

## **Chapter 2**

### **Evaluation and Selection of Methods**

#### **2-1.0 Introduction**

Criteria derivation is a process that can be broken down into a number of steps, starting with data collection and ending with numeric criteria that are protective of aquatic life with as much certainty as possible given the amount of data available. In this chapter, methods that may be used to achieve each step are presented, evaluated and selected for use in the new methodology. A full set of chlorpyrifos data was collected, processed according to suggested methods, and utilized to compare models. Eleven other pesticide data sets from USEPA (1980a; 1980b; 1980c; 1980d; 1980e; 1980f; 1986b; 2003d; 2005a) were also utilized.

#### **2-2.0 Data**

Criteria derivation requires ecotoxicological effects data. Good criteria must be based on good quality data of adequate taxonomic diversity. Physical-chemical data are also important for proper interpretation of toxicity test data, for estimation of freely dissolved fractions of chemicals, for understanding possible effects of water quality characteristics on toxicity, and for estimation of toxicity for some classes of chemicals. The most reliable, most certain criteria are derived from the largest and best quality data sets. The new methodology includes guidance on what kinds of data should be collected, where to collect it, and how to evaluate its quality.

#### **2-2.1 Data collection**

##### **2-2.1.1 Kinds of data**

For thorough evaluation of pesticide effects it is necessary to collect physical-chemical and ecotoxicity data. Although not used directly in derivation of aquatic life criteria, dietary exposure effects data for wildlife and humans should also be collected for assessment of potential hazards due to pesticide bioaccumulation. The new methodology includes a table summarizing the kinds of physical-chemical, ecotoxicity and other data required for criteria derivation. Because of the large variety of ecotoxicity data that may be found, the remainder of this section provides specific details regarding the kinds of ecotoxicity data that should be collected for criteria derivation. The goal is to collect high quality data from as many taxonomic groups as possible. As this methodology is for derivation of criteria specifically for the Sacramento and San Joaquin River watersheds, only data for freshwater species from families with reproducing populations residing in North America will be used in criteria derivation. However, all available data should be collected as they may be used as supporting information or for derivation of acute-to-chronic ratios if they are otherwise of high quality. The choice to consider geographic distribution at the family level, rather than the species level—as is done in current USEPA methodologies (USEPA 1985; 2003f)—is based on work by the USEPA showing that interspecies toxicity correlations work well at the family level (USEPA 2003e, see

discussion in section 2-2.2.1.2). A summary table that lists all of these data requirements is included in the new methodology (Table 3.3; Chapter 3, Appendix 3B).

### **2-2.1.1.1 Acute vs. chronic toxicity data**

Both acute and chronic toxicity data are needed for criteria derivation. As discussed in the Phase I report for this project (TenBrook & Tjeerdema 2006), the difference between acute and chronic toxicity is not always clear and thus it is important that this new methodology define what kinds of tests are considered acute vs. chronic. Good general definitions of acute and chronic are given in USEPA (2003f):

Acute toxicity: Concurrent and delayed adverse effect(s) that results from an acute exposure and occurs within any short observation period which begins when the exposure begins, may extend beyond the exposure period, and usually does not constitute a substantial portion of the life span of the organism.

Chronic toxicity: Concurrent and delayed adverse effect(s) that occurs only as a result of a chronic exposure. Chronic exposure is exposure of an organism for any long period or for a substantial portion of its life span.

These general definitions are helpful, but for clarity more specific guidance is needed. Following are definitions of acute and chronic data from existing methodologies. Most of these are incorporated into the new methodology:

#### Acute

- 1) Crustacean or insect tests lasting 24-96 h; (RIVM 2001; Siepmann & Finlayson 2000; USEPA 1985; 2003f);
- 2) Fish, mollusk or amphibian tests lasting 96 h (RIVM 2001);
- 3) Shellfish embryo, larval, or older life-stage tests lasting 96 h (USEPA 1985; 2003f).

#### Chronic

- 1) Algae, bacteria, or protozoa tests lasting 3-4 d (RIVM 2001);
- 2) Fish, mollusk or amphibian early life-stage tests and 28-d growth tests (RIVM 2001);
- 3) Single-celled organism tests of any duration (USEPA 1985; 2003f);
- 4) Any test that takes into account the number of young produced, regardless of duration (USEPA 2003f);
- 5) Full life-cycle (ranging from 7 d for mysids to 15 months for salmonids), partial life-cycle (all major life stages exposed in less than 15 mo; specifically for fish that require more than a year to reach sexual maturity), and early life-stage tests (ranging from 28-60 d; also specifically for fish (USEPA 1985; 2003f).

Endpoints in acute and chronic tests may be survival, growth, reproduction, measures of population growth rate, or other endpoints that have been linked to survival, growth or reproduction. See section 2-2.1.1.3 for further discussion of endpoints.

Definitions 1 and 3 in the chronic list both apply to single-celled organisms. Likewise, definitions 2 and 4 in the chronic list apply to early life-stage, or short-term chronic tests. The USEPA definitions (3 and 4 above) are included in the new methodology as they will result in the inclusion of a broader range of tests than those from the RIVM document. For example, algae, bacteria and protozoa tests shorter than 3 d are included by the USEPA definition, but excluded by the RIVM definition.

Typically, very few chronic data are available for a given chemical. Methods are available for deriving chronic toxicity values and chronic water quality criteria from acute toxicity data. These methods are discussed in 2-2.2 and 2-3.2.3.2.

#### **2-2.1.1.2 Hypothesis tests vs. regression analysis**

The Phase I report (TenBrook & Tjeerdema 2006) explored the use of statistical regression techniques versus hypothesis tests for analysis of toxicity data. This report concluded that statistical regression methods are commonly used and widely accepted for analysis of acute toxicity data, but for analysis of chronic data, hypothesis tests have been more widely used. However, hypothesis tests have fallen out of favor due to their dependence on experimental design and unrestrained type II error rates. Although regression methods are preferred, there is little agreement among scientists as to what level of statistical effect may be considered a no biological effect level (e.g., EC<sub>5</sub>, EC<sub>10</sub>, or some other value). In addition, most chronic toxicity studies reported in the literature use hypothesis tests to determine no observed effect concentrations (NOECs) lowest observed effect concentrations (LOECs) or maximum allowable toxicant concentrations (MATCs). The challenge, then, is to find a way to ensure that toxicity values derived from hypothesis tests are reliable values for use in criteria derivation.

A good approach is that proposed by participants in a 1994 workshop in The Netherlands (Van Der Hoeven *et al.* 1997). They concluded that NOEC data may be used as a summary statistic in ecotoxicity testing if the following are reported: a) the minimum significant difference; b) the actual observed difference from control; c) the statistical test used; and d) the test concentrations. These factors can be used to make case-by-case judgments as to whether a reported NOEC is reliable. For example, an extremely high minimum significant difference is a sign of a poorly conducted test, in which high variability within treatment groups has obscured differences between groups. Such a test should probably not be used. Likewise, the response at the NOEC should be reasonable compared to control (e.g., a 50% reduction compared to the control should certainly not be considered “no effect”), the statistical methods should be appropriate, and the test should be designed with an appropriate dilution factor (test-specific, but ranges from 1.5-3.2 in various methods from the Organization for Economic Co-operation and Development, OECD; the American Public Health Association, APHA; and the American Society for Testing and Materials, ASTM).

For the new methodology, acute toxicity data should be in the form of LC or EC<sub>50</sub> values derived from regression analysis. The use of chronic data expressed as EC<sub>x</sub> values (from regression analysis) is only acceptable if species-specific studies are available to show what level of *x* represents a biological no-effect level (see discussion in section 2-2.1.1.2). Species-specific studies are also required to determine what levels of effects can be detected in toxicity tests (Denton & Norberg-King 1996).

Chronic data expressed as results of hypothesis tests are acceptable, but must be evaluated to ensure that reported values are reasonable estimates of no-effect levels. The new methodology includes the following factors in test reliability rating schemes for results of hypothesis tests: minimum significant difference, observed difference from control at the NOEC, LOEC or MATC, statistical method used and test concentrations. Absence of these parameters, or unacceptable results for them, will not necessarily eliminate a test from the data set, but will reduce its reliability score.

The question still remains as to which hypothesis test value (NOEC, LOEC, MATC), should be used for criteria derivation. In a well-designed, well-conducted toxicity test, the true no-effect level lies between the NOEC and LOEC (each of which must be one of the toxicant concentrations actually tested). Although interpolation between these values is not strictly allowed (Stephan & Rogers 1985), the MATC, which is the geometric mean of the LOEC and NOEC, represents an accepted way of estimating the true no effect level. Therefore, the MATC is the chronic value used in the new methodology.

### **2-2.1.1.3 Non-traditional endpoints**

As discussed in the Phase I report (TenBrook & Tjeerdema 2006) most derivation methodologies use ecotoxicity data only from studies in which the evaluated endpoints were survival and/or immobility, and growth and/or reproduction, including effects such as histopathological effects on reproductive organs, spermatogenesis, fertility, pregnancy rate, number of eggs produced, egg fertility, and hatchability (RIVM 2001). These so-called traditional endpoints are favored because they can be readily linked to population-level effects. Linkages between effects at successive levels of organization are what define whether or not an observed effect is biologically significant (Suter & Barnthouse 1993). Non-traditional endpoints, such as endocrine disruption, enzyme induction, enzyme inhibition, behavioral effects (other than immobility), histological effects, stress protein induction, changes in RNA or DNA levels, mutagenicity, and carcinogenicity, have had very few links established between these effects seen at the individual level and effects at the population, community or ecosystem level. Many of these non-traditional endpoints are merely markers of exposure, with no link between that exposure and adverse effects on survival, growth or reproduction. Generally, non-traditional endpoints can be used as supporting information, but not directly in criteria derivation.

Two exceptions to this generalization are the endocrine disrupting effects of tributyltin and the inhibition of acetylcholinesterase by pesticides. Segner (2005) discusses three cases in which population-level effects in wildlife could be linked to

environmental substances with endocrine activity: reductions in dogwhelk (*Nucella lapillus*) populations due to imposex caused by exposure to tributyltin; reduction in predatory bird populations due to egg-shell thinning caused by exposure to DDE; and decline in Atlantic salmon populations due to effects of 4-nonylphenol on the ability of smolts to osmoregulate. However, only in the case of tributyltin is there a strong case for endocrine disruption as the mechanism of the observed toxic effects. As a result, the recent “Ambient Aquatic Life Water Quality Criteria for Tributyltin (TBT) –Final” (USEPA 2003c) utilizes data from several studies of imposex in gastropods to set the final chronic criterion.

In the case of effects on acetylcholinesterase (AChE) activity, mortality or immobility has been linked to enzyme inhibition of > 90% in larval walleye and > 71% in juvenile walleye in acute exposures to chlorpyrifos (Phillips *et al.* 2002), and 50-70% in *Daphnia magna* exposed to a variety of chemicals (Barata *et al.* 2004; Printes & Callaghan 2004). On the other hand, Ferrari *et al.* (2004) found that goldfish exposed to azinphosmethyl could withstand cholinesterase reductions > 90% without mortality. Printes & Callaghan (2004) found that different cholinesterase-inhibiting pesticides had different inhibition levels associated with mortality. These studies indicate that although AChE activity has been associated with mortality the association is species- and chemical- specific.

Whether AChE inhibition (or other biochemical endpoint) data can be used in criteria derivation has to be decided on a case-by-case basis. For example, in a study of Chinook salmon, Wheelock *et al.* (2005) determined a 96-h acetylcholinesterase inhibition NOEC for chlorpyrifos of 1.2 µg/L, LOEC of 7.3 µg/L and MATC of 3.0 µg/L. At the LOEC, inhibition was 85% in brain tissue and 92% in muscle. Raw data from this study were analyzed by linear regression (Excel v 11.2.5) to roughly estimate that 7.5% mortality would be expected at the MATC concentrations of 3.0 µg/L. Thus, in this case, a level of chlorpyrifos that causes less than 85% enzyme inhibition (i.e., at the MATC) is expected to result in just 7.5% mortality. At the LOEC of 7.3 µg/L chlorpyrifos, where 85-92% enzyme inhibition occurs, 18.2% mortality is expected. These levels of mortality would have to be shown to be both statistically and biologically significant for the AChE inhibition results to be used in criteria derivation. The statistical significance may be determined by analysis of toxicity test variability. For example, Denton & Norberg-King (1996) determined that a reduction of 11.2-14.9% in survival compared to controls could be detected in fish toxicity tests for some species. Biological significance is as not easily determined. Suter & Barnhouse (1993) explain that the biological significance of a property (in this case an effect) is determined by its importance to a higher level of hierarchy. Physiological changes (of which AChE inhibition is an example) are biologically significant if they affect a property of the whole organism, such as survival or fecundity; a change in survival or fecundity is biologically significant if it affects a property of the population, such as size or productivity. Thus, to determine the biological significance of a given level of mortality would require studies showing population-level effects due to the change in mortality. To be able to use AChE, or other biochemical, data for criteria derivation in this methodology, it would be necessary for a toxicity study to derive an inhibition concentration (IC<sub>x</sub>) value, where x is

equal to the enzyme inhibition level that is linked to statistically and biologically significant mortality, growth, or reproductive effects for a given chemical and species.

Another class of non-traditional endpoints are those that are directly linked to population-level effects, but are rarely determined in single-species toxicity studies. Population-level endpoints are suggested by Whitehouse *et al.* (2004) as a way to more directly predict toxic effects of chemicals on ecosystems. Using the population parameters  $r$  (intrinsic rate of population growth) and  $\lambda$  (factor by which a population increases in a given time), Whitehouse *et al.* (2004) found  $r$  to be a more sensitive endpoint than reproduction in tests with *Daphnia magna* exposed to zinc, and found EC<sub>20</sub> values based on  $r$  to be in good agreement with a NOEC value determined for effects of 17 $\alpha$ -ethinyloestradiol in fathead minnows (Lange *et al.* 2001). On the other hand Forbes & Calow (1999) found that, in most cases,  $r$  and  $\lambda$  were equally sensitive, or less sensitive to toxicant exposures compared to individual traits (e.g. reproduction). Whitehouse *et al.* (2004) note that while their intra-species examples of using population-level endpoints worked out well, there is little evidence to support their use across species for a given chemical. They attempted to collect data to expand the model across species, but out of 385 potentially usable studies, the needed mortality and fecundity data could only be obtained for 6. Due to lack of data, and lack of evidence that they are any more protective of ecosystems than traditional endpoints, population-level endpoints are not generally used in the new methodology, but can be used if available.

For the new methodology results of tests using individual level endpoints other than survival, growth and reproduction may be used to derive criteria, if those endpoints have been adequately linked to effects on survival, growth, reproduction, or population-level parameters, such as  $r$  or  $\lambda$ . Population level endpoints, such as  $r$  and  $\lambda$  can be used if they come from studies rated relevant and reliable, but only if a more sensitive endpoint is not available.

#### **2-2.1.1.4 Multispecies (field/semi-field, laboratory) data**

As discussed by TenBrook & Tjeerdema (2006) in the Phase I report, multispecies data is problematic for use in criteria derivation because there is very little of it, and what is available is highly variable. These kinds of data are not used for criteria derivation in the new methodology. Although not useful for direct derivation of criteria, field or semi-field data are very useful for comparison to criteria derived from single-species data (OECD 1995; RIVM 2001), and may provide justification for adjustment of a final criterion (RIVM 2001; USEPA 1985; 2003f; Zabel & Cole 1999).

#### **2-2.1.1.5 Data from multipathway exposures**

As discussed in Phase I (TenBrook & Tjeerdema 2006), until food web or other models are further developed to incorporate multipathway exposures into criteria derivation, the best approach is to do water-only assessments. If studies show these criteria to be underprotective, and if the substance has a log K<sub>OW</sub> between 5 and 7, then dietary uptake studies specific to the compound and species affected should be done to

determine if exposure has been significantly underestimated. Water-only exposures are used for criteria derivation by the new methodology, but if derived criteria for chemicals with log  $K_{OW}$  between 5 and 7 appear to be underprotective, then targeted studies are recommended to determine more precisely if dietary uptake is significant for particular species/chemical combinations. For pesticides with log  $K_{OW}$ s between 5 and 7, laboratory toxicity test data should be carefully reviewed to ensure that feeding regimes eliminated, or minimized any effects from interaction of the pesticide with food particles (e.g., reduction of test solution concentration due to partitioning into the food particles, or introduction of a dietary exposure route if animals ingest food that has had a chance to sorb pesticide).

#### **2-2.1.1.6. Toxicity data that incorporate time**

To address the effect of time on toxicity of chemicals, it would be ideal to be able to derive criteria that could be defined for any given exposure duration, thus eliminating the need to define separate acute and chronic criteria. In other words, different criteria would be derived for different exposure scenarios. Thus, environmental managers would be able to determine compliance with water quality standards for anything from brief pulse exposures to extended exposures of essentially infinite time. This could be done by, for example, segregating acute toxicity data according to exposure duration and deriving criteria for 24-, 48-, 72-h, etc. durations. Alternatively, toxicity test data could be analyzed using time-to-event methods to describe dose-time-response surfaces (Sun *et al.* 1995), or by kinetic models that describe the time course of toxicity (USEPA 2005b). As discussed in the Phase I report (TenBrook & Tjeerdema 2006), these models are data and resource intensive. Toxicity data, as they are currently (typically) reported, do not include information regarding multiple time points or kinetics. Thus, these time-to-event models are not feasible for general use in criteria derivation at this time and derivation of separate acute and chronic criteria is the approach adopted for the new methodology. However, as discussed in section 2-2.2.2.1, if data are available, concentration-time-effect models may be used to estimate chronic toxicity. Also if site- or situation-specific (i.e., for pulse exposures) criteria are desired, studies could be designed and conducted specifically to gather data for those models and the resulting toxicity data could be used to derive time-specific criteria.

#### **2-2.2 Filling data gaps with estimation techniques**

A common challenge in derivation of water quality criteria is that very few usable data are available. This is of particular concern in the case of chronic toxicity data. This section presents approaches for estimation of acute and chronic toxicity. Some, such as acute-to-chronic ratios (ACRs) are widely used and accepted. Some, such as quantitative structure activity relationships (QSARs) are widely accepted for some kinds of toxicants, but are still under development for most toxicants. Others, such as time-concentration-effect models are newer, have been validated for a large number of fish species, but are very data intensive procedures that are not feasible with most currently available data.

## **2-2.2.1 Estimating acute and chronic toxicity**

### **2-2.2.1.1 Quantitative Structure Activity Relationships (QSARs)**

QSARs are described and discussed in the Phase I report (TenBrook & Tjeerdema 2006). For chemicals with non-specific modes of action, and for which no other ecotoxicity data exist, QSARs may be used to estimate toxicity, and values derived from QSARs may be utilized in SSD and/or AF criteria derivation methods. However, if at least one measured toxicity datum is available, the assessment factor (AF) method should be used to derive criteria (section 2-3.2).

The RIVM (2001) guidelines provide 19 QSARs for estimating chronic effects of narcotic chemicals on aquatic species representing 9 different taxa. Other QSARs are available in the literature. For reactive and specifically-acting chemicals, QSAR models are not reliable for estimation of toxicity (Phase I report; TenBrook & Tjeerdema 2006). The ANZECC & ARMCANZ (2000) guidelines caution that QSARs should not be used as black boxes and considerable chemical expertise is required in their use. Using them only to predict toxicity of narcotic chemicals minimizes the risk of inappropriate use.

In reality, many industrial chemicals (e.g., solvents or other hydrocarbons) have a narcotic mode of action, but most pesticides have specific modes of action. Therefore, QSARs are of limited use for pesticide criteria derivation until such time as they are more fully developed for specifically-acting chemicals. Additionally, since pesticides used in California must have been tested at least minimally for registration, there should not be cases where no measured toxicity data are available. The new methodology does not include a QSAR component as a way to supplement data sets. However, QSARs are included as an option for estimating toxicity to threatened and endangered species for narcotic acting chemicals.

### **2-2.2.1.2 Interspecies correlations for estimation of toxicity**

The USEPA has developed interspecies correlation estimation software (ICE v 1.0), which can be used to estimate acute toxicity of all kinds of compounds to aquatic species, genera and families having little to no measured toxicity data, based on species with adequate data sets (USEPA 2003e). Toxicity estimates made by interspecies correlations work well within taxonomic families, but less well as taxonomic distance increases. The ICE models generate estimated acute toxicity values with confidence limits to quantify uncertainty. This technique is promising, but needs further development and validation before being used to generate data for criteria derivation. However, this model provides an excellent tool for assessment of potential effects of derived criteria on threatened and endangered species (discussed further in section 2-3.6.4) and it is included for this use in the new methodology.

### 2-2.2.2 Estimating chronic toxicity from acute data

In many cases, acute toxicity data are abundant, but there is very little acceptable chronic data available, making it difficult to derive chronic criteria. Two approaches are available for estimation of chronic toxicity from acute data. The first, the acute-to-chronic ratio (ACR) approach, is readily usable, even with very small data sets. The ACR approach is discussed in section 2-3.2.3.2 because the technique is applied during the criteria derivation process. The second approach is the use of time-concentration-effect models, and those are described in this section because they generate individual toxicity data that may be used in SSD derivation procedures.

#### 2-2.2.2.1 Time-concentration-effect (TCE) models

Analysis of ecotoxicity data by time-concentration-effect (TCE) methods provides a means to extrapolate from acute to chronic exposures. The USEPA has developed an acute-to-chronic estimation program that uses TCE models for estimating chronic toxicity from acute data (USEPA 2003b). Three slightly different models are included in the ACE v. 2.0 software package. These are the accelerated life testing model (Mayer *et al.* 2002; Sun *et al.* 1995), the multifactor probit analysis model (Lee *et al.* 1995; Mayer *et al.* 2002), and the linear regression analysis model (Mayer *et al.* 2002; Mayer *et al.* 1994). Each model considers three important factors in toxicity: exposure concentration, degree of response, and time course of effect. Analysis of these three factors from short-term (acute) toxicity tests allows for prediction of effects over long-term (chronic) exposures. The models only work for mortality data, thus will not provide the most sensitive estimate of chronic effects in cases where sub-lethal effects are more sensitive toxicity indicators. The Australia/New Zealand guidelines (ANZECC & ARMCANZ 2000) allow for the use of these same models for estimation of chronic toxicity from acute data.

Chronic values estimated by the models in the ACE program have been validated within species for 7 species of fish exposed to 17 different chemicals (Mayer *et al.* 2002), and across species for a variety of invertebrates and fish exposed to chlorpyrifos and ammonia (Whitehouse *et al.* 2004). Although TCE models hold promise for estimation of chronic toxicity, lack of appropriate data presents a barrier to their use. Typically, acute toxicity data are reported as LC<sub>50</sub> or EC<sub>50</sub> values at one or more time points. However, the TCE models must be populated with response data for each concentration at multiple time points. This kind of information is normally collected in acute toxicity tests, but is rarely reported. Whitehouse *et al.* (2004) contacted authors of 385 toxicity studies to try to request the raw data needed for TCE modeling. Only 85 replies were received, and only 34 of those actually contained the needed data. When data are available, TCE models should be used to supplement chronic toxicity data sets. For new methodology the USEPA ACE program may be used to estimate chronic toxicity from acute data if appropriate data are available. NOEC values derived from ACE may be used along with other chronic data in AF or SSD methods.

### **2-2.3 Data sources and literature searches**

To ensure that toxicity and physical-chemical data are collected without bias, a thorough search of numerous sources is necessary. While review articles and criteria documents are good starting points for data collection, original sources should be found and evaluated whenever possible. The Phase I report (TenBrook & Tjeerdema 2006) identified data sources from several existing criteria derivation methodologies. All of the sources mentioned are useful, and, as such, are simply compiled and presented, along with other useful sources, in a table (or tables) for the new methodology. The Dutch and Danish methodologies specify that literature searches should go back to 1970 and 1985, respectively (RIVM 2001; Samsøe-Petersen & Pedersen 1995). However, such limits are not necessary. Since pesticides are synthetic compounds (for the most part), any data available from the time a pesticide was first developed should be collected and evaluated.

The new methodology includes tables of physical-chemical and ecotoxicity data sources as well as instructions to conduct literature searches that encompass the lifetime of the pesticide in question.

### **2-2.4 Data summaries of ecotoxicity data**

In reviewing ecotoxicity data it is important to have a systematic way of rating the quality of a given study, but to rate diverse studies fairly requires that similar information be obtained from each. This particularly applies to single-species toxicity data; multi-species laboratory and field or semi-field tests are usually too complex to lend themselves to simplified summarization. To facilitate the data evaluation process in The Netherlands (RIVM 2001) data are put into data tables with the following headings: species (including scientific name), species properties (e.g. age, weight, lifestage), analysis of test compound (measured or not, Y of N), test type (flow-through, static-renewal, static), substance purity, test water, pH, water properties (e.g. hardness, salinity), exposure time, test criterion (e.g. LC<sub>50</sub> or NOEC, where LC<sub>50</sub> is the concentration that is lethal to 50% of organisms, and NOEC is the no observed effect concentration), ecotoxicological endpoint (growth, reproduction, mortality, immobilization, morphological effects, histopathological effects), LC<sub>50</sub> values, NOEC values, notes, and reference information.

This sort of summary is helpful, but does not include enough information for thorough evaluation of the quality of the study. Critical information missing from the Dutch data summary tables includes: where test organisms reside, control response, source of test organisms with confirmation that they were collected from non-polluted sites, detailed test design information, detailed water quality information, concentrations of any carrier solvents used, statistical methods used, and whether responses recorded at NOEC and LOEC concentrations are reasonable. All of this information is needed to adequately rate the quality of test data according to the methods outlined in section 2-2.5. Therefore, a new, more detailed data summary table has been developed to use with the new methodology. The table includes all of the elements mentioned above, as well as space to record any additional information that may be important to the study.

## 2-2.5 Data evaluation

In this section, the issue of data quality is explored. High quality data are both relevant and reliable. The EU Technical Guidance Document on Risk Assessment (TGD) describes reliability as the inherent quality of a test relating to test methodology and the way the that the performance and results of the test are described, while relevance refers to the extent to which a test is appropriate for a particular hazard or risk assessment (ECB 2003). Reliable data are from studies for which test reports describe the test in detail and indicate that tests were conducted according to generally accepted standards. Relevance is judged by whether a study included appropriate endpoints, was conducted under relevant conditions, and if the substance tested was representative of the substance being assessed. Existing approaches for evaluation of physical-chemical and ecotoxicity data are discussed below, and the strongest elements of many are included in the new methodology.

