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EPA's Framework for Ecological Effects Assessment

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ABSTRACT: The Office of Technology Assessment (OTA) is studying the implementation of the Toxic Substances Control Act (TSCA). One focus of the OTA study has been the TSCA existing chemical review program, which is administered by the U.S. Environmental Protection Agency's (EPA) Office of Pollution Prevention and Toxics (OPPT formerly the Office of Toxic Substances). The level and pace of EPA evaluation of the over 72,000 chemical substances on the TSCA Inventoty of existing chemicals lead the OTA to consider the adequacy of the testing and screening methods and technologies that are, or could be, used to assess such industrial chemicals in commerce.

One of the nine specified topics of interest to be addressed at the OTA Workshop was the testing and screening methods used by EPA (and others) to assess environmental toxicology, i.e., the testing and screening methodologies used to assess the potential ecological effects of TSCA regulated industrial chemicals. This chapter provides a review of OPPT's Environmental Effects Branch (EEB) efforts over the last 15 years in screening and assessing the potential ecological effects of industrial chemicals.

BACKGROUND

The Toxic Substances Control Act of 1976 (TSCA) provided the EPA (OPPT) with the authority to require development of adequate data for assessing the risk to human health and the natural environment from industrial chemicals identified as having risk potential. Within OPPT, the Environmental Effects Branch (EEB) has provided the expert scientific and technical evaluation of the environmental/ecological hazard of industrial chemicals, and has determined the type and adequacy of data needed to identify and assess their possible adverse effects. Over the past 15 years this group has provided significant direction to and rationale for how ecological hazard and risk assessment activities have been addressed under TSCA (32, 35, 36).

For example, from 1979 through 1994, EEB staff have been responsible for the screening and assessment of the potential ecotoxicity of over 26,000 new industrial chemicals (36). Since 1979, over 10,000 of the new chemicals that have been assessed as acceptable have been placed on the TSCA Inventory of existing chemicals because industry has commenced production and/or importation of them into the U.S.

To assure that adequate ecotoxicity data are developed to assess the possible adverse ecological effects of industrial chemicals, procedures and guidelines were established for developing data that are appropriate and adequate for assessing ecological hazard and risk. For industrial chemicals, the OPPT approach to ecological risk assessment (figure 8-1) is analogous to the risk assessment paradigm of the National Academy of Sciences (16) and is also consistent with the recently developed EPA Framework for Ecological Risk Assessment (12).

This approach ultimately required the active development of six specific areas: 1) defining appropriate ecological endpoints, 2) a tier-testing scheme for estimating impacts on these endpoints, 3) ecotoxicological testing guidelines, 4) structure-activity relationship technologies (SAR/QSAR) for estimating ecotoxicity from chemical structure, 5) hazard "assessment factors" for estimating chemical concentrations of concern, and 6) risk assessment methodologies that characterize risks by contrasting the ecotoxicity

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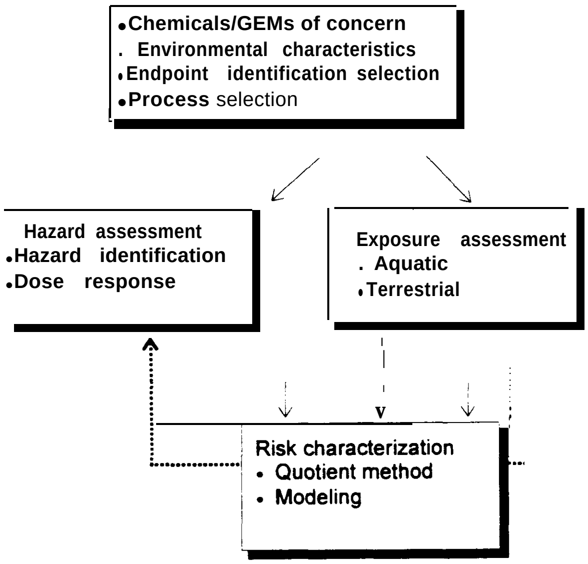
Figure 8-1: The OPPT Ecological Risk Assessment Process



SOURCE: Zeeman, M., and Gilford, J., "Ecological Hazard Evaluation and Risk Assessment Under EPA's Toxic Substances Control Act (TSCA)," *Environmental Toxicology and Risk Assessment: 1st Volume,* W.G. Landis, et al. (ads.) (Philadelphia, PA: ASTM, 1993).

and exposure data. These several sets of developments allows OPPT to estimate the adverse effects of industrial chemicals on ecological endpoints of concern.

