Endocrine Disrupting Substances and Ecological Risk Assessment of Commercial Chemicals in Canada

ROGER SUTCLIFFE*

Chemicals Evaluation Division, Commercial Chemicals Evaluation Branch, Environment Canada, 351 St. Joseph Boulevard, Hull, Quebec K1A OH3

The ecological risk assessment of commercial chemicals in Canada by the regulatory programs of the Commercial Chemicals Evaluation Branch, Environment Canada, are based on results from traditional toxicity data (e.g., lethality, effects to growth or reproduction). Some of the chemicals under consideration are known to alter endocrine systems in exposed organisms; however, effects to the endocrine system are used only as additional supporting information. Presently, there are no internationally accepted methodologies or tests for endocrine disrupting substances that can be used by these regulatory programs. The need for research with respect to hormone disrupting substances has been recognized in the revised Canadian Environmental Protection Act, 1999 (CEPA 1999). This paper describes the framework for the ecological risk assessment of new and existing substances and identifies issues and research needs in both screening level and in-depth ecological risk assessments with respect to the identification and assessment of potentially endocrine disrupting substances.

Key words: ecological risk assessment, endocrine disrupting substances

Introduction

Presently, the ecological risk assessment of commercial chemicals in Canada by the regulatory programs of the Commercial Chemicals Evaluation Branch (CCEB), Environment Canada, under the Canadian Environmental Protection Act, 1999 (CEPA 1999) and its predecessor (CEPA 1988) are based on results from traditional toxicity data (e.g., lethality, effects to growth or reproduction). Some of the chemicals under consideration are known to alter endocrine systems in exposed organisms; however, effects to the endocrine system are used only as additional supporting information. To move beyond the present situation, increased research activity is needed to develop screening and identification tools for endocrine disrupting substances (EDS) and demonstrate linkages between endocrine modulation and prediction of environmental effects. Indeed, CEPA 1999 recognized the need for supporting research on hormone disrupting substances. This paper focuses, firstly, on the ecological risk assessment of substances, excluding biotechnological products under

* roger.sutcliffe@ec.gc.ca
CEPA, and secondly, on identifying the research needs of the regulatory programs of CCEB to address the issue of substances which are potentially endocrine disrupting substances. Understanding of the legal mandates and regulatory assessment processes and their needs is a prerequisite if research on endocrine modulators is going to be undertaken that will advance the use and increase the profile of EDS data in regulatory decision making.

Ecological Risk Assessment within CCEB

Under the Canadian Environmental Protection Act, 1999 (CEPA 1999), the Commercial Chemicals Evaluation Branch (CCEB) of Environment Canada shares responsibility with Health Canada for identifying and assessing the risks posed by existing chemicals, new chemical substances and new products of biotechnology not regulated under other federal acts. CCEB has two divisions responsible for conducting environmental risk assessment of substances under CEPA, New Substances Division (NSD) and Chemicals Evaluation Division (CED). NSD conducts environmental risk assessments of substances that are new to Canada, including those that are biotechnology products, by implementing the New Substances Notification Regulations of CEPA. CED is responsible for the environmental risk assessments of existing substances: leading the Departmental program for assessing substances on the priority substances list (PSL); implementing the new mandates of categorizing and screening the Domestic Substances List (DSL); and the review of decisions by other jurisdictions.

Ecological risk assessment in CCEB for new or existing substances follow the same basic steps (Fig. 1). These assessments can be thought of on a continuum from screening level risk assessments (SLRA) as used in new substance assessment and as required under CEPA 1999 for DSL substances that proceed for a SLRA after being categorized, to the in-depth and often complex and time-consuming PSL assessments. The formulation of the approach may be represented differently because of the differences in availability of information and therefore methods and approaches used, and the legally mandated time for the assessments. In each case, the assessment is to determine whether the substance is “toxic” as defined under CEPA. The definition, contained in Section 64 of the Act (1999), takes into account the likelihood and magnitude of releases into the environment and the harm a substance may cause to human health or ecosystems at levels occurring in the Canadian environment:

A substance is toxic if it is entering or may enter the environment in a quantity of concentration or under conditions that (a) have or that may have an immediate or long-term harmful effect on the environment or its biological diversity; (b) constitute or may constitute a danger to the environment on which life depends; or (c) constitute or may constitute a danger in Canada to human life or health.

