Committee Secretary
Community Affairs Committee
Department of the Senate
Parliament House
Canberra ACT 2600
Australia

13th January, 2006

Re: Inquiry into *Therapeutic Goods Amendment (Repeal of Ministerial responsibility for approval of RU486) Bill 2005*

Summary.

The purpose of this submission is to address the issue of the safety of RU-486 (mifepristone) over surgical abortion using the most recent medical literature.

"The choice of mifepristone termination over surgical termination is based mainly on patient perceptions of safety, convenience, and privacy, but these perceptions do not accurately reflect the realities of the regimen. Furthermore, complete, accurate data concerning the public health risk posed by the mifepristone/misoprostol regimen currently in use are not being gathered through the FDA's Adverse Event Reporting System. After reviewing over 600 AERs, we believe that the FDA must promptly conduct a thorough review of this aspect of its postmarketing surveillance system to determine whether the failures described above are peculiar to mifepristone reports or are systemic to all drug reports."

Gary MM, Harrison DJ. Analysis of severe adverse events related to the use of mifepristone as an abortifacient. *Ann Pharmacother* Published online 27 Dec 2005. (viewed Jan 12 , 2006) http://www.theannals.com/cgi/reprint/aph.1G481v1

Author:
Mr John Wilks B.Pharm., MPS., MAACP
Consultant Pharmacist
Author, "A Consumer's Guide to the pill and other drugs." 3rd ed. National Bookstore, Manilla

The medical safety of RU-486 (mifepristone.)

A careful reading of recent publications by advocates of the mifepristone (RU-486) abortion procedure might lead one to conclude that this drug possesses a safety profile equal, if not superior to surgical termination of a pregnancy.

Prominent amongst the supporters of mifepristone is Prof. Caroline de Costa, who has been reported in many media outlets during the last six months advocating this opinion. [1] [2] [3] She has recently been co-joined in her view by the leadership of the Australian Medical Association, via a media release dated November 7, 2005.[4]

One November 9, the Royal Australian and New Zealand College of Obstetricians and Gynaecologists added their supportive voice to this proposition. [5]

[1] De Costa CM. Medical abortion for Australian women: its time. *MJA* 2005; 183 (7): 378-380 http://www.mja.com.au/public/issues/183_07_031005/dec10429fm.html

[2] AM- Fed Government considers conscience vote on RU-486 November 22 2005 http://www.abc.net.au/am/content/2005/s1513221.htm

[3] The Bulletin. Bitter Pill by Julie-Anne Davis. 12.7.05 (viewed 10.1.06) http://bulletin.ninemsn.com.au/bulletin/site/articleIDs/A4B745E0D6560003CA2570CB00087244

[4] http://www.ama.com.au/web.nsf/doc/WEEN-6HW5DZ (Viewed 12 Jan 2006)

[5] http://www.ranzcog.edu.au/media/pdfs/MR-Mifepristone_9-November05.pdf (Viewed 12 Jan 2006)

For many in the community and in Federal Parliament, such statements sound highly convincing, emanating as they do from such learned physicians.

Yet an objective review of the medical literature shows that, far from being safe, RU-486 represents a retrograde step in the healthcare of Australian women.

To begin I think it important that Committee Members have a clear understanding of what RU-486 is, and the procedure involved in its use.

The following information is taken from the American Food and Drug Administration (FDA) website and pertains to the termination of a pregnancy of up to 49 days. [6]

- Day one: 3 tablets of mifepristone (RU-486), each 200 milligrams, are taken orally.
- Day three: another drug, misoprostol is given **orally**, if the woman is still pregnant. The total dose is 400 micrograms.

[6] http://www.fda.gov/cder/foi/label/2005/020687s013lbl.pdf (Viewed 12th Jan 2006)

- Day 14: The woman must return to her doctor to confirm that the pregnancy has been terminated. If it has not, a surgical termination is recommended.

A number of features of this procedure require attention.

First, as will have been noted, the RU-486 procedure is a **two drug** process. The first drug, RU-486 (mifepristone) acts to cause fetal death by blocking the pregnancy maintaining actions of progesterone, a hormone produced by the woman's body. [7]

The second drug given, misoprostol, is a prostaglandin analogue.[8] Within the context of the RU-486 abortion procedure its primary function is to cause strong uterine contractions, thereby emptying the uterus of the death foetus.

The FDA website reports that in the USA clinical trials, 18.7% of women had to wait between 4 and 24 hours *after* taking misoprostol on day three before they delivered their foetus.

[7] http://www.fda.gov/cder/foi/label/2005/020687s013lbl.pdf
[8] E-MIMS 2005. Cytotec (misoprostol) approved product information

A further 8.2% of these American women had to wait more than 24 after taking misoprostol on day three before delivering their dead foetus.

