11 January 2006

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

Therapeutic Goods Amendment (Repeal of Ministerial responsibility for approval of RU486) Bill 2005

Attached is the submission of the Australian Federation of Right to Life Associations to the Inquiry being conducted by your Committee.

Yours sincerely

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The Australian Federation of Right to Life Associations submits that the decisions concerning the importation of abortifacient drugs, such as RU-486, into Australia should be taken openly in the parliamentary arena. Consequently the Federation opposes the Therapeutic Goods Amendment (Repeal of Ministerial responsibility for approval of RU486) Bill 2005 which would remove the decision on the importation of abortifacient drugs from the Minister for Health, as currently provided by the *Therapeutic Goods Act 1989*, to the Therapeutic Goods Administration (TGA).

The Federation can see no justification for allowing or facilitating the importation of RU-486 as an abortifacient intended to induce an abortion up to 9 weeks after conception. We oppose its introduction into Australia because the drug both causes the death of unborn children and it also subjects women taking it to additional physical and psychological risks, including death in a number of instances.

This Submission has five parts and three attachments:

A. Inappropriate wording of the Therapeutic Goods Amendment (Repeal of Ministerial responsibility for approval of RU486) Bill 2005.

B. Historical background of s. 6AA of the *Therapeutic Goods Act 1989* (an amendment made in 1996) which requires ministerial approval for importation of abortifacient drugs.

C. Reviews of Therapeutic Goods Administration (TGA) effectiveness.

D. Problems with RU-486.

E. Conclusion

Attachments

A: Audits of the Therapeutic Goods Administration 1996 to 2005

B: US Food and Drug Administration Information Sheet on Mifepristone

C: US Food and Drug Administration Patient Information Sheet on Mifepristone

A. Inappropriate wording of the Therapeutic Goods Amendment (Repeal of Ministerial responsibility for approval of RU486) Bill 2005

It should be noted that the discussion of the amendment Bill in the community and before this Committee has been focused exclusively on the regulation of RU-486. This is seriously misleading as to the full effect of the Bill were it to be passed**.** The very title of the amendment Bill fails to disclose adequately the scope of the amendments. The title of the Bill and its Purpose clause would suggest that its only effect would be to remove Ministerial responsibility for approval of RU 486:

> The purpose of this Act is to remove the responsibility for approval of RU486 from the Minister and to provide responsibility for approval of RU486 to the Therapeutic Goods Administration. [1]

The amendment Bill provides for the repeal of sections 6AA, 6AB, and 23AA of the *Therapeutic Goods Act 1989* and also for repeal of the definition of "restricted goods" in s 3(1).

However, s 6AA of the *Therapeutic Goods Act 1989* does not refer specifically to RU-486:

> "(1) In spite of any other provision of this Act, a person must not, without the written approval of the Minister, import any restricted goods into Australia. "

and s 3(1) provides:

> *restricted goods* means medicines (including progesterone antagonists and vaccines against human chorionic gonadotrophin) intended for use in women as abortifacients.

That means that if the amendment Bill is passed, it would remove from Ministerial responsibility approval of the importation of all abortifacient drugs/vaccines, not only of RU-486. This effect is conceded in the Explanatory Memorandum to the Bill:

> The amendments to the Therapeutic Goods Act 1989 in this Bill will bring the approval process for medications *such as RU486* into line with the evidence-based assessment used for all other medicines in Australia. (italics added)

B. Historical background of s 6AA of the *Therapeutic Goods Act 1989*

It is notable that the officials of the Department of Health and Ageing, in their evidence to the Senate Committee on 15 December, professed ignorance of the background in Parliament which led to the amendment in 1996 of the Act.[2] Only Senator Troeth of the four Senators proposing the Bill was a Federal MP at the time of the 1996 amendment; it is possible that neither she nor the other three sponsoring Senators are aware of the circumstances under which Ministerial responsibility came to be necessary for approval of abortifacient drugs.

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[1] **1 Short title** This Act may be cited as the *Therapeutic Goods Amendment (Repeal of Ministerial responsibility for approval of RU486) Act 200*5.
2 Commencement This Act commences on the day on which it receives the Royal Assent.
3 Purpose The purpose of this Act is to remove the responsibility for approval of RU486 from the Minister and to provide responsibility for approval of RU486 to the Therapeutic Goods Administration

[2] Senate – Legislation , Thursday 15 December 2005 CA 13.

Recalling how the present arrangements for approval of importation of RU-486 came about is, however, instructive of the caution which should govern its management.

In 1994 clinical trials were conducted on 300 Australian women subjects by the Sydney Centre for Reproductive Health and by Monash University Department of Obstetrics and Gynaecology at the facilities of the Family Planning Association of Victoria. Trials in Victoria and New South Wales were described erroneously as "emergency postcoital contraception" or "morning after" pill trials.

