SUMMARY REPORT OF THE 1996 OECD QUESTIONNAIRE

ON ENDOCRINE DISRUPTING SUBSTANCES

SUMMARY REPORT OF THE 1996 OECD QUESTIONNAIRE ON ENDOCRINE DISRUPTING SUBSTANCES

SUMMARY

1. In December 1996, a questionnaire was sent to Member countries to identify to what extent the possible risk of endocrine disruption should be a priority issue for the OECD and to obtain a snapshot of views on endocrine disruption as they were emerging in early 1997.

2. A high level of activity was reported on the topic in Member countries with reviews or national reports in preparation or available in almost all of them. Many projects concerning collection of use, exposure and toxicological and environmental data were identified.

3. Investigation of effects in reproductive systems were considered the most relevant to identify hazards in aquatic, terrestrial and mammalian species. Better knowledge of the mechanism of endocrine disruption would assist determining the most relevant endpoints to include in a testing strategy. At this stage, morphological and functional effects in mammals, and the effects on sex-hormones in mammals and morphological effects in the reproductive system of aquatic and terrestrial species were seen as priorities.

4. Countries indicated that enhancements to existing OECD test Guidelines are required in order to be able to detect endocrine disrupting effects. Consistent with the priority identified above, the most frequently identified priority was enhancing Test Guideline 416 (Two generation reproductive toxicity study) and Test Guideline 421 (Reproductive/developmental screening test) to include measurement of sex-hormone levels and morphological study of the gonads.

5. The need for new OECD Test Guidelines was also identified, with the most frequently identified area the reproductive system of aquatic species, and sex-hormones levels in both mammalian and environmental species.

6. Most countries have the possibility of addressing endocrine disrupters within their existing regulatory regimes. No action solely on the basis of possible endocrine disruption has yet been taken. However many of the substances identified as possible endocrine disrupters have already been regulated or controlled in countries.

INTRODUCTION

7. In December 1996 a questionnaire was sent to regulatory agencies in OECD Member countries for the purpose of:

- obtaining a better insight into Member countries' concerns about endocrine disrupting substances (EDS);
- developing an overview of current regulatory activities in the area; and
- identifying the need for test method development.

8. The questionnaire was designed to help identify to what extent the possible risk of endocrine disruption was a priority issue for the OECD, with the results to be taken into account when proposing the development or revision of OECD Guidelines for the Testing of Chemicals.

9. The survey was carried out using a questionnaire sent to National Co-ordinators of the OECD Test Guidelines Programme with copies to the members of the OECD Risk Assessment Advisory Body and Pesticide Forum to ensure that overlaps between testing, assessment and different classes of chemicals were covered.

10. The survey was conducted between 20 December 1996 and May 1997. Wherever possible one response per country was provided but given the timeframe for administering the survey and the various perspectives that exist this was not always possible. Given this, and the fact that scientific consensus on the issue is still developing, the survey results can only give a snapshot of county views and perspectives as they existed in early 1997.

11. Twenty-one countries completed the questionnaire, namely Australia, Austria, Belgium, Canada, the Czech Republic, Germany, Denmark, Finland, France, Greece, Ireland, Italy, Japan, the Netherlands, Norway, Poland, Spain, Sweden, Switzerland, the United Kingdom, and the United States of America. A total of 28 individual responses have been included in the analysis.

12. A summary and an evaluation of the responses received from the Member countries is given below. Many countries provided additional comments and these have been used to provide further insight and information when appropriate.

13. Relevant published research, national reports and reviews and details of contact persons for national expert groups are given in Annex 1, 2, 3 and 4 respectively. A copy of the original questionnaire is given in Annex 5.

RELEVANCE AND SCOPE

14. All countries considered endocrine disrupting substances candidates for regulatory or advisory activities with half suggesting that endocrine disrupting substances were of major concern.

15. Several reasons for this concern were given. The most frequently mentioned were wildlife and toxicological studies and public concern. Epidemiological studies, ecotoxicological studies, environmental and human exposure were mentioned in over half the countries as additional reason for concern. Uncertainty was identified as an important reason with conflicting research, unknown causes or the effects seen, lack of information on environmental and public exposure and other data gaps all stressed as important.

16. Concerns were derived from published literature and cases. A consolidated list of literature references is given in Annex 1.

17. Half the respondents stated that there was a good understanding in their country of what should be considered an endocrine disrupting substance and half did not, indicating that interest and consensus on this subject is still developing and emphasising that continuing provision of information will be important.

18. On 2-4 December 1996, a European Workshop was held on the Impact of Endocrine Disrupters on Human Health and Wildlife. There was general agreement at this Workshop that an endocrine disrupter

could only be adequately defined through the testing of chemicals in intact animals. It was accepted that the identification of **potential** endocrine disrupters could be based upon data derived from *in vitro* studies.

19. Definitions agreed at the Workshop were:

> **"An endocrine disrupter is an exogenous substance that causes adverse health effects in an intact organism, or its progeny, *consequent* to changes in endocrine function."**
>
> **"A potential endocrine disrupter is an exogenous substance that possesses properties that might be expected to lead to endocrine disruption in an intact organism."**

20. Almost all respondents (17/21) considered the definition of endocrine disrupting substance (referred to as the "Weybridge definition") as an acceptable or good starting point. In some countries or groups of countries there is further work in progress to develop a consensus on the definition of endocrine disrupting substance.

21. Many countries noted that while the Weybridge definition for an endocrine disrupter was acceptable it applied to all components of the endocrine system including the thyroid gland, testes, and suprarenal glands making a very broad area for work. Others were concerned that further consideration was needed to define the types of health effects that would be included and what was considered "adverse". For example, changes in hormone levels may occur that may go undetected or have undetected consequences. Several countries pointed to the fact that endocrine disruption describes a mechanism rather than being an adverse effect in itself.

CHEMICALS

22. Most countries regard the following chemicals and chemical groups as containing some potential endocrine disrupting substances namely; Phytoestrogens, PCB's and metabolites, phthalates, TBT, chlorinated hydrocarbons, chlorinated dioxins/furans, alkylphenols, DDT and metabolites, alkylphenolethoxylates, organometals, pesticides, pharmaceuticals, food additives. Other chemicals/categories noted in some countries responses included: bisphenol A and brominated flame retardants, optical brighteners, detergent derivatives and steroid hormones.

23. Many countries expressed concern that the questionnaire referred to broad use categories when only some members of these groups are of suspected of possible endocrine disruption. This comment applied especially to the following groups; pesticides, chlorinated hydrocarbons, organometals, pharmaceuticals and food additives.

24. In conclusion, while the listing of chemicals as endocrine disrupting substances is seen by some countries as premature, there is a level of agreement that certain specific chemicals have potential endocrine disrupting effects and a consensus on the need to develop agreed ways in which to identify potential endocrine disrupting substances was evident.

25. Table 1 lists the chemicals mentioned by countries in their answers to the questionnaire. It shows examples of those chemicals on which countries have current concerns and projects.

Table 1: **List of chemicals or chemical groups mentioned as of possible concern for endocrine disruption in Member countries**

Chemical/Chemical Group	**Examples of countries which mention concern about specific chemicals/classes of chemicals**	**Examples of countries which have specific projects on use, exposure, emission etc.**
Alkylphenols e.g. nonyl, octyl	DK, NO	AT, CH, NL, NO, SE, UK, US
Alkylphenolethoxylates eg nonyl, octyl	BE, CH, DK, NO, UK	DK, SE, UK
Bisphenol A		AT, NO, SE, UK, US
Brominated Flame Retardants		
Chlorinated Hydrocarbons		
DDT and metabolites	CH, SE	DK
Derivatives of detergents (e.g. amsonic acid)		
Dioxins/Furans		DK, FI, NL, UK
Fragrances		
Food additives		
Optical brighteners		
Organometals		BE
PCB's and metabolites	CH, NO, SE	DK, NL, SE, UK
Pesticides	FI	AT, BE, DK, ES, GR, IT, SP, UK
Vinclozin	FI, NO, SE	
Benomyl	SE	
Endosulphan	NO	
Dicofol	SE	
Atrazine	SE	
Pharmaceuticals		AT, ES
Phytoestrogens	UK	UK, US
Phthalates	UK	AT, ES, UK
DEHP	DK	DK
Di butylpthalate		
Butylbenzylphthalate		
Siloxanes		
Steroid Hormones		UK
Tributyltin	CH, NO, SE	NL, NO
UV absorbers in cosmetics		

PROPERTIES

26. Almost all countries (19/21) agreed that other than toxicity, biodegradation, formation of toxic by-products through biodegradation, persistence, stability and bioaccumulation are other important properties in risk assessment and regulatory work with endocrine disrupters. Almost all countries also considered the volume of production and use and the use/release pattern very important. Chemical structure of the substance was also considered important by about half the countries.

