

ENDOCRINE DISRUPTING CHEMICALS

INFORMATION PAPER

This document was prepared in April 1998 in response to public enquiries to relevant Commonwealth Government agencies about their current views on health and environmental aspects of the issue of endocrine disrupting chemicals (EDCs). It addresses a series of common questions. Input to responses is from Environment Australia (EA), the Department of Health and Family Services (DHFS), in particular the Therapeutic Goods Administration (TGA) and the Australia New Zealand Food Authority (ANZFA), and NICNAS (National Industrial Chemicals Notification and Assessment Scheme) and the Chemical Assessment Division of the National Occupational Health and Safety Commission (NOHSC).

EA and DHFS have the lead on environmental and health issues, respectively, but work cooperatively with other agencies involved in the assessment and regulation of chemicals, including ANZFA, NICNAS and the National Registration Authority for Agricultural and Veterinary Chemicals (NRA).

Chemicals Assessment and Management

International concerns about chemicals were a feature of the 1992 United Nations Conference on the Environment and Development (UNCED) (the so-called Rio World Summit). The resultant agreed global plan for sustainable development, Agenda 21, contained the program of action (Chapter 19) for improved international cooperation and strengthened national programs for the environmentally sound management of chemicals. As such, Chapter 19 is the agreed, endorsed international program of action of governments for developing and implementing national programs for chemicals management.

Since 1992, there has been a growing momentum towards international harmonisation of chemicals controls, building on the work of the OECD Chemicals Programme and the International Programme on Chemical Safety (IPCS), as a means of “sharing the burden” and eliminating duplication of effort and trade barriers. This provides for economic development whilst ensuring continued protection of human health and the environment.

The six key areas of activity under Chapter 19 are:

Program Area A:

Expanding and accelerating international assessment of chemicals risk.

Program Area B:

Harmonisation of classification and labelling of chemicals (seeking the development and implementation of a Globally Harmonised Scheme (GHS) for chemicals in manufacture, transport and use so that classification and labelling of hazardous chemicals are uniform and globally understood.

Program Area C:

Information Exchange on toxic chemicals and chemicals risks (includes work towards the treaty on Prior Informed Consent)

Program Area D:

Establishment of Risk reduction programs.

Program Area E:

Strengthening national capacity and capability for management of chemicals.

Program Area F:

Prevention of illegal international traffic in toxic and dangerous products.

Intergovernmental Forum on Chemical Safety

The Intergovernmental Forum on Chemicals Safety (IFCS) has been established to promote international cooperation in implementing the goals set out in Agenda 21 Chapter 19. Some 114 governments and associated partners are members of the IFCS. The IFCS is a mechanism for increasing cooperation between governments and other parties involved in strengthening chemical safety, and assists international agencies such as the OECD, IPCS, UNEP, ILO, FAO, UNIDO, in establishing priorities and cooperative and complementary work programs.

Australia is an active member of the IFCS, serving on the IFCS's Intersessional Group (ISG) and hosting the second ISG in March 1996. Australia has supported the work of the IFCS and supports its role in identifying priorities for action and in establishing the most effective and efficient manner in progressing activities in Chapter 19. Australia also sits on the Standing Committee of the IFCS.

IFCS and Endocrine Disrupting Chemicals

The IFCS considered EDCs at its second meeting in Ottawa in February 1997 where they were identified as an emerging issue. The IFCS made the following findings and recommendations.

The Forum agrees that a rapidly growing body of scientific research indicates that a number of substances have the potential to interfere with normal functions of the body governed by the endocrine system. Countries and other IFCS partners have expressed concern about these findings and many are investing significant resources into learning how and to what extent substances may be adversely affecting human health and the ecosystem via endocrine pathways.

