RU-486 is an oral contraceptive with abortifacient properties which has been used manufactured in Europe for approximately ten years and has been sold in France, Sweden and the United Kingdom. RU-486 is currently before the Food and Drug Administration for approval for use in the United States. According to the complaint, in 1994, the United States patent rights to RU-486 were obtained by the Population Council, Inc. ("Population Council"), a New York not-for-profit organization which engages in various biomedical and social research activities, and whose goal is to "advance the reproductive health and reproductive rights of women."

In an agreement dated September 15, 1995, the Population Council and Gedeon, a Hungarian pharmaceutical manufacturer, entered into a contract (hereinafter "Letter Agreement") pursuant to which Gedeon agreed to manufacture RU-486 in bulk form and to supply it to one or more of the Population Council's licensees or sub-licensees. In a separate agreement, also dated September 15, 1995, (hereinafter "Interim Agreement"), Gedeon and Danco entered into a contract pursuant to which Gedeon agreed to manufacture RU-486 in bulk form and sell it to Danco, as the sub-licensee of the Population Council. The bulk RU-486 would be converted to tablet form by another manufacturer and Danco would then market and sell the finished product. In May, 1995, Danco and Gedeon entered into a Manufacturing Agreement which more comprehensively set forth their respective obligations.

On May 9, 1997, Danco brought this action, asserting that Gedeon had breached the contract by refusing to manufacture RU-486. On May 12, 1997, Danco moved for an order sealing the record. In an order dated June 2, 1997, this court denied that motion on the grounds that the parties had failed to assert that any injury or adverse consequences would result from public access to the documents in this case. That decision went on to state that the sealing of any documents containing trade secrets would be considered if and when it became necessary.

On July 14, 1997, Danco's motion for a preliminary injunction was argued before this court. At that time, another request was made to seal the record. This Court issued an interim order sealing the record on the grounds that the parties had demonstrated good cause. On July 30, 1997, a final order was issued which stated that a showing of good cause had been established, given that the information contained in the court file contained trade secrets as well as identities of financial backers and financial interests.

Thereafter, the Post moved to intervene and to unseal the record, arguing that the public has a compelling interest in knowing if and when RU-486 will become available in the United States. Gedeon and Danco opposed the motion on the grounds that sealing the record is required both to protect trade secrets and to shield the parties from threats and boycotts from persons opposed to the introduction of RU-486 in the United States.

In a decision dated May 28, 1998, this court declined to unseal the record, finding that the interest of some members of the public in this case did not outweigh the interest of the parties in keeping numerous trade secrets and the identities of financial backers and financial interests confidential.

The Uniform Rules for New York State Trial Courts, 22 NYCRR 216.1(a), provides that

> Except where otherwise provided by statute or rule, a court shall not enter an order in any action or proceeding sealing the court records, whether in whole or in part, except upon a written finding of good cause, which shall specify the grounds thereof. In determining whether good cause has been shown, the court shall consider the interests of the public as well as of the parties. Where it appears necessary or desirable the court may prescribe appropriate notice and opportunity to be heard.

New York public policy is against the sealing of court proceedings. (Matter of the Conservatorship of Ethel Bronstone, 191 AD2d 167, 168). However, "the common-law right to inspect and copy judicial records is not absolute, particularly where such records are a source of business information which might harm a litigant's competitive standing, and the determination of whether access to such records is appropriate is best left to the sound discretion of the trial court, a discretion to be exercised in light of the relevant facts and circumstances of the particular case." (Matter of Crain Communications, Inc. v. Hughes, 135 AD2d 351, aff'd 74 NY2d 626, 628; see Nixon v. Warner Communications, 435 US 589, 598-599; 22 NYCRR 216.1(a)). In determining whether

to seal the record, the court must consider both the concerns of the public regarding the issues in the case as well as the movant's interest in keeping the information private. (See Dawson v. White & Case, 184 AD2d 246, 247). In some cases, confidentiality is "necessary in order to protect the litigants or encourage a fair resolution of the matter in controversy." (Matter of Twentieth Century Fox Film Corp., 190 AD2d 483, 486). In such cases, confidentiality must be provided. (Id.).

The court finds that the case at hand is one which requires confidentiality. None of the parties dispute that some members of the public have an interest in this case because they want to know if and when RU-486 will become available in the United States. It is also undisputed that the issue of abortion is a highly charged one, which has led to violence against persons seeking abortions as well as persons who provide abortion services. The question here is whether the interest of certain members of the public in keeping apprised of the availability of RU-486 outweighs the desire of the parties to protect their trade secrets and, potentially, their physical well being. This court cannot say that it does.

First, the court adheres to its earlier finding that sealing the record is necessary to protect the various parties' numerous trade secrets and the identities of financial backers and financial interests. This is especially true in connection with the parties' trade secrets, which must be kept confidential in

order to prevent harm to the parties' competitive standing. (See, Matter of Chair Communications, Inc. v. Hughes, 135 AD2d 351, aff'd 74 NY2d 526, 623).

Perhaps more importantly, the court finds that sealing the record is a necessary precaution to protect the well being of the persons involved in the manufacture and distribution of RU-486. Danco and Gedeon both point to evidence which indicates that such well-being is in increasing jeopardy.

