SUBMISSION TO THE SENATE COMMUNITY AFFAIRS REFERENCES COMMITTEE

INQUIRY INTO GYNAECOLOGICAL CANCER IN AUSTRALIA

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Background

Diethylstilboestrol (DES) is a synthetic oestrogen that was developed to supplement a woman's natural oestrogen production. It was first prescribed in 1938 for women experiencing miscarriages or premature deliveries and was originally considered effective and safe. In 1971 physicians were advised to stop prescribing DES to pregnant women because it was linked to a rare vaginal/cervical cancer in female offspring. Since 1971 research has shown:

- Women prescribed DES while pregnant, known as DES mothers, are at a modestly increased risk for breast cancer.
- Women exposed to DES before birth (in the womb), known as DES daughters, are at an increased risk for clear cell adenocarcinoma (CCA) of the vagina and cervix, reproductive tract structural differences, pregnancy complications and infertility. The risk for developing this cancer is approximately 1:1,000 DES daughters. Although DES daughters appear to be at highest risk for clear cell cancer in their teens and early 20s, cases have been reported in the 30-50 age groups. This cancer is aggressive and should be detected early.
- Men exposed to DES before birth (in the womb), known as DES sons, are at risk for non-cancerous epididymal cysts.

There is specific preventive health care for DES exposure. (See www.cdc.gov/des) The cancer risk to DES daughters has not passed, with cases now occurring in the 40s and 50s age groups. (See http://obgyn.bsd.uchicago.edu/registry.html#accessions)
Researchers are still following the health of the DES exposed population to determine whether other health problems occur with age. There may be many people who do not know they were exposed to DES and some women may not remember taking DES. DES information is important because people who were exposed must be vigilant about their own health care – to catch cancers early, demand high risk obstetric care when pregnant and factor in their exposure when making decisions about HRT use. It is as much part of a person's medical history as a family history toward heart disease or diabetes.

The Adverse Drug Reactions Unit has data of 15 cases of DES associated cancer. With the known 1:1,000 risk of DES daughters developing the associated cancer, this means there are conservatively at least 15,000 DES daughters, the equivalent number of DES sons and 30,000 DES mothers, thus totaling at least 60,000 Australians affected. There has been no complete reciprocal cross-check of Australian cases that have been reported to the International Registry. So far there is refusal by government to conduct regular reciprocal cross-checks with the International Registry held in Chicago US. There are also approximately 129 cases of the cancer type associated with DES in data held by the Australian Institute of Health and Welfare for which DES exposure has not been investigated.

Main Recommendation

The Commonwealth should establish a new government agency, the National Gynaecological Cancer Centre (NGCC) to include a specialist with proven updated consultation and liaison with the American College of Obstetricians and Gynaecologists, Kenneth Noller MD Ob-Gyn (New England Medical Center/Tufts University, Boston) and Arthur L. Herbst MD (Researcher, University of Chicago) in relation to the health of women exposed to DES.

Such a specialist should provide updated information to appointed specialists in each State and Territory major women's hospitals on DES health issues. Such a specialist should also act as consultant for the Commonwealth to ensure that when the public is provided with information about DES, that preventive health advice supported by medical research evidence is also given.

Summary of Recommendations to the Senate Inquiry

The Commonwealth and associated funding agencies should provide the funds to establish an accurate as possible figure of DES associated cancer cases.

The Commonwealth should establish a new government agency, the National Gynaecological Cancer Centre (NGCC). This agency could have a major role in overseeing the establishment and maintenance of a National Registry on Hormonal Transplacental Carcinogenesis.

The scope of screening programs should be expanded to ensure that the needs of DES exposed women are addressed, eg, information in Pap smear reminder letters, information provided when attending Breastscreen services, the provision of Breastscreen reminder letters to DES mothers over 69.

There should be increased funding to provide multidisciplinary care teams with knowledge of the psychosocial aspects of DES exposure.

Translated information about DES should be made available for the benefit of women from non-English speaking backgrounds.

Equivalent services as those provided in urban areas should be made available for DES exposed women in remote areas, including the provision of accessible DES knowledgeable specialists and the infrastructure for this should be coordinated by the NGCC.

An established NGCC should promote the educational program US *CDC DES Update: Educational Tools for Health Care Providers* and ensure the administration of credited points for the medical community, including general practitioners.

