

**Abortion Standards for Northern Ireland:
Deficiencies of the RCOG Guideline Pertaining to Medical Abortion
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The Draft Guidance on abortion references and includes the Royal College of Obstetrics and Gynaecology (RCOG) Guideline¹ which encourages use of medical (non-surgical) abortion procedures using mifepristone. But the 2004 RCOG Guideline is out of date and gravely harmful to women's health regarding its recommendations for medical abortion. Even if the Guideline were amended according to information below, medical abortion remains much less safe and less effective than surgical abortion. Medical abortion endangers women's lives and health. Although there are many different protocols for medical abortion used worldwide and in the research literature, with various combinations of several different drugs, this report will focus specifically on the mifepristone and misoprostol combination used in the U.S. and recommended in the RCOG Guidelines, though as we will see, the specific doses and recommendations differ between the U.S. and U.K.

The 2004 RCOG Guideline is out of date, and was not informed by “real-world” experience. It was published prior to the 2006 report by Gary and Harrison² which evaluated 607 unique mifepristone Adverse Event Reports submitted to the U.S. Food and Drug Administration (FDA). Results included 237 hemorrhages (1 fatal, 42 life threatening, 168 serious cases; 68 requiring transfusions); infections, including 7 cases of septic shock (3 fatal, 4 life threatening) and 43 cases requiring parenteral antibiotics; and ectopic pregnancies. Surgery was required in 513 cases, including 235 emergency surgeries. Since this study, additional reports have been received by the FDA, bringing the total reports to 1070 as of April 2006.³ U.S. physicians are not required to report adverse events, and the FDA estimates it receives reports for only 1 – 10% of drug complications.⁴ There is reason to believe that only about 3-4% of mifepristone adverse events have actually been reported.⁵

The FDA webpage displays copies of FDA required product labeling information,⁶ a Medication Guide,⁷ and a Patient Agreement,⁸ by which patients and providers are cautioned concerning risk of various complications associated with mifepristone abortions, including ectopic pregnancy, infections, septic shock, excessive hemorrhage, possible need for transfusions or D & C's. This information was updated on July 19, 2005⁹ to reflect post-marketing experience including deaths related to mifepristone abortion. These warnings are not currently included or discussed within the RCOG Guideline.

A general problem in regard to safety and efficacy data is the scarcity of fully randomized controlled trials comparing medical to surgical abortions. In the few head to head comparisons, surgical abortion is shown to be safer and more effective.^{10,11,12,13,14,15}

The U.S. House of Representatives Government Reform Committee in its report “The FDA and RU-486: Lowering the Standard for Women's Health” points out that the FDA typically “requires data from two clinical trials that are randomized, blinded and controlled against a ‘comparator’—often a placebo but more typically an alternative therapy.”¹⁶ This report discusses the necessity of matched controls so that there is a truly comparable control group. However, the report states that in regard to the French and U.S. studies on which FDA approval was based, “these trials were uncontrolled.”¹⁷

The RCOG Guideline references a small review article in which Say et al. searched the literature for randomized studies in which surgical and medical abortion were compared. Say et al. found only five studies, comparing

→ The authors have consistently opposed abortion and continue to do so; however, a careful examination of the claims made in this submission should alert people of conscience on either side of this contentious issue to the safety problems experienced by those who use mifepristone as an abortifacient.

four different abortion methods, concluding, “The results are derived from relatively small trials,” and that “there is inadequate evidence to comment on the acceptability and side effects of medical compared to surgical first trimester abortions.”¹⁸

A few studies do exist which compare medical abortion with mifepristone to surgical abortion, though the following are not randomized trials as in each case women chose the type of abortion they preferred. Cabeza’s study of 500 women found the medical abortion group had more side effects (including bleeding, cramping, nausea and vomiting).¹⁹ Elul et al. reported on data from 1,373 women in China, Cuba and India, finding that medical abortion patients at all locations experienced more side effects than surgical patients, particularly bleeding and pain.²⁰ Jensen’s study of 377 patients found more side effects (pain, nausea, vomiting and bleeding) in the medical abortion group.²¹ Each of these studies showed a higher failure rate for medical abortion.

