UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

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MEMORANDUM

SUBJECT: Guidance for using ECOSAR as a line of evidence for identifying residues of toxicological concern

FROM: Marietta Echeverria, Director
Environmental Fate and Effects Division (7507P)

TO: EFED Staff and Managers

The purpose of this document is to provide guidance to risk assessors for using ECOSAR predictions as a line of evidence to identify residues of toxicological concern (RoC). This document provides guidance on assessing ECOSAR toxicity estimates of degradates both when 1) the degradate and parent have one or more available ECOSAR chemical class(es) in common and 2) when the degradate and parent do not have any of those chemical class(es) in common. It provides a more efficient method for determining degradates of concern by giving staff clear instructions; increased consistency by reducing variability in outcomes between scientists; and a better justification for inclusion or exclusion of degradates.

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September 25, 2018

EFED Management Concurrence Form

Policy or Guidance: ECOSAR Guidance Document

By signing below, the EFED management team acknowledges that we are aware of the content and implications of the associated guidance or policy, we, or our designated expert, have participated in discussions surrounding this policy or guidance; and we are responsible for ensuring that the guidance is followed from the date of this signature and thereafter.

ERB1. Sujatha Sankula — Date: 9/26/18

ERB2. Elyssa Arnold (Acting) — Date: 9/25/18

ERB3. Dana Spatz — Date: 9/25/18

ERB4. Jean Holmes — Date: 9/25/18

ERB5. Justin Housenger — Date: 09/25/18

ERB6. Mark Corbin — Date: 9-25-18

EISB. Lee Kyle — Date: 9-25-2018

Deputy Director. Kimberly Nesci — Date: 9-26-2018

Associate Director. Brian Anderson — Date: 9-26-2018

Procedure for using ECOSAR as a Line of Evidence for Identifying Residues of Toxicological Concern

September 25, 2018

Executive Summary

This document provides guidance to risk assessors for using ECOSAR (ECOlogical Structure Activity Relationships) predictions as a line of evidence to identify residues of toxicological concern (RoC). The Ecological Structure Activity Relationships (ECOSAR) Class Program is a computerized predictive system that estimates aquatic toxicity. The program estimates a chemical's acute (short-term) toxicity and chronic (long-term or delayed) toxicity to aquatic organisms, such as fish, aquatic invertebrates, and aquatic plants, by using computerized Structure Activity Relationships (SARs). It supplements the 2012 general NAFTA guidance on QSARs (Quantitative Structure-Activity Relationships), which should be consulted for general considerations on the construction and use of QSARs in ecological risk assessment (https://www.epa.gov/sites/production/files/2016-01/documents/qsar-guidance.pdf). This document provides guidance on assessing ECOSAR toxicity estimates of degradates both when (1) the degradate and parent have one or more available ECOSAR chemical class(es) in common and (2) when the degradate and parent do not have any of those chemical class(es) in common.

Process. The first step is to run an ECOSAR prediction using the appropriate Simplified Molecular Input Line Entry System (SMILES) or the Chemical Abstracts Service Registry Number (CAS RN) for the parent and degradates to determine if they have ECOSAR chemical classes in common. If they do, the next step is to evaluate the ability of ECOSAR to predict the toxicity of the compounds of interest by comparing ECOSAR's predictions to measured (usually for the parent) toxicity data.

For degradates that do not fall within an ECOSAR chemical class in common with the parent, the comparison will be with a surrogate (analog) compound having measured toxicity data, and of the same ECOSAR chemical class as the degradate. The comparison occurs toward the end of the process of evaluating the degradates, to conserve resources.

In both cases, depending on the reliably of the predicted values from ECOSAR, this guidance will help evaluate the toxicity of degradates as a line-of-evidence for determining RoC.

To avoid duplication of effort, the user should consult the ROCKS (Residues of Concern Knowledge-based committee) memorandum for the pesticide of interest, to obtain SMILES codes, molecular weights, and water solubility values for the parent compound and degradates, as available.

Best Professional Judgment. While this guidance is not intended to be exhaustive, it provides staff with sufficient information with which to ensure consistency in employing ECOSAR as a line of evidence in ecological risk assessments in support of new and existing pesticide registration decisions. Best professional judgement (BPJ) should be applied throughout the process and in the ultimate decision to include or exclude a degradate from consideration, including integration of other lines of evidence.