There are some basic differences in the programs, the types of substances assessed, the time frames for the assessments, the available infor-
mation and powers to obtain information, the process requirements of the assessment and the certainty required in the decision making (Table 1). For a PSL assessment, if it is determined there is a risk to biota or the envi-

**Table 1.** Comparison of environmental risk assessments

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<tr>
<th>New substances screening assessments</th>
<th>Existing substances screening assessments</th>
<th>PSL assessments</th>
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<tbody>
<tr>
<td>Notified information prescribed in regulation + all available information</td>
<td>Available information, collection of up to date exposure and use pattern information</td>
<td>In-depth information collected on use patterns, exposure and effects</td>
</tr>
<tr>
<td>Regulatory timelines (days)</td>
<td>No regulatory timelines</td>
<td>5 years for publication of scientifically and publicly reviewed report</td>
</tr>
<tr>
<td>Predictive assessment of effects and exposure</td>
<td>Predictive and available test information for assessment of effects and exposure</td>
<td>Exposure and effects information can be generated</td>
</tr>
<tr>
<td>All types of substances assessed on a one-by-one basis pre-manufacture, pre-import</td>
<td>All types of substances in commerce assessed on a one-by-one basis</td>
<td>All types of substances, but also classes of substance, mixtures, environmental contaminants, effluents</td>
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vironment, the substance will be declared “toxic” under CEPA, Section 64, and will be recommended for addition to the List of Toxic Substances (Schedule 1). Substances added to this list are then subject to risk management activities (Government of Canada, Environment Canada 1995). For new substances, if an assessment of risk leads to a concern for a particular substance, control options may be considered based on a “suspicion of toxicity.” The latter phrase is used because any risk assessment is based upon available information and involves a degree of uncertainty. For substances subject to SLRA under the DSL Program the assessment outcomes can be the recommendation that the substance be added to List of Toxic Substances of CEPA, recommended for addition to the PSL, or no further action under the program.

**Environmental Assessment of Priority Substances**

**Introduction to PSL assessments — the three-tiered assessment approach**

Environment Canada has published a Guidance Manual for conducting environmental risk assessments under the Priority Substances Assessment Program (Table 2) (Environment Canada 1997). Environmental assessments can be complex and time-consuming, since the effects of substances on numerous species must be considered. Sometimes the effects are direct, such as death or reproductive abnormalities; at other times the effects are more subtle, such as disruptions to the structure or function of an ecosystem. Assessors at Environment Canada are assisted by an Environmental Resource Group (ERG) which is formed for each substance. The ERG can include experts from industry, academia and members of other government departments or other levels of government who have particular expertise in dealing with the substance.

Environmental risk assessments of priority substances involve three major steps: problem formulation, analysis and risk characterization. The

<table>
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<th>Table 2. Information sources related to environmental risk assessment</th>
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<td>Environmental Assessment of Priority Substances</td>
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<td>Guidance Manual for conducting environmental risk assessments under the Priority Substances Assessment Program</td>
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risk characterization process is further structured in three tiers to ensure that substances undergo rigorous analysis to determine if they are “toxic” under CEPA. This approach allows for a substance to be found not to be “toxic” after a Tier 1, Tier 2, or Tier 3 assessment, and eliminated from further study. The determination of whether or not a substance is “toxic” must be based on sound, scientifically reliable data.

A Tier 1 assessment typically uses very conservative estimates of exposure and effects to eliminate from further study substances that have almost no probability of causing environmental harm. For example, a Tier 1 or worst-case scenario (also known as “hyperconservative”) analysis could use for the exposure concentration the highest concentration of a substance ever measured in Canada. If no adverse effects are anticipated at this concentration, the substance would be judged not to be “toxic” under CEPA.

Tier 2 uses conservative, but more realistic, estimates of exposure and effects to eliminate from further study substances where the risk of environmental damage is very slight. For example, if releases of a substance have declined in recent years, the Tier 2 assessment could be based on the highest concentration measured in Canada in recent years.