27. Six Member countries specified exposure as important particularly when discussing endocrine disruption. Other aspects mentioned by one or two countries included information on substitution, epidemiological information, and pharmacodynamics.

KNOWLEDGE AND REVIEWS

Existing reviews and reports

28. Almost all responding countries (17/21) have issued or plan to issue reviews or national reports on the present knowledge of endocrine disrupting substances, emphasising the great interest in this area. Details of 26 reports were provided from Austria, Denmark, Finland, France, Germany, Ireland, Japan, Netherlands, Norway, Sweden, the United Kingdom, and the United States. An ECETOC Monograph (No 33) "Environmental Oestrogens: Compendium of Test Methods" was published in 1995. Most of the national reviews and reports were published in 1995/96. Annex 2 provides further information on these reviews.

Use and exposure

29. Many projects concerning the use, exposure and emission of endocrine disrupting substances are currently underway or are planned in Member countries. Most countries have some activity in this regard. The chemicals which are the focus of these activities are summarised in Table 1 (see above).

30. A variety of means are used to collect data e.g. pollutant release and transfer registers (PRTR), product register, surveys regarding release, environmental fate data and occupational exposure measurements. Measurement in the environment is by far the most common way to collect data with measurement of dietary intake and environmental fate data also frequently used.

31. European countries highlight the European Existing Substances Risk Assessment Programme as a means of gathering information on use and exposure. Other projects with a more research focus include e.g. kinetic studies on nonylphenol, ecological responses and toxicological research. Projects for the development of screening tests, and techniques for measuring and testing were mentioned by three countries.

32. Many studies on use, exposure and emission are also being carried out to address other issues such as persistent organic pollutants.

Expert committees

33. Member countries have different co-ordination mechanisms for their work on endocrine disrupting substances. Half the countries (10/21) have established expert committees with wide interdepartmental representation for example Environment, Health, Consumer Affairs, Occupational Health and Safety. A further two countries were planning to establish such committees. The national contact persons in each country are listed in Annex 3.

HAZARD CHARACTERISATION

Relevant endpoints

34. Countries were asked to score which biological endpoints are most relevant for the hazard characterisation of endocrine disrupting substances.

35. Effects in the reproduction systems were considered most relevant with: 1) morphological and 2) functional effects in the reproduction system of mammalian target species; 3) effects on sex-linked hormone level in mammalian species; 4) morphological effects in the reproductive system of aquatic target species; and 5) morphological effects in the reproduction system of terrestrial target species rated most highly.

36. The scores given by each respondent have been added in Table 2 to give an indicative importance of each endpoint.

Table 2: **Endpoints considered most relevant to the hazard characterisation of an endocrine disrupting substance.**

Endpoints	Total score
Aquatic target species	
Morphological effects in the reproductive system	92
Any morphological effect	42
Functional effects	75
Terrestrial target species	
Morphological effects in the reproductive system	91
Any morphological effect	35
Functional effects	72
Mammalian species	
Morphological effects in the reproductive system	121
Functional effects in the reproductive system	102
Morphological effects in the immune system	74
Effects on CNS	78
Other effects	
Reproductive system with evidence of a steroid dependent mechanism	22
Functional effects on the reproduction of aquatic species	9
effects on neuroendocrine and reproductive developments	
Evaluation of thyroid and adrenal function	
Possible dependent cancers	
New *in vitro* studies (receptor binding etc.)	
Effects on hormones/hormone levels	
Effects on sex-linked hormones/hormone levels in environmental species	76
Effects on sex-linked hormones/hormone levels in mammalian species	103
Effects on hormones/hormone levels	61
Clinical chemical parameters: thyroid hormones/hormone levels	18
Clinical Chemical parameters: circulating gonadotropins	20
Vitellogenin/zona radiata proteins in male fish	4

37. Thyroid hormones/hormone levels, receptor binding studies, reproduction/fecundity in Daphnia and fish and hormonally dependent cancers were relevant endpoints.

38. It was emphasized that as long as an understanding of the effects is insufficient all of the endpoints might be useful for hazard characterisation. Better knowledge of the actual mechanism of endocrine disruption is critical if the most relevant endpoints are to be identified.

TEST GUIDELINES

Existing Test Guidelines

39. Almost all respondents (24/26) felt that current OECD guidelines are insufficient for the testing of potential endocrine disrupting substances.

40. There was a clear preference in many responses to enhancing existing guidelines rather than developing new test guidelines particularly for human health effects. Many highlighted the need to consider the detail of what changes might be necessary in conjunction with consideration of the comments on the OECD Detailed Review Paper: Appraisal of Test Methods for Sex-Hormone Disrupting Chemicals.

41. Several Member countries emphasised again the scientific uncertainty surrounding endocrine disrupting substances and proposed that the development of new or the revision of existing test guidelines should take this into account and not proceed too quickly, allowing the necessary research to take place.

42. Table 3 shows the relevant endpoints suggested by Member countries which could enhance existing OECD Test Guidelines. The most frequently identified existing test guidelines were:

- TG 416: 2 generation reproductive toxicity; and
- TG 421: Reproduction/Developmental Screening Test.

The enhancements for these tests suggested most frequently were level of sex-linked hormones and morphological studies of the gonads.

Table 3: Relevant endpoints suggested by Member countries which could enhance existing OECD Test Guidelines

Existing Guideline	No. of country responses	Suggested relevant endpoints (references are explained in Annex 3)
TG 204, Fish, Prolonged Toxicity Test: 14-Day Study	10	Reproduction (CA2); Vitellogenin in young males (NO, CH); Morphological effects, changes in reproductive organs (NO)
TG 206, Avian Reproduction Test	10	Vitellogenin in young males, morphological effects, changes in reproductive organs (NO); Studies of F1-generation: sex organ morphology/histology, sex hormone levels, reproduction ability(SE); *In ovo* exposure, reproduction in offspring (US1)
TG 210, Fish, Early Life Stage Toxicity Test	9	Number of males/females (FI, NO); Developmental exposure, sexual maturation of adults (US1)
TG 414, Teratogenicity	11	Morphological studies of gonads (DE, JP1, SE); Sex ratio, duration of oestrus cycle, ano-vaginal distance (SE)
TG 415, One-Generation Reproduction Toxicity	11	Level of sex linked hormones (CA1, DE, UK); Morphological studies of gonads (DE, SE, UK); Sperm count and sperm morphology in F1-generation (CA1, NO); Sex ratio, duration of oestrus cycle, ano-vaginal distance (SE); Challenge test, weight of testes, uterus, epididymides, epididymal transition of sperm (CA1); Organ weight measurements in offspring (UK)
TG 416, Two-Generation Reproduction Toxicity	14	Level of sex linked hormones (CA1, DE, UK); Challenge test, weight of testes, uterus and epididymides, epididymal transition of sperm (CA1); Behaviour of F1 and F2 generation, ability of reproduction (JP1); Evaluation of fetal and postnatal development of testis (FR); Morphological studies of gonads (SE, DE, JP1); functional tests concerning mating (DE); Sperm count and sperm morphology in F1-generation (CA1, NO); Sex ratio, duration of oestrus cycle, ano-vaginal distance (SE); Organ weight measurements in offspring (UK)
TG 421, Reproduction/Developmental Toxicity Screening Test	13	Level of sex linked hormones and other hormones, challenge test (CA1); Sex ratio, duration of oestrus cycle , ano-vaginal distance, histopathology of testis (SE)
TG 422, Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test	10	Level of sex linked hormones and other hormones, challenge test (CA1); Morphological studies of gonads (DE, SE); Sex ratio, duration of oestrus cycle, ano-vaginal distance (SE); Hormone levels, semen analysis - enhanced endpoint analysis (UK)
TG 407, Repeated Dose 28-day Oral Toxicity Study in Rodents	9	Level of sex linked hormones and other hormones, challenge test (CA1); Endocrine effects on sex organs (SE)

New Test Guidelines

43. Almost all the responding countries (18/21) considered that there is a need to develop some new OECD Test Guidelines. The most frequently identified needs were a guideline for effects in the reproductive system of aquatic species (6 countries), guidelines for sex-linked hormone levels in mammalian target species (15 countries) and effects on sex-linked hormones in environmental target species (12 countries). Some specific effects to be assessed in new tests were proposed and are listed in Table 4.