According to the FDA’s medical review, written prior to initial U.S. approval, medical abortion patients had “far more frequent” nausea, vomiting, and cramping, than surgical abortion patients.²² This report also stated failure rates were higher for medical abortion, and that blood loss was significantly higher with medical compared to surgical abortion.²³

Bleeding that continues for a month or more after medical abortion has frequently been reported after medical abortion. Dr. James McGregor, speaking at a workshop presented by the U.S. Centers for Disease Control (CDC) and FDA, discussed a study from 1986 in which “many patients had prolonged, over a month of abnormal bleeding.”²⁴ The FDA product label information for mifepristone states, “According to data from the U.S. and French clinical trial studies, women should expect to experience vaginal bleeding or spotting for an average of nine to 16 days. Up to 8% of women may experience some type of bleeding for more than 30 days.”²⁵ The International Inquiry Commission on RU-486 expressed concern about uterine bleeding in over 90% of cases, lasting from 1 to 35 days, “in many cases an emergency” requiring surgery or transfusion.²⁶

In some cases, the bleeding is of massive proportions well beyond the amount of bleeding typically experienced in usual gynecological cases. Dr. Donna Harrison, co-author of a published report on 607 of the Adverse Event Reports received by the FDA on mifepristone, testified before a U.S. Congressional committee regarding the severity of some of the cases: “In my experience as an ob-gyn, the volume of blood loss seen in the life-threatening cases is comparable to that observed in major surgical trauma cases like motor-vehicle accidents. This volume of blood loss is rarely seen in early surgical abortion without perforation of the uterus, and it is rarely seen in spontaneous abortions.”²⁷

In her testimony, discussing studies from the U.S. and a number of international locations, Harrison concluded that the risk of a hemorrhage serious enough to require transfusion was between 0.1% to 0.2% (one to two per thousand).²⁸ Harrison concluded that the risk of hemorrhage from mifepristone abortions is much greater than the risk of hemorrhage from surgical abortion.²⁹

While some cases of severe hemorrhage do require transfusion, more frequently cases of severe bleeding are managed surgically. The FDA Medication Guide for mifepristone states that “in about 1 out of 100 women, bleeding can be so heavy that it requires a surgical procedure (surgical abortion/D&C) to stop it.”³⁰ The Medication Guide gives specific patient information as to how much bleeding is too much and when the patient should seek emergency treatment for bleeding, since it is expected that some women will have serious bleeding requiring surgical intervention following medical abortion. In fact, the mifepristone product label states that in the clinical trials that led to FDA approval, 5% of U.S. women experienced “uterine hemorrhage” and 6% of the French experienced a “decrease in hemoglobin greater than 2 g/dL.”³¹

RCOG Guideline does not address this serious risk of hemorrhage, stating, “The risk of hemorrhage at the time of abortion is low. It complicates around 1 in 1000 abortions overall.”³² Here, the Guideline appears to be referring to the risk of hemorrhage from all types of abortions in the UK, as it states, “The above rates of haemorrhage at the time of abortion are taken from National Office for Statistics . . . via the notification

process,” adding that “criteria for reporting are ill-defined and it is not known whether or not all these cases required transfusion.”³³ It is not stated whether the National Office for Statistics is plagued by a similar degree of under-reporting as is recognized for the FDA, but in any case it seems clear that the report is considering hemorrhaging after abortion generally, and not the specific case of medical abortion. Additionally it seems clear that there is some uncertainty as to the reporting.

Further along in the Guideline, in the section specifically pertaining to methods of medical abortion, a large study by Ashok is cited.^{34, 35} Conducted at the University of Aberdeen, this large study (4131 cases after one woman dropped out) reported 61 cases of serious bleeding, serious enough to require surgery, transfusion, or treatment with oxytocics. Although only 0.2% (two per thousand) required transfusion, a total of 1.5% actually had serious bleeding problems (calculations our own based on 61 women out of 4,131 reported as requiring surgery, transfusion or oxytocics for heavy bleeding). This is in the same range as that estimated by Dr. Harrison (above) and by the FDA’s Medication Guide for mifepristone (as above). Within the RCOG Guideline, the Calman scheme is used to describe “the degree of risk of complications and sequelae associated with abortions.”³⁶ In this scheme, shown in Table 5.1 of the Guideline, a risk occurring between 1 in 1,000 and 1 in 100 is considered moderate, while a risk greater than 1 in 100 is considered high.³⁷ By this definition, the risk of serious hemorrhage after medical abortion should not be described as “low.”

RCOG Guideline does not discuss mifepristone’s serious effects in disrupting the innate immune system. In an animal study, mifepristone increased death rate from sepsis from 13% to 100%.³⁸ “Numerous studies have been done which...show increased lethality in animal models in the presence of RU-486 or mifepristone.”³⁹ Immune system inhibition was a concern of the International Inquiry Commission on RU 486.⁴⁰ “During a mifepristone-induced abortion, the blockade of glucocorticoid receptors by mifepristone results in the disruption of the innate immune system.”⁴¹

There have now been six North American deaths from septic shock due to *Clostridium sordellii* in young women who have had medical abortion with mifepristone and misoprostol.⁴² Research presented at the Centers for Disease Control and Prevention (CDC)-FDA Workshop on “Emerging *Clostridial* Disease” supports a causal relationship between mifepristone immune suppression and death from *Clostridial* sepsis.^{43, 44} This workshop also reported on additional cases of medical abortion patients who have died of *Clostridium perfringens* infection which were at the time still being investigated.⁴⁵

