctor who does science," is how he always describes himself. Indeed, he explains his campaign for RU 486 as strictly a medical matter. "I want to help women. I have not dedicated my life to abortion. I am not anti-children. I have three children and seven grandchildren. But women die in botched abortions. Two hundred thousand every year. RU 486 can save them." Baulieu is quick to point out that he has no personal financial stake in the drug.

Baulieu's father too was a doctor, one of the first in Europe to examine the effects of insulin on diabetics, but he died when Baulieu was only four. For a time Baulieu and his mother disagreed over his career. She did not want him to study medicine, preferring something more like engineering for her son. "To please her, while I was studying medicine, I also studied biochemistry." The M.D. came just before the Ph.D., but although almost all of his subsequent career has been in research, Baulieu insists that "I am a real doctor. I don't have just a diplome. I had patients and everything, and I could have been a professor of internal medicine if I had wished."

Instead he became, at 29, France's youngest professor of biochemistry, at the new university in Reims. He was what the French call a "turboprof," commuting once a week on the fast turbotrains between his laboratories in Paris and a single day of 6 or 7 hours teaching in Reims, 85 miles to the east.

It was his medical training, and practice, that led him to patients with adrenal cancer, which in turn provided his 1959 discovery of soluble steroids. This work came to the attention of Seymour Lieberman, a famous steroid biochemist at Columbia. Lieberman invited the then 35-year-old Frenchman to spend a year in his lab, but at first Baulieu could not go.

"When I was young I was militant in leftist organizations," he told *Science*, "and I

didn't want to go to America." Then came 1956 and the Soviet invasion of Hungary. Like so many other people, Baulieu broke his connections with the left. But now that he had the desire, and the opportunity, to go to the United States, the Americans didn't want him. "I couldn't get a visa," he recalled. Despite interventions from leading scientists such as Lieberman, Baulieu was persona non grata.

As soon as John Kennedy got into the White House, though, Baulieu got his visa. Shortly after his arrival in New York, Lieberman introduced Baulieu to Gregory Pincus, a Boston University biochemist who had played a key role in the development of the contraceptive pill. It was Pincus who interested Baulieu in contraception and the regulation of pregnancy.

According to Baulieu, Pincus fixed it for him to detour on one of his flights between Paris and New York to Puerto Rico to visit a clinic in San Juan where the pill was being tested. And he arranged for Baulieu to join a World Health Organization committee on contraception, which kept Baulieu shuttling between his Paris laboratories and Geneva. Then, when Baulieu worked on the estrogen and progesterone receptors back in his labs at INSERM in the 1960s, he says Pincus was influential in securing plenty of research support from the Ford Foundation for his research. So when Baulieu isolated the progesterone receptor, his long association with research on contraception quickly led him to wonder how he might make practical use of this discovery to control pregnancy.

Baulieu could see three obvious approaches. One would be to prevent the body from making progesterone. He didn't like that because progesterone is on the direct path to other hormones; if you stop the synthesis of progesterone, you stop the synthesis of those other hormones too, with who knows what consequences. Another was somehow to remove all the progesterone from the body. At the time that seemed impossible, as it still does today. The third was to ignore the hormone and concentrate on the receptor, and that is exactly what Baulieu chose to do.

He already knew that compounds such as Tamoxifen, an antiestrogen drug made by Britain's Imperial Chemical Industries, occupied the receptor and substituted its own weak message for the more powerful signal from estrogen, thus preventing any estrogen present from having a major effect on the cell. All Baulieu had to do was find a similar compound that would block progesterone. "But it was all very vague," he recalls today. "We had no chemical idea how to devise a progesterone analogue."

Two lines of work converged on the

© P. Vauthey/Sygma

"We had no chemical idea how to devise a progesterone analogue."

solution. Robert Sutherland, an Australian postdoc working in Baulieu's lab, discovered that a derivative of Tamoxifen with an extra hydroxyl group was a much more potent antiestrogen than Tamoxifen itself. And George Teutsch, the chief chemist at Roussel, a company that had a reputation for fine steroid biochemistry, discovered an efficient way to tack appendages onto the progesterone molecule at a position equivalent to the point at which the hydroxyl group had been added to Tamoxifen. So they could produce a series of derivatives of progesterone and screen them to see whether they would block the receptor.

Despite this, the Roussel chemists nearly missed their target. All the compounds capable of blocking steroid receptors discovered at that time had low affinity for the receptor. That is, they bound weakly to the receptor and, it was believed, had a chemical effect on the cell that counteracted the action of the hormone proper. Baulieu discovered that hydroxy-Tamoxifen had a high affinity. It bound tightly to the receptor, but beyond that it did nothing. It worked by occupying the receptor entirely, thereby shutting off the estrogen molecule's access to the cell.

Screening takes time and money. So pharmacologists concentrate first on the most promising classes of compounds, and on the basis of their understanding at that time, they thought all antisteroids would bind weakly to the receptors. When Baulieu realized that hydroxy-Tamoxifen worked so well precisely because it had high affinity, he put the Roussel pharmacologists through a U-turn. "I said, 'Aha. Check all the high-affinity compounds.' " The result was RU 486.

Tests in the laboratory in 1978 showed that the new substance had a very high affinity for the progesterone receptor, completely blocking the effect of progesterone. At much higher doses, RU 486 blocked glucocorticoid receptors too. (Glucocorticoids are hormones responsible for the regulation of carbohydrates and proteins and many other important aspects of metabolism.) "As soon as we had it," Baulieu recalled, "I said the best way to test it is in vivo, to see if it blocks progesterone in pregnant women." This despite the fact that, although progesterone was known to be vital for pregnancy in a whole zoo of laboratory animals, its role had not yet been proven in women.

After tests had shown that RU 486 was not toxic to monkeys, Baulieu took it to Walter Herrmann, professor of obstetrics and gynecology at the University Hospital of Geneva and a long-time friend and collaborator of Baulieu's. Herrmann enlisted the help of 11 pregnant women who wanted an early abortion. Each received RU 486 for 4 days; nine aborted, eight of them within 5 days. Two did not abort and had to undergo suction to remove the fetus. This test proved that Baulieu's concept worked; RU 486 could put an end to pregnancy by blocking the progesterone receptor.

The drug has now been tested on thousands of women around the world, and although the dosage has been somewhat refined, the results have not changed all that much since that first Swiss trial.

Asked to sum up his view of his own career, Baulieu says: "If you have one adjective to attribute to me, I would say that I am full of curiosity." It is a curiosity often spurred by competition. "I like being in a race," Baulieu says. "Competition is amusing, and it certainly helps" to get results. And with competition come prizes, which he also relishes. "It's part of competition. If you are in a competition, you have to keep the score." Baulieu has had his share of awards, but "I would welcome a prize" for RU 486, he says, "because it helps the message to be spread."

Baulieu acknowledges that, as a scientist, he has been luckier than most, at least as far as the quantity and quality of his discoveries are concerned. But he is quick to quote Pasteur's remark: "Le hasard ne favorise que les esprits préparés"—chance favors only the prepared mind. ■ JEREMY CHERFAS

THE PRECEDING PAGES WERE TREATED
AS A UNIT IN THE ORIGINAL FILE

THE FOLLOWING PAGES WERE TREATED
AS A UNIT IN THE ORIGINAL FILE

TO: Representative Lincoln, members of House HESS Committee

Please accept this statement in lieu of testimony at today's hearing:

The Coalition of Alaskans for Choice wholeheartedly supports passage of HJR58. The French drug RU 486 offers the possibility of early, safe, effective termination of unwanted pregnancy without the need for surgical intervention. The drug may also offer other medical benefits to women, including the treatment of breast cancer and other types of cancer. The benefits of this drug were well documented at today's hearing by the Resolution's sponsor and other witnesses.

The Federal Food and Drug Administration has not only refused to allow importation of RU 486 into the United States, it has taken the further step of specifically banning the drug. This move is motivated by politics, not by concern for the health and safety of women.

The FDA does have the authority to allow, at its discretion, importation of drugs which have not yet been approved for use in the United States but which are thought to have efficacy in serious or life-threatening circumstances. An example of this would be controversial drugs for treating AIDS and certain types of cancer. Individuals are allowed to obtain these drugs in the countries where they are produced and to bring limited quantities to the U.S. for their own treatment.

In a letter from an FDA official to Alaska Senator Ted Stevens, the FDA's position is stated as follows: "the intended use of RU 486 makes it likely that it could be used without supervision by a physician, and that indiscriminate or unsupervised use could be hazardous to health."

In other words, the FDA has us in a closed loop: The FDA will not allow RU 486 to be safely prescribed by U.S. doctors, at the same time arguing that the drug must be banned because it is not safe unless its use is supervised by a doctor.

This situation reminds me of a bumper sticker I saw once which read: "Go To Health, FDA!"

Respectfully Submitted:

Eileen Self - March 11, 1992

Chair, Coalition of Alaskans for Choice

United States Senate
COMMITTEE ON APPROPRIATIONS
WASHINGTON, DC 20510-6025

June 14, 1991

Ileen Self
8209 Nadine Street, #2
Anchorage, Alaska 99507

Dear Ileen:

Enclosed is a copy of a letter I received from the Department of Health & Human Services in response to the inquiry I made on your behalf. I hope the information they provided is useful.

With best wishes,

Cordially,

TED STEVENS

Enclosure

Food and Drug Administration
Rockville MD 20857

1991 MAY -9 PM 1: MAY 8 1991

The Honorable Ted Stevens
United States Senate
Washington, D.C. 20510

Dear Senator Stevens:

This is in response to your letter of Apirl 12, 1991, on behalf of [redacted]silla, Alaska, concerning the unapproved new drug, RU-486.

As you may know, RU-486 is a drug that is approved in France for early abortion through a limited distribution system when used with one of two prostaglandins also approved in France. In addition, studies have been conducted on the treatment uses of this drug for diseases such as breast cancer, Cushing's syndrome, and other types of cancer.

To provide you background information, the Federal Food, Drug, and Cosmetic Act (FDC), which the Food and Drug Administration (FDA) administers, defines a new drug as one not generally recognized by qualified experts as safe and effective for the recommended uses. A new drug may not be distributed interstate (except for clinical study) until we have approved a new drug application (NDA) containing substantial scientific evidence of safety and effectiveness for use of the drug as labeled.

An investigational new drug (IND) application acceptable to the FDA is required of a sponsor (e.g., a drug manufacturer or a clinical investigator) to study the safety and effectiveness of an unapproved new drug. When the sponsor determines that adequate and well-controlled studies have been performed, which reflect favorably on a new drug's safety and effectiveness, the sponsor then submits that information, together with adequate information on manufacturing procedures and controls, in a new drug application to FDA. After a comprehensive review by the FDA the NDA is either approved or not approved; upon approval the drug may be marketed.

We are enclosing a publication, "New Drug Development in the United States," that describes in more detail the requirements for new drug clearance in the United States.

Strictly interpreted, the FDC Act prohibits the import and distribution in interstate commerce of drugs that have not been approved by the FDA. However, out of compassion for individual

patients, many of whom suffer from serious or life-threatening diseases, FDA has, as a matter of enforcement discretion, long permitted individuals to bring into the United States for personal use limited quantities of drugs sold abroad but not approved in the United States. In exercising this discretion, however, it is incumbent upon the Agency, in its charge to protect the public health, to allow the importation of unapproved drugs only if there is no unreasonable safety risk and only if the other criteria are met.

With regard to RU-486, a conclusion was reached that use of the drug posed unacceptable safety risks to the American public. This is because the intended use of RU-486 makes it likely that it could be used without supervision by a physician, and that indiscriminate or unsupervised use could be hazardous to health. In addition, to be optimally effective, RU-486 must be used in conjunction with another drug, a prostaglandin, also not approved in the United States, further complicating the safety issue.

Also, because RU-486 is not proposed for treatment of a serious condition for which no alternative treatment exists (one of the criteria set forth in the Pilot Guidance document), yet poses safety risks, we do not believe that our import policy can be appropriately applied to permit the importation of RU-486. Moreover, the publicity in this country regarding the availability of the drug overseas raised for FDA the possibility that a demand would be created in this country which in turn would foster importation of the drug for commercial use. Thus, we believe that our decision to restrict the importation of RU-486 is sound public health policy and is consistent with our policy guidance and the importation of unapproved drugs.

It is extremely important to point out that this import alert does in no way restrict the importation of this drug for research purposes to determine its usefulness for diseases such as Cushing's syndrome and some forms of cancer.

We hope the information provided will be helpful. If we can be of any further assistance, please let us know.

Sincerely yours,

Hugh C. Cannon
Associate Commissioner
for Legislative Affairs

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HJR # 58--- RU-486

March 11, 1992 House HESS

Madame Chairman, Members of the House HESS
I am Joan Heidersdorf and I'm here to testify in opposition to HJR 58 which supports bringing the drug RU 486 into the US.

The basic reason I am opposed to RU 486 is that it kills babies. This should be sufficient reason for ~~for~~ all of us to oppose it's use. However, for those who are not concerned about its effects on the child, there are a number of other disturbing aspects of this drug that should noted.

* RU 486 is a synthetic female hormone. DES is also a synthetic female hormone which had limited testing before being prescribed. We have seen its tragic results in the children of the women who used it. Other examples of medical procedures which have had women as their victims are breast implants, the Dalcon shield, ~~contraceptives and~~ fertility drugs. Therefore, as noted in a recent article in the magazine Vogue, pro-choice feminist Janice Raymond, an associate director of the Institute on Women and Technology at MIT, perceives RU 486 "as another assault on women's bodies by the medical profession." Really, RU 486 is just another example of experimentation on women which we don't need.

* The use of Ru 486 is open to widespread abuse because it is not a simple at-home do it yourself abortion method. It requires 4 visits to a doctor. The initial doctor's visit to receive the pill must have three follow-up

visits to the clinic or hospital for careful medical supervision. Because of this difficulty, especially for poor women, the Sixth International Women and Health Meeting passed a resolution opposing the use of RU 486.

* But even with careful medical supervision complications associated with the use of RU 486 are hemorrhaging, infection, permanent sterilization, heart attacks and even death. Thus, the French government has banned its use for heavy smokers and women over 35.

* Further, claims that RU 486 can cure a myriad of diseases is unfounded. There has been no proof that it will affect such ailments as brain tumors, depression, hypertension, Alsheimer's, obesity, glaucoma, breast cancer, severe wounds and burns, AIDS, diabetes etc. This magical miracle drug cannot possibly deliver and as Dr. Bernard Nathanson says "It begins to sound a little like Dr. Potter's Snake Oil."

* Ru 486 acts by blocking the babies use of the hormone Progesterone without which the baby starves to death. RU486 is effective in approximately 80 - 95% of the instances of its use. For the remaining cases the unborn babies may be injured and born with defects. Several days after taking RU 486 a prostaglandin must be administered to assure that the abortion is complete. We already know that prostaglandins affect the immune

systems but we don't know what a single dose might do. Really what is so wonderful about this drug that we must request the Food and Drug Administration to let it into our country?

We Alaskans should not be on record as supporting a drug that to be effective kills babies and puts the life and health of the mother in jeopardy.

Joan Heidersday
Po Box 020658
Juneau, AK - 99802
789-9858

TESTIMONY ON HOUSE JOINT RESOLUTION NO. 58

From: Ida Barnack, Representing Alaskan For Line Inc. -Juneau
8292 Garnet St.
Juneau Ak. 99801

The sole purpose of our organization is to support and advocate the right to life for the unborn members of society. All "born" members of our society (including you committee members) are first unborn members of our society.

The main purpose of RU 486 is to terminate pregnancy (end someone' life). Therefore, our organization is strongly opposed to this resolution.

The proponents of this drug indicate it can be used as a contraceptive, it is safe and it has other medical value.

