Electronic Mail Message

Date: 7/31/00 12:14:26 PM
From: [redacted]
Subject: BCC:URGENT!! Mifepristone Update

Electronic Mail Message

Date: 7/28/00 12:21:39 PM
From: [redacted]
Subject: Consult on mifepristone

Hi [redacted]

Here is the document that I have completed for above consult. The document is also saved under the folder [redacted]. The file name is [redacted]

I left 8 copies of signed signature pages in your office.

I want to thank you for your guidance and support. I will get more feedback from you and [redacted] after I return from China on August 20th.

Printed by

Electronic Mail Message

Sensitivity: COMPANY CONFIDENTIAL

Date: 27-Jul-2000 03:18pm.
From:

Dept: HFD-103 PKLN 13B45
Tel No:

TO: See Below
Subject: Mifepristone briefing for Dr. Henney post-industry meeting 8/4

I got a call from _____ that Dr. Henney would like an update the week of Aug 7th, which is after our industry meeting with Pop Council on 8/4.

Be prepared to see this on our calenders.

Distribution:

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Electronic Mail Message

Date: 7/25/00 2:28:08 PM
From: [redacted]
Subject: Epidemiologist for mifepristone

Hi, [redacted]

As we approach possible approval of Mifepristone (action date 9/30/00, we need to establish a relationship with an epidemiologist who will help review the phase 4 epi studies' results (your division was given a consult about the sponsor's proposals for phase 4 studies a few weeks back) and to help oversee the AEs with this drug. We expect there to be quite a lot of scrutiny on how well are we doing surveillance. Therefore, I'd like to discuss with you what skills from an epi person we'd need.

Once we get past an industry meeting and a manufacturing inspection, we will be in contact with you in mid August if the action is looking like approval. THis is just a heads up on needing to continue to collaborate on this drug. Speak to you soon. Thanks.

[redacted]

Electronic Mail Message

Date: 7/25/00 3:49:09 PM
From: [redacted]
Subject: FWD: Epidemiologist for mifepristone

FYI

Electronic Mail Message

Date: 7/18/00 10:03:44 AM
From:
To:
Subject: FWD: American Citizen Comments on RU 486..It should be distributed

Another RU-486 e mail.

f.c
RV488

Printed by [redacted]

Electronic Mail Message

Sensitivity: COMPANY CONFIDENTIAL

Date: 18-Jul-2000 11:02am
From: [redacted]

Dept: HFD-001 WOC2 6027
Tel No: [redacted]

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

Subject: Re: FWD: Drug listing information for Danco and the Chinese manuf

I understand Dr. Henney plans to meet again with us this Friday and we can explain it to her then. [redacted]

Printed by

Electronic Mail Message

Sensitivity: COMPANY CONFIDENTIAL

Date: 17-Jul-2000 11:37am
From:

Dept: HFD-103 PKLN 13B45
Tel No:

TO:
TO:
TO:

CC:
CC:
Subject: FWD: Drug listing information for Danco and the Chinese manuf

We have the information the Commissioner sought:

1) Shanghai Hualian Pharmaceuticals is It lists a variety of hormonal products.

2) We've inspected it and it passed. It does not list other drugs.

3) Danco is the distributor. They are working with others on training materials. They do not list any other drugs they distribute.

Please forward to the Commissioner, if needed. Thanks.

Electronic Mail Message

Date: 7/17/00 9:49:09 AM
From:
To:
Subject: FWD: RU486

Another RU-486 e mail.

Electronic Mail Message

Date: 7/14/00 10:53:28 AM
From:
To:
Subject: FWD: Mifepristone

Another RU-486 e mail.

Electronic Mail Message

Date: 7/14/00 1:27:43 PM
From:
To:
Subject: FWD: RU-486

Another RU-486 e mail. This is the first I received against approval.

Printed by [redacted]

Electronic Mail Message

Date: 17-Jul-2000 11:23am
From: [redacted]
Dept: HFD-580 PKLN 17B45
Tel No: [redacted]

Subject: Drug listing information for Danco and the Chinese manufact. site

Hi [redacted]

We have the following information re. Danco and the Chinese site. [redacted] was the source of this drug listing information. Do we need any additional followup or information that you can think of for background?

Danco - This firm is registered (LC 064875; CFN NY51309).
The address is
They have no products listed.

Shanghai Hualian Pharmaceutical
201419
Shanghai, China
(Note: We believe this firm has previously registered and listed...)

There is a firm "Shanghai Hualian Pharmaceutical Co, Ltd." registered in the data base (LC 064163; CFN FCCH442). With a Compliance Address: Jiang Wan Rd West, Shangai 200083 China. They have multiple listin

[redacted]

Let me know if you need/want more info on any of the above.

Printed by

Electronic Mail Message

Sensitivity: COMPANY CONFIDENTIAL

Date: 13-Jul-2000 03:30pm
From:
Dept: [illegible] PKLN 13B45
Tel No:

TO: See Below
Subject: Revised table for mifepristone

Attached is the revised table (from the discussion yesterday- 7/12) listing the "Issues for Discussion" on the labeling and distribution program for mifepristone.

Distribution:

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Electronic Mail Message

Date: 7/13/00 4:46:47 PM
From: [redacted]
To: See Below
Subject: FWD: use of mifepristone in France

Printed by

Electronic Mail Message

Date: 13-Jul-2000 08:19pm
From: [redacted]
Dept: HFD-103 PKLN 13B45
Tel No: [redacted]

TO: EUDRA - EUDRAWATCH (fr-h.eudrawatch@fr-h.eudra.org)

Subject: RE: use of mifepristone in France

Dr. [redacted]

Thank you for this information. I need one clarification:

Must the physicians who are authorized to prescirbe mifepristone also be authorized to perform surgical abortions?

Or, can the prescribing physician not have the ability to due surgical abortion and refer patients who need this procedure to other doctors who can perform surgical intervention?

In the US we are trying to decide on what skills the prescribing physician should have.

Your continued assistance is immensely appreciated.

[redacted]

Electronic Mail Message

Date: 7/13/00 11:50:42 AM
From: EUDRA - EUDRAWATCH (fr-h.eudrawatch@fr-h.eudra.org)
Subject: use of mifepristone in France

Dear [redacted]

Sorry to get back to you so late.

In France only physicians are authorized to prescribe mifepristone. However the tablet can be administrated to patient by nurses.

Only physicians are authorized to handle surgical abortions.They are either gynecologists, obstetricians or they have followed a particular training in pregnancy termination

The patients have to return for the second visit to receive the prostaglandin agent 2 days later. Following its administration, the patient need has to stay at the center to be monitored for 3 hours.

A third visit is required 10 to 12 days after to confirm expulsion in all cases of elective termination.

I called the biggest mifepristone user center in France, located at Broussais Hospital to get more informations about women who do not return at the center for the second visit. Their non-return rate is zero . They told me that the 3rd visit is not automatically necessary because most of patients have expulsion quickly after taking prostaglandin agent.

I hope that these informations answer your questions.

Best regards

[redacted]

Printed by

Electronic Mail Message

Date: 13-Jul-2000 11:50am
From: EUDRA - EUDRAWATCH
fr-h.eudrawatch@fr-h.eudra.org
Dept:
Tel No:

TO:

CC:
Subject: use of mifepristone in France

Dear

Sorry to get back to you so late.

In France only physicians are authorized to prescribe mifepristone. However the tablet can be administrated to patient by nurses.

Only physicians are authorized to handle surgical abortions.They are either gynecologists, obstetricians or they have followed a particular training in pregnancy termination

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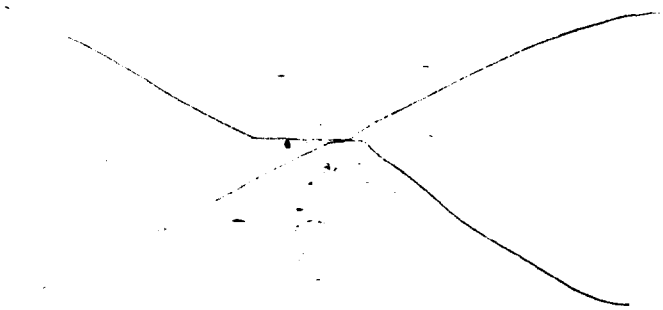
I hope that these informations answer your questions.

Best regards



<P>Dear [redacted]
<P>Sorry to get back to you so late.</P>
<P>In France only physicians are authorized to prescribe mifepristone. However the tablet can be administrated to patient by nurses.</P>
<P>Only physicians are authorized to handle surgical abortions.They are either gynecologists, obstetricians or they have followed a particular training in pregnancy termination</P>
<P>The patients have to return for the second visit to receive the prostaglandin agent 2 days later. Following its administration, the patient need has to stay at the center to be monitored for 3 hours.</P>
<P>A third visit is required 10 to 12 days after to confirm expulsion in all cases of elective termination.</P>
<P>I called the biggest mifepristone user center in France, located at Broussais Hospital to get more informations about women who do not return at the center for the second visit. Their non-return rate is zero . They told me that the 3rd visit is not automatically necessary because most of patients have expulsion quickly after taking prostaglandin agent.</P>
<P>I hope that these informations answer your questions.</P>
<P>Best regards</P>
<P><FONT color=#000000 face="Times New Roman">[redacted] of the Pharmacovigilance Unit</FONT></P></DIV></BODY></HTML>

Printed by

Electronic Mail Message

Sensitivity: COMPANY CONFIDENTIAL

Date: 07-Jul-2000 06:08pm
From:

Dept: HFD-103 PKLN 13B45
Tel No:

TO: See Below
Subject: Re: Golden Rod for Update on RU 486

Thanks for you help on this!

Distribution:

TO:

CC:
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CC:

Printed by [redacted]

Electronic Mail Message

Sensitivity: COMPANY CONFIDENTIAL

Date: 06-Jul-2000 04:11pm
From: [redacted]
Dept: HFD-103
Tel No: [redacted] 13B45

TO: [redacted]
TO:

CC:
CC:
CC:

Subject: Need for chemistry update on mifepristone

[redacted]

[redacted] d Dr. Henney would like an update about the chemistry manaufacturing issues with this drug. I know that Pop Council has submitted their response to manufacturing issues (did you get it? if not, see [redacted]. Please review and then write an email which I will incorporate into an updated document for the Drs. They are interested in issues dealing with approvability. I will need this paragraph (not a long email) by Monday if possible so I can forward the entire update document to [redacted] for processing to Dr. Henney. Thanks.

[redacted]

RU 486
Friday, October 8, 1999
PkIn 13B45

Agenda

1. Confidentiality
   - manufacturer's name
   - reviewers' names

2. Subpart H approval, consideration for restricted distribution
3. Cross labeling with Cytotec
4. How are we responding to (June 21, 1999) meeting request?
5. Other items

Printed by [redacted]

Electronic Mail Message

Sensitivity: COMPANY CONFIDENTIAL

Date: 21-Jun-2000 02:25pm
From: [redacted]

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

TO: [redacted]
TO. [redacted]

Subject: mife- confirming information

I'm not sure which source [redacted] used to get the information on state abortion law. However, [redacted] at the National Abortion Federation was very helpful. the law in Kentucky allows for first trimester abortion only by a physician or by the woman upon herself upon the advice of a licensed physician.

I also asked about the law for DC-- only under supervision of a licensed physician or no supervision. [redacted] said that the laws and issues concerning mid-level providers is a bit complicated. She is putting together a summary list for us on the mid-level provider issue by state. She said she could have this to us by COB tomorrow. I gave her [redacted] name and phone number since I will not be here tomorrow.

[redacted]

Printed by [redacted]

Electronic Mail Message

Sensitivity: COMPANY CONFIDENTIAL

Date: 07-Jun-2000 01:08pm
From: [redacted]

Dept: HRD-580
Tel No: PKLN 17B45

TO: [redacted]

CC: [redacted]
CC: [redacted]
Subject: Info from the EUropean labeling

Hi [redacted]

[redacted]

1. Under the Summary of Product Characteristics, page 1 No. 4 Clinical Particulars, there is a box that includes the following paragraph: "...As a consequence, they can only be prescribed by a medical doctor and in public or private hospital or centre (having approval to undertake termination of pregnancy). The product will be administered in the presence of the medical practitioner or of a delegated health professional."

The same box is included in the Patient Information Leaflet, page 3, b) under Special Warnings.

[redacted]

2. Section 4.4, No 1, Page 3:
"This method requires an active involvement of the woman who should be informed of the method's requirements:
- the necessity to combine treatment with prostaglandin to be administered at a second visit,
- the need for a control visit (3rd visit) within 10 to 14 days after MIFEGYNE's intake in order to check for complete expulsion,
- The possible failure of the method, leading to a pregnancy termination by another method."

This information is ~~also~~ included in a box under Special Warnings, No 1) on page 4 of the Patient Information Leaflet.

Also in Precautions for use, No. 2, Method of prostaglandin administration on page 6, "During intake and for three hours following the intake, the patients should be monitored in the treatment centre, which must be equipped with the appropriate equipment."

[redacted]

3.) In the Summary of Product Characteristics, page 4, under Risks related to the method; Bleeding: "The patient should be informed not to travel far away from the prescribing centre as long as expulsion has not been recorded. She will receive precise instructions as to whom she should contact and where to go in the event of any problems emerging, particularly in the case of very heavy vaginal bleeding." This is also emphasized in the Patient Information Leaflet, page 4 under Risks related to the method; Bleeding, 3rd paragraph.