However, as an abortifacient drug, RU-486 was a prohibited import to Australia unless exempted by the Department of Human Services and Health pursuant to the Customs (Prohibited Imports) Regulations. RU-486 gained access to Australia through a combination of events. Under the Clinical Trial Notification scheme which started in 1991 an ethics committee operating under NHMRC guidelines could approve a trial and then simply pay a fee to the Therapeutic Goods Administration (TGA) for the trial to proceed. Undertakings had been given and policy adopted, probably in 1988, that no such exemption would be given unless the Minister was consulted.[3]

Nonetheless an unidentified official with the TGA authorised the import of the banned abortion drug RU-486 in early 1994. This set in train a series of events culminating in the suspension of RU-486 trials, the ordering of a review into the consent forms used, and another review into the functions of Institutional Ethics Committees. The controversy surrounding the Australian trials brought to light the inadequate system of ethical evaluation and trial monitoring in Australia. It highlighted the unaccountable means by which hazardous drugs could be allowed for trial on Australian subjects.

Neither then Health Minister, Dr Carmen Lawrence, nor then Minister for Family Services, Senator Crowley (the TGA came under her portfolio), were consulted prior to the exemption granted for RU-486 trials by the TGA delegate. During the 1994 hearings of the Senate Estimates Committee Dr Malcolm Wright, head of the drug evaluation Branch of the TGA, admitted that the TGA had not carried out an assessment of the quality, safety and efficiency of RU-486; nor had it scrutinized legal and ethical implications of RU-486 before the exemption had been given for its importation and use in the clinical trials.

Committees approving the trials were the Victorian Family Planning Ethics Committee and the NSW Family Planning Association (FPA) Ethics Committee. They and the RU-486 researchers showed great reluctance to submit themselves and their work to public scrutiny, complaining to the NHMRC that Parliament's demands for trial details and consent forms were a threat to academic freedom.

However, then Health Minister Lawrence maintained that committees approving such trials bore a very substantial responsibility and that leaving the matters to “medical experts” was not satisfactory.[4] Serious questions were also raised by Dr Renate Klein and Dr Lynette Dumble about the adequacy of the trial consent form. The legality of the abortions procured in the trials was also questioned.

The outcome was the restriction now embodied in the provisions of s 6AA of the *Therapeutic Goods Act 1989* to ensure that the decision of the Minister would be accountable to the parliament through the tabling of the decision and open to public scrutiny. We note that the 1996 amendments were agreed, without a division being called, by both major parties and with the support of Greens Senator Chamarette.

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[3] Senate Hansard, 17 March 1994, p 1816, Questions without notice: Imports of drug RU-486.
[4] See Margo Kingston’s article in *The Canberra Times*, 17 August 1994

C Reviews of Therapeutic Goods Administration effectiveness

In addition to the lapse noted above in 1994 by a TGA official that led to the 1996 amendment to the *Therapeutic Goods Act 1989* there have been other problems which have featured in a series of audits of the TGA conducted by the Australian National Audit Office (ANAO) and, recently, by Deloitte.

ANAO Audits of the TGA

In the past decade there have been a number of audits conducted by the Australian National Audit Office (ANAO) into the efficiency, effectiveness and accountability of the TGA's performance in evaluating and approving prescription and non-prescription drugs for public use.

Significant findings of relevance to the Committee's Inquiry include:

- the TGA could increase the effectiveness of drug evaluation by closer monitoring of adverse drug reactions. (**ANAO Report no.8 of 1996-7**)
- although the TGA produced much information for the pharmaceutical industry, it could strengthen its external accountability through provision of clearer information on its activity to Parliamentarians and to consumers of prescription drugs. (**ANAO Report no.8 of 1996-7**)
- the TGA's performance indicators and performance reporting were not adequately informing the Parliament and consumers of its work. (**ANAO Report no.8 of 1996-7**)
- as the TGA relies primarily for its evaluation of a drug on the data provided by the manufacturer, the ANAO renewed its recommendations that the TGA should improve its management of the monitoring of adverse reactions to registered drugs. (**ANAO Follow-up Audit 2000**)
- progress and timeliness of the audit was adversely affected by limitations in the TGA's information and records management. (**ANAO Report No.18 2004-05)**
- an analysis of the performance management system for the regulation of *all therapeutic goods* to identify revised key outcomes, key performance indicator and targets for the regulation of therapeutic goods, including improved means for public reporting of outcomes, indicators and targets had not yet commenced. (**Deloitte Consultancy Findings June 2005**)

Further details of these audits are at **Attachment A.**

Comment

It is not the intention of the author of this submission to suggest that the TGA does not perform the bulk of its duties satisfactorily nor that it does not to intend to continue to address the deficiencies revealed in the series of audits cited above. However, the outcomes of these audits do reveal the need for substantial improvement in TGA processes for the sake of public safety.