Presumably, for many of these women, expulsion took place within the domestic setting.

From a psychological perspective one would conclude that this would be a traumatic experience for a woman, and one can only feel pity and grief for her. Interestingly, this is the clear view of pro-choice feminists such as Prof. Renata Klein, Associate Professor, Women's Studies, Deakin University.[9]

It is also the view of Edouard Sakiz the then president of French pharmaceutical company Roussel-Uclaf, the original developers of this drug. He has described the RU-486 procedure as:

> **"an appalling psychological ordeal because the woman ... has to 'live' with her abortion for at least a week using this technique."** [10] [11]

[9] Klein R, Raymond J, Dumble L. RU-486; Misconceptions, Myths and Morals Spinifex Press, Melbourne, Victoria, Aust. 1991
[10] Interview, Le Monde Aug 1 1990, reprinted in "*Guardian Weekly"* UK August 19th 1990.
[11] Peterson C. Risky drug of pro-choice. *The Australian.* Nov 12 , 2005

A second point to note from the aforementioned description of the RU-486 procedure is that there is a recommendation of a surgical abortion if the chemical abortion using RU-486 plus misoprostol has failed.

The reason for this recommendation is that misoprostol – the drug given to cause uterine contractions – has been reported in the medical literature to cause substantial birth defects, including scalp, cranial and limb abnormalities, hydrocephalus, abnormal digits, no kidneys, and, in one tragic case, a baby born with fused legs. This condition is called sirenomelia, or mermaid syndrome. [12] [13] [14] [15] [16] [17] [18] [19]

These events are documented in such well known, highly respected and peer-reviewed journals as *Studies in Family Planning, The Journal of Pediatrics* and *the Lancet.*

[12] Schonhofer PS *et al*, Brazil: misuse of misoprostol as an abortifacient may induce malformations. *Lancet* 1991; 337:1537-5
[13] Fonseca W, *et al*. Congenital malformations of the scalp and cranium after failed first trimester abortion attempt with misoprostol. *Cli Dysmorph* 1993; 2:76-80
[14] Gonzalez CH *et al*, Limb deficiency with or without Mobius sequence in seven Brazilian children associated with misoprostol use in the first trimester of pregnancy. *Am J Med Genet* 1993; 47:59-64
[15] Costa SH, Vessey MP. Misoprostol and illegal abortions in Rio de Janeiro, Brazil. *Lancet* 1993;341:1258- 61
[16] Barbosa RM *et al*. The Brazilian experience with Cytotec (misoprostol) *Stud Fam Planning* 1993;24:236-240
[17] Collins FS, Mahoney MJ. Hydrocephalus and abnormal digits after failed first-trimester prostaglandin abortion attempt. *Journ Ped* 1983;102(4):p.620
[18] Gonzalez CH, Marques-Dias MJ, et al. Congenital abnormalities in Brazilian children associated with misoprostol misuse in first trimester of pregnancy. *Lancet.* 1998;351:1624-1627
[19] Pons JC, Imbert MC, Elefant E, et al: Development after exposure to mifepristone in early pregnancy (letter). Lancet 1991; 338:763.

And how often does RU-486 (mifepristone) plus misoprostol fail?

According to the paper by Prof. Caroline de Costa, RU-486 plus misoprostol fails to cause an abortion in 2-7% of women. [20]

The *Canadian Medical Journal* (2005) reported similar data - the RU-486 procedure **failed** in 5-8% of cases and a woman required **"a surgical procedure because of incomplete abortion, excessive bleeding or continuing abortion."** [21]

A large study conducted in Denmark and also published in 2005 reported an 8**% failure rate**. [22]

This means approximately 1 in 12 women may require a surgical abortion because the chemical abortion has failed. This represents a gross pharmaceutical assault on the integrity of a woman's health.

[20] De Costa. CM. Medical abortion for Australian women: its time. *MJA* 2005; 183 (7): 378-380
[21] Murray S, Wooltorton E. Septric shock after medical abortions with mifepristone. *CMAJ*. 2005;175(5):485
[22] Ravn P, Rasmussen A, Knudsen UB, Kristiansen FV. An outpatient regimen of combined oral mifepristone 400mg and misoprostol 400mcg for first-trimester legal medical abortion. *Acta Obstet Gynecol Scand.*2005;84(11):1098-102

A third important issue arises from the proceeding matter - a matter of precision in terminology.

When speaking about the RU-486 plus misoprostol abortion procedure, advocates use the term **"medical abortion".**[23] In the view of experts in this field, this description is inaccurate and inappropriate.