In a Tier 3 assessment, the distributions of exposure and/or effects may be compared to estimate the likelihood that the substance will cause environmental harm. For example, a frequency distribution of environmental concentrations may be compared with a concentration-response curve from a toxicity test.

**Environmental risk assessment process**

**Problem formulation** is the planning stage of the process. The goals and focus of the assessment are established, an initial scoping is carried out, data gaps are identified, and a strategy for conducting the assessment is developed. Problem formulation is an iterative process and is updated when necessary as additional information is gathered during the assessment.

To determine how a substance enters the Canadian environment, a pathways analysis is conducted. Information on amounts manufactured, imported, exported, used and released is reviewed to predict a substance’s geographic distribution and its entry into various compartments of the environment, such as water, air, soil and sediment. These data are then used to identify the types of organisms that are potentially exposed to the substance and hence could potentially be harmed.

Data from toxicity tests conducted in the laboratory or in the field are used to identify species that are particularly sensitive to the substance. Assessors must develop an understanding of the ecological relevance of exposed organisms that are particularly sensitive to the substance in order to predict possible indirect effects on other components of the ecosystem, such as predators or prey species.

The next step is to select assessment endpoints pertaining to organisms that are likely to be most at risk from exposure to the substance. Assessment endpoints may pertain to populations of wild mammals or birds, aquatic organisms, soil organisms, etc. (for example, a decrease in
numbers of fish). Measurement endpoints are used to estimate effects on assessment endpoints (for example, the results of toxicity tests on rainbow trout). A conceptual model is then developed, summarizing the ways in which a substance acts in the ecosystem and its possible effects.

Once an initial problem formulation is completed, scientists from academia, industry, the federal government, provinces and territories, environmental groups and other interested parties are invited to comment on it.

The analysis phase consists of three parts: entry, exposure and effects characterization.

The objective of entry characterization is to identify the various sources of the substance in Canada, the quantity of the substance released from each of these sources, and how the substance is released over time to air, water or soil. Entry characterization includes all phases of the substance’s life cycle, from manufacture or importation, through transportation and use, to final disposal. Information gathered during this phase is the first step in determining exposure. If the substance is found to be “toxic” under CEPA, this information is also used to guide development of risk management options.

During exposure characterization, the exposure of each assessment endpoint to the substance is determined. Factors considered include where a substance is released, where it ends up, how long it stays there, what it breaks down into, and how or whether it is taken up by sensitive organisms. A numerical value, known as the estimated exposure value (EEV), is calculated for each assessment endpoint. In a Tier 1 assessment, the EEV is usually the highest concentration of the substance in air, soil, water, etc. For wildlife species, the EEV may be expressed as the maximum total daily intake through inhalation, drinking water and/or food.

The objective of effects characterization is to determine a critical toxicity value (CTV), or the lowest concentration of a substance that will cause a certain adverse effect for each assessment endpoint. For example, the concentration of a substance causing a 25% reduction in growth or reproduction of test organisms in a toxicity study could be selected as a CTV. A CTV is usually calculated from the results of short-term (acute) and long-term (chronic) laboratory toxicity tests on one or more species, or less often (due to their lack of availability), from the results of field studies. CTVs for Tier 1 assessments are typically based on toxicity to the most sensitive organism tested. For Tier 2 assessments, it may be possible to refine the CTV. For example, warm-water fish may be less sensitive to a substance than cold-water fish. If the substance is released only to warm waters, the Tier 2 CTV should be based on toxicity to the most sensitive warm-water species tested. A Tier 3 assessment may consider the entire concentration-effects curve derived from a toxicity study in order to determine potential effects at various concentrations of the substance.

Risk characterization, the third stage in environmental risk assessment, compares exposure concentrations and concentrations causing effects for each assessment endpoint in order to determine whether adverse effects are likely. The first step in risk characterization is to determine a level at which the substance would not be expected to affect the
assessment endpoints. This is known as the estimated no effects value (ENEV) and is usually derived by dividing the CTV by an application factor. An application factor is used to account for the uncertainties inherent in extrapolating between measurement and assessment endpoints, including variables such as the difference between laboratory animals and species found in the wild; fluctuations in environmental parameters, such as temperature, which may cause different effects; or other environmental stresses that organisms may face in their natural habitat.

