RU 486

Women's Domestic Issues

for RU 486

fate Rev 486

THE WHITE HOUSE

WASHINGTON

September 29, 2000

MEMORANDUM FOR HILLARY RODHAM CLINTON

FROM: **HEATHER HOWARD** HH

CC: **MELANNE VERVEER**
SHIRLEY SAGAWA
LISSA MUSCATINE
ANN O'LEARY

SUBJECT: **RU-486**

Attached please find guidance from the FDA and HHS on yesterday's RU-486 (mifepristone) decision. You asked whether the restrictions imposed by the FDA were comparable to those women face in Europe. Although the restrictions vary by country and health care system, I am told by advocates that they are comparable. For example, like the FDA plan, many countries require three visits to the physician's office.

Medicaid Coverage

Medicaid coverage of mifepristone should be similar to Medicaid coverage of surgical abortions. Thus, in the 16 states that cover abortion with their own state Medicaid funds (California, Connecticut, Hawaii, Idaho, Illinois, Maryland, Massachusetts, Minnesota, Montana, New Jersey, New Mexico, New York, Oregon, Vermont, Washington, and West Virginia), mifepristone should be covered, but in the other states, Medicaid would only cover under Hyde amendment situations: in case of rape or incest or life endangerment. HHS is currently in the process of determining whether to classify mifepristone a physician service or a drug.

Legal and Legislative Responses to the Decision

Opponents of mifepristone will respond in two ways to the decision. First, they have suggested they will sue the FDA, arguing that the approval process was flawed and political. If there is a more sympathetic FDA commissioner, they may also wait until women have been using the drug and sue on behalf of women who claim they were injured by it, and ask the FDA to reconsider the safety and efficacy.

Second, opponents are already contemplating a legislative response. Rep. Tom Coburn, who for the last three years has led the unsuccessful fight to prevent the FDA from approving mifepristone through Agriculture Appropriations riders, is planning to introduce legislation that would sharply curtail access to the drug. His proposed legislation would impose the following "patient protections:"

1) Only licensed physicians could distribute mifepristone. (Under the FDA plan, mid-level providers such as nurse-practitioners could dispense mifepristone under physician supervision, as allowed by state law.)

2) The physician must be trained and authorized by law to provide surgical abortions. This is clearly intended to limit the pool of providers.
3) The physician must be certified to provide ultrasound. Again, this would limit the pool of possible providers.
4) Distributing physicians must be certified to provide mifepristone through a curriculum approved by the FDA. This would require physicians to go through an FDA training program– creating hurdles for doctors and probably discouraging them from providing mifepristone.

Rep. Coburn, who is retiring this year, may try to attach these restrictions to an appropriations bill before the end of the session. The Republican leadership may prevent him, however, in order to keep the appropriations bills moving.

RU 486

June 7, 2000

MEMORANDUM FOR HILLARY RODHAM CLINTON

FROM: **HEATHER HOWARD**

CC: **MELANNE VERVEER**
SHIRLEY SAGAWA
LISSA MUSCATINE
ANN O'LEARY

SUBJECT: **RU-486**

As you know from news reports, pro-choice groups (Planned Parenthood, NARAL, National Abortion Federation and the Feminist Majority Foundation) are concerned that the FDA is considering placing restrictions on access to RU-486 (Mifepristone). I wanted to provide you with some background and context:

- Mifepristone is used in the first seven weeks of pregnancy. It has been shown in studies to be effective in ending pregnancy, but a small percentage of women require additional medical treatment such as blood transfusions or surgical procedures. It has been used over 500,000 times in Europe over the past 12 years.

- In 1989, the Bush Administration banned the importation of Mifepristone. In 1993, President Clinton reversed the importation ban. In 1998 and 1999, the Administration successfully fought for removal of an appropriations provision that would have prohibited the FDA from testing, developing or approving Mifepristone. We may face a similar amendment as early as next week when the House considers the Agriculture appropriations bill.

- In 1996 and again in February 2000, the FDA issued an "approvable" letter for Mifepristone, indicating that final approval was contingent upon additional information about manufacturing practices and labeling.

- Danco Laboratories – the company licensed for U.S. manufacture and distribution – is negotiating the conditions for the drug's manufacture, labeling and distribution. The groups have talked to Danco and claim that the FDA is considering requiring restrictions that would seriously limit access, including:

    - Requiring a "black box" to highlight certain warnings. According to the groups, the only other non-scheduled drug with such a black box is thalidomide.

- Requiring that it only be distributed by "qualified physicians" who are trained and certified to distribute it, and who are trained and authorized to perform surgical abortions. This would be problematic for two reasons: first, it would limit the number of doctors who would be able to prescribe, since there are already far too few doctors performing surgical abortions; second, it would require a registry to keep track of who is authorized to distribute the drug, which would discourage doctors who fear anti-choice violence.
- Requiring that Misoprostol, the second pill taken to induce contractions, be taken in a doctor's office, which would require women to make a second trip and would in particular limit the access of rural women. (Apparently in France women are required to make several trips to the doctor's office).

We do not know whether the press reports have accurately portrayed the conditions being considered by the FDA; we also do not know whether any of the restrictions are reasonable on their face. We have had no contact with the FDA because it is very important that the FDA's scientific approval process be credible; we should not interfere and politicize it. I have, however, been trying to see what I can find out from appropriate sources. We do know that the process is ongoing, and that the FDA is in negotiations with Danco – these restrictions may only be an early proposal. Danco will have an opportunity to respond to these proposals within the next few weeks, and will be able to make their arguments based on the science. The press reports are unfortunate because they politicize an issue that should be about the science, and hopefully the outcry has not boxed the FDA in.

Our message should be:

- We do not want women to face unnecessary access barriers, but we do want appropriate safety precautions.
- Mifepristone has been used safely and effectively in Europe for more than a decade, and the FDA has twice issued "approvable" letters, finding it safe and effective.
- The FDA is doing what it should be doing at this stage in the review process -- it is in negotiations with Danco about manufacturing and distribution issues. Danco will have an opportunity to be heard and present its arguments. The FDA's final decision must be based on the science.
- RU-486 is an important, non-surgical option for women early in their pregnancies and will not result in more abortions.

THE FIGHT FOR MIFEPRISTONE (RU 486)

1980 Researchers at Roussel Uclaf, a French pharmaceutical company, synthesize mifepristone (RU 486).

1981 The first study on the use of mifepristone to terminate early pregnancy is published.

1982 The U.S. Food and Drug Administration (FDA) issues a testing permit to the Population Council, a non-profit research organization, on the use of mifepristone as a method of early abortion.

1988 Mifepristone becomes available in France. In response to anti-abortion protests, Roussel Uclaf halts distribution of mifepristone. The French Minister of Health orders Roussel Uclaf to return the drug to the market, calling it "the moral property of women." Anti-abortion forces threaten a boycott of Roussel Uclaf's parent company. Hoechst A.G.

1989 In response to pressure from the Bush administration and anti-choice members of Congress the FDA bans the importation of mifepristone for personal use. Hoechst informs abortion opponents that it does not intend to market or distribute mifepristone outside of France.

1990 Leading scientists testify before Congress that the FDA import ban has hindered research on the broad medical benefits of mifepristone, including as a treatment for breast cancer.

Feb. 1991 The American Association for Advancement of Science (AAAS) urges the testing and use of mifepristone.

July 1991 Mifepristone is approved as an early option for nonsurgical abortion in the United Kingdom.

1991 Mifepristone is approved as an early option for nonsurgical abortion in Sweden.

July 1992 An American woman, Leona Benten, issues the first direct challenge to the FDA import alert when she returns from Europe with mifepristone. U.S. Customs officials seize the drug when Benten arrives. A U.S. District Court hears her case and examines the import alert, concluding, "[T]he decision to ban the drug was based not from any bona fide concern for the safety of users of the drug, but on political considerations having no place in FDA decisions on health and safety." The U.S. Supreme Court refuses to hear her case or to order the FDA to overturn the import ban.

Oct. 1992 A study published in the New England Journal of Medicine concludes that mifepristone is a safe and effective emergency contraceptive.

Jan. 1993 President Clinton issues an Executive Order directing the Secretary of Health and Human Services to instruct the FDA to re-evaluate the mifepristone import ban and to assess ways to promote the testing, licensing, and manufacturing of mifepristone.

Sept. 1993 The Institute of Medicine (IOM) releases a report recommending expedited submission to the FDA of a New Drug Application for the use of mifepristone as an early option for nonsurgical abortion. The IOM Report also calls for U.S. research on mifepristone and other antiprogestins as contraceptives and emergency contraceptives, and as possible treatments for endometriosis, some types of breast cancer, uterine fibroids, labor management, meningiomas, and other conditions.

Drug approval process

1994-1995 Roussel Uclaf donates U.S. patent rights for mifepristone to the Population Council. Clinical trials in the U.S. testing the combination of mifepristone and the prostaglandin misoprostol are conducted. Twenty-one hundred women in America participate in the trials.

July 1996 The FDA holds hearings on whether to approve mifepristone for use in the U.S. The FDA Advisory Committee for Reproductive Health Drugs recommends approval of mifepristone as a safe and effective early nonsurgical method of abortion. In addition, the committee concludes that the benefits of the procedure outweigh its risks.

"approvable" ?

Sept. 1996 The FDA issues an "approvable letter" for mifepristone, when used in combination with misoprostol, for early abortion. The FDA determines that "the submitted clinical data demonstrate the safety and efficacy of mifepristone in combination with misoprostol when used under close medical supervision, but additional information on other issues, including manufacturing practices and labeling, must be submitted before a final approval decision can be made."

Feb. 1997 Gedeon Richter, the European manufacturer responsible for producing mifepristone for the U.S. market, cancels its contract with the Population Council. While a new manufacturer is sought, mifepristone's introduction into the U.S. is delayed indefinitely.

April 1998 The New England Journal of Medicine reports on the clinical trials submitted to the FDA. The study finds mifepristone, in combination with a prostaglandin, is effective in medically terminating pregnancy in 92 percent of pregnancies lasting 49 or fewer days. (Women for whom the drug combination does not work may terminate the pregnancy surgically.) The study also finds this method of early nonsurgical abortion to be safe: side effects generally consist of nausea and cramping.

June 1998 U.S. Rep. Tom Coburn (R-OK) offers an amendment to the fiscal year 1999 Agriculture Appropriations bill to bar the FDA from using funds to test, develop, or approve any drug for the "chemical" inducement of abortion, including mifepristone. The amendment passes by a vote of 223-202.

July 1998 The Archives of Family Medicine reports that American women involved in clinical trials of mifepristone and misoprostol find the regimen highly acceptable. Ninety-six percent would recommend the method to a woman seeking an abortion, and over 90 percent would choose the method if they needed an abortion in the future. Even among women for whom the method failed, necessitating a traditional surgical abortion, 70 percent would try it again and 85 percent would recommend it to others.

Fall 1998 The Clinton Administration strongly opposes the inclusion of the Coburn amendment in the final Agriculture Appropriations bill and threatens to veto the bill if the ban is included. The Senate does not include a ban on FDA expenditure of funds to approve medical abortion in the Agriculture Appropriations bill. A conference committee is appointed to resolve the Senate and House differences in the Agriculture Appropriations bill, and ultimately the ban is removed.

1999 For the second time, the House votes to include the Coburn amendment, banning FDA expenditure of funds to approve medical abortion, in the Agriculture Appropriations bill. The Senate does not include such a ban, and a conference committee agrees to remove the language from the final version of the bill. Austria, Belgium, Denmark, Finland, Germany, Greece, Israel, Spain, and the Netherlands approve mifepristone for marketing.

Feb. 2000 The FDA issues a second "approvable letter" for mifepristone, when used in combination with misoprostol as an early option for nonsurgical abortion. The letter indicates that additional information is required before the FDA can grant final marketing approval. Final approval is expected in 2000.

Melanie
PYI - Heather

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Approval for RU-486

The Food and Drug Administration is expected to announce a decision next week on the fate of RU-486, the abortion pill that can offer women a safe, non-invasive alternative to surgical abortion. The agency faces a Sept. 30 deadline on whether to give final marketing approval for the drug, call for a delay of action or deny approval.

RU-486 would be a crucial breakthrough in abortion access in this country because it can be administered by primary care doctors in communities where surgical abortion services are nonexistent. Patients with RU-486 prescriptions would no longer need to travel to clinics that are targets of abortion protests. Not surprisingly, anti-abortion groups have vehemently opposed F.D.A. approval.

There is overwhelming evidence of RU-486's safety and effectiveness in a decade of use by more than 500,000 women in Europe and in clinical trials in this country. It is time the F.D.A. allowed women access to this important medical option without unnecessary restrictions.

RU-486, also known as mifepristone, was determined by the F.D.A. in 1996 to be safe and effective in terminating early pregnancies when used with another already approved drug called misoprostol. But RU-486 cannot be marketed until the F.D.A. resolves some manufacturing, labeling and distribution concerns. Those issues are being negotiated between the agency and Danco Laboratories, the group that seeks to market the drug.