Recommendations regarding infection control do not discuss possible infection with *C. sordellii*, nor atypical presentation of infection. At the CDC-FDA workshop on *Clostridial* disease, Dr. Marc Fischer said, “*C. sordellii* toxic shock syndrome. . . is an acute and rapidly progressive disease that is characterized by a lack of or minimal fever.”⁴⁶ The FDA Public Health Advisory: Sepsis and Medical Abortion points out that deaths have occurred without fever and other usual signs and symptoms of an infection.⁴⁷

Following the third and fourth mifepristone associated deaths, on July 19, 2005, the FDA updated the Mifeprex (mifepristone) Label,⁴⁸ Medication Guide,⁴⁹ and Patient Agreement⁵⁰ for Mifeprex (mifepristone) to include information concerning infection with *C. sordellii*.^{51, 52} The updated prescribing information alerts abortion providers and emergency room health care providers concerning how to evaluate for this diagnosis in patients who may not present with usual signs of infection. The information given to patients advises them as to what symptoms require emergency evaluation. Because the infections have had atypical presentations, and also have had a rapidly fatal course, it is of particular importance to caution patients and providers so that prompt diagnosis can be made.

The RCOG Guideline recommends prophylactic antibiotics to prevent infection from abortion, though several speakers at the CDC-FDA workshop recommended against routine use of prophylactic antibiotics due to issues relevant to *Clostridial* infection. Speaking of experience with *C. difficile*, (closely related to *C. sordellii*), Dr. Seligman pointed out that infections “occur mostly in association with antibiotic use,”⁵³ and Dr. Gerding agreed that prior antibiotic exposure was “the largest risk factor,” indicating that normal bacterial flora

was “protective.”⁵⁴ Elimination of the normal flora could allow *Clostridial* infection to flourish. Dr. McGregor, speaking specifically about possible antibiotic prophylaxis at the time of mifepristone abortion, stated, “I do not suggest ... that antimicrobial prophylaxis, either short or long course which has been suggested, would be likely effective. Indeed, it might be just the opposite.”⁵⁵ He stated that routine antibiotic prophylaxis was a “bad idea.”⁵⁶ The FDA’s Public Health Advisory: Sepsis and Abortion also recommended against this.⁵⁷

Speaking at the CDC-FDA workshop, Dr. Soper raised the concern that these infections have “such a rapid downhill course that there really is little opportunity for any kind of therapeutic intervention at all,”⁵⁸ commenting on the need for prevention, but also agreeing that antibiotic prophylaxis was not advisable. Dr. McGregor instead proposed, “I would suggest that we either reduce or eliminate mifepristone or at least consider that” as a means of prevention for abortion related *Clostridial* infection. And I note that there doesn’t appear to be a safe or specific alternative that only gets the progesterone receptor”⁵⁹ The best prevention of these fatal infections would be to eliminate use of mifepristone, and in addition, there is not going to be a safe alternative since there are alternatives which only act on the progesterone receptors without acting on the glucocorticoid receptors.

McGregor recommended aggressive management of *C. sordellii* infection should include “rapid” admission to hospital, that consultations should be obtained from infectious disease specialists and intensivists, and that multiple organ support is started “promptly.”⁶⁰ He also proposes that if *Clostridia sordellii*-associated toxic shock is definitely the diagnosis, that “immediate” hysterectomy or D & C be considered in order to remove the source of the infection.⁶¹

FDA’s Dr. Sandra Kweder expressed concern that there could be additional deaths due to *C. sordellii* sepsis which may be undiagnosed and attributed to unknown causes. She pointed out that these cases were likely to be attended by an emergency physician rather than an infectious disease specialist or a gynecologist.⁶²

The Guideline does not discuss issues related to pharmacokinetics of mifepristone including its long half-life, metabolic pathways, and drug interactions.

Dr. Miech, speaking at the CDC-FDA workshop stated that mifepristone normally has a half-life of 20-30 hours, so that it normally would take about four or five days before 95% of a single dose of mifepristone would be broken down. However, he said in some individuals who process the drug more slowly, it can have a 90 hour half-life and would then be active for 18 days.⁶³

Meich stated that mifepristone is broken down in the liver by cytochrome P450-3A4. “There is evidence that the enzyme itself can be inactivated during the metabolism of mifepristone. This probably accounts for the relatively long biologically half-life seen in humans.”⁶⁴ So mifepristone is normally broken down very slowly, but in addition, if mifepristone causes the suppression of the enzyme responsible for its breakdown, then that would explain mifepristone still being active in the body days or weeks later.