This drug is not a contraceptive. A contraceptive does not terminate a pregnancy. How can it be safe since it induces a miscarriage. With a miscarriage heavy bleeding occurs and it is always a concern whether or not the uterus will automatically "clamp down" or whether medical intervention is required. I am sure you have all known women who have had to be rushed to the emergency room due to heavy bleeding from a spontaneous miscarriage. Inducing a miscarriage through RU 486 will be no different. Often times a "D" & "C" is required after a miscarriage also.

This always ends the life of at least one person and could potientially end the life of another, the woman. In fact there are reported deaths of woman who have taken this drug.

Representative Boyer stated that this drug can be used to induce delivery thereby reducing the number of caesareans. This is all abortion-speak. If a caesarean is required, I sincerely doubt that there is any drug a woman could take to prevent it. It is common place to induce labor now only to have it end in a caesarean.

If there are other medical uses for the drug other than ending someone's life, we have no objections to it being tested.

Think about the reason Roussel will not bring it into a country where there is opposition. They themselves must be concerned that the pill will cause the death of some women or have bad side effects and they do not want to take the liability.

Our organization is pro-choice. We choose to protect the life of the innocent.

Thank you for accepting this testimony.

Alaska State Legislature

Please enter into the record my testimony to the HESS
committee name

committee on Resolution #58, dated March 10, 1992.
bill/subject

I want to first Thank all of you for being gutsy enough to represent us on very difficult moral issues.

I have never written testimony before.

The drug "RU486" will not only make it convenient for the individual, but society as a whole.

The value of life and its consequences, are the perspective we need in order to support each other.

Please vote no....

Signed: Lori Ralkar
Testifier

SELF
Representing (Optional)

820 CHARLES ST SITKA, AK 99835
Address

(907) 747-3641
Phone No.

Alaska State Legislature

Please enter into the record my testimony to the House HESS
committee name

committee on HJR 58 . dated 3/10/92 .
bill/subject

I would like to go on record before this committee stating that I am not in favor of abortion. The only exception to that would be in a case where the mothers life is threatened.

Signed: Michael W. LaGuire
Testifier

Representing (Optional)

Box 6369 Sitka, AK. 99835
Address

(907) 747-4880
Phone No.

TELECOPY COVER SHEET

Kodiak Legislative Information Office

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SENT BY: Tina

ALASKA WOMEN'S LOBBY
P.O. BOX 22156, JUNEAU, ALASKA 99802

March 11, 1992

RU486-HJR 58

RU 486 is a pharmaceutical which, among other uses, provides a means to medically terminate unwanted pregnancies.

American women should be allowed to benefit from this new advance in fertility control.

Use of the RU 486 requires no invasive procedure. There is no risk of any infection, nor need for anesthesia. It is 96% effective in the early stages of pregnancy.

Its use would put most early abortions into a very private realm, and would reduce the need for a majority of all surgical abortions in America.

In addition, it would end the open harassment and violence at abortion clinics that have characterized the bitter battle over reproductive rights.

Researchers believe that the drug has enormous promise in treating: breast cancer which affects one in nine women, endometriosis, a leading cause of infertility, ovarian cancer, glaucoma and ulcers.

RU 486 may be used to induce labor in a difficult delivery reducing the number of cesarean births.

It has been *proven* to effectively treat some forms of Cushing's Syndrome, a rare adrenal tumor which mostly affects women in their 30's to 40's.

The side effects that have been discovered have been minimal. No long term side effects have been observed

The current FDA ban on importation means that our doctors can't use RU 486 in therapy and our scientists can't use it for research even when their work has nothing to do with abortion.

Rep. Ron Wyden of Oregon who chairs the House Small Business subcommittee investigated the import ban for a year and concluded, "The Agency's decision was motivated by politics rather than by science or a desire to protect the public health from a clear and present danger." He charged the FDA with ignoring overwhelming evidence of the drug's safety.

When the distributor of the drug in France caved in to anti-abortion pressure and took the product from the French market, they were ordered to resume distribution two days later by France's Minister of Health who declared that RU 486 was "the moral property of women."

The Drug has been available in France since 1988 and it is licensed for use in Britain and Sweden.

The continued testing and availability of RU 486 is advocated by :

The American Medical Association (AMA),
The World Health Organization,
The American Public Health Association,
The World Congress of Obstetrics and Gynecology.

59% of all American adults think RU 486 should be made available in the U.S. (Harris poll).

RU 486 will come to America The chemistry for RU 486 is known. If it does not enter legally it will enter illegally within 2-5 years.

We must not have it enter the U.S. illegally. We want it properly tested and used with medical supervision to ensure its safety for women.

TELECOPY COVER SHEET

House HESS.

Kodiak Legislative Information Office

Office - (907) 486-8116 Fax - (907) 486-8264

TO: Rep. Lincoln - Chairman FAX: _____ PHONE: 465-3759

FROM: Kodiak L.I.O. PHONE: 486-8116

INSTRUCTIONS: Written Testimony for T/C 92-03-042

3-11-92 / Wednesday 8:30Am

RECEIVED: Date 3-12-92 Time _____

SENT: Date _____ Time _____

DISPOSAL OF ORIGINAL: Discard _____ Hold for Pickup _____

NUMBER OF PAGES: 2 (Not counting cover sheet)

SENT BY: LS

Alaska State Legislature

Please enter into the record my testimony to the House - HESS
committee name

committee on HJR 58 , dated March 11, 1997 .
bill/subject

Page (1)

As I await a turn to publicly testify against the passage of HJR 58, I wonder how many others with my viewpoint have been denied equal access to public and publicized (Channel 9) testimony. I suppose my ~~faxed~~ comments will not appear on Channel 9 news as did the "pro-abortion voice" of this morning.

At the outset, I would like to object to Rep. Boyer and the female from the Feminist Majority Foundation being introduced as "experts" on this subject they are politicians, nothing more; nothing less. I would hope in the future Reps. Boyer and Kapsner would leave testimony during teleconferences to the public their constituents, and who they are elected to represent.

I also wonder if there is any ~~room~~ room for the truth in all that is being said. A few facts may help.

1. RU 486 is not opposed by pro-lifers for legitimate research directed at saving lives.
2. To date, RU 486's only proven use is to destroy lives
3. Already one woman has died from use of RU 486, in addition to the as yet unmentioned side-

(over)

Signed: Margaret R Hennessy
Testifier

Representing (Optional)

3584 Woodland Drive, Kodiak AK
Address

(907) 486-3973

effects as excessive bleeding, requiring transfusions, intense pain and a 10-30% "failure rate" requiring a subsequent surgical abortion procedure, provided the woman does not change her mind.

4. RU 486 is touted as safer and easier than surgical abortion. In fact, it requires 4 trips to an abortionist, and if unsuccessful alone, is sometimes used in conjunction with prostaglandin a substance which at one time was also used to induce abortions but the pain and number of deaths resulting were considered intolerable.

5. Pro-abortion advocates want the public to think that RU 486 has many proven beneficial uses - yet none have been safely proven so far. They never mention the Institute on Women and Technology, a pro-abortion group, which came out against the import of RU 486 at this time, because of their concern about the side effects for women they, despite their viewpoint, could foresee the potential harm to women. The political lobby will probably never forgive them.

How many times does a society need to have a similar experience in order to see the truth? Women were told IUD's were safe, and thousands of women can no longer have children. Thalidomide was used for nausea in pregnancy by women, touted as perfectly safe, only to result in severely deformed human beings. What about the child that survives RU 486? What about Anna Rodriguez, a child who lost her arm to an abortionist during an 'incomplete' procedure and now lives? How will her mother answer her questions?

This bill has nothing to do with curing diseases or saving lives. The pro-abortion groups will stop at nothing to have abortion on demand, for any reason at any point in a pregnancy. They are not concerned with the health of women or those with Rh sensitivity Syndrome who are interested in the continued

Alaska State Legislature

Please enter into the record my testimony to the House HES
committee name

committee on HJR 58 , dated 3/16/92
bill/subject

I wish to voice my strong opposition to the legalization of the medication RU468 on the ~~grounds~~ (error) grounds that there is considerable evidence of its negative health effects for women and as well as evidence of fetal defects in children born for whom the drug was not effective (i.e. fatal).

I am concerned about a continuing birth control/abortion movement which does not fully take into account the health + psychological effects on women, and places on them the "burden of responsibility", subjecting their bodies to such "cures" as drugs and abortion which have considerable undesireable complications

Signed: Paul Ruff
Testifier

Representing (Optional)
PO 2648 Kodiak AK 99615

Address
(907) 486-3506

Phone No.

Alaska State Legislature

Please enter into the record my testimony to the House H&S
committee name

committee on HJR-52, dated 3-15-92.
bill/subject

As a concerned U.S. citizen I do not support this bill. It disregards potential dangers to women.

Signed: Janice VanRossen JANICE VAN ROSSEN
Testifier

The General Public
Representing (Optional)

Star Rt 3530 Kodiak AK 99615
Address

486-6050
Phone No.

FISCAL NOTE

STATE OF ALASKA
1992 LEGISLATIVE SESSION

BILL NO. HJR 58

Revision Date: _____ **Department Affected:** LEGISLATURE

Title: AVAILABILITY OF RU 486 DRUG **BRU:** _____

Component: _____

Sponsor: REP. BOYER

Requestor: _____ **COMPONENT SERIAL NO.** | | | | |

EXPENDITURES/REVENUES: (Thousands of Dollars)

OPERATING	FY 93	FY 94	FY 95	FY 96	FY 97	FY 98
PERSONAL SERVICES	-0-					
TRAVEL	-0-					
CONTRACTUAL	-0-					
SUPPLIES	-0-					
EQUIPMENT	-0-					
LAND & STRUCTURES	-0-					
GRANTS, CLAIMS	-0-					
MISCELLANEOUS	-0-					
TOTAL OPERATING	-0-					
CAPITAL	-0-					
REVENUE FUND SOURCE:	-0-					

FUNDING: (Thousands of Dollars)

GENERAL FUND	-0-					
FEDERAL FUNDS	-0-					
OTHER FUND SOURCE:	-0-					
TOTAL	-0-					

POSITIONS:

FULL-TIME	-0-					
PART-TIME	-0-					
TEMPORARY	-0-					

Estimate of current year impact: _____

ANALYSIS: (Attach a separate page if necessary.)

Prepared By: _____ **Phone:** 465-3732

Division: HOUSE HEALTH EDUCATION & SOCIAL SVCS CMTE **Date:** 3/10/92

Approved by Commissioner: _____

Agency: _____ **Date:** _____

Distribution (by preparer): Leg. Fin., Legislative Sponsor, Requestor, OMB/DBR, Gov. Legis. Ofc., & Impacted Agency(ies).

Rev 10/7/91

Statement of the American Medical Association

to the

Subcommittee on Regulation, Business Opportunities, and Energy

Committee on Small Business

U.S. House of Representatives

Presented by

P. John Seward, M.D.

RE: RU 486

November 19, 1990

American Medical Association
515 N. State Street
Chicago, Illinois 60610

Department of Federal Legislation
Division of Legislative Activities
(312) 464-4775

STATEMENT

of the

AMERICAN MEDICAL ASSOCIATION

to the

Subcommittee on Regulation, Business Opportunities, and Energy

Committee on Small Business

U.S. House of Representatives

Presented by

P. John Seward, M.D.

RE: RU 486

November 19, 1990

Mr. Chairman and Members of the Subcommittee:

My name is P. John Seward, M.D., and I am a physician in family practice in Rockford, Illinois. I also am a member of the Board of Trustees of the American Medical Association. Accompanying me is David L. Heidorn of the Association's Division of Legislative Activities. The AMA appreciates this opportunity to appear today to discuss the issue of RU 486 availability in the United States.

In the Subcommittee's letter of invitation to appear, you asked that the AMA respond to a number of special questions regarding the drug. In addressing those inquiries, I want there to be a clear understanding of the AMA's policy regarding RU 486 and what we believe to be the current legal status of that drug within the United States.

At its June 1990 meeting, the AMA's House of Delegates adopted the

following resolution:

> RESOLVED, That the American Medical Association support the legal availability of RU 486 for appropriate research and, if indicated, clinical practice.

The reason that the Association took this position was our very real concern that politics or ideology could interfere with a well established, legal decision-making process that is and must always be based on good science and proper medical practice, nothing more.

As you well know, RU 486, or mifepristone, which is a steroidal agent being used as an early abortifacient in some countries, has raised deep feelings among both the proponents and opponents of abortion and the prospective use of RU 486 in the United States. It is the AMA's position that any governmental decision regarding this drug, as with all other drugs, must not be influenced by political debates or social issues such as this one. This must not be taken to mean that the AMA supports the widespread availability of RU 486. We do not believe that there has been adequate research to establish that this drug is a safe and effective therapeutic modality. In fact, the central difficulty in evaluating this drug is that no research is being conducted in the United States to determine whether RU 486 has a role in medical practice, and the reason no research is going forward is its manufacturer's decision not to pursue clinical testing of the drug here.

As we understand the current situation, no Investigational New Drug (IND) applications (the legal precondition for a drug to be transported in interstate commerce for the purpose of clinical research) either are pending or have been approved by the Food and Drug Administration (FDA)

for RU 486. Since the Federal Food, Drug and Cosmetic Act requires that a drug be proven safe and effective for its intended purpose through well controlled clinical investigations, there is no basis for approval of a New Drug Application to allow the drug to be marketed. Therefore, no legal basis exists for this drug to be used in the United States for research or in marketing.

The only other basis for allowing importation of RU 486 would be for individual compassionate use. However, it is the AMA's understanding that RU 486 poses a severe risk to patients unless the drug is administered as part of a complete treatment plan under the supervision of a physician. During an appropriate course of treatment with the drug, it is common that three or four visits to a physician are necessary to avoid hemorrhaging and to ensure that a complete abortion has taken place. It also must be taken with a prostaglandin to increase the probability that a complete abortion occurs. Clearly, the importation of RU 486 for personal compassionate use would not be medically desirable given alternative available care methodologies.

These difficulties do not mean that research on RU 486 should not be conducted. On the contrary, we believe that if this drug can be shown to be a safe and effective medical treatment, it should be available for the appropriate care and treatment of patients. There has been some published conjecture that RU 486 may be an effective treatment for other indications besides its use as a contraceptive or abortifacient, including treatment of breast cancer, gynecological malignancies, glaucoma, infertility, and labor induction. While we do not believe this conjecture to be based on any substantiated tests of the drug, RU 486's

application to these conditions is certainly possible, although adequate drugs for these conditions already exist. It may even be possible that this drug is useful in treatments about which we have no current knowledge. No one, at this time, can say.

The only way to make these determinations and to establish the safety and efficacy of RU 486, as all other drugs, is to conduct the necessary research and clinical trials required by the FDA to market drugs in the United States. This is a highly effective process established to protect the health, safety, and welfare of the American people. For the same reasons drugs proven to be safe and effective should not be kept out of the United States for political reasons, so also should the high standards we have for drugs not be contravened for political purposes.

Rumors exist that the FDA, due to political pressure, is standing in the way of research on RU 486. We do not believe this to be true. On the contrary, it is the FDA's responsibility to ban a drug that has not met legal and regulatory requirements for importation into the United States. Because RU 486 has not met these requirements, the FDA complied with its charge and acted well within its authority in issuing its June 9, 1989, automatic detention import alert concerning the drug.

As we understand the situation, the actual impediment to research on RU 486 is the manufacturer's unwillingness to make the drug available in the United States. Without the drug, it is impossible to apply for an IND. The manufacturer is reportedly unwilling to allow clinical testing in the United States because of its concerns over the political controversy that has followed this drug and is sure to intensify if

research begins in this country. While the French government compelled the French manufacturer to make the drug available in that country, we do not believe that this is a problem that can be easily addressed under our current law.