Earlier this year there was considerable concern among pro-choice groups that the F.D.A. would impose strict distribution limits on RU-486. The F.D.A. was said to want only doctors who can perform surgical abortions to prescribe RU-486. Another proposal was to require prescribing doctors to have admitting privileges at hospitals within an hour of their offices. Such restrictions would greatly limit use of the drug, and do not seem medically necessary. The F.D.A. should approve RU-486 promptly without restrictions that undermine broad access.

The Wounded Euro

Yesterday's surprising decision by the United States to join with Japan and Europe in propping up the euro will not heal the ailing new currency, but it was a gesture worth making.

The euro's slide poses no grave threat to the world economy. Indeed, by cutting the cost of buying European goods, it helps American consumers and travelers to Europe. A lower euro does make American goods more expensive for Europeans to buy, hurting sales of American exports. But the American economy, according to the Federal Reserve, is in danger of overheating and needs no extra assist from more exports.

But the sagging euro has seriously hurt some American industries. It also hurts European consumers by driving up the price of imports and makes the European Central Bank's task of keeping inflation low that much harder. If, as the finance ministers believe, the slide of the euro is temporary, then there is an argument for returning it to its long-term value as soon as possible.

The theory behind intervention is that the euro is falling primarily because currency traders expect it to continue to fall. Intervention, so the argument goes, can swing currency traders around to the idea that the euro's slide is ending, inducing them to buy the euro, thus driving up its price.

In reality, interventions rarely work. The amount of money that governments are prepared to spend buying euros is tiny compared with the amounts that private currency traders are prepared to sell. Interventions can change currency values, but only if they are tied to changes in government policy. If, for example, the Federal Reserve had intervened yesterday as part of a decision to drive interest rates lower, investors would start selling dollars and buying euros. But that was not the Fed's intent in this case.

The best case for intervention is that America's European allies asked for help. Someday the United States might seek European assistance to prop up a falling dollar or to rein in a soaring dollar. If finance ministers feel compelled to help one another out, there is little danger in trying.

Weather
Today: Breezy, cool, rain.
High [illegible]. Low [illegible].
Sunday: Warmer, humid.
High [illegible]. Low [illegible].
Details, Page B8

123RD YEAR No. 295

The Washington Post

SATURDAY, SEPTEMBER 23, 2000

A Generation's Prime Time

Latino Youth's Emergence Drives New Kids' Shows

By Dale Russakoff
Washington Post Staff Writer

The newest American television family couldn't be more ordinary. The father is a history professor, the mother runs a beauty salon. They drive the official vehicle of the suburbs—an SUV—and they have four children, ages 9 to 14, three of them boys.

They wouldn't seem out of place living next door to June and Ward Cleaver or the Brady Bunch. Except for one thing: their name is Garcia, and they are the only middle-class Latino family in prime time, the first in 20 years.

The arrival over the summer of "The Brothers Garcia" on cable's Nickelodeon, the channel most watched by children under 12, is a barometer of changes being wrought by the current generation of youths, the most racially diverse and most Latino in the nation's history.

In the adult world, Latino advocates have denounced broadcasters for a "brownout" of Latino stars caused by executives' doubts that they draw enough adult viewers for advertisers. The only adult show with a Latino theme and stars—"Resurrection Boulevard," about the working-class Santiagos of East Los Angeles—premiered in June on the cable channel Showtime, which relies on subscriptions, not advertising.

But the walls are coming down in children's TV, reflecting much larger changes working

See LATINOS, A8, Col. 1

Bobby Gonzalez, Jeffrey Licon and Alvin Alvarez are "The Brothers Garcia" on Nickelodeon, the channel most watched by children under 12.

Oil Reserve To Be Tapped

30 Million Barrels To Be Released In Move Labeled Political by Bush

By Martha McNeil Hamilton
Washington Post Staff Writer

The Clinton administration announced yesterday that it will release 30 million barrels of oil from the Strategic Petroleum Reserve to help head off supply shortages of home heating oil this winter.

The decision, announced by Energy Secretary Bill Richardson, came just one day after Vice President Al Gore—who is campaigning against "big oil"—called for a withdrawal from the reserve to make heating oil more affordable.

Texas Gov. George W. Bush immediately criticized the decision, saying it was politically motivated and that the reserve "is meant for a national emergency, a national war, a major disruption of supply."

The decision means that 30 million barrels of crude oil—or about 5 percent of the reserve—will be released over 30 days with the option of releasing more if needed. The move is expected to reduce crude oil prices and increase home heating oil and gasoline supplies.

The action comes at a time when heating oil inventories are extremely low. In New England, where heating oil dominates, supplies on hand are 65 percent lower than last year, Richardson said. On the East Coast as a whole, where slightly more than a third of all homes use heating oil, stocks are 40 percent lower than this time last year.

The announcement represented a compromise within the Clinton administration, where some officials had argued vigorously against any

See OIL, A6, Col. 1

Energy Secretary Bill Richardson is said to have favored a larger release.

■ U.S. faces 'energy crisis,' Gore says | *Page A15*

Clintons Release Overnight Guest List

Link to Donations In N.Y. Race Denied

By Matthew Vita
Washington Post Staff Writer

The White House said yesterday that 404 people have stayed overnight at the executive mansion or Camp David since Hillary Rodham Clinton launched her campaign for the U.S. Senate, many of them donors who have given in excess of $100,000 to support her effort.

Seeking to quell a brewing controversy over whether the first lady improperly used government resources in her bid for a New York Senate seat, the White House denied that President Clinton or his wife were trading the perks of the presidency for political favors. It declared defiantly that they would continue to entertain their friends overnight until Clinton leaves office.

A spokesman for Hillary Clinton's campaign said about a quarter of the overnight guests were contributors to her campaign but that there was no "quid pro quo" between campaign checks and sleepover invitations.

"It is a basic, common-sense issue that your friends and people who you would have come stay at your home would also, in some instances, support your effort financially," White House spokesman Joe Lockhart said. "But any suggestion that there's anything more to that or there's any connection between that, is absolutely

See CLINTON, A13, Col. 1

OLYMPICS 2000

For U.S., a Win-Win Situation

U.S. swimmers Anthony Ervin, left, and Gary Hall Jr. are smiling for the same reason: They tied for gold in the 50-meter freestyle, part of a historic night that included golds for Brooke Bennett and Inge de Bruijn. Page D1

Golden Ride
David O'Connor of The Plains, Va., and his steed, Custom Made, jump over the equestrian competition. *Page C1*

Costly Foul in Shot
U.S. shot putter Adam Nelson fouled on his final throw, allowing Finland's Arsi Harju to win the gold. *Page D1*

For U.S., Gold to Go
After beating the top-ranked Dutch, the U.S. women's water polo team will face Australia for gold. *Page D16*

Complete, updated coverage of Olympics 2000 on www.washingtonpost.com

U.S., Japan and Europe Join to Prop Up Euro

Global Economy Threatened by Slump

By William Drozdiak
Washington Post Foreign Service

BRUSSELS, Sept. 22—Seeking to head off instability in the global economy, the world's leading central banks pumped billions of dollars into foreign exchange markets today in their first concerted effort to prop up the beleaguered euro, Europe's newest single currency.

The sudden rescue operation by the United States, Europe and Japan took markets by surprise. As traders in world financial centers watched their computer screens in suspense, the banks' buying spree drove the euro briefly above 90 cents for the first time in three weeks. Earlier it had dropped to just above 84 cents.

Officials hope the action will bolster the economies of the 11 European countries that use the euro, which are suffering from the currency's slump.

By making U.S. products cheaper for European buyers, a stronger euro could also create jobs in U.S. export industries whose sales in Europe have sagged. Likewise, it might boost the profits of U.S. companies whose European business has suffered under the cheap euro; a report by chipmaker Intel Corp. that euro problems would crimp its profits triggered a sell-off of technology stocks today.

See EURO, A19, Col. 1

Gore Holds $10 Million Edge for Final Push

By Ceci Connolly
Washington Post Staff Writer

Vice President Gore enters the final phase of the election with a $10 million advantage over Republican George W. Bush, an edge the Gore team plans to use to blanket the airwaves in key states between now and Election Day.

The financial gap comes as the Texas governor is struggling to regain his lead in the polls and calm party leaders who fear he has squandered precious time and money since the Republican National Convention.

Bush's heavy spending during August—$21 million to Gore's $11 million—is significant because both candidates began the general election with the same amount of public funding, about $67 million apiece.

Bush allies say his money gap can be bridged in part by the Republican National Committee, which has a large cash advantage over its Democratic counterpart. Still, Bush's quick spending during a month in which his advantage in the polls evaporated has raised questions among some of his own supporters about the GOP nominee's judgment.

"The fact that they spent one-third of their resources in August,

See GORE, A15, Col. 1

Jones Named Publisher, CEO of The Post

By Christopher Stern
Washington Post Staff Writer

Donald E. Graham, chairman of The Washington Post Co., yesterday appointed Boisfeuillet Jones Jr. publisher of the newspaper, the first time someone outside the Graham family has held that position in more than 30 years.

In an address to senior staff members yesterday, Graham, 55, said he will continue to hold the title of chairman of the newspaper, but Jones will be its chief executive. Graham also said he would continue to oversee the newspaper's editorial page policy "for a while."

While Jones may not be a member of the Graham family, his appointment represents continuity at The Washington Post. Jones, 53, has worked at the paper since 1980, when he was hired by Graham as vice president and general counsel. He and Graham have been friends since their days together at St. Albans School and later at Harvard College.

The announcement is not expected to herald big changes at the newspaper. Jones has been in charge of day-to-day operations since January, when Graham appointed him associate publisher. "Bo has really been running the newspaper to a great extent for years," Graham said in an interview.

The press of non-newspaper business at the growing Post com-

See POST, A7, Col. 1

Donald E. Graham, chairman of The Washington Post Co., left, with Boisfeuillet Jones Jr., newly appointed publisher of the newspaper.

Biotech Corn Fuels A Recall

Unapproved Variety Used in Taco Shells

By Marc Kaufman
Washington Post Staff Writer

Kraft Foods yesterday voluntarily recalled millions of taco shells sold in grocery stores after finding that some contained genetically modified corn only approved for farm animals.

The recall of shells sold under the name Taco Bell Home Originals is believed to be the first ever undertaken because a genetically engineered product was found in the food supply. The action comes at a time when the biotechnology industry has been defending itself against charges its products may be unsafe and poorly regulated.

While federal authorities called the presence of the unapproved corn "very serious" and "unlawful," they also said there is little known health risk from its presence in the taco shells. The corn was approved by the Environmental Protection Administration for animal feed in 1998, but the agency withheld approval for human use because of concerns that it might cause allergies in people.

The recall affects all varieties of Taco Bell shells sold in grocery stores. Consumers who purchased the shells should not eat them, and can return the packages for a refund, Kraft said.

See CORN, A6, Col. 1

INSIDE

Security Probe
The State Department has suspended the security clearance of U.S. Ambassador to Israel Martin S. Indyk.
NATION, *Page A11*

The Post on the Internet: www.washingtonpost.com

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Homes Overuse Drugs, Study Says

D.C.'s Retarded Adults at Risk From Medicine, Abuse, Neglect

By Lena H. Sun
Washington Post Staff Writer

The most comprehensive review of mentally retarded adults in the District's care has found that nearly 40 percent of those assessed are at risk because providers are overusing psychotropic drugs, improperly monitoring medication or failing to deliver routine health care.

In addition, 5 percent of those reviewed had been assaulted, according to a draft report provided to The Washington Post. The city is planning to release a final report by Monday.

The preliminary report by a team of consultants is the first systematic, independent assessment of those in the District's troubled system of care for the mentally retarded. City officials ordered the review in the spring after stories published in The Post last year detailed numerous instances of abuse, neglect and uninvestigated deaths among mentally retarded adults.

From April through August, the Delmarva Foundation for Medical Care Inc. and the William H. Mercer Group sent nurses, doctors and other specialists to review the health and safety of 1,155 mentally retarded individuals. Most live in group homes in the District.

"Although we knew things were bad, it's somewhat staggering to see the data laid out like this," said Kelly Bagby, managing lawyer at University Legal Services, a watchdog group charged with protecting the city's disabled population.

See RISK, A12, Col. 1

THE WHITE HOUSE

Office of the Press Secretary

For Immediate Release January 22, 1993

REMARKS BY THE PRESIDENT
DURING SIGNING OF PRESIDENTIAL MEMORANDA

The Roosevelt Room

3:22 P.M. EST

THE PRESIDENT: Please sit down, ladies and gentlemen.

Today I am acting to separate our national health and medical policy from the divisive conflict over abortion. This conflict, which stems from the Roe v. Wade decision of 20 years ago has brought to a halt promising research on treatment for serious conditions and diseases that affect millions of Americans -- millions of American men, women and children who include the members of my family and friends of mine and I'm sure virtually every other set of family and friends in the United States.

We must free science and medicine from the grasp of politics and give all Americans access to the very latest and best medical treatments.