Additionally, Miech stated that cytochrome P450-3A4 which breaks down mifepristone is also responsible for the metabolism of codeine. He stated, “In mifepristone abortions, women are frequently prescribed codeine for pain. Thus, codeine would compete for the enzyme that metabolizes mifepristone and prolong its biological half-life.”⁶⁵

In addition, Miech stated that mifepristone is broken down into six metabolites, and that some of these metabolites have biological activity.⁶⁶ McGregor also stated there are active metabolites, which he stated are active at both progesterone receptors and at glucocorticoid receptors.⁶⁷ It is through its action on the glucocorticoid receptors that mifepristone disrupts the innate immune system⁶⁸ but here we see that not only is it mifepristone but also its breakdown products which exert this effect.

Further, even “small concentrations of the molecule are quite efficient at saturating both progesterone receptors and glucocorticoid receptors,”⁶⁹ meaning that even when time has permitted the breakdown of

much of the original dose, small amounts that remain may continue to have an effect. McGregor gave an example of one study in which the effects on the innate immune system persisted for one week.⁷⁰

Recommendation 16 of the RCOG Guideline states that “abortion is safer than continuing a pregnancy to term and that complications are uncommon.”⁷¹ However, more recent reports have shown that the death rate from infection following medical abortion (mifepristone with misoprostol) has been ten times higher than the death rate from infections following surgical abortion^{72,73,74,75} and 50 times more compared to childbirth.⁷⁶ Dr. McGregor, speaking at the CDC-FDA workshop, stated that “surgical termination, which appears to be better studied, appears to have a lower risk in terms of patient mortality.⁷⁷ He also stated that informed consent forms should be changed to acknowledge the risk of serious infections and complications.⁷⁸

Recommendation 16 would inform women that complications of abortion are “uncommon,”⁷⁹ yet the FDA mandated labeling information for mifepristone states that “nearly all of the women who receive Mifeprex and misoprostol will report adverse reactions, and many can be expected to report more than one such reaction.”⁸⁰ The mifepristone label provides a list of 27 adverse effects which occurred in at least 1% of participants in the French and U.S. clinical trials.⁸¹ Of these listed symptoms, the most frequent were abdominal pain (reported by 96% of U.S. participants), cramping (reported by 83% of the French), nausea (61 % U.S.), headache (31% U.S.), vomiting (26% U.S.) and diarrhea (20% U.S.).⁸²

Especially worrisome, though lower in number, were the 5% who experienced uterine hemorrhage, the 6% (French) who experienced decrease in hemoglobin greater than 2 g/dl. and the 1% (U.S.) who experienced endometritis, salpingitis, and/or pelvic inflammatory disease.⁸³ The mifepristone label indicates that by day 14 reports of adverse effects were rare except for bleeding which is expected for an average of 9 days but which will continue for more than 30 days in 8% of the cases.⁸⁴

In regard to the severity of the various side effects the label states: “The percentage of women who considered any particular adverse event as severe ranged from 2 to 35% in the U.S. and French trials.”⁸⁵ The FDA’s Medical Officer’s review indicates that most patients reported more than one adverse event, and that “approximately 23% of the adverse events in each gestational age group were judged to be severe.”⁸⁶

The Guideline does not provide guidance on which patients must be excluded from use of mifepristone. For example, the FDA Medication Guide cautions the patients not to take Mifeprex if the patient is taking certain steroid medications, is taking anticoagulant medication, has a bleeding problem, if she cannot return for the next two visits, or if she could not easily get emergency medical help during the two weeks after taking Mifeprex.⁸⁷ The FDA mandated labeling in the U.S., under the heading “Contraindications,” cautions physicians that mifepristone must not be used in cases of chronic adrenal failure, in patients with hemorrhagic disorders or concurrent anticoagulant therapy, or in patients with receiving long-term corticosteroid therapy.⁸⁸ For the complete list of exclusions, refer to the Mifeprex Guide⁸⁹ and Mifeprex Label,⁹⁰ as these are examples and not a comprehensive list.

In a separate section titled “Precautions,” the FDA product label points out that “there are no data on the safety and efficacy of mifepristone in women with chronic medical conditions such as cardiovascular, hypertensive, hepatic, respiratory or renal disease; insulin dependent diabetes mellitus; severe anemia or heavy smoking.”⁹¹

The Spitz study specifically excluded “women with liver, respiratory, renal, adrenal, or cardiovascular disease, thromboembolism, hypertension, anemia, insulin-dependent diabetes mellitus, coagulopathy, or known allergy to prostaglandins . . . women less than 18 years. . . or those more than 35 years who smoked more than 10 cigarettes per day and had another cardiovascular risk factor.”⁹² Spitz had seven other exclusion criteria.