An established NGCC should liaise with the US Centers for Disease Control (CDC) and DES Action USA to formulate a program model of the US CDC *DES Update* to allow an effective educative campaign about DES in Australia.

There should be representation of people with proven updated DES knowledge from US experts on peak national bodies such as Cancer Australia (and its advisory council).Such representation will ensure that women who suffer from DES associated cancer and also the remaining population who suffer from other effects of DES will have a national voice and receive appropriate consideration.

Australian Background

The Australian Drug Evaluation Committee issued statements in 1972 in the Medical Journal of Australia (Med J. Aust.,Sept 9 1972. 2:622) and in 1975 in the Adverse Drug Reactions Bulletin (No:5, April 1, 1975) drawing the attention of medical professionals to the association of DES and the development of clear cell adenocarcinoma of the vagina in female offspring in adolescence and young adult life. In May 2003 the own journal of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists, (*O & G,* Vol. 15, No.2, May 2003, *DES 'daughters' - there is no 'safe period' for clear cell adenocarcinoma*) published an article informing doctors that there is no safe period for the development of clear cell adenocarcinoma of the vagina/cervix in DES daughters. In June 2004 a one-way cross check was conducted by the Australian government with the International Clear Cell Cancer Registry held in Chicago USA, showing a significant increase in the figure of known Australian cases from 7 to 15 cases. The government has recognised concerns about failure by doctors to report DES associated cancer to the Adverse Drug Reactions Unit.

To date there has been no concerted campaign to inform and educate the Australian population about DES. Up until 2004, there had only been small intermittent media coverage (not initiated by Government) informing the Australian public about the cancer risk with DES and the reproductive health effects caused by DES. The Therapeutic Goods Administration's (TGA) media release about DES in June 2004 (http://www.tga.gov.au/media/2004/040609_des.htm) was the first media release by the Government to inform the public about DES and its effects and required health care and this received nation-wide coverage. This media release followed a TGA Bulletin item about DES targeting doctors (http://www.tga.gov.au/adr/aadrb/aadr0406.htm#1) and contained information about the recommended health care for DES daughters and their ongoing cancer risks that is unsupported by available medical research evidence. Available medical research indicates that the advice given regarding DES daughters in the media release (the national cervical screening recommendation of Pap smear) does not always detect the aggressive type of cancer caused by DES. It is well-known in DES literature that DES daughters require annual DES examinations to prevent clear cell adenocarcinoma of the vagina/cervix. This media release also indicated that the cancer risk to DES daughters has passed. However, available medical research shows that there is no known upper age limit on the development of DES associated cancer, with cases recently appearing in the 40s and 50s age groups. (See http://obgyn.bsd.uchicago.edu/registry.html#accessions) Information readily available in Australia prior to June 2004 is as follows:

- The Royal Australian and New Zealand College of Obstetricians and Gynaecologists' own journal *O&G* Vol 5 No2 May 2003 (www.ranzcog.edu.au/publications/o-g_pdfs/OG-2000-2003/OG-May-2003.pdf)
- The Medical Journal of Australia, October 13, 1984 *The DES Story* by Professor Malcolm Coppleson, Head, Gynaecological Unit, King George V Memorial Hospital, Sydney.
- The NHMRC guidelines issued in 2005 has a reference dated year 2000 regarding the special care of annual pelvic examination for DES

daughters [Hacker NF. Vaginal carcinoma. In:Berek JS, Hacker NF eds. Practical Gynaecologic Oncology. 3rd ed. Philadelphia. Lippincott Williams and Wilkins. 2000. Ch 14. p605].

- The annual DES examination has been described on the NSW Health website www.health.nsw.gov.au/des since May 2003 and the US Centers for Disease Control website www.cdc.gov/des since 2003.
- The American College of Obstetricians and Gynaecologists agreed on 31st July 2003 that annual screenings are vital for DES daughters (see www.acog.org/from_home/publications/press_releases/nr07-31-03-1.cfm)
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- On 18th March 2003 Health Canada released a Health Professional Advisory *Advisory on diethylstilboestrol (DES) and the risk of genital and obstetrical complications* (http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2003/des_hpc-cps_e.html) in which the annual pelvic examination is outlined under the heading of *Systematic monitoring of women exposed in utero to DES.*

In October 2005, the TGA published a Bulletin item targeting doctors with information advising the annual DES examination for DES daughters. (See http://www.tga.gov.au/adr/aadrb/aadr0510.htm#3), but did **not** issue a media release to alert the population of the change in advice.