### 2-2.5.1 Physical-chemical data

In the context of deriving water quality criteria, physical-chemical data are relevant to the extent that they enhance the interpretation of toxicity data. For example, the organic carbon-water partition coefficient ( $K_{oc}$ ) can be used to predict concentrations of freely dissolved hydrophobic contaminants in water and whether dietary uptake might be important, while the acid dissociation constant ( $pK_a$ ) can be used to predict the predominant form of an ionizable compound, and the half-life ( $t_{1/2}$ ) can be used to determine if separate criteria are needed for degradative products. Toxicity tests can be evaluated based on whether test solution renewals were adequate considering the half-life ( $t_{1/2}$ ) of the compound, or whether reported toxicity values (i.e., LC50, NOEC, etc.) are reasonable given the water solubility of the compound. Octanol-water partition coefficients ( $K_{ow}$ ) may be used, in limited cases, to predict toxicity of chemicals using Quantitative Structure Activity Relationships (QSARs) if toxicity data are lacking. To the extent that physical-chemical parameters are affected by temperature, attention should be paid to whether a reported value was measured at a relevant temperature; if not, then values should be adjusted as necessary (RIVM 2001; Schwarzenbach *et al.* 1993).

The Phase I report (TenBrook & Tjeerdema 2006) concluded that reliable physical-chemical data are those determined by current, standard methods (e.g., ASTM, OECD, APHA) applied and performed correctly for the chemical of interest. Non-standard methods may also be appropriate, but only if valid reasons are given for deviation from standard methods, or if studies were done prior to the existence of standard methods, but generally followed currently acceptable methods. In regard to pesticides, which vary widely in characteristics such as hydrophobicity, water solubility, and ionizability, it is particularly important to verify that reported partition coefficients were determined correctly. Thus it is not acceptable to simply use a value reported in a handbook without verifying the value via the original reference. An exception to this is that recommended  $K_{ow}$  values may be taken without further review from the LOGKOW database (Sangster Research Laboratories 2004) because all values in this database have been reviewed by partition coefficient experts.

A number of web-based programs are available that can be used to estimate various physical-chemical parameters. These include ClogP3 ([www.biobyte.com](http://www.biobyte.com)), the USEPA's Estimation Program Interface Suite ([www.epa.gov/oppt/exposure/docs/episuite.htm](http://www.epa.gov/oppt/exposure/docs/episuite.htm)), and KowWin ([www.syrres.com/esc/est\\_soft.htm](http://www.syrres.com/esc/est_soft.htm)). Several databases containing physical-chemical data are also available on the web, including the Environmental Fate Database ([www.syrres.com/esc/efdb.htm](http://www.syrres.com/esc/efdb.htm)), EXTOXNET ([extoxnet.orts.edu](http://extoxnet.orts.edu)), PHYSPROP ([www.syrres.com/esc/physprop.htm](http://www.syrres.com/esc/physprop.htm)), and TOXNET ([toxnet.nlm.nih.gov](http://toxnet.nlm.nih.gov)). These are helpful resources, but should be used with caution. Estimated parameters should only be used in the absence of measured data. As with values taken from handbooks, any values taken from online databases should be fully referenced as to their original sources and those sources should be checked to ensure that the values were appropriately obtained.

While it is preferable to use only data from studies that can be reviewed and verified, in reality, the only information available may be in a handbook citing data that are not available for review. Such values should be used with caution. In some cases, values can be considered reliable without further review. For example, recommended values from the LOGKOW database (Sangster Research Laboratories 2004); due to the careful review process for values in the database, and physical-chemical data from unpublished manufacturer studies are acceptable (due to their wide acceptance). If several values are available for the same physical-chemical parameter, and all were obtained by acceptable methods, the geometric mean of the values measured at the same temperature should be used.

The new methodology provides general guidance on acceptability of physical-chemical data based on information in several existing methodologies (OECD 1995; RIVM 2001; USEPA 1985; 2003f). More specifically, tables are provided specifying acceptable test methods for determination of physical-chemical parameters such as log  $K_{OW}$ , water solubility, dissociation constants ( $pK_a$ ), and hydrolysis or other degradation rates. Also, a table of on-line databases and calculators that may be used to obtain or estimate physical-chemical parameters is provided.

### **2-2.5.2 Ecotoxicity data evaluation**

By studying criteria derivation methodologies for Phase I and working through the process of collecting and evaluating chlorpyrifos effects data it has become clear that ecotoxicity data need to be evaluated on three points: 1) relevance to criteria derivation; 2) documentation; and 3) acceptability. Documentation and acceptability together define the reliability of a study. The ECOTOX (2006) system for rating documentation of aquatic and terrestrial toxicity data from laboratory and field is widely accepted and is included in the new methodology, with some modifications by way of added detail. A similar system is used for evaluation of acceptability and relevance. The elements upon which a test is judged are similar for rating documentation and acceptability, but in the former case, scores are based solely upon whether or not an item was documented, while in the latter case, scores are based upon whether or not a given parameter was within

accepted testing guidelines and organism tolerances. Weighting of scores for acceptability is based upon test acceptability criteria as stated in standard methods (e.g., USEPA, OECD, APHA or ASTM toxicity test methods). For example, control response and temperature control, which are common measures of tests acceptability, are weighted more heavily as measures of reliability, than water hardness and alkalinity, which are not as critical. As there are no standard methods for multi-species lab, field or mesocosm/microcosm, or wildlife studies, these studies should be rated primarily on documentation, but also on a few key acceptability criteria as described by OECD (1995) and RIVM (2001). The new methodology includes detailed data scoring schemes, with point values assigned to each toxicity test element (see Tables 3.6-3.10, Chapter 3).

The elements for judging relevance of a study are somewhat different, but can be weighted and rated in a similar fashion. The relevance scores should be weighted such that failure of just one of a number of critical factors immediately renders the study irrelevant for criteria derivation. Tests that involve in vitro exposures of organs or tissues (i.e., were not whole-body exposures) and tests which report toxicity values greater than 2x the water solubility of the pesticide are not useful even as supporting information and can be eliminated without further consideration (see discussion below). For compounds with log  $K_{OW}$  between 5 and 7, laboratory tests should be eliminated from consideration if feeding regimes did not minimize or eliminate interaction of pesticide with food particles (see discussion in section 2-2.1.1.5). All other effects studies should be evaluated for relevance based on the following critical factors: controls must be documented and must meet minimum test acceptability requirements; tests must be with species belonging to families that reside in North America; endpoints must be linked to survival, growth or reproductive effects; tests must produce toxicity values (i.e., no  $>$  or  $<$  values); tests must be with freshwater species, and; tests must be conducted with pesticide that is  $\geq 80\%$  pure (i.e., no formulations and no mixtures). Only single-species toxicity tests need to be evaluated for relevance because they are the only ones that may be used directly for criteria derivation. Tests that fail to meet any one of these criteria may not be used to derive criteria or for derivation of acute-to-chronic ratios, but may be used as supporting information as long as they are rated highly enough (details of rating scheme follow).

The decision to include ecotoxicity data in cases where the reported toxicity values are greater than the water solubility of the pesticide is based on a recent review by Shen & Wania (2005) as well as data from the PAN and PHYSPROP databases (PAN 2006; PHYSPROP 2006). These sources show that water solubility values reported for a given pesticide can vary by greater than 100-fold, but it is common for reported values to vary by a factor of 2. Thus it seems reasonable to accept toxicity data that are within a factor of two of the geometric mean of acceptable solubility values.

For single-species toxicity data in this evaluation scheme, documentation and acceptability scores are averaged, resulting in one score for reliability. The reliability and relevance scores are then used to give the final rating. To establish a rating scale, the chlorpyrifos data set collected for this report was evaluated using the scoring systems detailed in Tables 3.6-3.8 of Chapter 3. The chlorpyrifos set was broken down as follows:

scores in the 75<sup>th</sup> or higher percentile of all scores were rated reliable; scores between the median and the 75<sup>th</sup> percentile were rated less reliable, and; scores below the median were rated unreliable. Similarly, relevance scores in the 90<sup>th</sup> or higher percentile were rated relevant; scores between the median and the 90<sup>th</sup> percentile were rated less relevant; scores below the median were rated not relevant. The 75<sup>th</sup> percentile of scores is suggested for the reliability rating because, in the case of the chlorpyrifos data set, higher percentiles were too restrictive, resulting in rejection of too much data that others have accepted for criteria derivation (Siepmann & Finlayson 2000; USEPA 1986a). On the other hand, the selection of the 75<sup>th</sup> percentile resulted in rejection of a few tests accepted by others, indicating that this rating system is a bit more rigorous than those used previously. The 90<sup>th</sup> percentile is suggested for the relevance scores because each element of this score is heavily weighted and scores falling below 90 should not be used for criteria derivation. Based on these ratings, the chlorpyrifos data fell into three categories: 1) those that may be used for criteria derivation (rating = RR); 2) those that may be used as supporting information (rating = RL, LR, LL); and 3) those that are not usable at all (any with an N in the rating), where R = relevant/reliable, L = less relevant/less reliable and N = not relevant/not reliable. Based on this translation of numeric scores into ratings for the chlorpyrifos data set, a numeric scale was established to be used for rating other pesticide data sets in the new methodology. The scale is shown in Table 3.11 (Chapter 3).

All other chlorpyrifos effects data (i.e., not single-species) were evaluated on documentation and reliability using the scoring schemes in Tables 3.9 and 3.10. Aquatic and terrestrial studies receiving R or L ratings may be used as supporting data in the criteria review process; studies rated N may not be used.

The data evaluation system presented here has been incorporated into the new methodology. The system includes procedures for scoring relevance and reliability of single-species, multispecies, laboratory, field, semi-field, microcosm and mesocosm studies, as well as a table describing ranges of scores that define the categories RR, RL, RN, etc.

## **2-2.6 Data quantity—ecotoxicity**

Based on conclusions from Phase I (TenBrook & Tjeerdema 2006), a sample size of 5 is the minimum needed for parametric statistical extrapolation procedures. For smaller data sets (as small as 1 datum), only assessment factor derivation methods are appropriate. Minimal data sets available for derivation of criteria in California will be those required for registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA, U. S. Code Title 7 1947) and those required by the California Department of Pesticide Regulation (California DPR 2005). According to 40 CFR Part 158.490 (USEPA 1993) the minimum data required for registration under FIFRA is an LC<sub>50</sub> for a fish and an LC<sub>50</sub> for a freshwater invertebrate. All other kinds of aquatic toxicity data are only conditionally required depending on planned pesticide usage, potential for transport to water, whether any acute LC/EC<sub>50</sub> values were < 1 mg/L, whether estimated environmental concentrations are > 0.01 times any LC/EC<sub>50</sub>, or if data indicate reproductive toxicity, persistence, or bioaccumulative potential. It is possible that for

many new chemicals, only the two acute toxicity data will be available. The DPR has tiered data requirements (California DPR 2005). The minimum data set includes LC<sub>50</sub>s for one warm water and one cold water fish and for a freshwater invertebrate. Further testing is required for the same reasons discussed for FIFRA. Again, it is possible that no more than the minimum data will be available for criteria derivation for new pesticides. An assessment factor criteria derivation method is needed for these very small data sets.

The overall quantity of data is one consideration, but it is also important to specify the range of taxonomic diversity that should be represented in the data set. The USEPA methodologies (USEPA 1985; 2003f) have the most comprehensive, specific taxonomic requirements among the reviewed methodologies and are used for the new methodology, with some modification to reflect species of importance to the Central Valley of California and to reduce the required number of data from 8 to 5.

First, consider the following taxonomic requirements in the USEPA (1985; 2003f) methods:

For derivation of acute or chronic criteria by the SSD method (minimum of 8 acute or chronic data):

- a. The family Salmonidae in the class Osteichthyes;
- b. One other family (preferably a commercially or recreationally important, warm water species) in the class Osteichthyes (e.g., bluegill, channel catfish);
- c. A third family in the phylum Chordata (e.g., fish, amphibian);
- d. A planktonic crustacean (e.g., a cladoceran, copepod);
- e. A benthic crustacean (e.g., ostracod, isopod, amphipod, crayfish);
- f. An insect (e.g., mayfly, dragonfly, damselfly, stonefly, caddisfly, mosquito, midge);
- g. A family in a phylum other than Arthropoda or Chordata (e.g., Rotifera, Annelida, Mollusca);
- h. A family in any order of insect or any phylum not already represented.

With regard to plants, the USEPA (1985) guidelines require results from at least one test with a freshwater alga or vascular plant, while the Great Lakes (USEPA 2003f) methodology indicates that plant data are desirable, but not required. In both cases, if plants are among the most sensitive (as is likely with herbicides), then tests with plants representing at least two phyla are required.

For derivation of acute criteria by the assessment factor method:

- a. At least one datum from the family Daphniidae; species must be from the genus *Daphnia*, *Ceriodaphnia*, or *Simocephalus* (USEPA 2003f).

For derivation of an acute-to-chronic ratio (minimum of 3 chronic data):

- a. At least one fish;
- b. At least one invertebrate;

c. At least one acutely sensitive freshwater species (the other two may be saltwater species).

With these requirements in mind, and with the minimal data sets available from pesticide registration, the following taxonomic requirements are in the new methodology:

For derivation of acute or chronic criteria by the SSD method (minimum of 5 data):

- a. The family Salmonidae;
- b. A warm water fish;
- c. A planktonic crustacean, of which one must be in the family Daphniida in the genus *Ceriodaphni*, *Daphnia*, or, *Simocephalus*;
- d. A benthic crustacean;
- e. For non-herbicides: an insect (aquatic exposure); for herbicides: an alga or vascular aquatic plant.

Rationale for exclusion of items c, g and h in USEPA list:

- c. Two fish species (one warm water and one cold water) are sufficient to represent the phylum Chordata;
- g. Rotifers, annelids and mollusks are typically insensitive to pesticides (e.g., Giesy *et al.* 1999);
- h. This category is very general and simply fills out the eight minimum data required by the USEPA SSD method (USEPA 1985; 2003f).

For determination of acute criteria by the assessment factor method (minimum of 1 datum):

- a. For non-herbicides: the family Daphniidae in the genus *Ceriodaphnia*, *Daphnia*, or *Simocephalus*; for herbicides: alga or aquatic vascular plant.
- b. Additional data must be from different families as per the list of those required for the SSD method. For example, to derive insecticide criteria, if data are available from two acceptable studies, then one must be from the family Daphniidae and the other must be either a member of the family Salmonidae, a warm water fish, a benthic crustacean or an insect. If three data are available, then one must be in the family Daphniidae and the others must be from two other, different families, and so on such that each additional datum contributes toward completing the minimum data set required for the SSD method.

The plant requirement for herbicides is added because herbicides are expected to be more toxic to plants than to animals. Item b. is added to ensure that the magnitude of the assessment factor is only reduced in cases where data are available for multiple families, and to encourage generation of data that would complete the minimum SSD set.

For determination of acute-to-chronic ratios, the requirements in USEPA guidance (USEPA 1985; 2003f) are acceptable, including the use of saltwater species if not enough freshwater data are available.

Based on the discussion here, the new methodology includes specific instructions regarding number and taxonomic diversity of data required for criteria derivation by SSD and AF methods.

## **2-2.7 Data reduction**

Data that have been rated as relevant and reliable require further reduction prior to criteria derivation so that no species receive undue weight in the derivation process. For example, if there are multiple data for a particular species, then some method has to be specified for reducing those data into a single point within the SSD for that species. As discussed in the Phase I report (TenBrook & Tjeerdema 2006) the geometric mean is a reasonable approach for reducing data from multiple tests to a single number for criteria derivation. No species should be represented more than once in the final SSD.

SSD procedures assume that toxicity data in the distribution represent an unbiased sample of the system to be protected (Forbes & Calow 2002). Current USEPA procedures (USEPA 1985; 2003f) utilize genus mean toxicity values on the grounds that this reduces potential bias due to overabundance of data for species from a few genera, and it minimizes statistical problems that arise due to non-random sampling (i.e., the close relationship between organisms within a species prevents organisms from responding independently). This approach does not seem entirely justified for a few reasons. First, Erickson & Stephan (1988) found that FAVs were comparable whether derived from species- or family-level data. Second, there is considerable variability of sensitivity between species within a genus in some cases. For example, Harmon *et al.* (2003) report an EC<sub>50</sub> (immobility) for *Daphnia ambigua* exposed to chlorpyrifos of 0.035 µg/L, while Van Der Hoeven & Gerritsen (1997) report an EC<sub>50</sub> (immobility) for *Daphnia pulex* of 0.42 µg/L, a 10-fold difference. In addition, sets of toxicity data acceptable for criteria derivation are usually quite small (e.g., in Erickson & Stephan 1988, data sets ranged from 8 to 45 values); thus, general statements about the intra-genus variability are not well-supported. For these reasons, and since no other existing methodology uses the genus-level approach, the new methodology utilizes data at the species level for both acute and chronic criteria derivation.

Specific data reduction methods used in existing methodologies were described in Phase I (TenBrook & Tjeerdema 2006). Following is a compilation of those methods that are used for reducing data to species mean acute values (SMAVs) and species mean chronic values (SMCVs) in the new methodology.

- 1) Calculate SMAVs/SMCVs as the geometric mean of toxicity values from one or more acceptable tests with the same endpoints (ANZECC & ARMCANZ 2000; ECB 2003; OECD 1995; RIVM 2001; USEPA 1985; 2003f);

- 2) If data are available for life stages that are at least a factor of two more resistant than another life stage for the same species, then do not use the data for the more resistant life stage to calculate the SMAV because the goal is to protect all life stages (RIVM 2001; USEPA 1985; 2003f);
- 3) If data are available for one species, but for multiple endpoints, then use the data for the most sensitive endpoint (ANZECC & ARMCANZ 2000; ECB 2003; OECD 1995; RIVM 2001); if multiple endpoints are equally sensitive, then note both endpoints, but use only one value for criteria calculation;
- 4) If a NOEC is not explicitly reported in chronic toxicity studies, but statistical analysis was done, the NOEC may be determined as the highest reported concentration not statistically different from the control ( $p < 0.05$ , RIVM 2001); the NOEC is not used in criteria derivation, but is needed for calculation of the MATC;
- 5) Similarly, if a LOEC is not explicitly reported in chronic toxicity studies, it may be determined as the lowest reported concentration that is statistically different from the control ( $p < 0.05$ ); the LOEC is not used in criteria derivation, but is needed for calculation of the MATC;
- 6) If a MATC is not reported, it may be calculated as the geometric mean of the NOEC and LOEC;
- 7) If no toxicity values were reported, but raw data are available, calculate values using appropriate statistical methods (ECB 2003);
- 8) If a MATC is expressed as a range of values, recalculate the MATC as the geometric mean of the high and low values (RIVM 2001);
- 9) If reasons for differences between tests for the same species/endpoints are found, then data may be grouped according to appropriate factors (e.g., pH or temperature; ECB 2003). Selection of the appropriate value to use in criteria derivation should be based on standard test parameters. Tests conducted under non-standard conditions (vs. standard conditions as defined in standard test methods) may be used to derive quantitative relationships between those conditions and toxicity (as in USEPA 1985; 2003f). If such a relationship is established then toxicity values derived under non-standard conditions may be translated to standard conditions and added to the criteria derivation data set. If no quantitative relationship can be derived then tests conducted under non-standard conditions should not be used for criteria derivation, but may be used as supporting information.
- 10) If data are available for multiple time points from crustacean or insect acute toxicity studies use the latest time point (i.e., 96-h tests are preferred over tests of  $< 96$  h);
- 11) For a given species, use data from flow-through tests in which concentrations were measured, if it is available. If such data are not available, then data from static or static-

renewal tests and/or tests in which concentrations were not measured may be used as long as they are rated otherwise relevant and reliable.

12) Further reduction may be needed in the course of SSD analysis. If data cannot be described by or fit to a distribution, then the set should be examined for outliers and/or bimodality. The new methodology includes detailed guidance for detection of outliers and exclusion of outliers. If data are bimodally distributed (as determined visually), use only the lower of the two groups for criteria derivation (ANZECC & ARMCANZ 2000); the effects of data exclusions on the criteria must be explored and explained (ECB 2003).

Data reduction procedures excluded from this list include those that equate NOECs with some percentage reduction from control responses and those that use factors to estimate NOECs from LOECs, with factor size dependent on level of response (ECB 2003; RIVM 2001). As discussed in section 2-2.1.1.2, there is little agreement as to what levels of effect constitute “no effect” (in terms of statistical or biological significance) so these extrapolations are unreliable. Also excluded was a procedure to exclude data for species in cases where toxicity values differ by more than a factor of 10 (USEPA 1985; 2003f). The approach for excluding data is not explained (USEPA 1985; 2003f) and step 12 in the data reduction procedure should adequately manage outliers. Also excluded was a procedure whereby multiple data for a given species were reduced by consideration of which studies best reflected regional environmental parameters (ECB 2003). This procedure makes little sense for laboratory toxicity data obtained in standardized tests, but could be useful in choosing field or semi-field data to support the criteria derivation process.

Based on this discussion, guidance is provided in the new methodology for selecting or calculating values for use in criteria derivation. Instructions are given for how to reduce multiple data for a given chemical/species combination to a single species mean acute or chronic value, and for how to manage bimodal distributions and outliers.

### **2-3.0 Criteria Calculation**

Criteria need to have components of magnitude, duration and frequency to be most useful to environmental managers (conclusion of Phase I report; (TenBrook & Tjeerdema 2006). Exposure duration is partially addressed through the derivation of separate acute and chronic criteria (USEPA 1985; 2003f). Further consideration of allowable duration and frequency of exceedances are discussed in sections 2-3.3 and 2-3.4. The use of species sensitivity distribution (SSD) and assessment factor (AF) extrapolation methods for determination of criteria magnitudes are addressed in this section.

The aim of both SSD and AF methods is to extrapolate from available toxicity data for a limited number of species to toxicity values that will be protective of all species in an ecosystem. The assessment factor (AF) method involves multiplying the lowest value of a set of toxicity data by a factor to arrive at a criterion. The statistical extrapolation method involves the use of one of several similar species sensitivity

distribution (SSD) techniques to determine the criterion. The Phase I report (TenBrook & Tjeerdema 2006) concluded that if at least five data are available from five taxonomic groups (defined in section 2-2.6), then the SSD method should be used. If fewer than five data are available, then the AF method should be used. There are a number of approaches to each of these methods, and the purpose of this section is to compare approaches using several example data sets, and to select the best ones for inclusion in the new methodology.

### **2-3.1 SSD methodology**

There are five points on which SSD methodologies may differ: 1) the shape of the distribution; 2) the kinds and quantity of data; 3) the level of confidence associated with derived criteria; 4) how data are aggregated; and 5) what percentile cutoff is the best predictor of no-effect concentrations. Item 2) has been addressed in sections 2-2.1.1 and 2-2.6. Items 1, 3 and 4 will be evaluated in more detail in the following sub-sections. Item 5 was discussed in the Phase I report (TenBrook & Tjeerdema 2006) and the 5<sup>th</sup> percentile was determined to be the best predictor of no-effect levels. However, since this is a critical issue in criteria derivation, the discussion is briefly revisited here.

#### **2-3.1.1 Appropriate distribution**

The first step in the SSD methodology is to plot data in a cumulative frequency distribution. One approach then is to assume that those data are a random sample of all species and that if all species were sampled, they could be described by some defined distribution. The USEPA (1985) assumes a log-triangular distribution while The Netherlands methodology utilizes a log-normal distribution as described by Aldenberg & Jaworska (2000). The OECD (1995) methodology offers a choice of either the log-normal distribution method of Wagner & Lokke (1991), the log-logistic distribution method of Aldenberg & Slob (1993), or the triangular distribution of USEPA (1985) depending upon which distribution best fits the available data. The Australia/New Zealand methodology (ANZECC & ARMCANZ 2000) utilizes a curve-fitting technique to fit distributions to data. The Burr Type III distributions utilized in the ANZECC & ARMCANZ methodology is a flexible 3-parameter distribution that approximates the log-triangular and log-normal distributions. In addition, the log-logistic distribution is a special case of the Burr III distribution (CSIRO 2001). Thus all of the distributions historically used for SSD analysis are considered by using the Burr III family.

In the Phase I report, all of these distributions were explored, as were non-parametric techniques, for estimation of community or ecosystem effects based on single-species toxicity tests (TenBrook & Tjeerdema 2006). Arguments for one or the other distribution, or for making no distributional assumptions, are based on how many samples are required, on which distributions are easier to work with, or which ones better quell the criticism that SSDs are not valid because data usually do not fit the assumed

Table 2.1. Acute toxicity data sets. Cpf = chlorpyrifos; Txp = toxaphene; End = endrin; Lin = lindane; Ald = aldrin; Diel = dieldren; Hept = heptachlor; Chl = chlordane; Endos = Endosulfan; Dia = diazinon; Atr = atrazine; all values in µg/L.