This audit information should be taken as a balance to the apparently unconsidered views expressed by some parties appearing previously before the Committee when they expressed their complete satisfaction with TGA management of drug approval.

Senator Nash repeatedly pressed witnesses for an opinion on the efficacy of TGA and its operations, as exemplified by the following exchange:

> **Senator Nash**-So to retain the current situation I guess would be to the detriment then of women? If it were going to be of benefit to move it to the TGA, retaining the current situation would then seem to be of detriment to women in Australia?
>
> **Dr Haikerwal**-Indeed. …….
>
> **Senator Nash**-Finally, do you have complete confidence that the TGA have the ability to put the appropriate process in place to manage this drug safely in Australia, if they approved it?
>
> **Dr Haikerwal**-Absolutely.[5] *
>
> * Notably, Dr Haikerwal went on to say that "[t]he TGA also act fearlessly", using as an example the withdrawal of Vioxx.[6] In fact, as explained later in the hearing by Dr David Graham, National Manager, Therapeutic Goods Administration, that drug was withdrawn by the manufacturer after the commencement of litigation against its manufacturers in the USA.[7]

In similar fashion, Senator Nettle elicited from Dr Haikerwal the response that the TGA would have handled the matter differently from the Minister for Health.[8]

At best, comments elicited from witnesses about the management of drug evaluation and monitoring were too sanguine and perhaps based on no more than incidental acquaintance, if any, with the operations of the TGA.

Ms Jane Halton, secretary of the Department of Health and Ageing, was far more circumspect about how the TGA would treat approval of, and/or issuing guidelines for the use of a drug such as RU-486:

> **Ms Halton**- …… The Therapeutic Goods Administration has no role in speculative consideration in relation to drugs that are not listed and for which there have been no applications received. …At the moment the TGA has no role in this area.[9]

In like vein Ms Halton declined to give a self-approval rating for the TGA in respect of management of abortifacient drugs:

> **Senator Nettle**-is the process for approval that the TGA uses for particular drugs a sound and appropriate one to be used for the evaluation of this particular drug?
>
> **Ms Halton**-You are asking for an opinion. As was indicated in the first instance, we cannot provide you with an opinion. We can say that we administer the legislation as it is provided to us, and I believe that we administer it with due diligence.[10]

To Senator Allison's erroneous assumption that there is a current ban on clinical trials for non-abortifacient uses of RU-486, Ms Halton replied:

> **Ms Halton**-…… there has been no barrier for people wishing to do that kind of research and for those alternative uses, particularly in respect to the treatment of some cancers.[11]

It is unfortunate Senator Allison, one of the sponsors of the amendment Bill, should display the same misunderstanding constantly repeated in the media[12] that there is currently a ban on RU-486.

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[5] Senate – Legislation , Thursday 15 December 2005 CA 7.
[6] see footnote 5.
[7] Senate – Legislation , Thursday 15 December 2005 CA 15
[8] Senate – Legislation , Thursday 15 December 2005 CA 9.
[9] Senate – Legislation , Thursday 15 December 2005 CA 14.
[10] Senate – Legislation , Thursday 15 December 2005 CA 16.
[11] Senate – Legislation , Thursday 15 December 2005 CA 18.
[12] For example, *The Sydney Morning Herald*, 3 January 2006, page 1.

Constant assertion by supporters of RU-486 that the TGA is indisputably the appropriate body to evaluate the safety and efficacy of abortifacient drugs should be tempered by the explanation of the role of the TGA in respect of trials of a drug supplied by an overseas manufacturer(s), by Dr Graham, National Manager TGA:

> [these trials are] "quite often done with fairly select groups where, although substantial, you have a limited number of patients that the products are tested on ….. [and] sometimes it is apparent that, when a product gets into the marketplace more generally, side effects which might be of fairly slow occurrence will start to show … [consequently] we would be monitoring the marketplace experience of that drug to identify if there were any consequences …….. "[13]

Dr Graham's remarks are in accord with the findings of *Performance Audit Report No.18 of 2004-05, Regulation of Non-prescription Medicinal Products*, where the ANAO urged an analysis of the performance management system for the regulation of *all therapeutic goods* (italics added). The subsequent Deloitte consultancy noted in June 2005 that this process had not yet commenced. (see Attachment A)

D. Problems with RU-486

It is fair to comment that the most recent information on the adverse effects of RU-486 were documented by individuals and organisations opposed to moving its regulation to the TGA. It renders their opinion that there should be parliamentary oversight and public input more than reasonable.