Conclusion

The AMA stands by the FDA's appropriate application of its legal responsibilities in protecting the health and well being of the American people from unsafe drugs. From our understanding of the current situation, the FDA has acted responsibly in issuing import restrictions for RU 486. At the same time, we would expect that, if an acceptable IND is submitted, the IND would be approved and importation allowed. We hope that the drug can be made available and research eventually can be conducted in this country to determine if the drug is safe and effective for its known uses and whether its use may be appropriate for other medical treatments. It is our primary concern that patients have every opportunity to receive the best possible medical treatment. When possible research into drug therapies does not occur, for whatever reason, the likelihood that the best possible care will not someday be available is greatly increased.

Frankly, we have no answer for this Subcommittee on how to ensure that all appropriate research occurs. Under our current system, which is the world's standard for the development of drugs, the manufacturer is well within its rights to hold the drug from distribution. We can only hope that the political climate will somehow not influence any future consideration of the introduction of RU 486 into the United States.

4239s

AMERICAN MEDICAL ASSOCIATION HOUSE OF DELEGATES

Resolution: 100
(A-90)

Introduced by: California Delegation

Subject: RU-486 Availability

Referred to: Reference Committee E
(Charles D. Sherman, Jr., M. D., Chairman)

Whereas, An antiprogesterone steroid, known as RU-486, has been developed and tested in Europe, and has been shown to be an efficacious and safe means of terminating early pregnancy when administered orally early in pregnancy by an appropriately trained physician; and

Whereas, The use of such a medication for terminating early pregancy constitutes a potentially significant medical and public health gain in terms of efficacy, safety, ease of use, cost and privacy of the physician-patient relationship; and

Whereas, RU-486 may also be an important treatment for other indications, including treatment of breast cancer, gynecological malignancies and labor induction; and

Whereas, Existing AMA policy holds that the early termination of pregnancy is a private medical matter to be decided between the patient and her physician, and AMA policy also does not prohibit abortion wherever legal and performed in accordance with good medical practice; and

Whereas, It is in keeping with basic medical standards to avoid surgical procedures whenever an equally effective non-invasive alternative is available; and

Whereas, The potential for a "black market" in RU 486 in this country is very real, with women's health activists already vowing to import the drug for use by American women, thus exposing them to the dangers of non-physician supervised use of the drug; therefore be it

RESOLVED, That the American Medical Association support the legal availability of RU-486 for appropriate research and, if indicated, clinical practice.

Fiscal Note: No significant fiscal impact

The Berkshire Eagle

Published daily by the Eagle Publishing Company,
33 Eagle Street, Pittsfield, Massachusetts 01202.

Editorials

Don't let U.S. politics thwart RU486

The French use it. So far 44,000 Frenchwomen have responded so favorably to RU486 — the pill used to terminate very early pregnancies — that the treatment has become the method of choice among one-third of Frenchwomen opting for abortion. The British and Swedes are enthusiastic about it, too: Next year RU486 will likely be available for marketing in those countries.

Even in the abortion-wary United States, there is a demand for RU486. A Harris poll conducted in 1988 found that 59 percent of Americans think the medication should be available here. And the American Medical Association — hardly a bastion of avant-garde thinking — endorses testing of RU486.

Evaluating the impact of RU486 from a scientific standpoint has been exciting. According to researchers, administered in conjuction with the steroid prostaglandin, the drug has proved to be 96 percent effective in terminating early pregnancies, with few side effects. Risks associated with chemical abortions are less than with surgical abortions. And RU486 shows promise in treating or preventing meningioma (a benign brain tumor), breast cancer, endometriosis, glaucoma and other diseases.

So why isn't it available in the United States?

It's a question of politics.

Although women indicate they prefer the option of monitoring their own abortions, anti-abortion activists in this country have effectively blocked the marketing of RU486 by any pharmaceutical company through the threat of boycotts and harassment. Roussel-Uclaf, the French manufacturer of RU486, has for now stayed out of the fray by keeping the drug from distribution until the political climate becomes more accepting.

But times may be changing. This summer, Eleanor Smeal, president of the non-profit Fund for the Feminist Majority, and a delegation of U.S. scientists delivered 115,000 petitions upholding RU486 and contraceptive research in America to the chief executive officers of Roussel and its German parent company, Hoechst. The manufacturers were impressed by the degree of support demonstrated by the U.S. public.

That support could be magnified in pharmaceutical board rooms if it were backed up by U.S. politicians lobbying in Europe to bring this medical advancement to the United States.

news articles

JUDY MANN

Facing the Abortion Issue

One of the reasons women feel so strongly about the abortion issue is that many of them have had to confront the question personally, and if they haven't, they have friends who have, and they know that they might have to. For women, abortion is not an abstract.

Women, as Harvard professor Carol Gilligan wrote in her book, "In a Different Voice," arrive at a decision about abortion in the context of their human connections and values about what is the right thing for them to do under their particular set of circumstances. Men, she wrote, tend to arrive at moral decisions in terms of absolutes of right and wrong.

When the decision about abortion is remote—as it has been for most men since the 1973 Supreme Court decision legalizing it—it is easier to take an absolute stand on it. This may account for the difference in the way men and women are voting in state legislatures that have recently considered abortion laws. The majority of men in most of the legislatures have voted to restrict access to abortion while the majority of women have voted against restricting access, according to a study done by the Feminist Majority.

Now, however, more and more politicians and organizations are having to take positions on abortion and are having to think through the consequences of that question in a far more personal way.

The American Bar Association is the latest to find itself embroiled in internal conflict over its stand on abortion. On Wednesday, its House of Delegates voted 200 to 188 to rescind its position that a woman's right to an abortion was guaranteed by the Constitution. That position, taken as recently as February, led to the resignation of more than 1,400 lawyers and a loss of about $300,000 in dues. The current ABA president backed the repeal while his successor opposes it, which suggests that the ABA hasn't seen the last of this.

The same day, the National Conference of State Legislatures met, and lawmakers on both sides of the abortion issue were clearly unhappy that they had to deal with it. According to a story in The Washington Post, Rep. Kelly Shockman, a Democrat from North Dakota who opposes abortion, got a round of applause from 200 of his colleagues after he said he resented "the fact that the Supreme Court dumped this whole issue back on the states."

President George Bush, anxious to avoid a firestorm over abortion, nominated to the Supreme Court an obscure federal judge who has been on the appellate bench so briefly that has no paper trail on abortion. What might have been called inexperience (particularly in a woman) was swiftly turned into a plus: "a clean slate," as Sen. Howard Metzenbaum (D-Ohio) called it.

It is clear that in the present political climate, no Supreme Court nominee with a record on abortion will get confirmed without the kind of bloodletting that will leave both sides of the battle exhausted. U.S. senators appear no more eager for these battles than are state legislators.

As the complexities—moral, personal and political—of the abortion debate reach beyond women and begin to embroil men in a direct way, with personal and political costs, they will realize that it is not only the most divisive issue of our time, it is the most personal one.

Each legislator who realizes how difficult the issue is to deal with will have made a giant step in understanding the ordeal that women go through. Politicians and members of professional organizations who have to vote on this will think twice before they parrot terms like "abortion on demand."

And they may find that it is in their best interests to lend their weight to efforts to import the French abortion pill, RU-486. The Feminist Majority recently led a delegation of 10 scientists, feminists and health-care professionals who met with the top officials of the companies that manufacture RU-486. They delivered 115,000 petitions and a list of 250 scientists and medical researchers who support importing the pill, which terminates pregnancies in the embryonic stage.

Myron Allukian, president of the American Public Health Association, who was a member of the delegation, said that RU-486, because it is non-surgical, produces less bleeding and less chance of infection and requires no anesthetic. He warned of a potential black market if it is not imported legally, which could lead to abuses in its use.

The French abortion pill has the potential of defusing much of the abortion controversy. It is cheaper and safer, and it puts a decision about abortion back where it belongs: Between women and their doctors. As more and more political organizations are discovering when they become embroiled in this fight, this is the only place for that decision to be made that makes any sense.

THE FOLLOWING DOCUMENT MAY NOT FILM
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THE ORIGINAL

SCIENTIFIC AMERICAN June 1990 Volume 262 Number 6

RU 486

This controversial drug is now used widely in France to terminate unwanted pregnancies. Yet the compound was not invented for that purpose and actually has many possible applications

by André Ulmann, Georges Teutsch and Daniel Philibert

In 1980 one of our colleagues synthesized a molecule with an unexpected property. Chemically it resembled the hormone progesterone, and like progesterone, it bound tightly to the progesterone receptor in cells. Yet instead of evoking the hormone's usual effects, this chemical blocked them. Because progesterone is crucial to the maintenance of pregnancy, the emergence of this unusual property raised the possibility that the new chemical might serve as a means of interrupting pregnancy.

The substance, designated RU 486 (after the maker, Roussel-Uclaf), is now on the market in France and the subject of worldwide controversy. International attention—both favorable and, in the case of antiabortion activists, unfavorable—has focused on the drug's role in the voluntary termination of early pregnancy.

Under the name mifepristone, RU 486 is administered as a tablet in conjunction with a small dose of a prostaglandin, which increases the frequency and strength of the uterine contractions needed to expel an embryo. In France the drug combination is approved for ending pregnancies of up to 49 days' duration (counting from the first day of the last menstrual period). There, between a quarter and a third of women who decide to interrupt an early pregnancy now choose this chemical approach over standard surgical procedures.

In the next few years RU 486 may also become available elsewhere for the same purpose. The manufacturer is considering distributing it in such countries as Great Britain, the Netherlands and Sweden, where the data required for licensing have already been amassed. The drug may also ultimately serve other functions as well. It has a number of possible therapeutic applications that are not limited to birth control and that include the treatment of certain cancers.

ANDRÉ ULMANN, GEORGES TEUTSCH and DANIEL PHILIBERT are colleagues at Roussel Uclaf in Romainville, France. Ulmann, a nephrologist and endocrinologist, is medical director; he headed the clinical testing of RU 486 by the company. Teutsch, a chemist who is director of endocrine research, focuses on the synthesis of steroids and peptides and on the production of new antibiotics. Philibert, a physicist and pharmacologist, supervised the research into how RU 486 acts in cells and in animals and is responsible for similar analyses of other steroid analogues synthesized at Roussel Uclaf.

RU 486 was not invented with the goal of pregnancy interruption in mind. Nevertheless, by the time it was synthesized, social concerns and scientific events had already helped set the stage for that use. International agencies were calling for the introduction of a variety of new birth control technologies. It was hoped that simplified or otherwise improved methods would help stem global population growth, which is accounted for by overwhelming growth in developing nations. The world's population expansion threatens the future availability of food, water and other resources and thus threatens the well being and the survival of the human species.

Among the desired technologies were new approaches to the termination of pregnancy. Many women in developing nations and, to a lesser extent, in industrialized countries rely on pregnancy interruption for birth control. Although legal surgical methods are safe and effective, they have well-known drawbacks. In the first three months of pregnancy, vacuum aspiration (sometimes preceded by dilation of the cervix) is the usual method of choice. In this approach, suction is applied to remove the embryo and the endometrial tissue in which it is embedded. After about three months of pregnancy, the required procedures generally become more complex. As pregnancy progresses, the risks of infection, hemorrhage, scarring and impaired fertility increase. In developing nations, where surgical facilities are often inadequate, the danger is greater. What is worse, where legally operated facilities are not readily accessible, many women die from having unsafe abortions, typically because of uncontrolled bleeding or infection.

Analyses of steroid hormones (of which progesterone is one) pointed to the possibility of a noninvasive and potentially safer means of interrupting pregnancy. Research suggested that if an agent with RU 486's particular antiprogesterone action could be identified and delivered as a tablet or by injection, it might offer a medical alternative to surgery.

This suggestion was informed by independent work done in the late 1960's and the 1970's by Edward T. Jones of the University of Chicago

Scientific American · 1990

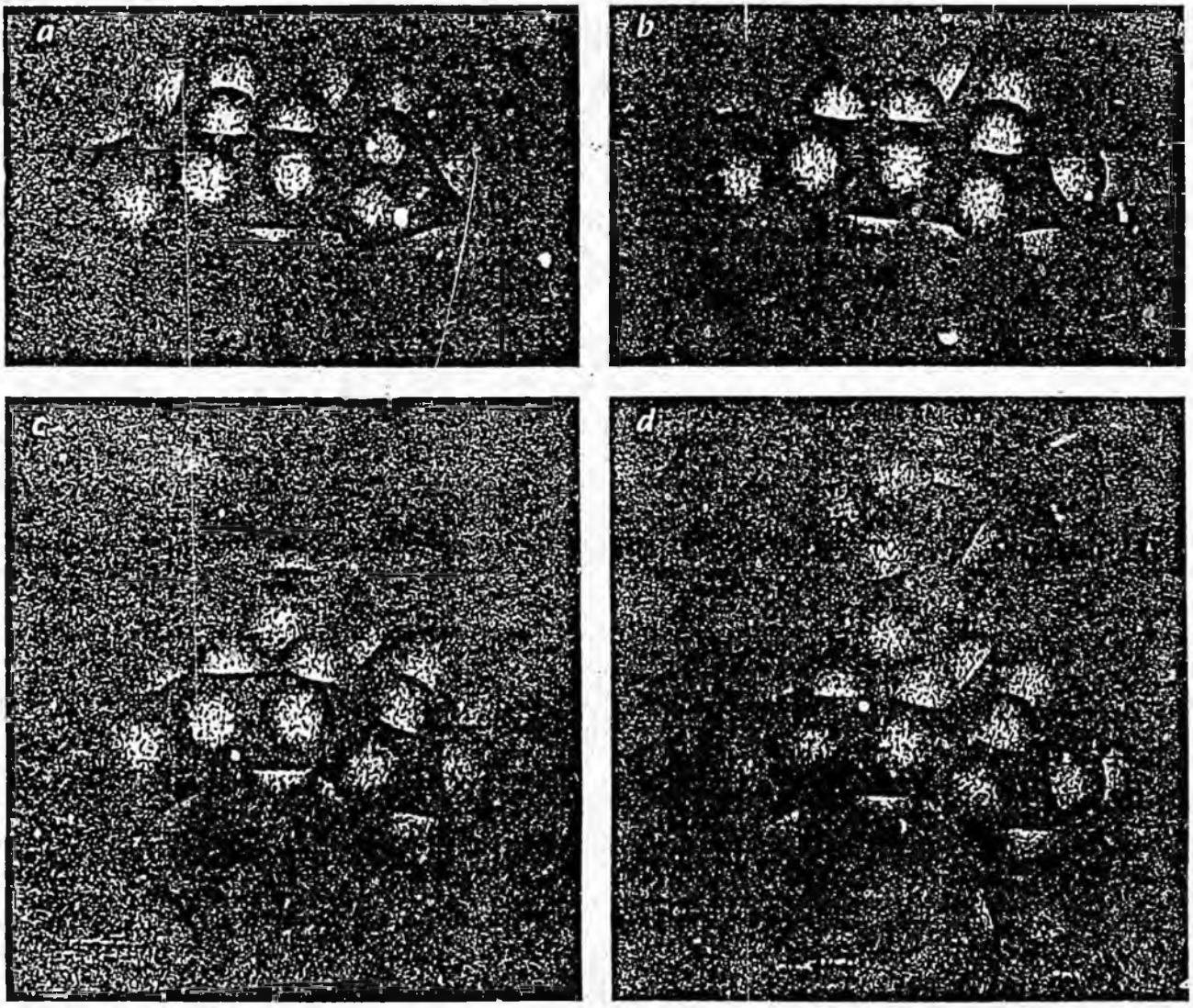
Etienne-Emile Baulieu of INSERM (the French institute for medical research) and Bert W. O'Malley of the Baylor College of Medicine in Houston, Tex. These investigators uncovered the basic mechanism by which steroid hormones induce cells to synthesize proteins. The steroids, which are derived from cholesterol, include not only progestins (progesterone and similar molecules) but also estrogens (such as estradiol), androgens (such as testosterone), glucocorticoids (such as cortisone) and mineralocorticoids (such as aldosterone).