For instance, pro-abortion feminist academic, Dr Renata Klien recently pointed out to Parliamentarians in an extensive email that the correct term for the RU-486/prostaglandin process is a **"chemical abortion"** because, as Dr Klein has stated:

> **"chemical is a much more appropriate term than 'medical' as it** (the treatment) **consists of a drug cocktail of two powerful chemicals…RU-486 and a prostaglandin – which is inherently unpredictable…"** [24] [My clarification]

[23] De Costa. CM. Medical abortion for Australian women: its time. *MJA* 2005; 183 (7): 378-380
[24] See email from Dr Renata Klein to all members of Parliament for a refutation of the term 'medical'.

Note her terminology – Dr Klein sees RU-486 plus misoprostol as a dangerous **"chemical cocktail".** In making this claim, Dr. Klein is raising the fundamental issue - the core issue in this debate; that of safety, the safety profile of this admixture of potent pharmaceutical products. It is this issue I now wish to draw to the Committee's attention.

The consistent theme of the RU-486 plus prostaglandin advocates is that this two drug procedure has a safety profile comparable to surgical abortion. [25] This is the recently stated view of Dr Haikerwal, President of the AMA. [26]

From an international perspective come similar conclusions. Vocal RU-486 advocate Dr David Grimes, from the Department of Obstetrics and Gynecology, North Carolina, recently wrote in the journal *Contraception* (2005) that :

> **"…the risk of death associated with medical** (meaning chemical) **abortion is remote and virtually identical to that with spontaneous and surgical abortion."** [27] (My clarification)

[25] http://www.abc.net.au/health/thepulse/s1509095.htm "the risks (with RU-486) are no greater than managing other obstetrics procedures like pregnancy and surgical abortion" Dr de Costa. (Viewed 12 Jan 2006)

[26] http://www.ama.com.au/web.nsf/doc/WEEN-6HX2LE Discussion of pregnancy termination drug RU-486. "…when you compare it with surgical terminations, this is a very safe and effective way to perform this procedure, where it's clinically indicated." Nov 8, 2005

Also adding to this view was a July 17 2005 health advisory issued by the FDA which stated that the RU-486/prostaglandin procedure **"doesn't present any special risk of infection."**[28]

Irrespective of the source of information selected, one can declare with certitude that statements asserting an acceptable level of safety for this drug combination are based upon dated and superceded scientific information.

The most up-to-the minute data unequivocally show that RU-486/prostaglandin procedure has a greatly inferior profile when compared to surgical abortion.

Evidence to support this statement can first be found in the leading journal dedicated to family planning and abortion - *Contraception.*

In the September edition, Dr PD Darney, a member of the Board of Associate Editors [29] of this journal stated the following:

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[27] Grimes DA. Risks of mifepristone abortion in context. *Contraception.* 2005;71:161
[28] http://www.fda.gov/medwatch/safety/2005/mifeprex_deardoc_071905.pdf
[29] http://authors.elsevier.com/JournalDetail.html?PubID=525002&Precis=EB

> **"… the death rate from medication abortion** (RU-486) **among Planned Parenthood patients [is]… roughly 1.5 per 100,000, compared to a U.S. rate of 0.5 for early surgical abortion."** [30] (my clarification)

In everyday language this means that the maternal death rate for the RU-486 plus prostaglandin combination is approximately **three times greater** than the maternal death rate recorded for early surgical abortions.

This is such a vital fact that I think it warrants repetition for the Honourable Members of this Committee.

The maternal death rate associated with the use of RU-486 is, according to this study, **three times greater** than the maternal death rate seen in surgical abortion. That is, three times as many women die during the RU-486(mifepristone) plus misoprostol procedure than die during surgical abortion.

Based upon this objective scientific data alone the position adopted by supporters of this drug mixture is untenable. Bluntly, their case is destroyed. They have no

[30] Darney PD. Deaths associated with medication abortion (Letter). *Contraception* 2005;71:319

facts to buttress their argument. The best scientific evidence is against them, pro-abortion feminists are against them, and, ironically, their position clashes with best medical practice, which in common parlance means the best interests of Australian women.

But on December 1 2005, any claims of scientific authority advanced by the AMA or the RANZCOG vanished, with the publishing of a paper in the *New England Journal of Medicine*.

The article, by Dr Michael F. Greene, professor of obstetrics, gynecology and reproductive biology at Harvard Medical School, Boston sets out a detailed comparison of the maternal death rates for surgical and chemical abortions. [31]

For surgical abortions up to 8 weeks gestation (56 days), the maternal death rate is **0.1 per 100,000.** [32]

[31] Greene MF. Fatal infections associated with mifepristone-induced abortion. *NEJM* 2005; 353:2317-2318 http://content.nejm.org/cgi/reprint/353/22/2317.pdf?search_tab=articles&excludeflag=TWEEK_element&sortspec=Score%2Bdesc%2BPUBDATE_SORTDATE%2Bdesc&hits=20&where=fulltext&FIRSTINDEX=0&andorexactfulltext=and&resourcetype=HWCIT&searchid=1&sendit=GO&searchterm=greene+misoprostol&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT

[32] Ibid, p. 2318

For ease of comparison this figure is the same as **1 maternal death for each 1,000,000 surgical abortions.** [33]

For chemical abortions up to 7 weeks and 2 days (51 days) the maternal death rate is 0.9 per 100,000. [34]

For ease of comparison this figure is the same as **9 maternal deaths for each 1,000,000 chemical abortions.**

Based upon this data from Prof. Greene, there are now two sets of data to compare for pregnancy termination for almost the same number of weeks gestation. For surgical abortions, the maternal death rate is 1 woman per 1,000,000 abortions. For chemical (RU-486) abortion, the maternal death rate is 9 women per 1,000,000 abortions.

It is now a simple question – why method is safer for women?

[33] This computation is done merely by multiplying both the incidence (0.1) and the population sample (100,000) by 10.
[34] 4 deaths in 460,000 procedures is cited in this paper, equalling a rate of 0.9 deaths per 100,000, or 9 per 1,000,000

The numbers are very clear: if the RU-486 maternal death rate is 9 per 1,000,000 and the surgical abortion maternal death rate is 1 per 1,000,000, then the death rate for RU-486 is 9 times greater than surgical abortion.

Put more simply, **nine times more woman die using RU-486 than die as a result of a surgical abortion.**

Clearly these data invalidate any claims that RU-486 is either a safe or safer alternative to surgical abortion.

Such an inference or assertion is scientific nonsense.

These are the facts as published in the *New England Journal of Medicine*. They are hard data from a pre-eminent journal, perhaps the most prestigious in the world.

Before proceeding further, a note of clarification is warranted.

In some medical reports it is stated that the maternal death rate for surgical abortion is about 1 per 100,000,[35] which, for ease of comparison with earlier data, equals 10 maternal deaths per 1,000,000 surgical abortions. On the basis of **this** figure, surgical and chemical abortion has (almost) the same mortality rate, and the view of the AMA and others is validated.

But this is a misleading figure. It is a global – or blended- risk assessment figure, derived by adding the very low maternal death rate from surgical abortion when done early in a pregnancy, with the increasingly higher risk of maternal death from surgical abortion when performed latter in the pregnancy.

This approach clouds right thinking and leads to erroneous comparative safety conclusions regarding RU-486 plus misoprostol and surgical abortion.

On this point Professor Greene clearly states that we must only compare like with like – that is, compare the risks associated with surgical and chemical *at the same gestational stage.* Whole-of-pregnancy risk data and their use are utterly deceptive.

[35] Henderson JT, Hwang AC, Harper CC. Safety of mifepristone abortions in clinical use. *Contraception* 2005;72:175-178

"The overall maternal mortality rate associated with induced abortion in the United States is approximately 1 per 100,000. That overall rate is a "blended" rate including all the procedures performed in the United States at all gestational ages. The gestational age–specific rate increases exponentially from 0.1 per 100,000 at 8 weeks' gestation to 8.9 per 100,000 at 21 or more weeks' gestation. Mifepristone is approved for the termination of pregnancies at less than seven weeks' gestation. Therefore, the appropriate comparison is with a risk of 0.1 per 100,000 for surgical abortions performed at less than eight weeks' gestation."[36]

Further medical evidence against RU-486 and misoprostol.

Also very damaging to the claim of relative safety of RU-486 plus misoprostol is a paper by Gary and Harrison, published on-line by *The Annals of Pharmacotherapy*. This paper was deemed to be of such social and medical importance that it was rushed onto *The Annals* internet site one month ahead of the scheduled publication date.[37]

In this paper, the authors assessed **"six hundred seven unique mifepristone AERs (adverse event reports) submitted to the FDA over a 4 year span…"** to

[36] Greene, op.cit., p.2318

[37] Gary MM, Harrison DJ. Analysis of severe adverse events related to the use of mifepristone as an abortifacient. *Ann Pharmacother* Published online 27 Dec 2005. (viewed Jan 12 , 2006) http://www.theannals.com/cgi/reprint/aph.1G481v1

assess the mortality, morbidity, sentinel events, and, importantly, the quality of postmarketing surveillance. [38]

The timespan of this data review was from September 2000, when the FDA approved the use of RU-486, until September 2004. The principle findings from this study of 607 notified AERs where:

Hemorrhage.

- 42 women experienced **"a life-threatening hemorrhage, as defined by active hemorrhaging with hemoglobin less than 7g/dL and the transfusion of 2 or more units of packed red blood cells (PRBCs)."**

- 168 women **"had severe hemorrhage, defined by hemoglobin of 7g/dl or above and transfusion."**

- **"Overall, 39% of AERs reported hemorrhage."** [39]

[38] Ibid.
[39] Gary, op.cit.