ECOLOGICAL ENDPOINTS

Ecological endpoints of concern are those adverse effects on the environment of sufficient importance to warrant regulatory action under TSCA (e.g., high fish toxicity). Ecological endpoints were a basic consideration in determining the kind and amount of ecotoxicological data needed to evaluate the potential hazard and risk posed by a chemical.

U.S. environmental legislation was examined to determine what ecological endpoints have been perceived by the U.S. Congress to be of sufficient importance to be protected by legislation. Resources such as wildlife, water, land, and air were to be protected from reduction, degradation, or loss in quality, quantity, or utility (5).

Also a search of the scientific literature on toxic effects of chemicals in the field identified occurrences of adverse environmental effects that resulted in some form of regulatory action. This search revealed nine cases of adverse environmental effects under field conditions, in which toxic chemicals reduced, or led to a loss of quality, quantity, or utility of the above valued resources. The adverse effects caused by the toxic chemicals were the result of: a) undesirable changes in the rates of mortality, growth, or reproduction of organisms; or b) through bioaccumulation of the chemical within a food chain to a level hazardous to other organisms in the environment (32).

Therefore **mortality, growth and development,** and **reproduction, and their potential impacts at the population level were selected as critical features to be considered when assessing the ecological impacts posed by industrial chemi**cals. These endpoints are still being used as the primary focus in OPPT in assessing the potential for industrial chemicals to cause adverse environmental effects that may be of regulatory significance.

TIER-TESTING SCHEME AND SURROGATE SPECIES

Next to be determined was the kind and amount of testing needed to develop data adequate to measure the potential hazard of a chemical and be useful in assessing its potential risk to the environment. That effort resulted in the development of a testing scheme (figure 8-2) that identifies the kind and amount of ecotoxicological testing required for ecological hazard and risk assessment (23, 32).

This scheme provides for sequencing (tiering) testing so that quick and inexpensive screening tests are performed first. Criteria or "triggers" for additional testing (e.g., for acute results to trigger chronic testing) and the logic for moving from one tier to another are provided and this limits testing to data essential for measuring hazard and assessing potential ecological risk (figure 8-3).

Figure 8-2: The OPPT Ecological Testing Scheme

Tier 1: toxicity tests

Aquatic vertebrate acute toxicity	Aquatic invertebrate acute toxicity	Aquatic plant acute toxicity	Terrestrial vertebrate acute toxicity	Terrestrial plant toxicity

Tier 2: toxicity tests

Additional aquatic vertebrate acute toxicity	Additional aquatic invertebrate acute toxicity	Additional aquatic plant acute toxicity	Additional terrestrial vertebrate acute toxicity	Additional terrestrial plant toxicity

Tier 3: toxicity tests

Aquatic vertebrate chronic toxicity	Aquatic invertebrate chronic toxicity	Aquatic bioconcentration	Terrestrial vertebrate reproduction	Terrestrial plant uptake

Tier 4: field tests

SOURCE: Zeeman, M., and Gilford, J., "Ecological Hazard Evaluation and Risk Assessment Under EPA's 'Toxic Substances Control Act (TSCA),'" *Environmental Toxicology and Risk Assessment: 1st Volume*, W.G. Landis, et al. (eds.) (Philadelphia, PA: ASTM, 1993)