4.)In the Summary of Product Characteristics, page 6, Section 4.6 Pregnancy and Lactation, 3rd paragraph, it states "In humans, the few reported cases of malformations do not allow a causality assessment for mifepristone alone or associated to prostaglandin. Therefore, data is too limited to determine whether the molecule is a human teratogen."

"Consequently:
- Women should be informed, that due to the risk of failure of the medical method of pregnancy termination and to the unknown risk to the foetus, the control visit is mandatory.
- Should a failure of the method be diagnosed at the control visit (viable ongoing pregnancy), and should the patient still agree, pregnancy termination should be completed by another method.
- Should the patient wish to continue with her pregnancy, the available data is too limited to justify a systematic termination of an exposed pregnancy. In that event, a careful ultra-sonographic monitoring of the pregnancy will be established."

Section 5.3 Preclinical safety data on page 9 also states that no teratogenic effect of mifepristone was observed in rats and mice surviving fetal exposure. In rabbits, isolated cases of severe abnormalities occurred (cranial vault, brain and spinal cord). The number of fetal anomalies was not statistically significant and no dose-effect was observed. In monkeys, the number of fetuses surviving the abortifacient action of mifepristone was insufficient for a conclusive assessment.

In the Patient Information Leaflet, page 5, 3) In any Case:

"It is possible for you to become pregnant again immediately after the termination is complete so you will need to start contraception as early as possible after taking the MIFEGYNE tablets. You should not be pregnant in the menstrual cycle following treatment."

Also, page 6 e) Pregnancy - Lactation, 4th paragraph: "The risks to the fetus in case of an ongoing pregnancy are unknown. Should you change your mind and wish to continue your pregnancy, ask your doctor. You would be proposed prenatal care with repeated ultrasonographies."

Thanks,

Printed by

Electronic Mail Message

Sensitivity: COMPANY CONFIDENTIAL

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

Dept: HFD-580 PKLN 17B30
Tel No:

TO:

CC:

Subject: Data from Current Literature Reporting Births of Children Exposed to Mifepristone and Misoprostol

Hi

I have been unable to find any current literature reporting births of children exposed to the mifepristone-misoprostol regimen. There is one letter to the editor (The Lancet; Vol. 352; July 25, 1998; p. 323) from Exelgyn SA in which they mention that they had reviewed 71 cases of continuing pregnancy after failed early termination of pregnancy occurring between 1987 and 1998 and found no reported cases of malformation associated with use of misoprostol when used with mifepristone. There was one report of sirenomelia and cleft palate in a patient who had a therapeutic termination of pregnancy at 7 weeks gestation associated with the use of mifepristone alone. This report was already known to us.

Safety Update Report # 3 submitted to the NDA March 31, 2000 contains Exelgyn Laboratories Periodic Safety Update Report # 9 for the period September 1, 1998 - November 30, 1999. This report contains an updated listing of ongoing pregnancies from 1987 to 1999. It lists the 38 ongoing pregnancies with mifepristone alone and the 36 ongoing pregnancies with mifepristone plus misoprostol which are mentioned in the draft labeling.

The European Summary of Product Characteristics dated July 6, 1999 for mifepristone contains the statement that in humans, the few reported cases of malformations do not allow a causality assessment for mifepristone alone or associated to prostaglandin. Therefore, data is too limited to determine whether the molecule is a human teratogen. It also states that should the patient wish to continue with her pregnancy, the available data is too limited to justify a systematic termination of an exposed pregnancy. In that event, a careful ultrasonographic monitoring of the pregnancy will be established.

Electronic Mail Message

Date: 10/4/00 6:49:52 AM
From:
To:
Subject: FWD: My comments re: misoprostol and gyn AEs

Sorry to bother you again, but I need your help. We have a letter from Representative Coburn re misoprostol and safety concerns when used with mifepristone. suggested address the exploding uteruses and deaths associated with misoprostol. has addressed this issue but suggested that comments be solicted from the division.

Please see her attached cover memo and the draft response to Representative Coburn.

Thanks for your help

Electronic Mail Message

Date: 10/4/00 5:38:22 PM
From:
To: See Below
Subject: Re: FWD: Mifeprex and commercial availability for oncology indications

Right. Drug's availability under IND's should remain unchanged!

To:
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Cc:
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Cc:

Electronic Mail Message

Date: 6/8/00 10:07:51 AM
From: [redacted]
Subject: Re: Telecon with Pop Council

Thanks, [redacted]

[redacted]

> -----Original Message-----
> [redacted]
>
> Sent: Wednesday, June 07, 2000 4:59 PM
> To: [redacted]
> Cc: [redacted]
>
> Subject: Telecon with Pop Council
> Sensitivity: Confidential
>
> I talked with the Pop Council today at 4:30pm. Sandy Arnold,
> and Nancy Buc were on the phone.
>
> They stated they did not interpret FDA was proposing a national public
> registry for physicians but that this idea must have been a
> misinterpretation on the part of others. I asked if they would consider
> correcting this misinterpretation and they said they would get back to
> me on this on Thursday or Friday.
>
> I further discussed the need for serious and candid discussions to move
> forward on the label and the distribution system and obtain agreement.
> I stated having proposals floated in the media will only serve to delay
> the process. They all assured me that this is what they want too.
> However, Ms. Buc did state we should expect that the pro-choice community
> continue to be highly engaged and they frequently use their first
> amendment rights. [redacted]
>
>
>
> We await their response to our proposals for the distribution system,
> due to us June 23.
>
> [redacted]
>
>
>
>
>

Electronic Mail Message

Date: 9/28/00 6:51:01 AM
From:
To:
To:
To:
Subject: FWD: Last minute Labeling Change for Ru 486!

I think there is a typo in — memo. The second sentence says the applications was initially submitted on Marach 14, 1966. Should that be 1996?

Electronic Mail Message

Date: 9/28/00 11:05:00 AM
From: [redacted]
To: See Below
Subject: Here's the Intro Text

The Food and Drug Administration has approved mifepristone (trade name Mifeprex) for the termination of early pregnancy, defined as 49 days or less, counting from the beginning of the last menstrual period. There is also an approved treatment regimen that stresses the importance of adherence to the regimen.

Mifepristone, which was developed by a French pharmaceutical firm, was first approved for use in France in 1988. Since then, the drug has also been approved in the United Kingdom, Sweden, and other countries. The approval of mifepristone in the U. S. is the result of the FDAs careful evaluation of the scientific evidence related to the safe and effective use of this drug, according to the Commissioner of Food and Drugs, and adheres "strictly to our legal mandate and mission as a science-based public health regulatory agency."

Electronic Mail Message

Date: 9/28/00 11:03:00 AM
From: [redacted]
To: See Below
Subject: FWD: Please look at Web Page Intro, etc.

Sorry, the address once again is http://internet-dev/cder/drug/infopage/mifepristone/default.htm

[redacted]

Electronic Mail Message

Date: 9/28/00 11:02:00 AM
From: [redacted]
Subject: Please look at Web Page Intro, etc.

Could you please look at the intro on the draft web page and see if you're okay with that?

From:
Sent: Thursday, September 28, 2000 9:38 AM
To:

this is the guts of what will be sending out today...it includes the telephone numbers.

This is to let you know that FDA has just announced the approval of the drug, MIFEPREX (mifepristone), for terminating a pregnancy in the early stages (49 days or less since last menstrual period began). I have attached a copy of the press release for your information.

Agency staff have agreed on a comprehensive roll out strategy to communicate with all of our external audiences about this approval. If you or your staff receive inquiries, you may direct them to FDA's website, http://www.fda.gov/cder/drug/infopage/mifepristone, or refer them to the designated contact below. The website contains the FDA press release, approval letter, package insert, medguide and other information on mifepristone. Please do not answer calls or emails directly.

Calls From:	Refer To:	
Health Professionals/Consumers	OTCOM	301-827-4570
Press/Trade Press		301-827-6250
		301-827-6248
Members of Congress/Staff		301-827-0087
Other gov't agencies/officials	FDA Exec Sec	301-827-4450

E-Mails should be forwarded to: druginfo@cder.fda.gov

Electronic Mail Message

Date: 9/27/00 1:35:33 PM
From: FDA.GOV)
Subject: Script folks may use re: RU 486 telephone calls

This is a script FDA staff, e.g., in the OC and in the ombudsman office may use when answering phone calls re: RU 486. This incorporates comments from as reviewed the script. Let me know if you think of additional questions.

n the spring of this year, the ombudsman office got many calls on RU 486 because their name appeared in a Christian Coalition pub - I've prepared them just in case their name is still out there.)

A: Office of the Commissioner

Caller: What is your name...who are you?

A: (You may give your office name and you may withhold your name, if you'd like.)

Caller: I'm calling about (mifepristone, mifeprex, misoprostle, RU 486, the Population (POP) Council drug approval, the abortion pill, etc.)

A: Hold on while I transfer you to the FDA people who are answering these calls...if you accidentally get cut off, I'm transferring you to 301-827-4570 (or you may transfer the call to 888-infoFDA) - (10:30 call (on Wed.)from .ating they WILL staff the 888 number). (If they identify themselves as congressional staff, transfer them to 301-827-0087 or if they are other gov't officials, transfer them to FDA exec sec at 301-827-4450.)

Caller: I don't want to be transferred (or I've already been transferred and the line is busy)...I want to talk with you or someone at this number.

A: I'm sorry, but all calls on this subject are being handled by one group of people. I'll be happy to take your name and number and forward it to the appropriate office. Or, you may write to the agency. (see addresses below.)

Caller: Who can I write to?

A: email: druginfo@cder.fda.gov

address: FDA
5600 Fishers Lane
OTCOM/CDER, HFD-200
Rockville, Md. 20857

fax: 301-827-4577

Printed by [redacted]

Electronic Mail Message

Sensitivity: COMPANY CONFIDENTIAL

Date: 25-Sep-2000 11:28am
From: [redacted]

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

TO: See Below
Subject: "Security Briefing"

For anyone interested in attending:

There will be a "Security Briefing" held tomorrow, September 26, 2000 at 10:30 am in Parklawn, CR "M" on the 3rd floor.

The purpose of this meeting is to discuss/clarify the appropriate steps to take for issues related to the upcoming mifepristone action.

If you have any questions, please see me.

[redacted]

Distribution:

Caller: Is this the Commissioner's office?

A: This is the Office of the Commissioner

Caller: I would like to leave a message for the Commissioner on this subject.

A: Sure, let me transfer you to a phone where you can leave a message (and then transfer to OTCOM - the 827 or 888 number above.)

Caller: How can I get more information on this topic?

A: The internet site is: http://www.fda.gov/cder/drug/infopage/mifepristone

Caller: (begins to cuss, say inappropriate things)

A: I'm sorry but I'm going to have to end this conversation.

Caller: (threatens the building, people, or the Commissioner)

A: (refer to security email/security procedures)

Caller: What do you think about the abortion pill...what is your opinion on FDA's action.

A: I'm sorry, but it is not appropriate for me to answer that question. If you'd like to comment or ask questions, call 301-827-4570 or 888-infofda (or refer them to the internet site.)

Electronic Mail Message

Date: 9/25/00 4:32:45 PM
From:
To:
To:
Cc:
Subject: RU label on teratogenicity

Nancy asked we change the wording from [redacted] to "...defects all have been reported after exposure during the first trimester." I agreed that is was fine. She now will check with both her clients on this.

I asked her to agree to final protocols for phase 4 in 6 months; she asked [redacted] months. I told her that the final in 6 months could be amended if [redacted] onths there is a problem (she anticipates the biggest unknown is the numbers of referring providers and only time will tell on their enrollment into the distribution system). I told her that this could be discussed and amended if it came up. She will get back to us on the timing of final phase 4.

Electronic Mail Message

Date: 9/21/00 9:23:36 AM
From: [redacted] (LIZ)
Subject: FWD: OPDRA consults on RU 486

I will bring copies of the revised consults (2nd review and addendum to 1st review) for your signature soon (with [redacted] name on it). However I am not sure if the electronic version of my first consult (1st review) in my computer is the most current one and I need to check with [redacted] on Monday. Some one needs to take care of the consult on name of the product. [redacted]

Electronic Mail Message

Date: 9/21/00 9:23:36 AM
From: [redacted]
To: [redacted]
To: [redacted]
Cc: [redacted]
Cc: [redacted]
Subject: FWD: OPDRA consults on RU 486

I will bring copies of the revised consults (2nd review and addendum to 1st review) for your signature soon (with [redacted] name on it). However I am not sure if the electronic version of my first consult (1st review) in my computer is the most current one and I need to check with [redacted] on Monday. Some one needs to take care of the consult on name of the product. [redacted]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

May 22, 1996

The Honorable Dan Coats
United States Senate
Washington, D.C. 20510

Dear Senator Coats:

This is in response to your letters of April 11, 1996 to Secretary Shalala and me in which you expressed concern for the public safety and the integrity of the drug approval process in relation to the future availability of mifepristone (RU-486) as an abortifacient in the United States. I want to assure you that neither the safety of the American public nor the integrity of the new drug approval process will be put in jeopardy by the Food and Drug Administration's (FDA's) actions.

As you may know, early in this Administration, the Secretary of Health and Human Services was directed by the President to promote the testing, licensing, and manufacturing in the United States of RU-486 and to direct the FDA to reassess whether RU-486 qualifies for FDA's personal use importation exemption. In response to that directive, FDA has been encouraging and facilitating the submission of a new drug application because we firmly believe that if a safe and effective medical alternative to any surgical procedure is available, American women should have access to that drug regimen. It is not unusual for FDA to encourage the development of new products for diseases and conditions for which there is an inadequate medical armamentarium, and if found to be safe and effective in accordance with established statutory and regulatory standards, to speed their availability to the American public. However, FDA's primary concern is public health and safety, and definitive conclusions about a drug's safety or effectiveness cannot be determined without first reviewing the studies and other data that would be submitted in a new drug application. Also, because of our concerns regarding the health and safety of American women, the import alert on mifepristone remains in effect and importation of the drug under the agency's personal use import policy is not appropriate.