Rank	Cpf <sup>1</sup>	DDT <sup>2</sup>	Txp <sup>2</sup>	End <sup>2</sup>	Lin <sup>2</sup>	Ald <sup>2</sup>	Diel <sup>2</sup>	Hept <sup>2</sup>	Chl <sup>2</sup>	Endos <sup>2</sup>	Dia <sup>2</sup>	Atr <sup>2</sup>
1	0.035	0.36	0.8	0.15	2.0	4.0	2.5	0.9	3.0	0.34	0.3773	3000
2	0.0427	1.1	1.3	0.32	10	4.5	4.5	1.1	6.3	0.83	0.7764	5300
3	0.06	1.4	1.962	0.33	10.5	6.1	5.0	1.8	15	2.3	1.048	6300
4	0.0654	1.6	2	0.41	32	7.4	6.1	2.8	26	3.2	1.587	6700
5	0.100	1.7	2.3	0.44	32	8.0	8.0	7.8	26	3.7	2.04	14700
6	0.150	1.7	3	0.46	40	9.0	8.1	13.1	37	3.8	6.51	20000
7	0.220	1.9	3.1	0.47	44	10	10.8	23.6	40	5.8	10.7	27000
8	0.25	1.9	3.446	0.54	44	16	15	24	45	6.0	16.82	49000
9	1.0	2.4	3.7	0.69	45	21	20	26	56	88	25	60000
10	4.7	2.6	3.822	0.75	48	27	22	29	57	261	425.8	
11	6	3.0	4.874	0.76	55.6	27	24	42	58		459.6	
12	8	3.0	5.782	0.78	64	28	39	47.3	59		602	
13	10	3.2	6	0.85	67.1	32	41	61.3	82		723	
14	15.96	3.5	6.7	1.0	68	34	130	78	190		800	
15	178	3.9	10	1.1	83	42	213	81.9			1643	
16	806	4.0	10.12	1.2	90	45.9	250	101			2166	
17	2410	4.3	10.8	1.3	138	50	567	148			3198	
18		4.9	11.85	1.5	141.1	143	620	320			7804	
19		5.0	12	1.8	207	180	740				7841	
20		7.3	13	2.1	460						8000	
21		7.8	13	3.1	485						9000	
22		7.8	13.78	4.7	676						11000	
23		8.0	14.59	5.9							11640	
24		8.5	14.6	32								
25		9.3	15.68	34								
26		10	16.71	60								
27		12	17.61	64								
28		14	18	352								
29		17	20									
30		18	24									
31		25	26									
32		33	31.75									
33		40	40									
34		48	73.48									
35		48	140									
36		54	210									
37		67	500									
38		68										
39		175										
40		192										
41		362										

<sup>1</sup> Data collected for this project

<sup>2</sup> USEPA criteria documents (USEPA 1980a; b; c; d; e; f; 1986a; b; 2003d; 2005a)

distribution. In the end, all of the methods currently in use appear to derive protective criteria. In The Netherlands, the log-normal distribution was selected over a log-log distribution (Aldenberg & Slob 1993) because, although the distributions are not all that different, and results obtained are not different, the normal distribution provides powerful

statistical tools (RIVM 2001). Likewise, the OECD (1995) concludes that the log-normal, log-logistic and triangular distribution methods give very similar results.

It is important to select a SSD method that minimizes violations of distributional assumptions. Species sensitivity distribution methodologies of USEPA (1985; 2003f), RIVM (2001) and ANZECC & ARMCANZ (2000) are discussed and compared further in section 2-3.1.4. The distributional assumptions of these three techniques are evaluated here using the chlorpyrifos acute toxicity data collected for this project (a more detailed table of this data set is included in Chapter 4), as well as acute pesticide data sets taken from Erickson & Stephan (1988) and diazinon and atrazine data sets from USEPA criteria documents (USEPA 2003d; 2005a). These data are shown in Table 2.1. Values in the USEPA diazinon and atrazine sets that were reported as > or < values were excluded from this analysis, as they are not usable in any but the USEPA SSD method. The highest DDT value and the two highest aldrin values were excluded because they were greater than two times the water solubility of the compound (as discussed in section 2-2.5.2.)

Figure 2.1 shows the log-normal distributional fits along with box plots and histograms of each data set (output from JMP IN v. 5.1.2, JMP 2004). Figure 2.2 shows log-triangular, log-normal and Burr Type III fits for these data sets (constructed using Excel v. 11.2.3). The log-triangular distributions were constructed according to the following parameters (Evans *et al.* 2000):

$$CDF = \frac{(x - a)^2}{(b - a)(c - a)} \text{ for } a \leq x \leq c; \quad (2.1)$$

$$\text{and } CDF = \frac{(b - x)^2}{((b - a)(b - c))} \text{ for } c \leq x \leq b \quad (2.2)$$

$$Mean = \frac{(a + b + c)}{3} \quad (2.3)$$

where:

CDF = cumulative distribution function

x = value in data set

a = minimum value in data set

b = maximum value in data set

c = mode

The mode of each log-triangular distribution was determined by dividing the data into bins and taking the average of the maximum and minimum values in largest bin.

The log-normal and Burr Type III distributions in Fig. 2.2 were constructed using Excel (v. 11.2.3). The Burr III distribution has the following cumulative distribution function:

$$F(x) = \frac{1}{\left[1 + \left(\frac{b}{x}\right)^c\right]^k} \quad (2.4)$$

Where:

$F(x)$  = probability of  $x$ ;  
 $b$ ,  $c$  and  $k$  are fit parameters;  
 $x$  = data point in the distribution

As  $k \rightarrow \infty$ , the Burr III distribution approaches the reciprocal Weibull distribution, and as  $c \rightarrow \infty$ , the Burr III distribution approaches the reciprocal Pareto distribution. Thus, these so called limiting distributions are used in cases where  $k > 100$  and  $c > 80$ , respectively (Campbell *et al.* 2000; CSIRO 2001).

The cumulative distribution function for the reciprocal Weibull distribution is:

$$F(x) = \exp^{-ax^{-\beta}} \quad (2.5)$$

Where:

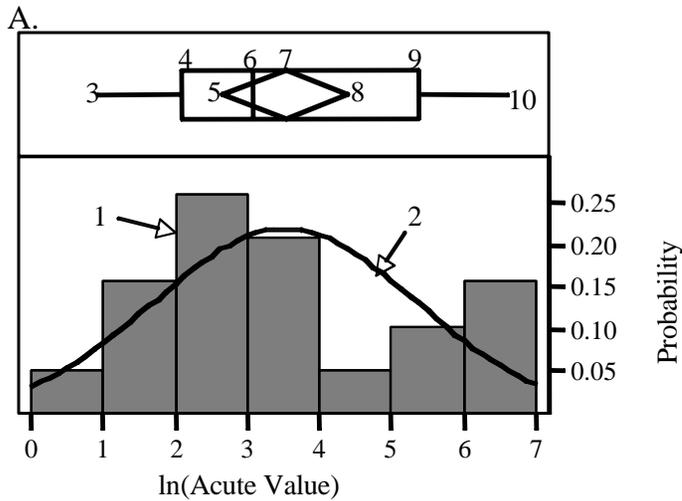
$F(x)$  = probability of  $x$ ;  
 $\alpha$  and  $\beta$  are fit parameters;  
 $x$  = data point in the distribution

For the reciprocal Pareto distribution the cumulative distribution function is:

$$F(x) = \left(\frac{x}{x_0}\right)^\theta \quad (2.6)$$

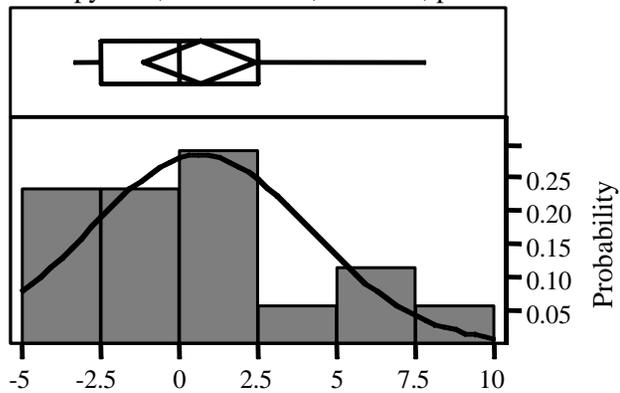
Where:

$F(x)$  = probability of  $x$ ;  
 $X_0$  and  $\theta$  are fit parameters;  
 $X$  = data point in the distribution



B.

Chlorpyrifos; mean = 0.65; sd = 3.5; p = 0.08



DDT; mean = 2.2; sd = 1.6; p = 0.26

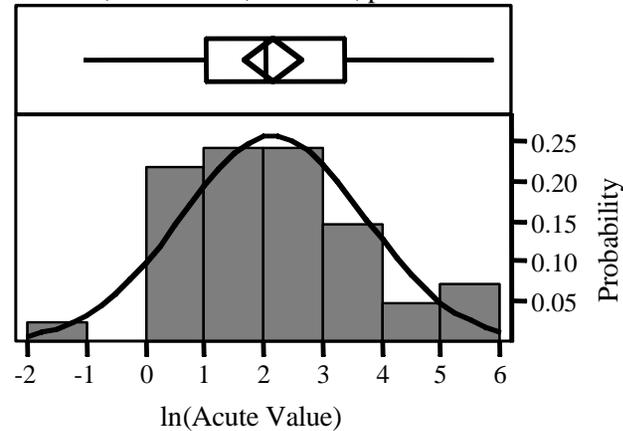


Figure 2.1. Tests for log-normal distribution of data sets. A. Key to distribution diagrams. B. Distributions for each of 12 data sets;  $p < 0.05$  indicates lack of fit. ■ indicates outliers (outside 1.5 times the interquartile range).

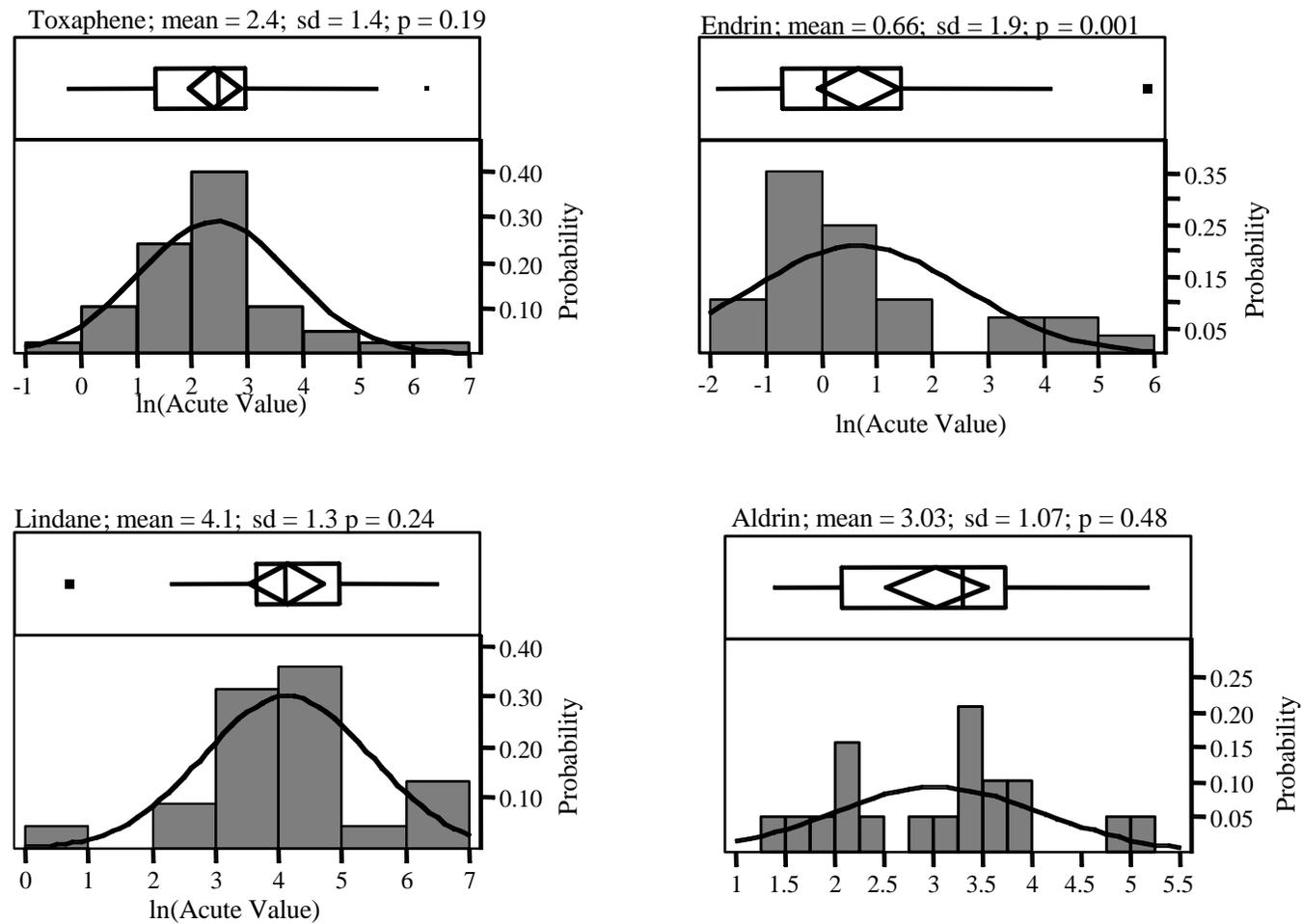
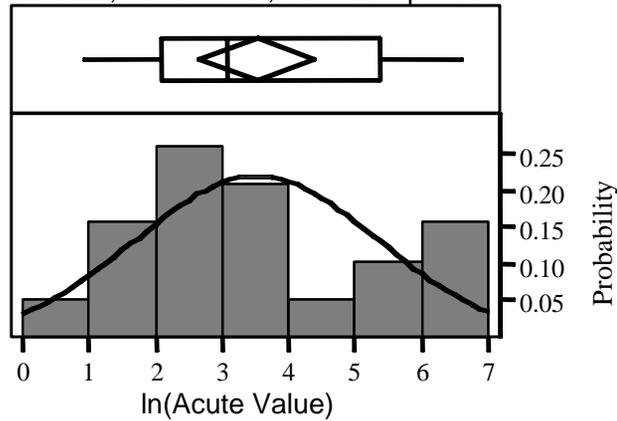
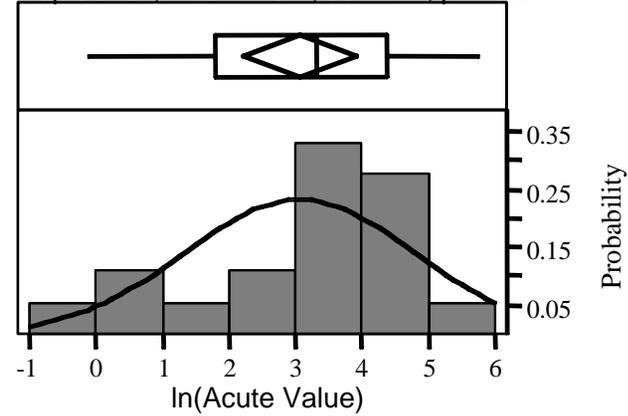


Figure 2.1 (cont.). Tests for log-normal distribution of data sets. A. Key to distribution diagrams. B. Distributions for each of 12 data sets;  $p < 0.05$  indicates lack of fit. n indicates outliers (outside 1.5 times the interquartile range).

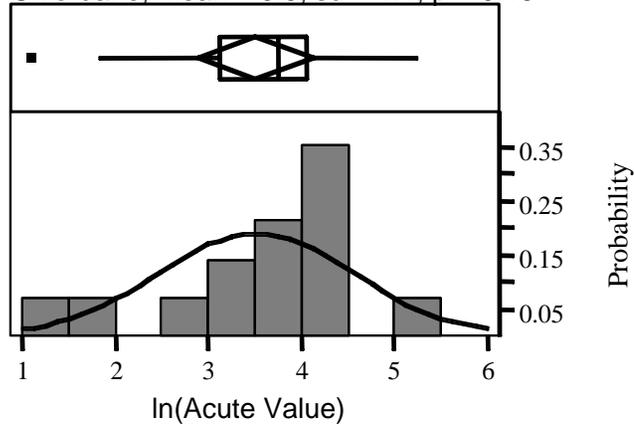
Dieldrin; mean = 3.5; sd = 1.08 p = 0.11



Heptachlor; mean = 3.1; sd = 1.7; p = 0.24



Chlordane; mean = 3.5; sd = 1.1; p = 0.18



Endosulfan; mean = 1.7; sd = 2.0; p = 0.20

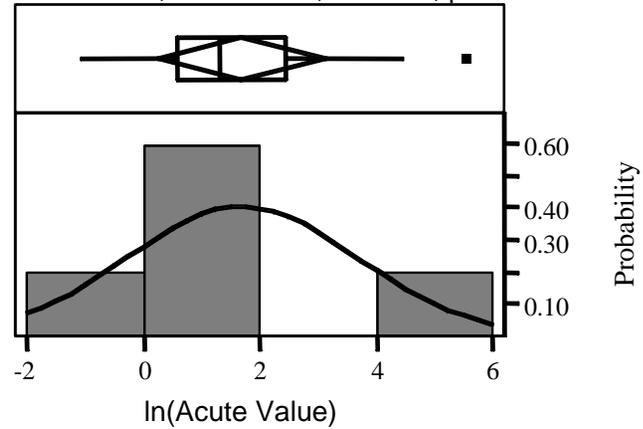


Figure 2.1 (cont.). Tests for log-normal distribution of data sets. A. Key to distribution diagrams. B. Distributions for each of 12 data sets;  $p < 0.05$  indicates lack of fit. ■ indicates outliers (outside 1.5 times the interquartile range).

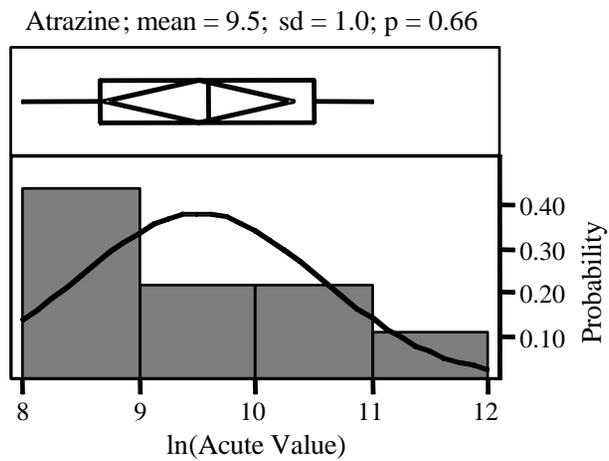
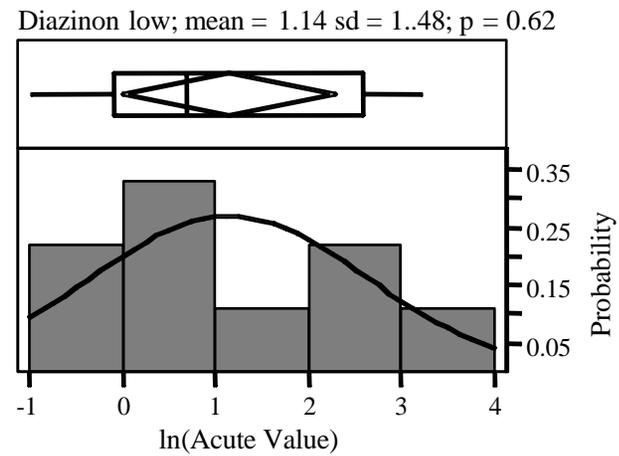
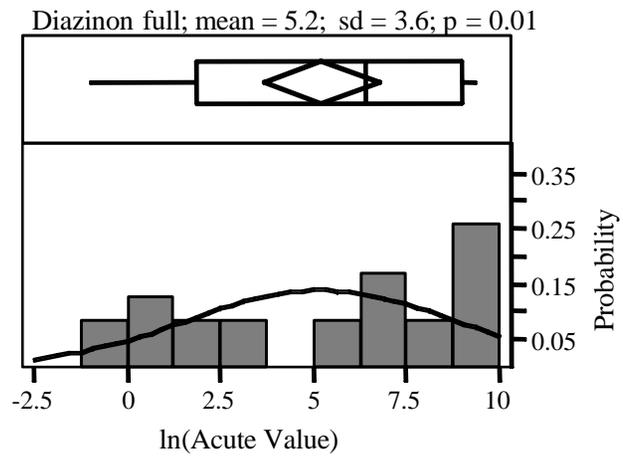


Figure 2.1 (cont.). Tests for log-normal distribution of data sets. A. Key to distribution diagrams. B. Distributions for each of 12 data sets;  $p < 0.05$  indicates lack of fit. ■ indicates outliers (outside 1.5 times the interquartile range).

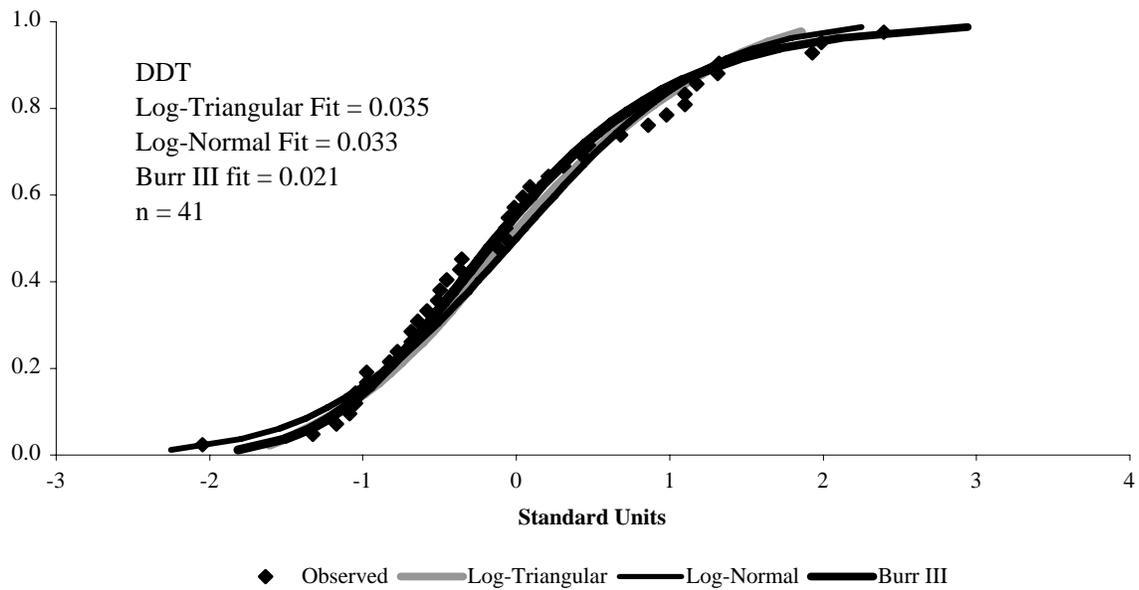
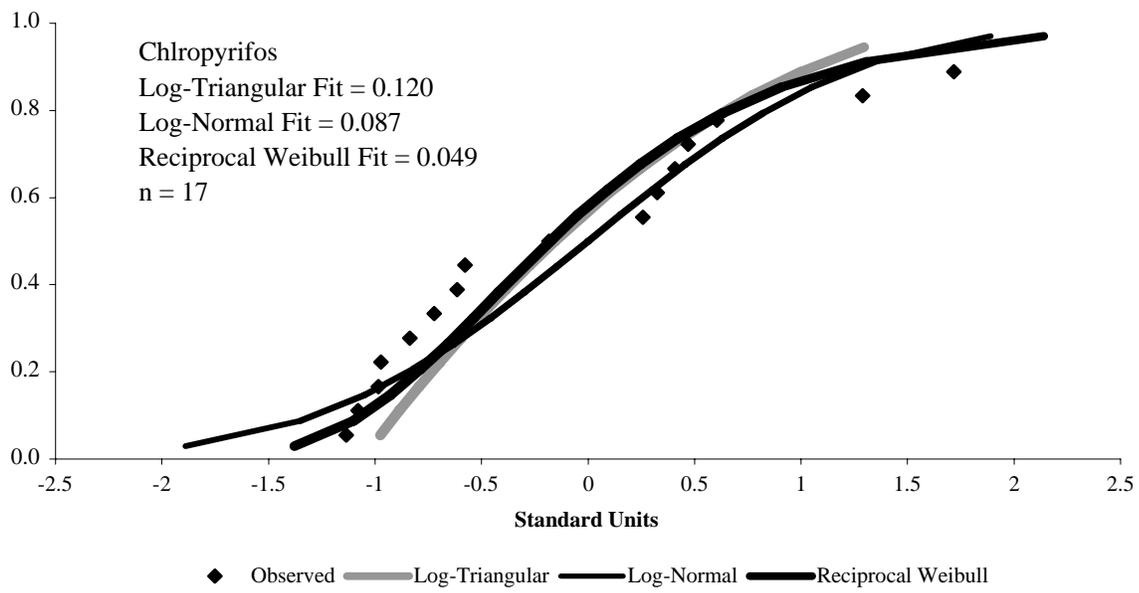


Figure 2.2. Comparison of fits of pesticide data to log-triangular, log-normal and Burr Type III distributions.