Considerable scientific uncertainty remains on the methodologies, exposures and effects of these substances. Therefore, new information and activities relevant to endocrine disrupting substances are rapidly emerging. This effort calls for coordinating effectively research, testing, assessment and sound management of endocrine disrupting substances, in ways that minimise duplication of efforts, make research and information more accessible to all interested parties on a global basis, and recognises that special needs and participation of developing countries and countries with economies in transition.

The Forum agreed on the need to investigate, in depth, the human, environmental and ecotoxicological aspects of endocrine disrupting substances, and made the following

Recommendation:

To address the concerns of endocrine disruption requires an open and transparent mechanism for assuring cooperation among governments, non-governmental organisations and other interested parties and therefore the Forum requests the IOMC through its participating organisations to:

- ⇒ compile and harmonise **DEFINITIONS** and terms appropriate to endocrine disruption*
- ⇒ promote coordinated **RESEARCH** strategies and processes, identify research priorities and gaps for all relevant research disciplines*
- ⇒ delineate **TESTING** methods, harmonise guidelines, identify testing priorities and gap*
- ⇒ adopt and maintain an **INVENTORY** of research activities and other relevant and related information*
- ⇒ facilitate **INFORMATION EXCHANGE** on:*
 - existing and new evaluations of scientific issues related to endocrine disruption*
 - research and testing results*
 - surveys and survey results*
 - meetings, workshops and conferences;*
 - actions and options to manage hazards and risks.*

Australian Approach

Given the wide-ranging implications in international chemicals issues, policy and technical work needs to be co-ordinated nationally to ensure effective and efficient chemicals management. This is achieved through coordinating mechanisms amongst federal agencies involved in assessment and regulation of chemicals. This is coupled with a system of designated national focal/contact points for various international programs. It is through such national co-ordination that a whole-of-government approach can be taken to chemicals issues.

Australia supports the findings and recommendations of the IFCS and has been actively participating in surveys and meetings within the OECD Chemicals Program (which is working on the testing requirements) and in other fora. Furthermore, lead Departments and chemical assessment/regulatory agencies are maintaining watching briefs on EDC. In addition, briefings on activities on EDCs have been provided to Community Consultative Committees, and non-government organisations through formal consultative mechanisms at the federal level.

Given the IFCS finding that further investigation is required, Australia sees benefit in supporting a concerted and co-ordinated program of research to investigate the possible links between demonstrated trends in human reproductive health and human exposure to chemicals in the environment. Further work is also needed to refine and clarify the measurement of trends in human reproductive health and the scope of research on wildlife should be extended to cover a range of populations, including those affected by point sources of pollution.

Until these matters are further clarified it would appear to be premature and unwarranted to divert scarce resources into developing major regulatory changes or action, acknowledging that the greatest benefit in ensuring responsible chemicals regulation will come from providing input where our expertise and resources allow and to utilise international efforts to guide our national decisions and actions.

COMMONLY ASKED QUESTIONS & ANSWERS

Q1. What is the Australian position on endocrine disrupters?

The Commonwealth Departments responsible for the assessment and regulation of chemicals take a coordinated policy position as outlined above. Australia supports the findings and recommendations of the IFCS on endocrine disrupting chemicals (EDCs) and maintains a watching brief on the latest developments in this area so as to inform its national assessment and regulation activities. This is true for both environmental and human health aspects of this issue.

In relation to human health issues

of EDCs (industrial chemicals and pesticides), the broad policy considerations to date are outlined as follows:

It is noted that in recent years concerns have been raised about the possible effects of chemicals present in the environment that could mimic and/or block the action of endogenous hormones such as oestrogens and androgens. It has been suggested that, at least in some parts of the world, several measures of human health, especially those related to reproduction and the incidence of certain cancers, have been somewhat compromised in recent decades. Included amongst reported adverse trends in human

health are decreased sperm counts and other testicular abnormalities, reproductive and immune dysfunction, neurobehavioural and developmental disorders, and an increased incidence of breast and testicular cancers. At the same time, various widely distributed environmental contaminants have been shown in the laboratory to possess oestrogenic and related activities. Thus, some scientists and epidemiologists working in the area have suggested a link between human health effects and endocrine disrupting chemicals in the environment.