Table 4: Possible new OECD Test Guidelines

Endpoint	No. of countries	Specific endpoints proposed
Effects in the reproductive system of aquatic target species	16	Reproductive success
Other effect in aquatic target species,	6	Behavioural aspects, morphological effects, reproductive success, effects on development
Effects in the reproductive system of terrestrial target species	11	Reproductive success
Other effect in terrestrial target species	4	Thyroid and behavioural effects, reproductive success, effects on development
Specific effects on mammalian target species, including:	8	Sertoli cell test and human oestrogen receptor test, Effects on brain development and sexually dimorphic brain functions, "*in vitro*" and "*in vivo*" hormonal screening tests, sperm analysis, paternal effects of exposure, specific effects on target cells
Effects on sex-linked hormones/hormone levels in environmental target species	12	
Effects on sex-linked hormones/hormone levels in mammal target species	15	*In vitro*/*in vivo* screens
Effects on other hormones/hormone levels	3	Thyroid and behavioural aspects and neuronal development Thyroid, adrenal and pituitary hormones

44. Countries emphasised the need for a cautious approach for developing new guidelines consistent with the need to improve understanding about the biological consequences of endocrine disrupting action.

REGULATORY ACTIVITIES

Administrative responsibility

45. The sectors of administration involved in work on endocrine disrupters in each Member country are listed in Annex 4.

Need for screening of chemicals

46. There was no clear answer when countries were asked whether there was a need to screen or test all new and existing chemicals for potential endocrine disrupting properties.

47. About half the countries replied that in principle "yes" there was a need to screen all new and existing chemicals for endocrine disrupting properties independent of their use. Many pointed to the need for an agreed validated, rapid screen and suggested strategies such as focusing on new chemicals. It was seen by others as premature to conclude what specific chemicals or chemical classes should be included in a screening program. Some countries suggested the need to establish criteria for which chemicals should be tested such as exposure, use, chemical structure/structure-activity-relationships, bioaccumulation, persistence and toxicological effects.

48. Those countries not supporting routine screening preferred to see testing restricted to chemicals substances and groups generally regarded as of concern for endocrine disruption, such as new chemicals or chemicals which are not covered by routine tests. Many countries stressed the need to also take exposure, use and chemical structure into consideration.

49. The availability of tests, both for *in vitro* screens, for adverse effects and for the mechanism of endocrine disruption should be addressed as a priority.

Regulation

50. With the exception of the United States, where new legislation, the US Food Quality Protection Act and the US Safe Drinking Water Act speak of a screening and testing program for certain environmental agents to identify their endocrine disrupting effect, other countries indicated that regulatory actions have not been taken or were being prepared to specifically address endocrine disrupting substances.

51. Countries are generally addressing endocrine disrupting substances within their existing regulatory framework, for example under the Canadian Environmental Protection Act (CEPA) substances which are persistent, bioaccumulative, toxic and predominantly anthropogenic sources may be virtually eliminated from the Canadian environment. Several persistent, bioaccumulative and toxic substances are currently being managed in this way.

52. In other countries there is the possibility of addressing endocrine disruptive chemicals within existing registration and assessment requirements, for example in the registration of pesticides and establishment of water quality regulations etc. The type of possible administrative measure varies and includes establishment and development of special developmental and reproductive toxicity test requirements, not registering for use or setting use restrictions, establishing limit values, voluntary agreements with industry for not using substances for certain uses and establishing residue limits in foodstuffs.

Policy documents and Information to the general public

53. Policy documents on endocrine disrupting substances are available or are planned to be available in approximately half the countries surveyed. The most common type of document was described as an advisory document or programme declaration for work within and between the agencies.

54. More frequently countries had informed the general public about the possible hazards and risks or available evidence on the effects of Endocrine Disrupting Substances, mostly through press releases. Public meetings and discussions have also been used.

Hazard and Risk Assessment

55. Approximately half the countries (11/21) quoted examples where hormone-like activity of a chemical was of a pivotal importance to the hazard and risk assessment process. In some cases this occurred in the registration of pesticides or veterinary medicines or systematic risk assessment of existing chemicals. A few chemicals were specifically identified vinclozolin (5 countries), TBT (3 countries), iprodione (2 countries); simazine, triazole fungicides, atrazine, dithiocarbamates, endosulfan, lindane, dicarboximide fungicides, nonylphenylethoxylates (1 country).

INTERNATIONAL CO-OPERATION

56. Most of the countries (19/21) already take part in international activities concerning risk management/control of endocrine disrupters. Organisations seen to be playing a leading role in the international activities are: EU (mentioned by 9 respondents), FAO (2), LRTAP (4), IFCS (9), IPCS (10), OECD (21), OSPARCOM (10), UNEP (9), WHO (6). OECD was identified as having a leading role in test guideline development, but otherwise there was no clear view from the questionnaire which organisation should be responsible for what area.

ANNEX 1

RELEVANT PUBLISHED RESEARCH

Ahlborg UG, Lipworth L, Titus-Ernstoff L, Hsieh C-C, Hanberg A, Baron J, Trichopoulos D & Adami H-O (1995) Organochlorine compounds in relation to breast cancer, endometrial cancer, and endometriosis: An assessment of the biological and epidemiological evidence. Crit Rev Tox 25: 463-531.

Arnold SF, Klotz DM, Collins BM, Vonier PM, Guillette LJ Jr & McLachlan JA (1996) Synergistic activation of estrogen receptor with combinations of environmental chemicals. Science 272: 1489-1492.

Auger J, Kunstmann JM, Czyglik F, Jouannet P. (1995) Decline in semen quality among fertile men in Paris during the past 20 years. New Engl J Med, 332, 281-285.

Berkowitz GS, Lapinski RH, Dolgin SE, Gazella JG, Bodian CA & Holzman IR (1993) Prevalence and natural history of cryptorchidism (Undescended testicles). Pediatr 92: 44-49.

Brotons JA et al. Xenoestrogens released from lacquer coating in food cons. Environ Health Perspect (in press).

Carlson E, Giwercman A, Keiding N & Skakkebaek NE (1992) Evidence for decreasing quality of semen during past 50 years. Brit Med J 305: 609-613.

Chemically Induced Alterations in Sexual and Functional Development: The Wildlife/Human Connection (1992). Editors: Colborn T and Clement C. Princeton Scientific Publishing, Princeton, NJ, US.

Colborn T, Dumanoski D & Peterson Myers J (1996) Our Stolen Future: Are we threatening our fertility, intelligence and survival? Dutton Press, US (ISBN-0525-939-822).

Danish Environmental Protection Agency (1995) Male Reproductive Health and Environmental Chemicals with Estrogenic Effects Miljoprojekt No. 2, Ministry of Environment and Energy, Denmark.

Davis DL, Bradlow HL, Wolff M, Woodruff T, Hoel DG & Anton-Culver H (1993) Medical hypothesis: Xenoestrogens as preventable causes of cancer. Environ Health Perspect 101: 372-377.