If Guidelines for Northern Ireland do not advise physicians regarding which patients are at higher risk and must be excluded, then they must expect a higher rate of serious adverse effects than that seen in the U.S. where the exclusions are required and where serious adverse events have nevertheless occurred. Without the exclusions, there is much greater potential for greater numbers of more serious complications, including death.

Recommendation 22 of the RCOG Guideline says ultrasounds are not essential, however ultrasounds must be required for dating of pregnancies and to detect possible ectopic pregnancies. Gary and Harrison, reviewing FDA adverse events reports, found 17 cases of ectopic pregnancies (11 ruptured; 1 death).⁹³ They state, “Ectopic pregnancy is an absolute contraindication to use of mifepristone,”⁹⁴ (also stated in FDA mandated product labeling).⁹⁵ Ultrasound documentation of intrauterine pregnancy before medical abortion would prevent this complication. This is essential because, “When an ectopic pregnancy ruptures, the women will rapidly bleed to death . . . unless she undergoes immediate surgery.”⁹⁶ However, “The signs and symptoms of ectopic pregnancy (*e.g.*, cramping and bleeding) resemble those experienced by a woman undergoing a medical abortion. [A] . . . patient might delay treatment thinking her symptoms were due to the [medical abortion]-- not an ectopic pregnancy.”⁹⁷

The Guideline encourages use of mifepristone in combination with vaginal misoprostol but does not discuss multiple serious issues concerning use of misoprostol, particularly when given by the vaginal route, which has been associated with serious complications such as sepsis, uterine rupture, and death.

Use of vaginal misoprostol for medical abortion is not approved by the FDA.⁹⁸ The Mifeprex (mifepristone) product label specifies the FDA-approved medical abortion protocol which includes 400 mg. of misoprostol taken orally at one time.⁹⁹ However, following FDA approval, a number of U.S. abortion providers adopted an unapproved regimen which involved use of misoprostol vaginally.

Some women developed fatal infections following medical abortion using this unapproved regimen which included both oral mifepristone (200 mg.) and vaginal misoprostol (800 mcg.).¹⁰⁰ To date, there have been six reported North American deaths by *C. sordellii* sepsis following medical abortion. Each of these deaths involved use of mifepristone with vaginal misoprostol.¹⁰¹

After the third and fourth septic shock deaths were made public, the FDA published “FDA public health advisory: sepsis and medical abortion” on July 19, 2005. In this document they gave several cautions related to possible serious infection and death after medical abortion, and they repeated that the approved dose of misoprostol was 400 mcg. taken orally (not vaginally).¹⁰² The FDA emphasized, “The safety and effectiveness of other Mifeprex dosing regimens, including use of oral misoprostol tablets intravaginally has not been established by the FDA.”¹⁰³

According to Dr. McDonald at the CDC workshop, an additional death has been reported which used only misoprostol but no mifepristone. This additional death was still under investigation at the time of the CDC-FDA workshop but involved a uterine infection by *Clostridium perfringens*, closely related to *C. sordellii*¹⁰⁴

Use of vaginal misoprostol has been prohibited in France according to Dr. McGregor¹⁰⁵ and Dr. Didier Sicard, Professor of Infectious Disease, Paris,¹⁰⁶ speaking at the CDC-FDA workshop.

Misoprostol causes uterine contractions and has been used to start labor in pregnant women.^{107, 108} FDA cautions that obstetrical uses of misoprostol are “not approved by the FDA. No company has sent the FDA scientific proof that misoprostol is safe and effective for these uses.”¹⁰⁹ FDA mandated label information for misoprostol (trade name Cytotec) states in a boxed warning, “Uterine rupture has been reported when Cytotec was administered in pregnant women to induce labor or to induce abortion beyond the eight week of pregnancy.”¹¹⁰ FDA explains that “a torn uterus may result in severe bleeding, having the uterus removed (hysterectomy), and death of the mother. . . .”¹¹¹

FDA’s Dr. Sandra Kweder stated out that vaginal misoprostol, in general obstetric use, has a “high rate of uterine rupture” which is “well reported.”¹¹² Kweder also stated that the oral misoprostol tablets have a “very unpredictable pharmacokinetic profile” when used vaginally.¹¹³ She suggested that misoprostol through vigorous uterine contractions, may have a role in setting the stage for *Clostridial* infections by deoxygenating the uterine tissue as well as by thrusting vaginal bacteria into the uterus.¹¹⁴

Dr. McGregor reported, “In our own work and others, we’ve shown that when the uterus contracts, that actually substances from the vagina are normally transported up inside the uterus so that would include *Clostridia sordellii* spores or other microorganisms. . . .”¹¹⁵ Thus misoprostol may play a role in facilitating transfer of the bacteria into the uterus. Dr. McGregor also stated misoprostol and the prostaglandins both primary and secondary roles in regard to innate immunity.¹¹⁶