Today I am directing Secretary of Health and Human Services Shalala immediately to lift the moratorium on federal funding for research involving transplantation of fetal tissue. This moratorium, which was first imposed in 1988, was extended indefinitely in 1989 despite the recommendation of a blue ribbon National Institute of Health advisory panel that it be ended. Five years later, the evidence is overwhelming. The moratorium has dramatically limited the development of possible treatment for millions of individuals who suffer from serious disorders, including Parkinson's disease, Alzheimer's disease, diabetes and leukemia. We must let medicine and science proceed unencumbered by anti-abortion politics.

Today also marks the beginning of a new national reproductive health policy that aims to prevent unintended pregnancies. Our administration is committed to providing the kind of prenatal care, child care and family and medical leave that will lead to healthy childbearing and support America's families.

As a nation, our goal should be to protect individual freedom while fostering responsible decision-making, an approach that seeks to protect the right to choose while reducing the number of abortions. Our vision should be of an America where abortion is safe and legal, but rare.

Let me also say that our administration is particularly concerned with the epidemic of teenage pregnancy. The greatest human cost of our continuing national debate over reproductive policy is borne by our children and by their children. A few teenagers choose to have and raise children, and we must help them to succeed. But for millions a teen pregnancy is unintended, leaving the young woman and her partner totally unprepared for the responsibilities of parenthood. The social

and economic price paid today and for the last several years by our nation is enormous.

So today I am also directing Secretary Shalala to act immediately to implement her intended suspension of the Title X family planning regulations that are also known as the "gag rule." For almost five years, HHS has prohibited Title X recipients from providing their patients with full information and counseling concerning pregnancy.

This dangerous restriction censors the medical information and advice that health care professionals can give their patients. As a result of today's action, every woman will be able to receive medical advice and referrals that will not be censored or distorted by ideological arguments that should not be a part of medicine.

I'm also ordering today the Director of the Agency for International Development to repeal immediately what has become known as the Mexico City policy, that has effectively applied the "gag rule" to organizations that receive United States funding, even when those organizations uses non-AID funds for those activities.

Today's actions will allow organizations that received AID funds to provide information regarding all family planning options to individuals in foreign nations. It will reverse a policy that has seriously undermined much needed efforts to promote safe and effective family planning programs abroad, and will allow us to once again provide leadership in helping to stabilize world population. Many believe that this is one of the most important environmental steps we can take.

Today I am also directing Secretary of Defense Aspin to lift immediately the near total ban on abortions at United States military facilites and to permit them to be performed at those facilities provided that the procedure is paid for entirely with private funds.

This action will allow military hospitals to perform abortions and to reverse a ban that has adversly affected the lives of scores of men and women who serve our nation around the world, or members of their families.

Finally, I am directing Secretary Shalala to instruct the Food and Drug Administration to determine whether the current import ban on the drug Mifepristone, commonly known as RU-486, is justified and to rescind the ban if there is no basis for it.

Here in the United States, RU-486 has been held hostage to politics. It is time to learn the truth about what the health and safety risks of the drug really are. If the FDA removes the ban, Americans will be able to bring the drug into the country for their personal use consistant with existing FDA policy that govern drugs not approved for distribution.

I've also ordered HHS to immediately explore the propriety of promoting testing in the United States as well as the possiblity of licsensing and manufacturing according to the standards which govern all other drugs so reviewed by our government.

Taken as a group, today's actions will go a long way toward protecting vital medical and health decisions from ideological and political debate. The American people deserve the best

medical treatment in the world. We're committed to providing with nothing less.

I'd like to say in closing a special word of personal thanks to the unbelievable number of Americans from all walks of life and all different political perspectives who have children with diabetes or who, like me, have lost relatives to Alzheimer's, or have friends suffering with Parkinson's and other diseases who came up to me over the last year and made a personal plea on the fetal tissue issue. Their statements to me and their life stories had a far greater impact on me even than the actions of the United States Congress, which included, as you know, a very broad spectrum of Republicans and Democrats on this issue.

I'd like now to sign these directives.

(Presidential Memoranda is signed.)

THE PRESIDENT: Thank you very much. (Applause.)

Q Mr. President, was it "William J." or "Bill"?

THE PRESIDENT: After a considered policy debate -- (laughter) -- we decided that I should sign my full name to all official documents of the government, and I'll continue to sign all my non -- my letters, Bill Clinton.

Q Let me ask you -- George was having a really hard time explaining to us what you knew about Zoe Baird's problem, when you knew it. Can you please explain that to us, so that the American public would really know?

THE PRESIDENT: No, I want to answer this. I think the American people are entitled to know that -- if you go back to my statement, I acknowledged that there were errors in the evaluation process, for which I take full responsibility. What happened was this. She voluntarily disclosed that; it was not in any way picked up in the vetting. It was, as you know, we were trying to make a Christmas deadline, which was probably my error, again, on this.

So just before she was announced, but after I had discussed the appointment with her, I was told that this matter had come up. Nobody said anything to me about the taxes. And what I was told was what you heard, in a very cursory way, was that an error had been made in the hiring of an illegal alien; that it had been made after consulting a lawyer, who was an expert in this area. So, basically, they had acted on counsel's advice. But they were wrong, they moved immediately to try to correct it, and the status had been corrected in terms of the legality of the person; and that the vettor's conclusion was there would be no problem.

I have to tell you that during the course of these inquiries, I received other "weightier warnings," if you will, of things which had to be worked through with other potential nominees. In retrospect, what I should have done is to basically delay the whole thing for a couple of days and look into it in greater depth.

But that was -- I take full responsibility for that. It is in no way -- this process is in no way a reflection on her. We would not have known any of this had she not disclosed it to us and to the United States Senate subseqently. So I will say again what I said this morning: I'm sorry about this. I still think she is an extraordinary person and a very able person who will

have a rich and successful career, and I take full responsibility for what happened in the review process.

Thank you. (Applause.)

END 3:30 P.M. EST

HHS NEWS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

P00-19
September 28, 2000
FOR IMMEDIATE RELEASE

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FDA APPROVES MIFEPRISTONE FOR THE TERMINATION OF EARLY PREGNANCY

The Food and Drug Administration today 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.

Under the approved treatment regimen, a woman first takes 600 milligrams of mifepristone (three 200 milligram pills) by mouth. Two days later, she takes 400 micrograms (two 200-microgram pills) of misoprostol, a prostaglandin. Women will return for a follow-up visit approximately 14 days after taking mifepristone to determine whether the pregnancy has been terminated.

Because of the importance of adhering to this treatment regimen, each woman receiving mifepristone will be given a Medication Guide that clearly explains how to take the drug, who should avoid taking it, and what side

-More-

effects can occur.

"The approval of mifepristone is the result of the FDA's careful evaluation of the scientific evidence related to the safe and effective use of this drug," said Jane E. Henney, M.D., Commissioner of Food and Drugs. "The FDA's review and approval of this drug has adhered strictly to our legal mandate and mission as a science-based public health regulatory agency."

FDA based its approval of mifepristone on data from clinical trials in the United States and France.

The labeling for mifepristone emphasizes that most women using the product will experience some side effects, primarily cramping and bleeding. Bleeding and spotting typically last for between 9 and 16 days. In about one of 100 women, bleeding can be so heavy that a surgical procedure will be required to stop the bleeding.

The drug's labeling also warns that it should not be used in women with the following conditions:

- Confirmed or suspected ectopic ("tubal") pregnancies
- Intrauterine device (IUD) in place
- Chronic failure of the adrenal glands

- Current long-term therapy with corticosteroids
- History of allergy to mifepristone, misoprostol or other prostaglandins
- Bleeding disorders or current anticoagulant (blood-thinning) therapy.

Under the terms of the approval, mifepristone 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.

To gather additional data about the use of mifepristone, the Population Council (sponsor of the product) has made a commitment to conduct postmarketing studies. These include a study comparing patient outcomes among physicians who refer their patients needing surgical intervention, compared to those who perform surgical procedures themselves; an audit of prescribers that will examine whether patients and their physicians are signing the patient agreement and placing it in the patient's

medical record, as required; and a system for surveillance, reporting and tracking rare ongoing pregnancies after treatment with mifepristone in the U.S.

Mifepristone, which was developed by a French pharmaceutical firm, was first approved for use in France in 1988. Since then, more than 620,000 European women have taken mifepristone in combination with a prostaglandin to terminate pregnancy. The drug has also been approved in the United Kingdom, Sweden, and other countries.

Mifepristone will be distributed in the U.S. by Danco Laboratories, LLC, New York, N.Y.

More detailed information about this product is available on FDA's website at http://www.fda.gov/cder/drug/infopage/mifepristone/

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Draft 09/28/00
INTERNAL USE ONLY

Questions and Answers on Mifepristone: INTERNAL USE ONLY

General

Q: What action did FDA take today?

A: Today, FDA approved mifepristone (trade name Mifeprex) for the termination of early pregnancy. The drug is approved to end pregnancies of 49 days or less, counting from the beginning of the last menstrual period.

Q: What treatment regimen did FDA approve?

A: The drug (mifepristone) is administered to a woman by mouth. Two days later, the woman returns to her doctor for oral administration of misoprostol, a prostaglandin that helps cause uterine contractions. Patients will return for a follow-up visit approximately 14 days after taking mifepristone to determine whether the pregnancy has been terminated.

Q: What is the basis for FDA's approval of this regimen?

A: FDA based its approval of mifepristone on data from clinical trials in the United States and in France.

Q: How effective was the regimen in clinical trials?

A: In the U.S. trials, medical termination of pregnancy was complete in 92% of the 827 women in the efficacy study – approximately six percent with mifepristone alone, and the remainder with mifepristone followed by misoprostol. In eight percent of patients, surgical intervention was required. Fewer than 1% of patients had ongoing pregnancies.

In the French trials, more than 95% of the 1,681 women experienced complete termination of pregnancy, 5.3% without misoprostol and the rest after taking both drugs. Surgical intervention was required in 4.5% of women.

Q: Is this the first drug approved in the U.S. for the termination of pregnancy?

A: No. Two other drugs are approved for the termination of pregnancy.

Restrictions

Q: What restrictions did FDA place on the use and distribution of this drug?

A: The drug may only be distributed to physicians who can accurately determine the duration of a woman'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.

FDA approved mifepristone under its "Subpart H" regulations, which specifically allow FDA to establish appropriate controls on the distribution of a drug.

Q: What about distribution?

A: Mifepristone will be distributed directly to qualified physicians. It will not be available through pharmacies or on the Internet.

Q: What decisions has FDA made about labeling this product?

A: FDA is requiring a "black box" warning in the mifepristone labeling for physicians. The "black box" warns that surgical intervention may be necessary and addresses the care patients should receive should such intervention be necessary. In addition, because of the importance of adhering to this treatment regimen, each woman receiving mifepristone will be given a Medication Guide that clearly explains how to take the drug, who should avoid taking it, and what side effects can occur. This Guide is also referenced in the "black box."

Q: Why did FDA impose these restrictions?

A: FDA always seeks to ensure that the products it approves are used appropriately, so that risks are minimized and benefits are maximized. FDA believes that, for this drug, these restrictions are needed to ensure safe use.

In addition, the agency believes that women should have as much accurate information as possible to make an informed decision about this regimen.

Q: According to FDA regulations, Subpart "H" applies to drugs for serious and life-threatening illnesses. Isn't it overkill to invoke this provision for the mifepristone regimen?

A: The sponsor proposed a restricted distribution system for its product, and the FDA advisory committee that discussed this application in July 1996 also recommended such a system. FDA has concluded that the termination of unwanted pregnancy is a serious condition, and that these restrictions are necessary for the safe use of this drug.

Moreover, mifepristone's distribution is typically restricted in other countries where it has been approved. FDA has concluded that establishing certain controls on the distribution of this drug are needed to help ensure that it is used appropriately.

Q: Has distribution of any other drugs been restricted? What are some examples?

A: The distribution of several other drugs has been restricted to assure that they are used safely. For example:

- Clozapine (Clozaril), a drug used to manage severe schizophrenia, is available only through a registry system that ensures monitoring of certain blood test results prior to the delivery of the drug.

- Transmucosal fentanyl (Oralet), a potent analgesic delivered on a lollipop as premedication in pediatric patients before surgery or before painful procedures, is restricted to certain registered hospitals, and is not available retail pharmacy outlets.

- The manufacturer of trovafloxacin/alatrofloxacin mesylate (Trovan/Trovan-IV) agreed to limit distribution only to hospitals and long-term nursing care facilities.

- Thalidomide (Thalomid) is marketed only under a special restricted distribution program. Under that program, only registered prescribers and pharmacists are allowed to prescribe and dispense the product.

Patients must also be registered and participate in mandatory pregnancy testing prior to receiving the drug.

Q: Why is FDA requiring a physician to be able to provide surgical intervention or to provide a plan for obtaining those services for each woman using mifepristone?