On June 12, 1997, before the record was first sealed, the Post published an article entitled "Abortion Pill's U.S. Sponsor Suing Hungarian Drug Firm." Sometime thereafter, apparently in 1998, an anti-abortion organization called Human Life International, published an article on its internet site which reported on the lawsuit at issue here and the progress of the effort to manufacture and distribute RU-486 in the United States. The report, which relied heavily on the Post's coverage of this action, specifically identified an individual who had invested in what was termed "the [Population] Council's abortion pill project." The report lists the location of the individual's residence, his educational background, employment history and many details about projects that he worked on at different jobs.

Another internet site, called "The Nuremberg Files", and run by a group known as the "Christian Gallery", solicits information about, among other things, individuals who perform abortions, or who own or operate abortion clinics. Among the information sought

are photographs and videotapes of the individuals in question. The site also provides a list of individuals who have already been identified, and lists them under the categories "working" "wounded" and "fatality". Finally, the site provides links to newspaper websites, including the Post, so that visitors to the site can have access to media coverage of the abortion issue.

In February of 1988, it was reported that an anti-abortion group called the "Army of God" had sent handwritten letters to various media outlets claiming responsibility for a fatal bombing of a Birmingham abortion clinic. The letters apparently included a statement that anyone who manufactures, markets, sells or distributes RU-486 would be targeted by the group.

The examples cited above demonstrate that there is an increasing likelihood that harm may come to individuals who are identified as being directly or indirectly involved in the manufacture and distribution of RU-486. The court finds, therefore, that the interest of the public in this litigation does not outweigh the threats to the individuals involved in the manufacture and distribution of RU-486. Accordingly, in the exercise of discretion, the court concludes that sealing the record in this case is necessary.

The Post argues that a more appropriate solution would be to redact ~~any~~ trade secrets and individual names from filed documents. However, as Gedeon points out, since there has already been a certain amount of disclosure of the identities of various

businesses and individuals involved in this case, it is possible that the Post or any other interested individuals could deduce the identities of individuals or businesses whose names are blacked-out in redacted documents, which would defeat the purpose of the redaction. Therefore, in the exercise of discretion, the court finds it appropriate to seal the entire record, rather than attempt to redact large portions of it. Accordingly, it is

ORDERED that plaintiff's motion to seal the court file and all proceedings of this case is granted.

DATED: June 23, 1999

ENTER:

J.S.C.

APPEARS THIS WAY
ON ORIGINAL

TOM A. COBURN, M.D.
2D DISTRICT, OKLAHOMA

COMMITTEE ON COMMERCE
SUBCOMMITTEES:
HEALTH AND ENVIRONMENT
ENERGY AND POWER

Congress of the United States
House of Representatives
Washington, DC 20515–3602

215 STATE STREET, SUITE 815
MUSKOGEE, OK 74401
(918) 687–2533
(918) 682–8503 (FAX)

120 S. MISSOURI, ROOM 105
CLAREMORE, OK 74017
(918) 341–9336
(918) 341–9437 (FAX)

34 "A" STREET N.E., ROOM 202
MIAMI, OK 74354
(918) 542–5337
(918) 542–5367 (FAX)

September 6, 2000

The Honorable Jane E. Henney, M.D.
Commissioner
Food and Drug Administration
Parklawn Building
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Henney,

An August 28 *Health News Daily* article regarding the FDA and Cytotec (or misoprostol, as it is more commonly known), referred to an August 23, 2000 letter to health care practitioners issued by Searle, the makers of Cytotec. I have recently obtained a copy of this drug-warning letter.

The Searle letter reiterates that Cytotec has not been tested or approved for use as "a cervical ripening agent prior to termination of pregnancy [abortion] or for induction of labor." The company states that: "Serious adverse events reported following off-label use of Cytotec in pregnant women include maternal or fetal death; uterine hyperstimulation, rupture or perforation requiring uterine surgical repair, hysterectomy or salpingo-oophorectomy; amniotic fluid embolism; severe vaginal bleeding, retained placenta, shock, fetal bradycardia and pelvic pain."

I would like to know the following information regarding your agency's involvement with this drug warning letter:

1) Since Cytotec is often used in conjunction with mifepristone (RU-486) as part of a two-drug regimen for inducing abortions, will Searle's letter be considered in the approval process for mifepristone?

2) If the FDA approves RU-486 for inducing abortions, will you take steps to warn pregnant mothers that their uteruses may explode and they may die if they use Cytotec for inducing abortion or labor?

3) The *Health News Daily* article said Searle's warning letter was "drafted jointly with the FDA." Did the FDA jointly draft a warning letter with Searle? And if so, is it standard procedure for the FDA to help pharmaceutical companies write drug warning letters?

00-5777

429 CANNON HOUSE OFFICE BUILDING
WASHINGTON, DC 20515
(202) 225–2701 Fax: (202) 225–3038

MF 008020

E-mail: rep.coburn@mail.house.gov
Web site: www.house.gov/coburn

4) Did the FDA provide Searle with information on published or unpublished "serious adverse events" which were reported following the off-label use of Cytotec? And if so, what were these sources?