Separate from *The Annals* report, Prof. de Costa has also cited the need for transfusions. She has stated that blood loss can be so severe that 100 to 250 women per 100,000 using RU-486 will require a transfusion.[40]

Infection.

- **"Serious or life-threatening infections were reported for at least 46 women, of whom 2 were aged 13-17 years."**

- **"Four women who had life-threatening infections but survived were in septic shock at the time of presentation to the emergency department. One patient (aged 15 years) presented with adult respiratory distress syndrome (ARDS) from sepsis. A second patient presented with ARDS from *Escherichia coli* sepsis. A third presented with toxic shock syndrome. A fourth (aged 16 y) presented with group B Streptococcus septicemia. In addition to these 4 patients with documented infectious etiology, a fifth patient presented with disseminated intravascular coagulopathy (DIC) with hepatic and renal failure."**

[40] De Costa, ibid, p.378 "Transfusion rates of 1 per 1000 and 2.5 per 1000 are cited in various studies." (multiply all the data by 100 to make the comparisons relevant to early data)

- **"Forty-three additional women required parenteral antibiotics for severe pelvic infection, and an additional 14 were treated for pelvic infections as outpatients. Overall, 11% of AERs reported an infectious complication."** [41]

Other journals have also reported on the need for antibiotic therapy. For example, Henderson and colleagues (*Contraception*, 2005) reported that 20 women in each 100,000 will require IV antibiotics. [42]

Undiagnosed ectopic pregnancy.

- **"Seventeen patients had ectopic pregnancies that were undetected at the time of mifepristone administration. Eleven of these were ruptured at the time of diagnosis (CTCAE genitourinary grade 4), including one death (CTCAE 5)."[43]**

Additional sentinel events.[44]

- myocardial infarction in a previously healthy 21- year-old woman
- prolongation of QT interval on electrocardiogram in another woman

[41] Gary, op.cit.
[42] Henderson JT, Hwang AC, Harper CC et al. Safety of mifepristone abortions in clinical use. *Contraception* 2005;72:175-178
[43] Gary, op.cit.
[44] Gary, op.cit.

- pulmonary embolism
- exacerbation of Crohn's disease
- precipitation of a sickle cell crisis
- acute pancreatitis
- drug interaction resulting in liver failure in an HIV- positive patient

Treatments required to treat adverse events.[45]

- **"Sixty-eight women received transfusions. Nineteen (28%) of these required 3 or more units of PRBCs. In 15% of cases with transfusion, the number of units was not documented in the AER."**

- **"At least 513 surgical procedures were performed in the 607 patients with adverse events."**

- **"There were 235 emergency surgeries performed. Of these, 17 (7%) were emergency laparotomies."**

[45] Gary, op.cit.

- **"16 were for ectopic pregnancies (1 ectopic pregnancy was managed laparoscopically) and one laparotomy was for sepsis. Two of the 5 deaths were intraoperative. The remaining 93% of emergency surgeries were emergency dilatation and curettage procedures performed to arrest hemorrhage."**

- **"At least 40% of the patients were hospitalized for treatment, including 12 admissions to the intensive care unit. Fifty-seven percent were managed as outpatients and, in 3%, the site of treatment was not documented."**

Allergic reaction.

- An **"unexpected finding was the number of allergic reactions ranging from hives to severe generalized urticaria."** One patient was hospitalized for 4 days, and 8 were treated on an outpatient basis.

Fetal abnormalities.

- Of the 278 pregnancies terminated after mifepristone failure, 21% **"had documented fetal viability by ultrasound on return visit … and 13% had documented fetal demise or retained products of conception**

without a fetus." [46]

- Despite poor record keeping that negated a clear and substantiated diagnosis in many cases – and these cases were excluded from the analysis – the rate of fetal malformation was at least 23% (3 of 13 fully documented cases). [47]

The two most striking conclusions made by the researchers were that (a) the perception of safety ascribed to this abortion procedure does not reflect the reality of the drugs poor safety history, and (b) the inadequacies of the American adverse drug reaction citing process mean that the safety profile of RU-486 plus misoprostol is actually worse than indicated above.

The following citation underscores both these aspects.

"The choice of mifepristone termination over surgical termination is based mainly on patient perceptions of safety, convenience, and privacy, but these perceptions do not accurately reflect the realities of the regimen. Furthermore, complete, accurate data concerning the public health risk

[46] Gary, op.cit.
[47] Gary, op.cit.

posed by the mifepristone/misoprostol regimen currently in use are not being gathered through the FDA's Adverse Event Reporting System. After reviewing over 600 AERs, we believe that the FDA must promptly conduct a thorough review of this aspect of its postmarketing surveillance system to determine whether the failures described above are peculiar to mifepristone reports or are systemic to all drug reports." [48]

Thus far I have spoken about the statistical evidence against RU-486's safety. What we must always keep in mind is that statistics do not die, but real people do.