A: Clinical trials and experience in countries where mifepristone is approved have shown that this regimen fails in five to eight of 100 women. Therefore, if the regimen fails and a woman still wants to terminate the pregnancy, a follow-up surgical procedure will be necessary and must be available.

Also, in about one of 100 women, bleeding can be so heavy that a surgical procedure will be required to stop the bleeding.

Q: Will FDA or the manufacturer establish a registry of physicians who have access to mifepristone?

A: Neither FDA nor the manufacturer has any plans to establish a registry of physicians.

Q: How can cancer patients obtain mifepristone?

A: Mifepristone is available for certain cancer patients through a single patient IND. Patients must be treated according to a specified treatment plan. The drug is provided by the Feminist Majority Foundation.

<u>Pressure on FDA</u>:

Q: There have been press reports that the politics of abortion have delayed FDA's action. How does the agency respond to those reports?

A: FDA is a scientific regulatory agency that makes decisions on the basis of science. The agency's review and approval of mifepristone adhered strictly to its legal mandate and mission as a science-based public health regulatory agency.

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Q: The average review time for priority drugs is now six months. The sponsor sent FDA its application in March, 1996. Why did this review take so much longer?

A: FDA sent the sponsor an "approvable" letter in September 1996, six months after receiving the application. The letter identified outstanding issues that needed to be resolved before FDA could approve mifepristone. The sponsor responded to those issues in September 1999. FDA issued another "approvable" letter in February, 2000, asking additional questions. The sponsor has now answered those questions.

Q: Some members of Congress have expressed their opposition to mifepristone. Could Congress overturn FDA's decision?

A: It would be unprecedented for Congress to overrule an FDA decision to approve a medical product.

Q: FDA is a regulatory agency in the executive branch of the Federal government. Could a new administration overrule FDA's approval of mifepristone?

A: As an executive branch agency in the Department of Health and Human Services, FDA has bases its judgments concerning medical and public health matters on sound science. FDA based its approval of mifepristone on data from clinical trials in the U.S. and in France. It would be unprecedented for a new administration to overrule an FDA decision to approve a medical product.

Q: Who manufactures and distributes mifepristone?

A: Danco Laboratories, LLC, based in New York City, distributes mifepristone. Neither the Population Council, the sponsor of this product, nor Danco Laboratories has disclosed the identity of the manufacturer.

Q: Why won't FDA disclose the identity and location of the manufacturing site?

A: Because many threats and acts of violence have been directed at persons associated with reproductive rights issues similar to those raised by mifepristone, FDA will not disclose the identity of the manufacturer or the manufacturing site.

Under these circumstances, this manufacturing information is considered confidential commercial information.

Q: Why is FDA withholding the names of its employees who reviewed the new drug application for mifepristone?

A: Because many threats and actions of violence have been directed at persons associated with reproductive rights issues similar to those raised by mifepristone, FDA will not disclose these employees' names. Under these circumstances, this employee information is considered personal privacy information.

The regimen:

Q: How can mifepristone be safely used?

A: Basically, a woman should follow all the instructions for taking the product. First, a woman must read the Medication Guide and sign the Patient Agreement Form.

Day 1: a patient will be given three 200 milligram tablets of mifepristone.

Day 3: a patient must return to determine if expulsion has occurred. (Expulsion is infrequent with mifepristone alone, happening only in five or six percent of cases.) If expulsion has not occurred, the patient will be given two 200 microgram tablets of misoprostol that she will take orally.

Day 14: the patient will return for a follow-up visit. This visit is very important to confirm that a complete termination of pregnancy has occurred.

Q: How did FDA conclude that mifepristone is safe when its use results in the termination of a pregnancy?

A: The sponsor submitted a new drug application to the FDA, seeking the agency's approval to market mifepristone for the termination of early pregnancy. FDA concluded that the results from the clinical trials established that mifepristone is safe and effective for its intended use. In its review and approval of this application, FDA adhered strictly to its legal mandate and mission as a science-based regulatory agency.

Q: Why did FDA require a second visit on Day 3, when the product is being studied and used in a U.S. clinical trial without a return visit on Day 3?

A: Mifepristone was approved on the basis of data from clinical trials, designed by the sponsor, in which every woman in the study was required to return to her physician for a second visit. Unless pregnancy termination through the use of mifepristone alone has been confirmed by clinical examination or an ultrasonographic scan, the woman will take misoprostol during this second visit.

A third visit, to confirm that a complete termination of pregnancy has occurred, is also required.

Q: Why can't all physicians prescribe mifepristone?

A: FDA is restricting the distribution of mifepristone to physicians with specific qualifications, such as the ability to diagnose a tubal pregnancy. These restrictions are designed to ensure safe and appropriate use of the product.

Q: Can nurse-practitioners, midwives, or others prescribe mifepristone? Why?

A: Some states allow physicians to supervise other health care practitioners such as certified registered nurse practitioners and nurse midwives, and these states may allow a supervised health care provider to dispense mifepristone.

Q: What about misoprostol? Is the use of misoprostol an unlabeled use?

A: Under the approved treatment regimen, misoprostol is administered on day three to help stimulate uterine contractions. This use of misoprostol is contained in the approved labeling of mifepristone. It is based on the clinical trials for the regimen of the two drugs, which FDA found to be safe and effective for the termination of early pregnancy.

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Q: The manufacturer of misoprostol just issued a warning to physicians not to use the drug in pregnant women, and there have been press reports that the manufacturer worked with FDA on this warning. How can FDA reconcile this warning with the approval of mifepristone when used with misoprostol?

A: Misoprostol (used alone) is currently approved for use in protecting patients from gastric ulcers induced by certain pain relievers. A women who is or may be pregnant – and who does NOT wish to terminate her pregnancy -- should know that she should not take misoprostol for prevention of gastric ulcers or any other reason.

The "Dear Doctor" letter issued by Searle on August 23, 2000, warns prescribers that misoprostol may cause abortion. It therefore emphasizes that misoprostol is contraindicated for use by any pregnant woman who does not wish to terminate her pregnancy.

As part of the mifepristone-misoprostol regimen, misoprostol is appropriate for use to terminate early pregnancy.

Q: Searle just distributed new labeling for its misoprostol product (Cytotec) that says the product is not approved for abortion. What is FDA's position on this labeling?

A: Now that FDA has approved the treatment plan for the use of mifepristone followed by the administration of misoprostol for the medical termination of intrauterine pregnancy through 49 days of pregnancy, the statement in the Searle label is inappropriate. FDA has asked that it be removed.

Patient Safety and Side Effects:

Q: What are the major side effects of mifepristone?

A: The Medication Guide provides information that women should be aware of concerning the incidence of side effects from administration of Mifeprex. These include cramping and, sometimes, heavy bleeding. After misoprostol administration on Day 3, there may be nausea, vomiting, and diarrhea. Before taking this medication, a woman must be fully aware of what to expect and will have to sign the Patient Agreement form.

The problems or side effects that women should be warned about include bleeding or spotting that is likely to occur from 9 to 16 days and that has been reported to last as long as 69 days. Up to eight percent of women may experience some kind of bleeding for 30 days or more. Surgical intervention may be needed to control the bleeding.

Q: What steps has FDA taken to ensure that women are adequately informed about how to use this regimen safely?

A: FDA is requiring that each woman who takes mifepristone receive a Medication Guide that clearly explains how to take the drug, who should avoid taking it, and what side effects can occur.

Each woman taking this drug must also read the Medication Guide and sign the patient agreement form before the drug will be administered.

Q: What if a woman changes her mind?

A: Among the many safeguards FDA has established for this treatment regimen are the requirements that each woman read the Medication Guide for mifepristone and that she also sign the Patient Agreement Form. These safeguards are designed to ensure that every woman knows and understands that this regimen is for the termination of early pregnancy and is committed to that course of action.

FDA and the sponsor have established a program to inform women about this regimen, including the risk of birth defects if the regimen does not end the pregnancy. Women are instructed that surgical termination may be needed, and the Patient Agreement Form certifies that they understand this possibility.

Q: Critics of this drug say it is dangerous to women and fetuses. How does FDA respond?

A: FDA and the sponsor have established a program to inform women about this regimen, including the risk of birth defects if the regimen does not end the pregnancy. Although the data on this risk are very limited, there are several reports in the medical literature of defects after first trimester exposure to prostaglandins, including misoprostol.

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As of May 2000, 82 cases had been reported in which women with ongoing pregnancies after using mifepristone, alone or followed by misoprostol, declined to have a surgical procedure. Of those, follow-up information is available for 36. Twenty-six of those 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.

Q: Has the sponsor agreed to carry out postmarketing studies of mifepristone?

A: To gather additional data about the use of mifepristone, the Population Council has made a commitment to conduct postmarketing studies. These include a study comparing patient outcomes among physicians who refer their patients needing surgical intervention, compared to those who perform surgical procedures themselves; an audit of prescribers that will examine whether patients and their physicians are signing the patient agreement and placing it in the patient's medical record, as required; and a system for surveillance, reporting and tracking of ongoing pregnancies after treatment with mifepristone in the U.S.

Q: The sponsor of mifepristone has agreed to conduct postmarketing studies involving this drug. Doesn't that mean FDA really thinks the regimen is unsafe?

A: No. It is not at all unusual for sponsors to conduct postmarketing studies on their approved products.

<u>Access</u>:

Q: Who may prescribe mifepristone?

A: The drug will be distributed only to physicians who can accurately determine the duration of a woman'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 for patients to obtain such care through others.

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Q: Will it be available in pharmacies?

A: No. Mifepristone will be available only through qualified physicians.

Q: What health professionals will have access to mifepristone?

A: Some states allow physicians to supervise other health care practitioners such as certified registered nurse practitioners and nurse midwives, and these states may allow a supervised health care provider to dispense mifepristone.

Q: Will mifepristone be available over the Internet?

A: No. FDA and the sponsor have established a treatment regimen with many safeguards, including the direct distribution of the drug only to qualified physicians.

Q: In 1990 FDA issued an Import Alert that banned the importation of mifepristone into the United States. The drug was listed under several other names. Is that Import Alert still valid?

A: FDA issued this Import Alert because of safety concerns for people taking the unapproved drug without adequate supervision from a health care professional. Now that FDA has approved Mifeprex, the Import Alert has been revised to exempt this specific product from the alert. Formulations of mifepristone not covered by the NDA or by an IND in effect would still be denied entry into the U.S., however.

Q: Has mifepristone been studied for other uses? If so, will those studies continue?

A: Mifepristone is being studied for a variety of uses, because it can block steroid receptors. In particular, it is being investigated as a potential treatment for cancers whose tumors have progesterone receptors.

ADDITIONAL QUESTIONS AND ANSWERS—INTERNAL USE ONLY

Q: Did the White House or Secretary Shalala intervene in FDA's review of mifepristone?

A: No. Neither the White House nor the Secretary were involved in FDA's decision. FDA based its decision on the science.

Q: Earlier this year there were reports that FDA was going to impose severe restrictions on the availability of mifepristone. What changed FDA's thinking?

A: Some early press reports on this issue were inaccurate. When FDA is nearing the end of a product review, give and take between the agency and the sponsor is normal.

Q: President Clinton in 1993 asked Secretary Shalala to see what could be done to expedite the availability of mifepristone. The Secretary in 1994 said that "FDA will do all it can to quickly evaluate mifepristone." What happened? Why did FDA not tell the sponsor until 1996 that mifepristone was "approvable?"

A: Many things had to occur before the FDA could take any action. The sponsor had to obtain patent rights on the drug, and this happened in May, 1994. The sponsor then had to identify a manufacturer for the drug, file an IND with the FDA, and design and conduct clinical studies of the product. Finally, the sponsor had to analyze the data and submit a marketing application to the FDA.

FDA received the new drug application in March 1996. It began reviewing the application immediately, held an advisory committee meeting in July, and issued an "approvable" letter in September 1996.

Q: Who made the decision to approve mifepristone?

A: Many FDA employees contribute to the review and approval of a new product. The "approval" letter FDA sends to the sponsor is typically signed by a senior official.

In the case of mifepristone, FDA is not disclosing the identity of the reviewers and others who reviewed this application.

Q: What about reports that FDA had hired armed guards and heightened security?

A: FDA does not comment on security matters.

External Q & A for FDA's Web Site

1. What is MIFEPREX (mifepristone) and how does it work?
Mifepristone is a drug that blocks a hormone called progesterone that is needed for pregnancy to continue. Mifepristone, when used together with another medicine called misoprostol, is used to end an early pregnancy (49 days or less since your last menstrual period began).

2. Is mifepristone approved in any other countries?
Yes, mifepristone is approved in many other countries including France, the United Kingdom, and Sweden.

3. Who should not take mifepristone?
Some women should not take mifepristone. Do not take mifepristone if it has been more than 49 days since your last menstrual period or if you have:

- a tubal pregnancy
- an intrauterine device (IUD) in place (must be removed before you take mifepristone)
- problems with your adrenal glands (glands near your kidneys)
- been treated with certain steroid medications for a long period of time
- bleeding problems or are taking anticoagulant (blood-thinning) drug products
- had an allergic reaction to mifepristone, misoprostol or similar drugs

It is important that you understand the need for follow-up visits with your health care provider and that you have access to a medical care facility in case of an emergency.