I would appreciate this information as soon as possible. If you have any questions, please contact Roland Foster of my staff at 202-225-2701.

Sincerely,

Tom A. Coburn, M.D.
Vice Chair
Commerce Subcommittee on Health & Environment

Attachment

APPEARS THIS WAY
ON ORIGINAL

SEARLE

SEARLE
5200 Old Orchard Road
Skokie, Illinois 60077
Phone (847) 982-7000
Fax (847) 470-1460

IMPORTANT DRUG WARNING CONCERNING UNAPPROVED USE OF INTRAVAGINAL OR ORAL MISOPROSTOL IN PREGNANT WOMEN FOR INDUCTION OF LABOR OR ABORTION

August 23, 2000

Re: Cytotec® (misoprostol)

Dear Health Care Practitioner:

The purpose of this letter is to remind you that Cytotec administration by any route is contraindicated in women who are pregnant because it can cause abortion. Cytotec is not approved for the induction of labor or abortion.

Cytotec is indicated for the prevention of NSAID (nonsteroidal anti-inflammatory drugs, including aspirin)-induced gastric ulcers in patients at high risk of complications from gastric ulcer, e.g., the elderly and patients with concomitant debilitating disease, as well as patients at high risk of developing gastric ulceration, such as patients with a history of ulcer.

The uterotonic effect of Cytotec is an inherent property of prostaglandin E_1 (PGE_1), of which Cytotec is a stable, orally active, synthetic analog. Searle has become aware of some instances where Cytotec, outside of its approved indication, was used as a cervical ripening agent prior to termination of pregnancy, or for induction of labor, in spite of the specific contraindications to its use during pregnancy.

Serious adverse events reported following off-label use of Cytotec in pregnant women include maternal or fetal death; uterine hyperstimulation, rupture or perforation requiring uterine surgical repair, hysterectomy or salpingo-oophorectomy; amniotic fluid embolism; severe vaginal bleeding, retained placenta, shock, fetal bradycardia and pelvic pain.

Searle has not conducted research concerning the use of Cytotec for cervical ripening prior to termination of pregnancy or for induction of labor, nor does Searle intend to study or support these uses. Therefore, Searle is unable to provide complete risk information for Cytotec when it is used for such purposes. In addition to the known and unknown acute risks to the mother and fetus, the effect of Cytotec on the later growth, development and functional maturation of the child when Cytotec is used for induction of labor or cervical ripening has not been established.

Searle promotes the use of Cytotec only for its approved indication. Please read the enclosed updated complete Prescribing Information for Cytotec.

Further information may be obtained by calling 1-800-323-4204.

Michael Cullen, MD
Medical Director, U.S.
Searle

CY20141A

APPEARS THIS WAY
ON ORIGINAL

April 6, 2001

Center for Drug Evaluation and Research
1451 Rockville Pike, Room 6027
Rockville, MD 20852

Dear

I am writing to advise you that Shanghai Hualian Pharmaceutical Co., Ltd. ("Shanghai Hualian") agrees that FDA may publicly identify Shanghai Hualian as the manufacturer of mifepristone for Danco.

By agreeing to the disclosure stated in the first paragraph, Shanghai Hualian does not waive or limit any right to confidentiality of other information, documents, and material under applicable law, including 18 U.S.C.A. § 1905, Section 301(j) of the Food, Drug, and Cosmetic Act, the Freedom of Information Act, and FDA's implementing regulations.

If you have further questions please contact me at

Sincerely,

/S/

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4/6/01 1:12 PM (25059-0002)

APPEARS THIS WAY
ON ORIGINAL

BUC & BEARDSLEY
919 EIGHTEENTH STREET, N.W.
SUITE 600
WASHINGTON, D.C. 20006-5503

WRITER'S TELEPHONE
202-736-3610

TELEPHONE
202-736-3600
FACSIMILE
202-736-3606

April 8, 2001

Center for Drug Evaluation and Research
Food and Drug Administration
1451 Rockville Pike, Room 6027
Rockville, MD 20852

Dear [redacted]

I am writing to advise you that Danco Laboratories, LLC ("Danco") and The Population Council agree that FDA may publicly identify Shanghai Hualian Pharmaceutical Co., Ltd. as the manufacturer of mifepristone for Danco.

By agreeing to the disclosure stated in the first paragraph, Danco and The Population Council do not waive or limit any right to confidentiality of other information, documents, and material under applicable law, including 18 U.S.C. § 1905, Section 301(j) of the Food, Drug, and Cosmetic Act, the Freedom of Information Act, and FDA's implementing regulations.

Sincerely,

Nancy L. Buc

APPEARS THIS WAY
ON ORIGINAL

TELEFAX

TO: _____

_____

_____

FAX: _____

PHONE: _____

FROM: _____

Food and Drug Administration
Division of Reproductive and Urologic Drug Products
5600 Fishers Lane, HFD-580
Rockville, Maryland 20857-1706

FAX:
PHONE:

DATE: 12/5/96

PAGES: 6 (Inclusive)

/S/

Approved for faxing.