The Cytotec (misoprostol) label states that congenital anomalies have been reported when misoprostol has been used unsuccessfully for medical abortion. “Several reports in the literature associate the use of misoprostol during the first trimester of pregnancy with skull defects, cranial nerve palsies, facial malformations, and limb defects.”¹¹⁷ Spitz also states says that misoprostol has been teratogenic in humans, citing two reports.¹¹⁸

In the study by Spitz et al. 5 percent of the women did not return for their final visit, and previously five of the women had ongoing pregnancies when last seen. The final visit which could provide for surgical intervention if necessary is important in order to avoid ongoing pregnancy and the risk of birth defects due to misoprostol.¹¹⁹

A report by Ashok et al. also states, “It is imperative to interrupt the pregnancy because of the possibility of birth defects following the administration of misoprostol.”¹²⁰

The Report of the International Inquiry Commission on RU 486 stated that “known side effects” of prostaglandins (such as misoprostol) include diarrhea, nausea, vomiting, severe pain, and also cardiovascular and respiratory risks. The report also cautioned on the lack of study of side effects when RU 486 and prostaglandins are used together.¹²¹

Misoprostol is used as an integral part of the approved RU486 abortion regimen in the U.S. and is also part of the “optimal” protocol recommended by the RCOG. However, the FDA has approved only the oral misoprostol, while the RCOG Guideline recommends at least the first dose should be vaginal, with subsequent doses in most cases being vaginal or oral depending on circumstances.¹²² The FDA approved only the 400 mg. dose, but RCOG recommends higher doses, starting with 800 mcg.¹²³ Additionally, FDA recommends one dose only, while the RCOG Guideline recommends multiple doses (depending on gestation and circumstances, 800 mg. initially and up to four doses of 400 mcg. subsequently).¹²⁴

A medical abortion is counted as a “failure” if surgery is needed afterward to remove retained tissue or to remove an intact ongoing pregnancy. The Guideline cites the work of Ashok et al.¹²⁵ whose 2002 study claimed, “The ongoing pregnancy rates in this series is the lowest reported to date,” which was attributed as possibly due to both the route of administration (vaginal) and the number of doses of misoprostol given.¹²⁶

However, even though the pregnancy has been successfully terminated, that is no guarantee against the complications that have been reported with use of mifepristone and misoprostol. The same vigorous contractions that successfully empty the uterus produce high risk of uterine rupture as stated by FDA’s Dr. Kweder.¹²⁷

Additionally, a successfully emptied uterus is no guarantee of protection against sepsis. At the CDC-FDA workshop, Dr. Fischer, discussed the first four U.S. deaths from *C. sordellii* sepsis following medical abortion. He stated that at autopsy, “none of the patients had retained fetal or placental tissue.”¹²⁸ The abortions were successful, their uteri were empty, and these young women were dead nevertheless. Based on an extensive investigation which included genetic testing of the bacteria for precise diagnosis, the four deaths were attributed to *C. sordellii* endometritis and toxic shock syndrome.¹²⁹

Dr. Fischer also made the point there may have been other deaths that have gone unrecognized. “Additional cases of pregnancy-associated *C. sordellii* infection in which the organism was not cultured or speciated may exist, but may not have been pursued because they did not receive the scrutiny afforded these four cases.”¹³⁰ Since the first four reported deaths all occurred in California, Dr. Fischer suggests that “local and regional attention around the first two cases in California may have increased the awareness of both the public and healthcare providers to this possible connection and stimulated reports of additional cases that may have not. . .

been detected in other states. In addition, the laboratory confirmation of *C. sordellii* in these cases resulted from extraordinary efforts at a national reference laboratory.”¹³¹

In short, deaths could occur in young women sent home following a “successful” abortion—young women from Derry or Belfast, for example—and these deaths might never be recognized as being related to the abortion. The empty uterus won’t give a clue about the abortion and there may be no fever or other signs of infection. In fact, it is possible a post-abortive young woman with a serious infection won’t make it to the hospital in time to give her medical history. Dr. Fischer stated that one of the California women “collapsed and died before reaching medical care.”¹³²

Dr. McGregor, after suggesting that eliminating mifepristone should be a consideration, also acknowledged that misoprostol, especially the vaginal use of misoprostol, was part of the problem. He stated that “certainly I would agree with practitioners, such as Planned Parenthood who’ve already gone to the oral only—oral only administration, which is actually what was approved by the FDA.”¹³³ By this time, following several deaths and the publication of the FDA Advisory, Planned Parenthood Federation of America, the largest U.S. abortion provider, had reportedly shifted from the unapproved regimen previously used to a more cautious unapproved regimen which used oral misoprostol in place of vaginal.