Notably, the proponents of importing RU-486 have progressively abandoned their earlier public extravagant and inaccurate claims as information about the workings of this 'medical abortion' drug and clinical experience with its use have been revealed. Initially, there were claims that this drug would mean that women need not require the intervention of any medical personnel (usually a male doctor) interfering with a woman's right to an abortion. Even 'over-the-counter' sales were mooted by a gullible media encouraged by this propaganda.

There still lingers in the media some confusion between this type of drug and the so-called 'morning-after' medication. While the latter can in some cases prevent conception, RU-486 is precisely intended to cause the death of the implanted fetus up to 9 weeks of an established pregnancy. Anyone who has experienced, or had acquaintance with a natural miscarriage of this type would be dismayed at such cavalier dismissal of its seriousness. Further, if the drug were to be available without prescription, as was at first proposed, women would have been deprived of any opportunity to receive counselling and advice on positive alternatives.

Following the unmasking of that furphy there then followed the claim that RU-486 would provide safe and easy abortion for women in isolated areas with access to a prescribing doctor but lacking easy access to an abortion clinic. This also has proved to be dangerously inaccurate propaganda with the belated admission that a woman taking RU-486 needs close medical monitoring and ready access to emergency room back-up in the not insignificant number of cases where the miscarriage will be incomplete.

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[13] Senate – Legislation , Thursday 15 December 2005 CA 15.

In sum, RU-486 is not designed to cause prompt abortion in a clinic or in a doctor's surgery. After the drug is taken the woman must wait for it to take effect (the documented interval is as long as several days); this is intended to occur without direct medical supervision (in most instances the woman will expel the foetus in a setting which is unpredictable: home, office, in transit etc.). There is ample evidence emerging from the period that the drug has been available overseas that RU-486 can pose serious health problems including haemorrhage and infections which may cause sterility. It is understood that RU-486 also acts to inhibit white blood cell activity which in turn may produce a suppression of the immune system. The woman's capacity to fight off infection is thus reduced.

The woman must herself decide whether any such complications require medical assistance. Her decision could be delayed by lack of knowledge, guilt, or desire to maintain privacy, increasing the risk of further trauma or even death. Moreover, studies show that RU486 fails to induce abortion in a significant number of cases with the woman subsequently needing surgical intervention to complete the miscarriage induced by the use of RU-486 which is usually followed by the taking of a prostaglandin type drug.

All these statements about the risk to the health of women posed by administration of RU-486 are confirmed by the attached, recently updated (July 2005) documents from the United States Federal Drugs Administration (USFDA):

- USFDA Patient Information Sheet Mifepristone (marketed as Mifeprex) details: those women who should not take this drug (the list is extensive);
  - the adverse outcomes which will need further medical attention including in some cases admission to an emergency room;
  - that in up to 8% of cases the abortion will be incomplete requiring surgical intervention to end the pregnancy or to stop too much bleeding.;
  - potential birth defects if the failed abortion is followed by the birth of a child. *(see* **Attachment B**)

- USFDA Patient Agreement *proforma* requires the woman to indicate that she has been warned of all the above and will undertake to contact her 'provider' if experiencing a high fever, severe abdominal pain, severe bleeding, vomiting or diarrhoea and so on. If the woman needs emergency room treatment then she undertakes to take the Patient Agreement with her so that the medical staff will understand that she is having an induced, incomplete abortion.
  (see **Attachment C**)

It is therefore evident that this drug is unsafe for provision not only to women who do not have easy access to the providing doctor and to emergency room back-up,[14] but carries significant risk of failure and adverse effects for all women who take it. It should also be noted that the mortality rate from use of RU-486 has been significantly understated. The death rate from RU-486, which is used to abort pregnancies up to 9 weeks gestation, has been inappropriately compared with that from surgical abortion for stages of pregnancy up to 21 weeks gestation. Comparison of mortality rates for abortions within the same gestational period show a death rate for RU-486 approximating 10 times that of surgical abortion.[15]

[14] See Submissions 1 (Dr D M Gawler) and 5 (World Federation of Doctors Who Respect Human Life)
[15] See Green, M *Fatal Infections Associated with Mifepristone-Induced Abortions, New England Journal of Medicine,2005; 353:2317-18*

It would appear to be incumbent on those who enthusiastically advocate the use of RU-486 to give assurance that they would support the mandatory provision of information about its effects to women whom they think it would benefit. This hope is unlikely of fulfilment when the support for RU-486 so far displayed by some witnesses to this Committee focus almost entirely on the expansion of choice in methods of abortion without sufficient regard for the safety of those 'choices'.[16] It is noted that Ms Roslyn Dundas, ACT Convenor for Women's Electoral Lobby Australia, while a Member of the ACT Legislative Assembly, voted in 2002 for the repeal of the *Health Regulation (Maternal Health Information) Act 1998*. The Act was repealed with the result that abortion providers are no longer required to give to women seeking abortion a booklet of information; this information had been authorised by the ACT Health Minister and set out a variety of material including adverse effects of abortion and other choices available to women.