Food and Drug Administration
Division of Reproductive and Urologic Drug Products
5600 Fishers Lane-HFD-580
Rockville, Maryland 20857-1706

List of Meetings for Mifepristone

Date of Meeting: February 27, 1989

External Attendees: David Andrews, Acting President, Planned Parenthood Federation of America (PPFA)
Louise Tyrer, M.D., Vice President, Medical Affairs (PPFA)
Eve Paul, Vice President, Legal Affairs (PPFA)
David Grimes, M.D., Chairman, National Medical Committee of PPFA
Nancy Buck, Attorney

FDA Attendees:

(HFD-510)	(HFD-510)
(HFD-510)	(HFD-510)
(HFD-510)	(HFD-510)
(HFD-510)	(HFD-510)
(HFD-510)	

Topic: Determination of the information required to apply for marketing approval for mifepristone.

Date of Meeting: June 18, 1990

External Attendees: Bernard Z. Gore, M.D.
Carl J. Levinson, M.D.
Steven Heilig, MPH

FDA Attendee: (HFD-510)

Topic: Initial deficiencies found in their submitted IND.

Date of Meeting: November 7, 1991

External Attendees: Etienne-Emile Bauliew, M.D., Ph.D. (Roussel Uclaf)

FDA Attendees:

(HFD-510)	(HFD-510)
(HFD-510)	(HFD-510)
(HFD-510)	(HFD-510)
(HFD-510)	(GCF-1)
(HFD-510)	(HFD-510)
(HFD-510)	(HFD-510)
(HFD-510)	

Topic: Current marketing plans for mifepristone.

Date of Meeting: May 4, 1993

External Attendees: Louise Tyrer, M.D., Association for Reproductive Health
Gary Hodgen, M.D., Jones Institute for Reproductive Medicine
[redacted]t, University Consultant
Lawrence Lader, Abortion Rights Mobilization

FDA Attendees:
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)

Topic: Development of a non-French mifepristone in the U.S.

Date of Meeting: July 16, 1993

External Attendees: The Population Council:
[redacted]
Dr. Ann Robbins
Dr. Irving Spitz
Dr. Irving Sivin
Dr. Wayne Bardin

FDA Attendees:
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (GCF-1)
[redacted] (HFD-713)

Topic: The development plan and time frame for submission of mifepristone NDA.

Date of Meeting: December 6, 1993

External Attendees: Lawrence Lader, President, Abortion Rights Mobilization
[redacted] University (Consultant)

FDA Attendees:
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-426)
[redacted] (HFD-713)

Topic: The regulatory process for development of a non-French mifepristone.

Date of Meeting: March 31, 1994

External Attendees: Lawrence Lader., President, Abortion Rights Mobilization
[redacted] Consultant)

FDA Attendees:
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (GFC-1)
[redacted] (HFD-426)
[redacted] (HFD-426)
[redacted] (HFD-510)
[redacted] (HFD-510)

Topic: Plans for pre-clinical and clinical studies using mifepristone.

Date of Meeting: July 7, 1994

External Attendees: Dr. C.W. Bardin (The Population Council)
Dr. A. Robbins (The Population Council)
Dr. I Spitz (The Population Council)
[redacted] ncil)
Dr. B. Winkoff (The Population Council)
[redacted]

FDA Attendees:
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-426)
[redacted] (OC)

Topic: The Population Council's proposed plans for an NDA.

Date of Meeting: October 12, 1994

External Attendees: Dr. Bardin, Population Council
[redacted]
Dr. Tyler, Gedeon Richter
Dr. Simon, Gedeon Richter

FDA Attendees:
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)
[redacted] (HFD-510)

Topic: Synthesis and manufacture of mifepristone.

Date of Meeting: June 23, 1995

External Attendees: Louise Tyrer, M.D., Principal Investigator for Abortion Rights Mobilization
Eric Schaff, M.D., Investigator for Abortion Rights Moblilization

FDA Attendees: ——— (HFD-510)
——— (HFD-510)
——— (HFD-510)
——— (HFD-510)

Topic: Proposed clinical protocol for mifepristone.

Date of Meeting: October 24, 1995

External Attendees: Dr. C.W. Bardin (The Population Council)
Dr. A. Robbins (The Population Council)
———
(Consultant to the Population Council)

FDA Attendees: ——— (HFD-510) ——— (HFD-510)
——— (HFD-510) ——— (HFD-510)
——— (HFD-510) ——— (HFD-426)
——— (HFD-510) ——— (HFD-713)
——— (HFD-510) ——— (HFD-510)

Topic: Upcoming NDA content and format.

Date of Meeting: February 7, 1996

External Attendees: Lawrence Lader., President, Abortion Rights Mobilization
——— (Consultant)
——— Steroids, LTD
——— President, Murty Pharmaceuticals

FDA Attendees: ——— (HFD-510)
——— (HFD-510)
——— (HFD-510)
——— (HFD-510)

Topic: Requirements for chemistry and toxicology to satisfy clinical hold deficiencies.