Concerns regarding the TGA's June 2004 media release and the disparity by not issuing a further media release are aggravated by the following factors:
(1) There would be women who do not yet know of their in utero DES exposure and also doctors, who for practical reasons, cannot be expected to identify the DES exposed population.
(2)There would be women who are aware of their DES exposure, but still unaware of their special health needs and so would not place importance on informing their doctors about their DES exposure.
It is highly impractical for doctors to be responsible for identifying DES exposed individuals and it is the right of Australian people to know the possibility of having been DES exposed and to know the risks and specific preventive health measures involved.

The TGA has stated the June 2004 media release was appropriate because prior to the media release there was no national agreement or any national guidelines for the care of DES daughters. The Minister for Health and Ageing, The Hon Tony Abbott has stated that a further media release to inform the public of the Government's changed position regarding health advice for DES daughters is not warranted.

The Australian Screening Advisory Committee is aware of the full details of the 2003 US Centers for Disease Control *DES Update* campaign with its strategy in targeting women in times of transition, ie, women seeking information about breast and cervical cancer. However, advice from the Australian Chief Medical Officer has been that the needs of DES exposed women are beyond the scope of the National Cervical Screening Program.

The obvious disparity in the TGA's actions in relation to the June 2004 media release and the October 2005 bulletin item by not issuing a media release to alert the Australian public of the change in advice is a very serious concern to the organisation, DES Action Australia-NSW. It is also of concern that the Australian Screening Program has no scope in its policy to address the needs of DES exposed women, including DES daughters for whom the National Cervical Screening recommendation is not appropriate. Most concerning of all to the organisation is that every reasonable effort has been made and all avenues have been exhausted merely to seek parity with the US health authorities in their enlightened management of their own patient cohort which differs only from that in our own developed western nation in terms of scale and population.

The terms of reference for the inquiry have been addressed below:

a) Level of Commonwealth and other funding for research addressing gynaecological cancers

Research about DES has largely been conducted in USA. There has been no research by Commonwealth to establish a figure that is as accurate as possible of DES associated cancer cases which would ultimately show the magnitude of the DES exposure problem in Australia. The available relevant data for this is scattered between the Adverse Drug Reactions Unit, the International Registry for Research on Hormonal Transplacental Carcinogenesis held in Chicago USA, the Australian Institute of Health and Welfare and State Cancer Registries (prior to 1982). Such research to establish a figure by the Commonwealth is fundamental to future research about DES in Australia to the benefit of those affected and would provide the information required for the establishment of an Australian Registry on Hormonal Transplacental Carcinogenesis.

Recommendations (a):

- The Commonwealth and associated funding agencies should provide the funds to establish an accurate as possible figure of DES associated cancer cases.
- The Commonwealth should establish a new government agency, the National Gynaecological Cancer Centre that could oversee the establishment and maintenance of a National Registry on Hormonal Transplacental Carcinogenesis.

b) Extent, adequacy and funding for screening programs, treatment services, and for wider health support programs for women with gynaecological cancer

There would be DES daughters, unknowing of the fact of their DES exposure and following the national cervical screening recommendation, and who would be at risk of clear cell adenocarcinoma of the vagina/cervix not being detected early. Women could be informed about DES within the services of the screening program, ie, in Pap smear reminder letters and information provided when attending Breastscreen services. There would be DES mothers over the age of 69, who due to their increased breast cancer risk, choose to be prudent with their breast health care. With memory not as intact with advancing years, these women are even more disadvantaged than the general population by Breastscreen’s decision to no longer send reminder letters for mammogram checks. There is inadequacy in the scope of screening programs to address the needs of DES exposed women**.** The psychological consequences of DES can be far greater and longer lasting than the physical effects. Specific government health support programs are non-existent for women who have developed DES associated cancer and for those DES exposed women who suffer depression, anxiety, guilt and fear of the unknown in relation to DES.

Recommendations (b):

- The scope of screening programs should be expanded to ensure that the needs of DES exposed women are addressed, eg, information in Pap smear reminder letters, information provided when attending Breastscreen services, the provision of Breastscreen reminder letters to DES mothers over 69.
- There should be increased funding to provide multidisciplinary care teams with knowledge of the psychosocial aspects of DES exposure.