In light of what is now known about this drug and the danger and distress it can cause to women the present provisions of s 6AA of the *Therapeutic Goods Act* 1989 (amendment passed in 1996) requiring ministerial approval for its importation should remain.

Further, it is undeniable that the procuring of abortion is not exclusively a matter to be considered from the exclusive viewpoint of drug administration. It is undeniable that a drug to procure abortion is of unique significance. It is not designed to cure any disease or medical condition; it is intended exclusively for procuring the miscarriage of a pregnancy absolutely irrespective of whether the pregnancy is a perfectly healthy one, as it would be in the vast majority of cases.

Abortion remains an issue of grave moral and social significance and is still governed by legal constraints in all Australian jurisdictions with the exception of the ACT where the repeal of abortion provisions in the Crimes Act 1900 (ACT) was achieved in 2002 by the margin of one vote. Ms Dundas voted for the repeal.

Doubt has been raised as to whether the prescription of RU-486 or any similar abortifacient drug in early pregnancy would meet the legal tests in Australian States and the Northern Territory. The test of necessity expounded in *Wald v Davidson* to protect the mother from serious risk of harm to her physical and/or mental health is usually applied to determine the lawfulness of abortion. This test is unlikely to be met in view of the circumstances where RU-486 would be prescribed. In almost all instances it would be too early in the pregnancy for a woman or doctor to form an opinion that continuance of the pregnancy would cause a serious risk to the life or health of the mother.

It might reasonably be concluded that the prescription of RU-486 as so lightly advocated by its proponents would breach, for example, s 83 of the *Crimes Act 1900* (NSW) and s 65 of the *Crimes Act 1958* (VIC) and carry grave legal risks for general practitioners beguiled by the easy reassurances of pro-choice advocates.

[16] For example, submission 4 (National Foundation for Australian Women) and evidence given to the Committee by Ms Roslyn Dundas (Senate – Legislation , Thursday 15 December 2005 CA 67 ff).

E. Conclusion

The Australian Federation of Right to Life Associations opposes the Therapeutic Goods Amendment (Repeal of Ministerial responsibility for approval of RU486) Bill 2005 which would remove the decision on the importation of abortifacient drugs from the Minister for Health, as currently provided by the *Therapeutic Goods Act 1989*, to the Therapeutic Goods Administration (TGA). However there are alternative methods by which parliamentary scrutiny for approval of abortifacient drugs could be achieved that might ensure more objective, considered debate. It is obvious that the current debate has been deflected from the obvious demerits of RU-486 to criticism of perceived personal beliefs of the Health Minister.

Alternative means other than the present provisions of the *Therapeutic Goods Act* include: approval by a panel of Ministers holding relevant portfolios; approval by Cabinet; approval given in a disallowable instrument. The Association submits that the essential principle is to retain parliamentary accountability for approval of this particular class of drugs which have the peculiar function neither of saving life nor of curing disease, but rather are intended only to kill. Parliamentary scrutiny is the best guarantee of robust public debate on the matter.

Attachment A

Audits of the Therapeutic Goods Administration 1996 to 2005

1. *Drug Evaluation by the Therapeutic Goods Administration* (Department of Health and Family Services), ANAO Report no. 8 of 1996-7.

The purpose of the audit was to examine the efficiency, effectiveness and accountability of the Therapeutic Goods Administration's performance in evaluating and approving prescription drugs for public use.

The audit found that the TGA could increase the effectiveness of its drug evaluation by giving more attention to the monitoring of adverse drug reactions. Further, although the TGA produced much information for the pharmaceutical industry, it could strengthen its external accountability through provision of clearer information on its activity to Parliamentarians and to consumers of prescription drugs. Finally, the ANAO concluded that TGA's performance indicators and performance reporting were not adequately informing the Parliament and consumers of its work.

2. *Drug Evaluation by the Therapeutic Goods Administration - Follow-up Audit 2000*

The ANAO continued to express concern about the TGA's reliance on cost recovery from industry, through charges and fees for services. The TGA relies primarily for its evaluation of a drug on the data provided by the manufacturer. When TGA receives an application from a pharmaceutical company for approval of a prescription drug, it first appraises the application for acceptability and calculates the fees payable by the drug sponsor for the evaluation. If an application is accepted for evaluation, TGA considers the sponsor's data in terms of the legislated quality, safety and efficacy requirements. After evaluating the proposed product, TGA may approve its inclusion in the Register. Further, the TGA requires pharmaceutical companies to supply it with data on any patients' adverse reactions to their medicines. In addition, it encourages reporting by medical personnel of all suspected adverse reactions to medicines.