A Tier 1 quotient is calculated by dividing the EEV (see above) by the ENEV. If the resulting value is less than 1, the substance is judged not to be “toxic” under CEPA for the assessment endpoint, and the assessment does not have to proceed further. If the value is greater than or equal to 1, the substance moves into a Tier 2 assessment.

A Tier 2 assessment may involve the use of more realistic, less conservative values for the EEV, or the ENEV, or both. It may also be possible to justify using a smaller application factor. There must be sound scientific reasons to support any changes that are made, and these reasons must be presented in the assessment report. If the numerical result of the Tier 2 assessment quotient is less than 1, the substance may be judged not to be “toxic” for the assessment endpoint. It is stressed that Tier 1 and Tier 2 quotients equal to or exceeding 1 do not result in a designation of “toxic” under CEPA for any substance. If the quotient is greater than or equal to 1, the assessment moves to Tier 3. Tier 3 involves consideration of all available data to characterize environmental risks to the greatest possible extent. For example, it could involve comparing the distribution of exposure concentrations with concentrations causing effects, in order to determine whether adverse effects are likely. A special analysis is used for naturally occurring substances, such as metals, which may cause harmful effects. This analysis considers natural background concentrations and takes into account the possibility that organisms found in naturally enriched areas may have developed a special tolerance to the substance. If it is concluded from a Tier 3 assessment that adverse effects are unlikely, the substance is judged not to be “toxic” based on the assessment endpoint.

If a Tier 3 analysis of any assessment endpoint indicates that adverse effects do occur or are likely to occur, the substance will be considered to be “toxic” under CEPA, paragraph 64(a), and will be recommended for addition to the List of Toxic Substances (Schedule 1 of CEPA), which will trigger actions to determine how best to reduce or eliminate the risk.

Screening Level Risk Assessments for Substances New to Canada and Existing Substances

The New Substance Notification Regulations

One of the objectives of CEPA is to ensure that no new substance be introduced into Canada without a formal review of its potential risks to human health and to the environment. The New Substance Notification (NSN) regulation is the authority under which the New Substances Notification Program performs the risk assessments and controls substances when a risk is identified. The NSN Regulations came into effect on
July 1, 1994. The NSN Regulations require importers and manufacturers to notify Environment Canada of substances new to Canada. New substances are defined as substances that do not appear on the Domestic Substances List (DSL). The DSL includes substances that were, between January 1, 1984, and December 31, 1986, in Canadian commerce, used for manufacturing purposes, or manufactured in or imported into Canada in a quantity of 100 kg or more in any calendar year. The List has been amended from time to time and currently contains approximately 23,000 substances.

The information notifiers must submit to government is described in regulatory “schedules.” The notification packages typically include test data in support of physico-chemical and/or toxicity information. Therefore, the initial information a risk assessor has to work with is dependent on the type of substance and notification schedule submitted.

**Screening level risk assessments of substances which have been categorized under Section 73 of CEPA**

Since most of the substances on the DSL have not undergone any environmental or human health assessment, CEPA 1999, provides for the systematic assessment of substances on the DSL that are to be carried out in two phases. The initial phase, referred to as the categorization of substances, identifies substances that will proceed to the second phase, a screening level risk assessment (Fig. 2). As identified in CEPA 1999, all substances on the DSL must be categorized within 7 years from the Bill receiving Royal Assent which occurred on September 14, 1999.