So who are these real people, these real victims of the RU-486 plus misoprostol "**chemical cocktail**"?

1991- Nadine Walkowiak, a French mother of eleven died as a result of the RU486/PG procedure. The prostaglandin Nalador®, which was given as an injection, caused cardiovascular shock (failure of the heart and circulation). This event was reported by *AAP* (25.3.91), the *Australian* (13-14th April 1991),

[48] Gary, op.cit.

Daytona Daily News (9th April 1991) [49] and confirmed on 8 April 1991 by the French Ministry of Health in an official *Communiqué.* This death has been minimized because the women was a heavy smoker and had cardio-vascular problems.

2001 - Brenda A. Vise, a 38-year-old Hamilton County, Tenn. resident, died on Sept. 12, 2001 from a massive infection resulting from a ruptured ectopic (tubal) pregnancy, five days after she visited the Knoxville abortion clinic and began taking the RU-486 drug combination.[50]

2003 – Holly Patterson. It is reported that the Planned Parenthood clinic failed to properly educate her on the correct use of the drugs. Her story appeared in *The Daily Telegraph* on 28/11/2005, as well as internationally.[51]
Her parents have filed suit against the drug company. A bill to review RU-486 – known as 'Holly's law' – may soon be presented to the US House of Representatives.

[49] French report on death in abortion pill treatment. *Dayton Daily News* Dayton. OHIO, USA. April 9th, 1991
[50] http://www.cnsnews.com/ViewCulture.asp?Page=%5CCulture%5Carchive%5C200209%5CCUL20020903a.html (viewed 12th Jan 2006)
[51] http://www.telegraph.co.uk/news/main.jhtml?xml=/news/2004/01/18/nabort18.xml

2003 – Rebecca Tell Berg, a 16-year old Swede died in her shower from a fatal hemorrhage. A coroner's report stated that the appropriate dose was given, and all proper procedures and rules were followed. [52]

2003 – Hoa Thuy Tran, aged 21, was a student teacher. Her parents have filed a law suit against Danco, the drug manufacturer, and Planned Parenthood, the drug licensor. She also died from septic shock. [53]

2005 – Oriane Shevin, 34, an attorney and mother of two died from RU-486 induced sepsis. [54]

Aside from these women, in 2004 the British Government announced that two women had died after taking RU-486, and in 2001 a Canadian woman died during a RU-486 trial. No names have been released for these victims. [55]

[52] http://www.gt.se/expressen/road/www/article/0/jsp/Render.jsp?a=115325&print=yes
[53] http://www.nctimes.com/articles/2005/10/08/news/state/15_12_2310_7_05.txt (viewed 12th Jan 2006)
[54] http://www.dhs.ca.gov/director/owh/owh_main/pubs_events/news_articles/repro/abortion_pill.pdf (viewed 12th Jan 2006)
[55] http://www.telegraph.co.uk/news/main.jhtml?xml=/news/2004/01/18/nabort18.xml (viewed 12th Jan 2006)

And it must not be overlooked that these deaths occurred in first world countries, with full emergency medical equipment at hand and a broad range of antibiotic therapies to call upon.

Yet, despite these superior facilities, four American women died. According to a summary of the autopsies, authored by Dr Marc Fisher and co-researchers, and published in the December 1st edition of the *New England Journal of Medicine* (2005), these women were all listed as "**previously healthy**." [56]

The cause of death in four of the American cases was a powerful bacterium known as *Clostridium sordellii.* According the experts in this field, notably Associate Professor Miech from Brown Medical School, there is a plausible biological link between the anti-immune system actions of RU-486 (mifepristone) and the rapid overgrowth of this fatal bacterium. [57]

[56] Fisher M, Bhatnagar J, Guarner J, et al. Fatal toxic shock syndrome associated with *Clostridium sordellii* after medical abortion. *NEJM.* 2005;353:2352-60

[57] Miech RP. Pathophysiology of mifepristone-induced septric shock due to Clsotrium sordellii. *Ann Pharmacotherapy* 2005;39:1483-8

Whilst *Clostridium sordellii* "**is an infrequent human pathogen**"[58] it causes a toxic shock-like syndrome due to the release of two lethal exotoxins called lethal toxin and hemorrhagic toxin and an endotoxin called lipoteichoic acid.[59]

The overgrowth by *C. sordellii* is caused by mifepristone (RU-486) acting to suppress the natural, innate immune system within the female reproductive tract.

