



Introduction

- Imidacloprid is a neonicotinoid insecticide currently undergoing registration review in US and Canada
- Widely used to control insect pests
 - Agriculture: Row and field crops, orchards and vineyards
 - Non-agriculture: Nurseries, turf (e.g., golf courses, residential)
- Imidacloprid is highly specific to nicotinic ACh receptors in the invertebrate central nervous system and thus aquatic invertebrates are a sensitive receptor group
- European Food Safety Authority, Dutch National Institute for Public Health and the Environment, and others have derived highly conservative water quality benchmarks for imidacloprid
 - Based on results of laboratory toxicity tests with the most sensitive receptors
 - Chronic benchmarks in Europe: 0.0083 to 0.009 µg/L
- Such an approach does not rely on the best available science, as more environmentally relevant data are available from mesocosm (cosm) studies
- Goal of this project was to derive a chronic benchmark for imidacloprid that is protective of invertebrate communities, but based on the results of more environmentally relevant cosm studies

Laboratory vs Cosm Studies for Deriving Benchmarks

Laboratory Studies

- Conducted under controlled conditions (e.g., temperature, photoperiod, pH, water hardness)
- Generally do not consider:
 - Influence of other media such as sediment
 - Natural variability in environmental conditions
 - Fluctuating concentrations
 - Indirect effects from changes in competitive hierarchies and predator-prey relationships, etc.
- Questionable relevance of findings to “real-world” aquatic communities

Cosm Studies

- Offer a level of realism not found in the laboratory
- Simulate realistic natural conditions
- Multiple species and trophic levels
- Long term endpoints from higher levels of organization
- Assess recovery after exposure
- Typically have lower statistical power



Imidacloprid: Available Studies

141 References

110 Tier I laboratory

+

31 Higher tier (microcosm, mesocosm, rice paddy)

- Primary literature
- Registrant-sponsored studies
- US EPA's ECOTOX database
- Water quality guideline documents
- Grey literature

Cosm Studies Evaluated for Relevance and Quality

Evaluation Scheme

- First screened for relevance (utility) with 5 questions
- If relevant, studies rated against 11 criteria, each scored from 0 to 3, to address:
 1. Objectivity
 2. Clarity and transparency
 3. Integrity
- Scheme informed by EPA ECOTOX; EPA OPP; Klimisch et al. (1997); de Jong et al. (2008); Breton et al. (2009); Hall et al. (2010, 2012); van der Kraak et al. (2013); Solomon (2014)

Step 1 – Relevance

Assessment Factor	Criteria	Score
Utility	Study community/ecosystem	YES/NO
	Single active ingredient tested	YES/NO
	Endpoints directly related to mortality, growth or reproduction	YES/NO
	Exposure route	YES/NO
	Exposure duration	YES/NO

* Only chronic community/ecosystem level studies involving imidacloprid exposure in aquatic media and measurements of apical endpoints moved to Step 2 of the evaluation

Step 2 - Quality

Assessment Factor	Criteria	Score
Objectivity	Use of standard guideline/complete description of test system and protocols	/3
	Identification of test substance	/3
Clarity and Transparency	Consideration of imidacloprid phys-chem properties (i.e., solubility, photolysis)	/3
	Controls	/3
	Statistical procedures	/3
	Exposure concentrations	/3
	Sufficient number of samplings	/3
	Concentration-response	/1
	Test species characteristics and acclimation	/3
Integrity	Test conditions	/3
	Good Laboratory Practices	/1

Evaluation Rubric – Example Questions

Assessment Factor	Questions	Score			
		0	1	2	3
Clarity and Transparency	Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?	No information provided on test substance	Imidacloprid technical or formulation reported	Product identification and purity, % a.i. reported	Product, purity, % a.i. and source reported
	Were appropriate controls included, reported and results adequate?	No controls reported	Controls used, but effects in controls not reported	Controls used, with effects in controls (e.g. mortality, immobilization) reported and within acceptable limits	Controls used, with effects in controls (e.g. mortality, immobilization) reported, within acceptable limits, and compared to treatment groups using statistical methods

Scores

- Acceptable score = 23-29
- Supplemental score = 13-22
- Unacceptable score = 0-12