![Fig. 2. Categorization of existing substances on the Domestic Substances List (DSL).](image-url)
Framework for screening assessments for non-human organisms

For both new and existing substances on the DSL the basic framework of the assessment is similar. The determination of suspicion of being toxic, or toxic, consists of integrating the assessment of potential predicted exposures of a substance with potential predicted adverse effects in the environment. In the case of some substances on the DSL, which are considered existing substances, there may be available measured exposure or effects data that can also be used in the assessment. The potential for exposure of a substance depends on the amount of substance released into the environment and its fate. The exposure assessment, therefore, consists of evaluating any known environmental concentrations of a substance as well as predicting environmental concentrations of a substance from releases resulting from its production, processing, uses and disposal, and its environmental fate evaluated on the basis of intrinsic physical-chemical properties, environmental mobility, and its persistence. The assessment will consider known uses of the substance as well as other possible ways the substance might be used (Fig. 3).

Exposure assessment at a screening level can contain considerable uncertainty in comparison to a risk assessment of the Priority Substances List type or site specific risk assessments, because of the dependence on available information and predictions of exposure. The quality and detail of information received from industry will influence the methods used and the level of uncertainty.

Environmental effects assessment involves establishing for a substance a toxicity profile that indicates the type of effect and the seriousness of that effect on a given organism at a known concentration of substance. Effects data can be based on available or submitted test data, or predictions using structure activity relationships and consider environ-
mental factors which may reduce or enhance the toxicity/toxic effect of a substance. The use of application factors to the effects concentrations provide concern concentrations (CC), or an ENEV. The subsequent risk assessment will be determined using a quotient method comparing concern concentrations and predicted environmental concentrations (PEC).

The environmental exposure assessment makes use of predicted or notified physical-chemical property information to predict how the substance will behave in the environment, including its persistence and bioaccumulation behavior. The entry characterization involves estimating the amounts and frequency of releases into the Canadian environment, for the notified use, as well as other possible end uses of the substance. For existing substances this involves finding present manufacture, processing and use information, and predicting other alternative uses. Entry characterization in screening risk level assessments focus primarily, but not exclusively, on aquatic systems, as the majority of releases of these substances have historically been to aquatic systems.

The exposure characterization consists of determining the fate of the substance in order to 1) estimate the exposure concentrations, and 2) estimate persistence and bioaccumulation in the medium to which it partitions. In order to determine the substance’s fate, the physical-chemical properties of the substance and the nature of the receiving bodies must be considered. Water solubility, octanol-water partition coefficient, vapour pressure and adsorption coefficient are examples of properties that can be used to determine the fate of the substance once it is released.

Environmental release information, from the previous “entry characterization”, is also employed in determining the fate of the substance. As noted earlier, most industrial and commercial chemicals are released to aquatic systems, either directly or via wastewater treatment plants. However, some substances can be released to the atmosphere or be disposed of on land. Monitoring data or measured concentrations where they exist will be incorporated into the assessment of existing substances. From physical-chemical properties and/or fugacity models with the types of environmental releases, the fate of the substance from the point(s) of release, and the subsequent partitioning to the various environmental compartments can be predicted. From these predictions, an indication of the order of magnitude of expected concentrations and an indication of the levels in biota and in each compartment to which these biota are exposed to can be made. Other predictions can be made for point-source type releases from manufacturing, processing and uses.

Bioavailability of the substance will also be considered in this section, if possible. Mitigation is a process whereby a substance (for example, with a high soil distribution coefficient) will be removed from aquatic systems as it adsorbs to suspended organic matter and settles out of the water column. Biotic and abiotic degradation may also play significant roles in determining compartmental concentrations. Substances may be removed from a compartment rapidly by chemical reactions and/or biodegradation to severely limit the exposure to organisms in that compartment. These processes and others may serve to decrease environmental exposure to biota.
The intent of the exposure characterization is to estimate the potential concentrations of the substance that may be found in each of the environmental compartments, based initially on conservative estimates of releases and anticipated partitioning. This provides a worst case scenario for exposures and as a result, the concentrations arrived at will be assumed to be the maximum concentrations that organisms will be exposed to in their respective media. These concentrations will be used in the risk assessment analysis and will be known as the predicted environmental concentrations (PEC), or in some cases for existing substances where data exist the estimated exposure value (EEV). These are values that are considered to be the worst case or, if data exist, representative concentrations that may be found in the environment as a result of the use, processing or manufacture of the substance in the prescribed manner. An EEV for biota exposed in surface water may be derived by, for example, dividing the amount of the substance expected to be discharged (in a given scenario) per day at a site by the flow rate of the receiving river (in L/day). More complex strategies may consider the results of fugacity modeling, with releases into specific, possibly multiple, compartments, biodegradation, mitigation, hydrolysis and other variables.

