# DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
## STATEMENT OF INVESTIGATOR
*(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) Part 312)*
(See instructions on reverse side.)

Form Approved: OMB No. 0910-0014.
Expiration Date: November 30, 1995.
*See OMB Statement on Reverse.*

NOTE: No investigator may participate in an investigation until he/she provides the sponsor with a completed, signed Statement of Investigator, Form FDA 1572 (21 CFR 312.53(c)).

**1. NAME AND ADDRESS OF INVESTIGATOR.**

Suzanne Poppema, M.D.
Aurora Medical Services, Inc. PS
1207 North 200th Street, Suite 214
Seattle, WA 98133

**2. EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFIES THE INVESTIGATOR AS AN EXPERT IN THE CLINICAL INVESTIGATION OF THE DRUG FOR THE USE UNDER INVESTIGATION. ONE OF THE FOLLOWING IS ATTACHED:**

☒ CURRICULUM VITAE ☐ OTHER STATEMENT OF QUALIFICATIONS

**3. NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL, OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATION(S) WILL BE CONDUCTED.**

Aurora Medical Services, Inc. PS
1207 North 200th Street, Suite 214
Seattle, WA 98133

**4. NAME AND ADDRESS OF ANY CLINICAL LABORATORY FACILITIES TO BE USED IN THE STUDY.**

Aurora Medical Services, Inc. PS
1207 North 200th Street, Suite 214
Seattle, WA 98133

**5. NAME AND ADDRESS OF THE INSTITUTIONAL REVIEW BOARD (IRB) THAT IS RESPONSIBLE FOR REVIEW AND APPROVAL OF THE STUDY(IES).**

Institutional Review Board
Under the auspices of

**6. NAMES OF THE SUBINVESTIGATORS *(e.g., research fellows, residents, associates)* WHO WILL BE ASSISTING THE INVESTIGATOR IN THE CONDUCT OF THE INVESTIGATION(S).**

Suzanne T. Poppema, M.D.
Seattle, WA CFN 3032921
EI: 11/01/99-11/05/99

Exhibit I Page 3 of 6

**7. NAME AND CODE NUMBER, IF ANY, OF THE PROTOCOL(S) IN THE IND FOR THE STUDY(IES) TO BE CONDUCTED BY THE INVESTIGATOR.**

Evaluation of the Efficacy, Safety and Acceptability of Mifepristone and Misoprostol in Inducing Abortion in Pregnant Women with Amenorrhea of up to 63 Days

Protocol #166A

8. ATTACH THE FOLLOWING CLINICAL PROTOCOL INFORMATION:

☐ FOR PHASE 1 INVESTIGATIONS, A GENERAL OUTLINE OF THE PLANNED INVESTIGATION INCLUDING THE ESTIMATED DURATION OF THE STUDY AND THE MAXIMUM NUMBER OF SUBJECTS THAT WILL BE INVOLVED.

☐ FOR PHASE 2 OR 3 INVESTIGATIONS, AN OUTLINE OF THE STUDY PROTOCOL INCLUDING AN APPROXIMATION OF THE NUMBER OF SUBJECTS TO BE TREATED WITH THE DRUG AND THE NUMBER TO BE EMPLOYED AS CONTROLS, IF ANY; THE CLINICAL USES TO BE INVESTIGATED; CHARACTERISTICS OF SUBJECTS BY AGE, SEX, AND CONDITION; THE KIND OF CLINICAL OBSERVATIONS AND LABORATORY TESTS TO BE CONDUCTED; THE ESTIMATED DURATION OF THE STUDY; AND COPIES OR A DESCRIPTION OF CASE REPORT FORMS TO BE USED.

9. COMMITMENTS:

I agree to conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, rights, or welfare of subjects.

I agree to personally conduct or supervise the described investigation(s).

I agree to inform any patients, or any persons used as controls, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent in 21 CFR Part 50 and institutional review board (IRB) review and approval in 21 CFR Part 56 are met.

I agree to report to the sponsor adverse experiences that occur in the course of the investigation(s) in accordance with 21 CFR 312.64.

I have read and understand the information in the investigator's brochure, including the potential risks and side effects of the drug.

I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.

I agree to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make those records available for inspection in accordance with 21 CFR 312.68.

I will ensure that an IRB that complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR Part 312.

## INSTRUCTIONS FOR COMPLETING FORM FDA 1572
## STATEMENT OF INVESTIGATOR:

1. Complete all sections. Attach a separate page if additional space is needed.

2. Attach curriculum vitae or other statement of qualifications as described i

3. Attach protocol outline as described in Section 8.

4. Sign and date below.

Suzanne T. Poppema, M.D.
Seattle, WA CFN 3032921
EI: 11/01/99-11/05/99
Exhibit 1 Page 4 of 6

5. FORWARD THE COMPLETED FORM AND ATTACHMENTS TO THE SPONSOR. The sponsor will incorporate this information along with other technical data into an Investigational New Drug Application (IND). INVESTIGATORS SHOULD NOT SEND THIS FORM DIRECTLY TO THE FOOD AND DRUG ADMINISTRATION.

| 10. SIGNATURE OF INVESTIGATOR | 11. DATE |
|---|---|
| Suzanne Poppema MD | 11-8-94 |

Public reporting burden for this collection of information is estimated to average 84 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

ports Clearance Officer, PHS
ubert H. Humphrey Building, Room 721-B
200 Independence Avenue, S.W.
Washington, DC 20201
Attn: PRA

and to:

Office of Management and Budget
Paperwork Reduction Project (0910-0014)
Washington, DC 20503

Please DO NOT RETURN this application to either of these addresses.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

# STATEMENT OF INVESTIGATOR

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Suzanne T. Poppema, M.D.
Seattle, WA CFN 3032921
EI: 11/01/99-11/05/99
Exhibit 1 Page 5 of 6

**7. NAME AND CODE NUMBER, IF ANY, OF THE PROTOCOL(S) IN THE IND FOR THE STUDY(IES) TO BE CONDUCTED BY THE INVESTIGATO**

Evaluation of the Efficacy, Safety and Acceptability of Mifepristone and Misoprostol in Inducing Abortion in Pregnant Women with Amenorrhea of up to 63 Days

Protocol #166A



MIF 002503

8. ATTACH THE FOLLOWING CLINICAL PROTOCOL INFORMATION:

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## INSTRUCTIONS FOR COMPLETING FORM FDA 1572

### STATEMENT OF INVESTIGATOR:

1. Complete all sections. Attach a separate page if additional space is needed.

2. Attach curriculum vitae or other statement of qualifications as described in Section 2.

3. Attach protocol outline as described in Section 8.

4. Sign and date below.

Suzanne T. Poppema, M.D.
Seattle, WA CFN 3032921
EI: 11/01/99-11/05/99 LSL
Exhibit I Page 6 of 6

5. FORWARD THE COMPLETED FORM AND ATTACHMENTS TO THE SPONSOR information along with other technical data into an Investigational New Drug Application (IND). INVESTIGATORS SHOULD NOT SEND THIS FORM DIRECTLY TO THE FOOD AND DRUG ADMINISTRATION.

| 10. SIGNATURE OF INVESTIGATOR | 11. DATE |
|---|---|
| Suzanne T. Poppema M.D. | 3/6/95 |

# *Suzanne T. Poppema*

1207 North 200th Street, Suite 214
Seattle, Washington 98133
(206) 546-8891


~~Assistant~~ Associate Clinical Professor / Family Medicine / Medical Director

## *Education*

**University of Washington School of Medicine** 1974-1977
Family Residency
Board Certified 1979, Re-certified 1987

**Harvard Medical School** 1970-1974
**M.D.**

**University of New Hampshire** 1964-1970
**Bachelor of Arts**, Government
*Summa Cum Laude*

## *Professional Summary*

### *Reproductive Experience*

**Aurora Medical Services, Inc. P.S.**, Seattle, Washington 1985-Present
**MEDICAL DIRECTOR**

- Women's health care clinic providing abortion services in conjunction with wellness care associated with reproductive services.
- Manage a staff of thirteen.

**Helen Jackson Center For Women,** Everett, Washington 1987-1989
**MEDICAL DIRECTOR**

- Women's health care clinic providing reproductive services

**Wyeth-Ayerst,** Philadelphia, Pennsylvania 1991-Present
**NORPLANT INSERTION AND REMOVAL TRAINER**

**Population Dynamics (now Aurora Medical Services),** Seattle, Washington 1975-1985
**MEDICAL CONSULTANT**

**Planned Parenthood - Snohomish County,** Everett, Washington 1980-1982
**MEDICAL DIRECTOR**

# *Suzanne T. Poppema*


(206) 546-8891

Associate ~~Assistant~~ Clinical Professor / Family Medicine / Medical Director

## *Professional Summary*

### *Reproductive Experience*

**Denver Women's Health Care Clinic,** Denver, Colorado — 1978-1979
**MEDICAL DIRECTOR AND FOUNDING MEMBER**

**Aradia Women's Health Center,** Seattle, Washington — 1975-1979
**MEDICAL DIRECTOR**

### *Professional Experience*

**NorthCreek Family Medicine,** Everett, Washington — 1980-1988
**PRESIDENT, FAMILY PRACTITIONER**

**Denver Health and Hospital,** Denver, Colorado — 1978-1979
**FAMILY PRACTITIONER**

### *Academic Appointments*

**ASSOCIATE ~~ASSISTANT~~ CLINICAL PROFESSOR** — 1999 → present ~~1986-Present~~
University of Washington, School of Medicine
Family Medicine Department, Seattle, Washington

**CLINICAL INSTRUCTOR** — 1978-1979
University of Colorado, School of Medicine
Family Practice Department, Denver, Colorado

### *Hospital Staff Appointment*

Providence General Hospital — 1980-Present
Everett, Washington

~~Assistant~~ Associate Clinical Professor / Family Medicine / Medical Director

## *Professional Organizations*

***Leadership***

*National Abortion Federation, 1991-present; President, 1998-2000*
*National Abortion Federation, Clinical Policies Committee Chair, 1992-1998*
*Society of Physicians for Reproductive Choice and Health, Secretary, Board of Directors, 1996-present*

***Current Membership***

*Association of Reproductive Health Care Professionals, 1990*
*National Abortion Federation, 1989*
*Washington State Association of Abortion Providers, 1986*
*National Abortion Rights Action League, 1980*
*Washington State Medical Association, 1980*
*Snohomish County Medical Society, 1979*
*American Medical Women's Association, 1977*
*American Academy of Family Practice, 1977*



## *Publications/Research*

**A Clinician's Guide to Medical and Surgical Abortion**, Editors Drs. Paul, Grimes, Lichtenberg, et al. **Ensuring Quality Care in Abortion Services**, Suzanne T. Poppema, M.D., et al, Churchill Livingston, February 1999

**Low Dose Mifepristone 200 mg. and Vaginal Misoprostol for Abortion**, Eric A. Schaff, M.D., Suzanne T. Poppema, M.D. et al; to be published.

