Reproductive Health Drugs Advisory Committee

FDA Technical Center
Gaithersburg, Maryland
19 July 1996

MINUTES

Members Present

Ezra C. Davidson, Jr, MD (Chair)
Janet R. Daling, PhD
Cassandra E. Henderson, MD
Thomas S. Kosasa, MD
Vivian Lewis, MD
Deborah L. Narrigan, MSN, CMN
Mary Jo O'Sullivan, MD
Diana B. Petitti, MD, MPH
Jane S. Zones, PhD

Members Absent

Kenneth Ryan, MD
Edward Wallach, MD

Invited Guests

Ricardo Azziz, MD

Executive Secretary

Philip A. Corfman, MD

"We certify that we attended the 19 July 1996 meeting of the Reproductive Health Drugs Advisory Committee and that these Summary Minutes accurately reflect what transpired."

Philip A. Corfman

Philip A. Corfman, MD
Executive Secretary

23 July 1996
Date

Ezra C. Davidson, Jr MD

Ezra C. Davidson, MD
Chair

July 23, 1996
Date

The Reproductive Health Drugs Advisory Committee of the Food and Drug Administration met on 19 July 1996 at the Food and Drug Adminstration's Technical Center in Gaithersburg, Maryland. A complete transcript of the meeting is available from the Dockets Management Branch. The following documents are annexed to these Summary Minutes:

1. The Agenda.
2. Questions put to the Committee.
3. A list of Committee members and the Guest invited by the FDA.

The meeting was opened by the Chair with comments concerning the exemplary service of the members whose terms on the Committee have ended, Drs. Janet Daling, Cassandra Henderson, and Jane Zones, and greetings to the Invited Guest, Dr. Ricardo Azziz, who becomes a member of the Committee this year. The Chair also introduced Agency staff at the Committee table: Commissioner David Kessler, Deputy Commissioner Mary Pendergast, and Acting Director of the Reproductive and Urologic Drugs Advisory Committee, Dr. Lisa Rarick.

Subsequent committee meeting dates were confirmed as follows:

20-22 November 1996
13-14 February 1997
5-6 June 1997

Ms. Marina Hooten, the Chief of the Ethics Branch in the Agency's Division of Ethics and Program Integrity, read the Conflict of Interest statement, noting that, due to the possibly apparent conflict of interest, Dr. Zones, though permitted to participate fully in the proceedings, has been asked not to vote, if votes are to be taken.

The Chair then opened the meeting to the principal topic.

NEW DRUG APPLICATION FOR THE USE OF MIFEPRISTONE FOR INTERRUPTION OF EARLY PREGNANCY

After an introduction to the topic by Commissioner David Kessler, the sponsor, the Population Council, presented its findings and recommendations. Presentations were given by Ms. Sandra Arnold, Drs. Ann Robbins, Irvin Spitz, Wayne Bardin, Beverly Winikoff, and Elizabeth Newhall. During these presentations there was discussion of the issues with Committee members. Dr. Robbins concluded the sponsor's presentations.

The next major agenda item was presentations of the Agency's review of the Application by staff of the Reproductive and Urologic Drugs Products Division, including the Acting Director, Dr. Lisa Rarick, and Drs. Alexander Jordan and Ridgely Bennett. There was discussion of the issues with Committee members during and after these presentations.

The afternoon session began with the Open Public Session, with presentations by the following individuals, speaking either as private citizens or on behalf of the organizations they represented:

Office of Congressman Tom Coburn
Member, United States House of Representatives
Michael Schwartz

Alan Guttmacher Institute
Lisa Kaeser, JD

American College of Obstetricians and Gynecologists
Carolyn L. Westoff, MD

American Life League, Inc.
Rebecca Lindstedt

American Medical Student Association
Paul Jung, MD

American Medical Women's Association
Diana Dell, MD

American Public Health Association
Allan Rosenfield, MD

American Victims of Abortion
Olivia L. Gans

Baruch College
Joel Brind, PhD

Private citizen
Randy O'Bannon, speaking for Charles Cargille, MD

Center for Reproductive Law and Policy
Janet Benshoof, JD

Private citizen
Helen M. Donovan, JD

Family Research Council
Gracie S. Hsu, MHS

Feminist Majority Foundation
Eleanor Smeal

Feminist Women's Health Center
Marie Head

Life Issues Institute
Richard D. Glasow, PhD

National Abortion and Reproductive Rights League
Marcy J. Wilder, JD

National Abortion Federation
Paul Blumenthal, MD

National Association of Nurse Practitioners
in Reproductive Health
Susan Wysocki, RNC, NP