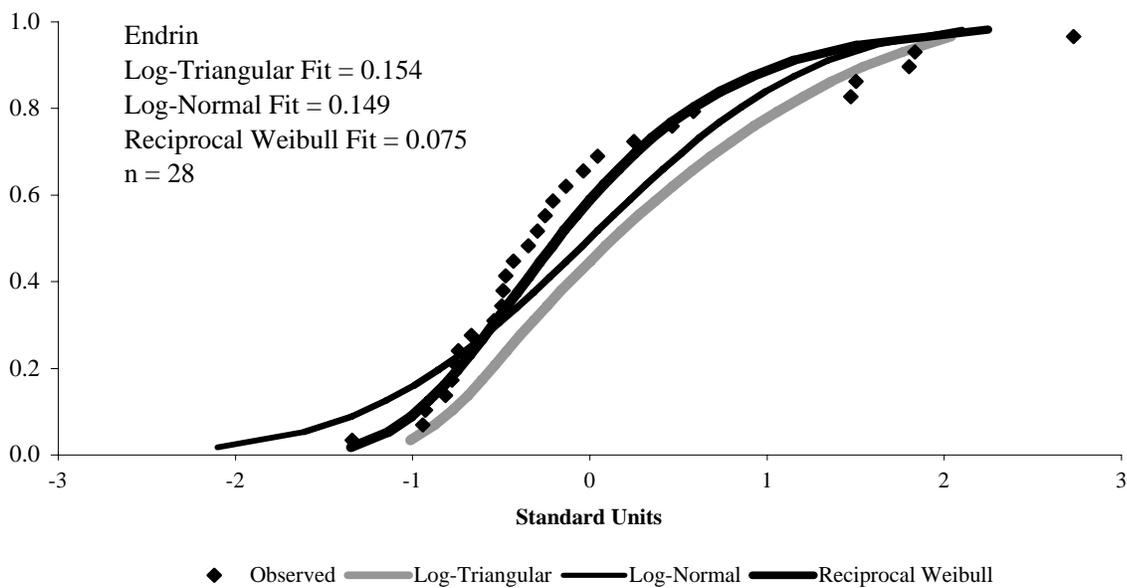
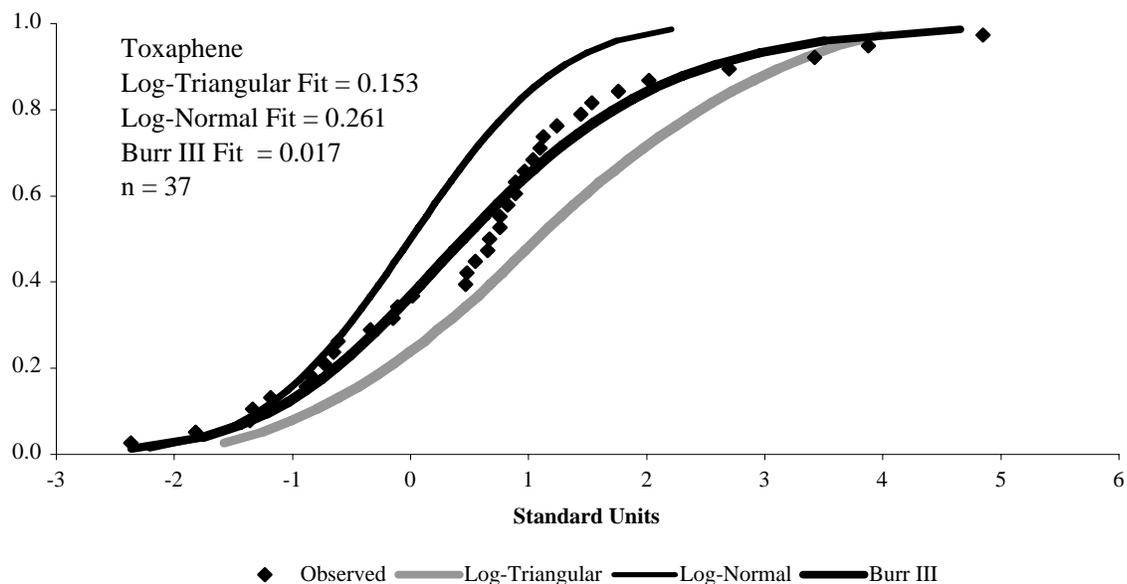


Figure 2.2 (cont.). Comparison of fits of pesticide data to log-triangular, log-normal and Burr Type III distributions.

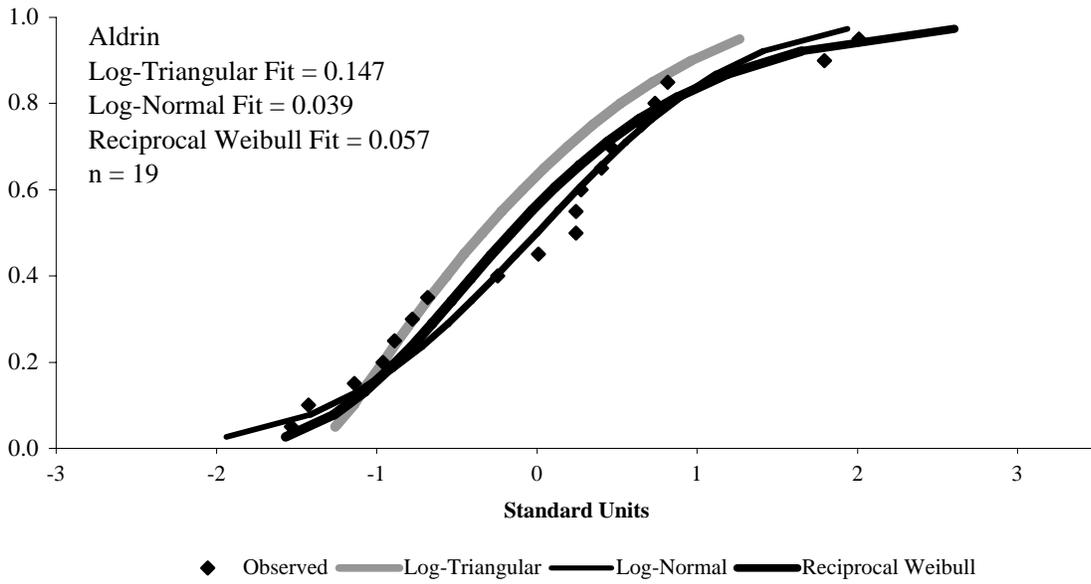
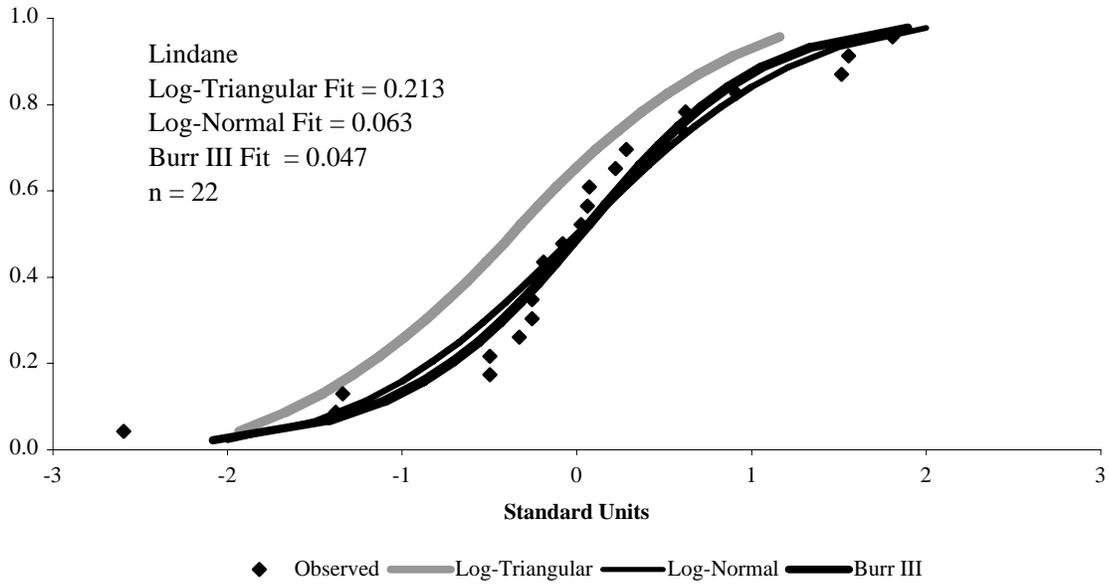


Figure 2.2 (cont.). Comparison of fits of pesticide data to log-triangular, log-normal and Burr Type III distributions.

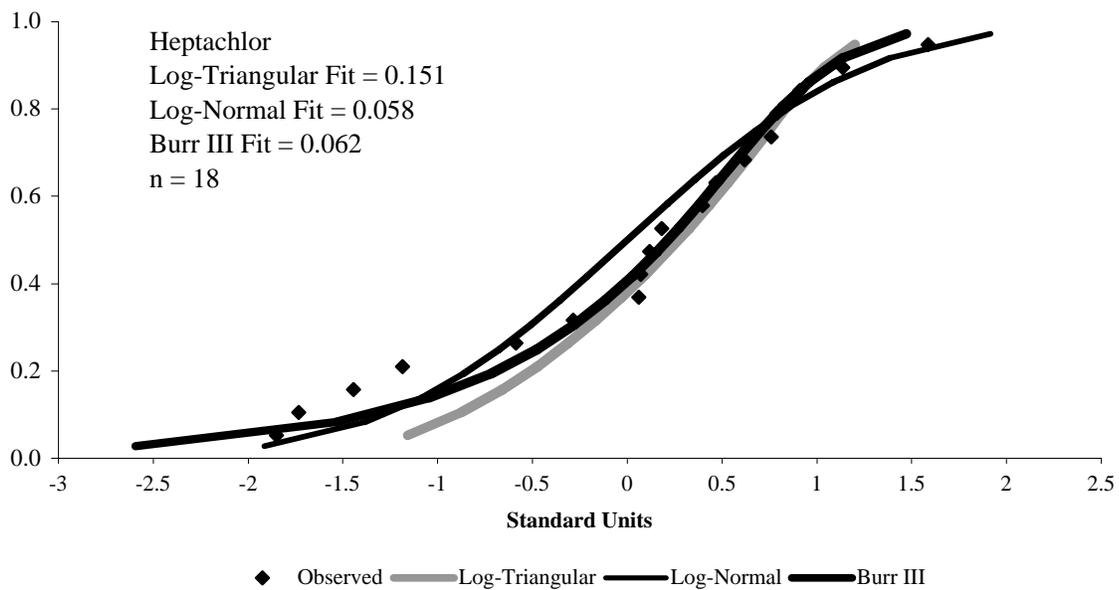
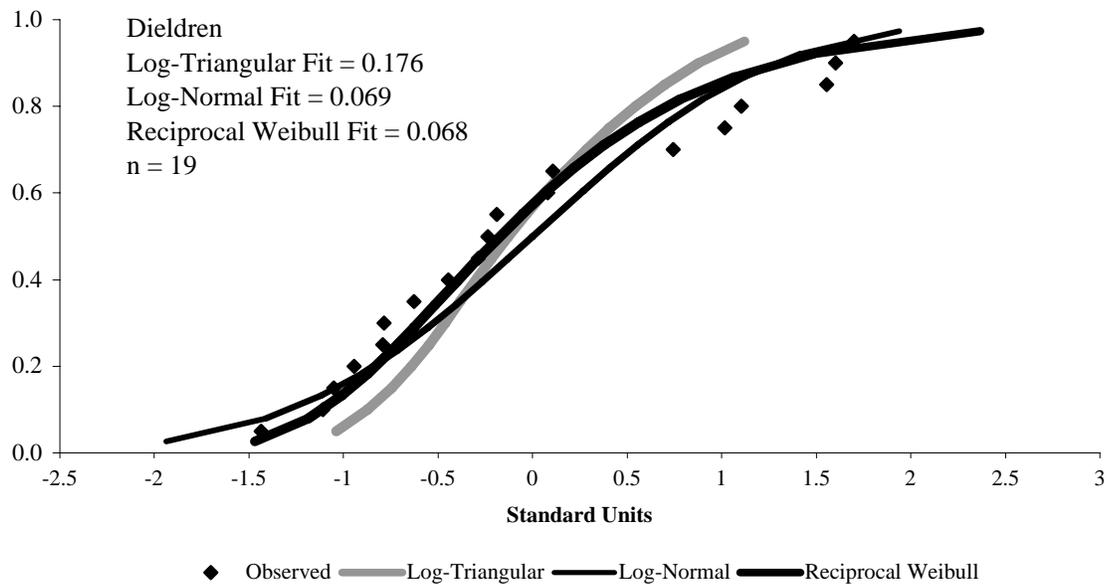


Figure 2.2 (cont.). Comparison of fits of pesticide data to log-triangular, log-normal and Burr Type III distributions.

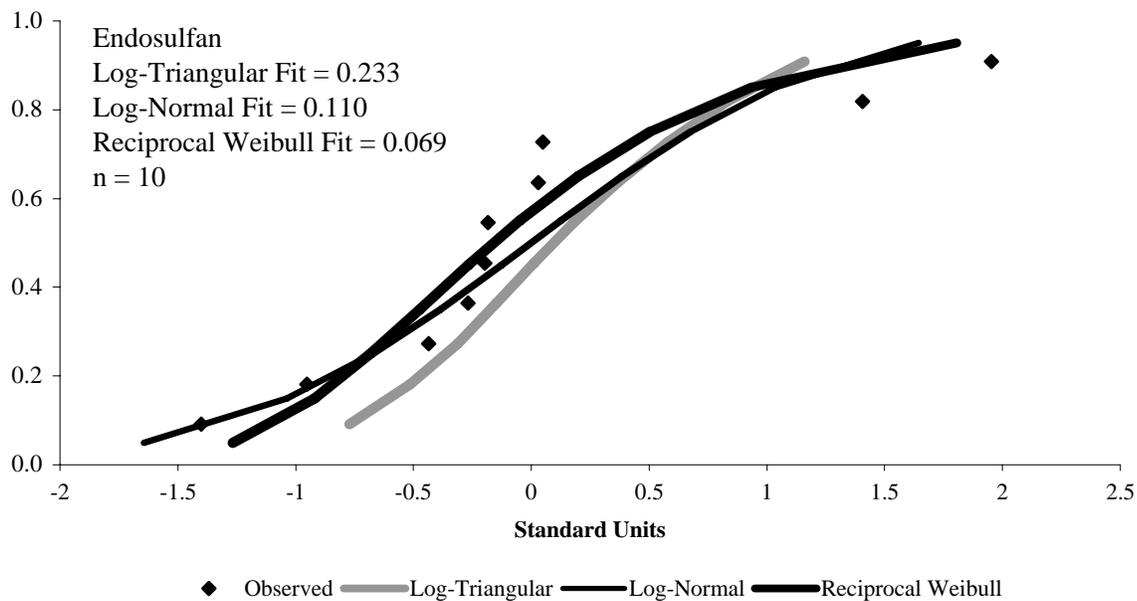
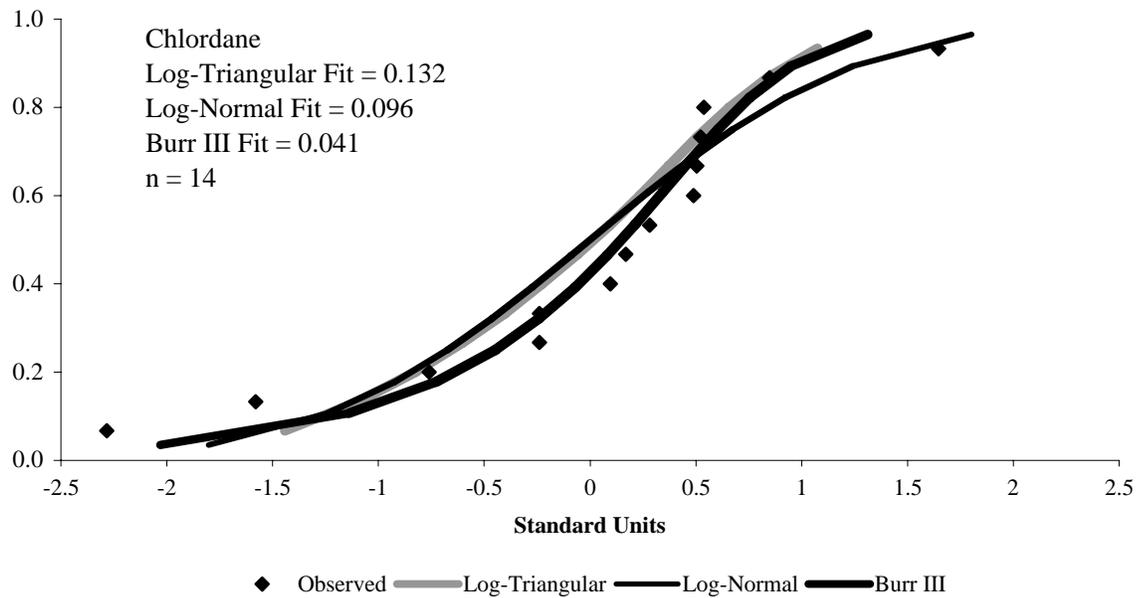


Figure 2.2 (cont.). Comparison of fits of pesticide data to log-triangular, log-normal and Burr Type III distributions.

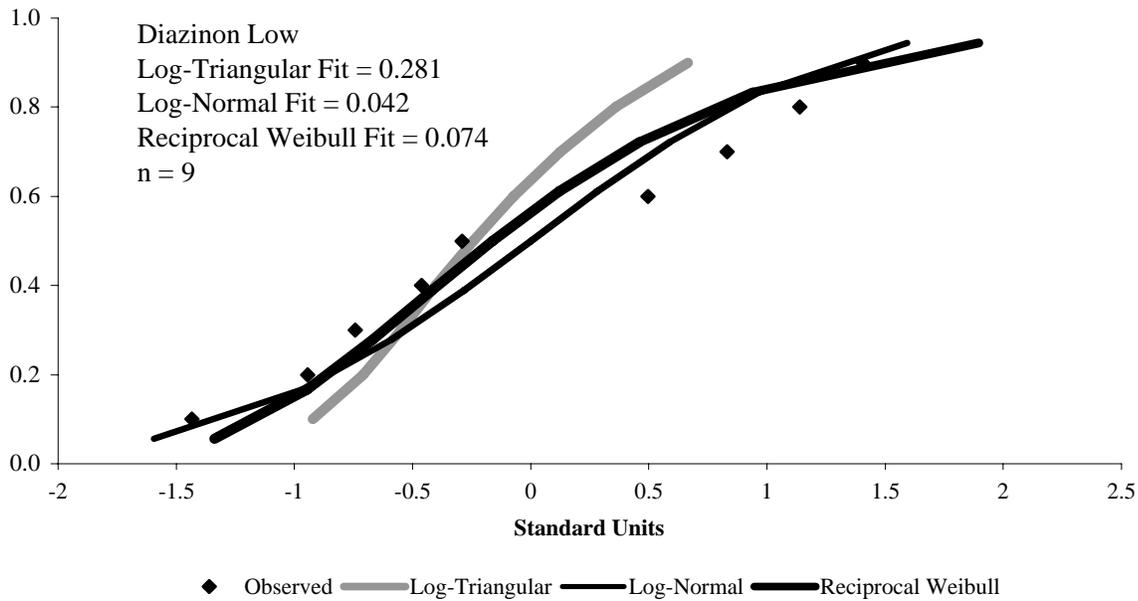
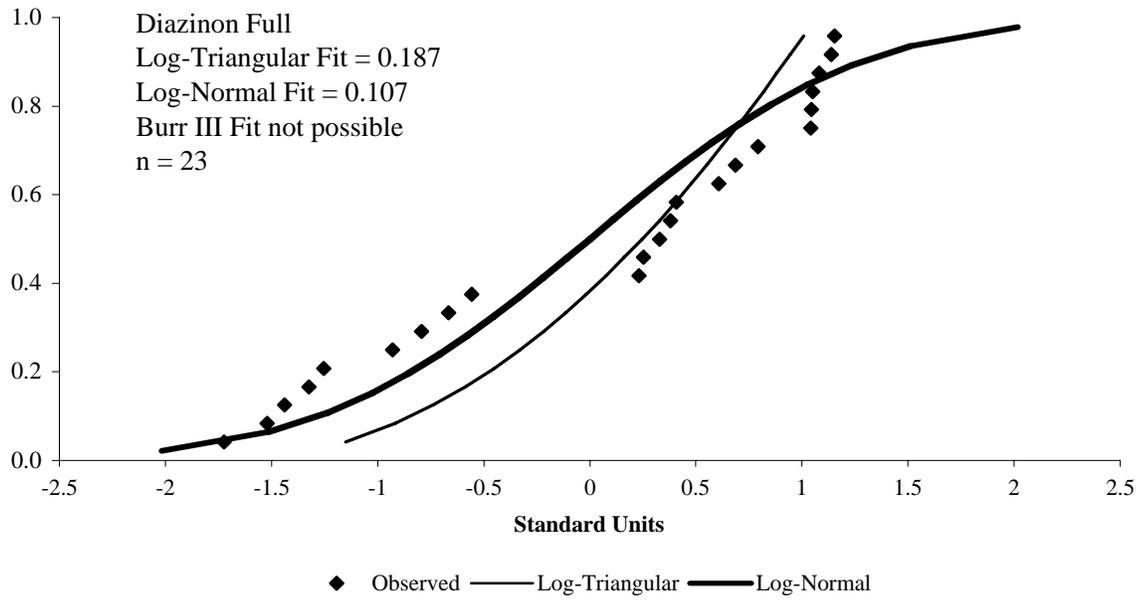


Figure 2.2 (cont.). Comparison of fits of pesticide data to log-triangular, log-normal and Burr Type III distributions.

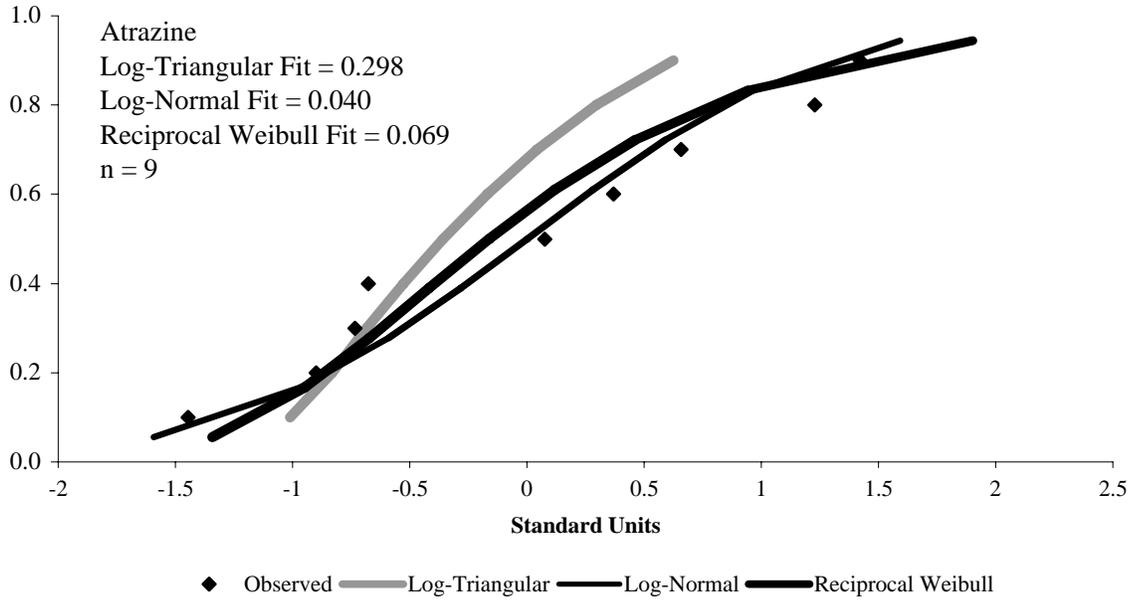


Figure 2.2 (cont.). Comparison of fits of pesticide data to log-triangular, log-normal and Burr Type III distributions.

Table 2.2 shows the results of curve-fitting for the 12 data sets in Table 2.1. The BurrliOZ v. 1.0.13 program (CSIRO 2001) was used to fit Burr Type III distributions to each data set, except the full diazinon set, which is bimodal (histogram, Fig. 2.1; observed data, Fig. 2.2). Using only the lowest 9 diazinon values, a reciprocal Weibull distribution was fit.

Table 2.2. Burr III family distribution fit parameters for data sets in Table 2.1. Parameters c, b and k apply to the Burr III distributions;  $\alpha$  and  $\beta$  apply to the reciprocal Weibull distribution.

Pesticide	Distribution	c or $\alpha$	b or $\beta$	k
Chlorpyrifos	Reciprocal Weibull	0.6979	0.3855	-----
DDT	Burr III	0.8576	0.7528	5.077
Toxaphene	Burr III	1.0852	3.6524	2.366
Endrin	Reciprocal Weibull	0.8914	0.7889	-----
Lindane	Burr III	1.552	76.521	0.8204
Aldrin	Reciprocal Weibull	15.908	1.095	-----
Dieldrin	Reciprocal Weibull	6.653	0.7061	-----
Heptachlor	Burr III	2.147	92.256	0.2830
Chlordane	Burr III	3.275	67.499	0.3572
Endosulfan	Reciprocal Weibull	1.743	0.667	-----
Diazinon Full	Could not fit	-----	-----	-----
Diazinon Low	Reciprocal Weibull	1.454	0.8207	-----
Atrazine	Reciprocal Weibull	34375	1.157	-----

Erickson & Stephan (1988) utilized the following formula to measure goodness of fit to a number of different distributions:

$$\frac{\sum (X_R - E(X_R))^2}{\sum_n (X_R - \bar{X}_R)^2} \quad (2.7)$$

Where:

- $n$  = number of data in set;
- $X_R$  = observed value of  $X$  at rank  $R$ ;
- $E(X_R)$  = expected value of  $X$  at rank  $R$ ;
- $\bar{X}_R$  = mean value of  $X$  for all ranks.

and:

$$E(X_R) = \hat{L} + \hat{S} \bullet E(Z_R) \quad (2.8)$$

Where:

$\hat{L}$  = location parameter estimate (mean)

$\hat{S}$  = scale parameter estimate (standard deviation)

Using equations 2.8 and 2.9, the data in Table 2.1 were tested for goodness of fit to the log-triangular, log-normal and Burr Type III distributions used in USEPA (1985; 2003f), RIVM (2001), and ANZECC & ARMCANZ (2000), respectively. Results are shown in Table 2.3 and are included in Fig. 2.2.

Table 2.3. Comparison of fit of log-triangular, log-normal, and Burr Type III distributions for data sets from Table 2.1. Lower number (shaded) indicates better fit. Where both are shaded, fits are equally good. Fit is measured as described in (Erickson & Stephan 1988); data were log-transformed prior to analysis.

	<b>Log-Triangular</b>	<b>Log-Normal</b>	<b>Burr Type III</b>
Chlropyrifos	0.120	.087	.049
DDT	0.035	.033	.021
Toxaphene	0.153	0.261	0.017
Endrin	0.154	0.149 <sup>1</sup>	0.075
Lindane	0.213	0.063	0.047
Aldrin	0.147	0.039	0.057
Dieldrin	0.176	0.069	0.068
Heptachlor	0.151	0.058	0.062
Chlordane	0.132	0.096	0.041
Endosulfan	0.233	0.110	0.069
Diazinon full	0.187	0.107 <sup>1</sup>	No fit
Diazinon low	0.281	0.042	0.074
Atrazine	0.298	0.040	0.069

<sup>1</sup> Normal fit rejected by ETX (Van Vlaardingén *et al.* 2004) and JMP (2004) analyses.