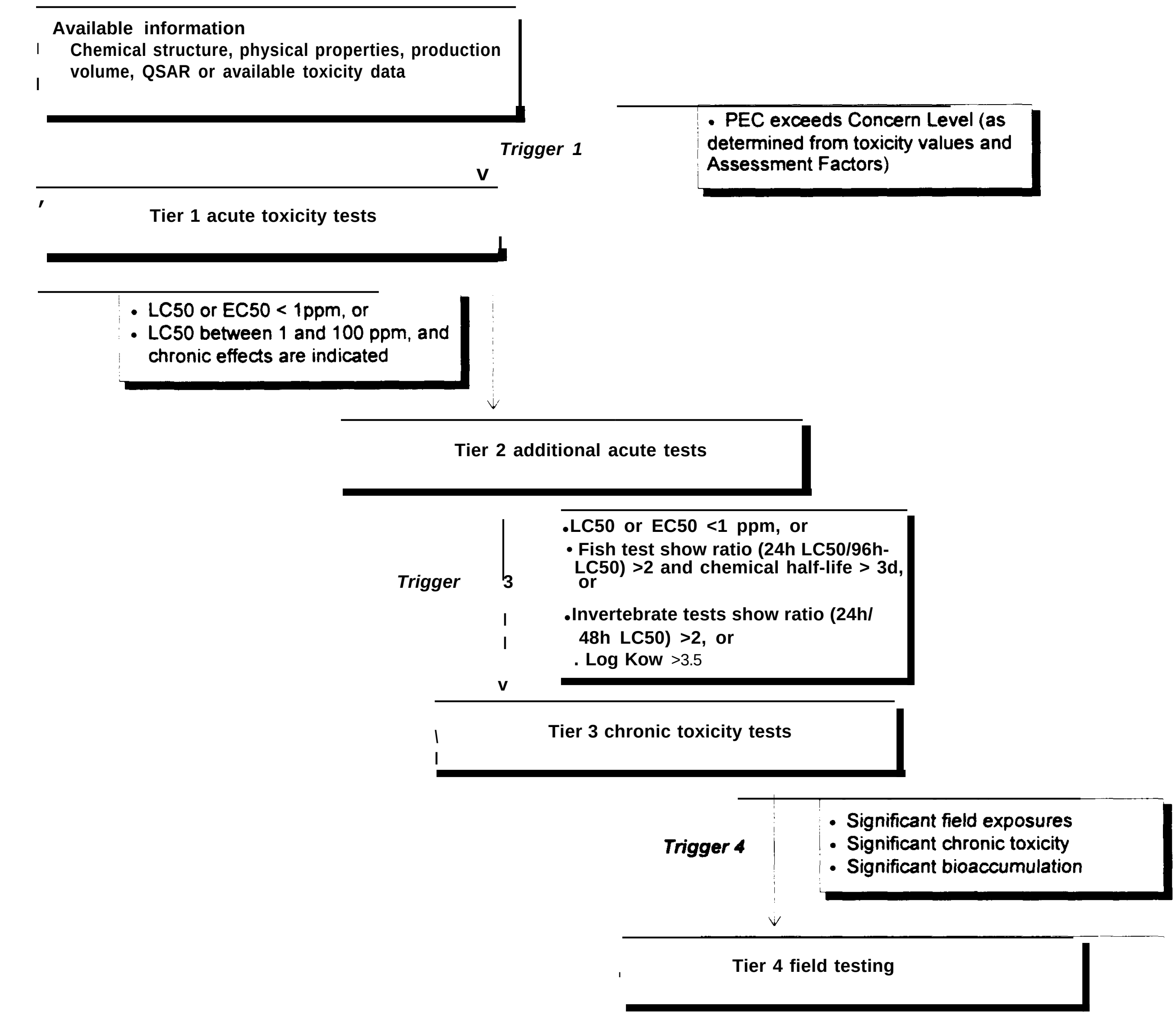
The question of using suitable surrogate test species under laboratory conditions for evaluating the ecotoxicity of chemicals in the field was also addressed. Representative organisms were selected for laboratory testing that would be acceptable as surrogate species (for example, fish suitably represent a species of aquatic vertebrates found in the water column). The number and variety of organisms that could serve as appropriate surrogates for evaluating the ecotoxicity of industrial chemicals were incorporated into the testing scheme (23).