Date of Meeting: June 18, 1996

External Attendees: Ms. Sandra Arnold (The Population Council)
Wayne C. Bardin, M.D. (The Population Council)
Mr. James Boynton (The Population Council)
Ms. Margaret Catley-Carlson (The Population Council)
Ann Robbins, Ph.D. (The Population Council)

FDA Attendees: [redacted] Division of Reproductive and Urologic Drug Products (DRUDP; HFD-580)
[redacted] (HFD-580)
[redacted] (HFD-580)
[redacted] (HFD-820)
[redacted] (HFD-580)
[redacted] (HFD-580)
[redacted] (HFD-580)
[redacted] (HFD-870)

Topic: The status of the NDA review including information requests, and the upcoming Advisory Committee.

Date of Meeting: September 12, 1996

External Participants: Ann Robbins, Ph.D., Scientist, Population Council
[redacted] Population Council
Tom Scarlett, Consultant for the Population Council from Hyman, Philips and MacNamara
Eliot Johanesson, M.D., Senior Scientist, Population Council
Sandra Arnold, Scientist, Population Council
James S. Boynton, Consultant from Christy and Viener

FDA Participants: [redacted] Drug Evaluation II (ODE II; HFD-102)
[redacted] Division of Reproductive and Urologic Drug Products (DRUDP; HFD-580)
[redacted] (HFD-580)
[redacted] (HFD-580)
[redacted] (HFD-580)
[redacted] (HFD-580)
[redacted] (HFD-580)

Topic: Labeling issues, Phase 4 issues, and the sponsors proposed distribution system.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

N 20-687

September 27, 2000

MEMORANDUM FOR THE RECORD

Re: Redacting Names and Addresses of Contract Manufacturers of Mifepristone

On June 23, 1999, The Danco Group (Danco) requested that the Food and Drug Administration treat the names and addresses of Danco's contract manufacturers as confidential commercial information. Danco supplemented its original request on July 14, 1999, January 11, 2000, and September 19, 2000.

FDA's Office of the Chief Counsel considered the information submitted by Danco and whether the Agency is authorized to redact the names and addresses of the contract manufacturers of mifepristone from agency records. See September 27, 2000 memorandum to Jane E. Henney re Redaction of Names and Addresses of Contract Manufacturers from Mifepristone Documents. The Office of the Chief Counsel has advised me that the Agency would be authorized to redact this information if the disclosure of the information is likely to cause substantial competitive harm to the entity from which the information was obtained.

Danco has provided the Agency with information on why it believes it is likely to suffer substantial competitive harm if this information is released. In addition, FDA also discussed the situation with attorneys in the Civil Rights Division at the Department of Justice. These attorneys, one of whom serves on the National Task Force on Violence Against Reproductive Health Care Providers, stated that, given their knowledge of the potential threats of violence against individuals or organizations involved in the provision of abortion services, they believe that there is a definite risk that the contract manufacturers would be the targets of threats or acts of violence by groups or individuals opposed to the use of mifepristone. More specifically, at least one individual involved in the development of mifepristone has been the target of threats of violence in the past, to the extent that the individual required armed protection for a period of time.

I have also considered the decision by the Supreme Court of the State of New York to seal the record in the on-going litigation between Danco and its former contract manufacturer. The Court in that case determined that sealing the record was a necessary precaution to protect the well-being of the individuals involved in the manufacturing and distribution of mifepristone. The Court based its decision in large part on the history of threats and acts of violence associated with the provision of abortion services in this country, and with the development of mifepristone.

The Agency also specifically considered whether information in its drug registration and listing system would be releasable under the Agency's drug listing regulations. The Office of the Chief Counsel has advised that the names and addresses of the contract manufacturers of mifepristone

can be redacted as confidential commercial information. Although, as a general matter, the release of information submitted pursuant to the drug registration and listing requirements is consistent with the protection of the public health, in this particular situation, I have decided that the public interest in knowing the specific manufacturing sites for mifepristone is outweighed by the potential risk of harm associated with the release of this information.

Before deciding to redact this information, the Agency attempted to determine whether this information is already publicly available and, if not, whether there are other channels through which it would ordinarily become publicly available. Danco states it has not released this information, nor is it aware that the information has been made public through other means. FDA considered whether the information would be available from, for example, the Securities and Exchange Commission, the Environmental Protection Agency, the United States Customs Service, or State or local government agencies. With regard to each of these, FDA has concluded that the information either would not be submitted to that agency or, if it were submitted, could be withheld as confidential commercial information.

After thorough review and careful consideration in discussion with other senior agency officials, I have concluded that the names and addresses of the contract manufacturers should be considered to be confidential commercial information under the Freedom of Information Act and the Trade Secrets Act because disclosure of this information is likely to cause substantial harm to the competitive position of Danco. Therefore, the names and addresses of the contract manufacturers will be redacted from all agency records prior to those records being made publicly available.

/S/

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

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

N 20-687

September 27, 2000

MEMORANDUM FOR THE RECORD

Re: Redacting Names of Individuals in Connection With Mifepristone Application

I have decided to redact the names of agency personnel from agency records related to the Population Council's new drug application for mifepristone prior to the release of those records. I have made this decision on privacy grounds after thorough review and careful consideration in discussion with other senior agency officials because I believe that doing so is necessary to reasonably assure the FDA employees' safety. This action is consistent with other decisions that have been made concerning employees' identities.