**The Future of Roe v. Wade**, Suzanne T. Poppema, M.D., Frances Kissling, Carol Sanger, Ms. Magazine, January/February 1998, Vol. 8 #4

**Why I am an Abortion Doctor**, Suzanne T. Poppema, M.D. & Mike Henderson, Prometheus Press, 1996

**Evaluation of the Efficacy, Safety and Acceptability of Mifepristone and Misoprostol in Inducing Abortion in Pregnant Women with Amenorrhea of up to 63 Days**, 1994-1995. The Population Council, Inc. New York, New York

**Depomedroxyprogesterone Acetate and Lipid Profile Alterations**. (Unpublished) 1986-1993 Aurora Medical Services, Seattle, Washington

RU-486, studied with Roussel Uclaf & Dr. Elisabeth Aubeny - Sabbatical, Paris, France 1989

Washington State Department of Health

# *MEDICAL TEST SITE LICENSE*

*This is to certify that*

**AURORA MEDICAL SERVICES**

*located at* **1207 N 200TH ST**
**SUITE 214**
**SEATTLE, WA 98133**

*is hereby licensed as a medical test site in accordance with Chapter 70.42 RCW subject to the provisions of this law, and the standards, rules and regulations of the Department of Health under Chapter 246-338 WAC.*

*License Number:* **MTS-0705**
*CLIA Number:* **50D0632980**
*Category:* **A**

*License Effective:* **11/01/94**
*License Expires:* **10/31/96**

THE SEAL OF THE STATE OF WASHINGTON 1889

Martha D. Simon

*Department of Health*

Suzanne T. Poppema, M.D.
Seattle, WA CFN 3032921
EI: 11/01/99-11/05/99
Exhibit 6 Page 1 of 8

MIF 002508

Washington State Department of Health

# MEDICAL TEST SITE LICENSE

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**AURORA MEDICAL SERVICES**

*located at* **1207 N 200TH ST #214 SEATTLE, WA 98133**

*is hereby licensed as a medical test site in accordance with Chapter 70.42 RCW subject to the provisions of this law, and the standards, rules and regulations of the Department of Health under Chapter 246-338 WAC.*

*License Number:* **MTS-0705** *Category:* **A**

*License Effective:* **11/01/93** *License Expires:* **10/31/94**

THE SEAL OF THE STATE OF WASHINGTON 1889

Suzanne T. Poppema, M.D.
Seattle, WA CFN 3032921
EI: 11/01/99-11/05/99
Exhibit 6 Page 2 of 8

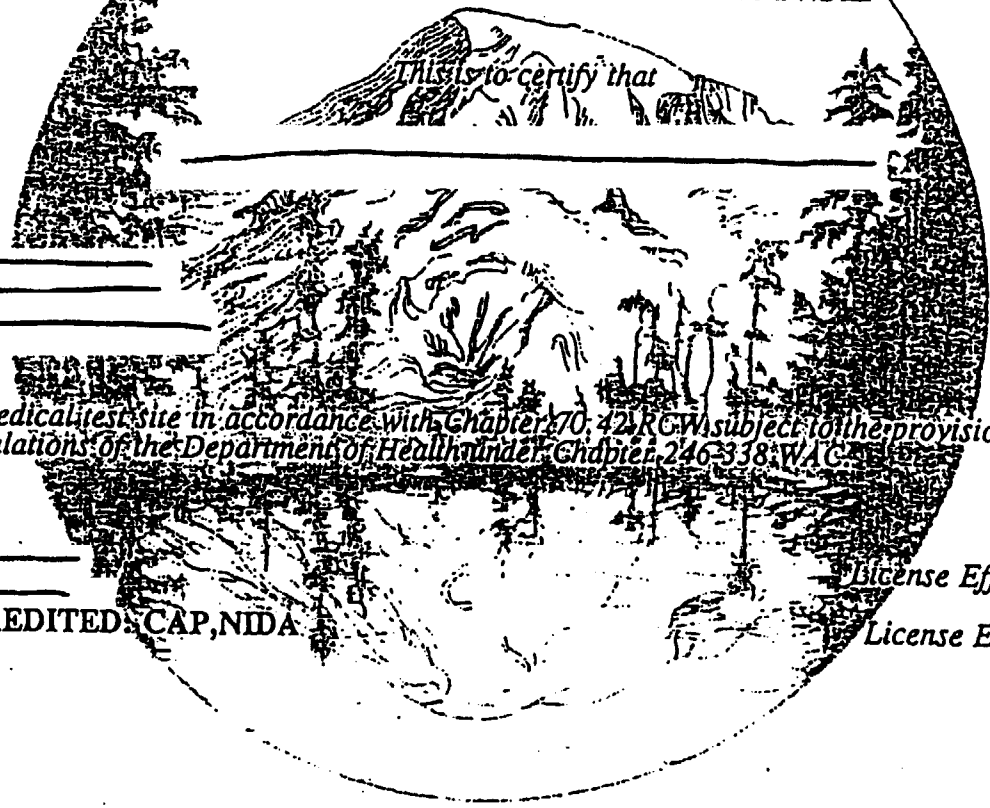
Martha D. Simon

*Department of Health*

MIF 002509

Washington State Department of Health

# MEDICAL TEST SITE LICENSE



*This is to certify that*

_____

*located at*

_____

_____

_____

*is hereby licensed as a medical test site in accordance with Chapter 70.42 RCW subject to the provisions of this law, and the standards, rules and regulations of the Department of Health under Chapter 246-338 WAC.*

*License Number:* _____
*CLIA Number:* _____
*Category:* ACCREDITED: CAP,NIDA

*License Effective:* 11/01/94

*License Expires:* 10/31/96

THE SEAL OF THE STATE OF WASHINGTON 1889

Martha G. Simon

*Department of Health*

Suzanne T. Poppema, M.D.
Seattle, WA CFN 3032921
EI: 11/01/99-11/05/99
Exhibit 6 Page 3 of 8

MIF 002510

May 24, 1995

APPEARS THIS WAY
ON ORIGINAL

**Note to File:**

**Re: Participation of laboratories in the mifepristone/misoprostol study at Aurora Medical Services, Seattle, WA**

βHcg assessments are being done at [redacted]

[redacted]

Clinical Research Department

[redacted] tab

APPEARS THIS WAY
ON ORIGINAL

Suzanne T. Poppema, M.D.
Seattle, WA CFN 3032921
EI: 11/01/99-11/05/99
Exhibit 6 Page 5 of 8

# MEMORANDUM

**TO:** File

**FROM:** _____

**DATE:** January 19, 1995

**RE:** M & M Study

**SITE:** Dr. Susan Poppema, Seattle, WA

Dr. Poppema is the Laboratory Director for the study center.

Suzanne T. Poppema, M.D.
Seattle, WA CFN 3032921
EI: 11/01/99-11/05/99
Exhibit 6 Page 7 of 8

FAX: (201) 777-1279
FAX: (201) 777-9847

# HEMATOCRIT

Hematocrit (HCT) testing is performed to determine the percentage of red bllod cells in a person's blood. An acceptable range of normal is 32 to 47 percent. A person with a hematocrit below this normal range may have anemia

## Principles of the Procedure:

The hematocrit represents the volume of circulating blood that is occupied by red blood cells measured as a percentage. Blood is drawn up into a capillary tube and the red end of the tube is packed with clay. The clay end of the tube is placed in the centrifuge facing the outside edge. The tube is spun in the centrifuge and this process packs the red blood cells at the bottom of the tube. The percentage of red blood cells to plasma is then measured.

## Storage:

The capillary tubes are to be stored at room temperature, 15 to 30 degrees C.

## Speciman Collection:

**Caution: All blood products should be treated as potentially infectious. Use universal precautions when collecting the speciman, performing the test, and disposing of test materials.**

Blood can be taken by finger puncture or venipuncture. The blood is then drawn up into a capillary tube and the end of the tube is packed with clay to prevent leakage.

## Materials necessary to perform test (Centrifugation Method):

- Capillary tubes
- Hematocrit clay
- Centrifuge
- Hematocrit graph

Printed by [redacted]

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 30-Jun-2000 02:02pm
**From:** [redacted]

**Dept:** HFD-580 PKLN 17B45
**Tel No:** 301-827-4260 FAX 301-827-4267

**TO:** [redacted]
**TO:** [redacted]

**CC:** [redacted]
**CC:** [redacted]
**Subject:** FWD: Registration/Listing Requested Info

**Information regarding the registration of the manufacturing firms from Compliance.**

[redacted]

Printed by

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 28-Jun-2000 06:39am
**From:**

**Dept:** HFD-103 PKLN 13B45
**Tel No:**

**TO:**
**TO:**

**CC:**
**CC:**
**CC:**
**Subject:** Re:

**Thanks for the email. I forwarded it to**

Printed by

# Electronic Mail Message

**Date:** 22-Jun-2000 05:06am
**From:** EUDRA - EUDRAWATCH
fr-h.eudrawatch@fr-h.eudra.org
**Dept:**
**Tel No:**

**TO:** [redacted]

**CC:** [redacted]
**Subject:** Use of mifepristone in France

Dear [redacted]

[redacted] gave me your e-mail and I will try to give you all the informations you need about the use of mifepristone in France.

Mifepristone was granted a marketing authorization in France in December 1988 for the following indication : " Medical alternative to vacum aspiration for termination of intrauterine pregnancy ( in combination with a prostaglandin analogue 36-48 hour later and up to 49 days'amenorrhea) ". Two other indications have been granted afterwards : in 1992 in " preparation for prostaglandin action in therapeutic pregnancy termination " and in "induction of labor in intra-uterine fetal death ".

Otherwise a marketing authoriszation has been obtained on July 1999 through the mutual recognition procedure in the following countries : Austria, Belgium, Denmark ? Finland ? Germany ? Greece Netherlands and Spain with France as Reference Member State.

The product is restricted to hospital practitionners who can use it in public or private centre having approval to undertake termination of pregnancy. Mifepristone must be administered to patients in the presence of the medical practitioner.

In France, the patient has to sign a letter of informed consent to certify that she has been fully informed about the method and its risks before.

Otherwise we do not have any special risk management program for this product in France.

We just have reviewed the 9th PSUR and have no special concerns at this time.

I can send you by fax the european SmPC of the product if you wish.

If you have other questions, please tell me !

Best regards

MIME-Version: 1.0

<P> </P>
<P>[redacted] gave me your e-mail and I will try to give you all the informations you need about the use of mifepristone in France.</P>
<P>Mifepristone was granted a marketing authorization in France in December 1988 for the following indication : " Medical alternative to vacum aspiration for termination of intrauterine pregnancy ( in combination with a prostaglandin analogue 36-48 hour later and up to 49 days’amenorrhea) ". Two other indications have been granted afterwards : in 1992 in " preparation for prostaglandin action in therapeutic pregnancy termination " and in "induction of labor in intra-uterine fetal death ".</P>
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<P>Otherwise we do not have any special risk management program for this product in France.</P>
<P>We just have reviewed the 9<SUP>th</SUP> PSUR and have no special concerns at this time.</P>
<P>I can send you by fax the european SmPC of the product if you wish.</P>
<P>If you have other questions, please tell me !</P>
<P>Best regards</P>
<P> [redacted] FONT color=#000000 face="Times New Roman">,
MD</FONT></P></DIV></BODY></HTML>

Printed by

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 20-Jun-2000 08:36pm
**From:**

**Dept:** HFD-103 PKLN 13B45
**Tel No:**

**TO:**

**Subject:** FWD: More info about Europe

# Electronic Mail Message

**Date:** 6/20/00 8:36:00 PM
**From:** [redacted]
**To:** [redacted]
**Subject:** FWD: More info about Europe

Printed by

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 20-Jun-2000 08:35pm
**From:** [redacted]
**Dept:** HFD-103 PKLN 13B45
**Tel No:** [redacted]

**TO:** [redacted]

**Subject:** FWD: Medical Abortion in England.

Printed by [redacted]

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 19-Jun-2000 05:50pm
**From:** [redacted]

**Dept:** HFD-580 PKLN 17B45
**Tel No:** [redacted]

**TO:** [redacted]
**TO:** [redacted]

**CC:** [redacted]
**Subject:** Ad Comm votes - from transcripts

I located the votes in the transcripts; they are in the third pdf file (c).

The vote to the first question - efficacy was 6 yes/ 2 no

The vote to the second question - safety was 7 yes/ 1 absention

The vote to the third question - risk/benefit was 6 yes/ 2 absentions

These votes are located between pages 275 and 298 of the transcripts.

Hope this helps,

[redacted]

# Electronic Mail Message

**Date:** 6/23/00 9:53:00 PM
**From:**
**To:** See Below
**Subject:** Nancy Buc Telecon 6/23/00 3pm

Nancy Buc called and expressed concern that we expected Pop Council to submit their revised proposed distribution system and labeling for the 7/19 meeting. She thought we would be discussing and "ready to make deals." She was concerned that we needed time to review their comments (not proposal) on our proposed distribution system and that if they submitted what they really want, we'd view their proposal as not responsive to FDA and "our noses would get bent out of shape." I reassured her that their comments are due to us on Monday. We'd review them and their proposals are due 2 weeks prior to the meeting and we'd have enough time to set expectations. I also said that we were looking to Pop Council to be a responsible entity in manufacturing, distributing, and shepherding this drug and that most responsible entities make proposals rather than expect FDA to write labels and distribution systems and obtain comments through the media.

Nancy also affirmed that the 1996 proposals for distribution system as presented by the Pop Council then and agreed to by the AC and FDA are NOT what the Pop Council wants today. I explained this change is very significant and that they need to present their justification/rationale. In this light, Nancy agreed that it is their turn to revise and present their current proposal and that they would get a proposal for both the system and label to us by July 5.