The importance of the testing scheme is that it provides a reasonable and consistent approach to developing those test data that are needed to assess the potential environmental hazard of an industrial chemical. It also develops ecotoxicity data in a manner that does not unduly impede or create unnecessary economic barriers to technological innovation while providing adequate information to protect the environment. An additional benefit of the testing scheme is that manufacturers and testing laboratories know in advance how much testing will be needed to meet OPPT concerns, thus alleviating industry's concern about open-ended testing requirements.

TESTING GUIDELINES

After settling on appropriate testing sequences, OPPT next developed and published guidelines for performing acute and chronic ecotoxicity tests, and for determining the capacity of chemicals to bioconcentrate (26). Included in that set of ecological test guidelines are procedures for conducting acute and chronic toxicity tests using invertebrates, fish, and birds. Also included are bioconcentration tests using fish and oysters, bioassays using freshwater and marine algae, and plant toxicity tests. Tests conducted using these guidelines result in ecotoxicological data that estimates the significant endpoints of mortality or impairment (i.e., LC50, LD50, or EC50), and effects on growth and development, and/or on

Figure 8-3: Triggers for Aquatic Tier Testing System



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reproduction (i.e., LOEC, NOEC, and MATC). New ecological guidelines have been added since the initial set was published (23).

These standardized test guidelines provide the means for OPPT to assure that ecotoxicological test data developed for existing chemicals (those already on the TSCA Inventory and subject to testing under TSCA Section 4) are suitable for performing adequate and reliable ecological hazard and risk assessments. These guidelines also provide a means for OPPT to assist manufacturers and testing laboratories in developing ecotoxicological test data suitable for evaluating the hazard and risk of the thousands of new chemicals subject to OPPT review under TSCA Section 5. The above testing scheme and guidelines are used routinely by industry and testing laboratories in developing ecotoxicological data for OPPT.

These test guidelines provide an additional benefit. Data based upon the use of standard test guidelines are of great value to OPPT for comparative purposes, in developing new structure-activity relationships (SAR), and for developing valid data suitable for inclusion in ecotoxicological data bases that can also be used to help develop quantitative SAR (QSAR). Reliable test data developed through these TSCA chemical testing requirements have provided OPPT with valuable information on chemical analogs and on chemical structure-activity relationships. These data have proven essential in evaluating the potential ecotoxicity of similar industrial chemicals for which test data are not available and in the ongoing validation efforts of the OPPT (Q)SAR technologies developed byEEB(15).

SAR/QSAR FOR ASSESSING ECOTOXICITY

The development and use of structure-activity relationships (SAR) and quantitative SAR (QSAR) to assess ecotoxicity has been an essential and active area of interest in OPPT/EEB for over a decade (1, 7, 8, 11, 13, 14, 35). This SAR/QSAR [or (Q)SAR] development became essential because estimations of ecotoxicity have to be provided in a very short time-frame for the risk assessments required for the thousands of new industrial chemicals that are submitted by industry to OPPT for evaluation every year.

Over the last decade, the new chemicals program has required the rapid assessment of about 2,300 chemicals/yr – almost 50/week, typically with these numerous ecotoxicity estimates needing to be available for preliminary risk assessment purposes within 2-3 weeks after industry submits the chemical for evaluation by OPPT. As up-front testing is not required for these submissions, the vast majority of OPPT new chemical notices (ea. 95°/0) contain no ecotoxicity data and, therefore, our (Q)SAR methodologies have been developed to fill these data gaps (34, 36).

SAR estimations can vary from simple similarities, such as using test data available for a similar chemical grouping or analogs, to being able to provide quantitative estimates of ecotoxicity (QSAR) because an empirical mathematical relationship has been established for a chemical grouping/class to which the new chemicals also belong. The 1988 version of the OPPT (Q)SAR Manual (6) has been updated and currently contains about 120 OPPT SAR/QSARs available for assessing the ecotoxicity of about 45 classes of chemicals (29). A computer program was also developed for the OPPT (Q)SAR Manual and was recently released as a PC Version, called ECOSAR, which is publically available (30).