The log-triangular distribution is not the best fit in any case, although it does well with the large DDT data set. Eleven of the data sets may be described by log-normal distributions ( $p > 0.05$ , Fig. 2.1), while that of endrin and the full, bimodal diazinon set may not. Burr III distributions were fit to 12 of the data sets, but could not be fit to the full diazinon set. For toxaphene, lindane, dieldrin and heptachlor, the log-normal and Burr III fits were equally good (ratio of fit numbers  $< 1.5$ ). For six of the sets, the Burr Type III distribution fits better than either the log-triangular or log-normal (Table 2.3), while the log-normal distribution is the best fit in two cases. When the log-normal fit is better, it is only slightly better (ratio of fit numbers = 1.5-1.8). On the other hand, there are cases where the Burr III fit is much better (ratio of fit numbers = 1.6-15). Although the goodness-of-fit test used in Table 2.3 indicates that the log-normal distribution is better than the log-triangular for the full diazinon set, Fig. 2.1 indicates that this set cannot be described by a normal distribution ( $p < 0.05$ ). Thus, the Burr Type III result of “no fit” (Table 2.3) is more accurate. For the lower portion of the diazinon set, the Burr

Type III distribution is the best fit. For endrin, the only distribution that fits is the Burr Type III.

The Burr family of distributions is used in the new methodology for derivation of criteria by the SSD technique because it provides a better fit than the log-triangular distribution in all cases tested, and provides an equivalent or far better fit than the log-normal distribution in most cases. This is expected because the Burr III family of distributions approximates the log-normal and log-triangular distributions (CSIRO 2001).

### **2-3.1.2 Percentile cutoff**

To use an SSD method for criteria derivation requires selection of a percentile of the distribution as a cutoff point. This is often interpreted to mean that species lying above this point in the distribution will be protected as long as the concentration of chemical is below the concentration at the selected percentile, but species lying below the percentile would be harmed. Van Straalen & Van Leeuwen (2002) note that it is not correct to interpret the 5<sup>th</sup> percentile to mean that 5% of species will be harmed (as was argued, for example, by Lillebo *et al.* 1988, regarding the USEPA 1985 methodology). Rather, this approach is one method for derivation of a predicted no-effect concentration, and although the choice of the 5<sup>th</sup> percentile is a purely a pragmatic one, it has been validated by field studies. Solomon *et al.* (2001), note that any percentile may be chosen as long as it can be validated against knowledge and understanding of ecosystem structure and function.

The USEPA rationale for choosing the 5<sup>th</sup> percentile is simply that criteria values derived using the 10<sup>th</sup> or 1<sup>st</sup> percentiles seemed too high and too low, respectively, and since the 5<sup>th</sup> falls between those, it was selected (Stephan 1985). By the USEPA methodology (USEPA 1985; 2003f) chronic criteria are derived directly from the 5<sup>th</sup> percentile of maximum acceptable toxicant concentrations (MATC) values. Acute criteria are derived from EC<sub>50</sub> or LC<sub>50</sub> data. Since 50% effect is not acceptable, the 5<sup>th</sup> percentile values are divided by a safety factor of 2 to arrive at the final acute criterion value. As with the 5<sup>th</sup> percentile, the factor of 2 was chosen without rigorous justification. Nonetheless, studies have shown good agreement between USEPA criteria and no-effect concentrations determined in experimental stream studies (USEPA 1991). The Dutch guidelines (RIVM 2001) use the 5<sup>th</sup> percentile for derivation of environmental limits. Specific reasons for this choice are not given, but the 5<sup>th</sup> percentile has been validated against field NOECs in studies by Emans *et al.* (1993) and Okkerman *et al.* (1993). The Australia/New Zealand guidelines (ANZECC & ARMCANZ 2000) consider the question more rigorously, but still arrive at the 5<sup>th</sup> percentile level for the simple reasons that it works well in the Dutch guidelines (RIVM 2001) and it gives criteria that agree with NOEC values from multi-species tests. The reason for not regularly using a lower percentile is that the uncertainty is very high in the extreme tail of the distribution and the uncertainty can contribute more to derived criteria than the data. However, the Australia/New Zealand guidelines do use the 1<sup>st</sup> percentile as a default value for high conservation ecosystems, for bioaccumulative substances, and for cases where an important species is not protected at the 5<sup>th</sup> percentile level. To provide further

information to water quality managers in Australia/New Zealand, other percentile levels are also calculated so that criteria are given based on the 1<sup>st</sup>, 5<sup>th</sup>, 10<sup>th</sup> and 20<sup>th</sup> percentiles.

Other researchers have also found good correlation between criteria derived from the 5<sup>th</sup> percentile of single-species SSDs and NOECs determined in multi-species tests (Hose & Van Den Brink 2004; Maltby *et al.* 2005; Versteeg *et al.* 1999). On the other hand, Zischke *et al.* (1985) found that a laboratory-derived criterion concentration of pentachlorophenol was not protective of invertebrates and fish in outdoor experimental channels. Maltby *et al.* (2005) determined that concentrations of pesticides derived from the 5<sup>th</sup> percentile of species sensitivity distributions with 95% confidence was protective of species in freshwater ecosystems, but concentrations derived with 50% confidence were not protective and required application of a safety factor.

The 5<sup>th</sup> percentile SSD cutoff, which has been validated against multi-species NOECs in many cases, is a level that balances the desire to select a percentile near zero with the need to avoid utilizing the highly uncertain tails of the distributions. The new methodology will use the 5<sup>th</sup> percentile, but, since a few studies have shown this level to be underprotective, criteria derived from this value will be evaluated against available data from tests with multi-species, ecosystem, sensitive species and threatened or endangered species. If evidence suggests that the 5<sup>th</sup> percentile will not be protective, criteria may be adjusted downward. The recommended means of making such an adjustment is to use either a lower 95% confidence limit estimate of the 5<sup>th</sup> percentile (see discussion in section 2-3.1.3), or a median or 95% confidence limit estimate of the 1<sup>st</sup> percentile.

### **2-3.1.3 Level of confidence**

With SSD methods it is necessary to decide what level of certainty is desired in the resulting concentration. The USEPA approach (USEPA 1985; 2003f) does not provide a means to determine levels of confidence for derived criteria; all are derived as the median estimate of the 5<sup>th</sup> percentile, meaning that the true value may be greater or less than the estimated value with equal probability. All other SSD methodologies result in a criterion derived from a specified percentile level and a specified level of confidence. Uncertainty in an extrapolated value is due to the risk that the extrapolated value is wrong (Aldenberg & Slob 1993). The distribution around the extrapolated value can be used to determine lower boundaries for the extrapolated value (Aldenberg & Slob 1993; Kooijman 1987; Van Straalen & Denneman 1989; Wagner & Lokke 1991). By evaluating this uncertainty, it is possible to state that the true 5<sup>th</sup> percentile value falls above (or below) the extrapolated value with, say, a 50%, 90%, 95% or other level of certainty. While all of these confidence levels may be calculated, the most statistically robust is the 50%, or median, estimate (ANZECC & ARMCANZ 2000; EVS 1999; Fox 1999). In cases where there is evidence that a median 5<sup>th</sup> percentile estimate is will not be adequately protective, a lower 95% confidence limit estimate of the 5<sup>th</sup> percentile may be used instead. Variability in the tails of the distributions tend to compound, rather than clarify, uncertainties. Ultimately, the selection of certainty levels is a policy decision, but one that can be informed by understanding the limitations of values derived from

distributional tails. The new methodology presents a method for derivation of criteria with multiple levels of certainty so that environmental managers can choose values that best suit their needs.

#### **2-3.1.4 Aggregation of taxa and outliers**

As discussed in section 2-3.1.1, one challenge in the use of SSDs is to fit the data to an appropriate distribution prior to extrapolation. One way to achieve a better fit is to break data into groups rather than to pool it all together in one SSD. Data may be grouped according to toxicant mode of action, habitat (e.g., lentic vs. lotic), reproductive strategy or life cycle (Solomon & Takacs 2002). The Phase I report (TenBrook & Tjeerdema 2006) concluded that it is important to include all species in the criteria derivation procedure. However, it is reasonable, especially in construction of SSDs, to separate species into groups if multimodal distributions are evident. Similarly, it is reasonable to exclude statistical outliers from a data set if distributional assumptions cannot be met. On the other hand, if there is no statistically significant difference between apparent groups (e.g., vertebrates and invertebrates, or plants and animals), or no statistically significant outliers, then the data should be pooled for criteria derivation.

#### **2-3.1.5 Comparison of methods**

Despite giving similar results, and deriving protective criteria, the various SSD methods do not have similar theoretical bases. Among methods currently used throughout the world, that of the USEPA (1985; 2003f) seems to be most often criticized. Typical criticisms are succinctly stated by the authors of the Australia/New Zealand guidelines (ANZECC & ARMCANZ 2000) who note that the USEPA (1985) data requirements are too stringent, that there is no biological basis for selecting a triangular distribution, that not all of the data are used, and that it assumes that a threshold toxicity value exists. Another problem is that the USEPA (1985) methodology derives criteria with no associated confidence levels. Thus, there is good reason to consider adopting a different SSD method for the new methodology.

Two widely used SSD techniques are those of RIVM (2001) and the USEPA (1985; 2003f). The ANZECC & ARMCANZ (2000) technique represents an improvement over RIVM (2001) in that it provides a way to fit distributions to data sets (a technique supported by OECD (a technique supported by OECD 1995)). In the following sub-sections these three techniques are compared using the data in Table 2.1. All three of the presented SSD methods are easy to use. The USEPA (1985; 2003f) method lends itself to hand or spreadsheet calculation, while computer programs are available for the RIVM (2001) and ANZECC & ARMCANZ (2000) methods. For each model, assumptions are stated, and equations are shown or described. Results of running all models with all data sets are given in Table 2.4.

### 2-3.1.5.1 Assumptions common to all models

Several assumptions apply to all SSD models and so are given here:

- 1) Surrogate species are good representatives of species of concern;
- 2) Protecting species from direct adverse effects will also protect them from indirect adverse effects;
- 3) Effects that occur on a species in laboratory tests will generally occur on the same species in comparable field situations;
- 4) Extrapolation of the 5<sup>th</sup> percentile of single-species toxicity values will produce a value that is protective of the all species in an ecosystem;
- 5) Protecting the most sensitive species will protect all species in an ecosystem.

### 2-3.1.5.2 USEPA (1985; 2003f)

To calculate the final acute value (FAV; the 5<sup>th</sup> percentile estimate), the SMAVs are ordered from highest to lowest and assigned ranks (R) from 1 to N. For each SMAV a cumulative probability (P) is calculated as  $P = R/(N+1)$ . The four SMAVs nearest to  $P = 0.05$  are selected (for data sets with fewer than 59 SMAVs, this will always be the four lowest values in the set). Note that the USEPA (1985; 2003f) SSD method is defined in terms of genus mean acute values (GMAVs), but, as discussed in section 2-2.7, species mean acute values (SMAVs) are used in the new methodology. Thus, for this comparison, SMAVs are substituted for GMAVs.

Using the selected SMAVs and P values, the FAV is calculated as follows (see Erickson & Stephan 1988 for derivation):

$$s^2 = \frac{\sum((\ln SMAV)^2) - ((\sum(\ln SMAV))^2 / 4)}{\sum(P) - ((\sum(\sqrt{P}))^2 / 4)} \quad (2.9)$$

$$L = (\sum(\ln SMAV) - s(\sum(\sqrt{P}))) / 4 \quad (2.10)$$

$$A = s(\sqrt{0.05}) + L \quad (2.11)$$

$$FAV = e^A \quad (2.12)$$

Where:

$s^2$  = variance of lowest four values in the data set

SMAV = species mean acute value

P = percentile rank of datum

L is as defined in equation (2.8)

A is as defined in equation (2.9)

FAV = final acute value; the 5<sup>th</sup> percentile estimate

e = base of the natural logarithm

The final chronic value (FCV) may be derived in the same manner if enough chronic data are available, however, the FCV is typically derived by application of an acute-to-chronic ratio (ACR; section 2-3.2.3.2) to the FAV.

Assumptions specific to this model:

- 1) Aquatic ecosystems can tolerate some stress and occasional adverse effects, therefore protection of all species at all times and places is not necessary;
- 2) Data sets represent independent random samples from symmetrical log-triangular distributions;
- 3) Using only the four values nearest the 5<sup>th</sup> percentile eliminates problems that arise when data sets do not meet the log-triangular distribution assumption;
- 4) No species succumbs to infinitesimal, or tolerates infinite, concentrations of toxicant (Erickson & Stephan 1988).

Minimum data required: 8

### **2-3.1.5.3 (RIVM 2001) formerly (MHSPE 1994)**

Environmental risk limits (ERLs; 5<sup>th</sup> percentile estimates) are derived using the SSD method of Aldenberg & Jaworska (2000). That is, HC<sub>p</sub> values (hazardous concentrations affecting p% of species) are calculated based on a log-normal SSD. Cumulative probabilities (P) for this procedure are calculated as  $P = (R-0.5)/N$ , where R is the rank with data ordered from lowest highest, and N is the number of data. The HC<sub>5</sub> and HC<sub>50</sub> are calculated as:

$$\log HC_p = \bar{x} - k \cdot s \quad (2.13)$$

Where:

HC<sub>p</sub> = Hazardous concentration for p% of species

$\bar{x}$  = mean of log-transformed NOEC data

k = extrapolation constant depending on percentile, level of certainty and sample size (Table 1 in Aldenberg & Jaworska 2000)

s = standard deviation of log-transformed data

Assumptions specific to this model:

- 1) Data sets represent independent random samples from symmetrical log-normal distributions;
- 2) No toxicity thresholds exist.

Minimum data required: 4

A computer program called ETX 2.0 is available for making these calculations (Van Vlaardingen *et al.* 2004); available for free at <http://www.rivm.nl/rvs/overig/risico/methoden/ETX.jsp>.

#### 2-3.1.5.4 ANZECC & ARMCANZ (2000)

The Australian/New Zealand guidelines use the same method as the Dutch, but with a curve-fitting procedure that overcomes the problem of data that do not fit an assumed distribution. Using the program BurrliOZ v. 1.0.13 (Campbell *et al.* 2000; CSIRO 2001), which is available for free at <http://www.cmis.csiro.au/Envir/burrlioz/>, data are first fit to a Burr III distribution (Burr 1942, discussed in section 2-3.1.1). As in the Dutch procedure, cumulative probabilities (P) for Burr III distributions are calculated as  $P = (R-0.5)/N$ , where R is the rank with data ordered from lowest highest, and N is the number of data.

After an appropriate distribution is chosen (either the Burr III or one of the limiting distributions), the median 5<sup>th</sup> percentile value is calculated from:

For Burr III:

$$PC(q) = \frac{b}{\left[ \left( \frac{1}{1-q} \right)^{\frac{1}{k}} - 1 \right]^{\frac{1}{c}}} \quad (2.14)$$

Where:

$PC(q)$  is the protecting concentration that will protect q% of species; thus, the 5<sup>th</sup> percentile is calculated by setting  $q = 95$ ;  
 $q$  = percent of species to protect;  
 $b, c, k$  are fit parameters.

For reciprocal Weibull:

$$PC(q) = (-\alpha / \ln(1-q))^{\frac{1}{\beta}} \quad (2.15)$$

Where:

$PC(q)$  and  $q$  are as described for Burr III;  
 $\alpha$  and  $\beta$  are fit parameters.

For reciprocal Pareto:

$$PC(q) = x_0(1 - q)^{1/\theta} \quad (2.16)$$

Where:

$PC(q)$  and  $q$  are as described for Burr III;  
 $x_0$  and  $\theta$  are fit parameters.

Assumptions specific to this model:

- 1) No toxicity thresholds exist.
- 2) Data sets represent independent random samples from symmetrical Burr Type III distributions.

Minimum data required: 5

One advantage of this method over the USEPA (1985; 2003f) and RIVM (2001) methods is that if a Burr III distribution, or one of the limiting distributions, cannot be fit to a data set, then no 5<sup>th</sup> (or other) percentile value can be calculated. It may still be possible to derive a 5<sup>th</sup> percentile value if modification of the data set is warranted due to bimodality or the presence of outliers. Using either the USEPA and RIVM methods, an unwitting user can determine a 5<sup>th</sup> percentile value whether or not the distributional assumptions are met. Such values would be unreliable.

### 2-3.1.5.5 Results and discussion of SSD model comparison

Table 2.4 shows the 5<sup>th</sup> percentile values derived for each of 12 pesticides using each of the three SSD methods. The USEPA method results in one value, the median estimate of the 5<sup>th</sup> percentile, while each of the others (ANZECC & ARMCANZ 2000; RIVM 2001) result in a median estimate, as well as a lower 95<sup>th</sup> percentile estimate. The true 5<sup>th</sup> percentile value has an equal certainty of falling above or below the median estimates, but has a 95% certainty of falling above the lower 95<sup>th</sup> percentile estimate. Other levels of certainty may be calculated with the ANZECC & ARMCANZ (2000) method as well, but these calculations become less and less reliable in the extreme tails of the distribution.

Many of the values derived by the various methods are similar. For example, the median 5<sup>th</sup> percentile values derived for DDT, toxaphene, aldrin, dieldrin, heptachlor, diazinon (low), and atrazine are within a factor of 2 by all three methods. The endrin median 5<sup>th</sup> percentile value is 2.5-2.75 times lower by the RIVM (2001) method compared to the other two, but that data set violated the assumption of log-normality, thus the RIVM (2001) method is not a good choice for the endrin data. The chlorpyrifos median 5<sup>th</sup> percentile value determined by the RIVM (2001) method is a factor of 4.6-6.6 lower than those obtained by the other methods. Although the chlorpyrifos data fit a normal distribution, the box plot in Fig. 2.1 A reveals that the distribution is right-skewed, which would cause the 5<sup>th</sup> percentile value to fall at a lower value than if the distribution were not skewed. The values obtained by USEPA (1985; 2003f) and ANZECC & ARMCANZ (2000) for endrin are very similar, in spite of the skewness of

the data.. For lindane, the median 5<sup>th</sup> percentile value obtained from the USEPA method is less than half that obtained by the other two methods. This is likely due to the presence of a low outlier (see Fig. 2.2) in the lindane set (outliers were left in for this analysis since they are part of the final USEPA criteria sets). As discussed in the Phase I report

Table 2.4. Results of analyzing pesticide data sets (Table 2.1) with SSD methods of USEPA (1985), the Netherlands (RIVM 2001), and Australia/New Zealand (ANZECC & ARMCANZ 2000); all values represent 5<sup>th</sup> percentile values (not criteria) expressed in µg/L; A/NZ = Australia/New Zealand; NC = not calculable.

<b>Pesticide</b>	<b>USEPA (median)</b>	<b>RIVM (median)</b>	<b>RIVM (95<sup>th</sup>)</b>	<b>A/NZ (median)</b>	<b>A/NZ (95<sup>th</sup>)</b>	<b>Lowest Value in Data Set<sup>1</sup></b>
Chlopyrifos	0.033	0.005	0.0003	0.023	0.018	0.035
DDT	0.845	0.659	0.322	0.97	0.61	0.36
Toxaphene	1.21	1.15	0.590	1.54	1.04	0.8
Endrin	0.20	0.081	0.027	0.22	0.15	0.15
Lindane	2.65	6.82	2.77	7.4	2.18	10
Aldrin	3.76	3.45	1.54	4.59	3.52	4
Dieldrin	2.67	1.62	0.415	3.10	2.22	2.5
Heptachlor	0.768	1.22	0.322	0.67	0.07	0.9
Chlordane	2.10	5.65	2.11	5.21	1.64	3
Endosulfan	0.183	0.188	0.017	0.44	0.24	0.34
Diazinon All	0.449	0.460	0.043	NC	NC	0.3773
Diazinon Low	0.260	0.251	0.036	0.41	0.25	0.3773
Atrazine	2,514	2,276	572	3,233	2,477	3,000

<sup>1</sup>From Table 2.1

(TenBrook & Tjeerdema 2006) and GLEC (2003), low outliers tend to lower the 5<sup>th</sup> percentile values derived by the USEPA method. The same phenomenon occurs for chlordane, where the USEPA value is less than half that of the other two. For endosulfan, the ANZECC & ARMCANZ (2000) method produces a median value that is more than twice the values obtained by the other two methods. In this case, figure 2.1 indicates a high outlier, which is handled better by the Burr III family of distributions than either the log-triangular or log-normal (Table 2.3).

An important consideration in assessing the various methods is whether or not they will produce protective criteria. The acute criterion will be derived by dividing the 5<sup>th</sup> percentile value by 2, so it is of interest to compare the lowest value in each data set with the resulting criterion. The last column of Table 2.4 shows the lowest value from each data set. For most of the pesticides, criteria derived from any of the median 5<sup>th</sup> percentile values would be lower than the lowest value. However, for DDT the median values derived by the USEPA (1985; 2003f) and ANZECC & ARMCANZ (2000) methods would result in criteria of 0.42 and 0.48 µg/L, respectively, which are higher than the lowest value of 0.36 µg/L. In such a case, the Australia/New Zealand approach provides the option of using the 95<sup>th</sup> percentile value to produce a number below the lowest value. By the USEPA method, an additional safety factor would have to be

applied to derive a protective criterion. The new methodology includes a step of checking derived criteria against available data and adjusting the criteria if they do not appear to be protective (section 2-3.6.1).

#### **2-3.1.5.6 SSDs in the new methodology**

The ANZECC & ARMCANZ (2000) methodology, utilizing the BurrliOZ program offers the best combination of data requirements, appropriate distributional assumptions, and flexibility in choosing protection and confidence levels. With some exceptions, median 5<sup>th</sup> percentile values obtained by this method are comparable to those obtained by the USEPA (1985; 2003f) methodology. The differences are likely due to the effects of outliers in the chlordane, lindane and endosulfan data sets. The new methodology uses the ANZECC & ARMCANZ (2000) SSD methodology utilizing the BurrliOZ program to calculate 5<sup>th</sup> percentile values with 50%, 95% and 99% confidence that the true 5<sup>th</sup> percentile value lies above the derived value. The acute criterion derived by the SSD methodology is equal to the median 5<sup>th</sup> percentile value divided by 2. The safety factor of 2 is applied because the SSD is constructed with toxicity values that indicate a 50% effect level. A 5<sup>th</sup> percentile value derived from chronic data is the chronic criterion without further adjustment.

#### **2-3.2 AF methodology**

When fewer than five data from an appropriate assortment of taxa are available, the SSD method cannot be used for criteria derivation. In such cases, an assessment factor (AF) method must be used. As discussed in Phase I (TenBrook & Tjeerdema 2006), assessment factors are recognized as a conservative approach for dealing with uncertainty in assessing risks posed by chemicals (Chapman *et al.* 1998). Assessment factors (also called safety factors, acute-to-chronic ratios, application factors, extrapolation factors) are usually applied to account for a wide range of possible effects and situations for which no data exist, including: lack of tests with relevant species; persistence or bioaccumulative potential of substances; genotoxic potential; laboratory to field extrapolation; acute-to-chronic extrapolation; variations in mesocosm types for multispecies tests; absence of most sensitive species in multispecies tests; mixture effects; experimental variability, and; lack of data (Phase I, TenBrook & Tjeerdema 2006). Further factors may be applied in some cases based on the professional judgment of the risk assessor. In all cases, the more toxicity data that are available for species of different trophic levels, different taxonomic groups, and different lifestyles, the smaller the applied factor.

Table 2.5 summarizes safety factors used by the methodologies reviewed by TenBrook & Tjeerdema (2006). They range from 1-1000 or more, and, with the exception of ACRs, are primarily based on the premise that 10 is a widely used factor in toxicology and should be applied for each step of an extrapolation from data at hand to real-world application.

Table 2.5. Assessment factors used in existing methodologies.

Methodology	Range of factors	Applied to	Reference
Australia/ New Zealand	Acute: NA <sup>1</sup> Chronic: 10-1000 Default ACR: 10+	Acute: NA Chronic: NOEC (single- or multispecies)	ANZECC & ARMCANZ (2000)
California (draft)	Acute: NA Chronic: 10	Acute: NA Chronic: LOEC	Lillebo <i>et al.</i> (1988)
Canada	Acute: NA Chronic: 10-100+ Default ACR: 10	Acute: NA Chronic: LC/EC <sub>50</sub> , LOEC	CCME (1999)
European Union/ Denmark	Acute: NA Chronic: 1-1000 Default ACR: 10	Acute: NA Chronic: LC/EC <sub>50</sub> , NOEC, QSAR estimates	OECD (1995); Samsoe-Petersen & Pedersen (1995); ECB (2003)
France	Acute: NA Chronic: 1-1000	Acute: NA Chronic: LC/EC <sub>50</sub> , NOEC	Lepper (2000)
Germany	Acute: NA Chronic: 10-1000 Default ACR: 10	Acute: NA Chronic: LC/EC <sub>50</sub> , NOEC	Irmer <i>et al.</i> (Irmer <i>et al.</i> 1995)
Great Lakes	Acute: 4.3-21.9 Chronic: NA Default ACR: 2 for FACR <sup>2</sup> 18 for SACR <sup>3</sup>	Acute: LC/EC <sub>50</sub> Chronic: NA	USEPA (2003f)
North Carolina	Acute: 3 Chronic: 1 Default ACR: 100 for t <sub>1/2</sub> > 96 h 20 for t <sub>1/2</sub> < 96 h	Acute: LC <sub>50</sub> Chronic: MATC	North Carolina DENR (2003)
South Africa	Acute: 1-100 Chronic: 1-1000	Acute: LC <sub>50</sub> Chronic: Final Acute Value	Roux <i>et al.</i> (1996)
Spain	Acute: NA Chronic: 1-100+	Acute: NA Chronic: LC/EC <sub>50</sub> , NOEC	Lepper (2000)
The Netherlands	Acute: NA Chronic: 1-1000	Acute: NA Chronic: LC/EC <sub>50</sub> , NOEC	RIVM (2001)
United Kingdom	Acute: 2-10 Chronic: 1-100	Acute: LC/EC <sub>50</sub> Chronic: NOEC	Zabel & Cole (1999)
USEPA	Acute: 2 Chronic: NA Default ACR: 2	Acute: Final Acute Value Chronic: NA	USEPA (1985)
USEPA	Acute: 100-1000 Chronic: 10 Default ACR: 10	Acute: LC/EC <sub>50</sub> Chronic: MATC	Nabholz (1991)

<sup>1</sup> Not applicable

<sup>2</sup> Final acute-to-chronic ratio

<sup>3</sup> Secondary acute-to-chronic ratio

### 2-3.2.1 Appropriate use of assessment factors

An important point to keep in mind in using assessment factors is that application of empirically based factors to toxicity data does not quantify uncertainty, but does reduce the probability of underestimating risk. At the same time, the use of AFs also greatly increases the possibility of overestimating risk (Chapman *et al.* 1998). It is worth restating and evaluating some of the specific points by Chapman *et al.* (1998) regarding the use of assessment factors: 1) data supercede extrapolation; that is, if data are available, they should be used; 2) extrapolation requires context; use of safety factors should be based on existing scientific knowledge; 3) extrapolation is not fact; estimates of effect levels obtained using safety factors should only be used as screening values, not as threshold values; 4) extrapolation is uncertain; safety factors should encompass a range rather than being a single value; 5) all substances are not the same; safety factors should be scaled relative to different substances, potential exposures and nature of effects; and 6) unnecessary overprotection is not useful; safety factors for individual extrapolation steps should not exceed 10, and may be much lower.