Before embarking on a structure activity relationship investigation using the ECOSAR tools the reviewer should first:

1. Carefully consider existing documentation regarding the declared mechanism of action for the active ingredient. If the registrant-supplied material has identified a specific substructure of the

chemical structure of the parent molecule that is responsible for the stated mechanism of action, the reviewer should inspect the degradates of the parent for the presence of this substructure.

2. Consult the mechanism of action lists in Insecticide Resistance Action Committee (IRAC), Herbicide Resistance Action Committee (HRAC), or Fungicide Resistance Action Committee (FRAC) for structural commonalities. Web links are given below. The purpose of this effort is to perform a read across with the structures of other compounds belonging to the stated mechanism of action for the parent compound under consideration to identify substructures held in common and putatively associated with the activity of the chemical class.

The main goal of this effort is to avoid ascribing parent compound toxicological similarity to degradates which no longer possess critical substructural components that are of established relationship to a chemical class mechanism of action. For example, the degradates of carbamate insecticides (acetylcholinesterase binding agents) should not be considered toxicologically equivalent to the parent compound if they no longer possess an intact carbamate structural moiety.

A. Purpose and Scope

The Ecological Structure Activity Relationship (ECOSAR v.2.1 or higher) program estimates chemical acute (short-term) and chronic (long-term) toxicity to aquatic organisms (fish, invertebrates, and plants) using SARs. The program groups structurally similar organic compounds with available measured effect levels that are correlated with physiochemical properties (*e.g.*, octanol water partition coefficient or K_{OW}) and uses these relationships to estimate toxicity values for chemicals without measured experimental toxicity data. Toxicity estimates for a degradate falling outside the domain of the models, as indicated by qualifiers given in the ECOSAR output, (*e.g.*, Log K_{OW}) should not be used.

This document supplements the 2012 general NAFTA guidance on QSARs, which should be consulted for general considerations on the construction and use of QSARs in ecological risk assessment (https://www.epa.gov/sites/production/files/2016-01/documents/qsar-guidance.pdf).

This guidance describes how to use ECOSAR (the most up-to-date version should be used and can be found at https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model) as a line of evidence for determining if a major degradate (*i.e.*, representing ≥10% of total residues in abiotic and/or biotic degradation/transformation studies) should be considered a RoC when assessing risks of a pesticide to aquatic organisms. This guidance document is useful by showing how to evaluate the reliability of ECOSAR's predictions by comparing the output values of the model to measured toxicity data. Generally, only major degradates (>10% of parent AR, Applied Radioactivity) should be considered, unless a group of minor degradates for a particular abiotic/biotic degradation/transformation study, all of which fall in the same ECOSAR class(es) as the parent, total to >10% of parent AR within a single fate study.

In judging the quality of ECOSAR estimates, the user should be aware that the quality of the underlying data sets and regressions varies from one structural class to another. The underlying data can be viewed in the ECOSAR program by following Help and On-line ECOSAR help in the tool bar.

The final judgement of the quality of the ECOSAR analysis for a particular data set should include consideration of the parent compound's mode of action, and the relevance of each ECOSAR structural class to the mode of action (*i.e.*, what moieties need to be retained for toxicity to be observed). This may be done by examining measured toxicity data for related active ingredients and their degradates (*i.e.*, a read-across exercise).