To date, however, information from studies in humans provides no firm evidence for a causal link between these two observations, and other hypotheses pertaining to trends in human reproductive health are just as plausible. Furthermore, reasonable doubts have been aired about the veracity of some of the reported adverse health trends. Nevertheless, some findings in wildlife studies increase the concern that a link may indeed exist.

An issue in developing research and testing strategies is that of **definition** of an endocrine disrupter. The focus largely has been on chemicals that affect the sex hormones. However, given that an 'hormone' is 'a chemical substance formed in one part of the body and carried by the blood to another organ or part where it can alter function and/or structure', and that 'endocrine' refers to the internal or hormonal secretion of a ductless gland, it is difficult, if not impossible, to think of an organ or body system which is not regulated by hormones in some way. Furthermore, the term 'endocrine disrupter' implies an ability to not only directly mimic or block the actions of endogenous hormones, but also could include modification of their release, clearance or balance. In considering the scope of what testing strategies will be needed, Australia has suggested an approach which firstly focuses on endocrine systems where the greatest research is available (ie the sex hormones) so as to avoid delays and maximise resource utilisation in this area.

Shortly after the publication in 1996 of *Our Stolen Future* (Theo Colburn et al. New York, Dutton Books) four key issues were identified by Australia which would need to be fully addressed in considering a research program, in developing appropriate tests, and in the assessment of potential endocrine disrupter chemicals.

These are detailed below and it is noted that these issues have been raised with international organisation and bodies undertaking activities arising from the IFCS recommendations on EDCs:-

⇒ ***What is an endocrine disrupter?***

Does it act as or mimic an oestrogen or androgen or both? Does it have agonist or antagonist action or both? Is it a disrupter through sex hormone receptor-mediated mechanisms or non-receptor mechanisms? Does it affect growth hormones? thyroid hormones? corticosteroids? Should compounds that affect any endocrine function be included in the definition? Most of the current discussion focuses on sex hormones as the main problem, both environmentally and with respect to human health issues. However, what about other compounds that may alter biological homeostasis but are not related to sexual function?

⇒ ***What are the biological endpoints we need to measure?***

Should the testing be related to function (eg. reproductive function) or absolute ie. related to a particular step in a pathway? Ideally the test battery should cover both mechanistic and functional assays. Do current toxicology test protocols adequately cover functional end-points?

⇒ ***Are currently available experimental models appropriate to address these issues?***

Are current toxicity testing requirements (Reproductive and Developmental Toxicity protocols) adequate to assess hormone disrupting potential eg. are male rats appropriate models for extrapolation to human males? Do we need to expand the testing to include, as routine, a standard battery of endocrine test measures (including measurement of hormone levels) and receptor binding studies?

⇒ ***What about the assessment of potency?***

Knowledge of the potency of the chemical, relative to the natural hormone, is essential in order to conduct a proper risk assessment and thus provide confidence in linking cause and effect. Any *in vitro* assays chosen should be adequate to address the issue of potency relative to naturally occurring hormones.

In the intervening period, moves have been made at the international level and by the US EPA in particular (in response to new legislation, the Food Quality Protection Act or FQPA), to address some of these issues (see responses below). However, there are still significant issues raised, which have not yet been fully addressed, or not yet agreed upon at the international level.