The objective of the effects characterization phase of the SLRA is to generate a critical toxicity value (CTV) for each assessment endpoint using the most sensitive measurement endpoint. The most sensitive measurement endpoint is the lowest concentration of the substance, observed during an experimental test or predicted using QSAR models, that produces an effect in biota. Effects characterization involves a review of eco-toxicological information on laboratory studies of exposed organisms, read-across data from analogous substances and QSAR estimates of toxicity from recommended programs. In most cases, these concentrations are expressed as LC₅₀ or EC₅₀. Other information may also be available, such as chronic toxicity studies (i.e., LOEL) or a low toxic effect (EC₂₅). Empirical data for the specific substance are given preference, but in the absence of quality experimental information, QSARs will be used to predict toxic effects of substances. Experimental data for surrogate substances may also be considered.

From the critical toxicity value, a concentration of concern (CC) will be derived for new substances or, if data exist, for an existing substances an estimated no effects value (ENEV) will be derived by dividing the CTV by an appropriate application factor (AF). Application factors are used to account for the uncertainties inherent in extrapolating data from empirical studies or QSAR estimates to ecological systems. The specific uncertainties that are typically represented by these factors include differences in age/development stage, sex, inter- and intraspecies variations, varying physical-chemical conditions of the environment, and extrapolating from acute endpoints to chronic endpoints. The ENEV uses known or predicted toxicity data and application factors to estimate the threshold concentration of a substance in the environment that would not illicit deleterious effects. Whenever possible more appropriate acute to chronic ratios will be used in place of the 10-fold factor.
**Risk characterization** combines the results of the exposure and effects characterizations. The ratio of estimated exposure to estimated effects or (PEC/CC) or known exposure to estimated no effects (EEV/ENEV) provides an indication of environmental risk. If this ratio is less than one, then there is a low probability of adverse effects occurring to biota. The assessment for that endpoint would not lead to the conclusion that the substance is “toxic” as defined under CEPA. If the ratio is greater than one, then a concern would exist and, for a new substance assessment, attempts would be made to refine the assessment. This would normally occur through discussions and requests for further information from the notifier of the new substance. Presently, for the DSL screening level risk assessment, it is unclear how after an initial determination of the risk using predicted and available information further refinement will be possible. Based on the level of uncertainty in the screening level risk assessment, this may be sufficient grounds for using other powers in CEPA to obtain additional information.

The risk characterization uses a weight-of-evidence approach to support conclusions, if possible. In assessment of existing substances, for example, assessors consider in determining the EEV and ENEV the relevance of the data presented in the assessment. Available data are ranked according to factors such as quality of the data presented — relevance of and adherence to test protocol, toxicity tests that use biota native to Canadian ecosystems, relevance of exposure data to Canadian environments, and others. By placing an emphasis on the more relevant data, uncertainty may be reduced in the assessment. If data-rich substances are evaluated, it may be possible to use a similar approach to a Tier 3 PSL assessment, which involves analysis of distributions of exposure and/or effects data.