I have been advised that, under 21 C.F.R. § 20.32, the names of FDA employees will not be deleted from disclosable records "except where such deletion is necessary to prevent . . . danger to the life or physical safety of the employee or under any other extraordinary circumstances." I have concluded that such extraordinary circumstances are present in this case and that there is a risk of danger to the lives or physical safety of agency employees. In evaluating this matter, FDA staff discussed the current situation with attorneys in the Civil Rights Division at the Department of Justice. These attorneys, one of whom serves on the National Task Force on Violence Against Reproductive Health Care Providers, stated that, given their knowledge of the potential threats of violence against individuals or organizations involved in the provision of abortion services, they believe that there is a risk that individuals or organizations who are publicly linked to mifepristone could be the targets of threats or acts of violence by groups or individuals opposed to the use of this drug product. More specifically, at least one individual involved in the development of mifepristone has been the target of threats of violence in the past, to the extent that the individual required armed protection for a period of time.

I have also considered the decision by the Supreme Court of the State of New York to seal the record in the on-going litigation between Danco (the contractor named in the mifepristone NDA) and the former contract manufacturer of mifepristone. The Court in that case determined that sealing the record was a necessary precaution to protect the well-being of the individuals involved in the manufacturing and distribution of mifepristone. The Court based its decision in large part on the history of threats and acts of violence associated with the provision of abortion services in this country, and with the development of mifepristone.

Given these conditions, I have concluded that there is a risk that individuals associated with the development, marketing, and distribution of mifepristone will become the targets of threats and acts of violence by individuals opposed to the use of mifepristone. I believe that this risk could extend to those FDA employees who were involved in the review of the new drug application for

mifepristone and in related activities. Therefore, to prevent danger to the lives and physical safety of those employees, I have decided that their names will be redacted from agency records on privacy grounds prior to the public release of those records. For similar reasons, I have also decided, in response to a request from The Population Council, to redact the names of the clinical investigators involved in the trials supporting the NDA for mifepristone if their names have not otherwise been made public.

/S/

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

APPEARS THIS WAY
ON ORIGINAL

ROUSSEL UCLAF

Romainville, October 16, 1995

CONFIDENTIAL

THE POPULATION COUNCIL Inc.
One Dag Hammarskjold Plaza
New-York / NEW-YORK 10017
USA

Attention of Ms CATLEY-CARLSON

Dear Sirs,

Re : MIFEPRISTONE-CMC Section of the ———— t

We are now completing the CMC section to be filed by the Council with the FDA as an amendment to the IND ———— t filed in the 1980's ; this will include information relating to methods validation. The Council will include reference to the CMC section in the NDA to be filed by it. Roussel Uclaf will also prepare four additional copies of said methods validation information contained in the IND for direct submission to the FDA in separate folders provided by the Council when the Council informs Roussel that it is submitting its full NDA.

The communication to the FDA of the CMC section and the above four additional copies will be made by Roussel Uclaf directly so as to preserve the confidentiality of the information.

We wish to emphasize that this communication is made subject to the following conditions :

a) The CMC section supplied by Roussel will be filed in the IND and not in the NDA.

b) If FDA hereafter requests samples of the drug product for any reason in connection with the NDA, the samples will be supplied by the Council and no reference to Roussel will be made.

c) Roussel Uclaf shall not be referred to, at any time, by the Council or its designees, as a manufacturer of mifepristone or as a supplier of information. The preceding sentence shall not preclude reference by the Council to the IND or to investigations of mifepristone conducted by or for Roussel,

.../

102, Route de Noisy 93235 Romainville Cedex
Tél. + 33 (1) 49 91 49 91 Fax. + 33 (1) 49 91 49 49
SIRET 542 008 081 00052

provided that any such reference shall be limited to communication between the FDA and Roussel and shall not be made public or be accessible to the public. We understand that the FDA policy is to keep the information referred to in the preceding sentence confidential, and the parties' agreement is based upon this policy and their belief that this policy will be followed.

d) Roussel Uclaf shall not supply mifepristone to the FDA, the Council, or any of its designees in any form, at any time. Roussel Uclaf shall not be considered as a manufacturer of mifepristone, and shall not be obliged to supply mifepristone to any person in any form, at any time.

e) The Council agrees that it shall not, and shall not permit any of its designees to sell or distribute mifepristone under an approved NDA, unless and until it has obtained a source of supply other than Roussel Uclaf.

f) An original copy of this letter signed by the parties will be submitted by the Council to the FDA.

Would you please confirm your agreement to the above by signing a copy of this letter, made in three originals, and returning it to us.

Sincerely yours,

ROUSSEL UCLAF

By .
Title .....President

Accepted by
THE POPULATION COUNCIL, Inc.