From the environmental perspective, further work is needed in a number of areas to help clarify our understanding of the effects of endocrine disrupting chemicals (EDCs) on wildlife populations. Overseas reviews have identified the following needs:

- ⇒ Develop and validate novel whole organism assays for endocrine disruption in birds and fishes, both to assess hazards to those species and as a possible replacement.
- ⇒ Evaluate the usefulness of monitoring arthropod metamorphosis and moulting.
- ⇒ Characterise a hierarchy of sensitivities for appropriate biomarkers in mammals, birds, fish and invertebrates, using a set of appropriately selected model chemicals.
- ⇒ Identify suitable sentinel species endpoints to use where an evaluation will most usefully commence in wildlife species; including a comparison of benefits of using species with either fixed or variable sex ratios.
- ⇒ Conduct effects-driven studies into exposure assessment in wildlife populations, both aquatic and terrestrial, targeted to well defined end-points to establish what is “normal” as a baseline.
- ⇒ Field studies are required where endocrine disrupting substance effects are suggested; these should involve a broadly based screen including assessment of gonadal function, behavioural patterns and offspring sex ratio, numbers and survival. Such studies should include comparison with control (unimpacted) areas.
- ⇒ Conduct basic research into comparative endocrinology and baseline (unaffected) populations.
- ⇒ Identify sentinel species using agreed selection criteria.
- ⇒ Develop biomarkers that predict impact on reproductive effectiveness.
- ⇒ Study the fate and bioavailability of known endocrinological disrupters; apply the insights gained to other substances.
- ⇒ Determine regional variations in the distribution of EDCs and wildlife populations.

The list, whilst not exhaustive, is already far too long to be addressed by any one country working alone. International cooperation, based on an agreed scientific foundation, is the only realistic way to proceed.

Q2. Have government agencies conducted or commissioned any Australian research on the reproductive effects of exposure- including *in vitro*- to the chemicals being considered as endocrine disrupting chemicals? If so, when do you expect the results to be available to the public?

Given the wide-ranging implications in international chemicals issues, policy and technical work needs to be co-ordinated nationally to ensure effective and efficient chemicals management. This is achieved through coordinating mechanisms amongst federal agencies involved in assessment and regulation of chemicals.

This is coupled with a system of designated national focal/contact points for various international programs. It is through such national co-ordination that a whole-of-government approach can be taken to chemicals issues.

Australia supports the findings and recommendations of the IFCS and has been actively participating in surveys and meetings within the OECD Chemicals Program (which is working on the testing requirements) and in other fora.

Furthermore, lead Departments and chemical assessment/regulatory agencies are maintaining watching briefs on EDC. In addition, briefings on activities on EDCs have been provided to Community Consultative Committees, and non-government organisations through formal consultative mechanisms at the federal level.

Given the IFCS finding that further investigation is required, Australia sees benefit in supporting a concerted and co-ordinated program of research to investigate the possible links between demonstrated trends in human reproductive health and human exposure to chemicals in the environment.

Further work is also needed to refine and clarify the measurement of trends in human reproductive health and the scope of research on wildlife should be extended to cover a range of populations, including those affected by point sources of pollution.

Until these matters are further clarified it would appear to be premature and unwarranted to divert scarce resources into developing major regulatory changes or action, acknowledging that the greatest benefit in ensuring responsible chemicals regulation will come from providing input where our expertise and resources allow and to utilise international efforts to guide our national decisions and actions.

Q3. Does your agency require the provision of test results on chemicals for their effects on the endocrine system in the notification and assessment of industrial chemicals? If not, do you plan to do so in the near future?

Industrial Chemicals

The National Industrial Chemicals Notification and assessment Scheme, NICNAS that is housed within the Office of the National Occupational Health & Safety Commission (NOHSC), undertake Notification and assessment of industrial chemical. Environmental

and public health assessments are conducted for NICNAS by Environment Australia and DHFS, respectively.)

Health Effects.

Test results of chemicals for their effects on the endocrine system are not included in the information specified for notification of new chemicals (Parts A, B or C of the schedule of the Industrial Chemicals (Notification and Assessment) Act 1989). The typical data requirements **for new chemical notification** are listed below:

If other data is available, for example reproductive toxicity or developmental toxicity studies these should also be provided to NICNAS for assessment. The Act does allow the Director of NICNAS to require further information during the assessment process in the event that certain information is considered necessary to complete the assessment. Furthermore, subsection 64(2)(e) of the Act requires the introducer of a chemical that has been assessed under the Act to provide any further information on adverse health effects, which has become available since the completion of the assessment.

