

Updating EnviroTox: developing transparent biology-driven approaches for defining acute and chronic experimental durations

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Abstract

The EnviroTox database was built to meet the needs of researchers and regulators to establish the ecological threshold of toxicological concern (ecoTTC), a pragmatic modeling approach that can be used to establish an exposure level for chemicals below which no appreciable risk to the environment would exist. The ecoTTCs are created from distributions of predicted no-observed-effect concentrations (PNECs) that can be derived using this uniquely curated chemical-effects database. Data contained within EnviroTox is curated to ensure each study meets the specifications for experimental duration, biological endpoint, and statistical approach required for an “acute” or “chronic” designation. The initial EnviroTox curation was completed entirely by hand using detailed decision diagrams. This required special considerations and expert review for all 1,500 unique species and 91,000+ entries in the database. A more streamlined approach is needed for standardizing and classifying new and relevant effects data so the EnviroTox database can be routinely updated.

Objectives

The EnviroTox database was initially curated entirely by hand. There has been a growing interest in expanding the EnviroTox database to include additional chemistries and studies and/or process privately held data using the same techniques and standards. A streamlined analysis approach is therefore needed. Transparent, automated logic needs to be developed to remove expert decision making, where possible.

- 1) Identify EnviroTox curation steps that require manual expert review
- 2) Review trophic level flow charts for accuracy and consistency
- 3) Create explicit trophic level / species level logic for assigning acute and chronic study durations
- 4) Identify outstanding steps remaining for EnviroTox updates

A word on relevance..

- “Acute” and “Chronic” are arbitrary designations based on:
 - Duration of study relative to organism life span and/or sensitive life stage
 - Biological endpoint
- Designations may vary based on regulatory jurisdictions
 - Algae are especially challenging, as the assay measures the effects at a population level. This is not typically considered an “acute” endpoint. Algae acute and chronic designations are determined based on test statistic.
- The A/C designations described here are “fit for purpose” for an ecoTTC PNEC derivation. These designations do not necessarily imply regulatory acceptance. However, regulatory designations were used to inform selections.
- Designations err on the side of data inclusivity. EnviroTox users could modify designations according to their own needs.
- For pragmatic reasons, A/C logic was set at the taxonomic level to avoid the development of unique guidelines for each of the 1500+ species in the database.

Considerations for Acute and Chronic designations

Logic diagrams were created to classify acute and chronic designations for photosynthetic microbial taxa, non-photosynthetic microinvertebrates, macroinvertebrates, and fish.

Key considerations for assigning test type:

- Select appropriate logic diagram based on taxonomic group / trophic level
- Experimental duration, often in relation to biological attributes
- Test statistic (e.g., NOEC, LOEC, ECx)
- Biological endpoint (e.g., survival, reproduction, growth, etc)