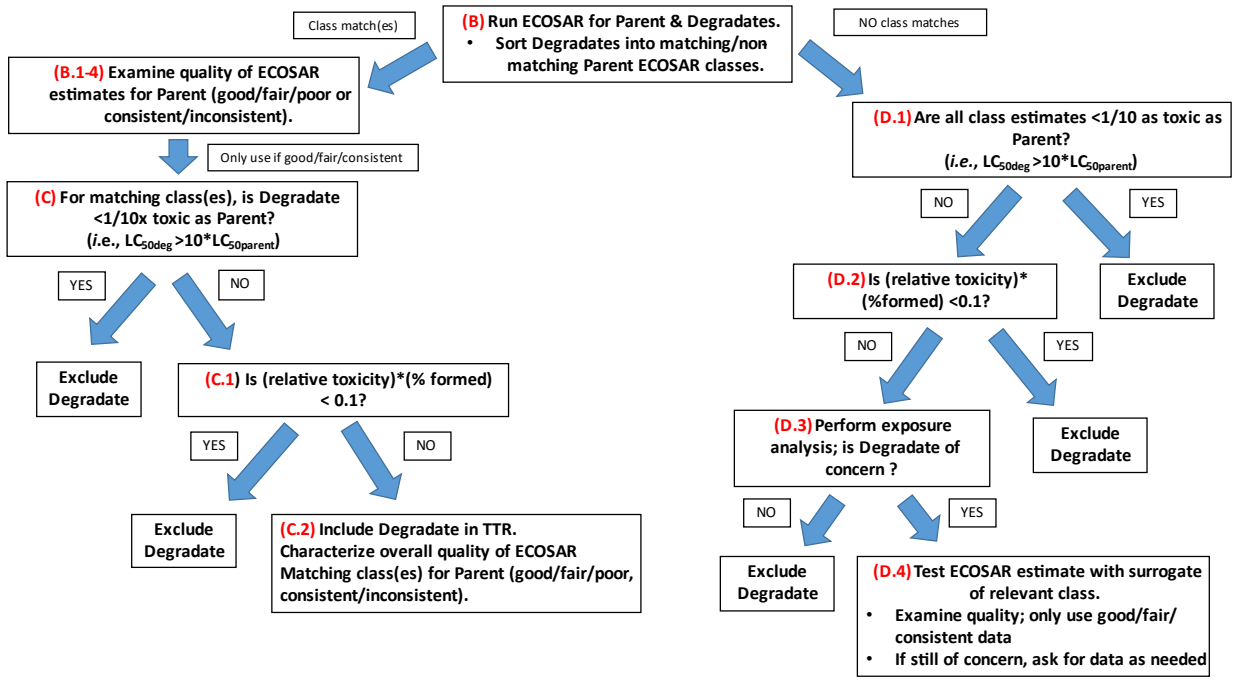
Consider other lines of evidence about the parent's mechanism of action when evaluating the ECOSAR fits, because a structurally complex parent may have moieties that place it in several ECOSAR structural classes. The accuracy of the fit in any one ECOSAR class is diminished by the overall complexity of a molecule, as the toxicological activity may be more than the "sum of the parts." The receptor-mediated toxicodynamics of the entire complex structure are less likely to be well-described by any one substructure. In exercising BPJ, be aware of the molecular mode of action and toxicodynamics, which can be determined from information supplied by the registrant, the Health Effects Division, and the scientific literature. Greater confidence in QSAR predictions come from a model based on a specific receptor-based mode of action (*e.g.*, GABA receptor binding), and the identification of substructures of parent and degradate that cause the toxicity. ECOSAR classes that account for these substructures should be given more weight. Mode of action information may be found at IRAC (Insecticide Resistance Action Committee, http://www.irac-online.org/), HRAC (Herbicide Resistance Action Committee, http://www.hracglobal.com/) and FRAC (Fungicide Resistance Action Committee, http://www.frac.info/), and the Organisation for Economic Co-operation and Development (OECD) QSAR Toolbox. Another source of mode of action information is the cumulative risk assessments produced by the Health Effects Division.

Because of the chance of a random "good" match between measured and estimated toxicity data for any one structural class, the quality of ECOSAR estimates is increased when multiple structural classes lead to the same conclusions, and when the structural class is specific to the parent compound.

Determination of the RoCs may consider lines of evidence in addition to ECOSAR, such as acute-to-chronic ratio analysis, toxicity data from the open literature, bridging (or read across) based on data from other similar compounds and other QSAR programs (*e.g.,* OECD QSAR Toolbox), as well as the EPA-ORD Chemistry Dashboard (https://www.epa.gov/chemical-research/chemistry-dashboard). However, ECOSAR should not be used for inorganic or organometallic chemicals, charged chemicals like acids or salts and chemicals with molecular weight greater than 1000 g/mol (ECOSAR v.2.0 has new modules for polymers and surfactants). Degradates that are RoCs may be considered in a total toxic residue (Guidance for Modeling Pesticides Total Toxic Residues (TTR) EFED May 6, 2009) or formation-decline expression, if they are in the same structural class(es) as the parent, or in individual RoC exposure estimates when the structural class (proxy for mode of action) is different from the parent chemical. **Figure 1** graphically summarizes the process and parts of the figure are displayed throughout the document as visual guides. Finally, guidance is given on when to ask for additional toxicity data for "non-matching" degradates.

In all cases, for both "parent" compounds and degradates, ECOSAR-estimated endpoints that exceed the known or estimated solubility of the compound should not be reported as definitive endpoints.