Under the Priority Existing Chemicals (PEC) Program of NICNAS, detailed reviews of existing industrial chemicals can be undertaken addressing potential adverse health and/or environmental concerns of a chemicals.

Review on the basis of concerns over adverse effects on the endocrine system are possible within the PEC program. This would include any studies that would detect effects on endocrine systems. Chemicals for consideration for PEC assessment can be nominated by the public, other government agencies and regulatory bodies, the jurisdictions and the Director of NICNAS.

PEC assessments cover a greater range of test data than that provided for new industrial chemicals reflecting the considerable body of test data and research information that is usually available on existing chemicals which has been generated either through the OECD SIDS (screening information data sets) program for High Production Volume (HPV) chemicals or through ongoing research and testing.

PEC assessments usually include assessment of reproductive toxicity, developmental toxicity and chronic toxicity including carcinogenicity data (see agvet table below for descriptions of these test data).

<i>Acute toxicity</i>	includes lethal dose studies by oral and dermal routes, eye irritation studies, dermal irritation studies and dermal sensitisation studies
<i>Short-term repeat-dose toxicity</i>	Studies involving multiple doses for up to 28 days
<i>Genotoxicity</i>	Determine the chemicals ability to interact with genetic material including DNA
<i>Special studies</i>	Includes special studies on neurotoxicity, immunotoxicity, and mechanism of action.
<i>Human studies</i> if available	Epidemiological reports, and case reports of poisonings or effects after occupational exposure.

Environmental Effects.

Industrial chemicals are also subject to environmental assessment when they are notified, or declared as priority existing chemicals. Information on use patterns, physico-chemical properties and environmental fate allows an exposure assessment to be conducted. Based on this exposure assessment, toxicity data are required for organisms likely to be exposed.

In general, environmental toxicity data requirements would focus on aquatic organisms (fish, water fleas and algae) as environmental exposure to industrial chemicals generally involves discharge to sewer. However, data requirements may extend to any organism likely to be exposed, and could be requested from notifiers in cases where suspected endocrine disrupting chemicals may be exerting adverse effects on reproductive outcomes.

Should the ongoing research and activity on developing testing strategies indicate a need, the development of cost-effective and reproducible tests for screening will allow both new and existing chemicals can be adequately investigated for their EDC hazard potential before they are considered suitable for introduction or continued use.

Based on the outcome of international work (predominantly the OECD) on EDC testing strategies, as directed by the IFCS, NICNAS will review its test data requirements for industrial chemicals as needed.

This reflects the fact that the majority of testing of chemicals is carried out overseas and that little compliance would result if Australia alone called for significant increases in the test data required for new chemicals notifications to NICNAS. Additional data requirements will only come from internationally agreed processes.

Agricultural and Veterinary Chemicals

(Agvet Chemicals are assessed and regulated by the National Registration Authority (NRA). Environmental assessments are undertaken by Environment Australia for the NRA and mammalian toxicology and public health assessments are carried out by DHFS for the NRA.)

Health Effects.

Within the area of agricultural and veterinary chemicals regulation, a wide range of toxicology studies is required to be submitted for registration/re-registration of agvet chemicals.).

Studies required include:-

<i>Metabolism and toxicokinetics</i>	
<i>Acute toxicity</i>	includes lethal dose studies by oral and dermal routes, eye irritation studies, dermal irritation studies and dermal sensitisation studies
<i>Short-term repeat-dose toxicity</i>	Studies involving multiple doses for up to 13 weeks
<i>Subchronic toxicity</i>	
<i>Chronic toxicity/Carcinogenicity</i>	Long-term studies \geq 1 year
<i>Reproductive toxicity</i>	Studies to examine the possible effects of the test material on all aspects of fertility and overall reproductive performance including duration of pregnancy, incidence of stillbirths, litter size,