> **"Mifepristone's multireceptor blockade interferes with the protective function of the innate immune system. Malfunction of the innate immune system in combating the invasion of the decidua by *C. sordellii* leads to septic shock…"** [60]

According to the paper by Fisher and colleagues in the *New England Journal of Medicine* this bacterium is:

1. **"Difficult to isolate and identify"** via blood tests
2. **"has been rarely been identified in the genital tract"** and
3. Is difficult to eradicate with antibiotics.[61]

[58] Fisher, op.cit. p.2356.
[59] Miech, op.cit., p.1486
[60] Miech, p.1487
[61] Fisher, p.2358

In fact, the effects of this bacterium are so difficult to eradicate that, according to Dr Marc Fisher, even the removal of the diseased uterus – this primary site of *Clostrium* infection in the dead women – **"will not mitigate the effects"** [62] of the poisonous secretions produced by this lethal bacterium. Why? Because these poisonous secretions have already flooded the body leading to low blood pressure, high heart rate and finally, death.

And, tragically, the most difficult aspect of this clostridium infection is the non-specific symptoms of abdominal cramping, normal temperature, nausea, vomiting and weakness that women first experience. A flow chart of the putative mechanism by which mifepristone (RU-486) causes septic shock and death is provided at the end of this submission.

And yet, despite this evidence, peak international institution such as the FDA do not, as the following citation shows, recognize that there is a straight line connection between the use of oral mifepristone (RU-486) and mildly symptomatic yet fatal sepsis.

[62] Ibid.

> **"Has any causal relationship between these events** (detection of Clostridium in 4 women) **and the use of Mifeprex and misoprostol been established?**
>
> **No. The FDA will continue to evaluate all case reports and other information to determine if there is any causal relationship."** [63] (My clarification)

Please note that this Q & A was posted on November 5 2005, two months *after* the publication of the paper by Miech.

Can ignorance be claimed apropos of the nexus between the use of mifepristone and a possibility of serious infection?

As Professor Miech has noted, the answer is clearly in the negative.

> **"As early as 1992, it was suggested that mifepristone might predispose bacterial contamination of tissue toward infection that could progress to septic shock."** [64]

Equally misleading are any attempts to downplay the significance of these deaths by inferring that the occurrence of this bacterium is a common aspect of

[63] http://www.fda.gov/cder/drug/infopage/mifepristone/mifepristone-qa20050719.htm (Viewed 12th Jan 2006)
[64] Miech, op.cit, p.1483

childbirth, and either via childbirth or chemical abortion, a woman will be exposed to the risk of infection. Again, from Associate Professor Emeritus Miech:

> **"Prior to the Food and Drug Administration's (FDA's) approval of mifepristone for medical abortions, fulminant lethal cases due to *Clostridium sordellii* in women of childbearing age were rare and exclusively associated with postpartum infections. Toxic shock syndrome due to *C. sordellii* has not been reported in surgical abortions."** [65]

The same conclusion has been stated by Abdulla and Yee (*J Clin Pathol*, 2000).

> **"*Clostridium sordellii* is rarely associated with disease in humans. Since its first report in 1922 only a few cases of bacteraemia have been reported."** [66]

[65] Miech, op.cit.
[66] Abdulla A, Yee, L. The clinical spectrum of *Clostridium sordellii* bacteraemia: two case reports and a review of the literature. *J Clin Pathol.* 2000; 53:709-712

Conclusion.

So, presented with these medical facts what conclusions should Honourable Committee Members consider?

First, the very best evidence shows that the RU-486/prostaglandin chemical abortion is **nine times** more lethal for a woman than surgical abortion.