The investigators showed that steroids, unlike polypeptide hormones, actually enter target cells. Inside a cell, they bind to receptors in the nucleus. The resulting unit—consisting of the bound steroid (the ligand) and its activated receptor—then binds to the chromatin in the nucleus (the complex of DNA and its associated proteins). That event then triggers the transcription of a selected gene from DNA into messenger RNA. Because the progesterone-stimulated synthesis of proteins in the uterus is essential to the maintenance of pregnancy, it was evident that the day scientists discovered a compound able to occupy progesterone receptors without inducing progesterone's effects, they would have an efficient and selective method for interrupting pregnancy.

It was expected that a progesterone antagonist would, depending on when it was administered, either prevent implantation of a fertilized egg or cause a more developed embryo to detach from the uterine wall. The details of how such effects might be induced were inferred from a long-held understanding of the menstrual cycle and pregnancy in mammals.

In the first half of the menstrual cycle—the follicular phase—estrogen and other hormones direct the development of a single ovarian follicle (an ovum and the cells that envelop it) and also induce the cells of the endometrium to proliferate. After the mid-cycle release of the egg at ovulation, the remnant of the follicle in the ovary becomes the corpus luteum, a transitory gland that secretes a continuous stream of progesterone.

The progesterone converts the proliferating endometrium into a tissue capable of accepting and nourishing a developing embryo. In particular, the



SHAPE of progesterone molecule (*a*) and three of its synthetic relatives was deduced by computer. Two of the molecules, norethindrone (*b*) and RU 42764 (*c*), mimic the hormone's activities, which are crucial to the maintenance of pregnancy. RU 486 (*d*) counteracts progesterone's effects, an antagonism that seems to stem from the bulky projection rising above the plane of the molecule. The green, blue, red and purple spheres represent carbon, hydrogen, oxygen and nitrogen, respectively.

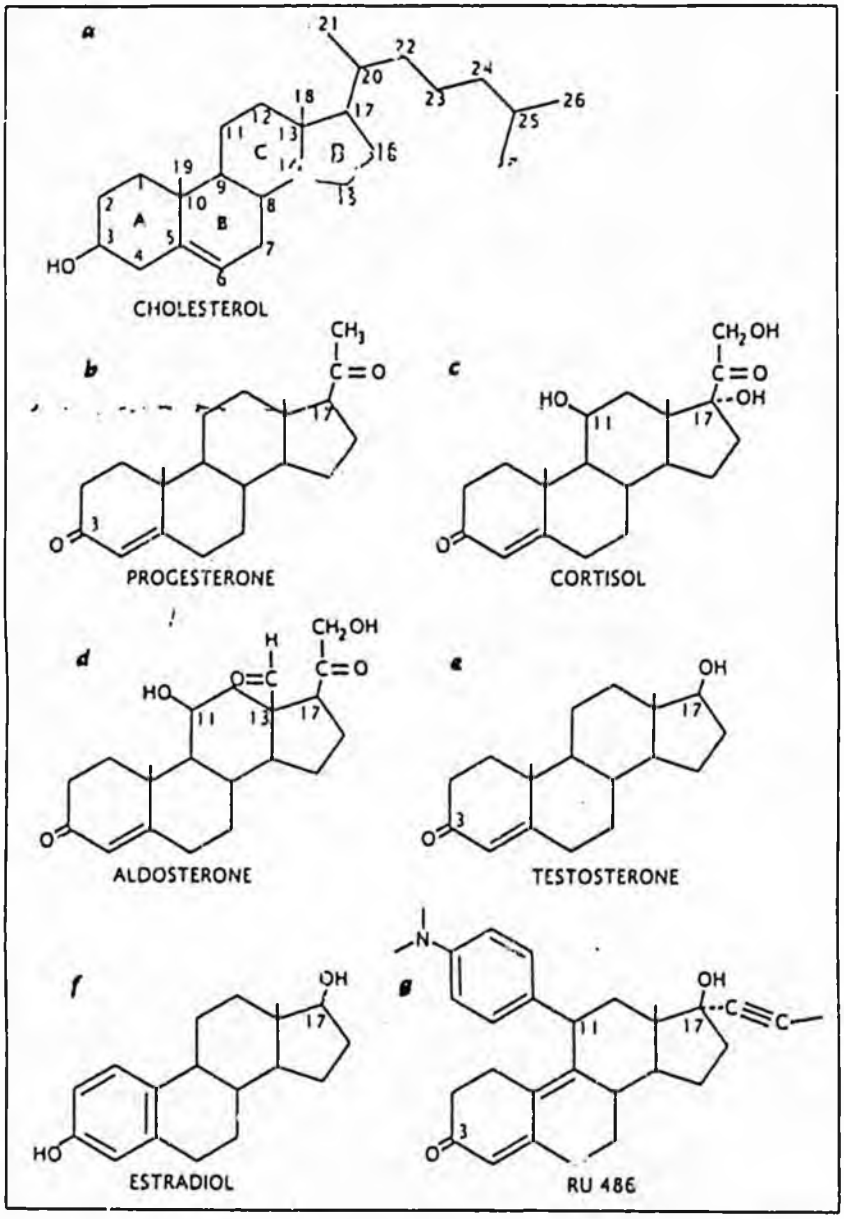
1310

hormone causes the endometrial cells to synthesize and store the sugar glycogen, promotes the growth of blood vessels in the expanded endometrium and increases the secretory activity of that tissue. Progesterone also relaxes the uterine muscle to forestall the contractions that might expel an embryo, and it further prevents expulsion by firming the cervix and inhibiting its dilation. These last effects derive in part from the ability of progesterone to inhibit the uterine secretion of prostaglandins.

If the egg is fertilized, it will begin to implant by about the sixth day after fertilization. Soon after, the trophoblast, or developing placenta, signals the corpus luteum to continue secreting progesterone until the placenta becomes fully functional in about the eighth week of pregnancy. If the egg is not fertilized, the corpus luteum begins to degrade after some 12 days, so that by about the 28th day of the cycle, the decline in progesterone results in the shedding of all but the basal (permanent) layer of the endometrium. Uterine bleeding follows, and the cycle begins anew.

The delivery of a progesterone antagonist before implantation, then, was expected to prevent the endometrium from undergoing the changes required for it to accept a new embryo. Given after implantation, the drug was expected to initiate a chain of events leading to the expulsion of the embryo. Blocking the secretory activity of the uterine lining would initiate endometrial erosion. That erosion would cause the developing placenta and the embryo to detach from the uterine lining. Then the corpus luteum would decay, resulting in a sharp decline in progesterone secretion. This decline would further erode the endometrium. At the same time, the decline in progesterone would lead to increased contractility of the uterine muscle and would facilitate the softening and dilation of the cervix, leading finally to the expulsion of the embryo.

In spite of such insight—and years of research, conducted primarily by the U.S. National Institutes of Health—no reasonable candidate for an antiprogesterone agent emerged until RU 486 was synthesized in 1980. It is ironic that, at the time, no one at Roussel-Uclaf was actively seeking a progesterone antagonist.



STEROIDS are derived from cholesterol (*a*), in which carbons are numbered according to a standard scheme. There is a structural similarity between representatives of each class: the progestins (*b*), glucocorticoids (*c*), mineralocorticoids (*d*), androgens (*e*) and estrogens (*f*). Because of this resemblance, synthetic steroids can sometimes bind to more than one kind of steroid receptor. For instance, RU 486 (*g*), which is a derivative of progesterone, binds strongly to both progestin and glucocorticoid receptors. RU 486 is known as an 11-substituted 19-norsteroid because an atomic grouping not found in progesterone is bound to the 11th carbon and because the methyl group (CH_3) that normally accounts for the 19th carbon has been removed.

The story of the compound's discovery actually begins a few years earlier, in 1975. One of us (Teutsch) was studying how small chemical alterations affect the ability of steroids to bind and activate their receptors. As part of his work, he developed a method of synthesizing versions of steroids that do not exist in nature. A young postdoctoral fellow, Alain Belanger, then produced the novel molecules.

As a matter of routine, each new steroidlike molecule made at Roussel-Uclaf is screened by the company's pharmacologists as a first step toward determining its possible effects in the body. On the assumption that a molecule capable of binding to a receptor might activate the receptor or block its activities, the pharmacologists determine the affinity of each new synthetic molecule for receptors representative of each of the five classes of steroids. The pharmacologists, led by Roger Deraedt, found that certain of the molecules made by Teutsch's

method bound extremely strongly to the progesterone receptor, some bound tightly to the glucocorticoid receptor and some bound well to both.

In many cases a molecule that binds tightly to a receptor is an agonist: it will produce the same effects as the natural ligand. Teutsch therefore decided to see if the same were true for the new creations. Because his responsibilities included research into glucocorticoids, he asked the pharmacologists to examine the activity of a molecule called RU 25055, which had a very high affinity for the glucocorticoid receptor.

RU 25055 did not behave as expected. When the molecule was mixed with cells that normally respond to glucocorticoids, it induced [illegible] able glucocorticoid activity, such as the shrinkage of thymic cells. That finding suggested the compound was actually a glucocorticoid antagonist. By binding strongly to the glucocorticoid receptor but failing to induce the usual effects, the molecule could presumably prevent such effects from occurring or from occurring with their usual intensity.

After this discovery was made, Teutsch and his colleagues gradually reversed their previous thinking about the relation between binding affinity and activity in this molecular series. They suspected that the molecules having the greatest affinity for the glucocorticoid receptor would actually have the strongest antagonistic, not agonistic, effect. This was an exciting notion because interesting therapeutic applications could be envisioned for an antagonist. For instance, a topically applied glucocorticoid antagonist might hasten the closure of burns or other skin lesions by counteracting the tendency of glucocorticoids to impair wound healing.

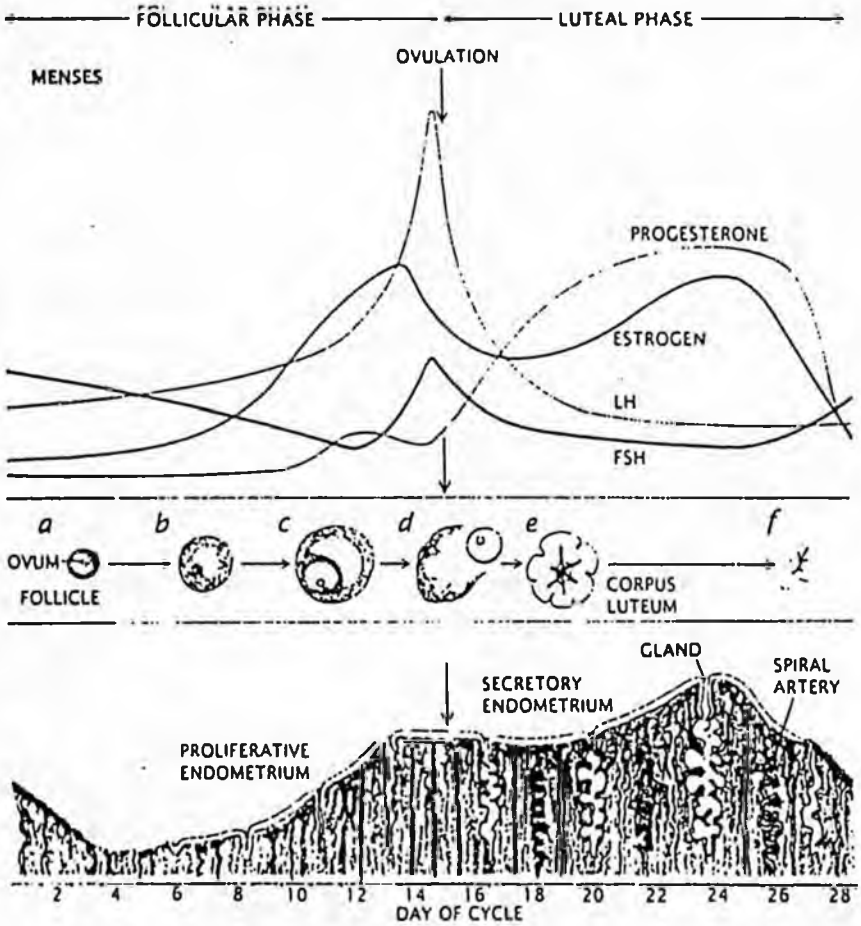
Toward the end of 1979 Edouard Sakiz, a company executive, created a formal research project for the development of glucocorticoid antagonists. Two of us (Teutsch and Philibert) participated in the project, as did other company employees and two scientific advisers from the outside: Sir Derek H. R. Barton, a 1969 winner of the Nobel prize for chemistry, and Baulieu, who by then was an established authority on steroid activity. One of us (Philibert) coordinated the project and supervised the studies of biological activity.

In April of 1980 three molecules synthesized as part of the new project were produced in succession and handed over to Philibert: RU 38140, RU 38473 and RU 38486—later shortened to RU 486. All bound strongly to the glucocorticoid receptor, and all interfered with certain activities of glucocorticoids in cell cultures. Of the three molecules, the last was the most potent; it was best able to block the actions of a powerful synthetic glucocorticoid (dexamethasone).

Yet the antiglucocorticoid activity of RU 486 was not the compound's only outstanding feature. Philibert's studies of its affinity for the five classes of steroid receptors indicated that the molecule also bound very strongly to the progesterone receptor. Initial tests in several animal species soon revealed that RU 486 was a progesterone antagonist.

Thus, the research group had inadvertently managed to produce the progesterone antagonist long awaited by investigators and clinicians interested in birth control. Baulieu, who himself had a long-standing interest in that area, was particularly struck by the importance of the discovery, and he convinced Roussel-Uclaf to pursue research into an antiprogesterone drug for fertility control. And so, serious testing of RU 486 for that purpose began.

Among the findings that convinced the company to proceed with investi-



MENSTRUAL CYCLE is regulated by several hormones (*top*). At the end of one cycle, the pituitary gland steps up secretion of follicle-stimulating hormone (FSH), which acts on the ovary (*middle*) to stimulate growth of an immature follicle (*a*). In the first half of the new cycle, the maturing follicle (*b* and *c*) secretes estrogen, which maintains follicle growth and both stimulates proliferation of the uterine lining (*bottom left*) and sensitizes the lining to progesterone. At midcycle, a surge of another pituitary factor, luteinizing hormone (LH), triggers ovulation (*d*). In the second half of the cycle, the remnant of the follicle in the ovary becomes the corpus luteum (*e*), which secretes progesterone and estrogen. The progesterone causes the endometrium to develop into a secretory, highly vascularized tissue (*bottom right*) that can receive and nourish a fertilized egg. If the egg is not fertilized, the corpus luteum eventually decays (*f*), and the resulting loss of progesterone leads to erosion of the endometrial lining. Bleeding then ensues, and the cycle begins once more.