Figure 1. Graphical representation of ECOSAR guidance

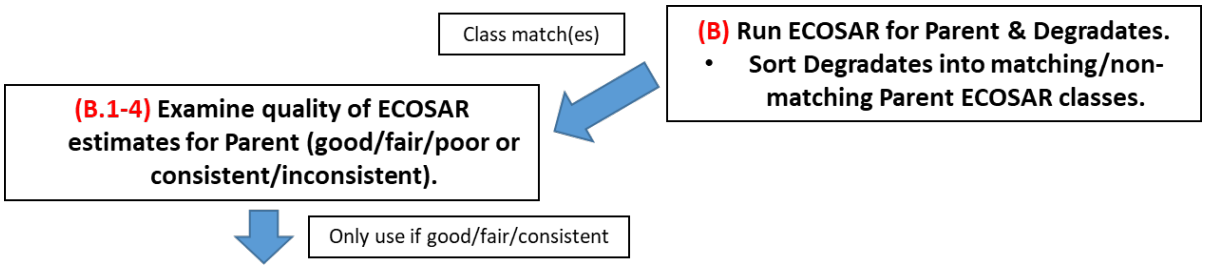


B. Parent: Comparison of Empirical Data and ECOSAR Estimates

This section gives guidance on how to compare the measured toxicity data for the parent compound to the ECOSAR estimates for each class into which the parent is categorized. This enables the user to judge the quality of the ECOSAR match for the parent, so that the utility of ECOSAR for the case at hand can be gauged, if the degradate is of the same SAR class as the parent. For definitive parent endpoints, the ECOSAR estimates are rated as good, fair, or poor based on the ratio (5x, 10x, >10x, respectively) of measurement to estimate. For non-definitive parent endpoints, the ECOSAR estimates are categorized as "consistent" or "inconsistent" with the parent measurement.

(B) Run ECOSAR for Parent & Degradates.
- **Sort Degradates into matching/non-matching Parent ECOSAR classes.**

Run ECOSAR for the "parent" compound. The "parent" compound should have toxicity data for the measurement endpoint (*e.g.*, survival, growth, reproduction) being estimated by ECOSAR. If all class matches are "poor" for the parent, then ECOSAR generally should not be used for determining whether degradates should be included as a RoC.



B.1. Comparison of Definitive Endpoints

This section provides guidance on the comparison of measured and estimated endpoints when neither of them is qualified as "greater than" or "less than" a numerical value (*i.e.,* both measured and estimated endpoints are definitive).

Rate the quality of the ECOSAR match for each structural class and endpoint versus the measured parent data as follows: within approximately 5x, good; within approximately 10x, fair; or greater than approximately 10x, poor.

B.2. Comparison of Definitive Endpoints to Non-Definitive Endpoints

This section provides guidance on comparing definitive and non-definitive endpoints. Usually, the non-definitive endpoint will be for the empirically derived endpoint; however, ECOSAR-estimated endpoints may also be considered non-definitive, as described below. In most if not all these situations, there is inherent uncertainty in the comparison of definitive and non-definitive endpoints. Ultimately, the degree of uncertainty is based on best professional judgement. These comparisons are rated as "consistent" or "inconsistent," rather than "good," "fair," or "poor." A few example situations are discussed below.

Most empirical data used to develop ECOSAR predictions of acute toxicity to fish, aquatic invertebrates, and aquatic plants[1] are definitive endpoints below 100 mg/L and non-definitive endpoints above 100 mg/L. Therefore, definitive ECOSAR predictions above 100 mg/L may be outside of the range of definitive empirical values used as the basis for the predicted value (*i.e.*, the ECOSAR prediction is based on extrapolation rather than interpolation). Given this limitation of the dataset, ECOSAR results for acute toxicity to fish, aquatic invertebrates, and aquatic plants should generally be reported as >100 mg/L if the ECOSAR result exceeds 100 mg/L (*e.g.*, 33,000 mg/L). That said, in those cases the added detail of an extrapolated definitive endpoint estimate above 100 mg/L may provide useful information for risk characterization. As for acute endpoints, the same considerations apply to chronic endpoints (fish and aquatic invertebrates) with definitive ECOSAR estimated values >10 mg/L.

ECOSAR-estimated endpoints may be considered generally consistent with empirical toxicity endpoints when both values are non-definitive, for ECOSAR results meaning above the measured or estimated water solubility limit (*e.g.*, both >50 mg/L or both <80 mg/L). That said, best professional judgment should be used, taking into consideration factors such as the relative difference in the magnitudes of the two non-definitive values and effects, if any, observed in the toxicity study.