<p><i>Developmental toxicity</i></p>	<p>incidences of malformations, development of young ie. Examination of reproduction parameters and pre- and postnatal development</p> <p>Studies to determine if the test material has potential for embryotoxic and/or teratogenic effects, with the material administered to the test species (usually rats and rabbits) during the period of organogenesis.</p> <p>Maternotoxicity and developmental effects (eg. foetal length and weight, number of live and dead foetuses, external malformations, resorptions and foetal anomalies and malformations) are investigated</p>
<p><i>Genotoxicity</i></p>	
<p><i>Special studies</i></p>	<p>Includes special studies on neurotoxicity, immunotoxicity, and mechanism of action.</p>
<p><i>Human studies</i></p>	<p>Epidemiological reports, and case reports of poisonings or effects after occupational exposure.</p>

In addition, information is required on the chemical identity (including the impurity profile) of the agvet chemical, its international status (esp. detail of its regulatory status in major countries/regions), and End Use Product (EUP) details (including

composition details and information about excipients). For agvet chemicals, the existing battery of tests would generally be sufficient to detect compounds which were having an adverse effect on reproduction and development.

Environmental Effects.

Environmental data requirements for agvet chemicals are more extensive than for industrial chemicals as agvet chemicals are deliberately released into the environment and are designed for biological activity. The extent of data requirements depends on the likely environmental exposure to the chemical. Environmental toxicity data may be required for birds, fish, aquatic invertebrates, algae, aquatic plants, earthworms, insects and other relevant organisms on a case-by-case basis. Acute and chronic data may be required, depending upon the properties and the use pattern of the chemical, and reproductive outcomes are carefully evaluated where there is significant exposure to suspected endocrine disrupting chemicals.

Food Additives and Contaminants

Health Effects

As noted above, agvet chemicals which may occur as residues in food are assessed and regulated by the NRA, based on recommendations and advice from other agencies participating in the National Registration Scheme (NRS) viz. DHFS, EA and NOHSC. MRLs established by the NRA are ultimately incorporated into the Food Standards Code maintained by ANZFA.

For specific food additive chemicals, data requirements are generally similar to those required for agvet chemicals. For other substances which may be found in food (eg. processing enzymes, naturally occurring phytoestrogens), there are no strict data requirements and assessments are based on all available information which can be retrieved.

Q4. Does your agency have any testing guidelines for evaluating the impact of pesticides and industrial chemicals on the endocrine system.

With respect to Test Guidelines (ie the guidelines for the actual conduct of toxicology tests in the laboratory), the standard international reference is the *OECD Guidelines for the Testing of Chemicals* (Vols 1 and 2).

All Australian assessment and regulatory agencies recognise the OECD guidelines (some, such as NICNAS and NRA, also recognise other internationally accepted test guidelines including those of the US EPA) In addition, most agencies are flexible with respect to data requirements and will accept test data under a variety of national and/or international protocols provided that the reports are well documented and provide sufficient details to allow independent assessment.

The OECD guidelines are equally applicable for all chemicals ie. agvet chemicals, therapeutics and industrial chemicals. Tests relating to developmental toxicology, reproductive toxicology, cancer-causing potential, immune-system toxicity etc. are covered in these OECD guidelines (but see also answer at question 7).

A number of national, regional and international initiatives have been taken to address EDCs.

The so called Weybridge meeting (European Workshop on the Impact of Endocrine Disrupters on Human Health and Wildlife, Weybridge, UK 1996) provided a key step towards consensus on EDC testing and assessment needs and proposed a two tier flexible approach.

This was followed by the EMWAT Workshop (SETAC Europe/OECD/EC Expert Workshop on Endocrine Modulators and Wildlife: Assessment and Testing, EMWAT, Netherlands, 1997) build on many of the issues raised at Weybridge and further elaborated details of a testing strategy for wildlife which involves three key levels of activity.