Mifepristone has not been studied in women who are heavy smokers. Please tell your doctor if you smoke more than 10 cigarettes a day.

4. Is mifepristone distribution restricted?
Yes, mifepristone is supplied directly to doctors who meet certain qualifications. It is not and will not be available in pharmacies. It is not legally available over the Internet.

5. Why are there restrictions for this drug?
Studies of mifepristone were conducted by doctors who had certain qualifications. Both the drug sponsor and the 1996 Reproductive Drug Products Advisory Committee also recommended that FDA restrict distribution of mifepristone to qualified doctors. FDA has concluded that these restrictions are necessary for the safe use of the drug.

6. What qualifications must doctors have to obtain mifepristone?
Doctors must have the ability to date pregnancies accurately and to diagnose tubal pregnancies. Doctors must also be qualified to provide any necessary surgery, or have

made arrangements for any necessary [redacted] doctors must ensure that women have access to medical facilities for emergency [redacted] must agree to other responsibilities, such as dispensing the Medication Guide [redacted] reporting any adverse events to the sponsor.

7. What authority does FDA have to re[redacted] consumption of a drug?
The law authorizes FDA to approve new [redacted] and if they have been demonstrated to be safe and effective for use under the condi[redacted] of use recommended in the label. FDA has broad authority to require restrictions [redacted] distribution to ensure safe and effective use. FDA's full legal authority to restrict distribution of a drug is described in more detail in the preamble to agency drug regulations. [redacted] (PDF or scanned copy)

8. Can health care providers other than [redacted] dispense mifepristone?
Some states allow physicians to supervise [redacted] health care practitioners, such as certified registered nurse practitioners and nurse [redacted] In these states may allow a supervised health care provider to dispense mifepristone. Health care providers should check their state law provisions.

9. Is there an age restriction for terminating a pregnancy?
States may set age restrictions on terminating a pregnancy if they believe such restrictions are appropriate.

10. Are there studies with mifepristone [redacted] under the age of 18?
Studies to evaluate mifepristone included women ages 18-45.

11. What are the possible side effects of [redacted] mifepristone?
Mifepristone treatment will cause vaginal [redacted] In some cases vaginal bleeding can be very heavy. In a few cases, this bleeding will need to be stopped by a surgical procedure.

Other possible side effects of the treatment include diarrhea, nausea, vomiting, headache, dizziness, back pain, and tiredness.

The possible side effects are described in the Medication Guide. Please read the **Medication Guide (LINK).**

12. What is a Medication Guide?
A Medication Guide contains FDA-approved information, written especially for patients.

13. Why did FDA develop a Medication Guide for mifepristone?
FDA determined that a Medication Guide is necessary for women to be able to use mifepristone effectively and safely. It is important for women to be fully informed about how mifepristone works and about its risks, including the need for follow-up visits with their health care provider, especially [redacted] after mifepristone is administered. The Medication Guide will help ensure [redacted] follow the directions for use and that they return to their health care provider [redacted] follow-up visits.

Before you receive mifepristone, your [illegible] will provide you with the Medication Guide and ask you to sign a statement (Patient [illegible]) that you have decided to end your pregnancy.

14. Can I become pregnant again [illegible] mifepristone?
You can become pregnant again right a[illegible] pregnancy ends. If you do not want to become pregnant again, start using a birth control method of your choice as soon as your pregnancy ends.

15. Does FDA endorse the use of [illegible]
FDA does not endorse or promote any [illegible]. The agency evaluates all drug applications submitted by sponsors to determine whether a drug is safe and effective for its proposed indication under the conditions specified in the labeling. This means that the benefits of the drug outweigh its risks. [illegible] standards were applied to the new drug application for mifepristone as are applied to all applications.

16. How much will mifepristone cost?
Manufacturers establish prices for [illegible] drugs. FDA has no jurisdiction over drug pricing.

17. Will insurance companies pay for [illegible]?
Insurance coverage is a decision made by [illegible] insurance provider. Please call your insurance company if you have questions.

FACSIMILE

DATE 9/28/00

TO: (NAME, ORGANIZATION, CITY/STATE AND PHONE NUMBER):

Ms. Maria Echaveste

FROM: (NAME, ORGANIZATION, CITY/STATE AND PHONE NUMBER):

Kevin Thurm

690-6133

RECIPIENT'S FAX NUMBER ( ) 202-456-1907

NUMBER OF PAGES TO SEND (INCLUDING COVER SHEET): 20

COMMENTS:

Draft 09/28/00
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File: Choice/ RU-486

Questions and Answers on Mifepristone: INTERNAL USE ONLY

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Q: What is the basis for FDA's approval of this regimen?

A: FDA based its approval of mifepristone on data from clinical trials in the United States and in France.

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A: In the U.S. trials, medical termination of pregnancy was complete in 92% of the 827 women in the efficacy study – approximately six percent with mifepristone alone, and the remainder with mifepristone followed by misoprostol. In eight percent of patients, surgical intervention was required. Fewer than 1% of patients had ongoing pregnancies.

In the French trials, more than 95% of the 1,681 women experienced complete termination of pregnancy, 5.3% without misoprostol and the rest after taking both drugs. Surgical intervention was required in 4.5% of women.

Q: Is this the first drug approved in the U.S. for the termination of pregnancy?

A: No. Two other drugs are approved for the termination of pregnancy.

Restrictions

Q: What restrictions did FDA place on the use and distribution of this drug?

A: The drug may only be distributed to physicians who can accurately determine the duration of a woman'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.

FDA approved mifepristone under its "Subpart H" regulations, which specifically allow FDA to establish appropriate controls on the distribution of a drug.

Q: What about distribution?

A: Mifepristone will be distributed directly to qualified physicians. It will not be available through pharmacies or on the Internet.

Q: What decisions has FDA made about labeling this product?

A: FDA is requiring a "black box" warning in the mifepristone labeling for physicians. The "black box" warns that surgical intervention may be necessary and addresses the care patients should receive should such intervention be necessary. In addition, because of the importance of adhering to this treatment regimen, each woman receiving mifepristone will be given a Medication Guide that clearly explains how to take the drug, who should avoid taking it, and what side effects can occur. This Guide is also referenced in the "black box."

Q: Why did FDA impose these restrictions?

A: FDA always seeks to ensure that the products it approves are used appropriately, so that risks are minimized and benefits are maximized. FDA believes that, for this drug, these restrictions are needed to ensure safe use.

In addition, the agency believes that women should have as much accurate information as possible to make an informed decision about this regimen.

Q: According to FDA regulations, Subpart "H" applies to drugs for serious and life-threatening illnesses. Isn't it overkill to invoke this provision for the mifepristone regimen?

A: The sponsor proposed a restricted distribution system for its product, and the FDA advisory committee that discussed this application in July 1996 also recommended such a system. FDA has concluded that the termination of unwanted pregnancy is a serious condition, and that these restrictions are necessary for the safe use of this drug.

Moreover, mifepristone's distribution is typically restricted in other countries where it has been approved. FDA has concluded that establishing certain controls on the distribution of this drug are needed to help ensure that it is used appropriately.

Q: Has distribution of any other drugs been restricted? What are some examples?

A: The distribution of several other drugs has been restricted to assure that they are used safely. For example:

- Clozapine (Clozaril), a drug used to manage severe schizophrenia, is available only through a registry system that ensures monitoring of certain blood test results prior to the delivery of the drug.

- Transmucosal fentanyl (Oralet), a potent analgesic delivered on a lollipop as premedication in pediatric patients before surgery or before painful procedures, is restricted to certain registered hospitals, and is not available retail pharmacy outlets.

- The manufacturer of trovafloxacin/alatrofloxacin mesylate (Trovan/Trovan-IV) agreed to limit distribution only to hospitals and long-term nursing care facilities.

- Thalidomide (Thalomid) is marketed only under a special restricted distribution program. Under that program, only registered prescribers and pharmacists are allowed to prescribe and dispense the product.

Patients must also be registered and participate in mandatory pregnancy testing prior to receiving the drug.

Q: Why is FDA requiring a physician to be able to provide surgical intervention or to provide a plan for obtaining those services for each woman using mifepristone?

A: Clinical trials and experience in countries where mifepristone is approved have shown that this regimen fails in five to eight of 100 women. Therefore, if the regimen fails and a woman still wants to terminate the pregnancy, a follow-up surgical procedure will be necessary and must be available.

Also, in about one of 100 women, bleeding can be so heavy that a surgical procedure will be required to stop the bleeding.

Q: Will FDA or the manufacturer establish a registry of physicians who have access to mifepristone?

A: Neither FDA nor the manufacturer has any plans to establish a registry of physicians.

Q: How can cancer patients obtain mifepristone?

A: Mifepristone is available for certain cancer patients through a single patient IND. Patients must be treated according to a specified treatment plan. The drug is provided by the Feminist Majority Foundation.

Pressure on FDA:

Q: There have been press reports that the politics of abortion have delayed FDA's action. How does the agency respond to those reports?

A: FDA is a scientific regulatory agency that makes decisions on the basis of science. The agency's review and approval of mifepristone adhered strictly to its legal mandate and mission as a science-based public health regulatory agency.

Draft 09/28/00
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Q: The average review time for priority drugs is now six months. The sponsor sent FDA its application in March, 1996. Why did this review take so much longer?

A: FDA sent the sponsor an "approvable" letter in September 1996, six months after receiving the application. The letter identified outstanding issues that needed to be resolved before FDA could approve mifepristone. The sponsor responded to those issues in September 1999. FDA issued another "approvable" letter in February, 2000, asking additional questions. The sponsor has now answered those questions.

Q: Some members of Congress have expressed their opposition to mifepristone. Could Congress overturn FDA's decision?

A: It would be unprecedented for Congress to overrule an FDA decision to approve a medical product.

Q: FDA is a regulatory agency in the executive branch of the Federal government. Could a new administration overrule FDA's approval of mifepristone?

A: As an executive branch agency in the Department of Health and Human Services, FDA has bases its judgments concerning medical and public health matters on sound science. FDA based its approval of mifepristone on data from clinical trials in the U.S. and in France. It would be unprecedented for a new administration to overrule an FDA decision to approve a medical product.

Q: Who manufactures and distributes mifepristone?

A: Danco Laboratories, LLC, based in New York City, distributes mifepristone. Neither the Population Council, the sponsor of this product, nor Danco Laboratories has disclosed the identity of the manufacturer.

Q: Why won't FDA disclose the identity and location of the manufacturing site?

A: Because many threats and acts of violence have been directed at persons associated with reproductive rights issues similar to those raised by mifepristone, FDA will not disclose the identity of the manufacturer or the manufacturing site.

Under these circumstances, this manufacturing information is considered confidential commercial information.

Q: Why is FDA withholding the names of its employees who reviewed the new drug application for mifepristone?

A: Because many threats and actions of violence have been directed at persons associated with reproductive rights issues similar to those raised by mifepristone, FDA will not disclose these employees' names. Under these circumstances, this employee information is considered personal privacy information.

The regimen:

Q: How can mifepristone be safely used?

A: Basically, a woman should follow all the instructions for taking the product. First, a woman must read the Medication Guide and sign the Patient Agreement Form.

Day 1: a patient will be given three 200 milligram tablets of mifepristone.

Day 3: a patient must return to determine if expulsion has occurred. (Expulsion is infrequent with mifepristone alone, happening only in five or six percent of cases.) If expulsion has not occurred, the patient will be given two 200 microgram tablets of misoprostol that she will take orally.

Day 14: the patient will return for a follow-up visit. This visit is very important to confirm that a complete termination of pregnancy has occurred.

Q: How did FDA conclude that mifepristone is safe when its use results in the termination of a pregnancy?

A: The sponsor submitted a new drug application to the FDA, seeking the agency's approval to market mifepristone for the termination of early pregnancy. FDA concluded that the results from the clinical trials established that mifepristone is safe and effective for its intended use. In its review and approval of this application, FDA adhered strictly to its legal mandate and mission as a science-based regulatory agency.

Q: Why did FDA require a second visit on Day 3, when the product is being studied and used in a U.S. clinical trial without a return visit on Day 3?

A: Mifepristone was approved on the basis of data from clinical trials, designed by the sponsor, in which every woman in the study was required to return to her physician for a second visit. Unless pregnancy termination through the use of mifepristone alone has been confirmed by clinical examination or an ultrasonographic scan, the woman will take misoprostol during this second visit.

A third visit, to confirm that a complete termination of pregnancy has occurred, is also required.

Q: Why can't all physicians prescribe mifepristone?

A: FDA is restricting the distribution of mifepristone to physicians with specific qualifications, such as the ability to diagnose a tubal pregnancy. These restrictions are designed to ensure safe and appropriate use of the product.

Q: Can nurse-practitioners, midwives, or others prescribe mifepristone? Why?