In order to be marketed in this country, a new drug product must, according to law, be shown by substantial evidence to be safe and effective for its labeled use. The manufacturer or sponsor of the drug has the responsibility for conducting studies on which safety and effectiveness is based and submitting these data to FDA in the form of a new drug application. FDA's role is to review the data submitted and then make a determination as to whether a product is safe and effective for its intended use.

As you may know, the Population Council recently announced that it had submitted to FDA a new drug application for mifepristone for use in the termination of pregnancy. You have my assurance that that application is being reviewed in accordance with the same stringent scientific and legal standards as any other application that is submitted to the agency.

Thank you for your interest and concern.

Sincerely,

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

APPEARS THIS WAY
ON ORIGINAL

DAN COATS
INDIANA

404 RUSSELL SENATE OFFICE BUILDING
(202) 224-5623

INDIANAPOLIS OFFICE
1180 MARKET TOWER, 10 WEST MARKET STREET
INDIANAPOLIS, IN 46204
(317) 226-5555

United States Senate

WASHINGTON, DC 20510

COMMITTEES:
ARMED SERVICES
LABOR AND HUMAN RESOURCES

April 11, 1996

SPECIAL

The Honorable Donna E. Shalala
Secretary
Department of Health and Human Services
200 Independence Avenue, Southwest
Washington, D.C. 20201

Dear Secretary Shalala:

As chairman of the Senate Committee on Labor and Human Resources Subcommittee on Children and Families, I request copies of documents in the possession of the Food and Drug Administration, including any of its advisory committees, relating to the drug known as RU 486 (mifepristone), developed by the company Roussel Uclaf SA.

I understand that the Population Council has an active investigational new drug application (IND) to use RU 486 for abortion. Several reports indicate extensive communications between representatives of the Clinton administration and private companies and organizations, including the Population Council, concerning the future availability of RU 486 for use as an abortion pill in the United States. These reports, together with issues raised in a Citizens' Petition on RU 486 submitted last year to the FDA, have generated serious concern for public safety and the integrity of the drug approval process. Consequently, I request that you provide the following information:

(1) Any and all written or recorded communications, including electronic or telephonic communications, involving one or more of the persons listed below and relating to RU 486 from January 1, 1992, up to the present (i.e., up until the time the document search is conducted).

When used in the above request, the word "communication" includes, but is not limited to: correspondence, electronic mail, memoranda, notes of conversations, calendars, notes of meetings (including the agenda, the list of those in attendance and the time, date and location of each meeting), telephone logs, message slips, and the travel logs of administration employees. It also includes all communications that do not specifically mention RU 486 but that may relate to its possible approval by FDA for use as an abortifacient (e.g., communications relating to the acceptability of foreign data in the drug approval process, communications with drug companies that produce a prostaglandin that is or could be used in conjunction with RU 486, etc.).

For each such communication, please indicate the date of the communication. the names and the professional or organization affiliations of all persons involved or present. and the offices within the FDA from which the communications were obtained. Also, please indicate which communications, if any, are confidential and may not be disclosed to the public.

This request includes all communications involving the following persons from January 1, 1992, up to the present:

President Clinton, Mrs. Clinton, and White House staff
Other administration officials or personnel, including yourself, _____, _____ and _____ of the Endocrine Drugs Division of the FDA
Edouard Sakiz, Dr. Andre Ulmann, and other officers, employees, or representatives of Roussel Uclaf
Margaret Catley-Carlson, Dr. Wayne Bardin, and other officers, employees. and representatives of the Population Council
David A. Grimes, M.D.
Daniel R. Mishell, M.D.
Suzanne Poppema, M.D.
Officers, employees and representatives of the following companies and organizations:
- Hoechst AG of Germany
- Hoechst Celanese Corporation
- Hoechst-Roussel Pharmaceuticals
- Rhone-Poulenc of France
- Schering AG of Germany
- G.D. Searle Company
- Upjohn Company
- Gynopharma, Inc.
- Cabot Medical Corporation
- Aurora Medical Services
- Fund for the Feminist Majority
- Planned Parenthood Federation of America
- Reproductive Health Technologies Project
- National Abortion Federation
- National Abortion and Reproductive Rights Action League (formerly the National Abortion Rights Action League)
- Oregon Science Health University of Portland, Oregon
- Center for Reproductive Law and Policy
- National Organization for Women
- Women's Issues Network

(2) Any and all documents relating to the implementation of President Clinton's January 22, 1993, memorandum for the Secretary of Health and Human Services regarding the importation of RU 486.

In this memorandum, the President asked the Secretary to take the following three actions:

a) "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" ;

b) " immediately take steps to rescind Import Alert 66-47" if the "FDA concludes that RU 486 meets the criteria for the personal use importation exemption"; and

c) "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 and other antiprogestins."

When used in the above request, the word "document" includes, but is not limited to: internal and external documents of the Food and Drug Administration, documents prepared by persons or offices outside the FDA (including documents prepared by non-governmental persons, organizations, or companies), correspondence, electronic mail, memoranda, notes of conversations, calendars, notes of meetings (including the agenda, the list of those in attendance and the time, date and location of each meeting), and telephone logs, message slips, and travel logs of administration employees. It also includes all documents that do not specifically mention RU 486 but which may relate to its possible approval by FDA for use as an abortifacient (e.g., criteria for the acceptance of foreign data, the use of a prostaglandin with RU 486, etc.). For each such document, please indicate the date of the document, the author or authors of the document, the persons to whom it was given or sent, and the offices within the Department from which the documents were obtained. Please separate the documents in this second request into three categories based on which of the three actions requested by the President the documents address. Again, please indicate which communications, if any, are confidential and may not be disclosed to the public.

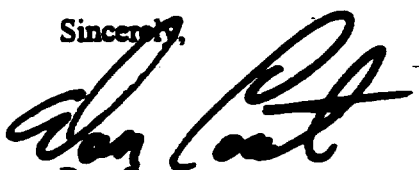
With respect to both requests (1) and (2) above, I ask that the information provided be complete, and that you not withhold documents or excise portions of documents on grounds of relevancy. If you assert executive privilege as to any document, please identify each one by providing the following information: the type of document and a summary of its contents; the date, author(s), and recipient(s) of document, the basis for withholding it from Congress, and an explanation if that basis was asserted on any document(s) in the 103rd Congress.

Please inform me if any communications (particularly, but not exclusively, e-mails) have been destroyed and the policy of the FDA on the destruction of e-mail messages. I request that every person involved in filling this requests, be asked if he or she has had e-mail messages related to RU 486 that have been destroyed and, if so, to provide a description of the subjects of those messages.

Finally, I wish to know the process used to comply with this letter, and to receive copies of all communications (memos, electronic mail, letters, etc.) produced in furtherance of filling this request for documents.

Thank you for your attention to this inquiry. I look forward to receiving the information by May 15, 1996. If you foresee any difficulty in fulfilling this request by that date, please notify me immediately. Vince Ventimiglia of my staff will be available to work with you if you have any questions. He can be reached at 202-224-1133.

Sincerely,



Dan Coats
U.S. Senator

SPECIAL

cc: Dr. David A. Kessler

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FILE

AUG 12 1996

The Honorable Tom A. Coburn
House of Representatives
Washington, D.C. 20515

Dear Dr. Coburn:

This is in response to your letter of July 1, 1996, regarding the drug RU-486 (mifepristone). Your letter asks questions about our previous responses to your November 1995 request for documents regarding RU-486.

You ask that we respond to seven specific questions. Our responses are as follows.

Questions 1,2,3,5 and 6: All the documents regarding RU-486 and its use as an abortion drug that are publicly available pursuant to the Freedom of Information Act (FOIA) and our regulations, have been previously provided to you or are included in this transmittal.

Question 4: "Why are there no documents relating to the citizens' petition on RU-486 in FDA's response to the earlier document request?"

These documents were provided to you on February 23, 1996. These documents are in the material from the Dockets Management Branch -- (items 1 through 3) that includes, both a copy of the citizen's petition and the comments we have received regarding the petition.

Question 7: We are including with this letter the most recent public calendars and a list of the members of the Advisory Committee for Reproductive Health Drugs.

As to the list of specific questions relating to itemized documents that were sent on May 3, 1996, by Ms. Maggie Wynne of your staff, as we stated previously in that letter, we have now transmitted everything publicly available under FOIA.

A few items do need to be clarified:

You stated that items 23 and 24, in the documents submitted by the Office of the Executive Secretariat, are missing. These items are confidential material and would not be released under FOIA. They were inadvertently listed in the index sent to you.

FILE COPY	OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE
	[illegible]		[illegible]						
	HFD-1		[illegible]						

MIF 002645

You asked about the attachments that appeared to not be included with item 9, in the documents submitted by the Office of Regulatory Affairs. It is our understanding that items 10 through 14 are in fact the attachments to which the last paragraph of S. Mayer's letter to Dr. Kessler (item 9) refers.

We are including four additional FOIA available documents regarding RU-486 that were not sent to you in our two prior responses.

We trust that this letter and the enclosed documents fully respond to your request. If you have any questions, please do not hesitate to contact me.

Sincerely,

Diane E. Thompson
Associate Commissioner
for Legislative Affairs

6 Enclosures

1) Memorandum dated April 12, 1994 to the Secretary of the Department of Health and Human Services, from the _____ to the Commissioner of Food and Drugs. Including Tabs A, B and C. Tab E is a two page "Summary of Other Events."

2) Note to Assistant Secretary of Health, from the _____ to the Commissioner of Food and Drugs, dated July 14, 1993.

3) Note to Secretary Donna Shalala, from , dated September 14, 1994.

4) Note to Claudia Cooley, from the _____ to the Commissioner of Food and Drugs; dated October 25, 1994 and attachments A and B.

5) Public Calendars from December 29, 1995 through July 13, 1996. (There is no public calendar for the dates March 3 through July 13, 1996).

6) List of members of the Advisory Committee for Reproductive Health Drugs.

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

OCT 20 2000

The Honorable Tim Hutchinson
United States Senate
Washington, D.C. 20510

Dear Senator Hutchinson:

Thank you for your interest in the Food and Drug Administration's (FDA or the Agency) recent approval of mifepristone. This is in response to your letter dated October 4, 2000, requesting responses to several questions concerning FDA's approval of mifepristone.

The Agency's responses follow your questions, which are repeated below.

1. **A detailed report in the September 5 edition of the *Wall Street Journal*, based in part from leaked documents from Danco Laboratories, strongly suggests that the RU-486 abortion pill that American women will receive is being manufactured in China. Those documents showed payments from Danco to an unnamed facility in China that is know to be manufacturing the pill for consumption within China, according to the *Journal*. As I understand it, the FDA has not made public the identify of the manufacturer of the abortion pill, ostensibly because of concerns for the security of the manufacturer. I am not asking for the name of the manufacturer if in fact it is located in the United States. However, I do want to know, is the abortion pill being imported from China? Is the pill being imported from another foreign nation? If so, which nation? If your response does not provide an explicit answer, please cite the legal authority to withhold the information.**

The Agency made a determination at the time of approval that it would not disclose the identity of the manufacturer or the manufacturing site because the information was protected from disclosure as commercial confidential or trade secret information under the Freedom of Information Act. 5 U.S.C. §552, the Trade Secrets Act, 18 U.S.C. §1905 and FDA's implementing regulations. If the Agency determines that

changed circumstances permit FDA to publicly disclose this information, we will provide it to you.

2. **Under the terms of the Food and Drug Administration's approval of Mifepristone, the drug will be distributed to physicians who can accurately determine the duration of a patient's pregnancy and detect an ectopic (or tubal) pregnancy. Physicians who prescribe Mifepristone must also be able to provide surgical intervention in cases of incomplete abortion or severe bleeding—or they must have plans in advance to provide such care through others. How does the FDA intend to ensure that this drug is only distributed to the appropriate physicians?**

The sponsor of the drug, the Population Council, agreed to distribution restrictions through an approved plan that ensures the drug is only distributed to physicians who meet specific qualifications. These restrictions are noted in the FDA approval letter to the Population Council, which can be found at the FDA website www.fda.gov/cder/drug/infopage/mifepristone/ under the heading "Mifepristone Approval Letter." Additional discussion can be found in the FDA Memo to the NDA file, dated September 28, 2000, which is on the FDA website at www.fda.gov/cder/drug/infopage/mifepristone/ under the heading "Office Memo to Population Council." FDA approved mifepristone under Subpart H of part 314 in Title 21 of the Code of Federal Regulations, which allows for such restricted distribution. If restrictions are not adhered to, FDA may withdraw approval. In addition, the Population Council has committed to several post-marketing studies as part of its Phase IV commitments, including a study that will address the adequacy of the distribution and credentialing system. The obligations under Subpart H and the Phase IV commitments will help to ensure that the drug is only distributed to qualified physicians.