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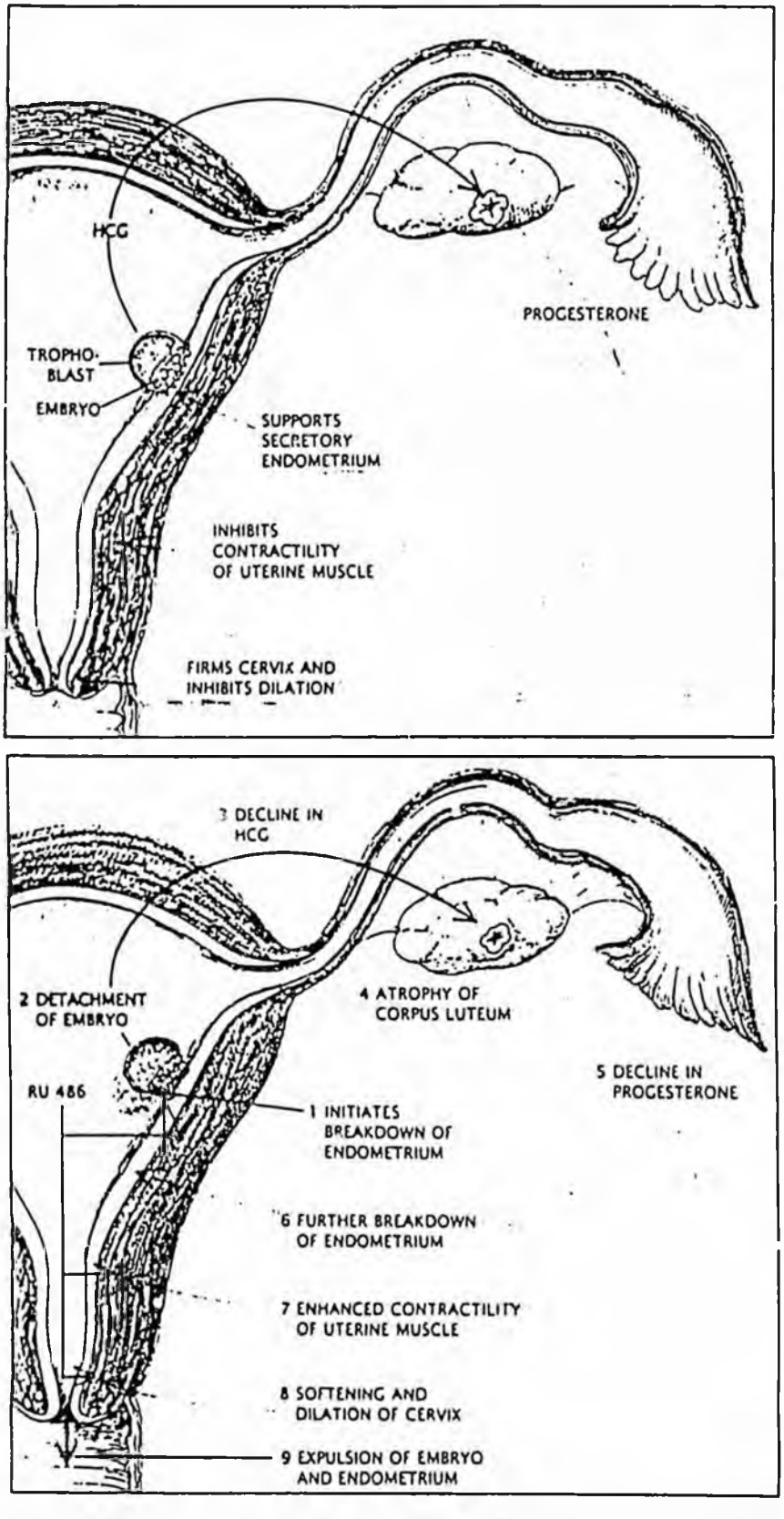


RU 486 interrupts pregnancy by opposing the action of progesterone at several sites in the uterus. In a normal pregnancy (*top*), the trophoblast (the future placenta) secretes human chorionic gonadotropin (HCG), which maintains the corpus luteum. Progesterone secreted by the corpus luteum has several effects that support the pregnancy. When that progesterone is blocked by RU 486 (*bottom*), the endometrium erodes and the embryo is detached and expelled along with the endometrial tissue.

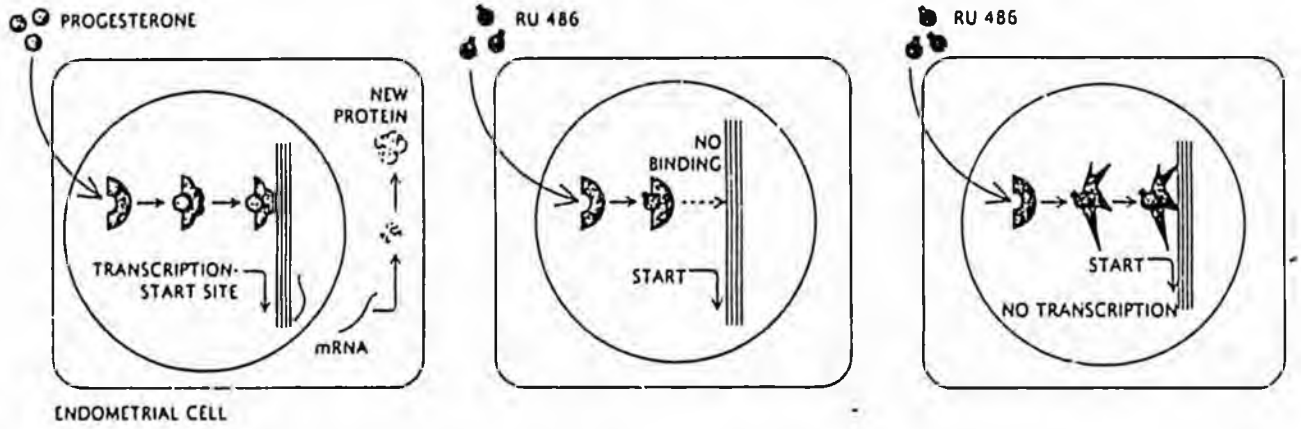
gations into the progesterone-antagonizing activity of RU 486 was the discovery that the in vitro binding affinity of RU 486 for the progesterone receptor was three times higher than that of progesterone. This activity suggested that the synthetic molecule would successfully compete with progesterone in the body and "win" occupancy of the receptor much of the time. Studies of cultured cells supported the idea, demonstrating that the effects of progesterone could be blocked in target cells that were exposed to a small amount of RU 486.

The true test of a compound's potential as a drug is its activity in vivo, and the results of the early animal studies had been encouraging as well. Some of these examined the effects of the compound on the endometrium of immature female rabbits. The rabbits were first injected with estradiol, an estrogen that both stimulates the growth of the endometrium and induces the cells to produce progesterone receptors. Next some of the animals were exposed to progesterone, which transformed the proliferating endometrium into a secretory tissue. Other rabbits were given RU 486 orally. The exposure to RU 486 alone did not induce the same transformation. Furthermore, when RU 486 was administered together with progesterone, the new compound actually blocked progesterone's ability to induce the change from a proliferative to a secretory state—as would be expected of a progesterone antagonist.

The findings of antagonism in vivo were important, but a crucial question still remained unanswered at the time Roussel-Uclaf decided to examine the potential of RU 486 to serve as an antiprogesterone drug: Could the antagonism that had been demonstrated thus far translate into the interruption of pregnancy? Studies of female rats, which do not have a menstrual cycle, confirmed that it could, and experiments with female monkeys (*Macaca fascicularis*), which do have such a cycle, offered further proof.

The first studies of monkeys were done with nonpregnant animals and revealed that a single oral or injected dose of RU 486 given in the second half of the cycle induced a premature menstrual period 48 hours after administration. Subsequently, Gary D. Hodgen and his colleagues at the Eastern Virginia University Medical School showed that the drug could also terminate pregnancy in monkeys. Other animal work established that RU 486, even at high doses, was nontoxic.

Such studies justified the initia-



PROGESTERONE acts within the cell (*left*). By occupying the progesterone receptor in the nucleus, the hormone modifies the receptor's shape, enabling it to bind to chromatin (DNA and associated proteins). Such binding leads to gene transcription and protein synthesis. RU 486 antagonizes these effects by occupying the receptor without stimulating gene transcription. It may block transcription by failing to induce the change in receptor shape required for chromatin binding (*center*). Or it may induce a change in shape that permits such binding but then prevents binding by critical transcription factors (*right*).

tion of clinical trials, and in October, 1981, Baulieu suggested to one of his colleagues, Walter Herrmann of the University Hospital of Geneva, that RU 486 be tested on human volunteers. The results were promising: RU 486 triggered expulsion of the embryo from the uterus in nine out of 11 women.

A number of clinical investigations soon followed under the auspices of Roussel-Uclaf, the World Health Organization and the Population Council, a nonprofit organization based in New York City. One of us (Ulmann) directed the clinical testing undertaken by Roussel-Uclaf.

The first large-scale studies were conducted in 1985 to determine the most effective administration schedule. It turned out that a single dose of 600 milligrams of RU 486 produced the best results. In the course of these studies, a consensus was reached as to exactly what constituted successful use of the drug. In short, RU 486 succeeded if no surgery was needed, that is, if the embryo and all but the deepest layer of the endometrium were expelled. (Incomplete expulsion calls for surgical removal, usually by vacuum aspiration, because the retained material can cause infection.)

By that standard, administration of RU 486 alone at best yielded an 80 percent success rate. The studies also found that the method worked only in early pregnancy, up to a week after menstruation would have been expected to begin. Considering that many women have a pregnancy test done only after that time, it became all too clear that RU 486 alone had limited applicability.

What accounted for the 20 percent failure rate? One reasonable hypothesis was that antagonism of progesterone could not by itself induce the frequent, strong uterine contractions required for complete expulsion of the embryo and the endometrial lining. To help correct that problem, Mark A. Bygdeman of the Karolinska Institute in Stockholm, who was overseeing a clinical trial, proposed adding a small dose of a prostaglandin to the protocol. He had earlier demonstrated that RU 486 increases the responsiveness of the uterine muscle to the contractile effects of prostaglandins.

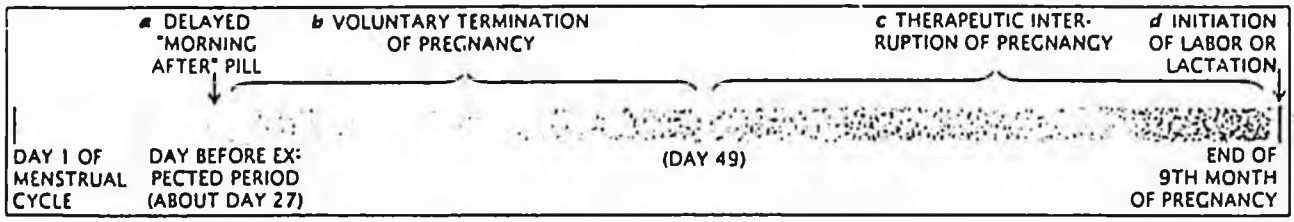
In accordance with Bygdeman's suggestion, new clinical trials were begun in France, Great Britain, Sweden and China to evaluate a new protocol: 600 milligrams of RU 486 delivered in a single dose, followed some 36 to 48 hours later by a prostaglandin. The interval cannot be shortened, because RU 486 takes time to sensitize the uterine muscle to prostaglandins.

The results improved dramatically. The success rate became 96 percent, close to the rate achieved with surgery, which itself is not foolproof. The studies also looked at the effects of the drug combination on somewhat more advanced pregnancies—those persisting up to three weeks past the missed period—and showed that the same 96 percent success rate could be achieved. In most cases the embryo and all endometrial fragments were expelled within 24 hours after the prostaglandin was administered.

As is true of miscarriages, in which a pregnancy is spontaneously arrested, the expulsion of the developing embryo and the endometrial lining was inevitably accompanied by uterine bleeding. In 4 to 5 percent of participants in these studies, the bleeding was heavy, as it can be during a normal miscarriage. Sometimes surgical intervention was needed to stop the bleeding, and in exceptional cases, a transfusion was needed. The results indicated that because of the risk of hemorrhage, the prostaglandin must be given in a medical facility where women can be monitored for several hours and, if necessary, treated.

The clinical studies further showed that abdominal pain, caused primarily by the contractile effects of the prostaglandin, is common. They also demonstrated that the 600-milligram dose of RU 486 needed to terminate a pregnancy did not cause clinically relevant antagonism of glucocorticoids. There was therefore no need to be concerned that RU 486 might produce undesirable antiglucocorticoid effects, such as profound fatigue and disturbances of electrolyte and glucose levels in the blood.

Once these studies were completed and reviewed, Roussel-Uclaf asked the French health authorities for permission to market the drug. This was duly granted on September 23, 1988. RU 486 is regulated by French law covering the termination of pregnancy, which stipulates that such terminations be performed only in authorized centers. There is one added restriction in the case of RU 486. Although the law permits voluntary termination of pregnancy through the 12th week, use of



APPLICATIONS OF RU 486 in fertility control and obstetrics are broad. The drug could serve as a delayed "morning after" pill (*a*) to be taken the day before menstruation is expected, for instance, in cases of rape. In France th. compound is given along with another drug, a prostaglandin, to terminate pregnancies of up to 49 days' duration (*b*). The combination of drugs is also able to interrupt pregnancy later and might be used when the mother's life is in danger or when the fetus is severely deformed or has died in utero (*c*). Studies of monkeys show that RU 486 can facilitate labor at term by sensitizing the uterus to the labor-inducing agent oxytocin; they also indicate that the compound can stimulate lactation (*d*).

RU 486 is limited to the seventh week of pregnancy because that is the outer limit examined in formal studies.

Since the autumn of 1988 more than 40,000 voluntary terminations have been performed with the combination of RU 486 and a prostaglandin. A recent study, published in March, of 2,115 of the women has confirmed the 96 percent success rate and the 4 to 5 percent rate of heavy bleeding. The study also showed that in 86 percent of the successful terminations, expulsion occurred within 24 hours of prostaglandin administration.

The average duration of bleeding in the subjects was nine days. Nevertheless, the time to expulsion, the duration of bleeding and the intensity of pain varied, depending on the dose of prostaglandin. A high dose was associated with faster expulsion but also with more prolonged bleeding and more intense pain.

Outside the study, physicians in the field have reported that two out of all the French women who received RU 486 have had severe disturbances in heart function after receiving the prostaglandin. The occurrence is rare and both women survived, but their difficulties suggest that prostaglandins should be administered cautiously in a woman who has heart disease or is at high risk for it, as in the case of heavy smokers.

It is now a decade since RU 486 was synthesized. The compound has begun to fulfill its potential as a nonsurgical method for interrupting early pregnancies, but that is only one of its many applications related to fertility control and obstetrics.

In theory, RU 486 might be taken as a delayed "morning after" pill, say, on the 27th day of a typical 28-day menstrual cycle. Because the drug is not always effective in this role, the woman must be tested some 10 to 15 days later to confirm she is not pregnant. For the same reason, the drug is not suitable as a routine postcoital birth-control agent.

The drug may have a place when a woman decides to end an early pregnancy by vacuum aspiration. Several clinical studies have found that the procedure is facilitated by taking RU 486 some 36 to 48 hours before the surgery. The compound helps by softening and dilating the cervix.

Still later in pregnancy, up through the third trimester, the combination of RU 486 and a prostaglandin might offer an alternative to surgery when a pregnancy must be ended because the fetus is seriously malformed or the health of the mother is endangered. Investigators have found that the approach can be effective in late pregnancy and is, in fact, less risky than the kinds of surgery usually required after the first trimester. The drug combination may also be helpful when the fetus dies in utero. In such cases the fetus is usually delivered vaginally, and so contractions are induced, often with much difficulty. Administration of RU 486 followed by a prostaglandin seems to facilitate expulsion of the fetus.

Studies of monkeys indicate that RU 486 may also help to induce labor at term. In the animals the drug has been shown to augment the labor-promoting effect of oxytocin, a pituitary hormone often infused in high doses in cases of stalled labor to stimulate uterine contractions. Hodgen has found that after RU 486 is administered, the frequency of uterine contractions can be increased with just a small amount of oxytocin. Thus, RU 486 may well help to avoid some cesarean deliveries. Hodgen's experiments also suggest yet another role for RU 486: in monkeys, at least, it triggers lactation and increases the volume of milk that is produced in the breasts.