RCOG Guideline supports medical abortion for up to 24 weeks (168 days)¹³⁴ while the FDA has approved only to 7 weeks (Day 49).¹³⁵ The study by Spitz et al. containing the mifepristone data submitted to the FDA, was able to support an approved use of mifepristone with oral misoprostol only to Day 49.¹³⁶ The failure rate increased from 8% in less than 49-days, to 17% in the 50-to-56-days group, to 23% in the 57-to-63-days group. Spitz et al. concluded the regimen was safe and effective only through Day 49. “With longer durations of pregnancy, the regimen is less effective and the incidence of adverse events is higher.”¹³⁷

Following U.S. approval of mifepristone, Planned Parenthood Federation of America, the largest U.S. abortion provider, had adopted an unapproved protocol allowing for medical abortion use up to 9 weeks (63 days). However, after several of the septic shock deaths had occurred and the second FDA Advisory had been published, Planned Parenthood adopted a new (also unapproved regimen) which used only oral (not vaginal) misoprostol, and limited medical abortion to starting no later than Day 56 after last menstrual period. Their website, in an article first published on May 1, 2006, which references the FDA Advisory of March 17, 2006, states, “Planned Parenthood currently provides medication abortion up to 56 days' gestation.”¹³⁸

To use medical abortion beyond the 9th week is completely beyond American experience, which has demonstrated sufficient complications as well as the known deaths that a U.S. Congressional report, following hearings, concluded that approval of mifepristone should be withdrawn. The reports conclusion states that mifepristone is a “dangerous and fatal product” which must be withdrawn “before more women suffer the known and anticipated consequences or fatalities. **RU-486 is a hazardous drug for women. . . and its withdrawal from the market is justified and necessary to protect the public’s health.**”¹³⁹ Several different U.S. physician groups have joined in litigation to require the FDA to withdraw approval of RU-486.

The RCOG Guideline specifically discusses abortion beyond 15 weeks (referring to the 15 to 24 week period), presenting evidence that at this stage, women undergoing medical abortion were “significantly more likely to have a complication” than women undergoing a D & E (dilatation and evacuation) surgical abortion (29% complications for medical vs. 4% for D & E).¹⁴⁰

Because of this, the RCOG recommends the D & E as method of choice for 15 weeks and beyond if the practitioner has the necessary instruments and sufficient skill.¹⁴¹ However, “for gynaecologists lacking the necessary expertise” use of mifepristone plus prostaglandin is appropriate” for an abortion at 15 to 24 weeks.¹⁴²

Here the RCOG has acknowledged that medical abortion has much higher rate of complications beyond 15 weeks, 29% in the study by Autry et al. which they reference. Nevertheless, the RCOG considers it appropriate

for less skilled abortion providers to use this method. Of note, the Guideline states that “the most common complication of medical abortion was retained products of conception requiring surgical evacuation,” but even excluding these, women undergoing “medical abortions still had more complications, including one case of uterine rupture.”¹⁴³ Thus, the less skilled providers for whom medical abortion methods are deemed more appropriate are then in many cases faced with managing a surgical procedure for the complications that arise.

The Guideline does not discuss whether the high complication rate for medical abortion at this stage, or the skill of the provider, are considered appropriate to include in the informed consent process. Autrey et al. do recommend that patients considering a second trimester medical abortion “should be advised that they have a significant risk (21%) of requiring surgery for retained products of conception.”¹⁴⁴

Autrey et al. also caution that the true rate of complications may be higher than reported. “Because these abortions were performed in referral centers, complications may have occurred that were treated by the referring physicians without our knowledge.”¹⁴⁵ In this study of less than 300 patients, some of the complications were quite serious including hemorrhage with transfusion, patients with cervical laceration, “organ damage,” and infections requiring intravenous antibiotics.¹⁴⁶

However, overall in the literature there seems to be a grave lack of data on medical abortion at the later gestational ages and it is unclear from the Guideline at the referenced studies how the RCOG was able to conclude that medical abortion to 24 weeks could be considered as “safe and effective.”

The RCOG Guideline cites a meta-analysis by Kahn et al. which showed clearly that “efficacy decreases with increasing gestational age”¹⁴⁷ with a rate of complete abortion being 91% at 50-56 days¹⁴⁸ (meaning, a 9% failure rate), and only 85% “success” for 57 days or greater¹⁴⁹ (meaning, a 15% failure rate at 57 days and onward). However, this meta-analysis did not clearly identify any abortions approaching 24 weeks. A few of the studies included had cases up to 63 days, in one case, 63+ days, and two that specifically included up to 70 days, but many of the studies included went up to 49 days or 56 days only. Some of the reports considered did not specify gestational age at all, but there was no evidence that they included cases in the 15 to 24 week range.