3. **Would you please outline the licensure requirements and any other criteria developed by the Food and Drug Administration for physicians who intend to prescribe and administer Mifepristone?**

FDA does not license physicians. State law addresses physician licensure. Under Subpart H of Part 314, however, FDA may restrict distribution to certain facilities or physicians with special training or experience, or require the performance of specified medical procedures. Doctors prescribing mifepristone must have the ability to date

pregnancies accurately and to diagnose tubal pregnancies. Doctors must be qualified to provide any necessary surgery, or have made arrangements through other qualified physicians for any necessary surgery. Also, doctors must assure that women have access to medical facilities for emergency care, and must agree to other responsibilities, such as dispensing the Medication Guide and reporting any adverse events to the sponsor. These qualification requirements are contained in the FDA approval letter to the Population Council, which can be found at the FDA website www.fda.gov/cder/drug/infopage/mifepristone/ under the heading "Mifepristone Approval Letter." Additional discussion on these qualification requirements can be found in the FDA memo to the NDA file, which is on the FDA website at www.fda.gov/cder/drug/infopage/mifepristone/ under the heading "Office Memo to Population Council."

4. **According to press reports, in early June the FDA sent Danco Laboratories a letter in which the FDA, based on its review of RU-486 going back to 1996, proposed a number of carefully crafted regulations regarding the distribution and use of RU-486. The regulations incorporated in the FDA announcement last week, however, were much weaker than what had originally been proposed. What was the basis for the FDA changing these regulations between June and September?**

To clarify, there are no "regulations" incorporated in the FDA announcement of the approval of mifepristone. There are documents and approved labeling which incorporate certain distribution restrictions. Since 1996, upon initial application by the sponsor and subsequent to the advisory committee recommendations made at the meeting held in July 1996, there have been ongoing discussions with the sponsor as to the extent and nature of the labeling, product distribution and physician qualifications. The final conditions and restrictions contained in the approval letter were based on a full review of the science and data and reflect what the Agency believes is necessary for the safe use of the product.

5. **Currently, the FDA requires that physicians report complications and compliance problems to the sponsor, and then Danco Laboratories will report those instances back to the FDA. Would you elaborate on this reporting requirement and how the FDA intends to ensure that complications and compliance problems are actually reported?**

FDA regulations require that all drug sponsors report adverse drug experiences that are both serious and unexpected to FDA within 15 days of the initial receipt of the information. All other adverse drug experiences must be reported to FDA quarterly for 3 years following application approval and annually thereafter. Additionally, as noted above in the response to question number 2, the sponsor of the drug, the Population Council has committed to several post-marketing studies as part of its Phase IV commitments. These include studies to collect certain additional information on the use of the drug. The sponsor's obligations for adverse event reporting and the Phase IV commitments made by the sponsor would be part of the review of compliance by the Agency.

6. **On January 22, 1993, President Clinton directed Secretary of Health and Human Services Donna Shalala to review the personal use import ban against Mifepristone and to assess initiatives for the agency's promotion of testing, licensing, and manufacturing Mifepristone. To your knowledge, is there any precedent for such a directive and has President Clinton ever issued a similar one?**

There always have been health issues that have generated different levels of interest and involvement by Administrations, Congress and the public. No matter what directive or interest, however, FDA cannot approve a drug product until a new drug application (NDA) has been filed with the Agency. FDA is a scientific regulatory agency that makes decisions on the basis of science. The Agency's review and approval of any drug adheres strictly to its legal mandate and mission as a science-based public health regulatory agency.

7. **To what extent did the Food and Drug Administration assist Roussell-Uclaf, the original manufacturer of Mifepristone, and the Population Council, the subsequent patent holder for the drug, in locating a manufacturer and distributor of Mifepristone?**

No assistance was provided by FDA to Roussell-Uclaf or the Population Council in locating a manufacturer and distributor of mifepristone.

8. **The clinical evidence suggested that Mifepristone is 99.5 percent successful if used in the first 49 days of**

pregnancy. Has the FDA examined the side effects resulting from the use of Mifepristone during any time period beyond 49 days for both the pregnant woman and the unborn fetus?

The labeling of mifepristone states that complete expulsion of the products of conception without the need for further surgical intervention was achieved in the U.S. study 92.1 percent of the time and in the French trials 95.5 percent of the time. The sponsor did not seek an indication beyond 7 weeks of pregnancy so no determination of the safety and effectiveness of administering mifepristone was made beyond the approved timeframe. As of May 2000, there were 82 cases reported in which women with ongoing pregnancies after using mifepristone, alone or followed by misoprostol, declined to have a surgical procedure. Of those, information is available for 36. Twenty-six of the women experienced live births and none of the infants had any abnormalities detected at birth. Ten of the women later decided to have a surgical termination, and of those, there was one case of fetal malformation. Also, the review division did review some French and English data that indicated that mifepristone when administered after the 49-day period did have a reduction in effectiveness.

Thanks again for contacting us concerning this matter. If you have further questions, please let us know.

Sincerely

/S/

Melinda K. Plaisier
Associate Commissioner
for Legislation

APPEARS THIS WAY
ON ORIGINAL

TIM HUTCHINSON
ARKANSAS

COMMITTEES:
ARMED SERVICES
HEALTH, EDUCATION, LABOR, AND PENSIONS
VETERANS' AFFAIRS

WASHINGTON OFFICE:
239 DIRKSEN SENATE OFFICE BUILDING
WASHINGTON, DC 20510
(202) 224-2353

http://hutchinson.senate.gov
E-mail: senator.hutchinson@hutchinson.senate.gov

United States Senate

WASHINGTON, DC 20510

October 4, 2000

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

Dear Dr. Henney:

I am writing to express my strong concerns regarding the Food and Drug Administration's recent approval of the drug Mifepristone, commonly known as RU-486. Knowing that the mission of the Food and Drug Administration is to protect the public health by ensuring drugs are safe and effective, I would appreciate your response to the following questions:

- A detailed report in the September 5 edition of the *Wall Street Journal*, based in part from leaked documents from Danco Laboratories, strongly suggests that the RU-486 abortion pill that American women will receive is being manufactured in China. Those documents showed payments from Danco to an unnamed facility in China that is known to be manufacturing the pill for consumption within China, according to the *Journal*. As I understand it, the FDA has not made public the identity of the manufacturer of the abortion pill, ostensibly because of concerns for the security of the manufacturer. I am not asking for the name of the manufacturer if in fact it is located in the United States. However, I do want to know, is the abortion pill being imported from China? Is the pill being imported from another foreign nation? If so, which nation? If your response does not provide an explicit answer, please cite the legal authority to withhold the information.

- Under the terms of the Food and Drug Administration's approval of Mifepristone, the drug will be distributed to physicians who can accurately determine the duration of a patient's pregnancy and detect an ectopic (or tubal) pregnancy. Physicians who prescribe Mifepristone must also be able to provide surgical intervention in cases of incomplete abortion or severe bleeding--or they must have made plans in advance to provide such care through others. How does the FDA intend to ensure that this drug is only distributed to the appropriate physicians?

- Would you please outline the licensure requirements and any other criteria developed by the Food and Drug Administration for physicians who intend to prescribe and administer Mifepristone?

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LITTLE ROCK, AR 72201
(501) 324-6336

101 NORTH WASHINGTON, SUITE 406
EL DORADO, AR 71730
(870) 863-6406

1 EAST CENTER, SUITE 212
FAYETTEVILLE, AR 72701
(501) 582-1935

ROOM 120, FEDERAL BUILDING
JONESBORO, AR 72401
(870) 935-6022

00-6123

- According to press reports, in early June the FDA sent Danco Laboratories a letter in which the FDA, based on its reviews of RU-486 going back to 1996, proposed a number of carefully crafted regulations regarding the distribution and use of RU-486. The regulations incorporated in the FDA announcement last week, however, were much weaker than what had originally been proposed. What was the basis for the FDA changing these regulations between June and September?

- Currently, the FDA requires that physicians report complications and compliance problems to the sponsor, and then Danco Laboratories will report those instances back to the FDA. Would you elaborate on this reporting requirement and how the FDA intends to ensure that complications and compliance problems are actually reported?

- On January 22, 1993, President Clinton directed Secretary of Health and Human Services Donna Shalala to review the personal use import ban against Mifepristone and to assess initiatives for the agency's promotion of testing, licensing, and manufacturing Mifepristone. To your knowledge, is there any precedent for such a directive and has President Clinton ever issued a similar one?

- To what extent did the Food and Drug Administration assist Roussel-Uclif, the original manufacturer of Mifepristone, and the Population Council, the subsequent patent holder for the drug, in locating a manufacturer and distributor of Mifepristone?

- The clinical evidence suggested that Mifepristone is 99.5 percent successful if used in the first 49 days of pregnancy. Has the FDA examined the side effects resulting from the use of Mifepristone during any time period beyond 49 days for both the pregnant woman and the unborn fetus?

Thank you for your immediate attention to the critical matter. Considering the limited time Congress has to examine this issue during the 106th Congress, I would ask that you provide your answers no later than close of business on Friday, October 6, 2000.

With kind regards,

Sincerely,

Tim Hutchinson
United States Senator

103d Congress

United States House of Representatives
Committee on Small Business

Subcommittee on Regulation,
Business Opportunities, and Technology
B-363 Rayburn House Office Building
Washington, DC 20515-6318

April 21, 1994

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

Via Fax: (301) 443-5930

Dear Dr. Kessler:

As you know, this subcommittee has been following, closely, the negotiations between Hoechst A.G. and the Population Council for the U.S. licensing of the abortifacient drug RU 486.

I have appreciated your office's frank assessments in recent months of the problems in reaching an agreement on this transfer of European technology so crucial to the health of American women. However, I must point out that these discussions have gone on for a year and significant obstacles seem to remain blocking their conclusion.

> I strongly sense there has been foot-dragging by one or both sides in these negotiations. My concern centers on the fact that further delay in U.S. clinical trials for this drug, and ultimately its availability should it prove safe and effective, will (1) pose a serious health risk to women who will be forced to choose a surgical alternative, (2) slow and perhaps even stop important, and perhaps life-saving experiments with this drug for non-abortifacient purposes, and (3) cloud, confound and delay the efforts of small, U.S. biomedical firms which may contemplating their own research and development involving anti-progestin drugs.

The failure so far to reach agreement on this license has a formidable impact on a variety of public policy issues of interest to this subcommittee, this government and the American public. After consulting with your office, the Secretary of Health and Human Services, and a number of interest groups following the RU 486 case, I have concluded that a congressional hearing is required to (1) obtain a full and complete description of the problems still

94-3692

unresolved in these negotiations, (2) the likelihood they will be overcome, and (3) the nature of the appropriate government response should Hoechst and the Population Council not be able to reach an agreement.

Therefore, we invite your testimony, or the testimony of your designee, time and place as follows:

Time: 10 a.m.
Date: Monday, May 16, 1994
Place: 2359 Rayburn House Office Building
Washington, D.C.

Should you wish to offer a substitute, please contact subcommittee staff by close-of-business Friday, April 29, with the name and title, and brief biography.

Your testimony should address, but not necessarily be limited to the following points and questions:

-- Please describe the history of the negotiations between the company and the Population Council, to date.

-- Please explain the key issues which must be decided upon, and included as part of the licensing agreement.

-- Please give a complete description of principal issues still unresolved, and your perspective regarding the reasons for that lack of resolution.

-- Please describe efforts made by your office, or other branches of government, to try to resolve these issues, or other obstacles placed in the way of complete and speedy clinical trials for RU 486.

-- Please explain why Hoechst has sought to negotiate this license rather than its subsidiary organization, Roussel-Uclaf, which we understand to be the patent-holder of RU 486 and the entity negotiating the license when talks began last year.

-- Please explain, from your own perspective, differences of opinion and philosophy between Hoechst and Roussel...if any exist...regarding the overseas licensing and/or marketing of this drug, and how those differences may be contributing to the delays in reaching an agreement.

-- Please describe the role played by federal health officials, if any, in the negotiation of this licensing agreement, and whether that role has been beneficial to the resolutions reached so far. By the same token, is there something more that the federal government could do to bring these discussions to a swift and successful conclusion?

-- It has been suggested that the federal government should seek to revoke the company's patent protection for this drug in the United States unless or until the company files for marketing approval, either on its own or through a licensing agreement.

In your view, would canceling the patent help or hinder, speed or delay, the introduction of RU 486 to the U.S. market?

Would the revocation of the patent, or the assumption of patent rights by the government, encourage or discourage other firms in the research and development of anti-progestin drugs?

At this stage, should the government seriously consider some action against the patent as a means of encouraging a successful conclusion to your negotiations?

Should the government consider supporting a targeted research and development program aimed at commercialization of a domestic version of RU 486?

-- The Population Council apparently has been in touch with a number of firms in North America and elsewhere which would be able to provide manufacturing and distribution facilities for this drug.

Do you have any misgivings about the Council's ability to select an appropriate partner(s) for these crucial tasks?

Your written testimony may be of any length. However, you should be prepared to summarize your key points in 10 to 12 minutes of oral presentation.

Please provide one copy of your written statement to subcommittee staff by close-of-business Tuesday, May 3, 1994. This copy may be submitted by fax at (202) 225-8950.

Please bring 100 copies of your statement to the subcommittee on the morning of the hearing.

Should you have any questions concerning this hearing, or my request, please don't hesitate to contact me, or Steve Jenning of the subcommittee staff at (202) 225-7797.

Sincerely,

RON WYDEN
Chairman

APPEARS THIS WAY
ON ORIGINAL

SEP 18 1995

The Honorable Tom A. Coburn
House of Representatives
Washington, D.C. 20515-3602

Dear Mr. Coburn:

This is in further response to your letter of July 10, 1995, regarding the development of a new "morning after" birth control pill similar to RU 486. Your letter asked about the involvement of the Food and Drug Administration (FDA) in the development of such a drug.