Outside the realm of pregnancy, RU 486 may one day help to treat cancers that bear progesterone receptors, including certain breast cancers. In test-tube studies, RU 486 has slowed the growth of tumors displaying such receptors. Certain noncancerous tumors that synthesize progesterone receptors might also be controlled or reduced with RU 486, among them meningiomas (tumors of the meninges, the membranes surrounding the brain). Clinical trials examining applications in cancerous and noncancerous tumors are now in progress.

Finally, RU 486 may yet find application as a glucocorticoid antagonist. For instance, it is being studied as a treatment of Cushing's syndrome, a disorder that results from the overproduction of cortisone and leads to such symptoms as hypertension, rapid fat storage in the upper body and osteoporosis.

Clearly, RU 486, the first progesterone antagonist ever brought to market, has potential beyond its value in terminating pregnancy. Its application in that area is but the first stage in the history of the compound.

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RU486

The Pill That Could End the Abortion Wars and Why American Women Don't Have It

LAWRENCE LADER

Founding Chair, National Abortion Rights Action League

misc. back-up

NATION'S HEALTH

August 1990

THE

Official Newspaper of the American Public Health Association

APHA President Myron Allukian, second from left, was part of a delegation presenting thousands of petition on RU486 to the Roussel Uclaf company in France. Center is Dr. Edouard Sakiz, CEO of Roussel Uclaf, and Eleanor Smeal, President of the Fund for the Feminist Majority.

APHA Joins Delegation To Ask for RU486

A delegation representing APHA and other organizations recently returned from a European meeting with makers of RU486, "the abortion pill," expressing confidence that the drug will be available in the United States without extraordinary delay.

The group, spearheaded by the Feminist Majority, included APHA President Myron Allukian and nine other scientists and leaders of women's organizations.

After meeting for several hours in Paris with Dr. Edouard Sakiz, the Chief Executive Office of the Roussel Uclaf company, which makes the drug, the group said that they felt significant progress had been made in getting the company to make the pill available in the United States. The drug interrupts pregnancy in the early stages.

Several recent press reports have in-

See Delegation...page 5.

Delegation Asks Company To Bring RU486 to the US

...from page 1.

dicated that the controversy in this country about abortion and RU486 have blocked the introduction of the drug here, seemingly indefinitely.

Right to Life groups have threatened a boycott on the company's other products if RU486 is introduced in the US. The Food and Drug Administration has banned imports of it saying that it could present an unreasonable safety risk.

At a news conference members of the US delegation said they found the French pharmaceutical company executives very concerned that the drug be used with proper precautions and that it not be abused. In France now, where reportedly 50,000 abortions have been carried out through this method and one in three abortions is currently done this way, there are a number of controls on the procedure. The woman must take the drug in front of a physician and sign a form saying that she will have a surgical abortion if the procedure does not work. Reportedly, the pills are numbered and the distribution of the pills is documented.

Also, the pill is not given to women over 35 who smoke because two women in that category have had cardiac problems, although both women recovered.

According to the delegation, many of the company's fears concerned the decentralized nature of the health system in this country and what they perceived as the lack of control that might apply to the drug once it was introduced. The delegation was able to allay many of those fears, according to its members.

The delegation presented the company with 115,000 petition signatures gathered in the US from people asking that the drug be made available here.

The group also met with top officials of the Hoechst company, which owns the majority of Roussel Uclaf.

At the press conference, APHA President Myron Allukian said, "RU486 is effective, easy to administer and use, non-intrusive, and allows women more control over the way their personal health services are delivered....As a result of this visit I am convinced that this is a major advance in women's health care. Women in America should not be denied, for any reason, this high quality of health service which is available to women in other countries."

Allukian also indicated that because women taking RU486 do not require surgery, there is no need for anesthesia,and there is less bleeding and less chance of infection. It is also much more acceptable to women, he said.

As the technique is refined over time, the APHA president said, the procedure may become even simpler to administer and cheaper.

Eleanor Smeal, the President of the Feminist Majority, said that RU486 is the first major breakthrough in fertility control in the 30 years since the advent of the birth control pill, and it will indeedcome to this country because American women will demand it.

At the same news conference the Feminist Majority announced a major push to combat laws requiring parental consent for abortion for women under 18 in the states where those laws are enforced. It will be appealing particularly to young people on the issue.

The side effects of RU 486.

DRUG OF CHOICE

By Dorothy Wickenden

In the mid-1980s, as word of the French abortion pill rippled across the world, the new drug was greeted as a thing of awesome powers. Pro-choicers eagerly proclaimed that RU 486 would render both surgical abortion and the anti-abortion movement obsolete. If a woman suspected she was pregnant, she would go to her medicine cabinet and, in peace and privacy, swallow the pill. With this simple act she could banish the emotional, the physical, and even much of the moral trauma accompanying the decision to have an abortion. Described by its inventor, Etienne-Emile Baulieu, as a "contra-gestive" (because it impedes gestation rather than conception), RU 486 would in effect erase the distinction between a contraceptive and an abortifacient. Anti-abortionists, horrified at the euphoria, quickly marshaled their forces against the drug, calling it a "chemical time bomb" and a "death pill."

The pro-choicers have sounded more sober about RU 486 over the past couple of years. Their initial hopes for the drug as "the ultimate act of reproductive privacy" proved to be, as Bill Hamilton of Planned Parenthood puts it, "a myopic dream." The anti-abortionists' continual boycott threats have cowed the patent owner and sole manufacturer, Roussel Uclaf of France, and its parent company, Hoechst AG, a German multinational, into tightly restricting access to the drug. In France, the only country where RU 486 is actually available to women outside of clinical trials, each pill must be registered, and the drug is dispensed only by designated clinics, only after a pregnancy has been confirmed, and only through the seventh week. And though French doctors report impressive success with it as an abortifacient, the procedure turns out to be neither quick nor painless nor totally private. Patients are required to make four visits to a designated clinic, on the second of which they are given synthetic prostaglandin to reduce the risk of hemorrhage and help induce contractions.

But the more recent news doesn't look good for the

anti-abortionists. Distribution of RU 486 will start in Great Britain within the next year. Scandinavia and the Netherlands are expected to follow soon, and Sweden has begun testing it as a once-a-month contraceptive. Spain's Ministry of Health has made an official demand for the pill, and Baulieu, who still works for Roussel, says the Soviet Union will likely be next. The World Health Organization continues its own clinical studies on RU 486 in China, India, Hong Kong, and Cuba. Perhaps most alarming of all from the anti-abortionists' point of view, RU 486 is once again being described as a miracle drug—this time by American doctors who say it may prove just as effective in treating a range of deadly diseases as it is in terminating pregnancy. William Regelson, an oncologist at the Medical College of Virginia, declares, "If RU 486 did not have abortion associated with it, it would be considered a major breakthrough drug."

In the August 22/29 issue of *The Journal of the American Medical Association*, Regelson and two co-authors describe the proven and potential uses for RU 486 in treating some kinds of breast cancer and brain tumors, Cushing's syndrome—a terminal disease characterized by hypertension, osteoporosis, diabetes, and infections—and even AIDS. RU 486 is known as a "hormone antagonist" because it prevents cells from responding to certain hormones as they normally would. It arrests the course of pregnancy by blocking the action of progesterone, without which an embryo cannot survive. Some tumors and cancers thrive on hormones as well, as do all steroid-related diseases. Cushing's syndrome, for example, is caused by an excess production of cortisol, which is blocked by RU 486.

A program at the University of Southern California School of Medicine is using RU 486 in a small group of patients with a type of meningioma, or brain cancer, that cannot be cured with surgery. Martin H. Weiss, who heads the study with Stephen Grunberg, says that it is the only medical treatment that has ever been shown to work on these patients; a third of them have been responding to the treatment. George Chrousos, a senior investigator at the National Institutes of Health, who conducted a five-year study of RU 486 on Cushing's syndrome sufferers, describes "miraculous improvement" on eight of the twelve patients in his study within weeks after treatment began. RU 486 may even be helpful to women who *want* to have a baby. Doctors at the University of California, San Diego, are doing a pilot study of RU 486 as a treatment for endometriosis, a common cause of infertility in women; and many believe that it could be used to induce labor in difficult deliveries, thus reducing the need for Caesarian sections.

All this sounds too good to be true, and some of it may be. The hopes that RU 486 may help AIDS patients, for example, are based on little more than informed speculation, and researchers who had hopes that it might cure glaucoma have been disappointed with the results of their animal studies. Arthur Caplan, director of the Center for Biomedical Ethics at the University of Minnesota, points out that "the rhetoric of the abortion debate has gotten the science inflamed." Doctors, no less than the pro-choice and anti-abortion forces, have their own interests to protect, and it's not surprising that they are among those who tend to make extravagant claims about RU 486.

Anti-abortionists, of course, are quick to downplay its curative potential—well aware that once it is approved in the United States for other uses, doctors could legally prescribe it as an abortifacient as well, as long as abortion itself remains legal. John Willke, president of the National Right to Life Committee, says, "People are using the theoretical possibility of therapeutic use to get the drug into the country on a massive level for lethal use." Yet he insists that his organization objects only to studies on RU 486 as an abortifacient. "We couldn't stop the other research if we wanted to," he declares.

That's true, but they can impede it. Hoechst hastily withdrew the drug in September 1988, only a month after the French government had approved it. A Roussel stockholders' meeting had been the scene of an anti-abortion protest, and the National Right to Life Committee in Washington and Catholic groups in France had issued a boycott threat against Hoechst and Roussel. Extremists proclaimed that I. G. Farben, the ancestor company of Hoechst, manufactured cyanide for Hitler's death camps. Distribution of RU 486 was resumed under orders from the French government, which owns 36 percent of Roussel Uclaf. Undeterred, the anti-abortionists kept up their boycott threats, and in December 1988 Roussel devised a set of criteria that countries have to meet before they can receive the drug: abortion must be legal and accepted by medical, public, and political opinion; prostaglandin must be available; distribution must be strictly controlled; and the patient must be required to sign a consent form declaring that if the treatment fails (as it does in up to 4 percent of women), she will have a surgical abortion. This would eliminate the possibility of babies born with defects—an unlikely prospect, many doctors claim, since RU 486 is taken in a single dose and the drug is metabolized quickly, but one that understandably concerns the manufacturer.

According to Roussel, the United States does not qualify for the drug—even though abortion is legal and supported by a majority of the American public. By "accepted by public opinion," the company clearly means "uncontroversial"—a much tougher standard, which thus far essentially has given a noisy minority veto power over a major medical development. Willke vows that if RU 486 comes to the United States, he'll mount a worldwide boycott of every product made by Roussel and Hoechst, and, he warns, "It'll be a whopper." Hoechst AG owns two New Jersey-based companies: Hoechst-Roussel Pharmaceuticals and Hoechst Celanese Corporation, a chemical company that produces everything from carpet fibers to tire cord. Hoechst Celanese alone has annual revenues in the

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United States of $6 billion. American pharmaceutical companies, which could push for a license from Roussel, apparently have no intention of doing so. "Do you have any idea what would happen in the U.S. if the drug were being distributed?" one unnamed senior executive at a drug company told *The Washington Post* when RU 486 was issued in France. "The market is potentially huge and the drug appears worthy. But who needs the headache?"

Some researchers who covet the new wonder drug are exasperated by Roussel's extreme caution about relinquishing it. William Regelson and his co-authors say that the threatened boycott has "largely frozen clinical trials," citing as evidence Roussel's cancellation of a meeting that it was to attend in April 1989 at Memorial Sloan-Kettering in New York to help the National Cancer Institute organize a multicenter study of RU 486 for treating breast cancer. Regelson says he was later told by a Hoechst employee that the company had pulled back because of the hostile political climate. Gary Hodgen, president of the Jones Institute for Reproductive Medicine, who has conducted numerous studies on RU 486 since 1982, says of Roussel and Hoechst, "They have limited access far more strictly than they did in years prior to 1989, no question about that." Baulieu denies these charges. It is high costs and the need for quality control, he insists, that have restricted the number of studies. And apparently not all doctors have had trouble getting the drug. Michael Kettle, who is working on the endometriosis study at San Diego, says that he and his co-workers have received active support from Roussel in their work.

On one point, at least, most people agree: Roussel's tight hold on RU 486 has crimped research in some critical areas. Since the early '80s the National Institutes of Health, which is barred from doing any abortion-related studies, has been conducting clinical trials of RU 486 for its use as a contraceptive and cellular studies on it as a possible future cure for breast cancer. However, one of NIH's most promising studies on RU 486 has come to a halt. Unlike women who use it as an abortifacient, patients with Cushing's syndrome require massive doses on a daily basis for extended periods throughout their lives. Although NIH researchers were excited by the extraordinary progress shown by the patients in the study, for whom no other medical treatment is effective, NIH decided not to continue its study in part because of concerns that it would be unable to obtain the quantities needed to sustain the patients' recovery.

One curious sign of the anti-abortionists' discomfort about RU 486 is their rhetoric. When Willke talks about the drug, he emphasizes the threat that it poses to women's health. He calls it a "chemical Dalkon Shield," "a powerful, poisonous steroid" that "kills unborn babies, will injure and kill women, and will cause an epidemic of fetal deformity." This would seem to be a shrewd tactic. The grisly history of fertility control—DES, Thalidomide, and the early birth control pill, as well as the Dalkon Shield—has made many women dubious about being subjected once again to an experimental drug whose long-term effects are unknown.

But this line of attack has already been shattered by the powerful medical establishment. The American Medical Association and *The New England Journal of Medicine*, among others, have declared that RU 486, when properly administered, is as safe as surgical abortion—one of the most common and least dangerous of all surgical procedures. The AMA has endorsed testing RU 486 here and is supporting efforts to convince Roussel to release it. Moreover, doctors are confident that as research continues, the drug—like the early birth control pill—will either be improved upon or replaced by a more sophisticated successor. NIH researchers hope that within the next several years they will have figured out the appropriate dose of RU 486 to be used as a birth control pill, perhaps taken only once or several times a month, and that it will have fewer side effects than the current pill.

Anti-abortionists should be the first to recognize the power of high-tech medicine to affect the political and ethical climate surrounding abortion. Sonograms have enabled us to peer inside the womb and detect the heartbeats of fetuses as young as six-and-a-half weeks, a development that helped to raise doubts among many whose support for abortion during the early months of pregnancy previously had been unqualified. RU 486 seems to be having precisely the opposite effect—removing some of the moral onus from abortion. Most people—even many in the anti-abortion rank and file—have fewer qualms about the idea of aborting a three-quarter-inch embryo than a fetus at three months, complete with tiny fingers and toes and all of its organs. So a pill that would both enable women to have earlier abortions and result in fewer late ones would doubtless be widely seen here, as it has been in France and other countries, as a welcome medical advance. And once its other potential uses are known, and the clamor for the drug increases, the issue will become even more problematic, not least among those who believe RU 486 should be available to prolong health and save lives but have serious scruples about it as an abortifacient.

On the other hand, Willke's health warnings about RU 486 have doubtless proved effective in raising the specter of lawsuits, which scare drug manufacturers in the United States as much as anti-abortion protesters do. Ever since the Dalkon Shield disaster, pharmaceuticals and insurance companies have retreated almost entirely from the field of birth control. In fact, insurance is no longer available in this country for clinical testing of most contraceptives. And even if a U.S. drug company decided to ignore the threat of political harassment and financial vulnerability, it would first have to wind its way through the byzantine—and politicized—regulatory maze. After getting a license from Roussel, a company would present a protocol to the Food and Drug Administration for its own round of expensive tests on RU 486 and

synthetic prostaglandin, and, finally, submit the drug application to the lengthy FDA approval process—an even more complex procedure when two drugs are involved. The FDA, for its part, has already revealed its susceptibility to political pressure: in June 1989, at the urging of Senator Jesse Helms, Representatives Henry Hyde and Robert Dornan, and others, it banned the import of RU 486 into the United States for private use.