If a definitive ECOSAR estimate of chronic toxicity (*e.g.*, ChV = 5 mg/L) is lower than the lowest observed effect concentration (*e.g.,* LOEC = 10 mg/L) of a toxicity test that did not define a no observed effect concentration (NOEC < 10 mg/L), then the ECOSAR-estimated value may be considered consistent with the empirical value.

Generally, estimated definitive endpoints exceeding estimated solubility or the Log Kow cut-off for the class should be reported and flagged as exceeding measured of estimated solubility or Kow limit.

B.3. Comparison of Inconsistent Endpoints

If the measured endpoint and the ECOSAR estimate qualitatively disagree, *i.e.*, when one is an undefined limit value ("<" or ">") and the other indicates a definitive or non-definitive endpoint inconsistent with the limit (*e.g.*, >10 mg/L measured and 5 mg/L estimated) then the quality rating for the comparison should rely on best professional judgment because the actual difference between the two values is unknown. This applies even if numerical values are within 5x or 10x evaluation criteria.

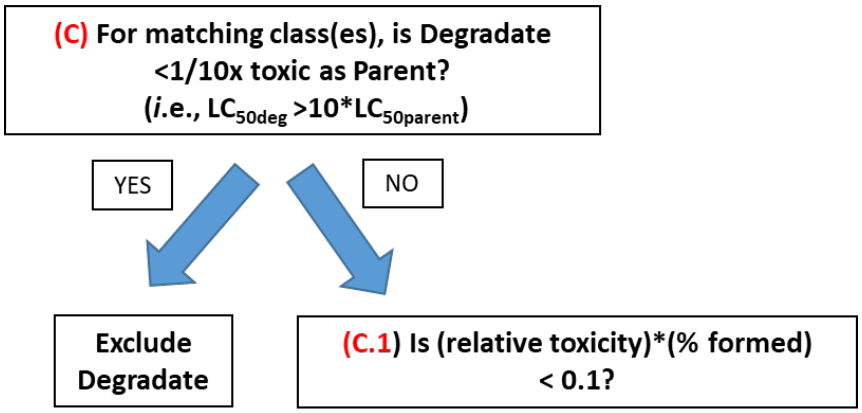
[1] EFED does not make a distinction between acute and chronic testing for aquatic plant studies. Guideline studies are typically conducted for 96-hours with algae and 7-days with non-vascular plants. These endpoints should be compared to the "acute" ECOSAR estimates.

Available information specific to the chemical (*e.g.*, solubility limit) or taxon (*e.g.*, unexpected degree of sensitivity of a test species to one or more chemicals in a class) should be considered and rated as "inconsistent" if the discrepancy cannot be explained.

B.4. Additional Considerations for Chronic Endpoints

For chronic endpoints, use the maximum acceptable toxic concentration (MATC), *i.e.*, the geometric mean of NOEC and LOEC, for comparison to the ECOSAR Chronic Value estimate (ChV). More leeway for endpoint matching may be given for chronic endpoints, given that the MATC depends on the spacing of the NOEC and LOEC. For categorization of chronic endpoints, the match may be considered "good" or "fair" if the ECOSAR prediction is between the NOEC and LOEC. ECOSAR assumes a constant acute-to-chronic ratio (ACR) of 10; if the actual ACR based on measured endpoints is different, this should be accounted for when judging the quality of ChV estimates.

C. Analysis of ECOSAR-estimated Toxicity Data for Degradates when ECOSAR Class(es) Matches the Parent

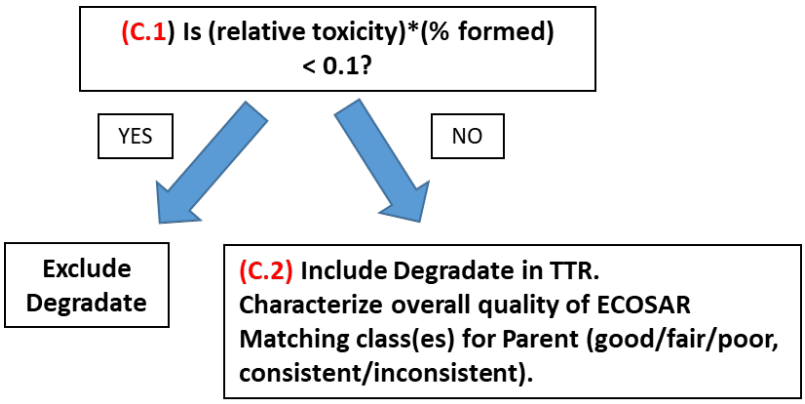


This section provides guidance on determining if a degradate is sufficiently abundant and toxic to include in the RoC, by comparing its estimated endpoints to the parent's estimated endpoints, within the same ECOSAR classes. Considerations for overall quality of ECOSAR analyses are given in **Section A**.