Further, the *US Food Quality and Protection Act* and amendments to the *US Safe Drinking Water Act* (passed in 1996) require the USEPA to develop and present a screening program for EDCs by August 1998 “using validated test systems and other scientifically relevant information”. This work is being progressed by EDSTAC (US EPA’s Endocrine Disrupter and Screening Testing and Advisory Committee) which has prepared a conceptual framework of the ordered sequence: priority setting, screening, testing.

Work is progressing in the OECD Test Guideline Program to develop a harmonised testing strategy for the screening and testing of EDCs taking into account the work of Weybridge, EMWAT and EDSTAC. The OECD is currently working on the development of an international testing strategy for EDCs. Through research and information exchange, a robust and scientifically reliable assessment can be made of the risk to wildlife and human health from exposure to EDCs.

Notwithstanding the caution required in interpretation of the available data relating to contaminants in the environment, Australia strongly supports the cooperative development by OECD of guidelines for any agreed additional testing and assessment of hormone disrupter chemicals. This will ensure that new and existing chemicals (pesticides, industrial and household products) can be adequately investigated before they are considered suitable for registration, re-registration, approval, or use.

The instigation of such test procedures will help prevent society from adding hormone disrupter chemicals to the environment (regardless of whether one agrees that existing environmental contaminants have xenoestrogenic actions or not).

At the international level, the modification of existing *in vivo* tests and development of new *in vitro* tests or new short-term *in vivo* tests, whilst also being developed by the US EPA, will benefit from the consideration by the OECD Test Guideline Program, which is the internationally recognised expert body. Australia is quite closely involved with the OECD Test Guidelines program, and has already completed a survey of current regulatory and assessment practices concerning EDCs.

ANZFA is aware of the phytoestrogen component of a range of plant-derived foods and the biological activities of such are considered in agency assessments; in view of the dietary intake of these compounds, they are following EDC testing proposals with interest.

Q5. Does your agency have any standards or recommendations for endocrine disrupter levels in industrial chemicals?

Industrial Chemicals

NICNAS, as an assessment agency, does not regulate level of contaminants for any class of chemical. However, when conducting a classification of health hazard, NICNAS uses the NOHSC Classification Criteria and the relevant concentration cut-offs used to determine whether a substance is hazardous. As such NICNAS does not publish any such standards relating to endocrine disrupters as such.

Environment Australia, when assessing chemicals, establish the predicted levels of exposure in the environment and compare these with toxicity levels as determined by testing. As a general rule, exposure concentrations that are less than 10% of effects concentrations are considered to present minimal environmental risk. For health assessment, in cases where an industrial chemical has been identified as having endocrine disrupting potential, NICNAS will make recommendations on minimising exposure.

Agricultural and Veterinary Chemicals

There are Australian standards for levels of certain highly toxic microcontaminants in various agvet chemicals. These standards [formerly listed in Appendix L ('Maximum Levels of Impurities') of earlier editions of the *Standard for the Uniform Scheduling of Drugs and Poisons*. Australian Health Ministers' Advisory Council] are maintained by the National Registration Authority, on the basis of advice received from the DHFS. However, these standards do not specifically relate to endocrine disrupter contaminants, but cover all toxic effects of concern.

Food Additives

Currently there are no specific standards for contaminants/impurities (in food additive chemicals) which may be EDCs.

Q6. Does your agency have any interest in the current hypothesis concerning the possible effects on the endocrine system posed by some chemicals used in the manufacture of certain plastics?

Relevant Australian agencies and Departments maintain a close watch on endocrine disrupter chemicals research and related issues. This is achieved through direct country to country interaction as well as via Internet and the use of the scientific literature. DHFS maintains a large database of papers, reports and other material. The issue of EDCs and plasticisers and phthalates is being monitored within NICNAS and ANZFA, and new chemicals with similar structures to those chemicals currently implicated as EDC, are watched for. In addition, under our PEC program, this hypothesis is being viewed for potential impact in selecting our next round of existing chemicals for assessment/review.