(c) Capability of existing health and medical services to meet the needs of Indigenous populations and other cultural backgrounds; and those living in remote regions

DES was prescribed to pregnant women in many countries of the world, including USA (estimated 5-10 million DES exposed*), Canada (estimated 400,000-800,000 DES exposed*), UK (estimated 20,000 DES exposed*), France (estimated 400,000 DES exposed*), The Netherlands (estimated 440,000 DES exposed*), Czechoslovakia (estimated 126,000 DES exposed*), Ireland, Belgium, Germany, Italy and Spain. Countries of possible usage are Finland, Norway, Portugal and Switzerland. (**Figure includes women and offspring.*)
DES was still prescribed to women outside the United States after 1971. As recently as 1993 there were concerns that DES may still be given to pregnant women in East and Central Europe, Africa, Asia and Latin America

There would be women from these overseas countries residing in Australia. There would be DES exposed women living in remote regions experiencing problems accessing DES knowledgeable specialists.

Recommendations (c):

- Translated information about DES should be made available for women from non-English speaking backgrounds.
- DES knowledgeable specialists and facility to address psychosocial needs should be accessible to DES exposed women in remote areas
- The infrastructure support required for the above two recommendations should be coordinated by an established NGCC.

(d) Extent to which the medical community needs to be educated on the risk factors, symptoms and treatment of gynaecological cancers

For many years it has been thought by the medical community that the cancer problem associated with DES has passed, when it has not. Because of this mistaken belief, all of the associated health problems with DES exposure have been "lost from the radar screens" of the medical community. The website of the US Centers for Disease Control (CDC) (www.cdc.gov/des) has a downloadable educational program for medical professionals without copyright. This program would have particular value for General Practitioners since they are the gatekeepers for referring DES daughters for specialist treatment and identifying the DES exposed population. However the Australian College of General Practitioners does not have the administration capacity to offer credited points for the US educational program about DES.

Recommendation (d):

- An established NGCC should promote the educational program US *CDC DES Update: Educational Tools for Health Care Providers* and ensure the administration of credited points for the medical community, including general practitioners.

(e) Extent to which women and the broader community require education of the risk factors, symptoms and treatment of gynaecological cancers

There has been no concerted educational campaign by the Commonwealth to inform the Australian population of the possibility of having been DES exposed when it is an individual's right to be informed and made aware of the associated preventive health measures. In 2003, in partnership with DES Action USA, the US Centers for Disease Control launched a new comprehensive information resource about exposure to DES (www.cdc.gov/des)*as* part of a multi-million dollar campaign so that individuals could access to learn more about DES exposure and how this could affect them, their families and their friends.

Recommendation (e):

- An established NGCC should liaise with the US Centers for Disease Control (CDC) and DES Action USA to formulate a program model of the US CDC *DES Update* to allow an effective educative campaign about DES in Australia.

(f) Extent to which experience and expertise in gynaecological cancer is appropriately represented on national health agencies, especially the recently established Cancer Australia

There is absence of representation of people on national health agencies with experience and expertise in DES health issues and who have proven updated liaison with US experts in the field of DES exposure.

Recommendations (f):

- There should be representation of people with proven updated DES knowledge from US experts on peak national bodies such as Cancer Australia (and its advisory council).
- Such representation will ensure that women who suffer from DES associated cancer and also the remaining population who suffer from other effects of DES will have a national voice and receive appropriate consideration.

INFORMATION SOURCES

www.cdc.gov/des

Website of DES Action USA http://www.desaction.org/
www.web.ca/~desact/anglais/anglais.html

UK Royal College of Obstetricians and Gynaecologists RCOG Statement No.2, April 2002.

Australian Adverse Drug Reactions Bulletin Vol. 23, No.3, June 2004

www.des-france.org/presse/presse_dates.asp

www.descentrum.nl

DES: A Drug with Consequences for Current Health Policy (Symposium, September 1990, Dublin Ireland, funded by Europe Against Cancer Programme and the Dutch foundation Fundraising Actions for Public Health).

Effects of diethylstilboestrol (DES) medication during pregnancy: report from a symposium at the 10th International Congress of ISPOG. J Psychosom. Obstet. Gynaecol. 14 (1993) 71-89.

www.health.nsw.gov.au/des

Adverse Drug Reactions Advisory Committee Minutes 1971-2003.

Australian Drug Evaluation Committee Minutes 1967-1981.