Donat H, Matthies J, Schwarz I (1990) Fertilität bei Exponierten genenüber Pflanzenschutz- und Schädlingbekämpfungsmitteln. Andrologia 22: 401-407.

Donat H, Schwarz I, Matthies J (1989) Untersuchungen über den Einfluss von Kohlenwasserstoffverbindungen am Arbeitsplatz auf die männliche Fertilität. Fertilität 5: 167-172.

Dunphy BC, Barratt CLR, von Tongelen BP, Cooke ID (1990) Male cigarette smoking and fecundity in couples attending an infertility clinic. Andrologia 23: 223-225.

Dunphy C, Barratt CLR, Cooke ID (1990) Male alcohol consumption and fecundity in couples attending and infertility clinic. Andrologia 23: 219-221.

Endocrine Issues Coalition (1996) Research Summary. April 1996.

Ensslen SC, Riedel H-H, Blüthgen H, Heeschen W, Grillo M, Jung H (1990) Chlorkohlenwasserstoffe in Follikelflüssigkeit und Sperma. Fertilität 6: 119-122.

Estrogens in the Environment, III: Global Health Implications (1995) Report of a symposium held on 9-11 January 1994, Washington DC, US. Environ Health Perspect 103, Suppl. 7, October 1995.

Frauenhofer-Institut für Umweltchemie und Ökotoxikologie (1995) Fachgespräch Umweltchemikalien mit Endocrine Wirkung. Berlin 9 - 10 March 1995. Umweltbundesamt Berlin, Germany. (CX/PLEN/GEN/39, January 1996).

Fullerton H. Sperm and diet. New Scientist, 1 June 1996 p 53 (letter).

García Rodriguez J et al. Exposure to pesticides and cryptorchidism geographical evidence of a possible association. Environ Health Perspect 104 (10): 1090-95.

García Rodriguez J et al. Exposure to xenoestrogens and cryptorchidism. Environ Health Perspect 1996.

Glass RI, Lyness RN, Mengle DC, Powell KE, Kahn E (1979) Sperm counts depression in pesticide exposed to dibromochlorpropane. Am J Epidemiol 109: 346-351.

Greenpeace (1995) Body of Evidence: The Effects of Chlorine on Human Health. Greenpeace International, London (May 1995).

Helzlsouer K, Comstock GW, Alberg AJ, Hoffman S, Kafonek S & Strickland P (1995) Molecular epidemiology of prostate cancer. Organochlorines and Cancer Workshop, Ottawa, Canada. 27-28 Sept. 1995.

Houghton DL & Ritter L (1995) Organochlorine residues and risk of breast cancer. J Amer Coll Toxicol 14: 71-89.

IEH (1995) Assessment on Environmental Oestrogens, Consequences to Human Health and Wildlife 1995, Medical Research Council, Institute for Environment and Health, University of Leicester, UK.

Key T & Reeves G (1994) Organochlorines in the environment and breast cancer. Brit Med J 308: 1520-1521.

Krieger N, Wolff MS, Hiatt RA, Rivera M, Vogelman J & Orentreich N (1994) Breast cancer and serum organochlorines: A prospective study among white, black and Asian women. J Natl Cancer Inst 86: 589-599.

Lawrence Wright (1996) Silent Sperm. New Yorker, Jan 15 1996.

MacLeod J & Wang Y (1979) Male fertility potential in terms of semen quality: A review of the past, a study of the present. Fertil Steril 3: 103-116.

Miller BA, Ries LA, Hankey BF et al. (1993) SEER Cancer Statistics Review, 1973-1990. National Cancer Institute Publication no. 93-2789. NIH, Bethesda, MD.

Mussalo-Rauhamaa H, Häsänen E, Pyysalo H, Antervo K, Kauppila R & Pantzar P. Occurrence of beta-hexachlorocyclohexane in breast cancer patients. Cancer 66: 2124-2128.

Olea F et al. Determination of estrogenic organochlorine compounds by performance liquid chromatography and assessment of their estrogenic activity. J Chromat (submitted).

Olsen GW, Bodner KM, Ramlow JM, Ross CE & Lipshultz LI (1995) Have sperm counts been reduced 50 percent in 50 years? A statistical model revisited. Fertil Steril 31: 887-893.

Olsen GW, Lanham JM, Bodner KM, Hylton DB, Bond GG (1990) Determinants of spermatogenesis recovery among workers exposed to 1,2-dibromo-3-chloropropane. J Occup Med 32(10): 979-984.

Olson JH, Birebaum R, Roseville MN, Golubroff ET, Seaman EK, Diamond B & Fisch H (1995) Semen analysis in 632 men over a 25 year period: No change in quality. J Urol 153, Suppl. p 323A.

Potashnik G, Ben-Aderet N, Insler R, Yanai-Inbar I, Sober I (1978) Suppressive effect of 1,2-dibromo-3-chloropropane on human spermatogenesis. Fertil Steril 30: 444-447.

Potosky AL, Miller BA, Albertsen PC & Kramer BS (1995) The role of increasing detection in the rising incidence of prostatic cancer. JAMA 273: 548-552.

Pusch H (1995) Einflüsse von Noxen, Umwelt und Stress auf die männliche Fertilität. J Fertil Reprod 18-21.

Safe S (1995) Environmental and dietary estrogens and human health: Is there a problem? Environ Health Perspect 103: 346-351.

Setc AM et al. The E-SCREEN assay as a tool to identify estrogens: an update. Environ Health Perspect (in press).

Shemi D, Marx Z, Kaplanski J, Potashnik G, Sod-Moriah UA (1988) Testicular damage development in rats injected with dibromochloropropane (DBCP). Andrologia 20: 331-337.

Suominen J & Vierula M (1993) Semen quality in Finnish men. Brit Med J 306: 1579.

Thomas JA (1995) Falling sperm counts. The Lancet 346: 636 (letter).

Whorton D, Krauss RM, Marshal S, Milby TH (1977) Infertility in male pesticide workers. Lancet 2: 1259-1261.

Wiimaak FM & Shapiro SS (1992) Longitudinal study of semen quality in Wisconsin men over one decade. Wiscons Med J 91: 477-479.

Williams KC, Blaney BJ & Magee MH (1988) Responses of pigs fed wheat naturally infected with 'Fusarium graminearum' and containing the mycotoxins 4-deoxynivalenol and zearaleone. Aust J Agr Res 39: 1095-1105.

Wolff MS, Toniolo PG, Lee EW, Rivera M & Dubin N (1993) Blood levels of organochlorine residues and risk of breast cancer. J Natl Cancer Inst 85: 648-653.

ANNEX 2

NATIONAL REPORTS AND REVIEWS
(Current as of 1996)

AT: Federal Environment Agency (Conference papers Vol. 19, 1996) Umweltchemikalien mit hormoneller Wirkung. Eine Standortbestimmung für Östreich. In German. (Andropogene Substances with Hormonal Effects.) Workshop Proceedings: Vienna, Apr. 22-23, 1996.

DE:
1) UBA (Texte 3/96). Endocrinically Active Chemicals in the Environment. Seminar Proceedings: Berlin, Mar. 9-10, 1995.

2) UBA, Frauenhofer Inst., Max Planck Inst. Effects of Endocrine Disrupters in the Environment on Neural Development and Behaviour (1997). Seminar Proceedings: Berlin, Feb. 17-18 1997.

DK: Miljøstyrelsen (Miljøprojekt 290, 1995). Male Reproductive Health and Environmental Chemicals with Estrogenic Effects.

FI:
1) Nordic Council of Ministers (TemaNord 1996:580). Chemicals with Estrogen-Like Effects.

2) P. Mellanen et al. (1966). Toxicol. Appl. Pharmacol 136:381-388.

FR: INSERM. Environnement et function masculine de la reproduction. Conference Proceedings: Aix-les-bains, Nov. 10-14 1996. In French.

JP: Japan Chemical Industry Ecology-Toxicology and Information Centre (Apr. 18, 1997). A Study on ”Hormone-Like (Hormone-Mimic) Effects of Exogenous Stubstances.