Each of the points raised by Chapman *et al.* (1998) need to be evaluated in the context of water quality criteria derivation, which is not the same as ecological risk assessment. Ecological risk assessment seeks to estimate risk based on a specific set of exposure and effects data, usually for a specific site. Numeric water quality criteria are derived considering only effects data along with a few exposure factors that directly affect toxicity. Criteria must be protective of aquatic life, and therefore must err on the side of conservatism when data are lacking. Criteria may be site-specific, but more often must be valid for a range of sites. When data are lacking, criteria will likely represent an over-estimation of risk. More data are required for extrapolated protective values to approach true values. With this in mind, consider each of the points raised by Chapman *et al.* (1998).

1) Data supercede extrapolation; that is if data are available, they should be used.

This point simply reinforces the idea that more data will result in better estimates of risk, and therefore, better estimates of appropriately protective criteria.

2) Extrapolation requires context; use of safety factors should be based on existing scientific knowledge.

This statement is true, but somewhat contradictory. In fact, safety factors are used to fill gaps in scientific knowledge. With the exception of measured acute-to-chronic ratios (ACRs; discussed in section 2-3.2.3.2), many existing criteria derivation methodologies use standardized factors of 10, 20 and 100, despite lack of supporting data (Chapman *et al.* 1998). Further, safety factors are often based on policy rather than empirical science. One methodology that has made use of existing scientific knowledge is that of the Great Lakes (USEPA 2003f), which uses empirically derived factors and

default ACRs. Details of the Great Lakes factors are discussed further in section 2-3.2.3.1 this approach is adapted for the new methodology.

3) Extrapolation is not fact; estimates of effect levels obtained using safety factors should only be used as screening values, not as threshold values.

All criteria are extrapolated values, and while those obtained by application of large factors to small data sets have a high level of conservatism and uncertainty, it is a policy decision whether or not to use them as threshold values. The new methodology includes an AF method to be used for data sets that are inadequate for SSD analysis. Less conservative, more certain numbers may be derived if more data become available.

4) Extrapolation is uncertain; safety factors should encompass a range rather than being a single value.

With the exception of the German methodology (Irmer *et al.* 1995), all existing methodologies utilize ranges of factors, and in all cases factors get smaller as data sets get larger. The AF procedure in the new methodology includes a range of factors.

5) All substances are not the same; safety factors should be scaled relative to different substances, potential exposures and nature of effects.

As noted in the response to 4), ranges of factors are used by nearly all existing methodologies. Among the reasons for using larger factors are lack of data, persistence, bioaccumulative potential, mixture toxicity, and potential for genotoxic effects. In effect, assessing factors for each of these variables achieves the scaling suggested by Chapman *et al.* (1998). Another example of how this is done is that the state of North Carolina utilizes different default ACRs depending on the half-life of the chemical of concern (North Carolina DENR 2003, shown in Table 2.5). The new methodology includes other means of addressing bioaccumulative potential, bioavailability and mixture toxicity and so does not incorporate these elements into assessment factors. Genotoxic effects are of concern in human health risk assessment, but not for protection of aquatic life (see section 2-2.1.1.3 regarding non-traditional endpoints), and thus are not incorporated into assessment factors either.

6) Unnecessary overprotection is not useful; safety factors for individual extrapolation steps should not exceed 10, and may be much lower.

This statement regarding overprotection is true, but should not be addressed by limiting the size of assessment factors. Chapman *et al.* (1998) found ACRs ranging from 1-20,000. Thus, for acute-to-chronic extrapolation, factors should definitely not be limited to 10. Also, empirically derived factors, such as those in the Great Lakes methodology (USEPA 2003f) should not be limited to 10. The best way to minimize overprotection is to expand available acute and chronic data sets.

### 2-3.2.2 Toxicity values

One of the choices to be made in using the AF method is what kind of toxicity data to use. For the new methodology, separate acute and chronic criteria are derived. Therefore, acute criteria are derived from LC<sub>50</sub> or EC<sub>50</sub> data. The situation is not so simple for chronic criteria. As shown in Table 2.5 most methodologies from the United States (Nabholz 1991; North Carolina DENR 2003; USEPA 1985; 2003f) use MATC values, while most other methodologies from around the world use NOEC values for derivation of chronic criteria; two utilize LOEC values (CCME 1999; Lillebo *et al.* 1988). The Netherlands (RIVM 2001) and the EU risk assessment technical guidance document (ECB 2003) accept EC<sub>10</sub> values to represent NOECs. As discussed in section 2-2.1.1.2 hypothesis test results can be used in criteria derivation, as long as results are evaluated with respect to test design, minimum significant difference (type II error), and effect levels at the NOEC and LOEC. As discussed in section 2-2.1.1.2, the MATC is the hypothesis test value used in the new methodology.

### 2-3.2.3 Magnitude of factors

As shown in Table 2.5, the magnitude of assessment factors ranges widely among existing methodologies. Aside from measured ACRs, little to no justification is given for the magnitude of most assessment factors (Phase I, TenBrook & Tjeerdema 2006). The exception is the Great Lakes methodology (USEPA 2003f), which utilizes final acute value factors and default acute-to-chronic ratios that are empirically based and theoretically supported (Host *et al.* 1995). These factors are discussed further in the following sections and the methods of Host *et al.* (1995) are used to derive factors for the new methodology.

#### 2-3.2.3.1 Acute factors

Most AF methods utilize standard factors that get larger and larger as more extrapolation steps are required. Such factors are widely used despite having little scientific basis (Chapman *et al.* 1998). The acute toxicity factors used in the Great Lakes methodology are based on work by Host *et al.* (1995) in which they described both empirical and theoretical methods for derivation of factors using data sets for all kinds of chemicals and based on log-triangular data distributions. Their methods were adapted to derive acute factors for the new methodology. The major differences in the approach used here are the use of only pesticide data (vs. all kinds of contaminants), and the use of Burr III distributions (vs. log-triangular distributions). This method requires that full data sets be available for several compounds, thus at this point it is only possible to derive acute (vs. chronic) factors by this method.

The goal of this process is to estimate a 5<sup>th</sup> percentile value when fewer than 5 data are available. The magnitude of the assessment factors needs to be set to achieve this. The factors are used as divisors for the lowest value in data sets that contains only 1-4 values.

As per Host *et al.* (1995), the following procedure was applied to each individual pesticide data set (from Table 2.1):

- 1) Ninety-nine (99) subsets of 5 values were randomly selected with the restriction that the first value had to be for an invertebrate from the genus *Daphnia*, *Ceriodaphnia*, or *Simocephalus*. Each successive sample had to fulfill a different requirement in the SSD minimum data set (section 2-2.6). The selection of which family to use for the second and subsequent values in each subset was made randomly;
- 2) For each subset of 5 values, subsets of 1-4 values were also created, resulting in 99 subsets of 1-5 values;
- 3) The lowest acute value in each subset of size 1-5 values was used as the numerator for calculating the assessment factor;
- 4) Each of the 99 5-sample subsets was used to generate 5<sup>th</sup> percentile values using BurrliOZ v. 1.0.13 (Campbell *et al.* 2000; CSIRO 2001).;
- 5) The geometric mean of the 99 5<sup>th</sup> percentile values was used as the denominator for calculating the assessment factor;
- 6) This procedure yielded 99 factors for each subset size;
- 7) The 95<sup>th</sup> percentile of the 99 factors was determined for each subset size.

This procedure was followed for chlorpyrifos, DDT, toxaphene, endrin, lindane, aldrin, dieldrin, heptachlor, chlordane, and endosulfan. Atrazine was not included since the data set is from a draft document. Diazinon was not included because the above procedure could not be applied to the data set. The bimodality of the full diazinon set resulted in many subsets that could not be fit to a Burr Type III distribution. The lower portion of the diazinon data did not include representatives from all five families required for the minimum SSD data set.

In accordance with USEPA (2003f), 95<sup>th</sup> percentile factors (from step 7, above) for all pesticides were compiled and the median of those factors for each subset size was selected to be the summary assessment factor (i.e., a factor to apply to all pesticides; Table 2.6). The summary factors for each sample size are shown in Table 2.7 along with the estimated 5<sup>th</sup> percentile toxicity values obtained for each pesticide using the summary factors together with the geometric mean lowest value for each subsample size. Diazinon was not used to derive factors, but the diazinon data set was used to estimate 5<sup>th</sup> percentile toxicity values using the factors. In all cases, the 5-sample factor produced an estimated 5<sup>th</sup> percentile value that is comparable to, or below, the median 5<sup>th</sup> percentile value determined from applying the SSD procedure to the full data set. The 4-, 3-, and 2-sample factors all produced estimated 5<sup>th</sup> percentile values below the value generated by the SSD method. Most of the 1-sample factors produced similar results. The exceptions are endrin and endosulfan for which the 1-sample factor overestimated the 5<sup>th</sup> percentile

value by 8-10-fold. This occurred because, for those two pesticides, the family Daphniidae was the most tolerant and the 1-sample subsets had very high toxicity values. To ensure that criteria derived by the assessment factor method are protective, even when based on a single toxicity value, an additional factor of 10 should be assessed. As shown in Table 2.6, this brings the endrin and endosulfan 1-sample values very near the SSD median value. The additional factor of 10 will lead to very conservative criteria in cases where Daphnids are among the most sensitive species, but such conservatism is reasonable when relying on a single datum to make predictions for an ecosystem.

Table 2.6. Compilation of 95<sup>th</sup> percentile of factors for subsets of 1-5 samples; the median values in the last row are the summary factors for each sample size.

<b>Subset size</b>	<b>5</b>	<b>4</b>	<b>3</b>	<b>2</b>	<b>1</b>
Chlopyrifos	5.56	11.81	52.95	52.95	52.95
DDT	4.08	4.08	4.08	4.08	4.08
Toxaphene	3.86	5.93	8.01	8.01	8.01
Endrin	3.65	5.1	8.49	148.49	1633.43
Lindane	4.03	4.12	4.37	18.83	61.48
Aldrin	5.13	5.13	5.32	5.32	5.32
Dieldrin	3.24	3.24	7.64	63.86	74.95
Heptachlor	3.48	16.3	32.71	97.02	97.02
Chlordane	2.23	3.86	5.94	8.62	8.62
Endosulfan	2.02	13.66	22.04	522.68	1550.24
Median	3.8	5.1	7.8	36	57

Table 2.7. Median 5<sup>th</sup> percentile toxicity value estimates for sample sizes of 1-5 acute toxicity values using summary pesticide assessment factors. All values are in µg/L.

<b>Sample size</b>	<b>5</b>	<b>4</b>	<b>3</b>	<b>2</b>	<b>1</b>	<b>1</b>	<b>SSD 5<sup>th</sup> percentile (median)</b>	<b>Lowest value in data set<sup>1</sup></b>
<b>Factor</b>	<b>3.8</b>	<b>5.1</b>	<b>7.8</b>	<b>36</b>	<b>57</b>	<b>57 x 10</b>		
Chlopyrifos	0.01	.012	.009	.003	0.002	0.0002	0.022	.035
DDT	0.25	0.20	0.13	0.03	0.02	0.002	0.97	0.36
Toxaphene	0.68	0.61	0.56	0.18	0.22	0.022	1.54	0.8
Endrin	0.10	0.09	0.08	0.03	1.80	0.18	0.22	0.15
Lindane	4.0	3.4	2.9	1.1	9.2	0.92	7.4	10
Aldrin	1.8	1.5	1.3	0.40	0.48	0.048	4.59	4
Dieldrin	1.2	1.0	0.82	0.40	3.5	0.35	3.10	2.5
Heptachlor	0.36	0.36	0.44	0.24	1.1	0.11	0.67	.9
Chlordane	2.2	2.1	2.0	0.63	1.0	0.10	5.21	3
Endosulfan	0.09	0.09	0.09	0.06	4.6	0.46	0.44	.34
Diazinon	0.22	0.22	0.22	0.22	0.22	0.022	0.20	.3373

<sup>1</sup>From Table 2.1

To derive an acute criterion by this method, the lowest value from an acceptable data set is divided by the appropriate factor from Table 2.6 (depending on sample size). The resulting value represents an estimate of the median 5<sup>th</sup> percentile value and is divided by 2 to determine the acute criterion. In all cases, for all pesticides shown in Table 2.6, criteria derived using the proposed factors are below the lowest values in each data set and would be expected to be protective.

#### **2-3.2.3.2 Acute-to-chronic ratios (ACRs)**

If at least five chronic data are available from five different families, the SSD method should be used to derive chronic criteria. However, when chronic data are lacking, the use of ACRs is necessary to extrapolate from acute to chronic toxicity. The ACR is calculated by dividing an acute LC/EC<sub>50</sub> value by a chronic value (e.g., MATC) derived from the same test, or from tests conducted by the same laboratory under identical conditions (USEPA 1985; 2003f). There are three basic approaches to deriving ACRs: 1) derive chemical-specific, multispecies ACRs using acute and chronic values derived from the same tests (ANZECC & ARMICANZ 2000; USEPA 1985; 2003f); 2) derive chemical-specific, multispecies ACRs using whatever chronic data are available, combined with one or more default ACR values (USEPA 2003f), and; 3) use default ACR values for all chemicals. As these approaches represent a stepwise procedure depending on available data, all are appropriate for inclusion in the new methodology.

##### **2-3.2.3.2.1 Single-chemical, multispecies ACR based on measured data**

The first approach is used in both the USEPA methodologies (USEPA 1985; 2003f) and in the Australia/New Zealand methodology (ANZECC & ARMICANZ 2000). However, only the USEPA methodologies give clear guidance for the procedure. The Great Lakes guidance, which is updated from the 1985 version, is presented here. The procedure requires acute and chronic data from organisms in at least three different families including a fish, an invertebrate, and at least one other acutely sensitive species. If there are not enough freshwater data to fulfill the ACR data requirements, then saltwater species may be used because freshwater and saltwater ACRs have been shown to be comparable (USEPA 1985) and this approach has been and accepted in numerous criteria derivations (Siepmann & Finlayson 2000; USEPA 1980a; b; c; d; 2003a; 2005a). For each chronic value (MATC) having at least one corresponding appropriate acute value, an ACR is calculated by dividing the geometric mean of all acceptable flow-through acute tests by the chronic value. Static tests are acceptable for midges, daphnids and other zooplankton. For fish, the acute test(s) should be conducted with juvenile or younger fish. For all species, the acute test(s) should be part of the same study and use the same dilution water as the chronic test. If acute tests were not conducted as part of the same study, but were conducted as part of a different study in the same laboratory and dilution water, then they may be used. If no such acute tests are available, results of acute tests conducted in the same dilution water in a different laboratory may be used. If no such acute tests are available, an ACR is not calculated by this method.

The species mean acute-to-chronic ratio (SMACR) is calculated for each species as the geometric mean of all ACRs available for that species. For some materials, the ACR seems to be the same for all species, but for other materials the ratio seems to increase or decrease as the SMAV increases. Thus the multispecies ACR can be obtained in one of three ways, depending on the data available:

1. If the SMACR seems to increase or decrease as the SMAVs increase, the ACR is calculated as the geometric mean of the ACRs for species whose SMAVs are close to the acute 5<sup>th</sup> percentile value.

The USEPA methodologies (USEPA 1985; 2003f) do not define what is meant by “SMAVs close to” the 5<sup>th</sup> percentile value. A definition for use in the new methodology can be developed based on the second approach to derivation of interspecies ACRs (item 2 below), which uses the geometric mean of SMACRs as long as they are within a factor of 10 of each other. Thus, it is reasonable to define species with “SMAVs close to” the 5<sup>th</sup> percentile as those whose SMACRs are within a factor of 10 of the SMACR of the species whose SMAV is nearest the 5<sup>th</sup> percentile value.

2. If no major trend is apparent and the ACRs for all species are within a factor of 10, the ACR is calculated as the geometric mean of all of the SMACRs.

3. If the most appropriate SMACRs are less than 2.0, and especially if they are less than 1.0, acclimation has probably occurred during the chronic test. In this situation, the final ACR should be assumed to be 2.0, so that the chronic criterion is equal to the acute criterion.

If the available SMACRs do not fit one of these cases, use the procedure described in section 2-3.2.3.2.2 to derive an ACR based partially on measured values and partially on assumed values.

#### **2-3.2.3.2.2 Single-chemical, multispecies ACR based on measured and assumed values**

If not enough data are available for calculation of an ACR by the preceding procedure, then an ACR is derived by using any available measured ACRs plus enough assumed ACRs to give a total of 3 ACRs (USEPA 2003f). For example, if no measured ACRs are available, then three assumed ACRs are used. If two measured values are available, then just one assumed value is used. The magnitude of the assumed, or default, ACR is discussed in the following section.

#### **2-3.2.3.2.3 Default ACRs**

In the Phase I report TenBrook & Tjeerdema (2006) concluded that there is no evidence that default ACR values are appropriate for pesticides in general. Nonetheless, adequate chronic data are often not available and some means of estimating an ACR is needed. The Great Lakes guidance uses a default ACR of 18 (USEPA 2003f), which

represents the 80<sup>th</sup> percentile value of all available ACRs from USEPA criteria documents (Host *et al.* 1995). This seems a reasonable approach because it is based on ACRs that have been derived from carefully reviewed studies. Some of the very high ACRs reported in the literature have been rejected by USEPA upon such review (e.g., diazinon ACRs determined by Kenaga 1982). For the new methodology the default ACR used in the Great Lakes guidance was recalculated to include only pesticide data from Host *et al.* (1995), as well as the ACR in the California Department of Fish and Game diazinon criteria document (Siepmann & Finlayson 2000) and a new chlorpyrifos value calculated by the new methodology. Table 2.8 shows this calculation. Based on this data set, a default ACR of 12.4 was calculated for the new methodology, with the following caveats: 1) if data sets collected according to this methodology lead to different ACR values, those values may be substituted into this table and the default ACR recalculated; 2) if previously calculated ACRs are shown to be invalid based on data sets collected according to this methodology, then those values should be removed and the default ACR recalculated; and 3) if additional pesticide ACR values become available, the default ACR should be recalculated.

The chronic criterion is calculated by dividing the acute 5<sup>th</sup> percentile value (derived by SSD method or estimated by AF method) by the ACR (derived by one of the three methods in sections 2-3.2.3.2.1 through 2-3.2.3.2.3):

$$\text{Chronic Criterion} = 5^{\text{th}} \text{ Percentile Value} \div \text{ACR} \quad (2.16)$$

Table 2.8. Calculation of default acute-to-chronic ratio (ACR).

<b>Chemical</b>	<b>ACR</b>
Chlordane <sup>1</sup>	14
Chlorpyrifos <sup>2</sup>	2.2
Diazinon <sup>3</sup>	3.0
Dieldrin <sup>1</sup>	8.5
Endosulfan <sup>1</sup>	3.9
Endrin <sup>1</sup>	4.0
Lindane <sup>1</sup>	25
Parathion <sup>1</sup>	10
80 <sup>th</sup> percentile	12.4

<sup>1</sup> Taken from Host *et al.* (1995); originally from USEPA criteria documents.

<sup>2</sup> Derived in Chapter 4 of this report .

<sup>3</sup> Siepmann & Finlayson (2000).

### 2-3.3 Averaging periods

Criteria derived according to either the SSD or AF methods are stated in terms of how much of a chemical may be in the water without causing harm (i.e., in terms of magnitude), but without consideration of for how long (duration) or how often (frequency) that level may be exceeded without harm. Section 2-3.4 addresses the frequency component. This section explores the question of duration.

Derivation of separate acute and chronic criteria, as is done in the new methodology, provides a duration component, but criteria derived from studies conducted under constant exposure scenarios do not account for the possibility of pulsed, or otherwise uneven, exposures. Such exposures are common in the Sacramento and San Joaquin River basins (Phase I, TenBrook & Tjeerdema 2006) and criteria need to reflect that. Time-to-event models could potentially provide a way to express criteria for any given exposure duration, but as discussed in section 2-2.1.1.6 such models are not currently feasible for use in criteria derivation. The best readily usable approach for determination of an appropriate duration component is to consult the literature. This is the approach used by the USEPA (1985; 2003f) to set both acute and chronic averaging periods. The averaging period is the period of time over which the receiving water concentration is averaged for comparison with criteria concentrations (USEPA 1994). There are two aspects to consider in setting an averaging period. First is to set the period long enough such that toxicity might occur due to an exceedance, and second is to set the period short enough that the effects of concentration fluctuations on the average concentration are minimized. For example, the USEPA (USEPA 1985; 2003f) sets the acute averaging period at 1 h based primarily on the fact that ammonia exerts its effects in that time frame, but also because if the period were longer, peak concentrations would be masked in the averaging process. Similarly, the chronic averaging period of 4 days has been shown to be long enough to observe the equivalent of chronic toxicity (USEPA 2002), but short enough to minimize the effect of concentrations fluctuations (USEPA 1991). As discussed in Phase I (TenBrook & Tjeerdema 2006), the 4-day averaging period used in the USEPA methodologies is reasonable and is used in the new methodology. Since the 1-h average is based on ammonia toxicity and may not be appropriate for pesticide criteria. This is explored in the following section.

### **2-3.3.1 Acute averaging period**

To establish an appropriate acute averaging period for the new methodology, a literature review was conducted to try to determine the time-course of acute pesticide toxicity. While many studies report pesticide effects after very short toxicant exposures, only a handful consider environmentally relevant concentrations. Often researchers expose organisms at concentrations many-fold higher than 96h-LC<sub>50</sub>s determined in continuous exposure tests, or at concentrations higher than would ever be expected in the environment (e.g., Barry *et al.* 1995a; Barry *et al.* 1995b; Jarvinen *et al.* 1988; Naddy *et al.* 2000; Peterson *et al.* 2001).

Among studies that consider environmentally relevant concentrations, Cold & Forbes (2004) report adverse effects on survival and reproduction in *Gammarus pulex* after 1-h pulses of esfenvalerate as low as 0.05 µg/L, with effects observed for as long as 2 weeks after the exposure. Forbes & Cold (2005) likewise report effects on larval survival and development rates of the midge *Chironomus riparius* with esfenvalerate exposures as brief as 1 h. Heckman and Friberg (2005) found similar results with pulsed exposures of streams to λ-cyhalothrin. A 1-h pulse application of lambda-cyhalothrin at ≥ 0.1 µg/L caused a nearly instantaneous increase in drift of stream macroinvertebrates,

with increases occurring within 2 h at concentrations  $\geq 0.01 \mu\text{g/L}$  (Lauridsen & Friberg 2005). In that same study, *Gammarus pulex* drift increased within 3 h after application at  $0.001 \mu\text{g/L}$ . Holdway *et al.* (1994) reported significant 96-h mortality to larval rainbowfish (*Melanotaenia fluviatilis*) with 1-h pulse exposures to fenvalerate at  $0.32 \mu\text{g/L}$ . Significant mortality occurred in 2 d to *Daphnia magna* exposed to a 24-h pulse of fenvalerate at  $3.2 \mu\text{g/L}$  (Reynaldi & Liess 2005). For the organophosphates pirimiphos-methyl and temephos Brown *et al.* (2002) reported 24-h  $\text{LC}_{50}$  values from 1-h pulse exposures of rainbowfish (*Melanotaenia duboulayi*) that were lower than estimated environmental concentrations. Schulz & Liess (2001) report reductions in emerged individuals of the insect *Limnephilus lunatus* at 154 d, as well as reduction in dry weight and reduction in biomass at 240 d after 1-h pulse exposures to fenvalerate. Sublethal responses in Schulz & Liess (2001) were observed at  $0.001 \mu\text{g/L}$  and lethal effects at  $0.1 \mu\text{g/L}$ . In tests of 1-h vs. 10-h equivalent doses of fenvalerate (measured in  $\mu\text{g h}$ ), Schulz & Liess (2000) reported long-term effects on emergence success and dry weight of caddisfly larvae, with significantly stronger effects from the stronger 1-h pulses vs. the lower level 10-h pulses. Chronic lethal and sublethal effects were observed in *Daphnia magna* after a 24-h pulse exposure of fenvalerate, with complete mortality occurring after 10 d at  $3.2 \mu\text{g/L}$  (Reynaldi & Liess 2005).

Another type of data that are useful in this analysis are the effects data from intermediate time points in standard toxicity tests. This type of data are regularly collected, but rarely reported. Several studies of acute toxicity of chlorpyrifos and diazinon with *Neomysis mercedis* (mysid), *Ceriodaphnia dubia*, and *Physa* sp. (pond snail) by the California Department of Fish and Game (CDFG 1992a; b; c; d; e; f; g; h; i; j; k; 1998a; b), and one of diazinon with *Lepomis macrochirus* (bluegill) by CIBA-GEIGY (1987) were obtained for review. All of these studies indicate that chlorpyrifos and diazinon are not particularly fast-acting toxicants, with mortality occurring at each 24-h observation period throughout the test (as opposed to only at the earliest observation period).

Based on the available pesticide literature, the 1-h acute averaging period utilized by the USEPA (1985; USEPA 2003f) is reasonable for the new methodology. This value is conservative for some pesticides that do not exert the (e.g., chlorpyrifos and diazinon), but should be protective for pyrethroids that exhibit latent effects after very short acute exposures, and for organophosphates (e.g., pirimiphos-methyl and temephos) that have been shown to exert their effects with 1-h pulse exposures of environmentally relevant magnitude.

To summarize, criteria derived by the new methodology include an expression of allowable exposure duration. For acute criteria, a 1-h averaging period is established, while for chronic criteria a 4-d period is established.