She stated strongly that she did not feel physician qualifications were justified for this drug (and not others). She thought many things could be handled in the label and that we had unreal concerns about misuse, abuse, or overuse of this drug.

**To:**
**To:**
**To:**
**Cc:**
**Cc:**
**Cc:**

Printed by

# Electronic Mail Message

**Date:** 23-Jun-2000 09:53pm
**From:**

**Dept:** HFD-103 PKLN 13B45
**Tel No:**

**TO:** See Below
**Subject:** Nancy Buc Telecon 6/23/00 3pm

Nancy Buc called and expressed concern that we expected Pop Council to submit their revised proposed distribution system and labeling for the 7/19 meeting. She thought we would be discussing and "ready to make deals." She was concerned that we needed time to review their comments (not proposal) on our proposed distribution system and that if they submitted what they really want, we'd view their proposal as not responsive to FDA and "our noses would get bent out of shape." I reassured her that their comments are due to us on Monday. We'd review them and their proposals are due 2 weeks prior to the meeting and we'd have enough time to set expectations. I also said that we were looking to Pop Council to be a responsible entity in manufacturing, distributing, and shepherding this drug and that most responsible entities make proposals rather than expect FDA to write labels and distribution systems and obtain comments through the media.

Nancy also affirmed that the 1996 proposals for distribution system as presented by the Pop Council then and agreed to by the AC and FDA are NOT what the Pop Council wants today. I explained this change is very significant and that they need to present their justification/rationale. In this light, Nancy agreed that it is their turn to revise and present their current proposal and that they would get a proposal for both the system and label to us by July 5.

She stated strongly that she did not feel physician qualifications were justified for this drug (and not others). She thought many things could be handled in the label and that we had unreal concerns about misuse, abuse, or overuse of this drug.

**Distribution:**

**TO:**
**TO:**
**TO:**

**CC:**
**CC:**
**CC:**

Printed by [redacted]

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 19-Jun-2000 04:50pm
**From:** [redacted]

**Dept:** HFD-580 PKLN 17B45
**Tel No:** [redacted]

**TO:**

**CC:**
**CC:**
**CC:**
**CC:**
**Subject:** mifepristone labeling recommendations - N 20-687

[redacted] asked that I provide you the attached documents for your information.

We have faxed the attached IR letter and labeling recommendations to the Population Council and Danco today. These will be sent hard copy to the sponsor as well.

Please let me know if you need any further information,

[redacted]

# Electronic Mail Message

**Date:** 6/19/00 4:50:37 PM
**From:**
**To:**
**Cc:**
**Cc:**
**Cc:**
**Cc:**
**Subject:** mifepristone labeling recommendations - N 20-687

asked that I provide you the attached documents for your information.

We have faxed the attached IR letter and labeling recommendations to the Population Council and Danco today. These will be sent hard copy to the sponsor as well.

Please let me know if you need any further information,

# Electronic Mail Message

**Date:** 6/19/00 10:06:38 AM
**From:**
**To:**
**To:**
**Subject:**

Thanks for the feedback. Let me know if he responds that he would prefer a "hard copy" of the 1996 Ad Comm transcript. Would you get that or would the Division need to provide him the copy? (Just trying to get all my references for his "package to review" in order before we need it.

Thanks again for your prompt responses and followup,

>
>The COI screening questions for RU-486 were sent t .ast
>week.... we are now waiting for his response.
>

Printed by

# Electronic Mail Message

**Date:** 19-Jun-2000 02:24pm
**From:**

**Dept:**
**Tel No:**

**TO:**

**CC:**
**CC:**
**CC**
**Subject:** Subpart H

The following language from section III.D (Withdrawal of Approved Drugs) of the preamble to the proposed rule for Subpart H (57 FR 13234, 13238) is

"For drugs approved under these proposed accelerated approval regulations, the risk/benefit assessment is dependent upon the likelihood that a surrogate endpoint will correlate with clinical benefit or that postmarketing restrictions will enable safe use. Without the assurances regarding demonstration of actual clinical benefit or the demonstrated adequacy of distribution restrictions, the risk/benefit assessment for these drugs changes significantly. The agency is proposing a streamlined, expeditious procedure for withdrawing approvals if: (1) A postmarketing clinical study fails to verify clinical benefit; (2) the drug's sponsor fails to perform the required postmarketing study with due diligence; (3) experience with the drug after marketing demonstrates that restrictions on distribution or use are inadequate to ensure safe use; (4) the drug's sponsor fails to adhere to the postmarketing restrictions agreed upon; (5) the promotional materials are false or misleading; or (6) other evidence demonstrates that the drug product is not shown to be safe or effective under its conditions ~~of use~~. FDA believes that if any of these circumstances exists, continued marketing of the drug to treat patients with a serious or life-threatening disease is inappropriate and marketing approval should be rapidly withdrawn."

Please let me know if you have additional questions.

MIF 002527

RFC-822-headers:
Received: from cdswss1.cder.fda.gov
("port 2390"@cdswss1.cder.fda.gov [150.148.150.21])
by Mail.cder.fda.gov (PMDF V5.2-32 #42130)
with SMTP id <01JQSGMK4XC491VSBC@Mail.cder.fda.gov>; Mon,
19 Jun 2000 14:24:28 -0400 (EDT)
Received: from 150.148.4.55 by cdswss1.cder.fda.gov with ESMTP
( WorldSecure Server SMTP Relay(WSS) v4.3); Mon, 19 Jun 2000 14:21:19 -0400
Received: by fdaress13.isa.fda.gov with Internet Mail Service ( 5.5.2650.10)
id <MQ5XSJKW>; Mon, 19 Jun 2000 14:20:32 -0400
X-Mailer: Internet Mail Service (5.5.2650.10)
X-Server-Uuid: 00796fd4-893e-11d3-8ed3-0008c75df4f2
X-WSS-ID: 1550BB1588869-01-01

# Electronic Mail Message

**Date:** 6/19/00 2:24:29 PM
**From:** [redacted]
**Subject:** Subpart H

Florence,

At our meeting on June 12, you asked me to confirm that the streamlined withdrawal procedures of Subpart H (21 CFR 314.530) apply to drugs approved under Subpart H with restrictions on distribution only (21 CFR 314.520), that is, drugs not also approved under 21 CFR 314.510 (based on a surrogate endpoint, etc.).

The following language from section III.D (Withdrawal of Approved Drugs) of the preamble to the proposed rule for Subpart H (57 FR 13234, 13238) is responsive to your request:

"For drugs approved under these proposed accelerated approval regulations, the risk/benefit assessment is dependent upon the likelihood that a surrogate endpoint will correlate with clinical benefit or that postmarketing restrictions will enable safe use. Without the assurances regarding demonstration of actual clinical benefit or the demonstrated adequacy of distribution restrictions, the risk/benefit assessment for these drugs changes significantly. The agency is proposing a streamlined, expeditious procedure for withdrawing approvals if: (1) A postmarketing clinical study fails to verify clinical benefit; (2) the drug's sponsor fails to perform the required postmarketing study with due diligence; (3) experience with the drug after marketing demonstrates that restrictions on distribution or use are inadequate to ensure safe use; (4) the drug's sponsor fails to adhere to the postmarketing restrictions agreed upon; (5) the promotional materials are false or misleading; or (6) other evidence demonstrates that the drug product is not shown to be safe or effective under its conditions of use. FDA believes that if any of these circumstances exists, continued marketing of the drug to treat patients with a serious or life-threatening disease is inappropriate and marketing approval should be rapidly withdrawn."

Please let me know ~~if~~ you have additional questions.

[redacted]

# Electronic Mail Message

**Date:** 6/14/00 11:57:03 AM
**From:** [redacted]
**Subject:** More info about Europe

Hi [redacted]

I just spoke with [redacted] at the [redacted] She formerly worked at [redacted] and is very knowledgeable about the status of mifepristone in Europe. I will try to summarize what I learned.

Mifepristone is distributed directly to clinics in most of Europe, except in Switzerland and Germany, and possibly Austria by now, where abortions are provided by physicians in their own practices, and the product is distributed to their offices in 1 week to 1 month supplies. In Belgium and Spain, distribution is linked to hospital pharmacies.

Medical abortions in France may be delegated by the physician to midwives or nurses. The physician is responsible for the decision to administer the drug, and it is then handled by the nurse-providers with physician supervision. The midwives/nurse providers do not perform surgical abortions. The physician is usually in the "ward" but may be available on call in case of a problem.

Surgical abortions and other family planning services are provided in the clinics in France. However, the clinics are closed at night and weekends, so patients are given the phone # of the hospital with 24 hour service and can contact the physician through that number. There is no specific distance requirement. There was a one-hour requirement for the clinical trials only.

The current labeling requires a second visit for administration of the misoprostol. Some physicians allow home administration, but they are cautious as this is not in the approved labeling. It is also administered at home in some places in the UK, but only with misoprostol. ( Gemeprost, which is used vaginally in the UK is a more potent prostaglandin and is used with more caution and closer monitoring.) The French regulatory agency is considering changing the requirement for the second visit for misoprostol administration based on US studies by [Eric Schaff?(I'm not sure I got the name right)]

Mifepristone along with the more potent prostaglandin gemeprost, which is given vaginally, is approved for gestations up to 63 days in the UK, Norway, and Sweden. The complete abortion rate is 94-97%.

Mifepristone is sometimes used off-label in doses other than 600 mg (most commonly 200 mg, but may be up to 800 mg with vaginal misoprostol 200-600 mcg). The UK was the first to shift to the 200 mg dose, along with the more potent gemeprost (still off-label, not approved except in the 600 mg dose)

The need for blood transfusion in France has been 0.1% of patients and is based on physician judgement, not based on hemoglobin changes.

I found this very interesting. However, it could make our labeling changes more difficult since it seems that there is more variability in actual use than the label indicates.

[redacted]

Printed by [redacted]

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 14-Jun-2000 12:00pm
**From:** [redacted]

**Dept:** HFD-580 PKLN 17B45
**Tel No:** [redacted]

**TO:** [redacted]

**CC:** [redacted]
**CC:** [redacted]
**Subject:** Info for Dr. Henney

Hi [redacted]

Here is my revised memo with the additional info that I reviewed yesterday and with the safety info added at the end. Both [redacted] and I have tried to locate a suitable text reference to get info about complications of spontaneous abortion, and we have not been sucessful. All of them refer to management of Sp AB and to etiologies and evaluation of recurrent pregnancy loss but do not give info regarding rates of complications of Sp AB. If warranted, we could do a literature search, but I am not hopeful that we will find anything.

**Abortion Provision in the U.S.**

RUDP

June 14, 2000

Number of abortions

1.37 million abortions were performed in the U.S. in 1996 (50 million worldwide, 20 million legal)

Procedures

- 98% by D&C
- 2,988 medical procedures were reported to CDC in 1997
- 4,200 medical abortions were reported to AGI in 1996, and 4,300 in 1st half of 1997, using mifepristone or off-label methotrexate. (AGI data is believed to be more complete than CDC data)
- According to NAF, for medical abortions, the misoprostol is taken at home.

Cost (1997)

Nonhospital facilities, surgical abortion at 10 wk gestation with local anesthesia, $150-$1535 (Average $316)

Medical abortion costs $100-$1250, average $401.

Demographics

- 2% of women ages 15-44 have abortions each year.
- 43% of women have at least 1 abortion by age 45
- 60% of abortions are provided to white women, BUT blacks are 3 times as likely and hispanics are 2 times as likely to have an abortion.