Limitations on birth control research, of course, mean fewer and less effective means of family planning for Americans. This only perpetuates the country's staggering rates of teenage pregnancy and abortion, both of which are among the highest in the industrialized world. A report of the National Research Council estimates that between 1.2 million and 3 million unwanted pregnancies occur in the United States each year, and that about half of the 1.5 million abortions each year are due to contraceptive failure.

Steps are being taken, though, to break the impasse. Some members of Congress, galvanized by an administration that, like its predecessor, has been more receptive to the demands of a powerful interest group than to the idea of pressing forward in controversial areas of medical research, have begun to move. In July, at the instigation of Representative Barbara Boxer of California, seventy members signed a letter urging Roussel to make RU 486 available for testing in the United States, in the hope that eventually Roussel will be convinced that the anti-abortionists represent neither the views of established medicine nor the will of the public at large. In late October the reauthorization bill for NIH collapsed after conservatives vehemently objected to several abortion-related provisions—among them proposals for new centers to study contraception and infertility, which they claimed might lead to federal funding of research on RU 486. But this month Representative Ron Wyden of Oregon is holding a hearing on RU 486, in an attempt to smoke out the administration's position on the drug, and to raise questions about the extent to which the politics of abortion is impeding research that could save lives.

As for the pharmaceutical companies, eventually they may find the lure of profits more compelling than the fear of boycotts and litigation—especially if RU 486 brings with it some of the health benefits that are predicted. The boycott threat could turn out to be a paper tiger: it will be hard to convince Americans not to buy a laxative made by Hoechst-Roussel Pharmaceuticals because its parent company also owns the company that produces RU 486. And Hoechst-Roussel specializes in prescription drugs rather than over-the-counter products. Even the liability conundrum is not insoluble. Many have proposed devising an insurance scheme for controversial new drugs and devices that would assure companies they would only be liable if culpable error could be proved. An insurance pool would cover unforeseen casualties.

Meanwhile, a group of physicians in San Francisco—unwilling to wait for drug companies and the FDA—has attempted to get the testing started themselves. Theirs would be the first trial in the United States of RU 486 with prostaglandin. (An earlier study, at the University of Southern California, examined the efficacy of the drug alone.) California's attorney general, John Van de Kamp, has proposed that the state invoke a statute that allows California to test, manufacture, and market drugs within its own borders that are not yet approved by the FDA. Three hospitals have agreed to conduct the trials, but the doctors' plan has stalled because Roussel has refused their request for the drug.

However, Baulieu, an irrepressible advocate of his invention, is confident that RU 486 will soon find its way to the United States—and "not through the back door," as the Californians are proposing. "I don't see any reason to have partial distribution," he says. "As in the U.K., the pressure will be so strong that it will go ahead in the USA. Roussel will help when the conditions are better." Baulieu is advocating a joint undertaking that would include Roussel, a non-profit organization here (most likely Planned Parenthood), and a group of venture capitalists.

The anti-abortionists have raised legitimate questions about how RU 486 might be misused if it becomes a legal commodity here. What happens if a pregnant teenager gets hold of some pills in her second trimester, and thinks they'll solve her problem? Because the U.S. regulatory system is so decentralized, it will be more difficult to maintain the scrupulous controls over distribution that France has imposed. But this country would doubtless require abortion patients to undergo the same series of doctors' visits, to receive the pills and the prostaglandin only at clinics and hospitals, and to sign the same strict consent forms. And the United States isn't exactly slack about drug safety standards. RU 486 could be handled like any prescription drug that poses a threat to the fetus (such as the acne treatment Accutane, with doctors strictly screening patients and the FDA requiring detailed warning inserts along with the prescription). Or, if necessary, it could be deemed a "Class 3" drug, like barbiturates and amphetamines, which doctors cannot prescribe without a special license, and which requires a detailed accounting on the part of physicians and pharmacists to avoid forgeries and other abuses.

There is no denying that RU 486 is an eerie drug. Even the most ardent pro-choice advocates have to ask whether there isn't a critical distinction between a contraceptive and a "contra-gestive." But RU 486, like abortion itself, isn't going to go away—regardless of the restrictions that are placed on it. As more countries begin using the drug, demand for it here will increase. And if it is not approved and carefully regulated in the United States, a black market will certainly develop, with predictably unpleasant consequences. Thus Willke and his colleagues will have succeeded in creating exactly the circumstance he claims to fear the most: widespread misuse of a potent drug with possibly serious health hazards for women. •

RU 486 and Abortion

A Feminist Majority Foundation Report

Developed by Roussel Uclaf, a French pharmaceutical company, RU 486 (or Mifepristone) is the first in a new generation of fertility control which can cause the interruption of an early pregnancy. But Roussel Uclaf refuses to make RU 486 available to American women.

RU 486: THE ABORTION PILL

As an anti-progestin, RU 486 works by blocking the action of the hormone progesterone. Without progesterone, the lining of the uterus breaks down (as it does prior to a menstrual cycle) and the conceptus is expelled. Because RU 486 stops gestation after fertilization of the egg, it has been called an abortion pill.

SAFETY AND EFFICACY

RU 486, taken in pill form, has been used by over 90,000 women in 20 different countries and has been found to be both safe and effective in terminating unwanted pregnancies. Taken alone, RU 486 causes complete evacuation of the uterus 80% of the time. **When a prostaglandin is administered 48 hours after RU 486 has been taken, the procedure is 96% successful through the first nine weeks following a missed menstrual period.**

PREGNANCY TERMINATION AND RU 486

In France, where RU 486 was approved for use in 1988, one out of three women seeking an abortion chooses the compound in place of another procedure. In France, there are currently four steps in the process:

Step 1: French law requires that a woman who wishes to terminate her pregnancy visit an authorized birth control center, where she is given a pregnancy test and a clinical examination. She must register her decision to have an abortion and then wait seven days before she can end the pregnancy.

Step 2: If she elects an abortion with RU 486, she returns to the center a second time and is given a 600 milligram oral dose of RU 486.

Step 3: After two days, she returns a third time for an injection or a vaginal suppository of prostaglandin. Prostaglandin causes contractions of the uterus and helps ensure its complete evacuation.

Step 4: Five to seven days later, she makes a final visit to her physician to make sure that the abortion is complete.

In countries with no mandatory waiting period for abortion, Steps 1 and 2 would be combined and the procedure would require only three visits instead of four. Leading scientists believe that RU 486 eventually will be combined with a slow-releasing prostaglandin, eliminating the need to administer these medications separately.

WHY MANY WOMEN PREFER RU 486

Many women prefer RU 486 because it allows them greater psychological control over the termination of pregnancy. Due to its its popularity, RU 486 could eventually replace 50% of vacuum aspiration or surgical abortions.

A woman can take RU 486 as soon as she knows that she is pregnant. Surgical abortion generally cannot be performed before the seventh week of pregnancy.

The administration of RU 486 is non-invasive, has no risk of infection, and does not require anesthesia. A vacuum aspiration abortion is invasive, has a slight risk of infection, and is commonly performed with local anesthesia in the United States.

RU 486 eventually ~~will be~~ less expensive than vacuum aspiration abortions.

BRINGING RU 486 INTO THE UNITED STATES

RU 486 was licensed in France in 1988 and in Great Britain in 1991. Shortly after its introduction in France, Roussel Uclaf pulled RU 486 off the market, attributing their decision to anti-abortion pressure. Two days later, the French government ordered Roussel to make the compound available to women in France, declaring RU 486 "the moral property of women."

Yet RU 486 remains unavailable to American women. On June 9, 1989, in response to lobbying by anti-abortion members of Congress, the U.S. Food and Drug Administration (FDA) issued an import alert on RU 486, banning importation of the compound for personal use.

Opponents of abortion rights have threatened boycotts against the French manufacturer of RU 486, Roussel Uclaf, and its German parent company, Hoechst, A.G. Thus far Roussel and Hoechst have decided not to apply for a license to distribute RU 486 in the United States.

FEMINIST MAJORITY PETITIONS PHARMACEUTICAL FIRMS

To visibly counter anti-abortion politics, the Feminist Majority Foundation is organizing the public, scientists, researchers, and health care professionals in the United States for the Campaign for RU 486 and Contraceptive Research.

Over 250,000 individuals have joined thousands of distinguished scientists, including winners of the Nobel Prize and the National Medal of Science, in signing petitions urging the manufacturers to release the drug.

In July, 1990, a Feminist Majority Foundation delegation of feminist leaders, scientists and health care professionals presented 800 pounds of some 115,000 petitions to Roussel Uclaf and Hoechst, A.G.

This delegation held a series of historic meetings with leading officials from both companies, including Roussel CEO Edouard Sakiz. The manufacturers were impressed by both the scientific and broad-based support for RU 486.

ORGANIZATIONS SUPPORT RU 486

Major American organizations have passed resolutions calling for release of the drug to the U.S. for research purposes:

American Medical Association
American Public Health Association
American Assoc. for the Advancement of Science
American Institute of Biological Sciences
American Pediatric Society
Zero Population Growth
National Organization for Women
Society for the Study of Reproduction
National Cushing's Syndrome Association
Endometrosis Association
Endocrine Society
National Association of Breast Cancer Organizations

RU 486 and Breast Cancer

A Feminist Majority Foundation Report

The French pill RU 486 has sparked international interest as a possible treatment for breast cancer. Yet the manufacturer of this compound has not provided RU 486 to any researcher for human clinical trials for breast cancer in the United States.

INCIDENCE OF BREAST CANCER

Breast cancer is an epidemic. Each year over 175,000 women will be diagnosed with breast cancer in this country alone. One in nine American women will develop breast cancer in her lifetime.

Breast cancer kills 44,500 women in the United States annually.

BREAST CANCER AND HORMONE TREATMENT

Breast cancer is the most common form of cancer in American women. Some types of breast cancer are "responsive" to different hormones: that is, tumors grow in response to levels of a particular hormone.

Great advances in breast cancer treatment have been made by using "anti-hormone" drugs to block the action of the hormone which causes tumors to grow.

For example, tamoxifen is an anti-estrogen drug which has been successfully used to delay breast cancer recurrence and reduce tumor growth in "estrogen-responsive" breast cancers.

RU 486 AND BREAST CANCER

Since RU 486 is an anti-progesterone drug, there is strong interest in testing RU 486 to see if its effects would be similar to tamoxifen when used as a new form of hormonal therapy for progesterone-responsive breast cancer.

In animal studies, conducted by Dr. Bakker *et al* in the Netherlands, RU 486 reduced breast cancer tumors as well as tamoxifen. The administration of both tamoxifen and RU 486 reduced tumor size more than each drug alone.

RU 486 also may be a second-line treatment for tumors that have become resistant to tamoxifen. In a preliminary clinical trial in France, Dr. Romieu *et al* found that RU 486 halted some cancer growth in 12 of 22 breast cancer patients after other treatments failed. Additionally, this study reported that RU 486 reduced pain from the metastasis of cancer cells to the bones.

RU 486 has been tested domestically at the National Institutes of Health (NIH) in Washington, D.C. and elsewhere to determine if its progesterone-blocking action might remove the stimulus for the growth of some breast cancer tumors.

All U.S.-based studies concerning RU 486 and breast cancer have consisted of basic laboratory research using only animal and human cell lines. In Europe, however, researchers in France and the Netherlands have progressed to human clinical trials using RU 486 for breast cancer.

SCIENTISTS SUPPORT RU 486

The most prestigous scientific organizations in the United States have passed resolutions calling for the release of RU 486 for research purposes. These organizations include:

American Medical Association
American Public Health Association
American Association for the Advancement of Science
American Institute of Biological Sciences
American Pediatric Society
Endocrine Society

WOMEN'S HEALTH CARE ADVOCATES SUPPORT RU 486

Advocates of women's health care also have expressed support for RU 486, including the **National Alliance of Breast Cancer Organizations**, National Organization for Women, Endometriosis Association, and National Cushing's Syndrome Association **believe research into RU 486's possible applications should move forward immediately.**

BRINGING RU 486 INTO THE UNITED STATES

Opponents of abortion rights have threatened boycotts against the French manufacturer of RU 486, Roussel Uclaf, and its German parent company, Hoechst, A.G. Thus far Roussel and Hoechst have not applied for a license to distribute RU 486 in the United States.

At the present time, RU 486 is licensed in France and Great Britain as a safe, effective abortifacient.

The U. S. Food and Drug Administration's politically-motivated ban on personal importation of RU 486 has caused confusion, delays and obstacles for researchers investigating the non-abortifacient indications of RU 486 as a treatment for breast cancer, Cushing's Syndrome, meningioma and endometriosis. The Feminist Majority Foundation believes that Roussel Uclaf and Hoechst, A.G. should make RU 486 more widely available for use and continued research.

FEMINIST MAJORITY PETITIONS AMERICAN PHARMACEUTICAL FIRMS

To visibly counter anti-abortion politics, the Feminist Majority Foundation is organizing the public, scientists, researchers and health care professionals in the United States for the Campaign for RU 486 and Contraceptive Research. Over 250,000 individuals have joined thousands of distinguished scientists, including winners of the Nobel Prize and the National Medal of Science, in signing Foundation petitions urging the manufacturers to release the drug.

In July, 1990, a Feminist Majority Foundation delegation of feminist leaders, scientists and health care professionals presented 800 pounds of some 115,000 petitions to Roussel Uclaf and Hoechst, A.G. This delegation held a series of historic meetings in Paris and Frankfurt with leading officials from both companies, including Roussel's CEO Edouard Sakiz. The manufacturers were impressed by both the scientific and broad-based support for RU 486.

RU 486 and Cushing's Syndrome

A Feminist Majority Foundation Report

Some forms of Cushing's Syndrome, a deadly disease, can be treated with the new French pill RU 486. But opponents of abortion have caused the near-halt of research into this and other life-saving applications of RU 486 simply because the compound is an effective abortifacient.

WHAT IS CUSHING'S SYNDROME?

Cushing's Syndrome results from an overproduction of **cortisol,** a natural glucocorticoid hormone produced by the endocrine system. Normally, the pituitary gland (located between the optic nerves) sends messages to the adrenal glands (found just above the kidneys) signalling how much cortisol is needed. In Cushing's Syndrome, this signal is not shut off and the adrenal glands begin massive overproduction of cortisol. Too much cortisol can be fatal.

The disease is triggered by the growth of a tumor in one of three locations in the body. "Spontaneous Cushing's" occurs when a small benign tumor develops on the pituitary gland, or on one of the adrenal glands. "Ectopic Cushing's" occurs more rarely when cancerous tumors, often on the lung, pancreas, or thymus gland, produce a hormone that stimulates cortisol secretion.

RU 486 AND CUSHING'S SYNDROME

The RU 486 compound is an anti-glucocorticoid: it binds to glucocorticoid receptors in the body and thus prevents the hormone cortisol from binding. Researchers at the National Institutes of Health (NIH) and elsewhere have investigated RU 486 as a possible treatment for Cushing's Syndrome since 1983.

One important NIH study has shown that when people gravely ill with inoperable tumors were given RU 486, over half experienced actual reversal and control of the disease as well as complete regression of the Syndrome's features. Administration of RU 486 enables the patient to regain strength, simultaneously allowing doctors enough time to find and remove the tumor(s). Without RU 486, the patient's condition continues to deteriorate, prevents surgery, and may result in death.

RU 486 already has helped patients in the United States with advanced Cushing's Syndrome symptoms. Two such survivors testified before Congress that RU 486 saved their lives.

The National Cushing's Association strongly supports making RU 486 available in the United States.

WHO IS AFFECTED BY CUSHING'S SYNDROME?