A: Some states allow physicians to supervise other health care practitioners such as certified registered nurse practitioners and nurse midwives, and these states may allow a supervised health care provider to dispense mifepristone.

Q: What about misoprostol? Is the use of misoprostol an unlabeled use?

A: Under the approved treatment regimen, misoprostol is administered on day three to help stimulate uterine contractions. This use of misoprostol is contained in the approved labeling of mifepristone. It is based on the clinical trials for the regimen of the two drugs, which FDA found to be safe and effective for the termination of early pregnancy.

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Q: The manufacturer of misoprostol just issued a warning to physicians not to use the drug in pregnant women, and there have been press reports that the manufacturer worked with FDA on this warning. How can FDA reconcile this warning with the approval of mifepristone when used with misoprostol?

A: Misoprostol (used alone) is currently approved for use in protecting patients from gastric ulcers induced by certain pain relievers. A women who is or may be pregnant – and who does NOT wish to terminate her pregnancy -- should know that she should not take misoprostol for prevention of gastric ulcers or any other reason.

The "Dear Doctor" letter issued by Searle on August 23, 2000, warns prescribers that misoprostol may cause abortion. It therefore emphasizes that misoprostol is contraindicated for use by any pregnant woman who does not wish to terminate her pregnancy.

As part of the mifepristone-misoprostol regimen, misoprostol is appropriate for use to terminate early pregnancy.

Q: Searle just distributed new labeling for its misoprostol product (Cytotec) that says the product is not approved for abortion. What is FDA's position on this labeling?

A: Now that FDA has approved the treatment plan for the use of mifepristone followed by the administration of misoprostol for the medical termination of intrauterine pregnancy through 49 days of pregnancy, the statement in the Searle label is inappropriate. FDA has asked that it be removed.

Patient Safety and Side Effects:

Q: What are the major side effects of mifepristone?

A: The Medication Guide provides information that women should be aware of concerning the incidence of side effects from administration of Mifeprex. These include cramping and, sometimes, heavy bleeding. After misoprostol administration on Day 3, there may be nausea, vomiting, and diarrhea. Before taking this medication, a woman must be fully aware of what to expect and will have to sign the Patient Agreement form.

The problems or side effects that women should be warned about include bleeding or spotting that is likely to occur from 9 to 16 days and that has been reported to last as long as 69 days. Up to eight percent of women may experience some kind of bleeding for 30 days or more. Surgical intervention may be needed to control the bleeding.

Q: What steps has FDA taken to ensure that women are adequately informed about how to use this regimen safely?

A: FDA is requiring that each woman who takes mifepristone receive a Medication Guide that clearly explains how to take the drug, who should avoid taking it, and what side effects can occur.

Each woman taking this drug must also read the Medication Guide and sign the patient agreement form before the drug will be administered.

Q: What if a woman changes her mind?

A: Among the many safeguards FDA has established for this treatment regimen are the requirements that each woman read the Medication Guide for mifepristone and that she also sign the Patient Agreement Form. These safeguards are designed to ensure that every woman knows and understands that this regimen is for the termination of early pregnancy and is committed to that course of action.

FDA and the sponsor have established a program to inform women about this regimen, including the risk of birth defects if the regimen does not end the pregnancy. Women are instructed that surgical termination may be needed, and the Patient Agreement Form certifies that they understand this possibility.

Q: Critics of this drug say it is dangerous to women and fetuses. How does FDA respond?

A: FDA and the sponsor have established a program to inform women about this regimen, including the risk of birth defects if the regimen does not end the pregnancy. Although the data on this risk are very limited, there are several reports in the medical literature of defects after first trimester exposure to prostaglandins, including misoprostol.

As of May 2000, 82 cases had been reported in which women with ongoing pregnancies after using mifepristone, alone or followed by misoprostol, declined to have a surgical procedure. Of those, follow-up information is available for 36. Twenty-six of those 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.

Q: Has the sponsor agreed to carry out postmarketing studies of mifepristone?

A: To gather additional data about the use of mifepristone, the Population Council has made a commitment to conduct postmarketing studies. These include a study comparing patient outcomes among physicians who refer their patients needing surgical intervention, compared to those who perform surgical procedures themselves; an audit of prescribers that will examine whether patients and their physicians are signing the patient agreement and placing it in the patient's medical record, as required; and a system for surveillance, reporting and tracking rare ongoing pregnancies after treatment with mifepristone in the U.S.

Q: The sponsor of mifepristone has agreed to conduct postmarketing studies involving this drug. Doesn't that mean FDA really thinks the regimen is unsafe?

A: No. It is not at all unusual for sponsors to conduct postmarketing studies on their approved products.

Access:

Q: Who may prescribe mifepristone?

A: The drug will be distributed only to physicians who can accurately determine the duration of a woman'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 for patients to obtain such care through others.

Q: Will it be available in pharmacies?

A: No. Mifepristone will be available only through qualified physicians.

Q: What health professionals will have access to mifepristone?

A: Some states allow physicians to supervise other health care practitioners such as certified registered nurse practitioners and nurse midwives, and these states may allow a supervised health care provider to dispense mifepristone.

Q: Will mifepristone be available over the Internet?

A: No. FDA and the sponsor have established a treatment regimen with many safeguards, including the direct distribution of the drug only to qualified physicians.

Q: In 1990 FDA issued an Import Alert that banned the importation of mifepristone into the United States. The drug was listed under several other names. Is that Import Alert still valid?

A: FDA issued this Import Alert because of safety concerns for people taking the unapproved drug without adequate supervision from a health care professional. Now that FDA has approved Mifeprex, the Import Alert has been revised to exempt this specific product from the alert. Formulations of mifepristone not covered by the NDA or by an IND in effect would still be denied entry into the U.S., however.

Q: Has mifepristone been studied for other uses? If so, will those studies continue?

A: Mifepristone is being studied for a variety of uses, because it can block steroid receptors. In particular, it is being investigated as a potential treatment for cancers whose tumors have progesterone receptors.

ADDITIONAL QUESTIONS AND ANSWERS—INERNAL USE ONLY

Q: Did the White House or Secretary Shalala intervene in FDA's review of mifepristone?

A: No. Neither the White House nor the Secretary were involved in FDA's decision. FDA based its decision on the science.

Q: Earlier this year there were reports that FDA was going to impose severe restrictions on the availability of mifepristone. What changed FDA's thinking?

A: Some early press reports on this issue were inaccurate. When FDA is nearing the end of a product review, give and take between the agency and the sponsor is normal.

Q: President Clinton in 1993 asked Secretary Shalala to see what could be done to expedite the availability of mifepristone. The Secretary in 1994 said that "FDA will do all it can to quickly evaluate mifepristone." What happened? Why did FDA not tell the sponsor until 1996 that mifepristone was "approvable?"

A: Many things had to occur before the FDA could take any action. The sponsor had to obtain patent rights to the drug, and this happened in May, 1994. The sponsor then had to identify a manufacturer for the drug, file an IND with the FDA, and design and conduct clinical studies of the product. Finally, the sponsor had to analyze the data and submit a marketing application to the FDA.

FDA received the new drug application in March 1996. It began reviewing the application immediately, held an advisory committee meeting in July, and issued an "approvable" letter in September 1996.

Q: Who made the decision to approve mifepristone?

A: Many FDA employees contribute to the review and approval of a new product. The "approval" letter FDA sends to the sponsor is typically signed by a senior official.

In the case of mifepristone, FDA is not disclosing the identity of the reviewers and others who reviewed this application.

Q: What about reports that FDA has hired armed guards and heightened security?

A: FDA does not comment on security matters.

External Q & A's for FDA's Web Site

1. What is MIFEPREX (mifepristone) and how does it work?
Mifepristone is a drug that blocks a hormone called progesterone that is needed for pregnancy to continue. Mifepristone, when used together with another medicine called misoprostol, is used to end an early pregnancy (49 days or less since your last menstrual period began).

2. Is mifepristone approved in any other countries?
Yes, mifepristone is approved in many other countries including France, the United Kingdom, and Sweden.

3. Who should not take mifepristone?
Some women should not take mifepristone. Do not take mifepristone if it has been more than 49 days since your last menstrual period or if you have:

- a tubal pregnancy
- an intrauterine device (IUD) in place (It must be removed before you take mifepristone)
- problems with your adrenal glands (the glands near your kidneys)
- been treated with certain steroid medications for a long period of time
- bleeding problems or are taking anticoagulant (blood thinning) drug products
- had an allergic reaction to mifepristone, misoprostol or similar drugs

It is important that you understand the need for 2 follow-up visits with your health care provider and that you have access to a medical care facility in case of an emergency.

Mifepristone has not been studied in women who are heavy smokers. Please tell your doctor if you smoke more than 10 cigarettes a day.

4. Is mifepristone distribution restricted?
Yes, mifepristone is supplied directly to doctors who meet certain qualifications. It is not and will not be available in pharmacies, and it is not legally available over the Internet.

5. Why are there restrictions for this drug?
Studies of mifepristone were conducted by doctors who had certain qualifications. Both the drug sponsor and the 1996 Reproductive Drug Products Advisory Committee also recommended that FDA restrict distribution of mifepristone to qualified doctors. FDA has concluded that these restrictions are necessary for the safe use of the drug.

6. What qualifications must doctors have to obtain mifepristone?
Doctors must have the ability to date pregnancies accurately and to diagnose tubal pregnancies. Doctors must also be qualified to provide any necessary surgery, or have

made arrangements for any necessary surgery. Doctors must ensure 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.

7. What authority does FDA have to restrict distribution of a drug?
The law authorizes FDA to approve new drugs only if they have been demonstrated to be safe and effective for use under the conditions of use recommended in the label. FDA has broad authority to require restrictions on distribution to ensure safe and effective use. FDA's full legal authority to restrict distribution of a drug is described in more detail in the preamble to agency drug regulations. **(LINK to CRF or scanned copy)**

8. Can health care providers other than doctors dispense mifepristone?
Some states allow physicians to supervise other health care practitioners, such as certified registered nurse practitioners and nurse midwives, and these states may allow a supervised health care provider to dispense mifepristone. Health care providers should check their state law provisions.

9. Is there an age restriction for termination of pregnancy?
States may set age restrictions on termination of pregnancy if they believe such restrictions are appropriate.

10. Are there studies with mifepristone in women under the age of 18?
Studies to evaluate mifepristone included women ages 18-45.

11. What are the possible side effects of using mifepristone?
Mifepristone treatment will cause vaginal bleeding. In some cases vaginal bleeding can be very heavy. In a few cases, this bleeding will need to be stopped by a surgical procedure.

Other possible side effects of the treatment include diarrhea, nausea, vomiting, headache, dizziness, back pain, and tiredness.

The possible side effects are described in the Medication Guide. Please read the **Medication Guide (LINK).**

12. What is a Medication Guide?
A Medication Guide contains FDA-approved information, written especially for patients.

13. Why did FDA develop a Medication Guide for mifepristone?
FDA determined that a Medication Guide was necessary for women to be able to use mifepristone effectively and safely. It is important for women to be fully informed about how mifepristone works and about its risks, as well as the need for follow-up visits with their health care provider, especially on the 14th day after mifepristone is administered. The Medication Guide will help ensure that women follow the directions for use and that they return to their health care provider for follow-up visits.

Before you receive mifepristone, your doctor will provide you with the Medication Guide and ask you to sign a statement (Patient Agreement) that you have decided to end your pregnancy.

14. Can I become pregnant again if I take mifepristone?
You can become pregnant again right after your pregnancy ends. If you do not want to become pregnant again, start using a birth control method of your choice as soon as your pregnancy ends.

15. Does FDA endorse the use of this drug?
FDA does not endorse or promote any drug product. The agency evaluates all drug applications submitted by sponsors to determine whether a drug is safe and effective for its proposed indication under the conditions of use in the labeling. This means that the benefits of the drug outweigh its risks. The same standards were applied to the new drug application for mifepristone as are applied to all applications.

16. How much will mifepristone cost?
Manufacturers establish prices for prescription drugs. FDA has no jurisdiction over drug pricing.

17. Will insurance companies pay for mifepristone?
Insurance coverage is a decision made by your insurance provider. Please call your insurance company if you have questions.

File: Choice/RJ-486

HHS NEWS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

P00-19
September 28, 2000
FOR IMMEDIATE RELEASE

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FDA APPROVES MIFEPRISTONE FOR THE TERMINATION OF EARLY PREGNANCY

The Food and Drug Administration today 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.

Under the approved treatment regimen, a woman first takes 600 milligrams of mifepristone (three 200 milligram pills) by mouth. Two days later, she takes 400 micrograms (two 200-microgram pills) of misoprostol, a prostaglandin. Women will return for a follow-up visit approximately 14 days after taking mifepristone to determine whether the pregnancy has been terminated.

Because of the importance of adhering to this treatment regimen, each woman receiving mifepristone will be given a Medication Guide that clearly explains how to take the drug, who should avoid taking it, and what side

-More-

ATTENTION TV BROADCASTERS: Please use open caption for the hearing impaired.

effects can occur.