Selecting Data for Deriving Higher Tier Benchmark

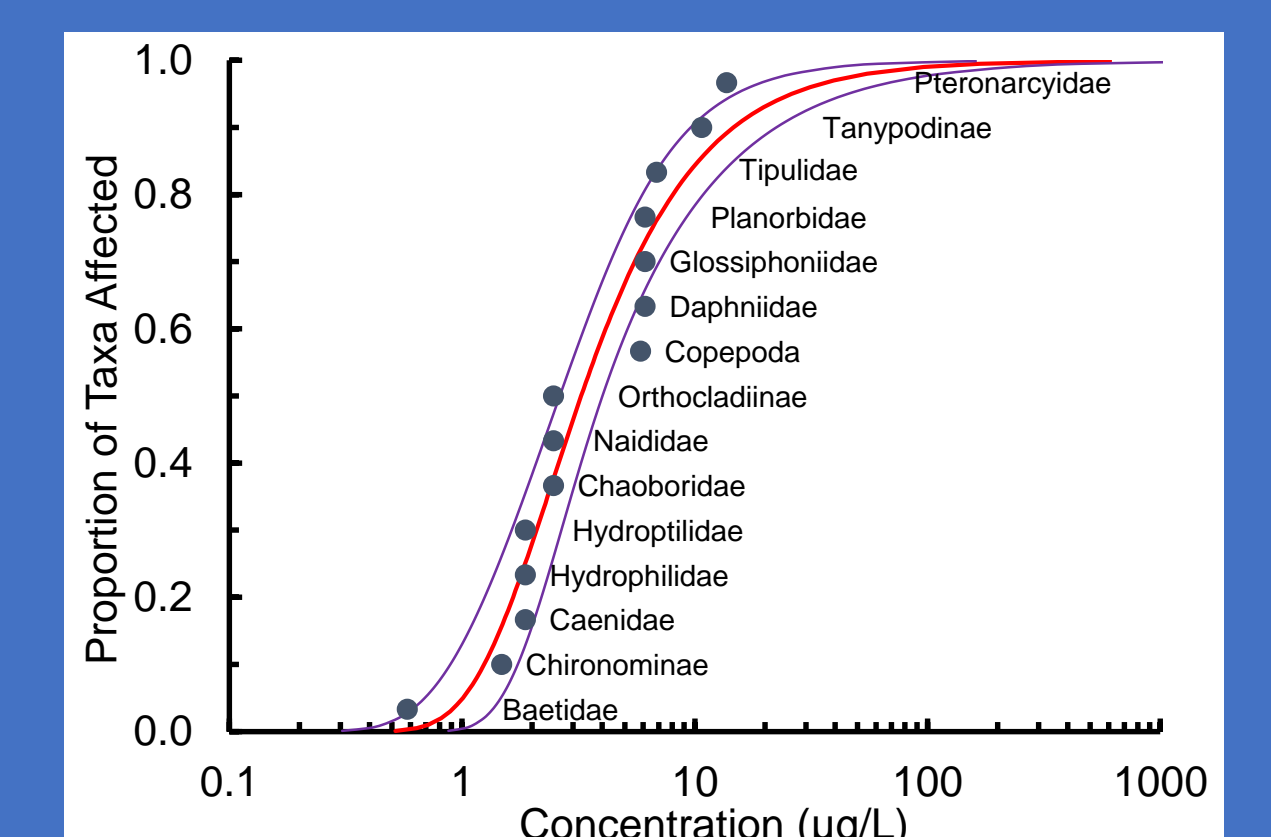
- Lowest NOEC determined for each taxon, generally at the family or subfamily level of organization
- Only 10 of 31 cosm studies found to be acceptable for quantitative use in a risk assessment
- Four of the acceptable studies only reported effects on overall invertebrate abundance and not taxon-specific endpoints (Hayasaka, 2012a,b; Kreuzweiser et al., 2009) or only reported endpoints for macrophytes and periphyton (Heimbach and Hendel, 2001)
- Remaining 6 acceptable cosm studies had varying exposure concentrations over time due to single or multiple applications, varying application intervals, and temporal decline following application as expected in the natural environment
- Studies with a single imidacloprid application conducted by Kreuzweiser et al. (2007, 2008)
- Studies with 2 applications and a 21-day retreatment interval conducted by Ratte and Memmert (2003), Roessink et al. (2015), and Roessink and Hartgers (2014)
- Other exposure regime included 4 applications with a 14-day retreatment interval (Moring et al., 1992)
- Several determined potential recovery of aquatic invertebrate populations (e.g., Moring et al., 1992; Ratte and Memmert, 2003), but we did not consider recovery in determining taxon NOECs for benchmark derivation