Gestational ages

- 88% of abortions are performed in 1st 12 weeks gestation
- 55% up to 8 weeks
- 36% up to 7 weeks (49 days)
- 43% of abortion facilities provide abortions only through 12 weeks gestation
- 42% of nonhospital facilities provided abortions under 6 weeks gestation in 1996, compared to 33% in 1992

Facilities

- 90% of abortions are performed in clinics
- 3% of abortions are performed in doctor's offices
- 7% of abortions are performed in hospitals
- 42% of nonhospital facilities provide abortion to women less than 6 weeks gestation
- 24 hour emergency contact must be readily available.
- NAF establishes guidelines for members

Providers

- In 43 states the law provides that only a physician may perform an abortion.
- The law in KY allows for first trimester abortion only by a physician or the woman herself. Later abortions are allowed by physician only
- In DC, abortions may be provided under the supervision of licensed physicians
- The following states permit midlevel providers to perform abortions: KS, OR, AZ, VT, WV, NH, DC
  - OR, NH, and DC have no requirement for an agreement with or supervision by a physician
  - AZ, VT, and WV require a collaborative arrangement between midlevel providers and a physician.
  - KS, VT, and WV require midlevel providers to follow designated protocols

- The number of abortion providers in the U.S. decreased by 14% (from 2380 to 2042) from 1992 to 1996
- 86% of U.S. counties had no abortion provider in 1996. These counties are home to 32% of women ages 15-44

NAF Guidelines:

- Must be performed by licensed physicians or licensed/certified/registered midlevel clinicians trained in the provision of abortion care, in accordance with state law.
- All personnel performing abortions must receive training in the performance of abortions and in the prevention, recognition and management of complications.
- When midlevel clinicians perform abortions, medical protocols should be in place that adhere to the midlevel provider scope of practice permitted by state law
- Rh immune globulin is to be administered to all Rh- women
- For early medical abortion, the patient must be informed about the need for follow-p contact to ensure that she is no longer pregnant.
- For early medical abortion, the patient must be informed about the efficacy, side effects, and risks, especially excessive bleeding and teratogenicity associated with the medications to be used.
- The patient's willingness to consent to surgical abortion if medical abortion fails must be documented.
- Guidelines are provided for management of complications, post-operative care, disposal of fetal tissue, and Emergency procedures.

Provision of Medical Abortion

- 12% of nonhospital abortion providers offered medical abortion in 1997 (163 providers)
- 43% of nonhospital facilities would provide medical abortion within the next year if mifepristone were approved
- 29% of nonhospital facilities would provide medical abortion within the next year even in mifepristone were not approved.
- Only 12% of OG/GYN residencies require training in 1st trimester surgical abortion. 69% of residents in a required program had clinical experience in the procedure.
- 29% of Family Medicine programs included 1st trimester abortion training (either optional or routine). Only 15% of chief residents had clinical experience with the procedure.
- 54% of OB/GYNs, 45% of FPs, and 54% of nurse practitioners and physician assistants would likely offer mifepristone if approved. ( Only 3% of FPs and 2% of NPs and Pas report ever performing surgical abortion)
- Only 19% of OB/GYNs. 11% of FPs, and 13% of NPs and PAs currently provide medical abortion with methotrexate and misoprostol

Safety of surgical abortion

- <1% major complications (1 in 200 procedures), including serious pelvic infection, hemorrhage requiring a blood transfusion or unintended major surgery.
- deaths 1:530,000 up to 8 wk gestation
  1: 17,000 at 16-20 wk gestation
  1: 6,000 at 21 wk gestation and beyond
- risk of death with childbirth is 10 times higher than with abortion

Safety of medical abortion (from French and US trials)

- 4.5% of 1800 French women and 7.9% of 859 US women participating in clinical trials received surgical intervention. 0.4% of French subjects and 1.6% of US subjects received medically indicated intervention, mostly for excessive bleeding. 2.9% of French subjects and 4.7% of US subjects had incomplete abortions at the end of the study protocol, and 1.3% and 1.0%, respectively, had ongoing pregnancies. In addition, 0.6% of US subjects received surgical interventions at the patient's request.

- The mean duration of bleeding was 9 days in the French trials and 16 days in the US trials. However, 0.5% of French subjects and 8.1% of US subjects had bleeding for more than 30 days. 4.3 % of French subjects received vasoconstrictor drugs and 5.5% had a decrease in hemoglobin of more than 2 g/dL. 2 of the 1800 subjects received blood transfusions. 4.8% of US subjects received uterotonic medications, 1.0% received intravenous fluids, and one subject of the 859 received a blood transfusion.
- No serious pelvic infections were reported.
- No deaths have been reported.

Complications of spontaneous abortions

Although spontaneous abortions are known to be complicated by hemorrhage, infection, and surgical intervention, the available texts do not provide information on the incidence of such complications, and focus instead on the etiologies and management of spontaneous abortion, and recurrent pregnancy loss.

Confidentiality of health care physicians who are distributed the drug

The distribution system as currently proposed by the sponsor does not guarantee confidentiality of the providers. However, it is reasonable to believe that with fairly minor modifications, such confidentiality can be assured.

References

The Henry J. Kaiser Family Foundation at http://www.kff.org/
The Alan Guttmacher Institute at http://www.agi-usa.org/pubs/fb_induced_abortion.html

# Electronic Mail Message

**Date:** 6/14/00 10:38:15 PM
**From:** [redacted]
**Subject:** FWD: More info about Europe

Enclosed are French Ab practices.

We are still pulling the data on complications of abs (the spontaneous ab info is lacking, but will pursue). Plan is to send this info and the confidentiality response for you to forward to Dr. Henney around Friday.

[redacted]

Printed by [redacted]

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 13-Jun-2000 10:03am
**From:** [redacted]

**Dept:** HFD-580 PKLN 17B45
**Tel No:** [redacted]

**TO:** [redacted]

**CC:** [redacted]
**CC:** [redacted]
**Subject:** Medical Abortion in England.

Hi [redacted]

I just spoke with [redacted] in London. He was very helpful in explaining their system. Mifepristone has been approved there since approximatedly 1993. All new drugs in the UK are marked with a black triangle for the first 2 years, which alerts practitioners that it is a new drug, and they can then report all AEs, not just serious AEs. There was no initial restriction on the use of mifepristone except as in the current labeling.

Abortions in the UK (both surgical and medical) are provided in Special Family Planning Clinics by specialists in Family Planning or OB/GYN, NOT by general practitioners. Legally, 2 physicians must certify that the patient's psychological or physical well-being is at risk before the procedure can be performed. There is no situation in which the surgical or medical procedure would be performed by a nurse provider or midwife without the direct supervision of a physician.

Mifepristone is distributed to the clinic pharmacies and administered at the clinic only, and the patient returns there for the prostaglandin. [redacted] is not aware of any situation where it may be administered at home. Because clinics are located in each region, and patients must attend the facility in their own region, the issue of specifying a given proximity is not addressed.

Although off-label use is possible [redacted] is not aware of any significant use of different doses or regimens of the drugs. There is some interest on the part of the MCA to look at lower doses, but no sponsor has applied for it, and the available data is old data from a WHO study.

I will keep trying to reach [redacted] who has past experience with the drug in France, and perhaps will call some other European practitioners tomorrow am if I am unable to reach her today.

Will keep you updated.

[redacted]

# Electronic Mail Message

**Date:** 6/12/00 3:39:34 PM
**From:** [redacted]
**To:** [redacted]
**Cc:** [redacted]
**Subject:** List of Competing products

Hi

Would you please pull the list of competing products that was used to screen the Adv. Com. members for the July 19, 1996 Reprod. Drugs Adv. Com. meeting. I need this as soon as you can pull it....the meeting concerned RU-486.

Thanks

[redacted]

Printed by [redacted]

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 09-Jun-2000 09:37am
**From:** [redacted]

**Dept:** HFD-103 PKLN 13B45
**Tel No:** [redacted]

**TO:** fr-h.pharmacovigilance@fr-h.eudra.org

**CC:** [redacted]
**Subject:** Question for [redacted]

Dear [redacted]

[redacted] gave me your email address. I work for the US FDA on mifepristone and am wondering if we could chat some about this drug and it's use in France. Thanks so much for your time!

[redacted]

Printed by [redacted]

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 31-May-2000 03:19pm
**From:** [redacted]

**Dept:** HFD-580 PKLN 17B30
**Tel No:** [redacted]

**TO:** [redacted]

**CC:** [redacted]
**CC:** [redacted]
**Subject:** U.S. Studies of Mifepristone

Demographics:
71% Caucasian
71% normal body mass index
61% aged 20-29 years. Mean age was 26.9 years
55% nulliparous
51% had a previous abortion

4.8% of subjects received administration of uterotonic medications which included oxytocin, methylergonovine, and vasopressin.

[redacted] is not available in the U.S.

Visit 3 was scheduled for day 15 (12 days after misoprostol administration).

Ultrasound examination was required at visit 1 and was at the discretion of the investigator at visits 2 and 3.

Printed by

# Electronic Mail Message

**Date:** 07-Jun-2000 07:04pm
**From:**

**Dept:** HFD-002 WOC2 6027
**Tel No:**

**TO:**

**CC:**
**CC:**
**Subject:** MESSAGE FOR - PLEASE DELIVER TO HER

Dear

Bonjour!

Hope this email finds you well. I hope by now that you have heard that I will be

I am really looking forward to this opportunity to work with you all more closely and get to know better the methods and ways you all perform your oversight responsibilities. I look forward very much to seeing you

I was wondering if you could please help us with something now though. We continue to struggle with the RU-486 (mifepristone) application and how to best assure its safe use. My question to you: (a) is it approved in the France (my understanding is that it is; but I just want to make sure); (b) if so, do you have it under any special risk management program or restriction; and (c) if so, to date are you satisfied with the results of any risk management program you have implemented for the product?

Many thanks for any perspectives you or someone on your staff could give us. If you or your staff would rather discuss this on the phone rather than in cyberspace, while I am on travel, please feel free to call (our office of drug evaluation 3 who is primarily responsible for this product). I've cced her on this email. Her phone number is

Many, many thanks as ever!

Take care. Hope to see you soon.

# Electronic Mail Message

**Date:** 4/28/00 2:16:45 PM
**From:** [redacted]
**Subject:** Meeting minutes for NDA 20-687 4/24/00

Please review and comment by COB 5/5/00. Please also add [redacted] as a cc in case I am o[redacted] leave.

Thanks,

[redacted]

Printed by [redacted]

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 28-Apr-2000 04:51pm
**From:** [redacted]

**Dept:** HFD-103 PKLN 13B45
**Tel No:** [redacted]

**TO:** See Below
**Subject:** Re: Meeting minutes for NDA 20-687 4/24/00

**My comments. Thanks.**

**>Please review and comment by COB 5/5/00. Please also add [redacted] as a cc in case I am on [redacted]eave.**
**>**
**>Thanks,**
**>**

**Distribution:**

**TO:**
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Printed by [redacted]

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** [redacted] pm
**From:** [redacted]

**Dept:** HFD-580 PKLN 17B45
**Tel No:** [redacted]

**TO:** [redacted]

**Subject:** FWD: Re:

**FY** [redacted]

# Electronic Mail Message

**Date:** 4/28/00 6:53:09 AM
**From:**
**To:**
**Subject:** Environmental information for 20-687

The information that they submitted to address the chemistry deficiency (submit a categorical exclusion under 21 CFR 25.31(b) for the drug substance manufacturer) is fine.

However in this packet of information they say they have submitted a categorical exclusion claim for the drug product. I have a completed environmental assessment and finding of no significant impact in my files for this application. These were signed 7/11/96. Could you look into this and let me know what is going on?

Thanks,

Printed by

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 25-Apr-2000 02:33pm
**From:**

**Dept:** HFD-580 PKLN 17B45
**Tel No:**

**TO:**

**Subject:** Re: Re:

**Thanks. I just wanted to confirm our policy. This is the mifepristone NDA.**

Printed by [redacted]

# Electronic Mail Message

**Date:** 14-Apr-2000 11:17am
**From:** [redacted]
**Dept:** HFD-103 PKLN 13B45
**Tel No:** [redacted]

**Subject:** RE: Reinspection of Chinese facility for NDA # 20687

Because of the need for reinspection of the Chinese facility, discussion of the applicant's restricted distribution system, and labeling, the user fee date for this submission is 9/30/00.

Please let me know if you need any assistance. Thanks so much.

[redacted]

Printed by

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** ~~15-Aug~~-2000 01:21

**From:**

**Dept:** HFD-580 PKLN 17B45

**Tel No:**

**TO:**

**Subject:** FWD: Re: NDA 20-687 mifipristone

**You can close EA review with her reply.**

# Electronic Mail Message

**Date:** 8/15/00 9:59:27 AM
**From:**
**To:** See Below
**Subject:** NDA 20-687

I've had to amend the due dates for the reviews for this NDA to Friday Sept 8th (not Monday Sept.11). This will allow me to take the package home the weekend and turn it over to on Monday 8/11. If you have a problem, please let know early (I am gone 8/16 to 9/5) and we can work with you on when you can get your review done.

Thanks for your patience and hard work on this NDA.