The ANAO noted:

> **6.** TGA's evaluation of products is crucial to pharmaceutical companies because no therapeutic good may be imported, exported, manufactured or supplied in Australia unless included in the Register. The research and development of a new medicine costs, on average, $750 million and takes 15 years. Effective and timely evaluations of registration applications, once they are received by TGA, are essential to a viable pharmaceutical sector in Australia.
>
> **7.** Australia's market for prescription drugs had a turnover of $6 billion in 1998–99. Between 1990 and 1995, the Australian pharmaceutical industry grew by 7.5 per cent and its ratio of exports to imports increased from 33.3 per cent to 41.9 per

cent. European manufacturers produced 77 per cent of the pharmaceutical drugs for human use that were imported to Australia in 1998–99.[17]

Attachment A (ii)

While there had been improvement in the TGA's efficiency, effectiveness and reporting to its stakeholders performance, the ANAO renewed its recommendations that the TGA should improve its management of the monitoring of adverse reactions to registered drugs.

3. Performance Audit Report No.18 of 2004-05, *Regulation of Non-prescription Medicinal Products*

The TGA is responsible for the regulation of the manufacture and supply of medicines, including complementary and over-the-counter medicines, in Australia, to protect public health and safety. The audit assessed the TGA's regulation of non-prescription medicinal products and addressed the systems, procedures and resource management processes used.

The ANAO noted:

> The progress and timeliness of this audit was adversely affected by limitations in the TGA's information and records management. Where necessary, the Australian National Audit Office (ANAO) has made estimates in key areas, for the purpose of this report.[18]

Licensing and certification of manufacturers

Approximately 60 per cent of manufacturers supplying the Australian market are located overseas, and are certified by an overseas regulator. These regulators are in countries with which Australia has either a Mutual Recognition Agreement (MRA) or a Memorandum of Understanding (MOU)/cooperative arrangements.

Only about 40 per cent of manufacturers of non-prescription medicinal products supplying the Australian market are directly approved by the TGA. Three out of five of these manufacturers are located in Australia.

Before TGA approval to manufacture is granted, it undertakes an audit so that compliance with the Code of GMP can be assessed. The TGA does not measure, or have a standard or target for, the timeliness of the approval process. This limits the TGA's ability to manage and monitor this aspect of its regulatory process.

While the TGA carries out a formal assessment to establish regulatory equivalence to Australian manufacturing standards for MRA signatories, this is not common practice for MOUs/cooperative arrangements. The TGA explained this by declaring that there was already a mutual understanding of each other's regulatory practices; and regular reassessment of regulatory equivalence is undertaken through an international inspection cooperation scheme for most countries that are signatories to the agreements.

However, for some countries, reassessments have been done on an informal basis only. The ANAO also found that one MOU established in 1993 had not been formally reassessed to ensure standards had remained appropriate.

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[17] *Follow-up Audit 2000,* page 10.
[18] Audit Report No.18 of 2004-05, page 13.

The author of this submission expresses concern that these arrangements for the approval on non-prescription drugs might be used for approval of the importation of prescription drugs with the potential effect that the TGA might be constrained to follow the regulatory practices of those countries with which Australia has a MOU/cooperative arrangements.

Attachment A (iii)

The author of this submission expresses concern that these arrangements for the approval on non-prescription drugs might be used for approval of the importation of prescription drugs with the potential effect that the TGA might be constrained to follow the regulatory practices of those countries with which Australia has a MOU/cooperative arrangements.

4. *Therapeutic Goods Administration – Consultancy Findings* June 2005 (Deloitte)

The Department of Health and Ageing engaged Deloitte to undertake a review of the TGA's progress

- in complying with the recommendations of the *ANAO report No.18*; and
- to develop broader recommendations to the TGA on issues such as governance, procedural improvement, risk management and performance management.

Briefly, Deloitte found that while a lot of work had been performed to improve procedures and performance, none of the recommendations had been fully implemented. There remained cause for concern in a number of areas:

- the current Manufacturer Assessment Section audit risk framework does not document the mechanism behind the risk definitions of 'High, Medium and Low' (**3.2.1.1**);
- the structure of the enforcement files reviewed was disorganized and difficult to follow. Decisions and support data were not always obvious (**3.3.1.2**); the level of detail provided and the structure of the audit work papers is inconsistent across files (**3.2.1.3**);
- the executive and management accountabilities are not always well understood by internal and external stakeholders (**4.3.1**);
- lack of clear accountability and consultation reinforced by the following limitations, including limited provisions for accountability and consultation requirements in the *Therapeutic Goods Act*;
- industry representative bodies identified the absence of a certified quality system impacting on the accountability, transparency and effectiveness of the audit program, complaints handling processes, performance reporting and stakeholder relations (**4.3.1**);
- limited coordination across the current compliance and risk management functions (**4.4.1**);
- limited visibility of strategic planning functions dedicated to managing crucial activities (**4.4.1**)