Run ECOSAR for all identified degradates that may be of concern (*i.e.*, structurally similar compounds representing ≥10% of total residues; exclude carbon dioxide). Generally, only major degradates (>10% of parent AR) should be considered, unless a group of minor degradates within a single study, all of which fall in the same ECOSAR class(es) as the parent, total to >10% of parent AR. If needed to document inclusion of degradates in a RoC, consider constructing a table showing parent compound with its measured toxicity data, and the ECOSAR toxicity estimates for parent and major degradates, including ECOSAR structural class as the column header. Also include any measured toxicity data for degradates. An example table is provided below (**Figure 2**).

For greater precision, the risk assessor may convert all endpoints to a molar basis (moles/liter) using the molecular weight before comparing endpoints across structures (*e.g.*, parent toxicity versus degradate toxicity). However, this step may not be warranted if an initial review reveals that the difference in molecular weight between parent and degradate(s) is small enough that the toxicity status of the degradate(s) is unaffected, and the difference would thus not affect the conclusions.

C.1. Analysis for Degradates with the same ECOSAR Class as the Parent



This section provides guidance for deciding whether degradates should be included in the Residues of Concern, when ECOSAR places the degradate in the same ECOSAR class(es) as the parent subject to overall quality considerations outlined in **Section A**.

For degradates ***included in*** any of the parent ECOSAR chemical classes, discard from the RoC any major degradates that are less than $^{1}/_{10}$ as toxic as the parent (mg/L or molar basis may be used) on an acute and chronic basis.

For degradates ***included in*** any of the parent ECOSAR chemical class(es), and within 10x of the parent's toxicity, compute the ***toxicity ratio*** as shown (**eq. 1**) using the maximum fraction degradate formed in the relevant environmental fate study (usually soil or aquatic metabolism, but not always). Use the ECOSAR estimated endpoints for parent and degradate for this calculation.

Toxicity Ratio = ((parent ECOSAR endpoint)/degradate ECOSAR endpoint)*(percent degradate formed)

(**eq. 1**)

If the Toxicity Ratio is less than 0.1, exclude the degradate from RoC. If the product is >0.1, include the degradate in RoC. Consider including in RoC, groups of minor (<0.1) degradates that sum to >0.1 when they are in the same ECOSAR class. Repeat for each endpoint and ECOSAR class.

If the toxicity estimate for any degradate is >10X lower or below the 95% confidence bound of the measured endpoint of the parent (*i.e.*, is more toxic than parent), consider requesting a toxicity test if warranted by refined exposure analysis, or evaluating the toxicity and exposure of that degradate outside of a RoC analysis.

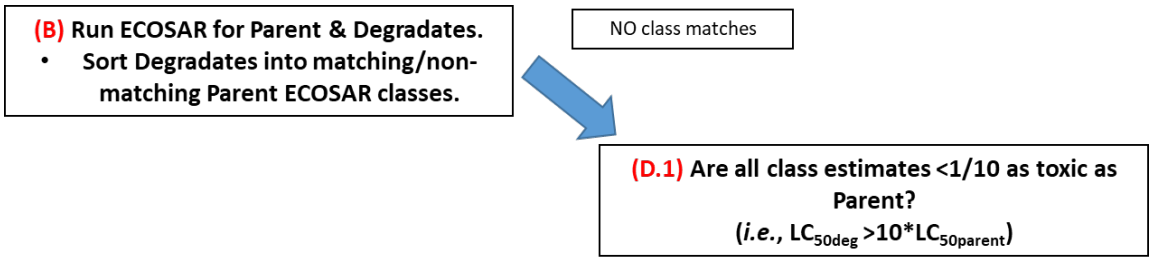
C.2. Final RoC Expression

(C.2) Include Degradate in RoC. Characterize overall quality of ECOSAR Matching class(es) for Parent (good/fair/poor, consistent/inconsistent).