**To:**
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# Electronic Mail Message

**Date:** 8/15/00 9:08:34 AM
**From:**
**To:**
**To:**
**To:**
**To:**
**To:**
**Subject:** LA Times today

Monday, August 14, 2000

THE ABORTION PILL: FINALLY AT HAND?
Although it has been used in Europe for a decade, its U.S. approval has been mired in bureaucratic and production delays as a crucial federal deadline approaches.

By SHARI ROAN, Los Angeles Times Health Writer

This was to have been the year that would change abortion in America. With the anticipated arrival of the abortion pill, mifepristone, or RU-486, American women were to have gained an alternative to surgical abortion that, most health experts believe, would make abortion safer, more accessible and more private.
But this is the United States, and nothing about abortion is predictable.
After a decade of use by women in France, England and many other countries and after approximately 500,000 abortions worldwide, mifepristone is still not available in this country. Instead, RU-486 has encountered a daunting obstacle course strewn with antiabortion politics, bureaucratic red tape and missteps by the abortion rights group that is shepherding efforts to get the drug on the U.S. market.
Now, as a crucial Sept. 30 federal deadline nears, the fate of the abortion pill remains uncertain. Abortion rights advocates fear that the Food and Drug Administration may delay approving the drug or so severely restrict it that women and their doctors will be reluctant to use it as an alternative to surgical abortion.
(The FDA earlier this year set Sept. 30 as its deadline for deciding whether to approve mifepristone. The agency could also decide to set a new deadline.)
"I don't think the public understands that because of politics, we are falling way behind other countries in terms of access to medical abortion," says Francine Coeytaux, co-founder of the Pacific Institute for Women's Health in Los Angeles.
Coeytaux and other abortion-rights supporters say that a window of opportunity for approving mifepristone may be slipping away, especially if the Republicans take control of the White House next year.
Mifepristone, used to terminate pregnancy, differs from the "morning-after" pill, which is used within days of unprotected intercourse to prevent pregnancy.
Though Al Gore supports abortion rights and opposes restricted access to abortion, George W. Bush would allow abortion only in cases of rape, incest or to save the life of the mother. Bush's father, former President George Bush, banned importation of RU-486 in the late 1980s.
Abortion rights supporters fear that if the FDA fails to act in September and Bush wins in November, the drug may never be available in this country.
"It's clear that mifepristone would increase access to abortion," something that Republicans have traditionally opposed, says Marie Harvey, an associate professor of public health at the University of Oregon and a researcher on reproductive health issues.
Access has been a hot-button issue for both sides of the abortion debate. Throughout the 1980s and '90s, legislatures across the country

passed laws that required parental consent for minors seeking abortions, mandatory counseling and waiting periods and other limitations. An estimated 86% of U.S. counties, the majority of them rural areas, lack abortion providers, and the number of abortion providers fell 14% from 1992 to 1996, according to surveys from the Alan Guttmacher Institute, a New York-based reproductive rights group.

About 49% of pregnancies among U.S. women are unintended, and about half of those--an estimated 1.37 million per year--are terminated by abortion, according to the institute.

An abortion pill, many reproductive health experts believe, would increase access because many doctors who don't perform surgical abortion would be more likely to offer the pill because it is relatively simple to use and could be given in the privacy of doctors' offices.

Taken early in a pregnancy, the abortion pill is expected to be less costly and less traumatic for a woman than surgical abortion, says Dr. Bryna Harwood, a reproductive health researcher at USC. "For many, many women in this country," she says, "access is a real problem."

Two-Drug Regimen Early in Pregnancy

Mifepristone, which is the chemical name for the French medication, is prescribed during the first seven weeks of pregnancy as part of a two-drug regimen. (The second drug used to trigger the abortion is misoprostol, already available for the prevention of ulcers.) Women undergoing a mifepristone abortion typically experience severe cramping, bleeding and nausea. However, the most serious potential side effect, heavy bleeding, is rare, researchers say. About one to three women per 1,000 required a blood transfusion, according to data from clinical trials of the drug in the United States.

In contrast, surgical abortion is typically performed no earlier than six weeks into pregnancy, requires anesthesia and carries risks, such as infection, associated with any surgery.

Mifepristone was developed in 1980 by the French pharmaceutical company Roussel Uclaf. France approved the pill in 1988, followed by England, Sweden, China, Israel, Russia, Spain and other countries.

In Europe, more than half of women who have a choice between RU-486 (sometimes called a medical abortion) and surgical abortion opt for the abortion pill, according to a 1996 survey.

The drug's safety record is part of its appeal for women seeking early abortions. Studies in Europe and the United States have shown the pill to be effective about 92% to 95% of the time. The mifepristone regimen fails to cause an abortion in 2% to 4% of women; those women can either opt to undergo a surgical abortion or to continue their pregnancies. For women who choose to continue their pregnancies after mifepristone fails, there is an increased risk of birth defects.

"Medical abortion is about physicians being able to give women a pill and then managing the effects of that pill, which is a miscarriage," says Sandra Waldman, a spokeswoman for the Population Council. The council is the nonprofit reproductive rights group that holds the U.S. patent on mifepristone and has been trying to gain its approval.

The acceptance of RU-486 in Europe and elsewhere did not smooth the way for its debut in this country. The senior Bush's import ban on RU-486 was not lifted until 1993, when President Clinton directed the FDA to investigate the drug. Shortly afterward, Roussel Uclaf donated U.S. patent rights for mifepristone to the Population Council.

From 1994 to 1996, mifepristone followed a fairly typical path through the federal drug approval process. U.S. research studies involving about 2,000 women produced results similar to those of earlier European studies.

Based on those findings, the FDA notified the Population Council in 1996 that it had given the drug an "approvable" designation. Approvable is agency jargon for a drug deemed safe and effective but for which there are still concerns about manufacturing, distribution or labeling. Most new drugs reach the market within a year, or sometimes just a few months, after receiving an "approvable" designation.

But an unusually rocky path lay ahead for the drug and its sponsor. In 1997, the company chosen to manufacture the drug backed out, leaving a trail of lawsuits and bad publicity. The council and its partner, Danco Laboratories, then had to convince the FDA that its new manufacturer could produce a quality substance.

Locating a new manufacturer "created a substantial delay," said Heather O'Neill, a spokeswoman for Danco, which would distribute the pill.

But more recent setbacks have been harder for abortion rights advocates to comprehend. There is lots of speculation about the reasons for the

delays--from political pressure by abortion opponents to bureaucratic timidity of FDA officials worried about job security in an election year--but few hard facts.
"There is growing resentment," said Coeytaux of the Pacific Institute, noting that four years have passed since the FDA cleared the drug for safety and effectiveness. "Every step of the way has been marked by delays and more delays."
Despite accusations from some abortion rights groups, there is no evidence that the FDA is bending to political pressure to keep mifepristone from U.S. women. The FDA declined to discuss the drug approval process for mifepristone, citing agency policy.
The FDA approval process for mifepristone has been unusually rigorous given the scientific evidence of the drug's safety and effectiveness, says Harwood. But the latest delay was the most unexpected. And it has prompted some abortion rights supporters to consider a future without mifepristone.

FDA Questions Dog Approval Process
In February, the FDA issued a second approvable letter, asking for detail on a few final issues.
"Those questions were fewer in number and narrower in scope" than the ones in the 1996 letter, says Danco's O'Neill, adding that responses were sent to the agency by late March.
Danco and the Population Council were so encouraged that they called a meeting on June 2 in New York to update health and reproductive rights leaders. The meeting was a turning point--but not the one they had hoped for.
On the eve of the meeting, the FDA unexpectedly issued a new list of questions and demands that had to be resolved before the drug would get final approval.
"The reaction was shock and confusion because we all thought we were moving in the same direction" as the FDA, says Coeytaux, who attended the meeting. "The Population Council was floored."
According to several people who attended the June meeting, the FDA proposed:
* That mifepristone be distributed only by health professionals trained in surgical abortion, medical abortion and sonography, a condition that would appear to limit the service to doctors and exclude nurse practitioners and physician's assistants who could help expand the pool of abortion providers.
* That doctors be situated within one hour of emergency rooms where they have admitting privileges.
* That a third party--such as the National Abortion Federation, a private accreditation group that trains health professionals--certify that the providers possess these qualifications and maintain a list of such providers.
The FDA often places conditions on a medication's use, and mifepristone does produce unusually severe side effects. However, the agency's proposals for the drug, particularly the suggestion of keeping a list of certified providers of a drug, is highly unusual, say industry experts.
None of the parties involved will discuss the negotiations in detail, but the Population Council's Waldman said: "We're really in the last stage, but it's a tricky stage. This is a safe drug."
And, Waldman adds, "the conditions the FDA has raised are not for safety reasons but because of politics."
Some observers suggest that the recent setback may simply reflect a changing FDA. Agency Commissioner Jane Henney is considered more cautious than her predecessor, David Kessler, who first approved mifepristone. And the agency is still feeling shock waves from the recent controversy over Rezulin, the diabetes drug that was pulled from the market after it was linked to dozens of deaths.
Opponents of abortion, however, praise the proposed restrictions, saying that mifepristone is dangerous and that women are being misled about what medical abortion is like.
"Mifepristone is killing life. We don't want to diminish that aspect of it. But it isn't good medicine, either," said Heather Cirmo, a spokeswoman for the Family Research Council in Washington, D.C. "There are complications associated with the drug that are similar with miscarriage. You can have the abortion at home. There is bleeding, severe cramping, and sometimes the woman doesn't come back for follow-up if the abortion isn't complete."
Advocates of the method, says Cirmo, "are painting this as a miracle

pill and the child vanishes."
Whatever the FDA's reasons, abortion rights advocates say that the proposed restrictions would significantly lessen the appeal of RU-486 to women and doctors.
"It would disqualify some current abortion providers, let alone other clinicians who want to add this to their practice," Vicki Saporta, executive director of the National Abortion Federation.
Requiring doctors who prescribe the drug to be certified and listed could dissuade physicians concerned about the personal safety of themselves or their patients, says Coeytaux.
"More and more physicians [providing abortions] fear for their lives," she says. "And if there is anything close to sounding like a registry or a list, they could be targeted."
Danco says it has not established a price for the pill, and whether insurance companies would cover the drug is not known. But there is evidence that more doctors would offer abortions if they could do so with an FDA-approved pill in the privacy of their offices.
According to a recent survey of 767 doctors by the Kaiser Family Foundation, a nonprofit health care philanthropy based in Menlo Park, Calif., 44% of gynecologists and 31% of family practice doctors said they were very likely or somewhat likely to offer mifepristone. But some of those doctors would reconsider their decisions if, for example, they had to be certified to prescribe the drug.
Abortion rights advocates acknowledge that, with or without restrictions, mifepristone will not dramatically change abortion services in America, says Saporta.
"Improving access is very important," she says, "but mifepristone is not a magic solution [for] ending the abortion debate in this country."

* * *

More interest in early abortion
Access to RU-486 in clinical trials or through "off-label," or non-approved, use of the drug methotrexate has allowed more women and medical clinics to consider these alternatives to surgical abortion.
Doctors' offices and clinics that offered abortion pills to women who were less than six weeks pregnant as part of clinical trials or in "off-label" uses of the drugs

| 1992 | 1996 |
|---|---|
| 33% | 42% |

Women who said they had abortions using pills seven or fewer weeks into their pregnancies:

| 1992 | 1996 |
|---|---|
| 30% | 33% |

FEWER ABORTION PROVIDERS
The number of U.S. doctors, hospitals and clinics providing abortion services has declined in the past 15 years, with most of the drop among hospitals and doctor's offices.

| | |
|---|---|
| 1996 | 2,042 |
| 1988 | 2,582 |
| 1982 | 2,908 |

ABORTION RATES DECLINE
The abortion rate among women ages 15 to 44 has declined from a peak in 1980.
(Number of abortions per 1,000 women)
1980: 29.3
1985: 28.0
1990: 27.4
1996: 22.9
Source: The Alan Guttmacher Institute

# Electronic Mail Message

**Date:** 8/15/00 8:34:53 AM
**From:**
**To:**
**To:**
**Cc:**
**Cc:**
**Cc:**
**Subject:** Re: Follow up to Tcon w/Nancy Buc

I've talked to and I'm tracking DDMAC I hope to resolve this today before I leave and will let you all know. agrees to a speedy review. I'm checking with DDMAC on the minimum number of days needed.