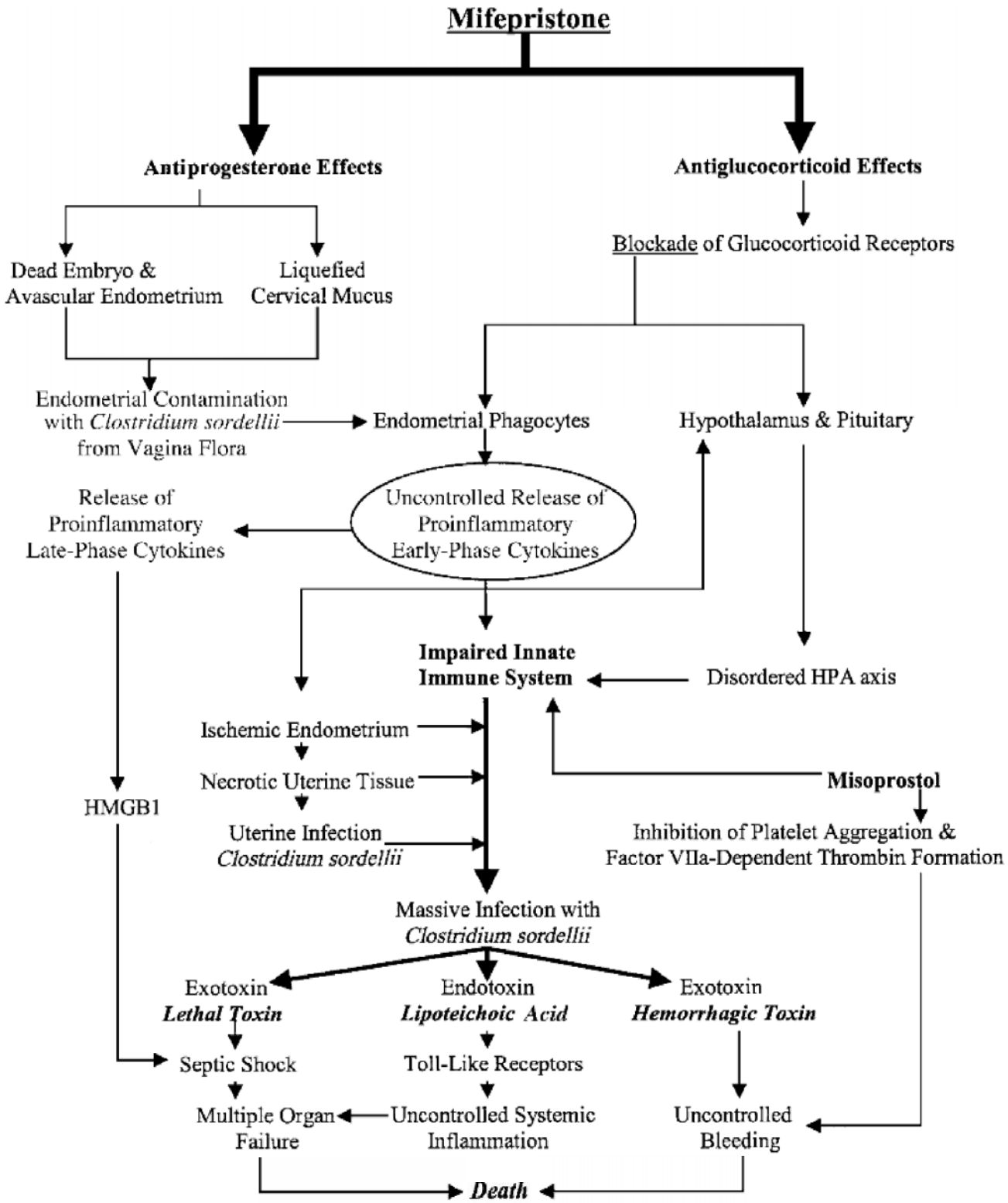
Second, the cause of recent American deaths has been the use of mifepristone (RU-486), not the use of the prostaglandin. It is mifepristone that disables a woman's' innate immune system, leading to a rapid growth of *Clostridium sordellii*. This bacterium produces lethal toxins.

Third, the symptoms of infection with *C. sordellii* are mild and deceptive, mimicking the expected symptoms of a chemical abortion (nausea, vomiting and stomach pain). Most problematic is the fact that women do not have a fever, a normal sign of bacterial infection.

Fourth, the fatal bacterium is both difficult to detect and to treat with antibiotics. Even removal of the diseased uterus is an action that will not save the woman's life.

Based upon the evidence presented in this detailed submission I would recommend to the Honourable Members of this Senate Committee that they support the current legal situation which allows for the Minister for Health to have the final determination as to the entry of this drug into our country. By maintaining the current legislative arrangement, it is the Minister and hence Parliament that decides. One matters of life and death, this is the most open and candid *modus operandi*.

Appendix 1 – The proposed mechanism of action of RU-486 induced Clostridium sordellii fatal sepsis. [67]

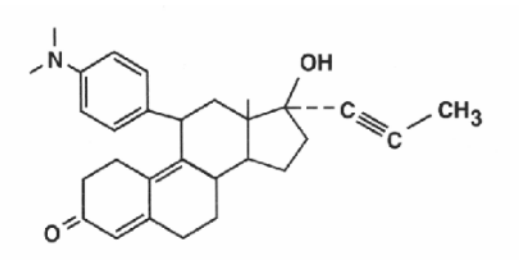


[67] Miech R. Pathophysiology of Mifepristone-Induced septic shock due to Clostridium sordellii. *Ann Pharmacotheraphy*. 2005;39:1483-8

Appendix 2 – the structure and chemical composition of RU-486.

Mifepristone is a substituted 19-nor steroid compound chemically designated as 11ß-[*p*- (Dimethylamino)phenyl]-17ß-hydroxy-17-(1-propynyl)estra-4,9-dien-3-one.

Its empirical formula is $C_{29}H_{35}NO_2$. Its structural formula is:



The compound is a yellow powder with a molecular weight of 429.6 and a melting point of 192- 196°C. It is very soluble in methanol, chloroform and acetone and poorly soluble in water, hexane and isopropyl ether.