NL:
1) National Institute for Public Health and Environment (1996). Public Health Aspects of “Oestrogenic Substances” in the Environment.

2) National Health Council (Report 1997/08, 1997). Hormon disruptors in humans. In Dutch with an English summary.

3) National Health Council (Draft 1997). Ecological aspects.

NO:
1) Food Control Authority: tins, cans, inside spray varnish. In Norwegian with an English summary.

2) SFT (Norwegian Pollution Control Authority) 96:21 (1996). Kartlegging av stoffer med mylige hormonliknende effekter. (Survey of chemicals with possible endocrine effects.) In Norwegian.

3) SFT 96:20 (1996). Kartlegging av mylige estrogenliknende effekter i miljöet i Norge. (Identification of possible estrogenic effects in the Norwegian environment - Biological effects.) In Norwegian.

SE:

1) National Chemicals Inspectorate (KemI Rapport 1/97, 1997). Hormonella effekter av kemikalier - en sammanfattning av kunskapsläget. In Swedish.

2) SEPA (Naturvårdsverket, Draft 1997). Endocrine Disrupting Chemicals Impairment of Reproduction and Development.

UK:

1) Institute for Environment and Health (IEH, A1 1995). Environmental Oestrogens - Consequences to Human Health and Wildlife.

2) Department of Environment (DoE, Draft 1997). UK Detailed Review Paper on Test Methods (for OECD).

3) MAFF (Draft). Review of Certain Aspects of the Literature on Phytoestrogens (especially beneficial effects and the influence of agricultural and food processing practices on content).

4) Environment Agency (EA). Endocrine Disrupting Substances - A Strategy for the Environment Agency.

US: Several reports exist from US-EPA.

1) US-EPA (EPA/630/R-96/Q12, 1997) Special Report on Environmental Endocrine Disruptors: an Effects Assessment and Analysis.

2) Environ. Health Perapectives Review (1996). Vol 104, Suppl. 4, 715-740. Kavlock et al.: Research Needs for the Risk Assessment of Health and Environmental Effects of Endocrine Disruptors. A report of the US-EPA sponsored Workshop.

3) US-EPA (EDSTAC-report, Draft 1997). Draft Report from the Workshop on Screening Methods for Endocrine Dirsruptors in Wildlife, Kansas City, Mar. 17-19, 1997.

4) De Rosa et al. (Draft 1997). Environmental Exposures that affect the Endocrine System: Public Health Implications.

5) U.S. Geological Survey (Report 96-627, 1997). Reconnaissance of 17-Estradiol, 11-Ketotestosterone, Vitellogenin, and Gonad Histopathology in Common Carp of United States Streams: Potential for Contaminant-Induced Endocrine Disruption.

BIAC: ECETOC (Document No.32, 1996) ”Environmental Oestrogens” Male Reproduction and Reproductive Development.

ANNEX 3

NATIONAL EXPERT GROUPS AND CONTACT PERSONS
(Current as of 1996)

AU: (1) Chemicals clearing house. Contact person: Dr. Brian Priestly, Chemicals and non-prescription drugs branch, Dept. of Health and Family Serv., Box 9848, Canberra, Act 2601, Australia, Phone: 61-6-289 7040

(2) Interdepartment committee on chemical treaties

BE: (1) Commission Technique Mer du Nord, Ministry of Public Health. Contact person: G. Pichot/C. Plasman, UGMM, Gulledelle 100, 1200 Brussels, Belgium, Phone: 32-2-773-21-22 (21-29)

(2) Special Working Group PCB. Ministry of Public Health. Contact person: M. Dequillier, RAC-Vésale, 1010 Brussels, Phone: 32-2-210-46-27

(3) Scientific Institute of Public Health, Ministry of Public Health Contact person: Dr.T.Lakhanisky, Rue J.Wytsman 14, 1050 Brussels Phone: 32-2-642-51-04

CA: Contact persons:

(1) Dr. Kelly Munkinttrick, AECB, NWRI, Environment Canada, 867 Lakeshore Blv. , Burlington, Ontario, Canada L 7R 4A6, Phone: 905-336-4864, Fax: 905-336-4972, E-mail; Kelly.munkittrick@cciw.ca

2) Karen Llyod, Environment Canada, Commercial Chemicals Evaluation Branch, Ottawa, Ontario, Canada K1A 0H3, Phone: 819-953-0356, Fax: 819-953-4936, E-mail: Karen.Llyod@EC.GC.ca

(3) Dr. Warren G. Foster, Room 338, PL#0803D, Environment Health Centre, Tunney´s Pasture, Ottawa, Ontario, Canada K1A 0L2, Phone: 613-957-8029, Fax: 613-941-4768, E-mail: Warren_Foster@isdtcp3.hwc.ca

CH: Working group ”Endokrine Effekte”. FOEFL. Contact person: Dr. G. Karlaganis, Federal Office of Environment, Forest and Landscape, CH-3000 Bern, Phone: 41-31-322 6955.

DE: Endocrine disruptor research advisory committe. Environmental Ministry,Contact person: Prof. Dr. Baseler, Environmental Ministry, IGII4, Kennedy Allee 5, D-531 75 Bonn, Phone: 49-305-2710

DK: Center for Xenoestrogenic Research. Biological Inst. Odense University. Contact person: Prof. Poul Bjerregård, Odense University, Campenvej 55, DK-5230 Odense M, Phone: 45-66-158 600

FR: (1) For scientific Research. INSERM. Contact person: Dr. Jegou , Germ. Inserm u 435 campers de Beaulieu, Avenue de General Leclerc, F-35042 Rennes Cedex, Phone: 33-2-9928 6911

(2) For information: Chimie ecologie*. Committee for administration, science and industy.Contact person: Mme. Schmitt, 28 rue Saint-Dominique, F-75 007 Paris, Phone: 33-145-56 02 49

(3) Commission d'evaluation de l'écotoxicité des substances chemiques*. Ministry of Environment.Contact person: Dr. Rault/Mme. Musset, Ministere de l'environnement, 20 Avenue de Ségur, F-753 02 Paris 07SP, Phone: 33-1-4219 1589/33-1-4219 1585

*These committees have not been established specially for EDS but it was decided that they will follow the activities on these chemicals.

IT: Contact person: Alessandro di Domenico, Instituto Superiore Di Sanitá, Viale Regina Elena 299, I-00161 Rome, Phone: 39-Rome-4990-2077

JP: (1) Research Group of ECD's, Ministry of Health and Welfare Contact person: Soichiro Isobe Chiyoda-ku, Tokyo 100-45, Japan, Phone: 81-3-3595-2298

(2) Committee for Endocrine Disrupter Issues, Japan Chemical Industry Ecology-Toxicology Center, Contact person: Dr. Junshi Miyamoto, New Sumitomo Bldg., 5-33, Kitahama 4-chome, Chuo-ku, Osaka 541, Japan

(3) Environment Agency, Contact person: Shigeki Shiiba, 1-2-2 Kasumigaseki, Chiyoda-ku, Tokyo, Japan Phone: 81-3-3581-2653

NO: Informal working group between authorities. Contact person: Berit Eyde Kjuus, Norwegian Pollution Control Authority, P.O. Box, 8100 Dep., N-0032 Oslo, Phone: 47-22-573400. Scientific group of the University of Oslo.

SE: Reference group for the investigation of the Swedish EPA (more agencies involved). Contact persons: Titus Kyrklund, S-EPA, S-106 48 Stockholm Phone: 46-8-698 1146/Ann Thuvander, NFA, Box 622, S-751 26 Uppsala Phone: 46-18-175763

UK: Interdepartmental Research Coordination Group on Endocrine Disrupters - including all interested departments, agencies, research councils.Contact person: Mrs. K. Cameron, DoE, Room A344, Romney House, 43 Marsham Street, UK-London SWIP 3P4, Phone: 44-171-276 8332

US: (1) US-EPA. Endocrine Disruptors Screening and Testing Advisory Committee (EDSTAC), Contact person: L. Goldman, OPPT, US-EPA, Room #637E, Mail Code 7101, 401 M Street, S.W., Washington, D.C. 20460.