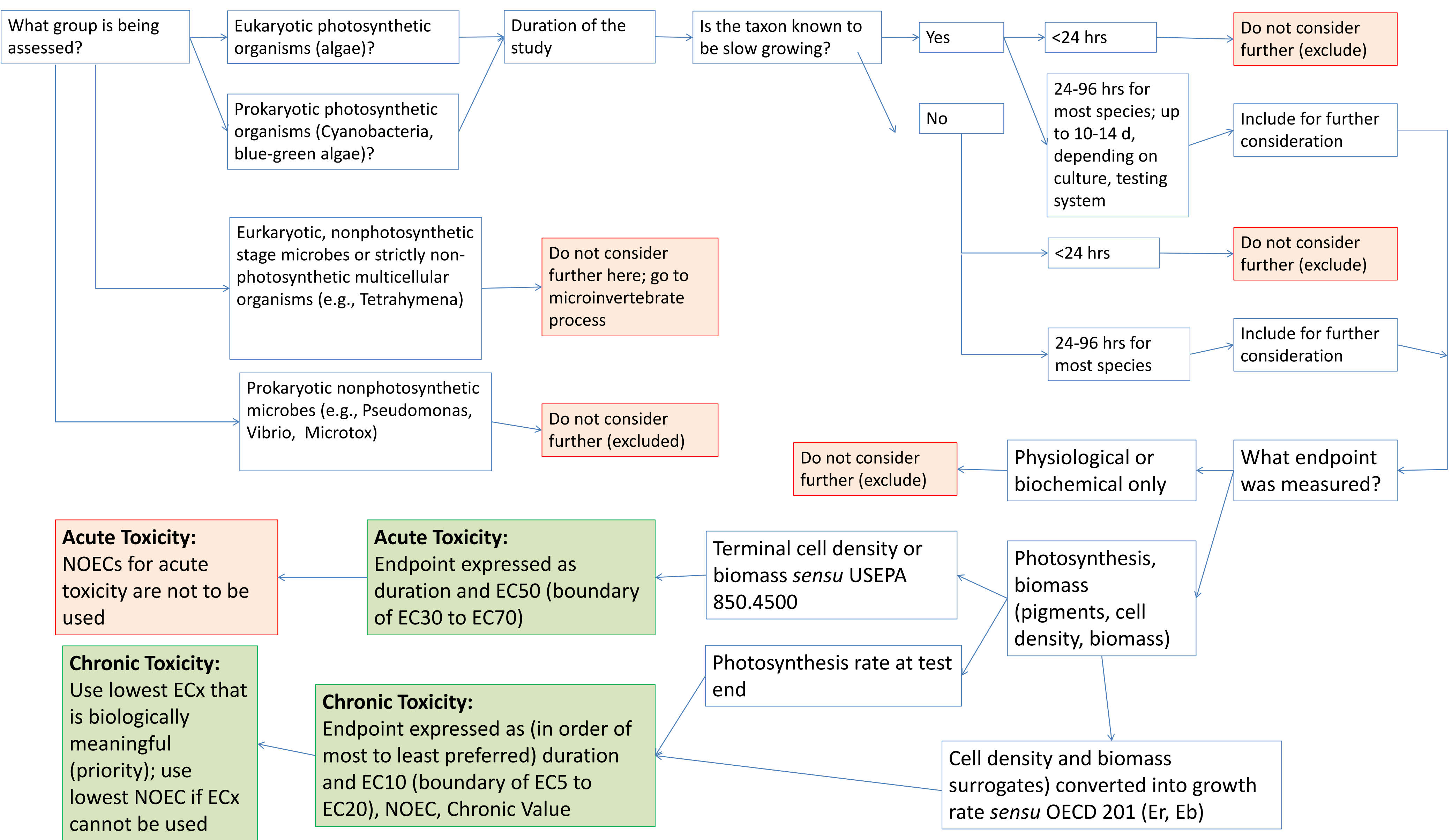
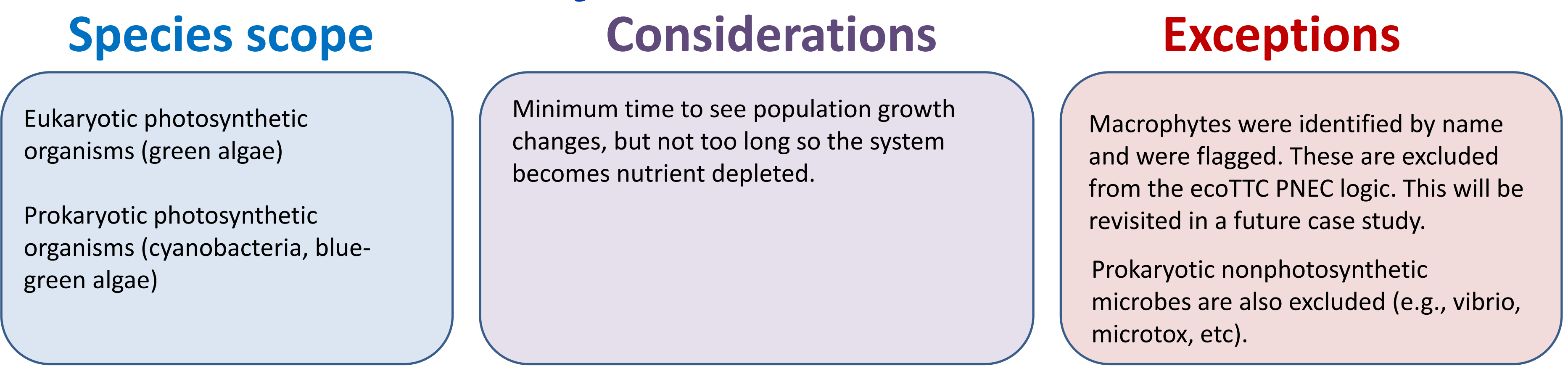
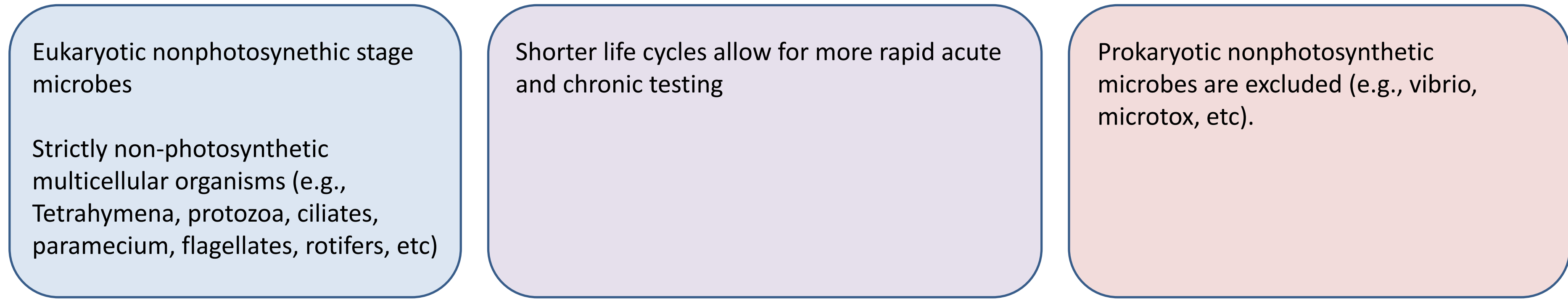