The final RoC expression should include all degradates that qualify for RoC for any of the endpoints (*i.e*., fish, invertebrate, or plant, and acute or chronic) from any matching ECOSAR class. In an effort to bound potential exposure estimates, exposure estimates may also be based on parent-only. Furthermore, the reviewer may also choose to calculate different RoC expressions when there is evidence that the RoC differ by taxa or exposure duration (acute vs. chronic). For risk quotient calculation, the measured parent toxicity endpoint is recommended as the toxicity estimate for the RoC. The final RoC expression is subject to Best Professional Judgment, based on several lines of evidence, and the reasoning for the final RoC should be documented in the risk assessment.

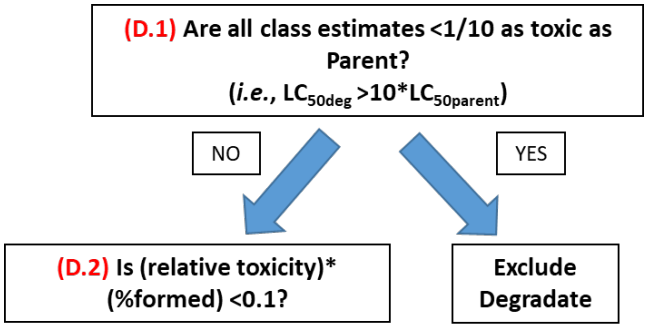
The quality of the RoC expression should be described, based on the parent-ECOSAR matching quality (within 5x, within 10x, consistent, inconsistent, *etc*.), and any other pertinent factors. These could include whether any of the ECOSAR class(es) match the parent's structural class (*e.g*., pyrethroid), and any factors described in the ECOSAR documentation.

D. Analysis for Degradates not in Parent ECOSAR Classes

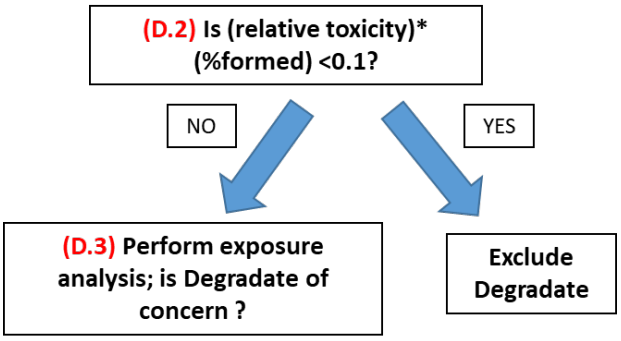


This section provides guidance for consideration of degradates that are not assigned by ECOSAR into any of the same structural classes as the parent. These degradates might be residues of concern but cannot be placed into a Total Toxic Residues expression based on ECOSAR class and would therefore need to be considered separately in the risk assessment.

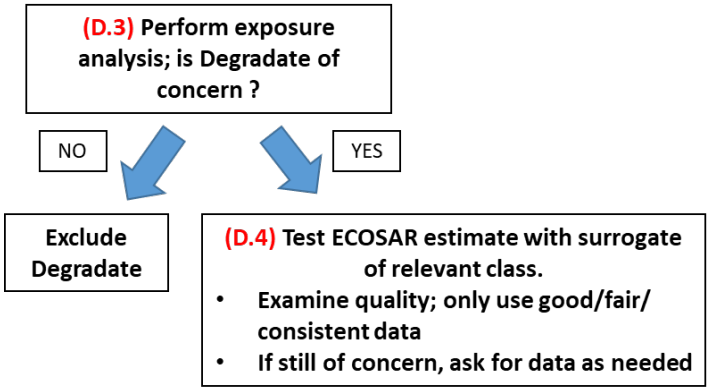
D.1. For degradates ***that are not included in*** any of the parent ECOSAR class(es), discard any degradates that are less than $^{1}/_{10}$ as toxic as the parent (compare ECOSAR estimate to measured parent data).



D.2. For degradates ***that are not included in*** any of the parent ECOSAR class(es) but are within 10x of the parent's toxicity, compute the toxicity ratio (**eq. 1**). Use measured parent and ECOSAR estimated degradate endpoints for this calculation. If this product is less than 0.1, exclude the degradate from consideration. If the toxicity ratio is > 0.1, continue to consider the degradate.



D.3. A qualitative exposure estimate may be used to determine if there is a potential risk concern and may identify a need to request measured toxicity data for the degradate(s) and associated endpoint, especially if there is a potential risk concern based on a refined exposure estimate, and not triggered by the parent or RoC.