Q7. Does your agency support the need for more toxicological information, in particular that relating to endocrine systems effects, for new and existing at-risk? chemicals in Australia?

Industrial Chemicals

Within the area of industrial chemicals, the standard package required for notification of **new** chemicals is generally confined to a package of acute toxicity studies, a short-term repeat-dose study (28 days) and several *in vitro* genotoxicity studies (noting the capacity to seek further data if needed as indicated in question 3 above) The development of a test battery of simple, robust *in vitro* tests for endocrine-disrupter activity would greatly progress safety testing in this area, in a cost-effective manner.

With respect to environmental assessment, further testing of chemicals for toxic effects wherever risks to non-target organisms are suspected is supported. Testing of endocrine disrupting activity would be supported on the basis that it provides useful information.

For existing chemicals, where any concerns about endocrine effects may arise, NICNAS would support a thorough investigation of those concerns. The science on whether there are any particular groups of chemicals that should be highlighted for such a study is not yet clear.

Agricultural and Veterinary Chemicals

Within the area of agvet chemicals, the DHFS considers that the toxicological investigation of most herbicides and pesticides is reasonably well covered. However, some test guidelines could be modified to further investigate the endocrine-disruptive potential of chemicals by relatively minor changes to test protocols eg. the period of dosing in developmental toxicity tests could be extended beyond the current standard (days 6-15 of pregnancy in rats, days 7-19 in rabbits) until just prior to term, to incorporate the period when the reproductive organs are undergoing major development. This would increase the chances of picking up EDCs and other reproductive toxicants.

With respect to environmental assessment, further testing of chemicals for toxic effects wherever risks to non-target organisms are suspected is supported. Testing for endocrine disrupting activity would be supported on the basis that it provide useful information.

Food Additives

ANZFA supports the need for more toxicological information relating to endocrine system effects for new and existing food additive chemicals.

Q8. Does your agency have contact with overseas agencies in the area of endocrine disrupter chemicals and an ability to share information with this agency.

Australia has formal contacts with overseas organisations and Fora involved in international chemicals negotiations on a broad range of chemicals assessment and management issues.

Environment Australia is the National Focal Point for activities carried out under the auspices of (1) the OECD Chemicals Programme; (2) for the UN Environment Programme (UNEP); and (3) UNCED Agenda 21 Chapter 19 activities including the IFCS. DHFS is the National Focal Point for the WHO and its International Programme on Chemical Safety (IPCS) and its assessment programs and Chapter 19 associated work including the CICADs (Concise International Chemicals Assessment Documents). NICNAS is a participating Institute of the IPCS.

Individual agencies have technical leads for programs within these international programs.

For example, the NRA and its service agencies provide technical policy input into, and actively participate in projects of, the OECD's Pesticide Forum. Similarly, NICNAS has active input into new and existing industrial chemicals programs of the OECD's chemical programme.

ANZFA takes part in the Joint FAO/WHO Expert Committee on Food Additives - Food Additives and Contaminants (JECFA) and in the Codex Committee on Food Additives.

When activities are at treaty level, the Department of Foreign Affairs and Trade is the lead agency, with technical policy input from the other agencies.

Through these formal contacts, Australia actively participates in EDC-related activities being undertaken by various international organisations.

In addition, individual agencies have direct working relations with their counterparts overseas and are in E-mail contact on a staff-to-staff basis, as well as having a range of informal scientific contacts. This allows agencies to be fully cognisant of developments within the US EPA and elsewhere, thus ensuring Australia's regulatory programs for chemical safety are informed by current knowledge and activities.

Useful Information Sources

The OECD home page (<http://www.oecd.org/ehs/test/endodrp.pds>) links to other relevant sites including:

- Endocrine Disrupters Research Inventory (in Europe)
- The Endocrine Disrupter Resource Center (outside Europe)