By .....
Title VP CORPORATE AFFAIRS
Date ...Oct...17, 1995

cc. : ——— Food and Drug Administration

BRIEF CLINICAL STUDY SUMMARY
Product: Mifepristone

Protocol EFR/91/486/14: Efficacy and Safety of Mifepristone (RU 486) at the Dose of 600 mg in a Single Administration in Combination with Misoprostol as an Alternative to Uterine Aspiration for Interruption of Pregnancies Aged Less Than or Equal to 49 Days Amenorrhea

1. Protocol Number: FFR/91/486/14 **2. Study Design:** Open label, multicenter study of a single administration of 600 mg of mifepristone in combination with misoprostol as an alternative to uterine aspiration for interruption of pregnancy. **3. Clinical Investigator:** Dr. E. Aubeny **4. Study Dates:** Start: June 1991 Completion: February 1992	**1. Age Range:** 14-39 (mean 25.8) years **2. Gestational Range:**: Calculated: 27-85 days (mean 45.1) Ultrasound: 24-55 days (mean 42.2) By ultrasound and calculation: 24-81 days (mean 42.6) **3. Patient Number:** Entered: 1286 Safety Evaluable: 1286 Efficacy Evaluable: 1205* Exposed to Study Drug: 1286 (1239 received mifepristone and misoprostol) **81 patients excluded from efficacy analysis for non-compliance with protocol* **4. Test Drug:** Mifepristone Dosage: 3 x 200 mg (600 mg) Formulation: 200 mg tablet Duration of Dosage: One day **5. Control Treatment:** None **6. Ancillary Drug:** Misoprostol Dosage: 2 x 0.2 mg (0.4 mg) Formulation: 0.2 mg tablet Duration of Dosage: One day Interval from Study Drug: 48 hours	**1. Outcome Variables:** Tolerance and Safety: •Occurrence of painful uterine contractions, gastrointestinal and other adverse events with severity and need for treatment. •Level of pain using a visual analog scale (VAS) assessed at the end of the four hour observation period. •Duration of uterine bleeding and need for any additional treatments and/or procedures to control bleeding. •Heart rate and blood pressure determined hourly before and after misoprostol. •Hemoglobin concentration and Rh status. Efficacy: •Evaluated by pelvic and ultrasound examinations and βHCG pregnancy tests. **2. Results:** Adverse Events: •1104 (86%) of all patients reported adverse events. •The most frequently reported were uterine pain (198 patients received treatment for painful uterine contractions), nausea, vomiting, diarrhea, headache and tiredness. •One patients required a blood transfusion and 5 patients required uterine evacuation. Tolerance and Safety: •Mean VAS score for uterine pain was 35.1 ± 0.76 (sem). •Mean duration of bleeding was 9.0 ± 0.12 (sem) days. •16% of the patients had an increase in blood pressure > 20% and 17 % of the patients had a decrease in blood pressure > 20%. •25 (2.3%) of patients had > 20% decrease in hemoglobin concentration. Efficacy: •Success rate for termination of pregnancy was 95.4%. •704 patients had complete expulsion within 4 hours after misoprostol.	**Status of Study:** **1. Study Classification:** Historically Controlled Studies - Mifepristone Plus Misoprostol **2. Location of CRF's:** **3. Status of Database:** SAS files on disk. **4. Status of Study Report:** Complete

Population Council
Center for Biomedical Research
1230 York Avenue
New York, NY 10021

Fax from Ann Robbins
Phone: 212-327-8748
Fax: 212-327-7678

Number of Pages (including this sheet):	5
Send to Facsimile Number:	[redacted]
Date:	9 February 1996
Send to Company:	FDA; Div. Metabolic & Endocrine Drug Products
Send to Person:	[redacted]
Subject:	Summary of NDA CMC status

Dear [redacted]

Thank you for your phone call yesterday. I'd like to summarize for you where things stand to date regarding the CMC section of the NDA.

1. Roussel submitted the CMC information directly to the FDA, as an amendment to the Population Council's mifepristone IND.

2. FDA reviewed the CMC section, and then, as per prior agreement with Roussel and the Population Council, sent Roussel a list of outstanding items on the section that need to be resolved before the CMC section could be accepted as complete. These issues must be resolved, in order to permit the Council to submit the NDA.

3. I received your phone call and fax of 26 January describing the response of Dr. [redacted] of Roussel to your list, which basically said the Population Council would have to handle all of these issues. I forwarded this information to the Population Council president, Margaret Catley-Carlson.

4. Ms. Catley-Carlson phoned Dr. Edouard Sakiz of Roussel on 29 January, and told him we were surprised by the content of Roussel's letter, as we are not in a position to answer the questions raised by the FDA since we do not have access to the CMC information. Dr. Sakiz agreed with this and promised to look into the situation.

5. Ms. Catley-Carlson also wrote an official letter to Dr. Sakiz, outlining the action needed from Roussel regarding the FDA list, which was faxed to Dr. Sakiz on 7 February. A copy of that letter is attached to this fax.