Procedure to Derive Benchmark

- To ensure that cosm-based NOECs were comparable, time-weighted average concentration estimates determined for each NOEC
- Approach standardized results between different studies with varying exposure regimes
- 21-day time-weighted average concentration estimates calculated assuming degradation half-life (DT50) of 11.6 days reported by Roessink et al. (2015)
- Duration of 21 days post final application corresponded to most common application interval
- Time-weighted NOECs reported in Table 1
- SSD Master v3.0 software used to derive taxon sensitivity distribution (TSD)
- SSD Master fits up to five non-linear regression models (normal, logistic, extreme value, Weibull, and Gumbel) in log or arithmetic space to establish the best-fitting cumulative distribution function (CDF)
- Model fit evaluated using the Anderson-Darling (AD) goodness-of-fit test statistic (A2) and various graphical plots of model residuals

Table 1 Data used to derive the chronic taxon sensitivity distribution (TSD) using results from cosm studies for imidacloprid.

Taxon (Family, Subfamily, Subclass)	NOEC (µg/L)	Geometric Mean NOEC (µg/L)	Time-weighted Average NOEC (µg/L)	Reference
Baetidae	0.6	0.816	0.581	Ratte & Memmert, 2003
	2			Moring et al., 1992
	1.52			Roessink and Hartgers, 2014
Chironominae	0.243	1.90	1.48	Roessink et al., 2015
	0.6			Ratte & Memmert, 2003
Caenidae	6	2	1.87	Moring et al., 1992
	2			Moring et al., 1992
Hydrophilidae	2	2	1.87	Moring et al., 1992
	2			Moring et al., 1992
Chaoboridae	3.8	3.8	2.47	Ratte & Memmert, 2003
	3.8			Ratte & Memmert, 2003
Naididae	3.8	3.8	2.47	Ratte & Memmert, 2003
	3.8			Ratte & Memmert, 2003
Orthocladinae	3.8	3.8	2.47	Ratte & Memmert, 2003
	3.8			Ratte & Memmert, 2003
Copepoda	6	7.51	5.85	Moring et al., 1992
	9.4			Ratte & Memmert, 2003
Daphniidae	9.4	9.4	6.12	Ratte & Memmert, 2003
	9.4			Ratte & Memmert, 2003
Glossiphoniidae	9.4	9.4	6.12	Ratte & Memmert, 2003
	9.4			Ratte & Memmert, 2003
Planorbidae	12	12	6.84	Kreuzweiser et al., 2007
	12			Moring et al., 1992
Tanytopodinae	20	13.7	10.7	Ratte & Memmert, 2003
	9.4			Kreuzweiser et al., 2007
Pteronarcyidae	12	24	13.7	Kreuzweiser et al., 2007
	48			Kreuzweiser et al., 2008



- Chronic HC5 = 1.01 µg/L, 26-fold higher than chronic HC5 from lab studies
- Recovery not considered, but commonly observed



Discussion and Conclusions

- Mesocosm, semi-field and field studies are environmentally more realistic than laboratory studies
- Concentrations of imidacloprid are temporally variable in the environment, as they were in the cosm studies, but not in standard toxicity tests conducted in the laboratory
- Cosm studies also important tools in testing and informing risk assessment conclusions (see, for example, Whitfield Aslund et al. (2017))
- Adverse effects observed in laboratory studies with single species are not necessarily translated to the community level of organization because adverse effects to a few sensitive species may be offset by increases in functionally similar, but more tolerant species
- Overall community structure and function may not be affected by adverse effects to a few sensitive species
- Functional redundancy likely partially explains why the aquatic invertebrate community is more resilient to imidacloprid exposure in cosm studies than predicted by laboratory studies on single species
- Cosms had varying concentrations and more realistic environmental conditions and habitats for receptors that likely also explain the additional resilience of invertebrate communities compared to laboratory studies
- Given the limitations of laboratory-based water quality benchmarks, we recommend adopting the chronic water quality benchmark for imidacloprid derived using the higher tier toxicity data, i.e., 1.01 µg/L