The FDA does not provide funding for clinical trials of drugs except for orphan drugs. A "morning after" birth control pill would not be considered an orphan drug. FDA, therefore, is not funding any studies for a "morning after" pill. If federal monies are being spent on such research, it is possible that the National Institutes of Health would have that information.

Please note that under the Federal Food, Drug, and Cosmetic Act and its implementing regulations, we may not release any information about unapproved new drugs, including the existence of an investigational new drug application for such a drug. Therefore, we cannot provide the names of any such drugs under investigation, the type of research being conducted, etc.

We regret that we cannot be more helpful. If we can be of any further assistance, please do not hesitate to contact us.

Sincerely,

Diane E. Thompson
Associate Commissioner
for Legislative Affairs

cc:HFW-10(2) HFD-1(2) HFD-500 HFD-510(3)
Drafted by: ——— :8.14.95:Cleared by: ——— :8.14.95
Initialed: ——— :8-14-95:Revised HFD-500/ ——— /8-30-95
Edited: ——— :8/31/95:Init: ——— :9/15/95
F/T: ——:9/16/95:(s:\wp\ ——— \mornaftr.tac)

FDA Control # 95 6397

APPEARS THIS WAY
ON ORIGINAL

TOM A. COBURN, M.D.
2D DISTRICT, OKLAHOMA
COMMITTEE ON COMMERCE
SUBCOMMITTEES:
TELECOMMUNICATIONS AND FINANCE
HEALTH AND ENVIRONMENT
ENERGY AND POWER

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

511 CANNON HOUSE OFFICE BUILDING
WASHINGTON, DC 20515
(202) 225-2701
(202) 225-3038 (FAX)

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

July 10, 1995

Commissioner David Kessler
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Commissioner Kessler,

I am writing to request all available information on the FDA's involvement in developing and funding a new 'morning after' birth control pill similar to RU 486. I understand the research trials are being conducted at _____

Specifically, I would like to know the name of the drug, type of research being conducted, how much federal money is being spent and any other relevant information. I would appreciate a prompt response.

Thank you for your attention to my request.

Sincerely,

Tom A. Coburn, M.D.
Member of Congress

APPEARS THIS WAY
ON ORIGINAL

95-637

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JAN 16 1998

The Honorable Joe Barton
Chairman, Subcommittee on
Oversight and Investigations
Committee on Commerce
House of Representatives
Washington, D.C. 20515-6115

Dear Mr. Chairman:

This is in response to your letter of December 18, 1997, to Secretary Shalala, requesting information and documents pertaining to the Food and Drug Administration's (FDA or the Agency) adverse drug reaction (ADR) reporting system and the disclosure of adverse event data received from foreign countries during consideration of the Population Council's pending new drug application (NDA) for mifepristone (RU-486).

The following are our responses to your questions:

1. **A description of the kind of adverse reaction information pertinent to assessing the safety of RU-486 or drugs that are considered similar to RU-486.**

In addition to collection of routine clinical and laboratory parameters, the following types of items were assessed prior to issuance of the "approvable" letter for mifepristone*:

- incidence of patients requiring dilatation & curettage (D&C) surgery, because of excessive bleeding;
- incidence of patients requiring a blood transfusion because of excessive bleeding;
- incidence of patients requiring intravenous (IV) fluids because of excessive bleeding;
- incidence of patients requiring hospitalization or an emergency room visit because of excessive bleeding;
- incidence and severity of patients experiencing hypotension, hypertension, tachycardia, or syncope;

*Note: Mifepristone has not received final approval.

- incidence and severity of painful uterine contractions, nausea, vomiting, and diarrhea occurring in treated patients; and,
- pregnancy outcome information in pregnancies reaching term.

Similar types of items would be considered in the safety assessment of applications filed for similar drugs.

2. The number of reports received by FDA from France of possible adverse reactions to RU-486 or drugs similar to RU-486 for each of the calendar years 1994, 1995, 1996, and to the extent the information is available, for calendar year 1997.

FDA collects information on adverse reactions both before and after a drug is approved. When trials are underway under a United States Investigational New Drug (IND) application, then ADRs are reported to that IND file. When a new drug application has been filed but not yet approved, then any ADRs detected are reported to the NDA file. After a drug is approved, then ADRs are reported to the Agency's post-marketing surveillance unit.

The number of ADRs for all indications shown below in Table I were reported to the NDA and include adverse event reports from France received on mifepristone. The NDA included summaries for patients using mifepristone as treatment for several different conditions and/or diseases, including: termination of pregnancy, labor induction, contraception, breast cancer, meningioma, [redacted] endometriosis, metastatic adrenal cancer, cervical ripening, ovarian cancer, and Cushing's syndrome. The numbers in Table I below are in accordance with the data submitted by the sponsor. One set of data was for 1993-1995 combined, other data were reported by individual year.

TABLE I

ADRs Reported During Use for Any Indication														
1993-1995			1994			1995			1996			1997		
FR	OT	UK	FR	OT	UK	FR	OT	UK	FR	OT	UK	FR	OT	UK
0	0	54	25	10	0	14	144	404	0	1	481	0	0	0

Code: FR=France, OT=Other Countries, UK=Unknown Countries

All clinical trials associated with the IND for mifepristone sponsored by the Population Council were conducted in the United States. Table II represents the number of ADRs reported under the Population Council's IND for patients being treated with mifepristone only for the indication "pregnancy termination."

TABLE II

ADRs Reported During Use for Pregnancy Termination							
1994		1995		1996		1997	
France	Other	France	Other	France	Other	France	Other
0	7	0	49	0	2	0	1

FDA has not received any reports from France of possible adverse reactions to drugs similar to mifepristone. FDA is unaware of any drugs either in France or any other country which are similar to mifepristone.

3. **All documents related to requests from FDA to the United Nations' World Health Organization for adverse reaction reports related to RU-486 or to drugs similar to RU-486 and the responses to those requests. If no such requests have been made, please explain if FDA will now make such a request.**

No such request was made from FDA's Division of Reproductive and Urologic Drug Products to the World Health Organization (WHO) regarding this issue. At this time, FDA does not intend to request information from WHO. FDA has received domestic and international adverse reaction reports and safety updates on mifepristone from the NDA sponsor.

4. **A description of all measures taken by the FDA to assure that all adverse event information about RU-486 was disclosed.**

In accordance with section 505(k)(2) of the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, an applicant " . . . must establish and maintain records . . . ." In addition, ". . . where the Secretary deems it appropriate, for the examination, upon request, by the persons to whom such regulations are applicable . . . ."

When the NDA was submitted, data from clinical trials conducted in France were submitted. Accordingly, two sites at which data were collected, were inspected by FDA's Division of Scientific Investigations; one in Paris, France, and one in Valencienes,

France. These two sites represented the majority of patients treated with mifepristone. There were no major audit violations found at either site that precluded recommending approval for the NDA.

In addition, FDA, on September 19, 1988, requested of the IND sponsor, data on adverse event reports from investigators doing studies with mifepristone. Over the life of the IND, the sponsor periodically has submitted such data. On July 24, 1996, FDA requested from the NDA sponsor a summary of the international post-marketing surveillance data on the use of mifepristone to ensure the information was available. The sponsor confirmed the data were available in the NDA and/or the NDA safety update.

This letter contains confidential information not releasable to the public under the Freedom of Information Act regulations. We ask that the Committee not publish or otherwise make public any information contained in this letter. We would be glad, of course, to discuss with the Committee staff the confidentiality of the information.

We hope this information is helpful.

Sincerely,

/S/

Sharon Smith Holston
Deputy Commissioner
for External Affairs

cc: Honorable Tom Bliley, Chairman
Committee on Commerce

Honorable John D. Dingell
Ranking Minority Member
Committee on Commerce

Honorable Ron Klink
Ranking Minority Member
Subcommittee on Oversight and Investigations

cc: HFW-1
HFW-2
HFW-10
HFW-14
HF-24
DHHS/OS/EXEC SEC (OS#1224970002)
R/D: [redacted] :01/05/98 (with clinical input from [redacted]
Concur: [redacted] :01/06/98
Concur: [redacted] :01/07/98
[redacted] :01/07/98
[redacted] :01/07/98
R/D: [redacted] :1/8/98
Reviewed: [redacted] :1/9/98
Reviewed: [redacted] :1/12/98
Reviewed: [redacted] :1/13/98
Reviewed: [redacted] 1/14/98
R/T: [redacted] 1/15/98 [redacted]
Reviewed: [redacted] :1/15/98
[redacted] 1/15/98
F/T: [redacted] 1/15/97
Control No. 97-10074

APPEARS THIS WAY
ON ORIGINAL

U.S. House of Representatives
Committee on Commerce
Room 2125, Rayburn House Office Building
Washington, DC 20515–6115

December 18, 1997

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

Dear Secretary Shalala:

Pursuant to Rules X and XI of the U.S. House of Representatives, the Subcommittee on Oversight and Investigations is examining the Food and Drug Administration's (FDA) adverse event reporting system and the disclosure of adverse event data from foreign countries.

An article in the December 11, 1997 edition of The Wall Street Journal reported that some European data on heart-valve problems in diet-pill users were undisclosed to the FDA as well as the FDA advisory panel that reviewed the diet drug known as Redux. That report has raised again questions about the FDA's adverse event reporting system, particularly with regard to drug approval decisions based on foreign data. My October 22, 1997 letter to you raised issues relating to adverse event reporting and about FDA's ability to exchange information about adverse reactions to drugs with foreign adverse event reporting systems. I am concerned that the issues raised in The Wall Street Journal article may also pertain to the FDA's consideration of safety data in the Population Council's pending new drug application (NDA) for RU 486 (mifepristone).

To assist the Subcommittee's work and assure the public that the FDA and the FDA advisory panel received and reviewed all foreign adverse reaction data about RU 486, please provide the following by January 9, 1998:

(1) A description of the kind of adverse reaction information pertinent to assessing the safety of RU 486 or drugs that are considered similar to RU 486.

(2) The number of reports received by FDA from France of possible adverse reactions to RU-486 or drugs similar to RU 486 for each of the calendar years 1994, 1995, 1996, and to the extent the information is available, for calendar year 1997.

(3) All documents related to requests from FDA to the United Nations' World Health Organization for adverse reaction reports related to RU-486 or to drugs similar to RU 486 and the responses to those requests. If no such requests have been made, please explain if FDA will now make such a request.

(4) A description of all measures taken by FDA to assure that all adverse event information about RU-486 was disclosed.

For purposes of responding to this request, the term "document" is used in its broadest sense, and includes originals and drafts of any kind of written or graphic matter, however produced or reproduced, of any kind or description, whether sent or received or neither, and all copies thereof that are different in any way from the original (whether by interlineation, receipt stamp, notation, indication of copies sent or received or otherwise), regardless of whether "confidential," "privileged," or otherwise, including without limitation any paper, book, account, photograph, blueprint, drawing, agreement, contract, memorandum, advertising material, letter, telegram, object, report, record, transcript, study, note, notation, working paper, intra-office communication, interoffice communication, intra-agency communication, interagency communication, intra-department communication, interdepartment communication, chart, minute, index sheet, routing sheet, computer software, computer data, delivery ticket, flow sheet, price list, quotation, bulletin, circular, manual, summary, recording of telephone or other conversation or of interviews, or of conferences, or any other written, recorded, transcribed, punched, taped, filmed, or graphic matter, however produced or reproduced. The term "document" also includes without limitation any tape, recording, videotape, computerization, or other electronic recording, whether digital or analog or a combination of the two.

If you have any questions, please contact Mr. Alan Slobodin of the Committee staff at (202) 225-2927. I thank you in advance for your courtesy and attention to this matter.

Sincerely,

Joe Barton
Chairman
Subcommittee on
Oversight and Investigations

cc: Honorable Tom Bliley, Chairman
Honorable John D. Dingell, Ranking Member
Honorable Ron Klink, Ranking Member
Subcommittee on Oversight and Investigations

12/24/97-0002

NOV 2 2 1996

The Honorable William L. Clay
House of Representatives
Washington, D.C. 20515-2501

Dear Mr. Clay:

This is in response to your letter of August 2, 1996, co-signed by several of your colleagues, regarding your strong endorsement of the recommendation for approval of mifepristone (RU-486) by the Food and Drug Administration's (FDA) Reproductive Health Drugs Advisory Committee.

As you know, on September 18, 1996, FDA issued an approvable letter to the Population Council for mifepristone. A copy of our announcement is attached. The Agency determined that the submitted clinical data demonstrate the safety and efficacy of mifepristone in combination with misoprostol when used under close medical supervision. Before a final decision on the approval for marketing of mifepristone in the United States, additional information on other issues, including manufacturing practices and labeling, must be submitted. We are continuing to work with the applicant on these issues.

Thank you for your interest. If we may be of any further assistance, please let us know. A similar response is being sent to your co-signers.

Sincerely,

Diane E. Thompson
Associate Commissioner
for Legislative Affairs

cc: HFW-10 (2)
HFW-14
R/D:
Review:

F/T: 11/20/96
Control 96-6109

SAM FARR
17TH DISTRICT, CALIFORNIA

COMMITTEE ON AGRICULTURE
SUBCOMMITTEES:
DEPARTMENT OPERATIONS, NUTRITION, AND FOREIGN AGRICULTURE
RISK MANAGEMENT AND SPECIALTY CROPS

COMMITTEE ON RESOURCES
SUBCOMMITTEES:
FISHERIES, WILDLIFE, AND OCEANS
WATER AND POWER RESOURCES

Congress of the United States
House of Representatives
Washington, DC 20515–0517

August 2, 1996

1117 LONGWORTH BUILDING
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100 WEST ALISAL
SALINAS, CA 93901
(408) 424–2229

701 OCEAN STREET
ROOM 318
SANTA CRUZ, CA 95060
(408) 429–1976

Dr. David Kessler
Commissioner
Food and Drug Administration
Dept. of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Dr. Kessler:

We are writing to let you know of our strong endorsement of the July 19 recommendation by the FDA Reproductive Health Drugs Advisory Committee for approval of Mifepristone, commonly called RU-486, for use in the United States.