(2) US-EPA. President's Office of Science and Technology Policy. Contact person: Dr. Larry Reiter, Research Triangle Park, NC 27711, Phone: 1-919-541-2281

(3) National Academy of Sciences Committee on Hormone Related Agents int he Environment, NAS/NRC Contact person: D.Policansky/C.Maczka.

(4) Committee on Environment and Natural Resources, Office of Presiden, Contact person: Ron Melius.

(5) FDA, Contact person: Dr. Susan Homire, 5600 Fishers Lane OC HF-32 Rockville MD, Phone:1-301-827-3366

BIAC: EMSG (Endocrine Modulators Steering Group), Contact person: Prof. André Lecloux, CEFIC-EMSG, Avenue E. Van Nieuwenhuyse 4, Box 2, 1160 Brussels, Phone: 32-2-6767306, Fax: 32-2-6767216, E-mail: ALE@CEFIC.BE.

ANNEX 4
ADMINISTRATIVE RESPONSIBILITY IN MEMBER COUNTRIES
(Current as of 1996)

AU

Aquatic environment	Environment Australia
Terrestrial environment	Environment Australia
Medicine/drugs	Drug Safety Evaluation Branch, Therapeutic Goods Administration, Dep't. of Health and family Services
Food additives,contamin.	Australia New Zealand Food Authority
Biotechnology	Departments of Industry, Science & Technology; Primary Industries and Energy; Others as listed here
Drinking water	Environmental Health Section,. Department of Health and Family Services
Workplace	Worksafe Australie (Dept. of Industrial Relations)
Others: Industrial chemicals	National Industrial Chemicals Notification and Assessment Scheme (Worksafe Australia)
Others: Agricultural and Veterinary Chem	National Registration Authority for Agricultural and Veterinary Chemicals)

AT

Aquatic environment	Ministry of Environment, Environment Agency
Terrestrial environment	Ministry of Environment, Environment Agency
Food additives,contamin.	Federal Chancellery
Drinking water	Federal Chancellery
Consumer products	Federal Chancellery

BE

Aquatic environment	VHM, BIM, DORNE
Terrestrial environment	AMINAL, BIM, DORNE
Drinking water	AMINAL, BIM, DORNE
Others:	Ministry of Public Health

CA

Aquatic environment	Department of Fisheries & Oceans - Environment Canada
Terrestrial environment	Environment Canada
Medicine/drugs	Health Canada, Drugs Directorate
Food additives,contamin.	Health Canada, Food Directorate
Biotechnology	Health Canada, Env. Health Directorate, Food Directorate, Environment Canada
Drinking water	Health Canada
Consumer products	Health Canada
Workplace	Health Canada
Others: environmental contaminants	Health Canada, Env. Health Directorate; Canadian Wildlife Service;
Others: pesticides	PMRA

CH

Aquatic environment	Federal Office of Environment, Forests and Landscapes (FOEFL)
Terrestrial environment	FOEFL
Medicine/drugs	Interkantonale Kontrollstelle für Heilmittel
Food additives,contamin.	Federal Office of Public Health
Biotechnology	FOEFL
Drinking water	Federal Office of Public Health
Consumer products	FOEFL, Federal Office of Public Health
Workplace	Bundesamt für Industrie, Gewerbe und Arbeit/Schweizerische Unfallversicherungsanstalt
Others: agricultural pesticides	Federal Office of Agriculture, Federal Office of Public Health , FOEF

CZ

Aquatic environment	Ministry of Environment
Terrestrial environment	Ministry of Environment
Medicine/drugs	Ministry of Health
Food additives,contamin.	Min. of Agriculture, Min. of Health, Min. of Environment
Biotechnology	Ministry of Environment, Ministry of Agriculture
Drinking water	Min. of Health
Consumer products	Ministry of Environment, Ministry of Health
Workplace	Ministry of Health

DK

Aquatic environment	Danish EPA
Terrestrial environment	Danish EPA
Medicine/drugs	Ministry of Health
Food additives,contamin.	Ministry of Food, Agriculture & Fisheries
Biotechnology	Ministry of Food, Agriculture & Fisheries, Danish EPA
Drinking water	Danish EPA (Bottled: Ministry of Food, Agric., Fisheries)
Consumer products	Danish EPA
Workplace	Ministry of Labour, Danish Work Directorate

ES

Aquatic Environment	Ministry of Environment
Terrestrial environment	Ministry of Environment
Medicine/drugs	Ministry of Health and Consumer
Food additives,contamin.	Ministry of Health and Consumer
Biotechnology	Ministry of Health and Consumer, Ministry of Environment
Drinking water	Ministry of Health and Consumerv
Consumer products	Ministry of Health and Consumer
Workplace	Ministry of Labour
Others:pesticides	Ministry of Health and Consumer

FI

Aquatic environment	Finnish Environment Institute
Medicine/drugs	National Agency for Medicines
Food additives,contamin.	National Food Administration
Biotechnology	The Board for Gene Technology
Drinking water	Ministry of Social Affaires and Health
Consumer products	National Consumer Administration
Workplace	Ministry of Social Affairs and Health
Others: Human Health	National Product Control Agency for Welfare and Health

FR

Aquatic environment	Ministry of Environment
Terrestrial environment	Ministry of Environment
Medicine/drugs	Ministry of Health
Food additives,contamin.	Ministry of Finance, Department of Consumption
Biotechnology	Ministry of Agriculture
Drinking water	Ministry of Health
Consumer products	Ministry of Finance, Department of Consumption
Workplace	Ministry of Labour (INRS)

GR

Aquatic environment	Ministry of Agriculture, Dept. of Pesticides
Terrestrial environment	Ministry of Agriculture
Medicine/drugs	National Drug Agency
Drinking water	Ministry of Agriculture
Consumer products	Ministry of Agriculture, Dept. of Pesticides

IE

Aquatic environment	Environmental Protection Agency and Dept. of the Environ.
Terrestrial environment	Environmental Protection Agency and Dept. of the Environ.
Biotechnology	Environmental Protection Agency
Drinking water	Environmental Protection Agency
Workplace	Health and Safety Authority

IT

Aquatic environment	Instituto Superiore di Sanitá - Ministry of Health
Terrestrial environment	Instituto Superiore di Sanitá - Ministry of Health
Medicine/drugs	Instituto Superiore di Sanitá - Ministry of Health
Food additives,contamin.	Instituto Superiore di Sanitá - Ministry of Health
Biotechnology	Instituto Superiore di Sanitá - Ministry of Health
Drinking water	Instituto Superiore di Sanitá - Ministry of Health

JP

Aquatic environment	Environment Agency
Terrestrial environment	Environment Agency
Medicine/drugs	Ministry of Health and Welfare (MHW)
Food additives,contamin.	MHW
Biotechnology	MHW
Drinking water	MHW
Consumer products	MHW, Ministry of International Trade and Industry (MITI)
Others: industrial chemicals;	MITI
Others: Agricultural pesticides	MHW, Ministry of Agriculture Forestry and Fisheries, Environment Agency

NL

Aquatic environment	Min. of Transport, Public Works and Water Management
Terrestrial environment	Ministry of Housing, Spatial Planning and Environment
Medicine/drugs	Ministry of Public Health, Welfare and Sports
Food additives,contamin.	Min. of Public Health, Welfare and Sports and Min. of Agriculture. Nature Management and Fisheries
Biotechnology	Min. of Public Health, Welfare and Sports and Min. of Agriculture. Nature Management and Fisheries
Drinking water	Ministry of Housing, Spatial Planning and Environment
Consumer products	Ministry of Public Health, Welfare and Sports
Workplace	Ministy of Social Affairs and Employment