### **2-3.4 Allowable frequency of exceedance**

In addition to magnitude and duration, it is necessary to consider the frequency with which a pesticide concentration may exceed a criterion without causing harm to

aquatic organisms. For the new methodology, the allowable frequency of exceedance is based on a review of studies of the ability of organisms to recover from brief exposures to pesticides. Generally, studies of post-exposure recovery are addressed to one of several levels of organization: ecosystem, community, population, species and individual. All levels should be considered in order to meet the mandate of the Central Valley Regional Water Quality Control Board is that “waters shall be maintained free of toxic substances in concentrations that produce detrimental physiological responses in...aquatic life” (CVRWQCB 2004).

### **2-3.4.1 Review of the literature**

Yount & Niemi (1990) provide a good review of studies of recovery of lotic communities and ecosystems after physical or chemical disturbances or stresses. They make an important distinction between press disturbances that occur over long periods of time causing sustained alterations in ecosystems, versus pulse disturbances that occur over shorter periods causing brief ecosystem alteration. The allowable duration of criteria exceedances included in this methodology (1 h for acute criteria; 1 h to 4 d for chronic criteria) are pulse disturbances by this definition. Thus, the same allowable frequency of exceedance applies to both acute and chronic criteria. This review focuses on studies of pulse, rather than press, disturbances. To examine recovery times, the review includes studies of recovery from brief, mild excursions of pesticide concentrations to toxic levels, as well as studies of recovery from catastrophic events (i.e., large spills). The latter are not really relevant for determination of time-to-recovery in cases of non-catastrophic events, but do provide good guidance on general aspects of ecosystem recovery.

The ability of an ecosystem to recover from a disturbance is dependent on several factors, which have been described by various authors in slightly different terms at different times. Cairns & Dickson (1977) give seven factors that determine how rapidly the recovery process will be after an ecosystem has suffered damage from one or more stressors (chemical or physical):

- 1) severity and duration of the stress
- 2) number and kinds of stressors
- 3) residual effects on the physical environment (e.g., from dredging or building dams)
- 4) presence of epicenters or refugia for recolonization
- 5) innate vulnerability of the system (e.g., lack of structural/functional redundancy)
- 6) inertia of the system (resistance to change)
- 7) resilience of the system (ability to readjust after exposure to a stressor)

Later, Cairns (1990) discussed, and quantified, six similar factors that affect an ecosystem’s ability to recover from major ecological disasters: a) existence of nearby sources of re-colonizing organisms; b) voluntary or involuntary transportability of eggs, spores, larvae, flying adults, or other life stage; c) condition of habitat following stress; d) presence and persistence of residual toxicants following stress; e) chemical-physical

environmental quality following stress; and f) potential for management/other agencies to assist in remediation. By rating each of these factors with a score of 1 = poor, 2 = moderate, or 3 = good, the following simple recovery index was defined:

$$\text{Recovery Index} = a \times b \times c \times d \times e \times f \quad (2.18)$$

A score of 400+ indicates that the ecosystem has an excellent chance of rapid recovery; 55-399 indicates a fair to good chance of rapid recovery; and < 55 indicates a poor chance. Rapid recovery is defined as having 40-60% of species reestablished within the first year after a major exposure event, and as many as 95% reestablished within 3 yr. Using this system (and recognizing that excursions above water quality criteria are not in the realm of ecological disasters, but are rare, brief, and mild events of limited scope), the following scores may be assigned to ecosystems in the Sacramento and San Joaquin River basins that have had excursions above water quality criteria:

*a* = 1-3; unaffected nearby tributaries are expected to be present, except in highly urbanized or heavily agricultural areas.

*b* = 1-3; depending on degree of transportability of species in damaged community

*c* = 3; exceedance is not expected to result in habitat alteration

*d* = 1-3; depending on chemical

*e* = 3; no chemical-physical alterations expected

*f* = 3; regulatory intervention expected

These values give a recovery index ranging from 27 to 729 indicating that the chance of rapid recovery within 3 yr following a major ecological disaster is poor to excellent. It is reasonable to assume that rapid recovery (as defined by Cairns 1990) is likely in much of the Sacramento and San Joaquin River basins following brief, mild, limited-scope excursions above criteria levels. However, in cases where all nearby tributaries are affected by the toxicant, where species in the affected are not readily transportable, and/or where the chemical either does not readily dissipate or has an ongoing source, recovery may be hindered. In such cases, site-specific frequency components of criteria may need to be derived.

In the same vein, Yount & Niemi (1990) report that in cases where rapid recovery has been observed in lotic systems it is because: 1) the life history characteristics of organisms allowed rapid recolonization and repopulation; 2) unaffected up- and downstream areas were available to supply new organisms; 3) lotic systems have high rates of flushing; and 4) organisms that live in lotic systems have evolved a lot of flexibility and adaptability because lotic systems are variable environments.

Yount & Niemi (1990) also summarized studies of ecosystem recovery following application of piscicides for eradication of undesired fish. In studies of rotenone treatments, fish recovery took from 12-16 mo and benthic macroinvertebrate recovery took 12 mo (Charles 1958; Little 1966). Similarly, in California macroinvertebrates recovered from rotenone applications within 6 mo (Cook & Moore 1969), while in Scotland they recovered within one year (Morrison 1977). Macroinvertebrates had not

recovered one year after application of toxaphene (Meehan & Sheridan 1966). Jacobi & Degan (1977) report full recovery of macroinvertebrates one year after antimycin application, and Minckley & Mihalick (1981) observed complete recovery of benthic invertebrates three years after antimycin application (in this case, recovery may have occurred sooner, but the investigators did not check).

Whiles & Wallace (1995) studied macroinvertebrates in headwater streams exposed to methoxychlor in four seasonal treatments over four years. They concluded that abundance measures were not necessarily the best measure of recovery, but that ecosystem structure is important. They found that ecosystem recovery was dependent on the life cycles of the taxa making up the system. For example, organisms with shorter life cycles or extended flight capability are able to recolonize more rapidly leading to more rapid ecosystem recovery. The ecosystem in this study took two years to recover nearly to its pre-treatment structure, but even then there were slight taxonomic and developmental stage differences.

In a review of studies of ecosystem recovery after damage from runoff of pesticides after forest application, Yount & Niemi (1990) report recovery times ranging from 2-3 mo for some species of insects exposed to DDT (Hoffman & Drooz 1953) to more than four years for other insects (Hastings *et al.* 1961). Ephemeroptera exposed to aldrin required more than 19 mo to recover, while Trichoptera and Chironomidae recovered in less than 19 mo (Moye & Luckmann 1964). Arthropod biomass was reduced by exposure to fenitrothion, but recovered in 50 d (Eidt 1981). Considering fish species in situations of exposure due to runoff, Warner & Fenderson (1962) reported recovery of trout populations three years after DDT exposure. Keenleyside (1959) concluded that Atlantic salmon populations were able to recover if DDT application was not repeated more than once every three years. Contrarily, when forests were sprayed with DDT during hatching and smolt migration periods, Atlantic salmon recovery required 4-6 years due to near elimination of an entire age class (Elson 1967). In areas where DDT had been sprayed repeatedly for several years, recovery took longer than 9 years. The longer recovery periods in this study were related to the relatively long (5-6-year) life cycle of Atlantic salmon, and to the fact that the DDT was applied on a watershed scale resulting in isolation of the affected areas from refugia that might have provided migrants to repopulate the affected area. Such a drastic exposure from watershed-scale pesticide applications are not likely to occur in the Sacramento and San Joaquin River basins, thus the probability of eliminating, or nearly eliminating, an age-class from an entire basin is remote.

Studies of recovery times are also summarized by Yount & Niemi (1990) for cases of direct application of pesticides to water bodies. Corbet (1958) reported recovery of insect larvae in 40 d after DDT application to streams in Uganda. After treatment with methoxychlor Chironomidae recovered in 1-2 wk, Plecoptera in 5 wk, and blackflies in 2-4 wk (Fredeen 1975; 1983). Snail populations recovered after treatment with the molluscicide, Bayluscid, after 10 mo in hard water, and after 22 mo in soft water (Harrison & Rattray 1966). After treatment with 3-trifluoromethyl-4-nitrophenol (TFM), benthic organisms in Lake Superior and Lake Michigan recovered in one year (Torblaa 1968),

while Dermott & Spence (1984) observed recolonization of invertebrates in streams within three weeks of TFM treatment. In a follow-up experiment, Jeffrey *et al.* (1986) found that benthic invertebrates had not recovered more than 35 days after TFM treatment of a stream. The difference between the two studies was that the Jeffrey *et al.* (1986) study was conducted in colder weather when convective currents caused mixing of TFM 55 cm into the hyporheic zone. The Dermott & Spence (1984) study was conducted in warmer weather when the convective forces were not present and the uncontaminated hyporheic zone served as a refuge from TFM exposure.

A few other studies of recovery after pesticide exposure were reviewed by Yount & Niemi (1990). Ghetti & Gorbi (1985) simulated an accidental spill of parathion that would produce measurable, but not catastrophic, effects on macroinvertebrates. Their test stream recovered in three months with macroinvertebrate density equaling or exceeding that of a reference stream after 117 days. However, macroinvertebrate trophic structure required two years for recovery (Wallace *et al.* 1986). In Nigeria, an isolated pool was treated with the insecticide Gammalin-20 in order to kill fish. After one month, no fish were found, but after three months the total number of taxa had returned to the pre-treatment state (Victor & Ogbeibu 1986).

One approach to measuring the ability of individuals or species to recover from pulse exposures to pesticides is to compare LC<sub>50</sub> values obtained in continuous exposure experiments with those obtained in pulsed exposure experiments. For example, Parsons & Surgeoner (1991a) found no difference in LC<sub>50</sub>s for mosquito larvae exposed to four 1-h pulses of carbaryl compared to those exposed continuously for four hours. They concluded that this indicated that there was no recovery during the 12-h intervals between pulses.

Turning to more recent studies, Liess & Schulz (1999) observed that in streams exposed to ethyl parathion, 4 of 11 species of macroinvertebrates that had disappeared after treatment recovered in 6 mo; 9 species had recovered after 11 mo; 2 species remained at low density for the full year of the study. Cold & Forbes (2004) found that *Gammarus pulex* recovered in 2 wk from a 1-h pulse exposure to esfenvalerate. Heckmann & Friberg (2005) showed that macroinvertebrate community structure had recovered within two weeks from two 30-min pulses of lambda-cyhalothrin. *Daphnia magna* recovered to control levels of total neonates per female and population growth rate within 21 d after a 24-h pulse exposure to fenvalerate (Reynaldi & Liess 2005). Schulz & Liess (2001) observed chronic effects on populations of insect larvae more than 240 d after 1-h exposures to fenvalerate. Parsons & Surgeoner (1991b) reported that mosquito larvae exposed to 0.5-4-h pulses of permethrin, carbaryl and carbofuran were able to recover from immobility, but not after 8-24-h exposures.

#### **2-3.4.2 Allowable frequency of exceedance-conclusion**

In setting an allowable frequency of exceedance of a water quality criterion, the question is how much time it would take for organisms at various organizational levels to recover from brief pulse exposures to contaminants. Yount & Niemi (1990) conclude that

ecosystem recovery from pulse exposures generally occurs in less than three years, and often in less than one year. Species that are slowest to recover are those with the longest life cycles. Likewise, Niemi *et al.* (1990) concluded that most ecosystems are able to recover from disturbances in less than 3 years except in cases where physical habitat was altered, the system was isolated, or residual pollutant remained. The majority of reviewed studies that consider community, population, or species-level effect indicate that recovery occurs in three years or less. The only exception is the study by Elson (1967), but, as discussed, the exposure conditions of that study were extreme and not really relevant to cases of brief, mild excursions above a water quality criterion.

Based on this review, three years between exposure events should allow full recovery from effects of an excursion above either acute or chronic water quality criteria in the Sacramento and San Joaquin River basins. This is in agreement with USEPA (1985; 2003f) methodologies, although the 3-year frequency component was supported by minimal data when it was first proposed. Acute and chronic criteria derived by the new methodology include a statement that exceedances should not occur more than once every three years.

### **2-3.5 Water quality effects**

Because water quality criteria are derived from laboratory studies conducted in carefully controlled systems, it is necessary to consider the effects that water quality characteristics may have on the toxicity of a chemical in the environment. For pesticides, the major concerns are the effects of suspended and dissolved particulate matter on bioavailability, the effects of pesticide mixtures, and the effects of temperature, pH, or other parameter on toxicity.

#### **2-3.5.1 Bioavailability**

The issue of bioavailability was discussed in the Phase I report (TenBrook & Tjeerdema 2006), but this important and complex topic merits further exploration because there is a level of uncertainty in deriving criteria with data from laboratory studies conducted in clean (i.e., solid-free water) and then using those criteria to protect aquatic organisms in an environment with varying levels of solids. Two questions need to be addressed. First, which phase or phases of a chemical in water are bioavailable? And, second, when bioavailability is well understood for a particular pesticide, what is the best way to determine compliance with water quality criteria? The first question is addressed through a literature review. Options for addressing the second question include equilibrium partitioning models, direct analysis of pesticides in different phases, and the use of passive sampling devices to estimate concentrations of bioavailable pesticides. Each of these is discussed below.

Staples *et al.* (1985) consider bioavailable chemicals to be those available to exert toxicity or to bioaccumulate. They hypothesized that most neutral organic chemicals must be in solution in order to be bioavailable, and they cite studies with polynuclear aromatic hydrocarbons (PAHs), crude oil components and polychlorinated biphenyls (PCBs) that

support this (Anderson *et al.* 1977; Halter & Johnson 1977; Neff 1979; Roesijadi *et al.* 1978a; Roesijadi *et al.* 1978b; Rossi 1977). Likewise, DiToro *et al.* (1991) conclude that compounds bound to either sediments or dissolved organic carbon (DOC) are not bioavailable. Reductions in accumulation and toxicity of synthetic pyrethroids in *Daphnia magna* have been related to the binding of these compounds to DOC (Day 1991), and reduction in bioconcentration of chlorobenzuron in *Daphnia magna* was attributed to binding of the compound to dissolved humic material (Steinberg *et al.* 1993). Kukkonen & Oikari (1991) showed that the total concentration of dissolved organic matter (DOM) in water is one of the main factors controlling bioavailability of organic contaminants. Pyrethroid uptake and toxicity in *Daphnia magna* and *Chironimus tentans* in water-sediment systems was reduced with increasing sediment organic carbon concentration (Maund *et al.* 2002). There is a species-specific aspect to the effects of solids on bioavailability. Sediment-biota accumulation factors (BSAF) for PAHs were reduced for the marine polychaete, *Nereis diversicolor*, in sediments amended with activated carbon, but there was no change in the BSAF for the gastropod *Hinia reticulata* (Cornelissen *et al.* 2006).

The studies discussed so far provide evidence that solids in water affect bioavailability of organic contaminants, but they do not necessarily support the hypothesis that only freely dissolved contaminants are bioavailable. Several studies refute the “dissolved = bioavailable” concept. Dissolved humic material (DHM) decreased the toxicity of diazinon, 4-chloroaniline, and 4-nitrophenol, had no effect on the toxicity of tetrabromobisphenol-A, o-toluidine, 3,4-dichloroaniline, and pentachlorophenol, but increased the toxicity of 2,4-dichlorophenol and 2,4,5-trichlorophenol to *Daphnia magna* (Steinberg *et al.* 1992). Fewer walleye survived exposure to chlorpyrifos-humic acid (HA) complexes than to either HA alone or chlorpyrifos alone, and no differences were seen in cholinesterase inhibition between chlorpyrifos-HA and aqueous chlorpyrifos exposures (Phillips *et al.* 2003). Schnürer *et al.* (2006) showed that glyphosate was microbially degraded even when sorbed to soil.

Without pesticide-specific, species-specific, site-specific information regarding which phases are bioavailable, compliance must be based on measurement of total pesticide concentration in water. If bioavailability information is available for a specific case, then there are several approaches that regulators may use to determine compliance. Each is discussed below.

Case 1: Pesticide is bioavailable in all three phases or no information is available. If studies show that a pesticide is bioavailable in solid, dissolved-solid and freely-dissolved phases, or if nothing is known about bioavailability for a particular pesticide on a site-specific basis, then compliance must be determined on the basis of the total concentration of pesticide in water.

Case 2: Pesticide is bioavailable in fewer than three phases. In this case, regulators still have the conservative option to determine compliance based on total pesticide concentration. However, if site-specific information is available, then compliance determination may be refined by consideration of just the bioavailable

fraction or pesticide in water. The most direct approach is to measure pesticides in each phase individually, and then determine the total bioavailable concentration by adding together the results from each bioavailable phase. Exploring analytical options is beyond the scope of this project, but several studies have measured pesticide concentrations in three phases by various methods (e.g., Eadie *et al.* 1990; Liu *et al.* 2004; Rogers 1993). Two other options for determining compliance based on bioavailable pesticide are discussed below. The first is a modeling approach applicable in cases where only the dissolved fraction is bioavailable. The second is the use of passive sampling devices, which are applicable to any combination of phase bioavailability.

To address the case of bioavailability in the freely-dissolved phase, Staples *et al.* (1985) developed a simple model to describe the relationship between total and dissolved concentrations of a contaminant in water based on the concentration of suspended sediment in the water and the solid-water partition coefficient. This model is the one used in RIVM (2001), for converting total concentrations to dissolved concentrations:

$$C_{dissolved} = \frac{C_{total}}{1 + (K \cdot S)} \quad (2.19)$$

Where:  $C_{dissolved}$  = concentration of chemical in dissolved phase  
 $C_{total}$  = total concentration of chemical in water  
 $K$  = solid-water partition coefficient (l/kg); expressed as  $K_{oc}/f_{oc}$   
 $S$  = concentration of sediment in water (kg/L)

One problem with this approach is that it makes no distinction between suspended solids and dissolved solids, which both affect bioavailability (Ditoro *et al.* 1991; McCarthy *et al.* 1985), but which can have very different partition coefficients (Delle Site 2001). Measured DOC-water partition coefficients ( $K_{DOC}$ ) for fluoanthene were incorrectly estimated in 11 different sediment pore waters using models that assume  $K_{DOC} = K_{OC}$  (Brannon *et al.* 1995). In a study of phenanthrene binding and sorption to humic acids (HA), Laor *et al.* (1998) found that partition coefficients for dissolved HA were at least an order of magnitude higher than coefficients for mineral-associated HA. Thus, trying to describe the partitioning process based only on a  $K_{oc}$  value is an oversimplification.

To improve this model, researchers have expanded it to include three phases: freely-dissolved, adsorbed to dissolved organic matter, and adsorbed to solids (Eadie *et al.* 1990; Liu *et al.* 2004). The Great Lakes criteria derivation methodology uses a three-phase model for derivation of human health and wildlife criteria (Eadie *et al.* 1990; USEPA 2003f). The three-phase model is an improvement over the two-phase model, but it does not acknowledge that partition coefficients vary considerably depending on the nature of the solids. Normalizing the partition coefficient to organic carbon is a common approach to reduce that variability, but even  $K_{oc}$  values vary depending on the nature of the organic carbon. Delle Site (2001) notes that the sorptivity of organic matter depends on the relative proportion of humic and fulvic acids, lipids and humins (based on studies by Chiou *et al.* 1987; Chiou *et al.* 1986; Garbarini & Lion 1986; Gauthier *et al.* 1987).

Kukkonen & Oikari (1991) reported that the degree of aromaticity and portion of hydrophobic acids in DOM are important controlling factors in the sorption of organic compounds. The log  $K_{OC}$  values for nonylphenol were 1.71, 3.08, 4.15, 4.50, and 4.71 for cellulose, chitin, lignin, humic acid, a natural sediment, respectively (Burgess *et al.* 2005). In a study of chlorpyrifos binding to colloidal materials, Wu & Laird (2004) found that chlorpyrifos sorbed strongly to a calcium-humate and did not desorb, but moderately sorbed to, and desorbed from, a river sediment. They concluded that both the organic and inorganic materials in suspended sediment affect the adsorption and desorption of chlorpyrifos. In light of these studies, simple partitioning models are not useful for making general predictions about phase distributions for organic contaminants. It may be possible to use them in site-specific situations in which partition coefficients are available for the specific types of solids present in the site water.

Simple partitioning models also assume that the mechanism for reduced bioavailability and toxicity of organic contaminants in the presence of solids is adsorption or binding of the contaminant to the solids. However, Steinberg *et al.* (1992) found that DHM and sunlight enhanced diazinon degradation, which is another mechanism reducing toxicity. This is not surprising in that photolysis of DOM is a known source of hydroxyl radicals in waters (Takahashi *et al.* 1988).

Semi-permeable membrane devices (SPMDs) are passive sampling devices that are intended to mimic uptake of bioavailable contaminants (Huckins *et al.* 1990). Using laboratory-determined uptake rate constants, SPMDs can be used to determine time-integrated ambient water concentrations of bioavailable contaminants. These devices work well both qualitatively and quantitatively for hydrophobic organic chemicals (Huckins *et al.* 1990; Lu & Wang 2003), but do not give reliable quantitative results for polar organics (Alvarez *et al.* 2004). Using SPMDs for quantitative analysis of ambient waters is problematic because each device has a specific membrane permeability, and uptake rates are affected by flow rates, temperatures, and fouling (Huckins *et al.* 1990). For measuring hydrophobic compounds, performance reference compounds (PRCs) have been developed to counter these variables (Huckins *et al.* 2002), but attempts to develop PRCs for polar organics have not been successful (Alvarez *et al.* 2004).

SPMDs are promoted for their ability to take time-integrated water samples such that contaminant pulses can be detected. However, this type of sampling is not useful for determination of short-term variability in ambient water contaminant concentrations (Gustafson & Dickhut 1997; Prest *et al.* 1998), and thus would be of little value in measuring compliance with acute criteria that must be met on the basis of 1-h average concentrations. Other problems with SPMDs include the fact that compounds are subject to photolysis if devices are deployed in shallow water or near the surface (USGS 2000), and that they are not accurate measures of bioaccumulation because devices do not mimic biological processes (i.e., metabolism, excretion chemical, movement, feeding) that affect equilibrium concentrations in organisms (Huckins *et al.* 2004).

There is much evidence that solids in natural waters affect the uptake and toxicity of organic contaminants. As discussed in Phase I (TenBrook & Tjeerdema 2006)

pesticide loadings to surface waters are typically due to storm or agricultural runoff, and since suspended solids are also higher than normal during runoff events, it would be ideal if criteria could be expressed, or compliance could be determined, in terms that reflect this covariance of pesticides and suspended solids. This is particularly important in the Central Valley of California where suspended solids levels are quite variable. The US Geological Survey reports levels ranging from 1-330 mg/L in samples from various streams in the Sacramento River Basin and from 1-5280 mg/L in the San Joaquin River Basin (USGS 2005a; b).

As the discussion in this section has shown, there is no simple way to incorporate the effects of solids on bioavailability into either criteria derivation or compliance determinations. It is not correct to assume that freely dissolved compounds are equivalent to bioavailable compounds. Further, it is too simplistic to assume that general partition coefficients are valid for all kinds of solids. Thus, there is no general way to predict bioavailability from physical-chemical parameters and water quality data. However, if studies are available that show which fraction, or fractions, of a particular pesticide is bioavailable, then it may be of interest to directly measure the pesticide concentrations in those fractions to determine compliance. For pesticides which are only bioavailable in the freely dissolved phase, and for which  $K_{OC}$  and  $K_{DOC}$  values are available, use of a three-phase partitioning model is an option for translating measured total pesticide concentrations into dissolved concentrations. If technical limitations of passive sampling devices can be overcome, they offer another option for estimating bioavailable pesticide in water samples, but only for determination of compliance with chronic criteria. The new criteria derivation methodology includes brief guidance regarding how to address bioavailability.

### **2-3.5.2 Mixtures**

Various approaches to addressing toxicity of mixtures were discussed in Phase I (TenBrook & Tjeerdema 2006). They concluded that there really is no way to derive criteria for all of the potential mixtures of pesticides that could occur a water body. Nonetheless, there are many models available for determination of mixture toxicity. The question is whether such models, which are designed to predict toxicity of a mixture to a single species, can be adapted for use in determination of compliance to a water quality criterion that applies to multiple species. The CVRWQCB (2004) has done this by substituting water quality criteria for LC/EC<sub>50</sub> values and in a simple concentrations addition model and using the results to assess compliance. Felsot (2005) has shown that this is also possible with a toxic equivalence model.

How to best model chemical mixtures will depend on the nature of the mixture. All models must be applicable to mixtures of two or more components. Where models will differ is in whether they apply to chemicals of similar or different modes of action, and whether the mixtures show additive toxicity, or if there are known interactions leading to antagonistic (less than additive) or synergistic (greater than additive) effects. Pesticide modes of action are often known; pesticide interactions are not as well-studied. The following discussion is broken down according to the mixture models that are

available. Each is described and discussed in terms of its applicability to particular types of mixtures or to determination of compliance with water quality criteria. The SSD approach to mixtures (Traas *et al.* 2002) was explored in Phase I (TenBrook & Tjeerdema 2006), but is not discussed further here as it is fairly complex, it is not readily adaptable for use in compliance determination, and it requires that SSDs be available for each component of the mixture, which would limit its applicability.

### 2-3.5.2.1 Additivity

There are two basic models to describe additive mixture toxicity. The concentration addition model is used for chemicals with similar modes of action, while the independent action model is used for chemicals with different modes of action (Plackett & Hewlett 1952).

#### 2-3.5.2.1.1 Concentration addition—for similar modes of action

The basic concentration addition model is expressed as (acc. to Olmstead & LeBlanc 2005; PapeLindstrom & Lydy 1997):

$$\sum_n^{i=1} \frac{C_i}{ECx_i} = 1 \text{ TU} \quad (2.20)$$

where

$C_i$  = concentration of the  $i$ th chemical in the mixture

$ECx_i$  = concentration of the  $i$ th chemical that elicits the same response ( $x$ ) as the full mixture

TU = toxic unit

If the sum is 1TU, then the mixture exhibits additivity. If the sum is greater than 1 TU, the mixture is less than additive (antagonistic); if less than 1 TU, the mixture is greater than additive (synergistic). For example, if the  $EC_{50}$  is the chosen level of effect, then it is expected that the sum of the concentration: $EC_{50}$  ratios for each component of the mixture will equal 1 TU. If less than 1 TU is required to elicit 50% effect in the mixture, then the mixture is showing more than additivity (synergism); if more than 1 TU is required, then the mixture is showing less than additivity (antagonism).