The vast majority of Cushing's victims are women, primarily in their 20's - 40's. But it also affects men, and can strike children too. Cushing's Syndrome is not a common disorder. However, many more people have Cushing's than are diagnosed with the disease. In fact, many people who have the disease have suffered for years before proper diagnosis is made. Widespread use of pharmacological doses of glucocorticoids

administered for a wide range of other diseases may have given **millions** of people mild variants of this disorder.

WHAT HAPPENS TO PEOPLE WITH THIS DISORDER?

- excessive weight gain, especially fat deposits on upper body leading to "buffalo hump" and "moon face" features
- severe muscular weakness, impotence, and urinary incontinence
- mental depression, memory loss, severe mood swings
- osteoporosis (bone thinning)
- thinning of the hair
- development of diabetes mellitus
- atherosclerosis
- acne, facial hair growth in women
- loss of menstrual periods
- hypertension (high blood pressure)
- suppression of the immune system

If left untreated, Cushing's Syndrome can be fatal.

WHAT TREATMENTS EXIST?

Selective surgical removal of the tumor in the pituitary gland, complete removal of the adrenal gland which has the tumor, or complete resection of an ectopic tumor are treatments for Cushing's. Surgical treatment relieves the predominant symptoms and reverses the process. But surgery is often not possible for people with Ectopic Cushing's, or when the cancer has metastasized. For these cases, RU 486 may be the only possible treatment.

BRINGING RU 486 TO THE U.S.

Opponents of abortion rights have threatened boycotts against the French manufacturer of RU 486, Roussel Uclaf, and its German parent company, Hoechst, A.G. Thus far Roussel and Hoechst have not applied for a license to distribute RU 486 in the United States. At the present time, RU 486 is licensed in France and Great Britain.

The U.S. Food and Drug Administration's ban on personal importation of RU 486 has caused confusion, delays and obstacles for researchers. Scientists who need RU 486 for the treatment of Cushing's Syndrome and for research into the medication's potential as a life-saving treatment for diseases such as breast cancer have had difficulties obtaining RU 486. The Feminist Majority Foundation believes that Roussel Uclaf and Hoechst, A. G. should make RU 486 more widely available for use and continued research.

FEMINIST MAJORITY PETITIONS PHARMACEUTICAL FIRMS

To visibly counter anti-abortion politics, the Feminist Majority Foundation is organizing the public, scientists, researchers and health care professionals in the United States for the Campaign for RU 486 and Contraceptive Research. Over 250,000 individuals have joined thousands of distinguished scientists, including winners of the Nobel Prize and the National Medal of Science, in signing petitions urging the manufacturers to release the drug.

Major American organizations, such as the American Association for the Advancement of Science, American Medical Association, the American Public Health Association, Endocrine Society, Endometriosis Association, Society for the Study of Reproduction, National Organization for Women, **National Cushing's Syndrome Association**, and the National Association of Breast Cancer Organizations, also have passed resolutions calling for release of the drug to the U.S. at least for research purposes.

In July 1990, a Feminist Majority delegation of feminist leaders, scientists and health care professionals presented 800 lbs. of some 115,000 petitions to Roussel Uclaf and Hoechst, A.G. This delegation held a series of historic meetings in Paris and Frankfurt with leading officials from both companies, including Roussel's CEO Edouard Sakiz.

RU 486 and Meningioma

A Feminist Majority Foundation Report

The new French pill RU 486 shows promise as a treatment for meningioma, a type of brain or spinal cord tumor. But opponents of abortion have caused the near-halt of research into this and other life-saving applications of RU 486 simply because the compound is an effective abortifacient.

WHAT IS MENINGIOMA?

Meningiomas develop from the middle of the three layers of membrane that cover the brain and spinal cord. As meningiomas grow, they erode the outer membranes and cause thickening of the bones of the skull. Eventually, they may protrude through the skull and appear beneath the scalp as a firm lump. Depending upon the location of the meningioma, the tumor can cause a host of symptoms. Symptoms of brain tumors range from headaches, vision problems, seizures and memory loss to difficulty speaking, reading and writing.

Tumors of the spinal cord can cause pain in the neck and shoulders, loss of sensation in the upper part of the body, numbness or tingling in the arms or legs, difficulty walking, and a gradual weakness of the body. Usually benign, meningiomas are very slow growing tumors, that can cause debilitating symptoms and are sometimes fatal.

INCIDENCE OF MENINGIOMA

Meningiomas account for between 15 and 20% of all brain tumors, and 32% of all spinal cord tumors. **Meningiomas occur two times more frequently in women than in men.**

Surgery is usually the treatment recommended for tumors located in an accessible area of the brain or spinal cord. Radiation therapy is used for inaccessible tumors, or those which can only be partially removed.

RU 486 AND MENINGIOMA

According to the Association for Brain Tumor Research, meningiomas are more common in women, may enlarge or become symptomatic during pregnancy or the menstrual cycle, and are positively associated with breast cancer.

These indications suggest that the hormones estrogen and progesterone influence tumor growth. Meningioma cells have been found to contain progesterone and estrogen receptors, lending physical support to this theory. Meningiomas are more commonly positive for progesterone receptors than for estrogen receptors.

By binding with progesterone receptors, RU 486 -- an anti-progesterone -- may inhibit the growth of, or actually reduce meningiomas.

In a study by Dr. Grunberg *et al* at the University of Southern California School of Medicine,

RU 486 was found to have some efficacy in the treatment of patients with inoperable meningioma. Of 14 patients, 5 experienced objective tumor regression (reduced tumor measurement). Four patients also experienced subjective improvement (improved extraocular muscle function or relief for headache). Because meningiomas occur within closed spaces - the skull or spinal cord - even small amounts of shrinkage can mean important improvement for the patient.

BRINGING RU 486 INTO THE U.S.

Opponents of abortion rights have threatened boycotts against the French manufacturer of RU 486, Roussel Uclaf, and its German parent company, Hoechst, A.G. Thus far Roussel and Hoechst have not applied for a license to distribute RU 486 in the United States. At the present time, RU 486 is licensed in France and Great Britain as a safe, effective abortifacient.

The U. S. Food and Drug Administration's politically-motivated ban on personal importation of RU 486 has caused confusion, delays and obstacles for researchers investigating the non-abortifacient indications of RU 486 as a treatment for breast cancer, Cushing's Syndrome, meningioma and endometriosis.

The Feminist Majority Foundation believes that Roussel Uclaf and Hoechst A.G. should make RU 486 more widely available for use and continued research.

FEMINIST MAJORITY PETITIONS PHARMACEUTICAL FIRMS

To visibly counter anti-abortion politics, the Feminist Majority Foundation is organizing the public, scientists, researchers and health care professionals in the United States for the Campaign for RU 486 and Contraceptive Research. Over 250,000 individuals have joined thousands of distinguished scientists, including winners of the Nobel Prize and the National Medal of Science, in signing Foundation petitions urging the manufacturers to release the drug.

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This delegation held a series of historic meetings in Paris and Frankfurt with leading officials from both companies, including Roussel's CEO Edouard Sakiz. The manufacturers were impressed by both the scientific and broad-based support for RU 486.

ORGANIZATIONS FOR RU 486

Major American organizations now have passed resolutions calling for release of the drug to the U.S. at least for research purposes:

American Medical Association
American Public Health Association
American Association for the Advancement of Science
American Institute of Biological Sciences
American Pediatric Society
Zero Population Growth
National Organization for Women
Society for the Study of Reproduction
Endometriosis Association
National Cushing's Syndrome Association
Endocrine Society
National Association of Breast Cancer Organizations

RU 486 and Endometriosis

A Feminist Majority Foundation Report

The new French pill RU 486 shows promise as a treatment for endometriosis, a chronic, long-term, painful disease that can affect women for their entire reproductive lives. But opponents of abortion have caused the near-halt of research into this and other life-saving applications of RU 486 simply because the compound is an effective abortifacient.

WHAT IS ENDOMETRIOSIS?

Endometriosis is the growth of uterine tissue outside of the uterus: in the abdomen, on the ovaries and abdominal lining, bowel and bladder. Endometrial growths usually respond to the hormones of the menstrual cycle just as the lining of the uterus does. Tissue builds up each month and is sloughed off. But endometrial tissue outside of the uterus has no way of leaving the body. The result is internal bleeding, formation of scar tissue, inflammation, and other medical problems.

Endometriosis is one of the three leading causes of female infertility.

WHO IS AFFECTED BY ENDOMETRIOSIS?

At least 5 million women between the ages of 11 and 50 are affected by endometriosis in the United States.

The most common symptoms of the disease are pain before and during menstrual periods, pain during or after sexual activity, infertility, and heavy or irregular bleeding. It is difficult to diagnose because these symptoms, as well as other less common ones, may be caused by other conditions.

Another barrier to accurate diagnosis is the unfortunate ignorance of many health professionals about the disease. As recently as the 1980's many medical students were taught that the symptoms of endometriosis originate in the mind or in mental or emotional conflict, and many women were referred to psychiatrists or given tranquilizers to "treat" this physiological condition.

Only ten to fifteen percent of girls and women in the United States with endometriosis are properly diagnosed.

RU 486 AND ENDOMETRIOSIS

The cause of endometriosis is unknown, and currently there is no cure. One method of treatment involves using male and female hormonal preparations to try to shrink endometrial growths.

In addition to being an anti-progestin and an anti-glucocorticoid, RU 486 appears to be a non-competitive anti-estrogen. As such, it is a possible new hormonal treatment for endometriosis. Through an unknown mechanism, RU 486 seems to block the capacity of the endometrial tissue to grow in response to estrogen.

RU 486 also inhibits the secretion of estrogen in the body, lowering the amount of estrogen available to exacerbate endometrial growths.

There is currently only one human clinical trial in the United States investigating the efficacy of RU 486 in treating endometriosis. Much more data is needed before RU 486 could be used to treat women with endometriosis. But scientific research into the many potential applications of RU 486 is being slowed, if not stopped altogether, by non-scientific obstacles.

BRINGING RU 486 INTO THE UNITED STATES

Opponents of abortion rights have threatened boycotts against the French manufacturer of RU 486, Roussel Uclaf, and its German parent company, Hoechst, A.G. Thus far Roussel and Hoechst have not applied for a license to distribute RU 486 in the United States. At the present time, RU 486 is licensed in France and Great Britain as a safe, effective abortifacient.

The U. S. Food and Drug Administration's politically-motivated ban on personal importation of RU 486 has caused confusion, delays and obstacles for researchers investigating the non-abortifacient indications of RU 486 as a treatment for breast cancer, Cushing's Syndrome, meningioma (brain tumors) and endometriosis.

The Feminist Majority Foundation believes that Roussel Uclaf and Hoechst A.G. should make RU 486 more widely available for use and continued research.

The critical need for research into endometriosis, both causes and treatments, cannot be underestimated. It is unconscionable that research into a promising treatment for this little understood disease is being hindered.

FEMINIST MAJORITY PETITIONS PHARMACEUTICAL FIRMS

To visibly counter anti-abortion politics, the Feminist Majority Foundation is organizing the public, scientists, researchers and health care professionals in the United States for the Campaign for RU 486 and Contraceptive Research. Over 250,000 individuals have joined thousands of distinguished scientists, including winners of the Nobel Prize and the National Medal of Science, in signing Foundation petitions urging the manufacturers to release the drug.

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ORGAINIZATIONS FOR RU 486

Major American organizations now have passed resolutions calling for release of the drug to the U.S. for research purposes:

Endometriosis Association
American Medical Association
American Public Health Assocation
American Association for the Advancement of Science
American Institute of Biological Sciences
American Pediatric Society
Zero Population Growth
National Organization for Women
National Cushing's Syndrome Association
Endocrine Society
Society for the Study of Reproduction
National Association of Breast Cancer Organizations

RU 486 and Women in Developing Nations

A Feminist Majority Foundation Report

"If it is important, as I believe it is, to make a humanitarian effort to reduce the complications of abortion -- in countries where it is illegal, in countries when it is badly done, in countries where the health service infrastructure is inadequate -- then it has to be admitted that RU 486 presents an opportunity of doing better and cheaper abortions." - Dr. Etienne Baulieu

RU 486 CAN SAVE WOMEN'S LIVES

For women in poor nations in Latin America, Asia and Africa, RU 486 represents a significant and potentially life-saving discovery. **According to the World Health Organization (WHO), an estimated 200,000 young women die each year (one every three minutes) in these countries as a result of unsafe and illegal abortion.**

The vast majority of women in poor nations terminate their pregnancies outside the formal health sector using unsafe methods that often result in infections and bleeding.

In hospitals in developing nations, dilation and curettage (D&C), although twice as risky as either the use of RU 486 or vacuum aspiration abortion, remains the most frequently employed means of ending a pregnancy.

The availability of better technology, already used in wealthy nations, could vastly improve the quality of care women receive. RU 486 is a safe and inexpensive alternative for women in poor nations who lack fertility control options.

HOW RU 486 WORKS

Developed by Roussel Uclaf, a French pharmaceutical company, RU 486 (or Mifepristone) is the first in a new generation of fertility control methods which can cause the interruption of an early pregnancy.

By blocking the action of the hormone progesterone, RU 486 causes the lining of the uterus to break down (as it does prior to a menstrual cycle) and the conceptus to be expelled. Because RU 486 stops gestation after fertilization of the egg, it has been called an abortion pill.

To date, RU 486 has been used by over 90,000 women in 20 different countries.

Taken alone, RU 486 causes complete evacuation of the uterus 80% of the time.

When a prostaglandin is administered 36 to 48 hours after RU 486 has been given, the procedure is 96% successful through the first nine weeks following a missed menstrual period.

WHY MANY WOMEN PREFER RU486

For a variety of reasons, many women favor RU 486:

•Pregnancy termination with RU 486 is a non-invasive procedure, requiring no anesthesia and putting women at no risk of infection.

• RU 486 affords women relative privacy - both in making and in carrying out their reproductive decisions.

• RU 486 can be administered to a woman as soon as she knows that she is pregnant and wants to have an abortion. By contrast, a woman must wait until the seventh week of pregnancy before she is able to have a vacuum aspiration abortion.

• Many women prefer RU 486 because it allows them greater psychological control over the termination of pregnancy.

RU 486: ADVANTAGES IN POOR NATIONS

There are some particular advantages in the use of RU 486 in poor countries:

• Minimal time from skilled practitioners is needed to administer RU 486. Its use would free up scarce and valuable medical personnel to attend to other work.

• RU 486 is safer and more effective than both currently used methods of self-induced abortion and D&C, the most frequently used method of pregnancy termination in hospitals in developing nations.

• Through a Roussel Uclaf - WHO agreement, RU 486 is available to the public sector in developing countries at a low price, estimated to be between $2 and $4 per treatment.

• Because RU 486 affords women relative privacy, it is culturally more acceptable than more invasive procedures in many settings.

AVAILABILITY OF RU 486

To date, however, RU 486 is available only in France and in the UK. Although China was the first country to approve RU 486 following extensive clinical trials, the drug has not been made available to that country. The Chinese have synthesized their own version of the compound which is being tested in Shanghai.

The bulk of the research on RU 486 in poor countries has been sponsored by the Special Programme of Research, Development and Research Training in Human Reproduction at the World Health Organization (HRP/WHO) under a contract with Roussel. Clinical studies with RU 486 have been conducted in China, Cuba, India, Singapore, and Viet Nam. WHO studies on the efficacy of RU 486 as an abortifacient have been limited to countries where abortion is legal.

The lack of appropriate equipment and technology, restrictive abortion laws, the Reagan-Bush gag rule (the so-called "Mexico City Policy"), weak health-care infrastructures, and the over-medicalization of abortion and other health-care services all deny women access to safe, legal abortion.

Expanding the availability of RU 486 is a critical step toward preventing the needless deaths of women in poor nations.