The OPPT aquatic toxicity (Q)SARs used for estimating the acute toxicity of industrial chemicals to fish, daphnia, and algae have generally been proven to be quite reliable. The validation of these OPPT SAR/QSAR relationships is an ongoing effort (15, 34, 36). In addition, a joint EPA/European Union evaluation of the accuracy of the OPPT SARs was undertaken from 1991-93 and it was termed the “Structure Activity Relationship/Minimum Premarketing Dataset” (SAR/MPD) study (17, 23). For the EPA ecotoxicity (Q)SAR methodology, the European Union experts concluded that these OPPT QSAR methods “performed extremely well in predicting acute toxicity to fish and daphnia” (23, 36).

The structure-activity relationship (SAR) and quantitative SAR (QSAR) technologies that have been actively developed by EEB for the formidable new chemical endeavor were also recently applied to the ecotoxicity screening and assessment of over 8,000 discrete organic industrial chemicals on the TSCA Inventory of existing chemical substances. This technology was useful in assessing the hazard distributions for different chemical classes and the proportions of such chemicals displaying high acute or chronic ecotoxicity (8, 9,34,35, 36).

HAZARD “ASSESSMENT FACTORS”

As so little up-front ecotoxicity test data was provided to assess new or existing chemicals, EEB dealt with the several levels of uncertainty created due to this lack of data by developing “assessment factors” (25). Pragmatically, these

Table 8-1: OPPT Assessment Factors Used in Setting "Concern Levels"

Available data on chemical or analogue	Assessment factor
Limited (e.g., only One Acute LC50 via SAR/QSAR)	1000
Base Set Acute Toxicity (e.g., Fish and Daphnid LC50's, and Algal EC50)	100
Chronic Toxicity MATC's	10
Field Test Data for Chemical	1

SOURCE: Zeeman, M., "Ecotoxicity Testing and Estimation Methods Developed Under Section 5 of the Toxic Substances Control Act (TSCA)," *Fundamentals of Aquatic Toxicology: Effects, Environmental Fate, and Risk Assessment,* Chapter 23, G. Rand (cd.) (Washington, DC: Taylor & Francis, 1995).

assessment factors are used in a fashion somewhat akin to uncertainty factors to provide a consistent regulatory basis for assessing the potential for ecological risks.

These factors vary by three orders of magnitude (see table 8-1) in an attempt to account for uncertainties such as a) estimating chronic toxicity from acute toxicity, b) accounting for species-to-species differences, and c) extrapolating from laboratory toxicity tests to field toxic effect levels. The hazard estimate, even a (Q)SAR estimate, is divided by an appropriate assessment factor, and this results in predictions of concentrations of concern (concern level) in the environment.

Environmental exposures (often PECs, predicted environmental concentrations) below this concern level are not presumed to be safe or without risk. However, for practical purposes, if this level is not exceeded, it has typically been assumed by OPPT that the likelihood of a significant environmental risk is probably too low to warrant taking any regulatory action (13).

For regulatory purposes, the concern level is the environmental concentration above which risk in the aquatic environment could be inferred. When risk to organisms in the environment is estimated to be likely (due to sufficient potential exposures), that forms one possible basis for requesting the development of ecotoxicity test data to further refine the potential hazards of the chemical.

Although some would argue that these concern level estimates may be too conservative because of what may seem large assessment factors, in reality there are additional factors that need to be considered. First, the assessment factor of 1,000 is seldom used because we can often estimate through (Q)SARs the acute toxicity to fish, daphnia, and algae, and/or chronic toxicity to one or more of these aquatic species. Therefore assessment factors of 10 or 100 are more typical.