D.4. For degradates ***that are not included in*** the parent ECOSAR class(es), and whose toxicity ratio is within 10x of parent toxicity, identify surrogate compound(s) matching the ECOSAR structural class(es) of the degradate, with measured toxicity data if available. Another degradate, with measured toxicity data, and of the same ECOSAR class, may be used as a surrogate. If the measured toxicity data are matched by ECOSAR within a factor of 5 for the surrogate(s), or if the underlying regression for that class in ECOSAR is of high quality, characterize the potential risk for the degradate(s) in that ECOSAR class, characterizing the measured endpoint (from the surrogate) as an estimate of toxicity.

(D.4) Test ECOSAR estimate with surrogate of relevant class.

- **Examine quality; only use good/fair/ consistent data**
- **If still of concern, ask for data as needed**

More leeway for endpoint matching may be given for chronic endpoints, given that the MATC depends on the spacing of the NOEC and LOEC. An ECOSAR estimate (ChV) falling between the NOEC and LOEC may be considered "good" or "fair." ECOSAR assumes a constant ACR of 10; if the actual ACR based on measured endpoints is different, this should be accounted for when judging the quality of Chronic Value (ChV) estimates.

E. Glossary

ACR, Acute to Chronic Ratio: Calculation of a chronic endpoint for species A from acute and chronic endpoints for species B.

AR, Applied Radioactivity: The amount of radioactivity added to an environmental fate study as parent compound.

BPJ, Best Professional Judgment: the user of this guidance is expected to characterize the results with multiple lines of relevant scientific evidence.

ChV, Chronic Value: Chronic endpoint estimated by ECOSAR. Equivalent to MATC.

Consistent endpoints: A situation when a definitive NOAEC endpoint is lower than a LOAEC (effects at all test concentrations), higher than a limit dose ("greater than" value), or when two non-definitive endpoints have the same inequality sign (< or >).

Definitive endpoint: A toxicity endpoint, measured or estimated, not qualified as "greater than" or "less than."

Degradate: A metabolite or breakdown product of the parent active ingredient.

EC_{50}: Median effective concentration. Acute toxicity endpoint not limited to lethality, typically including counts of individuals exhibiting either mortality or another condition approaching fatality (e.g., moribundity) in the calculation.

ECOSAR class: A chemical class automatically assigned by ECOSAR based on the structure of the chemical entered.

Empirical endpoint: A toxicity endpoint measured in the laboratory.

Inconsistent endpoints: A situation when two endpoints are mutually exclusive, such as when a definitive endpoint is numerically less than a limit dose ("greater than" value), *e.g.*, 50 and >100; or when a definitive endpoint is greater than a LOAEC (*e.g.*, 50 and <10).

LC_{50}: Median lethal concentration. Acute toxicity endpoint.

LOAEC: Lowest Observed Adverse Effect Concentration.

MATC: Maximum Acceptable Toxicant Concentration. Geometric mean of the LOAEC and NOAEC.

Major degradate: A degradate formed at greater than 10% of the parent applied radiation in a relevant environmental fate study.

Matching classes: A situation when the parent and degradate are assigned the same ECOSAR class.

Measured endpoint: A toxicity endpoint measured in the laboratory.

Minor degradate: A degradate formed at less than 10% of the parent applied radiation in a relevant environmental fate study.

NOAEC: No Observed Adverse Effect Concentration.

Non-definitive endpoint: A toxicity endpoint, usually measured, that is qualified as "greater than' or less than."

Parent compound: The pesticide active ingredient, or its principal residue, for which laboratory toxicity measurements have been conducted.

QSAR: Quantitative Structure-Activity Relationship.

RoC, Residues of Concern: The collection of parent and degradates that are deemed toxic and considered in the risk assessment.

ROCKS: Residues of Concern Knowledge Subcommittee. A joint EFED-HED committee that selects degradates for the human health risk assessment.

Toxicity ratio: The product of the percent formation of a degradate in the relevant environmental fate study, with the ratio of the parent to degradate toxicity endpoints.

TTR, Total Toxic Residues: An expression of the residues of concern in risk assessment; calculated by summing radioactivity of all residues of concern.

Figure 2. Example data table to be completed for each endpoint

chemical	data	molecular weight	solubility (mg/l or mole/L)	Neutral Organic	qsar 1	qsar 2	qsar 3
parent/principal residue	(measured endpoint)	(for converting mg/L to mole/L)		est. endpoint or >solubility			
deg 1							
deg 2							
deg 3							
deg 4							
deg 5							
deg 6							
deg 7							
deg 8							
deg 9							