6. This week, Ms. Catley-Carlson phoned Dr. Sakiz to follow-up on this situation but Dr. Sakiz is on vacation. In his absence, she has spoken to ——— and today (9 February 1996), Ms. Catley-Carlson asked me to phone ——— directly, which I have done. ——— confirmed that Roussel is working on the CMC items outlined by the FDA. He hopes to be able to give us a written response and/or answer to all of these items by Wed. February 14. However, he wanted to alert the Council to two important points: a) he does not believe that Roussel has enough information to write a complete Environmental Assessment and believes we may need to seek an exemption or at least determine if an abbreviated EA can be submitted and b) Roussel does not have enough active drug substance from the batch used to produce the drug product we have in-house to provide the samples required for the methods validation section. He suggested we discuss with the FDA the possibility of submitting active substance from a different batch, one that does not correspond to the batch used to produce the tablets we have.

7. ——— called Ms. Catley-Carlson this week to inquire about the status of the NDA. Ms. Catley-Carlson explained that we are waiting on several things, some of which are slow responses from Roussel and perhaps ———, could help. ——— indicated she would get more details on the situation.

This is where things stand as of today. I will keep you posted on the progress of this situation, as we are all quite anxious to have this situation resolved so we can proceed with the submission.

Best regards,

Ann Robbins

Ann Robbins, Ph.D.
Scientist

cc: M. Catley-Carlson (fax: 212-755-6052)
J. Boynton (fax: 212-632-5555)
E. Sakiz (fax: 011-33-1-4991-4490)
——— (fax: 011-33-1-4991-4048)

APPEARS THIS WAY
ON ORIGINAL

The Population Council

One Dag

Margaret Catley-Carlson
President

by fax: 33 14 991 4490 (three pages)

February 7.

Dr. Edouard Sakiz
Roussel Uclaf
102, route de Noisy
93235 Romainville Cedex - France

Dear Edouard:

Thank you for the letter from ——— I did not have it in hand when last we spoke. We are glad to have some movement on that issue.

As we discussed last Monday, we were very distressed when we received from the FDA a copy of ——— letter of January 26, 1996. He was responding to ——— inquiries concerning the CMC section submitted by Roussel under the NDA for mifepristone. Consequently, I was delighted to learn from ——— earlier this week that work is underway on the various responses.

As a preliminary matter, let me first reiterate as we did by signing the letters pertaining to the FDA which were submitted to us by Roussel last fall that we completely understand that Roussel is not and will not be the manufacturer of the drug substance or the drug product for the US market. If Roussel needs a similar assurance from the US Government, please let us know and we will see what we can do.

Subsequent to my conversation with you last week, we have carefully reviewed the items covered in ——— Memorandum of Internal Meeting to determine which require Roussel's further cooperation and which can be handled by the Population Council. Our view is as follows:

(1) The Environmental Assessment is specific to the facility in which the drug product used in the French and American trials was manufactured and thus must be completed by Roussel since only Roussel possesses the requisite information concerning the facility (and we assume that that information is confidential.)

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

(2) The Population Council is submitting proposed labelling as part of the NDA and has so informed the FDA. Nothing is required from Roussel with regard to this item, and we have assumed that Roussel does not wish to review the proposed labelling.

(3) This query requires in response only a simple letter from Roussel confirming that the formulation of the substance used in the French and American trials is the same as that described in the CMC section as submitted. A letter requesting this confirmation was sent to Dr. Remi Peyron on January 26th.

(4) The method validation packages must be prepared by Roussel because they must tie into the CMC section. However, we have prepared the binders in which this information can be incorporated into the NDA, and are ready to forward these to Roussel at any time so you can submit this information directly to the FDA. These packages must include drug samples of the kind described in Ann Robbins' letter of January 30th to ——— and must also include drug reference standards. We have assumed that these materials would be submitted to the FDA upon their request via the Population Council as specified in our correspondence last fall. Thus, we must have those samples in-house prior to submission.

(5) This query requires in response a simple statement that Roussel will cooperate with the FDA by permitting required facility inspections.

(6) We believe that what the FDA needs in regard to the starting material is a simple reference to a Roussel Drug Master File for the precursor. Only Roussel is in a position to provide this information whether directly or via the Population Council.

(7) The response to the seventh query could take the form of a statement from Roussel addressed either directly to the FDA or the Population Council to the effect that it will use its best efforts to respond to further inquiries. So far as we are aware, the FDA has no other questions in mind.

As the foregoing indicates and as I mentioned in our discussion last week, each of ——— questions other than item 2 pertaining to labeling requires some further cooperation from Roussel. We do not care whether that cooperation takes the form of a supplemental submission to the FDA under the IND directly by Roussel or incorporation of information and certifications provided by Roussel into the Population Council's NDA. Whatever form it takes we need it urgently to prevent further delay in the filing of the NDA which is otherwise ready to be filed.

We have come a long way in this project at great risk to the Population Council. We signed, as of the end of last year, a license agreement with a distribution organization which is now also participating in those risks. All of these actions have been predicated on continued cooperation which we know from experience we can expect from Roussel. Please call me after you have had a chance to review this letter so that we can verify that we have the same view of what needs to be provided and by whom.

All best regards to you and Catherine.

Yours sincerely,

Margaret Catley-Carlson

cc: _____ (fax: 33 1 49 91 31 19)
_____ (fax: 33 1 49 91 40 48)

APPEARS THIS WAY
ON ORIGINAL