Deloitte's report of TGA progress against ANAO recommendations included:

- the approach to monitor the standards and procedures, performance measures and targets, currency of agreement , resources required to monitor equivalence, including management arrangements, and reporting arrangements, is still to be defined (**Attachment A: ANAO Findings: page 2**);
- the business requirements for trend analysis are still to be clearly defined (**Attachment A: ANAO Findings: page 6**);
- an analysis of the performance management system for the regulation of *all therapeutic goods* in order to identify appropriate revised key outcomes, key performance indicator and targets for the regulation of therapeutic goods, including

improved means for public reporting of outcomes, indicators and targets had not yet commenced (**ANAO Findings: page 12 of Attachment A to the Report**).

Attachment B

Patient Information Sheet
Mifepristone (marketed as Mifeprex)

This is a summary of the most important information about Mifeprex. For details, talk to your healthcare professional.

FDA ALERT– [07/2005] FDA is aware of four women in the United States who died from sepsis (severe illness caused by infection of the bloodstream) after medical abortion with Mifeprex and misoprostol. Sepsis is a known risk related to any type of abortion. The symptoms in these cases were not the usual symptoms of sepsis. We do not know whether using Mifeprex or misoprostol caused these deaths. Patients should contact a healthcare professional right away if they have taken these medicines and develop stomach pain or discomfort, or have weakness, nausea, vomiting, or diarrhea with or without fever, more than 24 hours after taking misoprostol. These symptoms, even without a fever, may indicate sepsis. Make sure your healthcare practitioner knows you are undergoing a medical abortion.
This information reflects FDA's current analysis of data available to FDA concerning this drug. FDA intends to update this sheet when additional information or analyses become available.

What Is Mifeprex?

Mifeprex is used to end an early pregnancy. It blocks a hormone needed for your pregnancy to continue. It is not approved for ending later pregnancies. Early pregnancy means it has been 49 days (7 weeks) or less since your last menstrual period began. When you use Mifeprex (Day 1), you also need to take another medicine, misoprostol, 2 days after you take Mifeprex (Day 3), to end your pregnancy. About 5-8 out of 100 women taking Mifeprex will need a surgical procedure to end the pregnancy or to stop too much bleeding.

Who Should Not Take Mifeprex?

Do not take Mifeprex if:

- It has been more than 49 days (7 weeks) since your last menstrual period began.
- You have an IUD. It must be taken out before you take Mifeprex.
- Your doctor has told you that you have a pregnancy outside the uterus (ectopic pregnancy).
- You have problems with your adrenal glands (chronic adrenal failure).
- You take a medicine to thin your blood.
- You have a bleeding problem.
- You take certain steroid medicines.
- You cannot return for the next 2 doctor's office visits.

- You cannot easily get emergency medical help in the 2 weeks after you take Mifeprex, if you need it.
- You are allergic to mifepristone, misoprostol, or medicines that contain misoprostol, such as Cytotec or Arthrotec.

Attachment B (ii)

What Are The Risks?

The following are the major possible risks and side effects of Mifeprex therapy. This list is not complete.

- **Cramping and Bleeding** are expected with this treatment. Usually, these symptoms mean that the treatment is working. But sometimes, you can get cramping and bleeding and still be pregnant. This is why you must return to your healthcare professional on Day 3 and on about Day 14. See the Medication Guide for more information on when to return to your healthcare professional. If you are not already bleeding after taking Mifeprex, you probably will begin to bleed once you take misoprostol, the medicine you take on Day 3. Bleeding or spotting can be expected for an average of 9–16 days and may last for up to 30 days. Your bleeding may be similar to, or greater than, a normal heavy period. You may see blood clots and tissue. This is an expected part of ending the pregnancy.

Although cramping and bleeding are an expected part of ending a pregnancy, rarely, serious and potentially life-threatening bleeding, infections, or other problems can occur following a miscarriage, surgical abortion, medical abortion, or childbirth. Prompt medical attention is needed in these cases.