National Council of Jewish Women
Donna Gary

National Organization for Women, Inc.
Janice E. Erickson

National Women's Health Network
Cynthia A. Pearson

National Women's Health Organization
Susan Hill

National Women's Law Center
Ann Kolker

Northeast Waterloo Family Practice
M. Louviere, MD

Pharmacists for Life, International
Mary Jasinski Caldwell

Planned Parenthood Federation of America
Gloria M. Feldt

Planned Parenthood of Westchester and Rockland, Inc.
Lynn Borgatta, MD, MPH

Reproductive Health Technologies Project
Marie Bass

Private citizen
Wendy Simonds, PhD

Society of Physicians for
Reproductive Choice and Health
Seymour L. Romney, MD

Southwestern Medical Clinic, PC
Donna J. Harrison, MD

Women's Legal Defense Fund
Joanne L. Hustead

After completion of the Open Public Hearing, the Chair directed the attention of the Committee to the questions.

ANSWERS TO THE QUESTIONS

AGENCY STATEMENT INTRODUCING THE QUESTIONS
"The regimen proposed for the use of mifepristone for the termination of early pregnancy consists of the oral administration of 600 milligrams of mifepristone within 49 days after the beginning of the last menstrual period, followed by oral administration of 400 micrograms of misoprostol 48 hours later."
CHANGE IN STATEMENT
The Committee began its deliberations on the questions by changing the phrase "48 hours" to "2 days" in this statement.

QUESTION 1.

a. Do the results of the open-label, historically controlled studies conducted in France establish the efficacy of this regimen for use in the United States?
ANSWER
The Committee voted 6 in favor and 2 opposed in response to this question.

b. If not, what additional efficacy information should the applicant provide?
ANSWER
In response to this question, the Committee voted unanimously (8 to 0) in favor of the following motion:
"The Committee has some reservations about finally determining efficacy without access to the US data and recommends to the Agency that the Committee would like the opportunity to review the data when they are available."

QUESTION 2.
The safety database for this regimen consists of trials conducted in France, preliminary data from U.S. trials, and foreign post-marketing experience.

a. Do these data adequately demonstrate that the regimen is safe for use in the United States when used for the proposed indication?
In your discussion, please include comments on the following issues:
- o Whether the adverse events associated with the regimen can be adequately managed when the regimen is administered as labeled.
- o The acceptability of the frequency of adverse events.

ANSWER
The Committee voted 7 in favor and 1 in abstention in response to this question. (The Committee provided no specific responses to the two issues on this questions presented by the Agency.)

b. If not, what additional safety information should the applicant provide?
ANSWER
The Committee discussed the issue of safety at length and stated that it would like be to be informed of the final analysis of the safety data from the US studies.

QUESTION 3.
Taking into consideration the overall evidence for safety and effectiveness of the regimen, do you believe the benefits outweigh the risks for use of the regimen for the proposed indication in the United States?
ANSWER
The Committee voted 6 in favor and 2 in abstention in response to this question.

QUESTIONS 4 and 5.
4. If the regimen were to be approved, do you consider the labeling proposed by the applicant on how to administer the regimen and how to monitor patients who receive it to be appropriate?
5. If the regimen were to be approved, what further information, if any, do you recommend be included in the written information to be provided to the patient?
ANSWER
In response to Questions 4 and 5, the Committee made the following statement:
"With regards to labeling for both physicians and the patients, the Committee is concerned that the precautions and conditions employed in the clinical trials - such as under age 18, over age 35, smoking, and certain chronic medical conditions - be described in the labeling and noting that there are as yet no data concerning the safety of the use of the regimen by women with such conditions. The Committee also recommended that patient labeling include what is known about possible teratogenicity in humans, that the risk to fetuses of pregnancies that are not terminated by the regimen is not certain, but women should be offered surgical terminations when failures occur."

QUESTION 6.
If the regimen were to be approved, do you have recommendations concerning the drug distribution system proposed by the applicant?
ANSWER
The Committee voted unanimously (8 to 0) in favor of the following statement:
"We agree in concept with the proposal but have serious reservations on how it is currently described in terms of assuring safe and adequate credentialing of providers."

QUESTION 7.
If the regimen were to be approved, what recommendations, if any, do you have for post-marketing studies?
ANSWER
The Committee recommended that several issues be studied after the regimen is marketed including the following:

- *monitor the adequacy of the distribution and credentialing system by determining, among other end points, the frequency of post-surgical complications;*
- *follow-up on the outcome of all women who have surgical abortion because of method failure;*
- *studies of the long-term effects of multiple use of the regimen;*
- *ascertainment of the number of women who follow the complete regimen of treatment, and follow-up of women who do not;*
- *studies of the efficacy and safety of the regimen in women under age 18, over age 35, and in smokers; and*
- *ascertainment of the effect of the regimen on children born after treatment failure.*

The Committee having completed the agenda, the Chair closed the meeting.