"The approval of mifepristone is the result of the FDA's careful evaluation of the scientific evidence related to the safe and effective use of this drug," said Jane E. Henney, M.D., Commissioner of Food and Drugs. "The FDA's review and approval of this drug has adhered strictly to our legal mandate and mission as a science-based public health regulatory agency."

FDA based its approval of mifepristone on data from clinical trials in the United States and France.

The labeling for mifepristone emphasizes that most women using the product will experience some side effects, primarily cramping and bleeding. Bleeding and spotting typically last for between 9 and 16 days. In about one of 100 women, bleeding can be so heavy that a surgical procedure will be required to stop the bleeding.

The drug's labeling also warns that it should not be used in women with the following conditions:

- Confirmed or suspected ectopic ("tubal") pregnancies
- Intrauterine device (IUD) in place
- Chronic failure of the adrenal glands

-More-

- Current long-term therapy with corticosteroids
- History of allergy to mifepristone, misoprostol or other prostaglandins
- Bleeding disorders or current anticoagulant (blood-thinning) therapy.

Under the terms of the approval, mifepristone 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.

To gather additional data about the use of mifepristone, the Population Council (sponsor of the product) has made a commitment to conduct postmarketing studies. These include a study comparing patient outcomes among physicians who refer their patients needing surgical intervention, compared to those who perform surgical procedures themselves; an audit of prescribers that will examine whether patients and their physicians are signing the patient agreement and placing it in the patient's

medical record, as required; and a system for surveillance, reporting and tracking rare ongoing pregnancies after treatment with mifepristone in the U.S.

Mifepristone, which was developed by a French pharmaceutical firm, was first approved for use in France in 1988. Since then, more than 620,000 European women have taken mifepristone in combination with a prostaglandin to terminate pregnancy. The drug has also been approved in the United Kingdom, Sweden, and other countries.

Mifepristone will be distributed in the U.S. by Danco Laboratories, LLC, New York, N.Y.

More detailed information about this product is available on FDA's website at http://www.fda.gov/cder/drug/infopage/mifepristone/

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HHS NEWS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

P00-19
September 28, 2000
FOR IMMEDIATE RELEASE

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FDA APPROVES MIFEPRISTONE FOR THE TERMINATION OF EARLY PREGNANCY

The Food and Drug Administration today 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.

Under the approved treatment regimen, a woman first takes 600 milligrams of mifepristone (three 200 milligram pills) by mouth. Two days later, she takes 400 micrograms (two 200-microgram pills) of misoprostol, a prostaglandin. Women will return for a follow-up visit approximately 14 days after taking mifepristone to determine whether the pregnancy has been terminated.

Because of the importance of adhering to this treatment regimen, each woman receiving mifepristone will be given a Medication Guide that clearly explains how to take the drug, who should avoid taking it, and what side

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effects can occur.

"The approval of mifepristone is the result of the FDA's careful evaluation of the scientific evidence related to the safe and effective use of this drug," said Jane E. Henney, M.D., Commissioner of Food and Drugs. "The FDA's review and approval of this drug has adhered strictly to our legal mandate and mission as a science-based public health regulatory agency."

FDA based its approval of mifepristone on data from clinical trials in the United States and France.

The labeling for mifepristone emphasizes that most women using the product will experience some side effects, primarily cramping and bleeding. Bleeding and spotting typically last for between 9 and 16 days. In about one of 100 women, bleeding can be so heavy that a surgical procedure will be required to stop the bleeding.

The drug's labeling also warns that it should not be used in women with the following conditions:

- Confirmed or suspected ectopic ("tubal") pregnancies
- Intrauterine device (IUD) in place
- Chronic failure of the adrenal glands

- Current long-term therapy with corticosteroids
- History of allergy to mifepristone, misoprostol or other prostaglandins
- Bleeding disorders or current anticoagulant (blood-thinning) therapy.

Under the terms of the approval, mifepristone 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.

To gather additional data about the use of mifepristone, the Population Council (sponsor of the product) has made a commitment to conduct postmarketing studies. These include a study comparing patient outcomes among physicians who refer their patients needing surgical intervention, compared to those who perform surgical procedures themselves; an audit of prescribers that will examine whether patients and their physicians are signing the patient agreement and placing it in the patient's

medical record, as required; and a system for surveillance, reporting and tracking rare ongoing pregnancies after treatment with mifepristone in the U.S.

Mifepristone, which was developed by a French pharmaceutical firm, was first approved for use in France in 1988. Since then, more than 620,000 European women have taken mifepristone in combination with a prostaglandin to terminate pregnancy. The drug has also been approved in the United Kingdom, Sweden, and other countries.

Mifepristone will be distributed in the U.S. by Danco Laboratories, LLC, New York, N.Y.

More detailed information about this product is available on FDA's website at http://www.fda.gov/cder/drug/infopage/mifepristone/

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DEPARTMENT OF HEALTH & HUMAN SERVICES

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Questions and Answers on Mifepristone: INTERNAL USE ONLY

General

Q: What action did FDA take today?

A: Today, FDA approved mifepristone (trade name Mifeprex) for the termination of early pregnancy. The drug is approved to end pregnancies of 49 days or less, counting from the beginning of the last menstrual period.

Q: What treatment regimen did FDA approve?

A: The drug (mifepristone) is administered to a woman by mouth. Two days later, the woman returns to her doctor for oral administration of misoprostol, a prostaglandin that helps cause uterine contractions. Patients will return for a follow-up visit approximately 14 days after taking mifepristone to determine whether the pregnancy has been terminated.

Q: What is the basis for FDA's approval of this regimen?

A: FDA based its approval of mifepristone on data from clinical trials in the United States and in France.

Q: How effective was the regimen in clinical trials?

A: In the U.S. trials, medical termination of pregnancy was complete in 92% of the 827 women in the efficacy study – approximately six percent with mifepristone alone, and the remainder with mifepristone followed by misoprostol. In eight percent of patients, surgical intervention was required. Fewer than 1% of patients had ongoing pregnancies.

In the French trials, more than 95% of the 1,681 women experienced complete termination of pregnancy, 5.3% without misoprostol and the rest after taking both drugs. Surgical intervention was required in 4.5% of women.

Q: Is this the first drug approved in the U.S. for the termination of pregnancy?

A: No. Two other drugs are approved for the termination of pregnancy.

Restrictions

Q: What restrictions did FDA place on the use and distribution of this drug?

A: The drug may only be distributed to physicians who can accurately determine the duration of a woman'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.

FDA approved mifepristone under its "Subpart H" regulations, which specifically allow FDA to establish appropriate controls on the distribution of a drug.

Q: What about distribution?

A: Mifepristone will be distributed directly to qualified physicians. It will not be available through pharmacies or on the Internet.

Q: What decisions has FDA made about labeling this product?

A: FDA is requiring a "black box" warning in the mifepristone labeling for physicians. The "black box" warns that surgical intervention may be necessary and addresses the care patients should receive should such intervention be necessary. In addition, because of the importance of adhering to this treatment regimen, each woman receiving mifepristone will be given a Medication Guide that clearly explains how to take the drug, who should avoid taking it, and what side effects can occur. This Guide is also referenced in the "black box."

Q: Why did FDA impose these restrictions?

A: FDA always seeks to ensure that the products it approves are used appropriately, so that risks are minimized and benefits are maximized. FDA believes that, for this drug, these restrictions are needed to ensure safe use.

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In addition, the agency believes that women should have as much accurate information as possible to make an informed decision about this regimen.

Q: According to FDA regulations, Subpart "H" applies to drugs for serious and life-threatening illnesses. Isn't it overkill to invoke this provision for the mifepristone regimen?

A: The sponsor proposed a restricted distribution system for its product, and the FDA advisory committee that discussed this application in July 1996 also recommended such a system. FDA has concluded that the termination of unwanted pregnancy is a serious condition, and that these restrictions are necessary for the safe use of this drug.

Moreover, mifepristone's distribution is typically restricted in other countries where it has been approved. FDA has concluded that establishing certain controls on the distribution of this drug are needed to help ensure that it is used appropriately.

Q: Has distribution of any other drugs been restricted? What are some examples?

A: The distribution of several other drugs has been restricted to assure that they are used safely. For example:

- Clozapine (Clozaril), a drug used to manage severe schizophrenia, is available only through a registry system that ensures monitoring of certain blood test results prior to the delivery of the drug.

- Transmucosal fentanyl (Oralet), a potent analgesic delivered on a lollipop as premedication in pediatric patients before surgery or before painful procedures, is restricted to certain registered hospitals, and is not available retail pharmacy outlets.

- The manufacturer of trovafloxacin/alatrofloxacin mesylate (Trovan/Trovan-IV) agreed to limit distribution only to hospitals and long-term nursing care facilities.

- Thalidomide (Thalomid) is marketed only under a special restricted distribution program. Under that program, only registered prescribers and pharmacists are allowed to prescribe and dispense the product.

Patients must also be registered and participate in mandatory pregnancy testing prior to receiving the drug.

Q: Why is FDA requiring a physician to be able to provide surgical intervention or to provide a plan for obtaining those services for each woman using mifepristone?

A: Clinical trials and experience in countries where mifepristone is approved have shown that this regimen fails in five to eight of 100 women. Therefore, if the regimen fails and a woman still wants to terminate the pregnancy, a follow-up surgical procedure will be necessary and must be available.

Also, in about one of 100 women, bleeding can be so heavy that a surgical procedure will be required to stop the bleeding.

Q: Will FDA or the manufacturer establish a registry of physicians who have access to mifepristone?

A: Neither FDA nor the manufacturer has any plans to establish a registry of physicians.

Q: How can cancer patients obtain mifepristone?

A: Mifepristone is available for certain cancer patients through a single patient IND. Patients must be treated according to a specified treatment plan. The drug is provided by the Feminist Majority Foundation.

<u>Pressure on FDA</u>:

Q: There have been press reports that the politics of abortion have delayed FDA's action. How does the agency respond to those reports?

A: FDA is a scientific regulatory agency that makes decisions on the basis of science. The agency's review and approval of mifepristone adhered strictly to its legal mandate and mission as a science-based public health regulatory agency.

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Q: The average review time for priority drugs is now six months. The sponsor sent FDA its application in March, 1996. Why did this review take so much longer?

A: FDA sent the sponsor an "approvable" letter in September 1996, six months after receiving the application. The letter identified outstanding issues that needed to be resolved before FDA could approve mifepristone. The sponsor responded to those issues in September 1999. FDA issued another "approvable" letter in February, 2000, asking additional questions. The sponsor has now answered those questions.

Q: Some members of Congress have expressed their opposition to mifepristone. Could Congress overturn FDA's decision?

A: It would be unprecedented for Congress to overrule an FDA decision to approve a medical product.

Q: FDA is a regulatory agency in the executive branch of the Federal government. Could a new administration overrule FDA's approval of mifepristone?

A: As an executive branch agency in the Department of Health and Human Services, FDA has bases its judgments concerning medical and public health matters on sound science. FDA based its approval of mifepristone on data from clinical trials in the U.S. and in France. It would be unprecedented for a new administration to overrule an FDA decision to approve a medical product.

Q: Who manufactures and distributes mifepristone?

A: Danco Laboratories, LLC, based in New York City, distributes mifepristone. Neither the Population Council, the sponsor of this product, nor Danco Laboratories has disclosed the identity of the manufacturer.

Q: Why won't FDA disclose the identity and location of the manufacturing site?

A: Because many threats and acts of violence have been directed at persons associated with reproductive rights issues similar to those raised by mifepristone, FDA will not disclose the identity of the manufacturer or the manufacturing site.

Under these circumstances, this manufacturing information is considered confidential commercial information.

Q: Why is FDA withholding the names of its employees who reviewed the new drug application for mifepristone?

A: Because many threats and actions of violence have been directed at persons associated with reproductive rights issues similar to those raised by mifepristone, FDA will not disclose these employees' names. Under these circumstances, this employee information is considered personal privacy information.

The regimen:

Q: How can mifepristone be safely used?

A: Basically, a woman should follow all the instructions for taking the product. First, a woman must read the Medication Guide and sign the Patient Agreement Form.

Day 1: a patient will be given three 200 milligram tablets of mifepristone.

Day 3: a patient must return to determine if expulsion has occurred. (Expulsion is infrequent with mifepristone alone, happening only in five or six percent of cases.) If expulsion has not occurred, the patient will be given two 200 microgram tablets of misoprostol that she will take orally.

Day 14: the patient will return for a follow-up visit. This visit is very important to confirm that a complete termination of pregnancy has occurred.

Q: How did FDA conclude that mifepristone is safe when its use results in the termination of a pregnancy?

A: The sponsor submitted a new drug application to the FDA, seeking the agency's approval to market mifepristone for the termination of early pregnancy. FDA concluded that the results from the clinical trials established that mifepristone is safe and effective for its intended use. In its review and approval of this application, FDA adhered strictly to its legal mandate and mission as a science-based regulatory agency.