Mifepristone is one of the most important scientific advances in women's reproductive health care since the birth control pill. With a success rate of 95 percent both in the American trials and among the 200,000 French women who have taken Mifepristone since it was approved in France in 1988, the drug offers American women a medically safe alternative to surgical abortions. The availability of Mifepristone will restore privacy to a deeply personal decision between a woman and her doctor and, hopefully, reduce clinic violence.

With seven of the eight advisory committee members determining that Mifepristone is safe and effective for terminating early pregnancies, we urge you to act favorably and promptly on the application by Advances in Health Technology, the non-profit organization that holds the exclusive legal rights to manufacture and distribute Mifepristone in the United States.

American women deserve access to a safe, and effective reproductive choices -- this must include Mifepristone.

Sincerely,

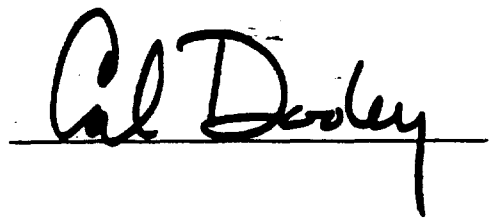
Sam Farr

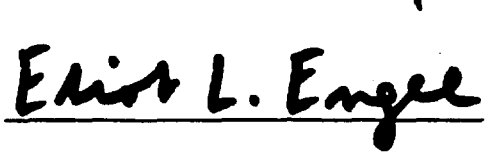
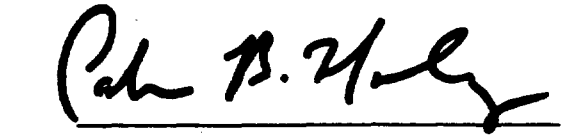
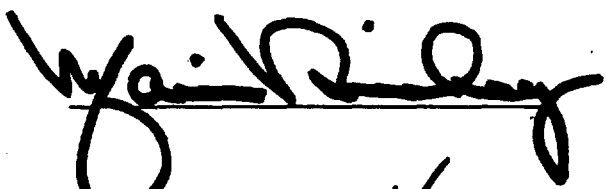
Lane Evans

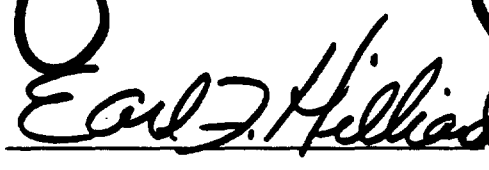
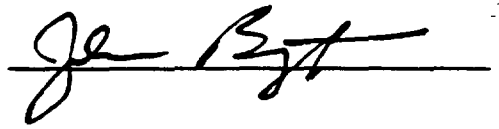
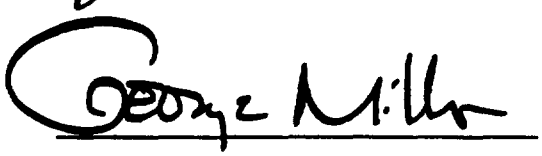
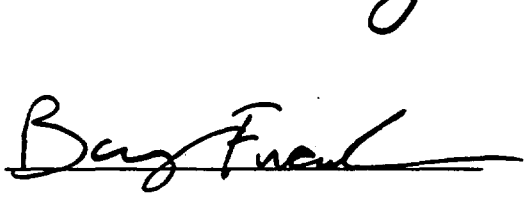
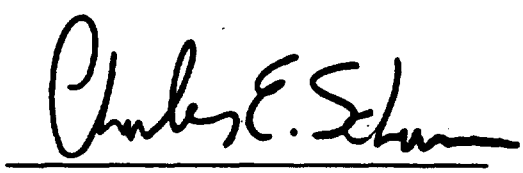
John W. Olver

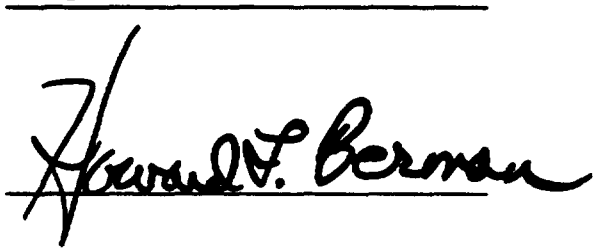
Alcee L. Hastings

N6.96-6109

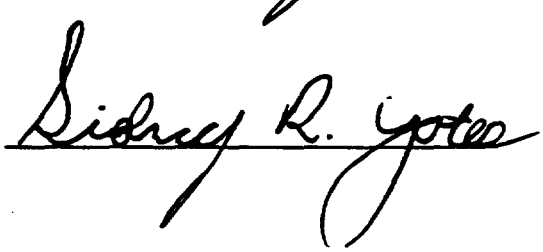


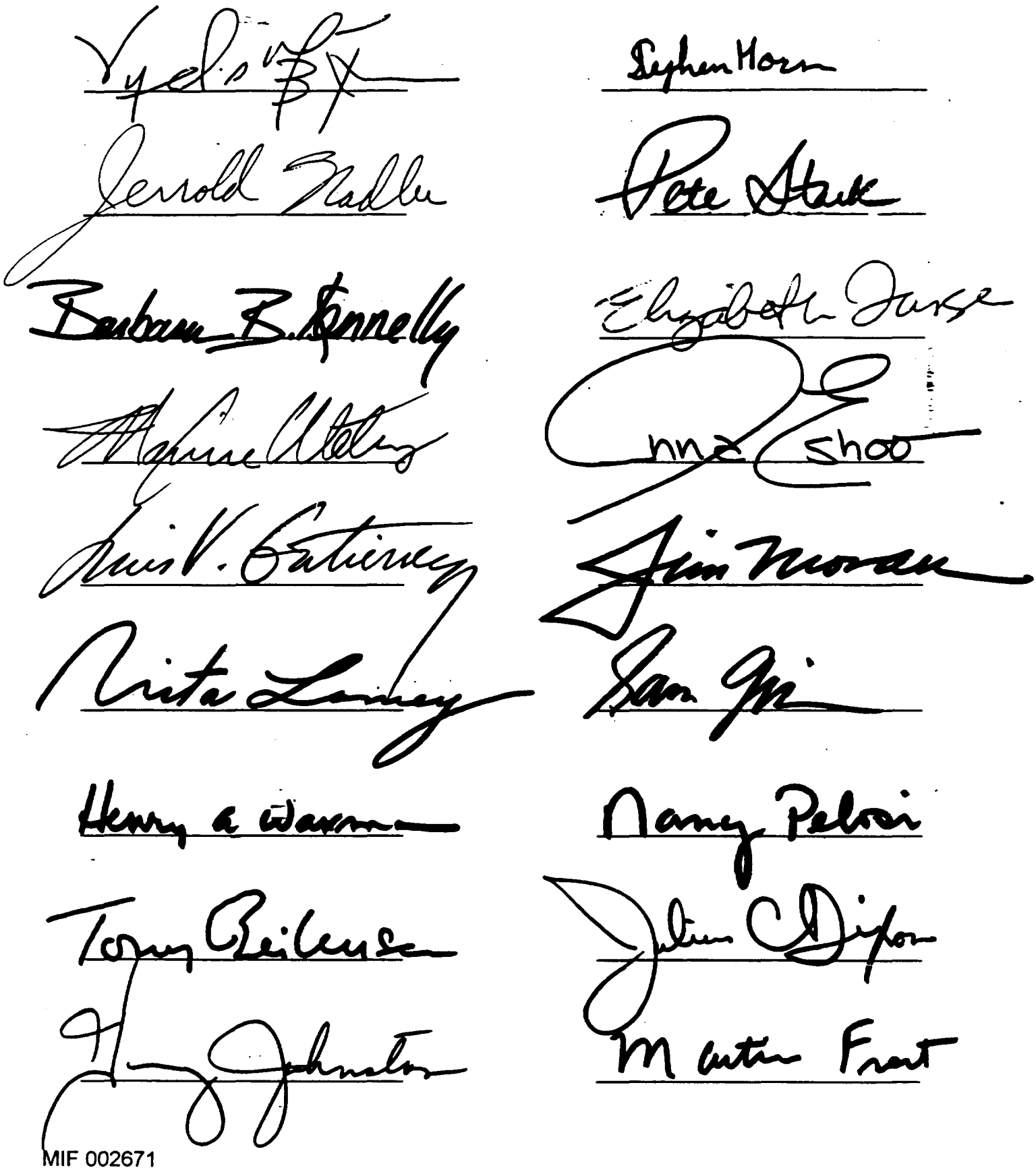












James Greenwood

Bill Sander

Pete Hoekstra

Bob Filner

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

See attached forged typed list of 45 member signatures

SAM FARR
17TH DISTRICT, CALIFORNIA

COMMITTEE ON AGRICULTURE
SUBCOMMITTEES:
DEPARTMENT OPERATIONS, NUTRITION, AND FOREIGN AGRICULTURE
RISK MANAGEMENT AND SPECIALTY CROPS

COMMITTEE ON RESOURCES
SUBCOMMITTEES
FISHERIES, WILDLIFE, AND OCEANS
WATER AND POWER RESOURCES

Congress of the United States
House of Representatives
Washington, DC 20515–0517

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100 WEST ALISAL
SALINAS, CA 93901
(408) 424–2229

701 OCEAN STREET
ROOM 318
SANTA CRUZ, CA 95060
(408) 429–1976

FASCIMILE TRANSMISSION
WASHINGTON OFFICE OF REP. SAM FARR
(202) 225-2861
fax 225-6791

TO: _____

FROM: Debbie Merrill

DATE: 8/15/96

NUMBER OF PAGES (including this cover): 2

MESSAGE: Members who signed RU486 letter to Dr. Kessler - I forget Gerry Studds

APPEARS THIS WAY
ON ORIGINAL

Members who signed letter to Dr. David Kessler of the FDA regarding RU486.

Sam Farr	Barney Frank
Charles Schumer	George Miller
Edolphus Towns	Howard Berman
Gary Ackerman	Peter DeFazio
Jan Meyers	Sidney Yates
Nydia Velazquez	Stephen Horn
Jerrold Nadler	Pete Stark
Barbara Kennelly	Elizabeth Furse
Maxine Waters	Anna Eshoo
Luis Gutierrez	Jim Moran
Nita Lowey	Sam Gejdenson
Henry Waxman	Nancy Pelosi
Anthony Beilenson	Julian Dixon
Martin Frost	Harry Johnston
James Greenwood	Bernard Sanders
Peter Deutsch	Earl Blumenauer
Bob Filner	John Olver
Alcee Hastings	Cal Dooley
Neil Abercrombie	Eliot Engel
Carolyn Maloney	Maurice Hinchey
Corrine Brown	Earl Hilliard
John Bryant	William Clay

Gerry Studds

APPEARS THIS WAY
ON ORIGINAL

TOTAL P.02

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

APR 12 2000

The Honorable Lynn Woolsey
House of Representatives
Washington, D.C. 20515-0529

Dear Ms. Woolsey:

Thank you for the letter of March 27, 2000, co-signed by thirty-four of your colleagues, expressing your views concerning the new drug application (NDA) of the drug product, mifepristone, (French brand name - RU486). This NDA, sponsored by the Population Council of New York City, is currently pending before the Food and Drug Administration (FDA or the Agency).

On February 18, 2000, FDA issued a second "approvable" letter concerning the Population Council's NDA for mifepristone. A copy of the Agency's Talk Paper explaining this action is enclosed. An approvable letter is one of several actions the Agency can take during the drug approval process. Such letters are a formal communication to the sponsor, informing them in detail, of the remaining information that must be submitted to complete an application. As explained in the Talk Paper, under the requirements for FDA set out in the Prescription Drug User Fee Act, the Agency has a six-month goal for acting on information submitted in response to an original action. The February 2000 approvable letter was the Agency's response to that requirement.

FDA regulations, 21 CFR § 20.61, prevent the Agency from discussing any information about a pending NDA that has not been made public by the sponsor. Please be assured that the Agency is aware of your concerns on this matter and is acting as expeditiously as possible to process the application within the requirements of the law.

APPEARS THIS WAY
ON ORIGINAL

We trust this responds to your concerns. If we may be of further assistance, please contact us again. A similar letter has been sent to all co-signers of the letter.

Sincerely,

/S/

for Melinda K. Plaisier
Associate Commissioner
for Legislation

Enclosure

APPEARS THIS WAY
ON ORIGINAL

bcc: HFW-10
HFW-1
HFW-14
R/D: 3/30/00
Rev: :3/31/00
Cleared: :3/31/00
Edits: 4/3/00
Edits: :4/4/00
F/T:frw:4/7/00:(G:\WP
Control No.:00-2187

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

FEB 07 1997

The Honorable Joe Barton
Chairman, Subcommittee on Oversight
and Investigations
Committee on Commerce
House of Representatives
Washington, D.C. 20515-6116

Dear Mr. Chairman:

This is to complete our response to your letter dated September 17, 1996, regarding further information related to the Food and Drug Administration's (FDA) consideration of RU 486 (mifepristone).