>We need to get DDMAC involved.
can you put this on your list of things to do?
>
>>Thanks. Will you arrange an internal meeting or conference call to
>discuss
>>the promotional materials issue?
>>
>>
>>This e-mail message is intended for the exclusive use of the
>>recipient(s) named above. It may contain information that is
>protected,
>>privileged, or confidential, and it should not be disseminated,
>>distributed, or copied to persons not authorized to receive such
>>information. If you are not the intended recipient, any
dissemination,
>>distribution or copying is strictly prohibited. If you think you have
>>received this e-mail message in error, please e-mail the sender
>>immediately at
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>>-----Original Message-----
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>> Call me if you have questions.
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>>

Printed by

# Electronic Mail Message

Date: 14-Aug-2000 08:11am
From:

Dept: HFD-357 WOC2 3073
Tel No:

**Subject:** Re: NDA 20-687 mifipristone

I've looked over the information you sent to me on consult. A claim of categorical exclusion or requirement for an EA only applies to an entire application. Therefore a request for a categorical exclusion for a part of an application (e.g., drug substance manufacture) is not appropriate. Additionally since the EA regulations were revised in 1997 environmental information for manufacturing sites is not normally required.

On July 11, 1996 we signed a finding of no significant impact (FONSI) for At that time (before regulation change) a categorical exclusion claim could not be made for NDA applications and an abbreviated EA was submitted for this NDA. The additional information (I assume for a different manufacturer of ds) does not affect the previous EA and FONSI because no ds manufacturing site was identified in the public part of the EA.

>Hi
>
>Per s request, last week I forwarded to you via office mail
>the "Environmental Assessment" for this NDA. They had refused to submit
>a request for categorical exclusion is what I understand. Our due date
>(action goal date) is September 30, 2000.
>
>Could you confirm when you recieve the consult request and if you
>anticipate any problems in returning the consult by early September?
>
>Thanks,
>

# Electronic Mail Message

**Date:** 8/14/00 8:41:19 AM
**From:** [redacted]
**To:** [redacted]
**Subject:** Re: NDA 20-687 mifipristone

[redacted]

I've looked over the information you sent to me on consult. A claim of categorical exclusion or requirement for an EA only applies to an entire application. Therefore a request for a categorical exclusion for a part of an application (e.g., drug substance manufacture) is not appropriate. Additionally since the EA regulations were revised in 1997 environmental information for manufacturing sites is not normally required.

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[redacted]

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>
>Thanks,
>

[redacted]

# Electronic Mail Message

**Date:** 8/14/00 8:41:19 AM
**From:** [redacted]
**Subject:** Re: NDA 20-687 mifipristone

[redacted]

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>Thanks,
>

[redacted]

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**Date:** 8/14/00 8:41:19 AM
**From:**
**Subject:** Re: NDA 20-687 mifipristone

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>(action goal date) is September 30, 2000.
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>Could you confirm when you recieve the consult request and if you
>anticipate any problems in returning the consult by early September?
>
>Thanks,
>

Printed by

# Electronic Mail Message

**Date:** 15-Aug-2000 01:11pm
**From:** [redacted]
**Dept:** HFD-357 WOC2 3073
**Tel No:** [redacted]

**Subject:** FWD: Re: NDA 20-687 mifipristone

[redacted]

Printed by

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 15-Aug-2000 01:11pm
**From:**

**Dept:** HFD-357 WOC2 3073
**Tel No:**

**TO:**

**Subject:** FWD: Re: NDA 20-687 mifipristone

# Electronic Mail Message

**Date:** 8/14/00 9:43:32 AM
**From:**
**To:**
**Subject:** FWD: RU-486

Another RU-486 e mail.

Printed by

# Electronic Mail Message

**Date:** 11-Aug-2000 10:00am
**From:**

**Dept:**
**Tel No:**

**TO:**

**Subject:** FW: Germany company to drop unprofitable RU-486 abortion pill bus iness

FYI
> -----Original Message-----
> From:
> Sent:
> To:
>
> Subject: FW: Germany company to drop unprofitable RU-486 abortion
> pill business
>
> FYI...
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> -----Original Message-----
> From:
> Sent: Friday, August 11, 2000 8:06 AM
> To:
> Special
> Subject: Germany company to drop unprofitable RU-486 abortion pill
> business
>
> Germany company to drop unprofitable RU-486 abortion pill business
> August 11, 2000
> BERLIN (AP) via NewsEdge Corporation -
> A German company licensed to sell the RU-486 abortion pill said Thursday
> it is going to give up on marketing the French-produced item, with sales
> over the past nine months only a third of what had been anticipated.
> The Femagen pharmaceutical company, based in Holzkirchen near Munich, said
> that in all likelihood it would return its marketing license for the pill,
> also known as Mifegyne, to its French patent holder.
> Femagen, which began marketing the pills in November, had anticipated
> selling about 20,000 packages of RU-486 in the first year, but only
> between 500 to 600 packages were sold per month, business manager Petra
> Schoettler said.
> ``One can't expect us to let the economic problems pile up indefinitely,''
> she said.
> The reason for the disappointing sales is that German doctors receive 649
> marks (dlrs 325) for surgical abortions, compared to only 280 marks (dlrs
> 140) for using Mifegyne, she said.
> During the first quarter of 2000, only 4.5 percent of abortions in Germany
> were induced through Mifegyne, while they accounted for 35 percent in
> France.
> Berlin gynecologists on Wednesday announced they would no longer use the
> pills for abortions unless women pay privately to make up the difference
> over surgical abortions.
> Ulrike Busch of Pro Familia in Berlin said that seven of eight of its
> family counseling centers had discontinued assuming the costs of
> medication-induced abortions.

> The abortion pill was first marketed in France in 1988, and is also sold
> in Sweden and Britain.
> After years of being blocked in Germany by the conservative government of
> former Chancellor Helmut Kohl, the current center-left government of
> Chancellor Gerhard Schroeder opened the way for RU-486 to be imported last
> year to the ire of the Roman Catholic church, which has labeled it a
> ``murder pill.''
> German regulators said under European Union rules, they had to present
> reasons for withholding approval and they had found none.
> Schoettler said the company was checking to see if doctors and hospitals
> could obtain the pills on their own directly from France to eliminate the
> current costs of import documentation for packaging and delivery.
>

THE WHITE HOUSE

Office of the Press Secretary

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For Immediate Release January 22, 1993

January 22, 1993

MEMORANDUM FOR THE SECRETARY OF HEALTH AND HUMAN SERVICES

SUBJECT: Importation of RU-486

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

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

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

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

WILLIAM J. CLINTON

# # #

# Electronic Mail Message

**Date:** 8/10/00 4:32:05 PM
**From:**
**To:**
**Cc:**
**Cc:**
**Subject:** NDA 20-687 mifipristone

Hi

Per request, last week I forwarded to you via office mail the "Environmental Assessment" for this NDA. They had refused to submit a request for categorical exclusion is what I understand. Our due date (action goal date) is September 30, 2000.

Could you confirm when you recieve the consult request and if you anticipate any problems in returning the consult by early September?

Thanks,

# Electronic Mail Message

**Date:** 8/10/00 4:39:34 PM
**From:** [redacted]
**To:** [redacted]
**Subject:** Re: NDA 20-687 mifipristone

Yes I got it and I don't see a problem with the deadline.

**Percentage Rates for Abortion(Abs) Complications**
(per 100 patients)

| Complications | Medical Abs* (<49 days gestation) | Surgical Abs** (all gestations) | Spontaneous Abs*** (all gestations) |
|---|---|---|---|
| Death | None in Trials | 0.001% (1:100,000) | 0.0007[1] (0.7:100,000) (0.3:100,000 ≤ 12 wk GA) 59% due to infection 18% due to hemorrhage 13% due to embolism 5% due to anesthesia 5% other causes |
| Perforations | None in Trials | 0.004 | |
| Transfusions | 0.1 | 0.06 | |
| Hemorrhage[2] (>500cc or >2gm/dl) | 0.6-2.0 | 0.05-5.0[3] | |
| Retained products | 3-5 | 0.5-1.0 | |
| Endometritis/ Salpingitis | None in Trials | 1.0-5.0 | [4] |
| Ashermann's (scarring down of uterine cavity) | unknown | 0.1-2.3[5] | |
| Anesthetic | None in Trials | 0.2 | |

*Data from NDA 20-687
**Scott JR, Di Saia PH, Hammond CB, Spellacy WN (eds.) Danforth's obstretics and gynecology, 8th edition. Philadelphia, PA: Lippincott Williams and Wilkins, 1999, p. 577.
***Saraiya Marvelon®, Green C, Berg C, Hopkins F, Koonin L, Atrash H, Obstetrics and Gynecology, Vol. 94; No. 2, August 1999. Pp 172-176.

[1] Databases on spontaneous abortion are incomplete, as there is no required reporting, and not all are managed in hospitals. No references could be found to establish the incidence of hemorrhage, transfusion, retained products, endometritis/salpingitis, Ashermann's syndrome, or anesthetic complications.
[2] A study of measured blood loss with first trimester medical vs surgical abortions by YF Chan, PC Ho, HK Ma, 1993 (*Contraception, Vol 47:pp 85-95, 1993)* revealed >400 cc blood loss in 2.1% of medical Ab vs. 0% of surgical AB, and 300-400 cc blood loss by 5.2% of medical Ab vs. 0% of surgical Ab.
[3] This includes more advanced gestational ages than for medical Ab, and these would be expected to result in larger blood losses
[4] Some spontaneous abortions may be caused by pelvic infection.
[5] This includes more advanced gestational ages than for medical Ab, and these would be expected to result in a higher incidence of Ashermann's Syndrome.

9/12/02
+ Success by Age
+ update teratog

Table 10 (Continued)
Success Rates and 95% Confidence Limits by Patient Characteristics
Complete Expulsion (Success)
(Efficacy Evaluable Patients)

**stational Age Group [1]: ≤49 Days (Group 1)**

| Variable | Successes/Total N | Success Rate (%) | Confidence Limits (95%) |
|---|---|---|---|
| All Patients | 390 / 420 | 92.86 | 89.85, 95.05 |
| AGE (years) | | | |
| <20 | 30 / 30 | 100.00 | 85.87,100.00 |
| 20-24 | 114 / 125 | 91.20 | 84.45, 95.31 |
| 25-29 | 117 / 123 | 95.12 | 89.24, 98.00 |
| 30-34 | 80 / 88 | 90.91 | 82.38, 95.71 |
| >35 | 49 / 54 | 90.74 | 78.94, 96.54 |
| RACE | | | |
| AFRICAN AMERICAN | 37 / 41 | 90.24 | 75.94, 96.83 |
| CAUCASIAN | 281 / 298 | 94.30 | 90.85, 96.54 |
| EAST ASIAN | 23 / 25 | 92.00 | 72.50, 98.60 |
| HISPANIC | 42 / 49 | 85.71 | 72.14, 93.59 |
| OTHER | 7 / 7 | 100.00 | 56.09,100.00 |
| BODY MASS INDEX (kg/m²) | | | |
| MISSING | 0 / 1 | 0.00 | |
| NORMAL (≤25) | 307 / 328 | 93.60 | 90.23, 95.90 |
| OVERWEIGHT (25-30) | 54 / 60 | 90.00 | 78.83, 95.87 |
| OBESE (>30) | 29 / 31 | 93.55 | 77.16, 98.87 |
| GRAVIDITY | | | |
| 1 | 102 / 108 | 94.44 | 87.81, 97.72 |
| 2 | 99 / 107 | 92.52 | 85.36, 96.48 |
| 3 | 63 / 71 | 88.73 | 78.47, 94.66 |
| 4+ | 126 / 134 | 94.03 | 88.19, 97.20 |
| PARITY | | | |
| 0 | 224 / 239 | 93.72 | 89.65, 96.32 |
| 1 | 76 / 83 | 91.57 | 82.86, 96.25 |
| 2 | 51 / 56 | 91.07 | 79.63, 96.67 |
| 3+ | 39 / 42 | 92.86 | 79.45, 98.14 |
| NUMBER OF PREVIOUS SPONTANEOUS ABORTIONS | | | |
| 0 | 331 / 357 | 92.72 | 89.38, 95.10 |
| 1 | 47 / 51 | 92.16 | 80.25, 97.46 |
| 2+ | 12 / 12 | 100.00 | 69.87,100.00 |
| NUMBER OF PREVIOUS ELECTIVE ABORTIONS | | | |
| 0 | 178 / 191 | 93.19 | 88.39, 96.18 |
| 1 | 129 / 138 | 93.48 | 87.62, 96.78 |
| 2+ | 83 / 91 | 91.21 | 82.93, 95.85 |
| DAYS OF AMENORRHEA (PATIENT ESTIMATE) | | | |
| MISSING | 6 / 7 | 85.71 | 42.01, 99.25 |
| < 36 days | 16 / 18 | 88.89 | 63.93, 98.05 |
| 36 to <43 days | 100 / 103 | 97.09 | 91.10, 99.24 |
| 43 to ≤49 days | 180 / 196 | 91.84 | 86.85, 95.11 |
| 50 to ≤56 days | 69 / 71 | 97.18 | 89.28, 99.51 |
| 57 to ≤63 days | 14 / 18 | 77.78 | 51.92, 92.63 |
| >63 days | 5 / 7 | 71.43 | 30.26, 94.89 |

[1] Gestational age group was assigned by the investigator based upon menstrual history, pelvic examination and vaginal ultrasonography.