Be sure to contact your healthcare professional right away if you have any of the following:

- ***Heavy Bleeding***. Contact your healthcare professional right away if you bleed enough to soak through two thick full-size sanitary pads per hour for two consecutive hours or if you are concerned about heavy bleeding. 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.
- ***Abdominal Pain or Feeling Sick***. If you have abdominal pain or discomfort, or you are feeling sick with symptoms including weakness, nausea, vomiting or diarrhea, with or without fever, more than 24 hours after taking the misoprostol, you should contact your healthcare professional right away. These symptoms may be a sign of a serious infection or another problem (including an ectopic pregnancy, a pregnancy outside the womb).
- ***Fever***. In the days after treatment, if you have severe abdominal pain or a fever of 100.4°F or higher that lasts for more than 4 hours, you should contact your healthcare professional right away. Fever may be a symptom of a serious infection or another problem (including an ectopic pregnancy, a pregnancy outside the womb).

What Should I Tell My Healthcare Professional?

Before you take Mifeprex, tell your healthcare professional about all of your medical conditions and problems, especially if you:

- ***Are Breastfeeding***: If you are breastfeeding at the time you take Mifeprex and misoprostol, discuss with your healthcare professional if you should stop breastfeeding for a few days.
- ***Smoke*** at least 10 cigarettes a day.

Attachment B (iii)

Can Other Medicines or Foods Affect Mifeprex?

Mifeprex and certain other medicines can interact with each other. Tell your healthcare professional about all the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them with you to show your healthcare professional.

What Else Should I Know About Mifeprex?

- You must have 3 visits to your doctor's office during the treatment procedure. It is ***extremely important*** that you attend all three visits. Please read the Medication Guide for information on how to take Mifeprex.
- You can become pregnant again right after your pregnancy ends. If you do not want to become pregnant again, start using birth control as soon as your pregnancy ends or before you start having sexual intercourse again.

Patient Information Sheet Revised 07/2005

Attachment C*

Patient Agreement
Mifeprex (mifepristone) Tablets

1. I have read the attached MEDICATION GUIDE for using Mifeprex and misoprostol to end my pregnancy.
2. I discussed the information with my health care provider (provider).
3. My provider answered all my questions and told me about the risks and benefits of using Mifeprex and misoprostol to end my pregnancy.
4. I believe I am no more than 49 days (7 weeks) pregnant.
5. I understand that I will take Mifeprex in my provider's office (Day 1).
6. I understand that I will take misoprostol in my provider's office two days after I take Mifeprex (Day 3).
7. My provider gave me advice on what to do if I develop heavy bleeding or need emergency care due to the treatment.
8. Bleeding and cramping do not mean that my pregnancy has ended. Therefore, I must return to my provider's office in about 2 weeks (about Day 14) after I take Mifeprex to be sure that my pregnancy has ended and that I am well.
9. I know that, in some cases, the treatment will not work. This happens in about 5 to 8 women out of 100 who use this treatment.
10. I understand that if my pregnancy continues after any part of the treatment, there is a chance that there may be birth defects. If my pregnancy continues after treatment with Mifeprex and misoprostol, I will talk with my provider about my choices, which may include a surgical procedure to end my pregnancy.
11. I understand that if the medicines I take do not end my pregnancy and I decide to have a surgical procedure to end my pregnancy, or if I need a surgical procedure to stop bleeding, my provider will do the procedure or refer me to another provider who will. I have that provider's name, address and phone number.
12. I have my provider's name, address and phone number and know that I can call if I have any questions or concerns.
13. I have decided to take Mifeprex and misoprostol to end my pregnancy and will follow my provider's advice about when to take each drug and what to do in an emergency.
14. I will do the following:
    - contact my provider right away if in the days after treatment I have a fever of 100.4°F or higher that lasts for more than 4 hours or severe abdominal pain
    - contact my provider right away if I have heavy bleeding (soaking through two thick full-size sanitary pads per hour for two consecutive hours).
    - contact my provider right away if I have abdominal pain or discomfort, or I am "feeling sick", including weakness, nausea, vomiting or diarrhea, more than 24 hours after taking misoprostol.
    - take the MEDICATION GUIDE with me when I visit an emergency room or a provider who did not give me Mifeprex, so that they will understand that I am having a medical abortion with Mifeprex.
    - return to my provider's office in 2 days (Day 3) to check if my pregnancy has ended. My provider will give me misoprostol if I am still pregnant.
    - return to my provider's office about 14 days after beginning treatment to be sure that my pregnancy has ended and that I am well.

Attachment C (ii)

Patient Signature: _____

Patient Name (print): _____

Date: _____

The patient signed the PATIENT AGREEMENT in my presence after I counseled her and answered all her questions. I have given her the MEDICATION GUIDE for mifepristone.

Provider's Signature: _____

Name of Provider (print): _____

Date: _____

After the patient and the provider sign this PATIENT AGREEMENT, give 1 copy to the patient before she leaves the office and put 1 copy in her medical record. Give a copy of the MEDICATION GUIDE to the patient.

Rev 2: 7/19/05

* **Note:** re-formatted from the US FDA website.