### Endocrine Disrupting Substances in Regulatory Ecological Risk Assessments

**Present Status**

CEPA 1999, reconfirms that the basis of all decisions under this law must continue to be based on sound science. It is fundamental to the foundation of all regulatory action. However, CEPA also recognizes explicitly that absolute certainty in science and absolute scientific guarantees are rarely achievable. It recognizes that science is the foundation, but that in the face of uncertainty in the science where the threat is severe and irreversible to either the environment or to health, measured and thoughtful action is not only appropriate but required. The regulator must act reasonably and judiciously in the face of scientific uncertainty. CEPA actually obligates the Minister to conduct research on hormone disrupting substances. At present, from the perspective of the ecological assessment programs within CCEB, there are no internationally accepted methodologies/tests that will address specific issues of EDS that we can use within our regulatory programs to identify these types of substance. Therefore, there is no basis to request information under regulation.
The question is then how do we presently address substances that are endocrine disruptors, or are suspected of being endocrine disrupters? The New Substances and Priority Substances Program believe that the most harmful substances and many classes of substances suspected of being EDS are captured by considering the traditional toxicity endpoints which are used in the risk assessments. A substantial number of chemicals which are on various lists as suspected EDS are already subject to regulatory measures. These measures were taken on the basis of reported toxic effects of the individual substance without necessarily identifying the underlying mechanism. This is recognized as not being a totally satisfactory position for the programs. Questions that need to be addressed are: Do these effects occur at levels significantly lower, or at levels similar to traditional endpoints? Can programs be confident that our assessment factors on traditional endpoints are protective enough of EDS effects? How are chemicals in classes beyond those currently suspected of being EDS to be identified?

What Are the Requirements for CCEB To Address Risks Posed by EDS?

What do we need to address risks posed by an EDS? The programs require the establishment of screening tools and test methods which will be able to detect major effects which have been linked to EDS and identify which substances are of concern. This applies across all programs: new substances, DSL categorization and the PSL programs. In establishing these methods, dose-response considerations have to be established in order to factor this information into the risk assessment processes. In identifying which classes of substance require the establishment of screening and identification processes, it is also necessary to identify which classes can be excluded. Also, the cost efficiency considerations of regulations require that unnecessary testing be minimized.

With respect to identification and testing for EDS, it is acknowledged that ongoing activities through the Task Force on Endocrine Disrupter Testing and Assessment (EDTA), established under the Test Guidelines Program and the Risk Assessment Advisory Body of the OECD, and the U.S. EPA established Endocrine Disrupter Screening and Testing Advisory Committee (EDSTAC) and subsequent Endocrine Disrupter Screening Program (EDSP) have made progress in the development of a strategies to identify and test substances to identify EDS. At present, we see limitations that need to be addressed before the goals of these groups can be implemented into Canadian regulatory programs. There is a need to link the results of testing for EDS effects to the prediction of environmental effects. This needs the establishment of the causal link between potential effects and potential exposure in the environment. Furthermore, how this testing and screening data are to be used has to be further developed. Then there are the practical issues of whether or not the screening and testing is appropriate and practical for all types of substances with which the regulatory programs deal. Cost effective screening tools, either tests or predic-
tive modeling, which can identify candidates for further testing are required. In addition, there are issues related to the purity of the substances that will be subjected to testing. Commercial chemicals are not necessarily of the purity of standards used in test method development, and the relevance and interpretation of the results is therefore an issue.

The ecological risk assessments of CCEB will need, with respect to effects assessment, to address emerging concerns such as long-term exposure to low concentration of substances, potential synergistic effects, and multi-generational effects. There are also more specific issues that will require addressing with respect to species: Are effects species specific? Are some species more sensitive? What are the stages of development that are important to specific species and are there differences? Which vertebrates and invertebrates should be used as representative species, or is there no representative species?

With respect to exposure issues there will be a need to link potential effects to the sources and pathways of exposure, including the magnitudes, duration and frequency of exposure.

Specifically for screening assessments of existing and new substances, the programs require the demonstration and availability of scientifically validated predictive screening tools or screening tests and tiers of validated test protocols that can deal with all types of substance, including difficult to test substances. In test protocols, there is a need for a demonstrated link between effect and dose levels. The PSL assessment program will need the above as well as field studies and monitoring data which link effect to specific substances.

Summary

CEPA 1999, requires research on hormone disrupting substances and allows for use of endocrine disruption test data in regulatory programs. In CEPA assessment programs, endocrine effects can be examined using the same approach as traditional endpoints; however, at present, decisions are based on traditional toxicological end-points.

CCEB for its legally mandated programs needs research that supports risk characterization. For the Tier 1 and screening level assessments, this is the development of validated screening tests, and identification of which substances will require screening and which will not. For Tier 2 conservative or more in-depth screening assessments, the need is for the development of dose-response relationships. Finally, Tier 3 probabilistic assessment development of specific links of adverse effects to effects in the field is required.

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