54 + 52 = 106
Total
735

Source Data: Appendix A.1, Tables 2, 6, 7 and 9, and Appendix B.1, Table 1

J:\USA\166A\SASPGMS\TABLES\FINAL\succ1.SAS 22JUL98:16:23 FINAL

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Proportion | 0.04 | 0.04 | 0.04 | 0.05 | 0.05 | 0.05 | 0.06 | 0.06 | 0.06 | 0.07 | 0.07 |
| Upper limit of 95% CI | 0.05 | 0.08 | 0.1 | 0.05 | 0.08 | 0.1 | 0.05 | 0.08 | 0.1 | 0.05 | 0.08 |
| N per group | 225 | 100 | 70 | 260 | 110 | 80 | 300 | 130 | 85 | 340 | 140 |

# Electronic Mail Message

**Date:** 8/9/00 4:15:33 PM
**From:**
**To:**
**To:**
**To:**
**To:**
**Cc:**
**Subject:** FWD: More info about Europe

more European info

# Electronic Mail Message

**Date:** 8/9/00 4:11:44 PM
**From:**
**To:**
**To:**
**To:**
**To:**
**Cc:**
**Subject:** FWD: Medical Abortion in England.

email re. the UK findings

# Electronic Mail Message

**Date:** 8/9/00 4:13:49 PM
**From:**
**To:**
**To:**
**To:**
**To:**
**Cc:**
**Subject:** FWD: More info about Europe

more in f/u to UK data

# Electronic Mail Message

**Date:** 8/9/00 10:41:48 AM
**From:**
**To:** See Below
**Subject:** Update Briefing for the Commissioner

Attendees:

You are invited to an Update Briefing for the Commissioner on mifepristone. The briefing will be held on Friday, August 11@11:00 a.m.(1 hour) in room 14-68.

**To:**
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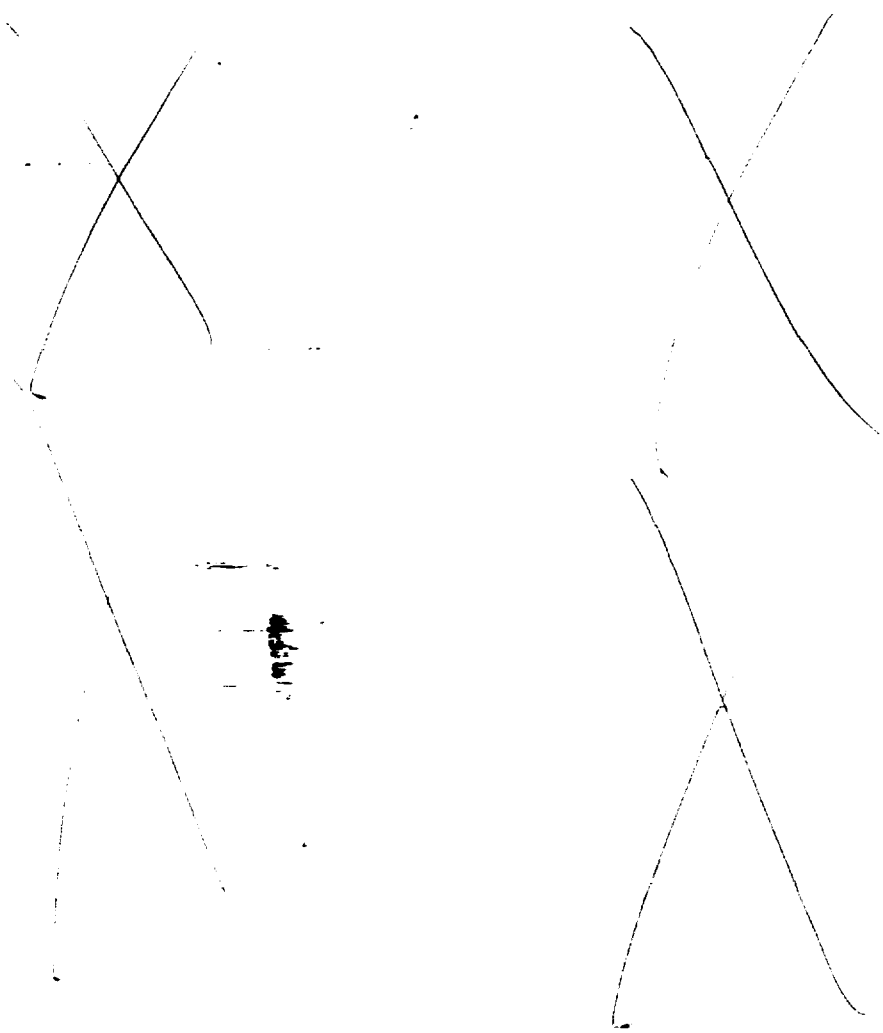

# Electronic Mail Message

**Date:** 8/9/00 1:53:48 PM
**From:** [redacted]
**To:** See Below
**Subject:** mifepristone Exhibit E comments by Fri (if possible)

Hi all,

As discussed in yesterday's meeting, we will try to compile the list of revisions to Exhibit E before many of us leave for vacation (by Fri 8/11). We can discuss more perhaps in the Fri. 8/11/00 meeting at 1pm in 17B43, if you can attend.

Please email me your comments/revisions and cc: [redacted] who will be covering for me while I am away next week.

Reminder that Exhibit E is located in the last meeting package dated July 27, 2000 as Attachment A.

I hope to mail out the comments to sponsor the week of 8/21, when I return.

Thanks,

[redacted]

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# Electronic Mail Message

**Date:** 08/07/2000 7:17:02 PM
**From:**
**To:** See Below
**Subject:** Re: Urgetnt-Outcomes for pop council

I need to talk to _____ (as I too will be away 8/16-9/5) this week about these studies_____ .et's talk. I may wish you to attend the commissioner's briefing on this drug this Friday; but before that, we need to talk as it was clear at the meeting last Friday, we have to agree on some things first. Thanks!

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# Electronic Mail Message

**Date:** 8/7/00 7:17:02 PM
**From:** [redacted]
**Subject:** Re: Urgetnt-Outcomes for pop council

[redacted]

I need to talk to [redacted] (as I too will be away 8/16-9/5) this week about these studies. [redacted] let's talk. I may wish you to attend the commissioner's briefing on this drug this Friday; but before that, we need to talk as it was clear at the meeting last Friday, we have to agree on some things first. Thanks!

[redacted]

# Electronic Mail Message

**Date:** 8/2/00 7:43:33 AM
**From:** [redacted]
**To:** See Below
**Subject:** Pop Council

I called our epidemiologist who is out of the country last night and updated him regarding our meeting yesterday. He had the following comments (see attachment) on the outline of the study reports and the concept of combining objectives 1, 2 and 4.

**To:**
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**To:**

# Electronic Mail Message

**Date:** 8/2/00 7:43:33 AM
**From:** [redacted]
**Subject:** Pop Council

I called our epidemiologist who is out of the country last night and updated him regarding our meeting yesterday. He had the following comments (see attachment) on the outline of the study reports and the concept of combining objectives 1, 2 and 4.

# Electronic Mail Message

**Date:** 8/2/00 3:46:44 PM
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**Cc:**
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**Cc:**
**Subject:** Re: JEH Invitation Request #00-4974

As additional info when considering the request to meet with ACOG on mifepristone, received the following email from in ASL.

Request to meet attached as pdf below.

Thanks,

<<0004974.pdf>>
**********

requests such as this are managed by I only manage hill requests. II defer to to manage this request.

-----Original Message-----
From:
<mailto:[SMTP
Sent: Friday, July 28, 2000 4:52 PM
To:
Subject: letter to Dr. Henney from ACOG re: RU486

ACOG has requested a meeting with Dr. Henney. ACOG sent me a copy of the letter. asked me to help you coordinate the meeting. I know ACOG's leg. director well -- Please let me know how you were planning on handling this request. Thanks.

-----Original Message-----
From:
Sent: Wednesday, August 02, 2000 2:52 PM
To: OC Invitation Reviewers; Execsec, Cder ;

Cc:
Subject: JEH Invitation Request #00-4974
Importance: High

Attached is a MEETING request for Dr. Henney to meet with them to discuss FDA's restrictions on the distribution and administration of mifepristone.

Please indicate the priority for JEH accepting this request:
___ LOW ___ MEDIUM ___ HIGH

If this is important to FDA but it would be more appropriate for another Agency representative to accept in the Commissioner's place, who would you recommend?

Rationale/What other information is relevant to this decision?

Please provide me with your input by COB 8/4/00.

Thanks,

[redacted]

<< [redacted]

[redacted]

[redacted]

July 24, 2000

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

Dear Dr. Henney:

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

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

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

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

Sincerely,

Ralph W. Hale MD

E. Ratcliffe Anderson MD

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

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

00-4974

July 24, 2000

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

Dear Dr. Henney:

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

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

Thank you for your interest in this important issue.

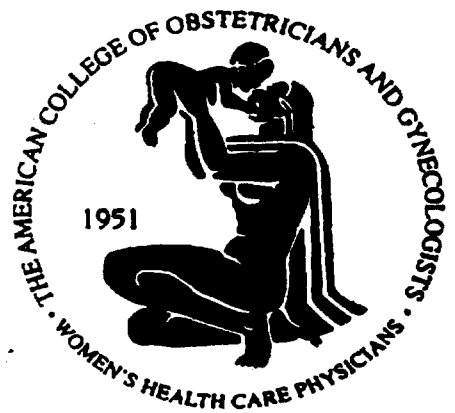
Sincerely,

Ralph W. Hale MD

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

00-4973

THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS • WOMEN'S HEALTH CARE PHYSICIANS
409 12TH STREET SW WASHINGTON DC 20024-2188
MAILING ADDRESS: PO BOX 96920 WASHINGTON DC 20090-6920
202/638-5577




# American College of Obstetricians and Gynecologists

## Analysis of the Possible FDA Mifepristone Restrictions

July 27, 2000

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

# Electronic Mail Message

**Date:** 8/1/00 12:50:49 PM
**From:** [redacted]
**To:** [redacted]
**To:** [redacted]
**Cc:** [redacted]
**Subject:** mifepristone tradename review - NDA 20-687

[redacted]

We are nearing the end of the resubmission review for this application (goal date is September 30, 2000 - although action may be taken earlier).

Your Office reviewed the proposed tradename(s) for this NDA and recommended that "Mifiprex", which the sponsor continues to request, was unacceptable.

[redacted] was reviewed as an alternative tradename and was found to be acceptable according to your review.

Would you please provide for the NDA "record" an update to your tradename reviews for "Mifeprix" and [redacted]

Thanks in advance for your feedback,

[redacted]

HFD-580
Sponsor: Population Council

[redacted]

# Electronic Mail Message

**Date:** 8/1/00 6:34:30 PM
**From:** [redacted]
**To:** [redacted]
**To:** [redacted]
**Cc:** [redacted]
**Subject:** mifepristone tradename review - N 20-687

Hi [redacted]

In your ongoing review of the tradename for mifepristone, the review team would like you to reconsider and/or comment once again on the acceptability of the tradename "Mifeprix" as well as [redacted]

This product will be approved under a restricted distribution to physicians only. In light of this specific distribution system (direct to physicians for distribution to patients) and the lack of the pharmacy involvement with the drug product, would your conclusions/ recommendations re. this tradename ("Mifeprix") be different?