NO

Aquatic environment	Norwegian Pollution Control Authority (SFT)
Terrestrial environment	Norwegian Pollution Control Authority (SFT)
Food additives,contamin.	Nowegian Food Control Authority (SNT)
Biotechnology	Environmental authorities
Drinking water	Nowegian Food Control Authority (SNT)
Consumer products	Nowegian Food Control Authority (SNT), Norwegian Pollution Control Authority (SFT (SNT food additives, cosmetic products))
Workplace	Directorate of Labour Inspection
Others: Pesticides	Norwegian Agricultural Inspection Service

SE

Aquatic environment	Swedish EPA, National Chemicals Inspectorate (KemI)
Terrestrial environment	Swedish EPA, National Chemicals Inspectorate (KemI)
Food additives,contamin.	National Food Administration (NFA)
Drinking water	National Food Administration (NFA)
Consumer products	National Chemicals Inspectorate (KemI)
Others: material and articles in contact with foodstuffs	National Food Administration (NFA)

UK

Aquatic environment	DOE, MAFF, Environment Agency (EA), Scottish Environmental Protection Agency (SEPA), DOE (Northern Ireland)
Terrestrial environment	DOE, MAFF, EA, SEPA, DOE (NI)
Medicine/drugs	Medicines Control Agency
Food additives,contamin.	MAFF, Department of Health (DH)
Biotechnology	MAFF
Drinking water	DOE
Consumer products	MAFF(Food), Department of Trade and Industry
Workplace	Health and Safety Executive
Others: Health effects generally	DH
Others: Animal feed	MAFF

US

Aquatic environment	EPA
Terrestrial environment	EPA
Medicine/drugs	FDA
Food additives,contamin.	FDA, EPA, USDA
Biotechnology	EPA, FDA, USDA
Drinking water	EPA
Consumer products	CPSC
Workplace	NIOSH/OSHA
Others: hazardous waste facilities	ATSDR

ANNEX 5

QUESTIONNAIRE TO THE RESPONSIBLE REGULATORY AGENCIES IN OECD MEMBER COUNTRIES ON ENDOCRINE DISRUPTERS

1. INTRODUCTION

This survey is being conducted by OECD with help of the Nordic countries for the purpose of:

- obtaining a better insight in Member countries' concern with endocrine disrupting chemicals (EDC's);
- developing an overview of current regulatory activities in the area; and
- identifying the need for test method development.

The OECD Secretariat has been directed by the National Co-ordinators (NCs) of the Test Guidelines Programme to develop the inventory in order to identify to what extent the possible risk of EDC's for human health and the environment is a priority issue for OECD. The analysis of responses to this questionnaire will be included in the final version of a Detailed Review Paper (DRP) on this subject which is currently prepared by the UK.

The information provided by the questionnaire and the DRP will be discussed by the NCs at their 8th Meeting in April 1997. During this meeting, they will take this information into account when proposing the development of new and the revision of existing Test Guidelines.

This questionnaire has been sent to the National Co-ordinators of the Test Guidelines Programme with copies to the members of the Risk Assessment Advisory Body and members of the Pesticide Forum. You are requested to co-ordinate your response via the National Co-ordinator of your country so that a National Position will be forwarded to the Secretariat.

2. RELEVANCE AND SCOPE

2.1. Concern

Do you consider endocrine disrupting chemicals (EDC's) candidates for regulatory or advisory activities or for control measures in your country?

❑ yes
❑ no (if no, continue with item 3.1)

If yes, please give a score for your level of concern by circling one of the following numbers (1 is minor concern and 5 is major concern)

1 2 3 4 5

Why are EDC's of special concern in your country ?
(more than one reason can be selected)

Because there is evidence of adverse effects of ECD's from:
❑ epidemiological studies
❑ wildlife studies
❑ toxicological studies
❑ ecotoxicological studies

❑ Because there is widespread environmental exposure
❑ Because there is widespread human exposure
❑ Because there appears to be a public concern
❑ Other reasons, please specify: .....

Is your country's concern based on published research and/or cases?

❑ no
❑ yes, the most relevant studies/cases are: .....

2.2. Definitions/criteria

Is there a good understanding in your country of what should be considered an EDC?

❑ yes
❑ no (if no, continue with item 2.3)

A recently held EC/WHO/OECD Workshop (Weybridge, UK, 2-4 December 1996) provisionally agreed on the following definitions:

"An endocrine disrupter is an exogenous substance that causes adverse health effects in an intact organism, or its progeny, secondary to changes in endocrine function."

"A potential endocrine disrupter is an exogenous substance that possesses properties that might be expected to lead to endocrine disruption in an intact organism."

Are these definitions acceptable to your country:

❑ yes?
❑ no, The following alternative definition(s) are proposed (add the source if available):
.....

2.3. Chemicals

Which chemical-use-categories/chemical classes are considered potential EDC's in your country?

❑ Phytoestrogens ❑ PCB's and metabolites ❑ Pesticides
❑ TBT ❑ Chlorinated hydrocarbons ❑ Pharmaceuticals
❑ Alkylphenols ❑ Chlorinated dioxins/furans ❑ Food additives
❑ Alkylphenolethoxylates ❑ DDT and metabolites
❑ Phtalates ❑ Organometals

❑ Others, please specify .....

2.4 Properties

Which aspects of potential EDC's other than toxicity are considered important in regulatory work and risk assessment?

- ❑ Biodegradation/Formation of toxic by-products through biodegradation
- ❑ Persistence/stability/bioaccumulation
- ❑ Volume of production and use
- ❑ Use/release pattern
- ❑ Structure of the substance
- ❑ Others, please specify .....

3. KNOWLEDGE AND RESEARCH

3.1 Reviews

Are there plans for reviews/national reports on the present knowledge of EDCs or have such reviews already been made in your country?

- ❑ yes, reviews/reports are already available
- ❑ plans are made
- ❑ no reviews, no plans

If yes, please list the most significant reviews (use a separate list/annex when necessary):

3.2. Use, exposure, emission

Are there projects concerning the use, release and/or exposure of potential EDC's in your country or are there plans for such projects?

- ❑ yes, there are projects
- ❑ projects are being developed or planned
- ❑ no projects, no plans

If yes or planned, please specify in which areas you collect data.

projects considered	***projects in place***		***specify the chemical/class or chemical use category***
❑	❑	Pollutant Release and Transfer register PRTR (OECD activity)	
❑	❑	Product register	.....
❑	❑	Surveys regarding release	.....
❑	❑	Measurements in the environment	.....
❑	❑	Measurements of dietary intake	.....
❑	❑	Environmental fate data	.....
❑	❑	Occupational exposure measurements/assessments	
❑	❑	Others, please specify:	.....
❑	❑		

3.3. Expert committees

Have expert committees been established, or are they being planned in your country (committees in an agency or committees for several agencies) or do you have other instruments to co-ordinate the work on EDC's?

- ❑ yes, established or planned committees
- ❑ other instruments
- ❑ no committees or other instruments, no plans

If yes, please name contact person(s):

Committee:

Ministry/Agency: ..... Contact person: .....

Address:

Phone:

Committee:

Ministry/Agency: ..... Contact person: .....

Address:

Phone:

Committee:

Ministry/Agency: ..... Contact person: .....

Address:

Phone:

4. HAZARD CHARACTERISATION

4.1. Relevant endpoints

Which of the listed biological endpoints related to hormonally mediated mechanisms are considered most relevant for the hazard characterisation of EDC's? (more than one endpoint can be selected)

score [1)]

- ❑ morphological effects in the reproduction system of aquatic target species ❑
- ❑ any morphological effect in aquatic target species ❑
- ❑ functional effects in aquatic target species ❑
- ❑ morphological effect in the reproduction system of terrestrial target species ❑
- ❑ any morphological effects in terrestrial target species ❑
- ❑ functional effects in terrestrial species ❑
- ❑ morphological effects in the reproduction system of mammalian target species ❑
- ❑ functional effects in the reproduction system of mammalian target species ❑
- ❑ morphological effects of the immune system of mammalian target species ❑
- ❑ effects on the CNS of mammalian target species ❑
- ❑ other effects: ..... ❑

- ❑ effects on sex-linked hormones/hormone levels in environmental target species ❑
- ❑ effects on sex-linked hormones/hormone levels in mammalian target species ❑
- ❑ effects on other hormones/hormone levels: ..... ❑
- ❑ clinical chemical parameters such as: ..... ❑
- ❑ other: ❑

[1)] 1 = of minor relevance, 5 = most relevant

4.2. Test Guidelines

Are currently available OECD Test Guidelines sufficient for the testing of potential EDC's?