Next, the uncertainty factor approach used for the estimation of risk to organisms in the environment would seem to be substantially less rigorous than that used for estimating risk to humans. For example, results of toxicity testing in a few rodent and other mammalian species are all typically used, along with appropriate uncertainty factors, to estimate the chemical risks to only one species, humans. The extrapolations that are used here for environmental species should often seem more uncertain. How many would argue that a short-term laboratory toxicity test result for only one species of fish is suitable enough to extrapolate such limited data as being representative of, let alone being protective for, the other 20,000 species of fish found in the real world?

Other more refined ecological protection methods, based on fairly extensive ecotoxicity test data and on sets of complex statistical methodologies that may protect 95% of the species are being developed by the Dutch and have been proposed in the ecological assessment schemes of the OECD (18). Independent evaluations of the simple EPA/OPPT assessment factor approach and these complex statistical schemes seem to find that often there is not that much difference in predicting the respective levels of concern in the environment (4, 10, 35).

ECOLOGICAL RISK ASSESSMENT

Unlike human health risk assessment, ecological risk assessment must consider adverse effects of chemicals on many species, not just one. As is seen in the previous discussion on assessment factors, one way that this has been done is to use the hazard estimates for several species and to apply such "uncertainty" factors to estimate the environmental concentrations of concern.

A slightly more refined method also used by OPPT for its chemical assessments is to contrast these hazard estimates with predictions of exposure concentrations (PECs) expected in the environment. This is called the quotient method and it is very widely used as a measure of potential ecological risk. As predicted exposures approach the lowest hazard estimate (for toxicity, reproductive effect, etc.) more of a risk for such impacts in the environment is inferred (21, 28, 32).

The quotient method is most typically used in the ecological assessment of existing chemicals. An example would be the assessment of the potential impacts on terrestrial organisms in the environment from the dioxins and furans (TCDD/TCDF) found as contaminants in the sludges of the paper and pulp industries that are applied to lands and forests as soil conditioners (12, 19,20, 31). The quotient method allows for a simple comparison of the best estimates of toxic thresholds and the no-observed-adverse-effect levels (NOAELs) for terrestrial birds and mammals with the TCDD and TCDF concentrations likely to be in their food (soil organisms) that had become contaminated from the soils amended with such sludges.

Through the expanded development of population and ecosystem models, the typical ecotoxicity test data on mortality, growth, and reproduction may be extended to more adequately deal with population- and ecosystem-level effects (24). Such models are starting to be used to augment the typical existing chemical assessments, such as in the assessment of the potential adverse aquatic effects of the chlorinated paraffins, a widely used industrial chemical (3, 21). The continued development of pragmatic and user-friendly population and ecosystem models is essential for these powerful methods to be useful to regulators needing quick and simple responses to the difficult issues posed in the ecological risk assessment of industrial chemicals.

The goal of an OPPT ecological risk assessment is to be as realistic as is reasonable with the data available. When data are scarce, as typically occurs in new chemical assessment, the estimates made of hazard, exposure, and risk must be viewed as being somewhat preliminary. Ecological data provided for existing chemical assessments may be almost as scanty as for new chemi-cals, however, it is more common that additional ecotoxicological data will be provided for these major chemicals in commerce. Hopefully this additional data allows for more reasoned decisions on hazard, exposure, and risk to be made.

CONCLUSION

The many years of experience by OPPT/EEB in screening and assessing the ecotoxicity and risks of the thousands of new industrial chemicals submitted for evaluation each year has resulted in procedures and technologies, i.e., (Q)SARs and concern concentrations, that are extremely versatile and efficient in assessing chemicals. These efficient ecotoxicity assessment procedures and technologies are now also being applied to the discrete organic substances in the existing chemical arena, especially to those existing chemicals for which little or no reliable ecotoxicity data is readily available.

The use of the chemical class (Q)SAR methodology by OPPT should continue to expand. As new test data for terrestrial organisms on specific chemical classes have become available, OPPT/EEB has already expanded the use of (Q)SAR into that environment (e.g., earthworm QSAR for neutral organics). Also, as additional targeted ecotoxicity test data are provided, there are many areas into which this screening and assessment technology could be expanded further, e.g., the development of (Q)SARs for sediment-dwelling organisms and for avian species should be of high priority.

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