Q: Why did FDA require a second visit on Day 3, when the product is being studied and used in a U.S. clinical trial without a return visit on Day 3?

A: Mifepristone was approved on the basis of data from clinical trials, designed by the sponsor, in which every woman in the study was required to return to her physician for a second visit. Unless pregnancy termination through the use of mifepristone alone has been confirmed by clinical examination or an ultrasonographic scan, the woman will take misoprostol during this second visit.

A third visit, to confirm that a complete termination of pregnancy has occurred, is also required.

Q: Why can't all physicians prescribe mifepristone?

A: FDA is restricting the distribution of mifepristone to physicians with specific qualifications, such as the ability to diagnose a tubal pregnancy. These restrictions are designed to ensure safe and appropriate use of the product.

Q: Can nurse-practitioners, midwives, or others prescribe mifepristone? Why?

A: Some states allow physicians to supervise other health care practitioners such as certified registered nurse practitioners and nurse midwives, and these states may allow a supervised health care provider to dispense mifepristone.

Q: What about misoprostol? Is the use of misoprostol an unlabeled use?

A: Under the approved treatment regimen, misoprostol is administered on day three to help stimulate uterine contractions. This use of misoprostol is contained in the approved labeling of mifepristone. It is based on the clinical trials for the regimen of the two drugs, which FDA found to be safe and effective for the termination of early pregnancy.

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Q: The manufacturer of misoprostol just issued a warning to physicians not to use the drug in pregnant women, and there have been press reports that the manufacturer worked with FDA on this warning. How can FDA reconcile this warning with the approval of mifepristone when used with misoprostol?

A: Misoprostol (used alone) is currently approved for use in protecting patients from gastric ulcers induced by certain pain relievers. A women who is or may be pregnant – and who does NOT wish to terminate her pregnancy -- should know that she should not take misoprostol for prevention of gastric ulcers or any other reason.

The "Dear Doctor" letter issued by Searle on August 23, 2000, warns prescribers that misoprostol may cause abortion. It therefore emphasizes that misoprostol is contraindicated for use by any pregnant woman who does not wish to terminate her pregnancy.

As part of the mifepristone-misoprostol regimen, misoprostol is appropriate for use to terminate early pregnancy.

Q: Searle just distributed new labeling for its misoprostol product (Cytotec) that says the product is not approved for abortion. What is FDA's position on this labeling?

A: Now that FDA has approved the treatment plan for the use of mifepristone followed by the administration of misoprostol for the medical termination of intrauterine pregnancy through 49 days of pregnancy, the statement in the Searle label is inappropriate. FDA has asked that it be removed.

<u>Patient Safety and Side Effects</u>:

Q: What are the major side effects of mifepristone?

A: The Medication Guide provides information that women should be aware of concerning the incidence of side effects from administration of Mifeprex. These include cramping and, sometimes, heavy bleeding. After misoprostol administration on Day 3, there may be nausea, vomiting, and diarrhea. Before taking this medication, a woman must be fully aware of what to expect and will have to sign the Patient Agreement form.

The problems or side effects that women should be warned about include bleeding or spotting that is likely to occur from 9 to 16 days and that has been reported to last as long as 69 days. Up to eight percent of women may experience some kind of bleeding for 30 days or more. Surgical intervention may be needed to control the bleeding.

Q: What steps has FDA taken to ensure that women are adequately informed about how to use this regimen safely?

A: FDA is requiring that each woman who takes mifepristone receive a Medication Guide that clearly explains how to take the drug, who should avoid taking it, and what side effects can occur.

Each woman taking this drug must also read the Medication Guide and sign the patient agreement form before the drug will be administered.

Q: What if a woman changes her mind?

A: Among the many safeguards FDA has established for this treatment regimen are the requirements that each woman read the Medication Guide for mifepristone and that she also sign the Patient Agreement Form. These safeguards are designed to ensure that every woman knows and understands that this regimen is for the termination of early pregnancy and is committed to that course of action.

FDA and the sponsor have established a program to inform women about this regimen, including the risk of birth defects if the regimen does not end the pregnancy. Women are instructed that surgical termination may be needed, and the Patient Agreement Form certifies that they understand this possibility.

Q: Critics of this drug say it is dangerous to women and fetuses. How does FDA respond?

A: FDA and the sponsor have established a program to inform women about this regimen, including the risk of birth defects if the regimen does not end the pregnancy. Although the data on this risk are very limited, there are several reports in the medical literature of defects after first trimester exposure to prostaglandins, including misoprostol.

As of May 2000, 82 cases had been reported in which women with ongoing pregnancies after using mifepristone, alone or followed by misoprostol, declined to have a surgical procedure. Of those, follow-up information is available for 36. Twenty-six of those 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.

Q: Has the sponsor agreed to carry out postmarketing studies of mifepristone?

A: To gather additional data about the use of mifepristone, the Population Council has made a commitment to conduct postmarketing studies. These include a study comparing patient outcomes among physicians who refer their patients needing surgical intervention, compared to those who perform surgical procedures themselves; an audit of prescribers that will examine whether patients and their physicians are signing the patient agreement and placing it in the patient's medical record, as required; and a system for surveillance, reporting and tracking rare ongoing pregnancies after treatment with mifepristone in the U.S.

Q: The sponsor of mifepristone has agreed to conduct postmarketing studies involving this drug. Doesn't that mean FDA really thinks the regimen is unsafe?

A: No. It is not at all unusual for sponsors to conduct postmarketing studies on their approved products.

Access:

Q: Who may prescribe mifepristone?

A: The drug will be distributed only to physicians who can accurately determine the duration of a woman'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 for patients to obtain such care through others.

Q: Will it be available in pharmacies?

A: No. Mifepristone will be available only through qualified physicians.

Q: What health professionals will have access to mifepristone?

A: Some states allow physicians to supervise other health care practitioners such as certified registered nurse practitioners and nurse midwives, and these states may allow a supervised health care provider to dispense mifepristone.

Q: Will mifepristone be available over the Internet?

A: No. FDA and the sponsor have established a treatment regimen with many safeguards, including the direct distribution of the drug only to qualified physicians.

Q: In 1990 FDA issued an Import Alert that banned the importation of mifepristone into the United States. The drug was listed under several other names. Is that Import Alert still valid?

A: FDA issued this Import Alert because of safety concerns for people taking the unapproved drug without adequate supervision from a health care professional. Now that FDA has approved Mifeprex, the Import Alert has been revised to exempt this specific product from the alert. Formulations of mifepristone not covered by the NDA or by an IND in effect would still be denied entry into the U.S., however.

Q: Has mifepristone been studied for other uses? If so, will those studies continue?

A: Mifepristone is being studied for a variety of uses, because it can block steroid receptors. In particular, it is being investigated as a potential treatment for cancers whose tumors have progesterone receptors.

ADDITIONAL QUESTIONS AND ANSWERS—INERNAL USE ONLY

Q: Did the White House or Secretary Shalala intervene in FDA's review of mifepristone?

A: No. Neither the White House nor the Secretary were involved in FDA's decision. FDA based its decision on the science.

Q: Earlier this year there were reports that FDA was going to impose severe restrictions on the availability of mifepristone. What changed FDA's thinking?

A: Some early press reports on this issue were inaccurate. When FDA is nearing the end of a product review, give and take between the agency and the sponsor is normal.

Q: President Clinton in 1993 asked Secretary Shalala to see what could be done to expedite the availability of mifepristone. The Secretary in 1994 said that "FDA will do all it can to quickly evaluate mifepristone." What happened? Why did FDA not tell the sponsor until 1996 that mifepristone was "approvable?"

A: Many things had to occur before the FDA could take any action. The sponsor had to obtain patent rights to the drug, and this happened in May, 1994. The sponsor then had to identify a manufacturer for the drug, file an IND with the FDA, and design and conduct clinical studies of the product. Finally, the sponsor had to analyze the data and submit a marketing application to the FDA.

FDA received the new drug application in March 1996. It began reviewing the application immediately, held an advisory committee meeting in July, and issued an "approvable" letter in September 1996.

Q: Who made the decision to approve mifepristone?

A: Many FDA employees contribute to the review and approval of a new product. The "approval" letter FDA sends to the sponsor is typically signed by a senior official.

In the case of mifepristone, FDA is not disclosing the identity of the reviewers and others who reviewed this application.

Q: What about reports that FDA has hired armed guards and heightened security?

A: FDA does not comment on security matters.

External Q & A's for FDA's Web Site

1. What is MIFEPREX (mifepristone) and how does it work?
Mifepristone is a drug that blocks a hormone called progesterone that is needed for pregnancy to continue. Mifepristone, when used together with another medicine called misoprostol, is used to end an early pregnancy (49 days or less since your last menstrual period began).

2. Is mifepristone approved in any other countries?
Yes, mifepristone is approved in many other countries including France, the United Kingdom, and Sweden.

3. Who should not take mifepristone?
Some women should not take mifepristone. Do not take mifepristone if it has been more than 49 days since your last menstrual period or if you have:

- a tubal pregnancy
- an intrauterine device (IUD) in place (It must be removed before you take mifepristone)
- problems with your adrenal glands (the glands near your kidneys)
- been treated with certain steroid medications for a long period of time
- bleeding problems or are taking anticoagulant (blood thinning) drug products
- had an allergic reaction to mifepristone, misoprostol or similar drugs

It is important that you understand the need for 2 follow-up visits with your health care provider and that you have access to a medical care facility in case of an emergency.

Mifepristone has not been studied in women who are heavy smokers. Please tell your doctor if you smoke more than 10 cigarettes a day.

4. Is mifepristone distribution restricted?
Yes, mifepristone is supplied directly to doctors who meet certain qualifications. It is not and will not be available in pharmacies, and it is not legally available over the Internet.

5. Why are there restrictions for this drug?
Studies of mifepristone were conducted by doctors who had certain qualifications. Both the drug sponsor and the 1996 Reproductive Drug Products Advisory Committee also recommended that FDA restrict distribution of mifepristone to qualified doctors. FDA has concluded that these restrictions are necessary for the safe use of the drug.

6. What qualifications must doctors have to obtain mifepristone?
Doctors must have the ability to date pregnancies accurately and to diagnose tubal pregnancies. Doctors must also be qualified to provide any necessary surgery, or have

made arrangements for any necessary surgery. Doctors must ensure 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.

7. What authority does FDA have to restrict distribution of a drug?
The law authorizes FDA to approve new drugs only if they have been demonstrated to be safe and effective for use under the conditions of use recommended in the label. FDA has broad authority to require restrictions on distribution to ensure safe and effective use. FDA's full legal authority to restrict distribution of a drug is described in more detail in the preamble to agency drug regulations. **(LINK to CRF or scanned copy)**

8. Can health care providers other than doctors dispense mifepristone?
Some states allow physicians to supervise other health care practitioners, such as certified registered nurse practitioners and nurse midwives, and these states may allow a supervised health care provider to dispense mifepristone. Health care providers should check their state law provisions.

9. Is there an age restriction for termination of pregnancy?
States may set age restrictions on termination of pregnancy if they believe such restrictions are appropriate.

10. Are there studies with mifepristone in women under the age of 18?
Studies to evaluate mifepristone included women ages 18-45.

11. What are the possible side effects of using mifepristone?
Mifepristone treatment will cause vaginal bleeding. In some cases vaginal bleeding can be very heavy. In a few cases, this bleeding will need to be stopped by a surgical procedure.

Other possible side effects of the treatment include diarrhea, nausea, vomiting, headache, dizziness, back pain, and tiredness.

The possible side effects are described in the Medication Guide. Please read the **Medication Guide (LINK).**

12. What is a Medication Guide?
A Medication Guide contains FDA-approved information, written especially for patients.

13. Why did FDA develop a Medication Guide for mifepristone?
FDA determined that a Medication Guide was necessary for women to be able to use mifepristone effectively and safely. It is important for women to be fully informed about how mifepristone works and about its risks, as well as the need for follow-up visits with their health care provider, especially on the 14th day after mifepristone is administered. The Medication Guide will help ensure that women follow the directions for use and that they return to their health care provider for follow-up visits.

Before you receive mifepristone, your doctor will provide you with the Medication Guide and ask you to sign a statement (Patient Agreement) that you have decided to end your pregnancy.

14. Can I become pregnant again if I take mifepristone?
You can become pregnant again right after your pregnancy ends. If you do not want to become pregnant again, start using a birth control method of your choice as soon as your pregnancy ends.

15. Does FDA endorse the use of this drug?
FDA does not endorse or promote any drug product. The agency evaluates all drug applications submitted by sponsors to determine whether a drug is safe and effective for its proposed indication under the conditions of use in the labeling. This means that the benefits of the drug outweigh its risks. The same standards were applied to the new drug application for mifepristone as are applied to all applications.

16. How much will mifepristone cost?
Manufacturers establish prices for prescription drugs. FDA has no jurisdiction over drug pricing.

17. Will insurance companies pay for mifepristone?
Insurance coverage is a decision made by your insurance provider. Please call your insurance company if you have questions.