❑ yes (if yes, continue with item 5.1)

❑ no

If no, is there a need to revise existing OECD Test Guidelines and/or is there a need to develop new Test Guidelines?

❑ yes, the following existing Test Guideline(s) need updating specifically to cover testing of EDC's: relevant endpoints

- ❑ TG 204 Fish, Prolonged Toxicity Test: 14-Day Study
- ❑ TG 206 Avian Reproduction Test .....
- ❑ TG 210 Fish, Early-Life Stage Toxicity Test .....
- ❑ TG 414 Teratogenicity .....
- ❑ TG 415 One-Generation Reproduction Toxicity .....
- ❑ TG 416 Two-Generation Reproduction Toxicity .....
- ❑ TG 421 Reproduction/Developmental Toxicity ..... Screening Test .....
- ❑ TG 422 Combined Repeated Dose Toxicity Study ..... with the Reproduction/Developmental Toxicity ..... Screening Test .....
- ❑ TG 407 Repeated Dose 28-day Oral Toxicity ..... Study in Rodents.....
  - ❑ other TGs:.....

❑ yes, there is need to develop new Test Guideline(s), focusing on:

- ❑ effects in the reproductive system of aquatic target species
- ❑ other effect in aquatic target species, including:
- ❑ effects in the reproductive system of terrestrial target species
- ❑ other effect in terrestrial target species .....
- ❑ specific effects on mammalian target species, including:.....
- ❑ effects on sex-linked hormones/hormone levels in environmental target species
- ❑ effects on sex-linked hormones/hormone levels in mammal target species
- ❑ effects on other hormones/hormone levels:.....

5. REGULATORY ACTIVITIES

5.1. Administration responsibility

Which sectors of administration are involved in the work on EDC's in your country. Please, specify ministries/agencies.

<u>ministry/agency</u>

- ❑ Aquatic environment (surface waters, effluent waters, sewage) .....
- ❑ Terrestrial environment, including above ground .....
- ❑ Medicines/drugs .....
- ❑ Food additives, contaminants .....
- ❑ Products of modern biotechnology .....
- ❑ Drinking water .....
- ❑ Consumer products .....
- ❑ Workplace .....
- ❑ Others, please specify .....

5.2. Regulation

Is there a need to screen or test all new and existing chemicals for potential endocrine disrupting properties independent of their use?

- ❑ yes, in principal all chemicals
- ❑ not all chemicals; testing should be restricted to chemical substances of the following chemical use categories/chemical classes:

❑ Phytoestrogens	❑ PCB's and metabolites	❑ Pesticides
❑ TBT ❑ Chlorinated dioxins/furans		❑ Pharmaceuticals
❑ Alkylphenols	❑ DDT and metabolites	❑ Food additives
❑ Alkylphenolethoxylates	❑ Organometals	
❑ Phtalates ❑ Chlorinated hydrocarbons		
❑ Others		

- ❑ no additional testing is needed.

Is regulatory action taken or being prepared to specifically control EDC's in your country?

- ❑ yes, action taken
- ❑ action prepared
- ❑ no

If yes, please specify the regulatory action/decision:

action taken	***action prepared***		***specify the chemical/class or chemical use category***
❑	❑	Legislation/act/statutory orders	.....
❑	❑	Decision	.....
❑	❑	Approval/registration	.....
❑	❑	Discharge permits	.....
❑	❑	Voluntary agreement	.....
❑	❑	Recommendations/guidance	.....
❑	❑	Others, please specify:	.....

Please provide a copy of relevant documents when appropriate.

5.2 Regulation (continued)

If the regulations concern specific chemical(s), please specify the chemical(s) if not confidential, or provide the chemical class:

5.3. Policy documents

Are policy documents addressing EDC's available or are they under preparation in your country ?

- ❑ yes
- ❑ in preparation
- ❑ no

If yes or in preparation, in which form:

- ❑ Advisory document
- ❑ Political declaration (e.g. for Parliament or for the relevant ministry or state department)
- ❑ Programme declaration for the work within and between the agencies
- ❑ other

Please give titles, year of publication and language and attach if possible (use a separate list/annex when necessary):

5.4. Information to the general public

Has the general public or media been informed by authorities in your country about the possible hazards/risks or available evidence on the effects of EDC's?

- ❑ yes, this information is provided through:
- ❑ no
- ❑ information campaigns
- ❑ press releases
- ❑ leaflets
- ❑ brochures
- ❑ recommendations/warnings against some products
- ❑ others, please specify .....

5.5. Hazard and risk assessment

Are you aware of cases of hazard and risk assessment in your country where hormone-like activity of a chemical was of pivotal importance in the assessment?

❑ yes
❑ no

If yes, in which areas? ***<u>specify chemical(s), if not confidential,</u>***
<u>or provide the chemical class</u>

❑ Classification and labelling .....
❑ Drug registration .....
❑ Pesticide registration .....
❑ Food additive registration .....
❑ Other registration .....

6. INTERNATIONAL CO-OPERATION

6.1. International co-operation and other initiatives

Does your country already take part in international activities aiming at the risk management/control of EDC's?

❑ yes
❑ no

If yes, do any of the following organisations play a leading role in the activity?

❑ EU ❑ FAO
❑ ILO ❑ LRTAP (The Convention on Long-Range Transboundry Air Pollution)
❑ IFCS ❑ IPCS
❑ OECD ❑ OSPARCOM (Oslo and Paris Commission)
❑ UNEP ❑ WHO
❑ others, please specify

Do you co-operate with other countries in this respect?

❑ yes, with .....
❑ no

6.1 continued

Is there a need for extended international co-operation in this field?

❑ yes
❑ no

If yes, in which <u>area(s):</u>

❑ 1. Research programmes
❑ 2. Test guidelines development
❑ 3. Collecting data on the mechanisms of ecotoxicity and toxicity of EDC's
❑ 4. Collecting data on the use and exposure of EDC's
❑ 5. Regulatory decisions on risk reduction of EDC's
❑ 6. other

Which international organisation should take the lead on work in these areas? (Please circle relevant areas)

❑ EU for activity	1	2	3	4	5	6
❑ FAO for activity	1	2	3	4	5	6
❑ ILO for activity	1	2	3	4	5	6
❑ LRTAP for activity	1	2	3	4	5	6
❑ IFCS for activity	1	2	3	4	5	6
❑ IPCS for activity	1	2	3	4	5	6
❑ OECD for activity	1	2	3	4	5	6
❑ OSPARCOM for activity	1	2	3	4	5	6
❑ UNEP for activity	1	2	3	4	5	6
❑ WHO for activity	1	2	3	4	5	6
❑ others for activity	1	2	3	4	5	6

7. CONTACTS

7.1 Contacts

Please provide names, addresses, telephone, fax numbers and e-mail addresses of persons we may contact in each ministry or agency if clarification of the information provided is necessary.

1) Area of questionnaire.....
Name:
Address:
Tel:
Fax:
E-mail:

2) Area of questionnaire.....
Name:
Address:
Tel:
Fax:
E-mail:

3) Area of questionnaire..... .....
Name:
Address:
Tel:
Fax:
E-mail:

4) Area of questionnaire.....
Name:
Address:
Tel:
Fax:
E-mail:

7.2 National Co-ordinators

If the questionnaire was not completed by the National Co-ordinator; please provide information on who co-ordinated the response: .....

Did you consult with colleagues in other ministries/agencies?

- ❑ yes, with colleagues from:.....
- ❑ no

Do the answers to the questions represent a co-ordinated national position?

- ❑ yes
- ❑ predominantly the position of ..... (agency/ministry)