Assuming the true failure rate of medical abortion is 15% at 57 days as Kahn found, and also assuming it is true as Kahn concluded that “efficacy decreases with increasing gestational age,” then what might be expected for failure rates even beyond 70 days, much less 24 weeks? Data for both safety and efficacy of medical abortion during the second trimester seem to be quite limited but what little is available should be sufficient to raise grave concern about this method at this gestational period.

In regard to failure rates of medical abortion in general, Recommendation 16.5 states that the failure rate for medical abortion is between 1 and 14 per thousand (from 0.1% to 1.4%),¹⁵⁰ but studies from U.S. and throughout the world have shown a much higher failure rate for medical abortion.^{151, 152, 153, 154, 155} The RCOG Guideline is able to demonstrate this lower failure rate by citing two studies of consecutive cases (one a continuation of the other) by Ashok et. al.^{156, 157} in which vaginal misoprostol was used, and in the half of the cases, the protocol was altered to allow for a second dose of vaginal misoprostol.

Vaginal misoprostol, and with repeated, multiple doses, as we have already seen, is more effective at emptying the uterus. However, as we have shown above, it is also much more dangerous for the woman. Vaginal misoprostol was abandoned by Planned Parenthood in the U.S. following deaths of several North American young women after abortions using mifepristone along with vaginal misoprostol. Indeed, as we have seen, these deaths occurred after “successful” complete abortion, with no retained products. Vaginal misoprostol is prohibited in France. There has been at least one death reported from vaginal misoprostol without mifepristone.

In any event, Ashok et al. only included cases up through Day 63 so their efficacy data does not in any way address the efficacy of later medical abortions.¹⁵⁸

Limitations of current research: Kahn et al. state, in their report on 54 studies of medical abortion: “Data on complications were very difficult to interpret because of the lack of standardized clinical protocols (eg. when surgical hemostasis is indicated for bleeding) and even shifting practices during the study period.”¹⁵⁹

In some reports, there are limitations on follow up data. For example, Ashok et al. concluded that 70% of women undergoing medical abortion would opt for the same procedure in the future,¹⁶⁰ though recognizing that only one third of all women who underwent medical abortion returned the questionnaire.¹⁶¹

Conclusion: The U.S. experience continues to demonstrate an increasing number of adverse events reported to the FDA, with multiple physician groups litigating for withdrawal of this product. A U.S. Congressional committee report, following Congressional committee hearings, has concluded that mifepristone is a hazard to women’s health, and that this product should be withdrawn, as we have seen above. The information we have presented here is only a small portion of the extensive evidence on the extreme health hazards associated with mifepristone.

The FDA Medical Officer Review¹⁶² as well as the Congressional report “The FDA and RU-486: lowering the standard for women’s health”¹⁶³ give a very different picture of the safety and efficacy of RU-486 compared to what is suggested in the RCOG Guideline. These two U.S. reports which include information from the French and U.S. clinical trials, from world wide studies and from recent U.S. experience, all bear reading and study. The actual transcript of the 2006 CDC-FDA workshop¹⁶⁴ also is well worth study before action is taken to make mifepristone abortion readily available to the women of Northern Ireland, particularly under the specifications of the RCOG Guideline.

The State of Tennessee Senate Judiciary Committee has just recently (April, 2007) held hearings regarding the information which physicians should be required to disclose to women considering medical abortion. Although we believe the evidence would strongly recommend against moving forward with use of RU-486 in Northern Ireland, nevertheless, if it is to be used it is a necessity that detailed, accurate informed consent be provided to anyone consideration use of this dangerous drug.

Many young women, including the young teens who will be able to access medical abortion without their parents knowledge under the draft Guideline, will be led to believe that medical abortion is easy and safe, as easy and safe as taking a tablet. Yet if women were given accurate information about what they could expect to experience, they might well choose differently.

In the U.K., are most young women informed about bleeding that may go on for a month (as we have seen above) or that research demonstrates more pain with medical than with surgical abortion (according to a number of head to head comparison studies^{165, 166, 167, 168, 169, 170, 171})? Is she cautioned about less frequent but more serious complications that may occur, the immune suppression, the risk of death from sepsis or hemorrhage (as discussed above)? Are those women considering a second trimester medical abortion informed of the complication rate at that stage, or of the relative lack of data at the higher gestational stages? The literature is limited on what information women are actually receiving in the informed consent process. In the U.S., there has been reason for concern that it is not sufficient, which is the reason for the Tennessee Senate hearings.

Did this young woman, quoted in the New York Times, have any idea of the experience she was in for when she took her tablets? “I felt like I was dying...it hurt so much. I had contractions coming so fast, and I was sick to my stomach and dry heaving. I couldn’t stop trembling and I felt so hot.”¹⁷²

If the people of Northern Ireland were acquainted with the information presented in the Congressional hearing, very likely few would want this legally available for their daughters, and very few would choose it themselves.

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