Thanks for your consideration and feedback on this tradename as part of the review of the tradenames for this product.

[redacted]

# Electronic Mail Message

**Date:** 8/1/2000 5:43:40 PM
**From:**
**To:** See Below
**Subject:** Item from Pop Council meeting today

FYI,

Attached is the very rough draft of a paper distributed tc today re:Pop Council. It includes a list for items needed in a Phase 4 Epi protocol. This is provided FYI and for comment.

**To:**
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# Electronic Mail Message

**Date:** 8/1/00 5:43:40 PM
**From:** [redacted]
**Subject:** Item from Pop Council meeting today

FYI,

Attached is the very rough draft of a paper distributed to [redacted] today re:Pop Council. It includes a list for items needed in a Phase 4 Epi protocol. This is provided FYI and for comment.

[redacted]

Printed by

# Electronic Mail Message

**Sensitivity:** COMPANY CONFIDENTIAL

**Date:** 01-Aug-2000 03:55pm
**From:**
**Dept:** HFD-103 PKLN 13B45
**Tel No:**

**TO:**
**TO:**

**CC**
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**CC**
**Subject:** Re: FWD: Re: mifepristone tradename review - NDA 20-687

Yes, have them relook at Mifeprix given direct physician distribution.

>I was thinking that since you implied that the acceptability of the
>Mifeprix tradename may be ok, given that it will be distributed
directly
>to the physician, perhaps we would want OPDRA to reconsider their
>original recommendation.
>
>Would you recommend that I resend my request with the direct
>distribution to physicians as part of their consideration for review
and
>directly ask them to reconsider the name?
>
>Thanks for your feedback and advice,
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>
>>
>>Did you want them to relook at Mifeprix, too?
>>
>>
>>
>>>Hello
>>>
>>>I have processed your request for the secondary review of for
>>>NDA 20-687. It is OPDRA consult #00-0203. We should be getting back
>>to
>>>you in the next few weeks with an e-mail response. will be
>>>compared against any drug names approved since our initial review for
>>>sound-alike/look alike problems.
>>>
>>>Thanks,
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>>>Hi
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>>>>We are nearing the end of the resubmission review for this
>application
>>>>(goal date is September 30, 2000 - although action may be taken
>>>>earlier).
>>>>
>>>>Your Office reviewed the proposed tradename(s) for this NDA and
>>>>recommended that "Mifiprex", which the sponsor continues to request,
>>>was
>>>>unacceptable.
>>>>
>>> was reviewed as an alternative tradename and was found to be

> > > > acceptable according to your review.
> > > >
> > > > Would you please provide for the NDA "record" an update to your
> > > > tradename reviews for "Mifeprix" and
> > > >
> > > > Thanks in advance for your feedback,
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> > > > HFD-580
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# Electronic Mail Message

**Date:** 8/1/00 9:55:09 AM
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**Subject:** POP COUNCIL - premtg conf room changed to Pkln. 17-53 (DDMAC conf. rm in

Re. Population Council meetings this week:

Please note that the pre-meeting conference room for our Pop Council internal meeting has changed to:

Wed., Aug. 2, 2000
10:30-11:30
~~Parklawn~~ 17-53 - Headhouse (~~DDMAC conf~~ rm.)

We will be preparing to discuss the following issues for Friday's mtg agenda:

1) labeling
2) physician qualifications
3) patient agreement issues including Medication Guide
4) Phase 4 studies, especially as they pertain to items 1, 2, and 3

Friday's meeting with Population Council, Danco and Nancy Buc will be as follows:

Friday, Aug. 4, 2000
11:00 - 12:30
Chesapeake Rm - Pkln. 3rd floor

Please let me know if you need any additional materials to review before the internal or industry meeting. (The meeting package dated 7/28/00 only addressed/responded to the label and distribution system as discussed at the 7/19 industry meeting with sponsor. The Phase 4 summaries were presented in the background materials submitted on 7/5/00 for our 7/19 mtg.)

I will bring additional copies of the 7/28 mtg package and the Phase 4 summaries to the pre-meeting on Wed.

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**Date:** 8/1/00 9:55:09 AM
**From:** [redacted]
**To:** See Below
**Subject:** POP COUNCIL - premtg conf room changed to Pkln. 17-53 (DDMAC conf. rm in

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[redacted]

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**Date:** 8/1/00 9:55:09 AM
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**Subject:** POP COUNCIL - premtg conf room changed to Pkln. 17-53 (DDMAC conf. rm in

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Thanks,

[redacted]

# Electronic Mail Message

**Date:** 7/31/00 9:09:52 AM
**From:**
**To:**
**Cc:**
**Subject:** FYI - RU-486

In case you haven't seen it, below is a copy of an article on RU-486 posted on Medscape, which is a medical opinion leader on the Web.

From
Medscape Women's Health

The Approval of Mifepristone (RU486) in the United States: What's Wrong With this Picture?
Paul Blumenthal, MD, Jane Johnson, and Felicia Stewart MD
[Medscape Women's Health 5(4), 2000. © 2000 Medscape, Inc.]

Since its approval in France in 1988, the abortifacient mifepristone (RU486) has proven to be a safe, effective, acceptable option for millions of women seeking abortion during the first several weeks of pregnancy. More than 500,000 women in Europe and millions of women in Asia have used the mifepristone/misoprostol regimen.[1] Women in the United States have waited long enough for this safe and effective early abortion option.

After more than 5 years and at least 1 false start, the Population Council, a nonprofit entity which holds the US rights to mifepristone, was able to identify a private industry partner, Danco, willing to confront threats of economic boycotts and protests to bring mifepristone to American women. In the meantime, violent acts and protests meant to intimidate women and healthcare providers have continued, culminating in the murder of Dr. Barnett Slepian in October 1998.

Women's health advocates have recently learned of yet another development in the ongoing saga regarding final approval of mifepristone. At a meeting of early abortion providers and abortion rights advocates, the Population Council and Danco revealed that the U.S. Food and Drug Administration (FDA) had made a series of proposals regarding the labeling and distribution of mifepristone that would severely limit women's access to the drug if and when it is approved.

The labeling and distribution restriction described by Danco would be unprecedented and without any clinical or scientific merit. More than 8000 women in the United States have had a medical abortion using mifepristone in combination with misoprostol in clinics, doctors' offices, and their own homes.[2-5]

In 1996 and again in February 2000, the FDA had declared mifepristone safe and effective for use as a very early abortion method. So why don't American women have access to this drug? Given the safe and efficacious profile that has been established for mifepristone and misoprostol, the answer apparently lies neither in science nor the practice of medicine, but in the politics of abortion and women's reproductive health.

Mifepristone can be administered safely by a wide array of healthcare providers. As a result, mifepristone availability not only could expand the options available to women who want to terminate their pregnancy early, but it could expand the number of providers willing to offer safe and accessible abortion services. A recent national survey by the Kaiser Family Foundation found that more than 1 in 3 gynecologists who do not now perform abortions would offer mifepristone.[6]

In addition, 31% of family practice physicians -- most of whom do not perform abortions now -- say they would also offer the drug. Rather than have to face a barrage of angry or even violent protestors outside an abortion clinic, women potentially could access abortion services in the privacy of their own doctor's office.

Unfortunately, the distribution limitations being discussed would virtually eliminate that possibility. One provision, limiting sale of the drug only to physicians trained in 3 procedures -- surgical abortion, mifepristone abortion, and the use of ultrasonography -- would mean that few new providers would be likely to begin providing medical abortion services. Another provision being considered, limiting its use to physicians who have admitting privileges to an emergency room within an hour's distance of their office or clinic, would make many current abortion providers ineligible to use this option.

These restrictions might be appropriate if mifepristone was a dangerous drug. But it is not. No woman has died as a result of using mifepristone. In fact, a blood transfusion, the most severe adverse outcome, has been required in only 0.1% of cases (or 8 out of more than 8000) in the United States[2-5] (Schaff EA, et al. Randomized trial of vaginal misoprostol at 24, 48, and 72 hours after mifepristone for abortion up to 56 days pregnant. Submitted for publication).

By comparison, Viagra -- known to have caused far more serious health consequences, including at least 60 reported deaths -- carries no such training or certification restrictions.[7]

Furthermore, the proposals' scope translates into an unprecedented and unwarranted intrusion in the nature of clinical practice. Midwives, for example, can and do deliver babies without having to be certified in backup procedures such as cesarean sections. Cardiologists routinely provide medication for chest pain without being trained and certified in cardiovascular surgery should medication fail. Ultrasonography is certainly not an essential part of early abortion care. In fact, a recent study in Lancet shows that a majority of women can accurately predict for themselves when they became pregnant.[8]

Even if one accepts ultrasound as a prerequisite to eligibility for a mifepristone abortion, isn't a consultant radiologist perfectly competent to perform this test and relay the results to the clinician providing the abortion procedure? Isn't such consultation an established, proven pattern for the safe and expeditious practice of medicine in the United States and elsewhere?

While final US approval of mifepristone continues to languish, clinical trials have been under way that clearly demonstrate that a variety of healthcare providers, including obstetricians/gynecologists, family physicians, and nurse/midwives, can and do provide safe medical abortions using mifepristone without any certification procedures. When an optometrist in rural Montana can write a prescription for Viagra -- no questions asked -- but a family practice physician in suburban Maryland has to jump through multiple certification hoops to offer the far safer mifepristone, something is clearly wrong.

Organizations such as the American College of Obstetricians and Gynecologists, Physicians for Reproductive Choice and Health and the National Abortion Federation are in strong agreement that mifepristone

should be made available to women without imposing any unnecessary, unprecedented, or politically motivated restrictions that are not supported by scientific data (Physicians for Reproductive Choice and Health, personal communication).

Although disappointing, the slow and cautious pace to final approval for mifepristone is not altogether surprising. In 1998 and again in 1999, the House of Representatives approved an amendment to the Agriculture Appropriations bill that would prohibit the FDA from using any public funds to review and approve mifepristone. As long as social conservatives remain in power, review and approval process at the FDA will continue to come under heavy partisan scrutiny. Allowing decisions about medical science to be delayed by political pressure or fear of pressure, however, is surely not appropriate. This is especially unacceptable when such significant clinical issues are involved for women and their families. Indeed, the FDA's principal role in the drug-approval process is as a regulatory agency and, as such, is mandated to be concerned solely with the science and medicine of new drugs and devices.

In the past, despite political pressure, the FDA has relied on supportive scientific information to make courageous regulatory decisions. We urge that in determining how this regimen will be approved and regulated in the United States, the FDA should consider the enviable safety and efficacy record of mifepristone and misoprostol and make it's recommendations solely on the basis of the scientific data without being influenced by partisan political pressures.

---

Paul Blumenthal, MD, Jane Johnson, and Felicia Stewart, MD, are members of the board of the Reproductive Health Technologies Project.

References

1. Christin-Maitre S, Bouchard P, et al. Medical termination of pregnancy. 2000;342:946.
2. Spitz IM, Bardin CW, Benton L, Robbins A. Early pregnancy termination with mifepristone and misoprostol in the United States. N Engl J Med. 1998;338:1241.
3. Schaff EA, Stadalius L, Eisinger SH, Franks P. Vaginal misoprostol administered at home after mifepristone for abortion. J Fam Pract. 1997;44:353.
4. Schaff EA, Eisinger SH, Stadalius LS, Franks P, Gore BZ, Poppema S. Low-dose mifepristone 200 mg and vaginal misoprostol for induced abortion. Contraception. 1999;59:1.
5. Schaff EA, Fielding, SL, Eisinger SH, Stadalius LS, Fuller L. Low-dose mifepristone followed by vaginal misoprostol at 48 hours for abortion up to 63 days. Contraception. 2000;61:41-46.
6. Kaiser Family Foundation. A National Survey: Views of Women's Health Care Providers on Abortion (Conducted Jan. 19-Apr. 27, 2000). Released June 13, 2000.
7. Mitka M. Some men who take Viagra Die. Why? JAMA. 2000;283:590.
8. Ellertson C, Elul B, Ambardekar S, Wood L, Carroll J, Coyaji K. Accuracy of assessment of pregnancy duration by women seeking early abortions. Lancet. 2000;355:877-881.

# Electronic Mail Message

**Date:** 7/31/00 8:28:12 AM
**From:**
**To:**
**Subject:** FWD: RU486

Another RU-486