The CVRWQCB (2004) adapts this equation for determination of compliance with water quality criteria:

$$\sum_{i=1}^n \frac{C_i}{O_i} < 1.0 \quad (2.21)$$

where

$C_i$  = concentration of toxicant  $i$  in water

$O_i$  = water quality objective/criterion for toxicant  $i$

As long as the sum is < 1.0, the water body is considered to be in compliance with respect to the mixture.

Felsot (2005) argued that actual toxicity values (e.g., LC<sub>50</sub>s) should be used in these equations instead of water quality objectives for criteria to more accurately reflect toxicity of the mixture. This argument was made in regards to acute criteria that include a safety factor of 2 after determination of an acute value. However, for determination of compliance, the question is simply whether concentrations of chemicals in a water body are below criteria levels. To answer this question, using water quality criteria in these equations is appropriate.

As an alternative to equation 2.21, Felsot (2005) suggested using the relative potency factor (RPF) approach to determine compliance in cases of additive toxicity for compounds with similar modes of action. The RPF approach, which is analogous to the toxic equivalency factor (TEF) approach used in assessing toxicity of dioxin and dioxin-like compounds (Van den Berg *et al.* 1998). By the RPF approach, one chemical (usually the most toxic) is chosen to be the reference chemical and the potency of all other similarly-acting chemicals is expressed relative to the reference. The potency of each chemical is divided by the potency of the reference chemical and this ratio, the RPF, is multiplied by measured concentrations of each non-reference chemical to produce concentrations in terms of equivalents of the reference chemical. Compliance with the objective for the reference chemical is based on the sum of the measured concentration of the reference chemical plus the concentrations of the equivalents. Mathematically, this is expressed as:

$$TE_{total} = C_R + \sum_n^i TE_i \quad (2.22)$$

where:

$TE_{total}$  = total toxic equivalents of mixture (µg/L)

$C_R$  = Concentration of reference chemical (µg/L)

$TE_i$  = toxic equivalents of *i*the component of the mixture (µg/L)

and

$$TE_i = RPF_i * C_i \quad (2.23)$$

where:

$RPF_i$  = relative potency factor of the *i*th component of the mixture

$C_i$  = concentration of the *i*th component of the mixture (µg/L)

and

$$RPF_i = \frac{EC_{xR}}{EC_{xi}} \quad (2.24)$$

where:

$EC_{xR}$  = concentration of reference chemical causing  $x\%$  effect when tested alone ( $\mu\text{g/L}$ )

$EC_{xi}$  = concentration of mixture component  $i$  causing  $x\%$  effect when tested alone ( $\mu\text{g/L}$ )

For compliance determination, a multispecies RPF is needed, so equation 2.24 can be written:

$$RPF_i = \frac{\text{Criterion}_{xR}}{\text{Criterion}_{xi}} \quad (2.25)$$

where:

$\text{Criterion}_{xR}$  = water quality criterion of reference chemical ( $\mu\text{g/L}$ )

$\text{Criterion}_{xi}$  = water quality criterion of the  $i$ th chemical ( $\mu\text{g/L}$ )

Using these equations, if  $TE_{total} \leq$  the criterion for the reference compound, then the water body is in compliance.

Both the concentration addition approach and the TEF approach are valid for determination of compliance in cases of additive toxicity when chemicals in the mixture have similar modes of action. Both are included in the new methodology allowing regulators to select which one works best for them.

### 2-3.5.2.1.2 Response addition—for independent modes of action

For chemicals that do not have similar modes of action, the response addition, or independent action, model is used. It is expressed mathematically as (acc. to Belden & Lydy 2006):

$$R_{mix} = 1 - \prod_{n=1}^{I=1} (1 - R_I) \quad (2.26)$$

where:

$R_{mix}$  = response of the mixture (i.e., percent response)

$R_I$  = response expected from the  $I$ th component the mixture

This model is not applicable for determination of compliance. To illustrate, consider an example in which two pesticides are each present at concentrations equal to its water quality criterion. Since the criteria are based on a concentration that might affect 5% of species, the  $R_I$  value for each pesticide is 0.05 and the equation is:

$$R_{mix} = 1 - (1 - 0.05) * (1 - 0.05) = 0.10, \text{ or } 10\% \quad (2.27)$$

Thus, the mixture could harm as many as 10% of species, which is unacceptable. To ensure compliance, each of the two chemicals would have to be present at a level that might be expected to harm 2.5% of species, so that  $R_{mix}$  would be at or below 5%. Estimates of percentile values below the 5<sup>th</sup> percentile are highly variable (Phase I, TenBrook & Tjeerdema 2006), and yet all values of interest for application of the independent action model to compliance determination for mixtures lie below this level (values above the 5<sup>th</sup> percentile would indicate non-compliance with individual criteria). While the independent action model works well for predicting toxicity of mixtures when individual toxicities are known, it is not adaptable for compliance determination.

### 2-3.5.2.2 Non-additivity; synergism and antagonism

Chemical mixtures may display non-additive toxicity in the form of either antagonistic or synergistic effects. This indicates an interaction between chemicals such that the response observed for a mixture is either less than (antagonism) or greater than (synergism) that predicted by additivity models. Although the concept of synergy is often used in reference to cases where one chemical present at non-toxic concentrations increases the toxicity of a second chemical, but it can be applied to mixtures in which both chemicals are at toxic levels. Mu & LeBlanc (2004) utilized the coefficient of interaction ( $K$ ) to define this relationship. First described by Finney (1942), the basic equation is:

$$K_x = \frac{EC50_0}{EC50_x} \quad (2.28)$$

where:

$K_x$  = coefficient of interaction at synergist/antagonist concentration  $x$

$EC50_0$  = EC50 of chemical in absence of synergist/antagonist

$EC50_x$  = EC50 of chemical in presence of synergist/antagonist at concentration  $x$

When a measured concentration of a chemical is multiplied by the  $K_x$  value for a given concentration of a synergist/antagonist, the value that results is an adjusted, or effective, concentration of the chemical. Mathematically, this is expressed as:

$$C_a = C_m(K) \quad (2.29)$$

where:

$C_a$  = adjusted, or effective, concentration of chemical

$C_m$  = concentration measured

$K$  = coefficient of interaction

For application to compliance determination equation 2.29 could be used and the effective concentration compared to the water quality criterion. Additionally, the effective concentration could be used in additivity models described in section 2-3.5.2.1.1. The difficulty is in determination of an appropriate K value. Rider & LeBlanc (2005) fit logistic functions to describe the relationship between K values and piperonyl butoxide (PBO) concentration, such that K values could be estimated for a wide range of PBO concentrations. Unfortunately, K values derived in that manner are not generally applicable. In the case of Rider & LeBlanc (2005) they are specific to the interaction of PBO with either malathion or parathion and the toxicity of binary or ternary mixtures of those chemicals to *Daphnia magna*.

Equation 2.29 can be modified, in theory, for mixtures containing both synergists and antagonists, or multiple synergists/antagonists, (LeBlanc, pers. comm. 2006):

$$C_a = C_m (K_1 K_2 \dots K_n) \quad (2.30)$$

where:

$C_a$  and  $C_m$  are as defined in equation 2.29

$K_1, K_2, K_n = K$  values for synergist/antagonist 1, 2...n

Dr. LeBlanc cautions that as more K values are strung together, the error of each term will lead to large error in the adjusted concentration. Thus, this approach should not be used for compliance determination, but may be used to assess research needs.

To use the interaction coefficient concept in determination of water quality criteria compliance would require the establishment of relationships between K values and synergist/antagonist concentrations. That is, for pesticides that commonly occur together, it might be worth the research effort to establish relationships (i.e., predictive equations) between K and concentrations of known synergists/antagonists for a range of species. This issue is discussed further at the end of section 2-3.5.2.3.

### 2-3.5.2.3 Combined models

Each of the models discussed so far apply to only one type of mixture effect. In the environment, it would not be unusual to find complex mixtures that include chemicals that show all three of the basic mixture effects: additivity with similar modes of action, additivity with different modes of action, and interaction leading to synergism or antagonism. Olmstead & LeBlanc (2005) developed a model that combines concentration addition and response addition models in to one. Rider & LeBlanc (2005) expanded on that model to include an interaction component. The basic model equation is:

$$R = 1 - \prod_{I=1}^N \left\{ 1 - \frac{1}{1 + \left( \sum_{i=1}^n \frac{k_{a,i}(C_a) \times C_i}{EC50_i} \right)^{\rho'}} \right\} \quad (2.31)$$

where:

$R$  = response of the mixture (percent of individuals responding)

$N$  = number of cassettes (cassette = group of chemicals of similar mode of action)

$I$  =  $I$ th cassette

$n$  = number of chemicals

$i$  =  $i$ th chemical

$k_{a,i}$  = interaction coefficient for chemical  $a$  (synergist/antagonist) interacting with chemical  $i$

$C_a$  = concentration of chemical  $a$  in the mixture

$C_i$  = concentration of chemical  $I$  in the mixture

$EC50_i$  =  $EC50$  for chemical  $i$  alone

$\rho'$  = average power (slope) of dose-response curves of chemicals in cassette  $I$

This model integrates all aspects of mixture toxicity, but can only be applied to one species at a time. Gerald LeBlanc was contacted to discuss the possibility of adapting this model for determination of criteria compliance (pers. comm. 2006). The proposal was put forth that some of the variables in equation 2.31 be redefined as follows:

$R$  = response to the mixture (percent of species responding)

$k_{a,i}$  = multi-species interaction coefficient

$EC50_i$  = replace with water quality criterion

$\rho'$  = average slope of species sensitivity distributions in cassette  $I$

Using the model in this way, when  $R > 0.05$ , the criterion would not be met, because the criterion is based on the 5<sup>th</sup> percentile of the SSD. Likewise, for  $R \leq 0.05$ , the mixture would be in compliance.

LeBlanc's response was that this approach seemed reasonable in all respects except that it may not be possible to derive a reliable multi-species  $K$  value. His concern was that since  $K$  is a mechanism-dependent value, assuming a common value across species would be equivalent to assuming similar toxicity mechanisms across species. He gave the example of a chemical mixture containing an androgen receptor antagonist and an androgen synthesis inhibitor. In vertebrates, these chemicals interact synergistically, but in invertebrates they do not because invertebrates lack androgen receptors. Thus it may not be possible to derive a valid ecosystem  $K$  value for this mixture. Before it can be used for compliance assessment, the Rider & LeBlanc (2005) model would have to be

validated for use across species. However, K-values for individual species could be used to assess the potential harm from non-additive toxicity on a species by species basis.

#### **2-3.5.2.4 Conclusions on mixtures**

Among the mixture approaches presented, only the concentration addition models are readily applicable for determination of compliance with water quality criteria. The interaction coefficient concept could be used if further research provided K values applicable to multiple species over a range of synergist/antagonist concentrations. The combination model of Rider & LeBlanc (2005) that incorporates concentration addition, response addition and interaction components holds promise as a way to assess toxicity of complex mixtures, but further research and testing is needed to find a way to utilize it in compliance determination.

The new methodology includes both of the concentration addition approaches discussed in section 2-3.5.2.1.1. The non-additive model (section 2-3.5.2.2) is also included, with the caveat that it can only be used if reliable K values are available (either a multispecies value, or individual species values). The response addition and combined models are not incorporated into the methodology. Regulators can choose among the models and apply them to determine compliance with water quality criteria or to assess the potential for harm due to non-additive toxicity.

#### **2-3.5.3 Other water quality effects**

As described in USEPA (1985; 2003f), if data are available to establish quantitative relationships between water quality characteristics and toxicity, then criteria should be expressed as equations reflecting that relationship. Both USEPA methodologies (1985; 2003f) provide detailed instructions for an acceptable method for determination of acute and chronic criteria in cases where toxicity to two or more species is related to a water quality characteristic (hardness, pH, temperature, etc.). The USEPA approach is included in the new methodology. Details are not reproduced here, but may be found in Chapter 3, section 3-5.3.

#### **2-3.6 Other considerations after criteria have been derived**

Once derived according to methods discussed in the procedures in section 2-3.0, criteria must be evaluated to ensure that they are set at levels that will protect against adverse effects to: 1) particularly sensitive species; 2) wildlife and human health due to bioaccumulation; 3) species within ecosystems; 4) threatened and endangered species (TES); and, 5) other environmental compartments due to partitioning of chemicals from the water compartment.

### 2-3.6.1 Sensitive species

Derived criteria should be compared to studies of the most sensitive species in the data set to ensure that these species will be protected. If a calculated criterion is higher than toxicity values reported for a particularly sensitive species, then the criterion may require downward adjustment, for example, by using the lower 95 or 99% confidence interval estimate of the 5<sup>th</sup> percentile, rather than the median.

### 2-3.6.2 Bioaccumulation/secondary poisoning

This methodology is concerned with setting water quality criteria for the protection of aquatic life, thus it is not directly concerned with the protection of terrestrial wildlife or human health. However, for potentially bioaccumulative chemicals it is important to be sure that water quality criteria are set at levels that do not lead to unacceptable levels of chemicals in food items. The new methodology includes a procedure for checking calculated chronic criteria for the possibility of secondary poisoning of wildlife, or possible human health effects, due to bioaccumulation in fish or other food items. Acute criteria do not require this check because they are intended to protect against short periods of elevated pesticide concentrations, making the equilibrium model inappropriate. For wildlife, this requires the availability of studies that demonstrate adverse effects from dietary intake of toxicants; for human health, this requires the availability of FDA action limits for the chemical of concern. The procedure described here is based on the discussion in section 7.3.2 of the Phase I report (TenBrook & Tjeerdema 2006). The discussion is framed in terms of fish tissue, but the procedure may be applied to any potential food items.

The first step in the process is to determine if the chemical of interest has the potential to bioaccumulate. The OECD (1995) provides useful guidance, which is incorporated into the new methodology. According to this guidance, chemicals are likely to bioaccumulate if they have a  $\log K_{OW} > 3$ , molecular weight  $< 1000$ , molecular diameter  $< 5.5 \text{ \AA}$ , and molecular length  $< 5.5 \text{ nm}$ . The latter two parameters are not readily available for many chemicals, but may be used as guidelines if available. Chemicals are not expected to bioaccumulate if they are reactive and/or readily metabolized.

The next steps only apply if a chemical is determined to have bioaccumulative potential, and if dietary toxicity data or FDA action levels are available. Based on an equation in the EU risk assessment technical guidance document (ECB 2003), the Phase I report (TenBrook & Tjeerdema 2006) proposed the following equation for translating dietary NOEC or LC<sub>50</sub> values, or FDA action, levels to water NOEC values:

$$NOEC_{water} = \frac{NOEC_{oral-predator}}{BCF_{fish} \cdot BMF_{fish}} \quad (2.32)$$

or:

$$NOEC_{water} = \frac{LC_{50,oral-predator}}{BCF_{fish} \cdot BMF_{fish}} \quad (2.33)$$

where:

$NOEC_{water}$  = NOEC in water; concentration in water below this level is not expected to lead to bioaccumulation to harmful levels in food items;

$NOEC_{oral-predator}$  = dietary NOEC value for wildlife or FDA action level;

$LC_{50,oral-predator}$  = dietary  $LC_{50}$  value for wildlife (mg pesticide/kg food);

$BCF_{fish}$  = bioconcentration factor; ratio of concentration of chemical in tissue due to water-only exposure to concentration in water; whole-body, wet weight value (ECB 2003; OECD 1995);

$BMF_{fish}$  = biomagnification factor in food item; ratio of concentration of chemical in predator to concentration in prey items; based on lipid-normalized values, if available (ECB 2003)

If no measured BMF is available, then an appropriate default value (Table 2.9; based on  $\log K_{OW}$  or BCF) should be used (ECB 2003).

Table 2.9. Default BMF values (ECB 2003).

<b><math>\log K_{OW}</math></b>	<b>BCF</b>	<b>BMF</b>
< 4.5	< 2,000	1
4.5 - < 5	2,000-5,000	2
5 - 8	5,000	10
> 8 - 9	2,000-5,000	3
> 9	< 2,000	1

Alternatively, if a bioaccumulation factor (BAF) is available for fish, then equation (2.32) may be modified to:

$$NOEC_{water} = \frac{NOEC_{oral-predator}}{BAF_{fish}} \quad (2.34)$$

where:

$NOEC_{water}$  = NOEC in water;

$NOEC_{oral-predator}$  = dietary NOEC for wildlife or FDA action level (mg pesticide/kg food);

$BAF_{fish}$  = bioaccumulation factor in fish; ratio of concentration of chemical in tissue due to water plus dietary exposure to concentration in water.

In this form, the equation is similar to the USEPA (USEPA 1985; 2003f) method for determination of a final residue value, but for the new methodology, the BAF may not simply be replaced with a BCF value. If no BAF value is available, then equation 2.32 or

2.33 must be used, and if no measured BMF value is available, then the appropriate default value should be used (Table 2.8). If multiple BCF, BAF or BMF values are available for a chemical, the geometric mean of all acceptable values should be used.

To determine compliance the  $NOEC_{\text{water}}$  derived from either equation 2.32, 2.33, or 2.34 would be compared to the chronic water quality criterion. If it is above the criterion, then the no adjustment of the criterion is necessary. If the  $NOEC_{\text{water}}$  is below the criterion, then the criterion may have to be adjusted downward to ensure protection.

### **2-3.6.3 Ecosystem and other studies**

As recommended in section 2-2.1.1.4, criteria should be evaluated against field or semi-field data to judge whether they will be protective of all species within ecosystems. If not, then criteria may need to be adjusted downward. This is consistent with several criteria derivation methodologies (OECD 1995; RIVM 2001; USEPA 1985; 2003f; Zabel & Cole 1999) and is included in the new methodology.

### **2-3.6.4 Threatened and endangered species**

A number of threatened and endangered species (TES) live in the waters of the Central Valley. Due to their protected status, it is likely that very little toxicity test data will be available for these species (TES). However, it is important to ensure that they are protected by water quality criteria. Certainly, if data of acceptable quality are available for TES, then those data should be included in sets used for criteria derivation. Once derived criteria should be checked against toxicity values for TES to ensure that criteria will be protective of those species. Since criteria were calculated to be estimates of ecosystem no effect levels, they should be protective of TES. However, it is worthwhile to use available data and tools to confirm this.

When effects data are lacking for TES, both the USEPA (2003f) and the Australia/New Zealand (ANZECC & ARMCANZ 2000) guidelines suggest that studies with appropriate surrogate species may be used to set criteria. Deciding on appropriate surrogate species is left to professional judgment. More rigorous methods for estimating toxicity to TES based on surrogates are provided by both QSARs and interspecies correlation estimates (ICE). The ICE model (USEPA 2003e) is available for free download at <http://www.epa.gov/ceampubl/fchain/index.htm> (documentation included in Chapter 3, Appendix 3C). It can be used to estimate toxicity for any chemical for which a toxicity value is available for a surrogate, but, so far, has only been developed for estimation of acute toxicity. Also, the ICE model works best when making correlations within families. It can be used for larger taxonomic distances, but estimates will not be as good. QSARs are available for both acute and chronic toxicity (e.g., RIVM 2001), but, as discussed in section 2-2.2.1.1, application of QSARs is limited to chemicals with non-narcotic modes of action, which severely limits their usefulness in estimating pesticide toxicity.

To assess whether criteria derived by the new methodology will be protective of TES (based on the most recent list available), the following procedure is included:

For comparison to acute criteria:

- 1) Compare criteria to toxicity values from acceptable studies of effects on TES.
- 2) If no toxicity values are available for a TES, but an acceptable acute toxicity value is available for a surrogate species in the same family or genus as the TES, then use the ICE (v. 1.0) program to estimate a toxicity value for the TES; compare this estimated value to the acute criterion.
- 3) If no surrogate value is available, and if the chemical of interest has a narcotic mode of action, select a QSAR (e.g., from OECD 1995; RIVM 2001) that can be used to estimate toxicity based on a log  $K_{OW}$  value.

For comparison to chronic criteria:

- 1) Compare criteria to toxicity values from acceptable studies of effects on TES.
- 2) If the chemical of interest has a narcotic mode of action, select QSARs (e.g., from OECD 1995; RIVM 2001) that can be used to estimate toxicity based on a log  $K_{OW}$  value.

If no data for the TES or acceptable surrogates are available, or if QSARs are not applicable, then it will not be possible to assess whether changes in the criteria are required to be protective of these species. If any of the above comparisons reveal that a criterion is higher than any of the TES toxicity values (or estimated values), then the criterion may need to be adjusted downward.

### **2-3.6.5 Harmonization/coherence across media**

The final element that regulators may wish to consider is whether a pesticide that is present in the water at criterion levels might have the potential to move from the water compartment into another environmental compartment (i.e., sediment, biota, air) where it may exceed levels of concern established for those compartments. This is the concept of harmonization as discussed in the Phase I report (TenBrook & Tjeerdema 2006). Consideration of bioaccumulation and secondary poisoning is a specific case of harmonization of criteria between two compartments. As this is an assessment of equilibrium conditions, it is only necessary to consider chronic criteria concentrations, as discussed for bioaccumulation (section 2-3.6.2). This procedure is not necessary if levels of concern have not been established, and toxicity data are not available, for air, sediment or biota compartments.

Steady-state environmental models are tools that may be used to assess harmony, or coherence, across environmental media. Acceptable models are available for free over

the internet. The Exposure Analysis Modeling System (EXAMS, Burns 2004) is available from the USEPA Center for Exposure Assessment Modeling (CEAM; <http://www.epa.gov/ceampubl/swater/index.htm>). Mackay's (2001) Fugacity-Based Environmental Equilibrium Partitioning Models Levels I, II and III, are available for free download from the Canadian Environmental Monitoring Center (CEMC; <http://www.trentu.ca/cemc/welcome.html>). To estimate equilibrium concentrations of pesticides in various compartments at equilibrium, the easiest-to-use and most appropriate model is the Level I fugacity model. The EXAMS and Level II and III fugacity models can be used, but are more complex and require more site-specific input. The Level I fugacity model requires several input parameters including water solubility, vapor pressure, melting point and log  $K_{OW}$  for prediction of steady-state concentrations of chemicals in air, water, suspended sediment, bed sediment and biota. Note that steady state environmental models determine equilibrium concentrations in various compartments. The equilibrium that exists between any two compartments may be described by the following equation (based on a simple first-order kinetic model):

$$C_1k_{12} = C_2k_{21} \quad (2.35)$$

where:

$C_1$  = concentration of pesticide in compartment 1

$C_2$  = concentration of pesticide in compartment 2

$k_{12}$  = rate constant for transfer of pesticide from compartment 1 to compartment 2

$k_{21}$  = rate constant for transfer of pesticide from compartment 2 to compartment 1

Equation 2.35 can be rearranged:

$$C_1/C_2 = k_{21}/k_{12} = K \quad (2.36)$$

where:

$K$  = the equilibrium constant between the two compartments

In the simulations that will be run to assess harmonization in the new methodology, the concentration of pesticide in water will be set at the chronic criterion level by adjusting the total mass of pesticide in the system. According to equation 2.36, as long as  $C_1$  is constant,  $C_2$  will also be constant for a given equilibrium constant. Thus, the only kinds of model input changes that will affect final concentrations in non-water compartments are those that affect the equilibrium constant. For example, changing lipid levels in fish, or organic carbon content in suspended sediments will cause changes in equilibria, but changing concentrations of solids, or volumes of air or water will not. Model simulations can be run over a range of values to provide information applicable to a variety of site-specific situations.

Model outputs, based on having a chemical of concern at its chronic criterion level in water, should be compared to appropriate levels of concern (if any) established

for the non-water compartments (e.g., sediment or air quality criteria or FDA action levels). If the steady-state concentrations in all compartments are below their respective levels of concern, then the water quality criterion is acceptable. If not, then the criterion may need to be adjusted downward to a point where all compartments are protected. Before such an adjustment is made, though, further site-specific modeling is recommended. The new methodology includes a harmonization procedure and a list of available, acceptable models with documentation.

#### **2-4.0 Guideline Format**

As discussed in Phase I (TenBrook & Tjeerdema 2006), the methodology must be understandable, navigable and usable by environmental managers. The new methodology, presented in Chapter 3 of this Phase II report, includes a flow chart outlining the derivation procedure, explicit guidance and instructions for each step of the process, details of calculations, and numerous tables of information. For clarity, background and supporting information have been separated from the methodology itself. The rationale for selecting various components and approaches is discussed in the Phase I report (TenBrook & Tjeerdema 2006) and in this chapter (Chapter 2) of the Phase II report. A complete criteria derivation is also included in Chapter 4 of the Phase II report to demonstrate application of the methodology.

#### **2-5.0 Conclusion**

Each aspect of criteria derivation identified in the Phase I report (TenBrook & Tjeerdema 2006) as potential components of the new methodology has been evaluated in more detail. Methods have been selected for data collection, evaluation and reduction. The SSD approach utilized in the Australia/New Zealand criteria derivation guidelines (ANZECC & ARMCANZ 2000) was selected for use in the new methodology, but with the modification that it may be used to derive acute or chronic criteria when at least 5 toxicity data representing 5 different families are available.

To arrive at the acute criterion the 5<sup>th</sup> percentile values derived from acute SSDs is divided by two, while 5<sup>th</sup> percentile values derived from chronic data would become chronic criteria. For smaller acute data sets, an AF method similar to that in the Great Lakes methodology (USEPA 2003f) is included, but new factors, specific to pesticides, have been developed. In cases when fewer than 5 chronic data are available, chronic criteria are to be derived from acute criteria divided by an acute-to-chronic ratio.

Criteria are stated in terms of magnitude, duration and frequency. For acute criteria a 1-h averaging period is established, while for chronic criteria a 4-d averaging period is established. For both acute and chronic criteria, an allowable frequency of criteria exceedance of once-in-three-years is established.

To determine compliance with derived criteria, guidance is given for how to account for bioavailability, pesticide mixture effects, and water quality effects. Methods are also presented for evaluating criteria in terms of their ability to protect species

(including threatened and endangered species) within ecosystems, and their potential for partitioning into other environmental media.

## 2-6.0 References

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