As we discussed with Mr. Alan Slobodin of your staff on November 14, 1996, we indicated that we would send you, once a compilation had been made, a list of all meetings on RU 486 between the review division and persons outside the executive branch concerning or related to RU 486. We have enclosed this list of all the meetings between FDA's Division of Reproductive and Urologic Drug Products (and previously, the Division of Metabolic and Endocrine Drug Products) and the outside persons.

The enclosed 5-page list contains confidential commercial information and other privileged information not releasable to the public under the Freedom of Information regulations promulgated by FDA. We request that the Subcommittee not publish or otherwise make public any part of this letter or any information contained within it. In addition, given the sensitivity of this subject, we have redacted the names of certain individuals associated with the clinical trials and application review.

These review division meetings are not listed in the FDA public calendar because such meetings are confidential meetings with the investigational new drug application (IND) or new drug application (NDA) sponsor. These meetings deal with confidential commercial information and we are careful not to publicize this information. Also, such meetings are typically attended by the team of reviewers who will actually work on the application. Sometimes the division director may attend. Neither division directors nor review staff (medical officers, chemists, pharmacologists, project officers, etc.) are required to report their meetings on the public calendar pursuant to Title 21, Code of Federal Regulations, section 10.100(b)(3).

We trust this information responds to your concerns. Please let us know if you have any questions.

Sincerely,

/S/

Sharon Smith Holston
Deputy Commissioner
for External Affairs

Enclosures

cc: The Honorable Thomas J. Bliley, Jr.
Chairman, Committee on Commerce

The Honorable John Dingell
Ranking Minority Member
Committee on Commerce

The Honorable Ron Klink
Ranking Minority Member
Subcommittee on Oversight and Investigations

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

FEB 26 1998

The Honorable Joe Barton
Chairman, Subcommittee on
Oversight and Investigations
Committee on Commerce
House of Representatives
Washington, D. C. 20515-6115

Dear Mr. Chairman:

This is in response to your letter of February 4, in which you asked two follow-up questions to the Food and Drug Administration's (FDA) January 16 response to your inquiry concerning the disclosure of adverse drug report (ADR) data for mifepristone (RU 486).

The following are our responses to your questions:

1. **Denominator data on overall use of RU 486 for the relevant categories in Tables I and II.**

Table I in FDA's January 16 response represented the serious ADRs reported to the new drug application (NDA). These reports represent "spontaneous" reports submitted to the sponsor by any source, as well as those that occurred in the two French clinical trials sponsored by the applicant. The total number of patients in the French trials is known (total n=2480 patients). A denominator for reports received after marketing is not known as the total number of persons using the drug is not known.

Table II represented the serious ADRs reported in the investigational new drug (IND) application and represents the United States clinical investigation. The total number of patients treated in that clinical trial was 2121.

2. **A written explanation as to why the FDA does not intend to request information from WHO.**

Throughout the NDA review process, FDA reviews the available data, including reported adverse events. A sponsor is required to provide, present and discuss all known adverse experiences. If the World Health Organization, or any other organization, maintains a database of adverse experiences, the sponsor would be expected to seek the information and provide it to their NDA.

This letter contains confidential information not releasable to the public under the Freedom of Information Act regulations. We ask that the Committee not publish or otherwise make public any information contained in this letter. We would be glad, of course, to discuss with the Committee staff the confidentiality of the information.

We hope this information is helpful.

Sincerely,

/S/

Sharon Smith Holston
Deputy Commissioner
for External Affairs

cc: Honorable Thomas J. Bliley, Chairman
Committee on Commerce

Honorable John D. Dingell
Ranking Minority Member
Committee on Commerce

Honorable Ron Klink
Ranking Minority Member
Subcommittee on Oversight and Investigations
Committee on Commerce

APPEARS THIS WAY
ON ORIGINAL

U.S. House of Representatives
Committee on Commerce
Room 2125, Rayburn House Office Building
Washington, DC 20515–6115

February 4, 1998

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

Dear Secretary Shalala:

I have reviewed FDA's January 16, 1998 response to my inquiry about the disclosure of adverse event data for mifepristone (RU 486) from foreign countries. In its response, FDA provided the numbers of adverse drug reactions (ADRs) related to RU 486, but omitted denominator data on overall use of RU 486 for the relevant categories. In addition, FDA stated that FDA's Division of Reproductive and Urologic Drug Products had not requested ADRs related to RU 486 from the World Health Organization and that FDA does not intend to request information from WHO.

To assist the Subcommittee's work, please provide the following by February 18, 1998:

(1) Denominator data on overall use of RU 486 for the relevant categories in Tables I and II.

(2) A written explanation as to why the FDA does not intend to request information from WHO.

If you have any questions, please contact Mr. Alan Slobodin of the Committee staff at (202) 225-2927. I thank you in advance for your courtesy and attention to this matter.

Sincerely,

Joe Barton

Joe Barton
Chairman
Subcommittee on
Oversight and Investigations

No. 98-1116

02/07/98 CC 32

cc: Honorable Tom Bliley, Chairman
Honorable John D. Dingell, Ranking Member
Honorable Ron Klink, Ranking Member
Subcommittee on Oversight and Investigations

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

FEB 2 3 1996

The Honorable Tom A. Coburn
House of Representatives
Washington, D.C. 20515-3602

Dear Dr. Coburn:

This is in further response to your letters of November 10, 1995, to Secretary Donna E. Shalala and Commissioner David A. Kessler, requesting copies of documents relating to the drug RU-486 (mifepristone). As we stated in our December 28, 1995 letter to you, because of the government shut-down, we were unable to ascertain if additional responsive documents existed.

We are enclosing additional correspondence located in the files of the Food and Drug Administration (FDA). These documents have been redacted to remove patient identifiers. Also enclosed are copies of FDA public calendars for the years 1992-1995.

We now have provided all releasable documents in FDA's files that are responsive to this request. The Department will be responding to your request to Secretary Shalala separately.

If you have any questions, or need further assistance, please let us know.

Sincerely,

/S/

for Diane E. Thompson
Associate Commissioner
for Legislative Affairs

Enclosures

See separate folder for Docs

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

September 14, 1994

Note to: Secretary Donna Shalala

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

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

APPEARS THIS WAY ON ORIGINAL

151

cc: Dr. Philip Lee

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

DEC 13 1996

The Honorable Joe Barton
Chairman
Subcommittee on Oversight and Investigations
Committee on Commerce
House of Representatives
Washington, D.C. 20515

Dear Mr. Chairman:

This is in further response to your letter dated September 17, 1996, regarding further information related to the Food and Drug Administration's (FDA) consideration of RU 486 (mifepristone). You raised five issues.

As per discussions with Mr. Alan Slobodin of your staff, on November 14, FDA provided documents responsive to questions two and three. Answers to the remaining questions follow:

Issue 1
Concerning senior officials did not report several meetings on the public calendar as required by Agency regulations (21 C.F.R. 10.100) . . .

(a) Please list the dates, brief description of subject matter, and attendees of all meetings between FDA officials and persons outside the executive branch concerning or relating to RU 486.

(c) You asked that we provide an explanation as to why the meetings were not reported on the public calendar pursuant to 21 C.F.R. 10.100.

As discussed with Mr. Slobodin, the following is a list of all meetings between senior FDA officials and persons outside the executive branch concerning or related to RU 486. We indicate if the meeting was on the public calendar and if not, why it was not reported. This list does not include meetings the review division may have had, if the meeting did not include a senior FDA official. We will provide information on any other meetings that may have occurred between review division staff and persons outside the executive branch as soon as that information is gathered.

2/24/93 David Kessler, ——— and ——— of FDA met with Dr. Sakiz and Dr. Ulmann, from Roussel Uclaf. Subject was a discussion of RU 486.[1]

Discussed clinical and manufacturing data on the drug that FDA would need in considering an NDA for an abortificient indication. At that meeting, FDA received a strong commitment from Roussel Uclaf to continue to make the drug available for research on other potential uses. While asserting that RU 486 should be made available in the United States, the firm emphasized the importance of finding a way to achieve that goal without the involvement of Roussel Uclaf. FDA and Roussel Uclaf agreed to continue to work on this matter until remaining issues can be resolved.[2,3] This meeting was reported in FDA public calendar for the week of February 19, 1993.

4/20/93 David Kessler, [redacted], and others from the Center for Biologics Evaluation and Research, Drew Altman of the Kaiser Family Foundation, Wayne Bardin, George Brown, Margaret Catley-Carlson, James Boynton, and Beverly Winikoff of the Population Council, Edouard Sakiz and Catherine Evouard of Roussel Uclaf. Discussed RU 486.[1]

This meeting was listed in the FDA public calendar for the week of April 16, 1993.

10/4/93 Meeting with Chief of Staff, [redacted] Roussel Uclaf's lawyers from Swidler and Berlin, and [redacted] during which it is explained that the company's demands for indemnification and patent seizure are not likely to be met in the United States.[2] This meeting was not listed in the FDA public calendar because a meeting is to be reported by the most senior official attending (21 CFR 10.100(b)(1), 40 FR 40602, 40693, September 3, 1975). The most senior official was [redacted] of the Department of Health and Human Services, and therefore, was not reported by any FDA official in the FDA public calendar.

In your letter you cited that the meetings of December 6, 1993 and April 14, 1994, were not listed in the public calendar.

The "December 6, 1993 pre-IND meeting" was not listed in the FDA public calendar because such meetings are confidential meetings with the investigational new drug application (IND) sponsor. The pre-IND meetings deal with confidential commercial information and we are careful not to publicize this information. Pre-IND meetings are typically attended by the team of reviewers who will actually work on the application.

Sometimes the division director may attend. Neither division directors nor review staff (medical officers, chemists, pharmacologist, project officers, etc.) are required to report meetings on the public calendar pursuant to 21 CFR 10.100(b)(3). Consequently, the fact that this meeting was not listed on the public calendar is typical for such meetings.

You asked about the "April 14, 1994 meeting between Lester Hyman and David Kessler, [redacted]." We have researched this meeting and have not been able to establish that this meeting occurred.

You also asked about a trip or trips by [redacted] to France to meet with Roussel Uclaf officials. [redacted] has not traveled to France or Europe to meet with Roussel Uclaf officials regarding RU 486. Consequently, there are no listings of any such meetings in the FDA public calendar.

(b) Please provide all unexpurgated books, records, . . . mentioning or pertaining to all meetings and telephone conversations between FDA officials and persons outside the executive branch concerning or relating to RU 486.

All relevant documents are enclosed at Tab A. The documents that are public and releaseable under the Freedom of Information Act are listed separately from those documents that are confidential. The confidential documents or confidential versions of public documents have not previously been released.

(4) All precedents and legal authority that support the propriety of FDA officials encouraging, urging or soliciting a submission of an IND or new drug application.

Pursuant to a presidential memorandum dated January 22, 1993, the Secretary of Health and Human Services directed that FDA promptly assess initiatives to promote testing, licensing, and manufacturing of RU 486 in the United States. 58 Fed. Reg. 7459, 7468 (February 5, 1993). Under section 903(b)(2)(E) of the Federal Food, Drug, and Cosmetic (FDC) Act, the Commissioner of Food and Drugs is responsible for executing the Act and performing such other functions as the Secretary may prescribe. In carrying out the directive, FDA officials acted to facilitate the submission of a new drug application for RU 486.

FDA's mission is, essentially, to promote and protect the public health. The promotion and protection of the public health often requires the Agency to be proactive in disseminating information about public health issues. See sections 705, 903(b)(2)(E) of the FDC Act; see also section 310(b) of the Public Health Service Act. FDA believes

that facilitating the submission of marketing applications for potentially significant drug products is appropriate and consistent with the Agency's mission. Although it is not possible to identify "all precedents" in this area, as requested, the following are among many possible examples.

In a 1973 Federal Register publication, FDA announced its intention to consider new drug applications on diethylstilbestrol for use as an emergency postcoital contraceptive. 38 Fed. Reg. 26809 (September 26, 1973). Similarly, in 1978, the Agency published in the Federal Register a request for the submission of new drug applications for potassium iodide for use as a thyroid blocking agent in radiation emergencies. 43 Fed. Reg. 58798 (December 15, 1978).

More frequently, however, FDA facilitates the submission of marketing applications through more informal interactions with potential sponsors. For example, where a promising combination drug to treat ——— had been approved in several foreign countries, FDA contacted the sponsor to encourage the submission of an NDA for that product.

In another case, FDA asked the sponsor of an approved animal drug to submit an NDA for use of the same drug in humans to treat ——— Among other examples, FDA made special efforts to facilitate the submission of a marketing application for an ——— and solicited NDAs for a drug to treat ——— and a drug for ——— FDA also facilitated the submission of marketing applications for a drug to assist ——— and for a drug to be used with ——— In another case, ———

It is very common for FDA to engage in dialogue with potential sponsors beginning at the initial research stages and continuing until the Agency ultimately decides to approve or deny an application. FDA involvement at the research stage occasionally results in the Agency asking the sponsor to submit a treatment IND based on the preliminary analysis of test results. See 21 CFR 312.83.

FDA solicitations have resulted in NDA submissions for many orphan drugs, including drugs to treat ——— disorders. As a result of FDA's initiative, INDs were submitted for drugs to treat ———

FDA has also played an active role in facilitating marketing applications to alleviate shortages of many medically necessary drug products. For example, FDA widely encouraged firms to seek marketing approval for a drug to treat a type of drug-resistant tuberculosis and succeeded in finding a sponsor for an application that was subsequently approved.