Fig. 1. Determination of acute and chronic toxicity for photosynthetic microbial taxa

Photosynthetic microbial taxa



Non-photosynthetic micro-invertebrates



Macroinvertebrates

Species scope

Aquatic invertebrates: Ceriodaphnia, Daphnia, Chironomous species, various amphipods, bivalves, etc

Considerations

Acute and Chronic experimental durations are longer, due to longer life cycles.

Some species have complex life stages (e.g., clams/bivalves, snails, others with hydrozoan life cycles). Appropriate acute and chronic duration will depend on the life stage tested.

Exceptions

Species must have a fully aquatic life stage (e.g., water mites are in scope, water spiders are out of scope).

Fish

All bony fish
Superclass: Osteichtyes

Acute: Tests generally do not include feeding. Consider how long an organism can survive without food.

Chronic: Consider duration needed to characterize the chronic effect. Shorter experiments at earlier life stages may still give chronic results (e.g., fish ELS studies).

Cartilaginous fish

Preliminary duration cut-offs

Table 1. Taxonomic group Acute and Chronic duration guidelines, in days

| Taxonomic group | Acute | | Chronic | |
|---------------------------------------|-------|-----|---------|-----|
| | min | max | min | max |
| Photosynthetic microbial taxa | 1 | 10 | 1 | 10 |
| Non-photosynthetic microinvertebrates | 1 | 4 | 1 | 4 |
| Macroinvertebrates * | 1 | 7 | 8 | |
| Fish | 1 | 6 | 7 | |

*Some macroinvertebrates will require expert review due to unique life stage considerations

Take-aways

- Preliminary acute and chronic designations were created based on operationalized definitions establish per taxonomic group / trophic level
- Manual expert review will still be required for:
 - Bivalves and other macroinvertebrate species with complex life stages (e.g., hydrozoan life cycles)
 - Review relevance and validity of biological endpoints, and if they are appropriate an acute or chronic test
- Final designation will be made based on duration, biological endpoint and statistical endpoint, as outlined in Figure 1.
- EnviroTox will be updated with new experimental data in the coming months.
- Algae acute and chronic durations could be further curated in the future to account for slow-growing species (e.g., Navicula, Anabaena, etc).

Acknowledgements

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