In addition, on several occasions, the Agency has facilitated the submission of an IND, sometimes in coordination with the CDC, to allow the importation of a medically necessary drug that was not available domestically. In this manner, FDA facilitated the availability of drugs to treat _____ In other instances, FDA's assistance in locating sources of scarce bulk drug substances, and soliciting application supplements to allow the use of such substances, has averted shortages of drugs necessary to treat _____

(5) All unexpurgated books, records, . . . mentioning or pertaining to FDA's implementation of President Clinton's memorandum of January 22, 1993 concerning RU 486.

A list of the documents and the documents are enclosed at Tab B.

This letter and the enclosed lists and documents contain confidential commercial information and other privileged information not releasable to the public under the Freedom of Information regulations promulgated by FDA. We request that the Subcommittee not publish or otherwise make public any part of this letter or any information contained within it. In addition, given the sensitivity of this issue, we have redacted the names of certain individuals associated with the clinical trials and application review.

We trust this information responds to your concerns. Please let us know if you have any questions.

Sincerely,

/S/

Sharon Smith Holston
Deputy Commissioner
for External Affairs

Enclosures

cc: The Honorable Thomas J. Bliley, Jr.
Chairman, Committee on Commerce

The Honorable John Dingell
Ranking Minority Member
Committee on Commerce

The Honorable Ron Klink
Ranking Minority Member
Subcommittee on Oversight and Investigations

TAB A:

FOIA documents:

- Letter to [redacted] FDA, dated January 3, 1992 form Andre Ulmann, Rousell Sanei R. et D.
- Memorandum to Subcommittee on Regulation, Business Opportunities, and Energy, dated January 6, 1992, from [redacted] FDA.
- Letter to Ron Wyden, dated January xx, 1992, from Kay Holcombe, FDA.
- Statement by President Clinton, dated January 22, 1992 -- Remarks by the President During the Signing of Presidential Memoranda.
- Memorandum for the Secretary of Health and Human Services, regarding the Importation of RU-485, signed by the President, dated January 22, 1992.
- Letter to Ron Wyden, dated August 7, 1992, from Carol Scheman, FDA.
- Statement of Ruth Merkatz, FDA before the Subcommittee on Regulation, Business Opportunities, and Energy, Committee on Small Business, May 8, 1992.
- Letter to Ron Wyden, dated December 8, 1992, from Edouard Sakiz, Roussel Uclaf.
- Letter to Dr. E. Sakiz, Roussel uclaf, dated December 14, 1992, from David Kessler, FDA.
- Letter to David Kessler, FDA, dated December 17, 1992, from Dr. E. Sakiz, Roussel uclaf.
- Letter to Ron Wyden, dated January 19, 1993, from Marc Scheineson, FDA. Attached--Letters to Dr. Edouard Sakiz, dated December 14, 1992, from David Kessler; letter to David Kessler, dated December 17, 1992, from Edouard Sakiz, Roussel Uclaf, and letter to David Kessler, dated January 14, 1993, from Ron Wyden, House of Representatives.
- Letter to Dr. Edouard Sakiz, dated January 22, 1993, from David Kessler, FDA.
- Record of Telephone conversation with Andre Ulmann, Roussel Uclaf, dated January 25, 1996, from [redacted] FDA.

- Email Talk Paper on RU 486, to all States, dated February 25, 1993, from [redacted] FDA.
- Letter to David Kessler, FDA, dated January 27, 1993, from [redacted], Professor, [redacted]
- Talk Paper on Meeting with Roussel uclaf on RU 486, dated February 25, 1993, from FDA.
- Letter to Dr. Edouard Sakiz, Roussel uclaf, dated March 3, 1993, from [redacted]
- Letter to Professor Wolfgang Hilger, dated March 12, 1993, from Secretary Shalala.
- Letter to Secretary Shalala, DHHS, dated March 18, 1993, from Dr. Edouard Sakiz, Roussel uclaf.
- Letter to Secretary Shalala, DHHS, dated March 23, 1993, from Professor Wolfgang Hilger, Hoechst.
- Letter to Secretary Shalala, DHHS, dated March 31, 1993, from Lawrence Lader, Abortion Rights Mobilization.
- Letter to David Kessler, FDA, dated April 15, 1993, from Professor W. Hilger, Hoechst.
- Letter to Lawrence Lader, Abortion Rights Mobilization, dated May 11, 1993, from [redacted] DHHS.
- Letter to [redacted] FDA, dated January 11, 1994, from John R. Fleder, Olsson, Frank and Weeda.
- Letter to Ron Wyden, dated February 8, 1994, from Secretary Shalala. Attached--Letter to Secretary Shalala, dated December 22, 1993, from Ron Wyden, House of Representatives
- Memorandum to Secretary, DHHS, dated April 13, 1994, from Deputy Commissioner/Senior Advisor to the Commissioner of Food and Drugs.
- HHS Fact Sheet on Mifepristone (RU 486): Brief Overview, dated May 16, 1994.
- HHS News on Roussel Uclaf donates US Patent Rights for RU 486 to Population Council, dated May 16, 1994.
- Testimony of David Kessler, FDA before the Subcommittee on Regulation, Business Opportunities, and Technology, Committee on Small Business, dated May 16, 1994.

- Letter to James Boynton, Christy and Viener, and Lester Hyman, Swidler and Berlin, dated April 22, 1994, from ——— ——————— FDA.

- Memorandum to Assistant Secretary for Health, DHHS, dated July 14, 1993, from ———————, FDA. Attached -- Memorandum to the Secretary, not dated or signed, from the Assistant Secretary for Health, DHHS.

- Note to Secretary Donna Shalala, dated September 14, 1994, from ——————— FDA.

- Memorandum for ——————— undated, from ———

- Note to ——————— Executive Secretary, dated October 25, 1994, from Deputy Commissioner/Senior Advisor to the Commissioner. Attached -- Summary, and Population Council Press Package.

- Memorandum to the Secretary, DHHS, dated October 25, 1994, from the Commissioner of Food and Drugs. Attached -- Summary Update on Medical Abortion, Talking Points, and Questions and Answers.

- Note to ——————————————————————————— ——————— DHHS, dated August 14, 1995, from ——— ——————————— Includes faxed cover sheets. Attached -- Subject Areas for Fact Sheets on Women's Health, Fact Sheet on Alcohol and Illicit Drugs.

- Letter to Andre Ullman, Roussel Uclaf, dated September 14, 1994, from ——————— FDA.

APPEARS THIS WAY
ON ORIGINAL

- Letter to [redacted] FDA, dated May 19, 1994, from Pascal Chevit, French Ambassador to the United States. Copy of Letter to David Kessler attached, dated May 19, 1994, from Pascal Chevit, French Ambassador.

- Letter to Secretary Shalala, dated May 30, 1994, from Dr. Edouard Sakiz, Roussel Uclaf.

- Letter to Secretary Shalala, dated June 8, 1994, from Marie Bass, Reproductive Health Technologies Project.

- Letter to Ron Wyden, dated June 16, 1994, from Diane E. Thompson, FDA.

Confidential Documents:

These documents contain confidential commercial information and other privileged information not releasable to the public under the Freedom of Information regulations promulgated by FDA. We request that the Subcommittee not publish or otherwise make public any part of this letter or any information contained within it.

- Telefax letter to [redacted] FDA, dated February 28, 1993, from Catherine Euvrard, Roussel Uclaf.

- [redacted]

- Memorandum to the Secretary of DHHS, dated April 12, 1994, from Deputy Commissioner and [redacted] Food and Drugs.

- Fax to [redacted], FDA, dated April 11, 1994, from [redacted], Esq. with [redacted].

- Note to Monica Mullens, Presidential Letters, Office of Correspondence, dated May 31, 1994, from [redacted] FDA.

- Memorandum to [redacted] FDA, dated May 17, 1994, from Monica Mullens, Presidential Letters. Office of Correspondence.

TAB B

- Statement by President Clinton, dated January 22, 1992 -- Remarks by the President During the Signing of Presidential Memoranda.
- Memorandum for the Secretary of Health and Human Services, regarding the Importation of RU 486, signed by the President, dated January 22, 1992.
- Memorandum for the Secretary of Health and Human Services, from the Deputy Commissioner/Senior Advisor to the Commissioner of Food and Drugs, dated April 12, 1994.
- HHS News on Roussel Uclaf Donates US Patent Rights for RU 486 to Population Council, May 16, 1994.
- HHS Fact Sheet, Mifepristone (RU 486): Brief Overview, dated May 16, 1994.

Sources:

1. Source -- Public Calendar

2. Source -- Confidential version of the "RU 486 Overview Chronology", attachment to April 12, 1994 memorandum to the Secretary from Deputy Commissioner/Senior Advisor to the Commissioner of Food and Drugs.

3. Source -- FDA Talk Paper dated February 25, 1993.

APPEARS THIS WAY
ON ORIGINAL

DOMAINE THÉRAPEUTIQUE ENDOCRINOLOGIE
AD/CR - 92/08

Romainville, 3 janvier 1992

FOOD AND DRUG ADMINISTRATION

Division of Metabolism and
Endocrine Drug Products, HFD-510

5600, Fishers Lane
ROCKVILLE, MD 20857
U S A

Dear ———

I wish to confirm you that Roussel Uclaf fully agrees to help US investigators to perform clinical studies with RU 486 (Mifepristone), provided that :

1) the studies are not in relation with abortion ;

2) the protocols are medically and ethically acceptable ;

3) the investigators will comply to the FDA rules, and to the internal Roussel Uclaf procedures as regards reporting of side-effects, publications, etc...

We are prepared to provide the investigators with the amount of RU 486 necessary for the planned studies, provided that adequate monitoring of drug distribution and storage is followed.

Roussel Uclaf also agrees to provide investigators with the material necessary to obtain their personal IND number.

Please, do not hesitate to contact me for any problem in this field.

Yours Sincerely,

André ULMANN, M.D., Ph.D.

[illegible] route de Noisy 93230 Romainville - Tél. [illegible] - Telex : ROUSS 235 477 F

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

Dear Mr. Wyden:

We are writing because we are concerned about statements made at your December 5, 1991, hearing on RU-486.

Specifically, on page 147, lines 3357-3361, of the transcript, you attribute to [redacted] a statement regarding the Administration's position on abortion research. You stated: "He said that there was no problem with abortion research as far as the Bush Administration is concerned." We believe that you may be referring to [redacted] comments at your Subcommittee's November 19, 1990, hearing on RU-486. I refer specifically to page 40 of the printed record of that hearing, where [redacted] is discussing the RU-486 import alert and its impact on research on potential uses of this drug. He said: "Even in regard to abortion, the agency has not taken a position of stopping investigational use." This is a correct statement of the FDA policy. Because we believe this statement is not in accord with your characterization at the December 5 hearing, we respectfully request that this hearing record be corrected.

In addition, you stated at the December 5 hearing (page 141, lines 3236-3242) that "now we checked with the FDA as of yesterday, there were two compassionate use approvals, no new investigational drug applications for research within the last three years." I would like to clarify for the record conversations between our staffs just prior to the December 5 hearing regarding investigational new drug applications (INDs). Specifically, your staff was informed that while we could (and did) share with the Subcommittee information on the existence of new INDs, our regulations prohibit public discussion of such new applications. Further, we advised your staff that because a number of the previously disclosed studies (applications) had been either completed or discontinued, the number of active ongoing studies had declined. We did not characterize the status of current research as "moribund." The agency currently has six active research INDs for RU-486 (one of which was submitted in 1991) and five compassionate use INDs for RU-486 (five of which were submitted since June 1991).

We would greatly appreciate a clarification of the record of your December 5, 1991, hearing. If you have any questions, please feel free to contact me.

Sincerely yours,

Kay Holcombe
Acting Associate Commissioner
for Legislative Affairs

cc: HFW-1
HFW-10(2)
HFW-12
R/D: ———:11492
R/T: —:1/14/92
Edit: ———:1/15/92
Edit: —— :1/15/92
———:1/15/92
Concur on citing numbers of applications: ——— 1/16/92
cc: ——— 1/16/92
Edit: — :1/21/92
F/T: — 1/21/92
——— DRUGLTRS\RU-486.TX)

APPEARS THIS WAY
ON ORIGINAL

AUG 7

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

Dear Mr. Chairman:

As a followup to discussions with your staff, the Food and Drug Administration (FDA) is gravely concerned about the public release of confidential proprietary information in conjunction with the Subcommittee's July 28, 1992, hearing on the drug RU-486. The release of this information violates our fundamental understanding with the Subcommittee concerning the Agency's responses to document requests.

On two different occasions, at the request of the Subcommittee, FDA provided the Subcommittee with a list of applications for investigational new drugs (INDs) on file with the Agency for studies involving RU-486 -- after the Subcommittee's May 8, 1992, field hearing on women's health issues, and more recently in response to your written requests dated July 22, 1992. In both instances, the information was transmitted to the Subcommittee with a cover letter emphasizing the confidential nature of some of the information provided. As is FDA's practice, we offered to discuss the matter with your staff in the event you sought the public release of any of this information. Your staff did not discuss the public release of the IND list with the Agency, yet either at the hearing, or subsequent to it, information from those lists was made publicly available.

FDA's regulations implementing the Freedom of Information Act are very specific with regard to the availability for public disclosure of information in INDs. In fact, the very existence of an IND is confidential by law unless the sponsor has publicly disclosed such information. (See 21 CFR 312.130 and 314.430, enclosed for your information.)

FDA takes very seriously its responsibility to protect the confidentiality of data and information submitted to us. We also take very seriously our responsibility to provide Congress with information requested in the conduct of its oversight of the FDA. It is extremely important that this