



Augmenting Species Diversity in Water Quality Criteria Derivation using Interspecies Correlation Models

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**USEPA Office of Research and Development
Gulf Ecology Division**

Office of Research and Development
NHEERL, Gulf Ecology Division, Gulf Breeze, FL 32561



The Problem of Species Diversity

Most Commonly Reported Aquatic Toxicity Test Records in ECOTOX

Taxa	Test Type	Number of Records ^a
Fish	Acute	10,566
	Chronic	4,184
	Bioconcentration	796
Arthropods	Acute	8,134
	Chronic	698
Mollusk	Acute	1,722
	Bioconcentration	239
Plant	Acute	933
Algae	Acute	468
	Chronic	571
Amphibian	Acute	393
	Chronic	323
Annelid	Acute	234
	Chronic	121
Rotifer	Acute	210
Echinoderm	Acute	74

Species	Common Name	Percentage of Records ^a
<i>Oncorhynchus mykiss</i>	Rainbow trout	7.7
<i>Daphnia magna</i>	Water flea	6.2
<i>Pimephales promelas</i>	Fathead minnow	5.3
<i>Lepomis macrochirus</i>	Bluegill	2.8
<i>Cyprinus carpio</i>	Common carp	2.0
<i>Danio rerio</i>	Zebra danio	1.8
<i>Oryzias latipes</i>	Japanese medaka	1.4
<i>Ceriodaphnia dubia</i>	Water flea	1.3
<i>Pseudokirchneriella subcapitata</i>	Green algae	1.3
<i>Ictalurus punctatus</i>	Channel catfish	1.2

2012 Download: Fairbrother, Barron, Johnson 2015

Web-ICE developed to address problem of species diversity

ICE (Interspecies Correlation Estimation)

- log-linear models of the relationship between the acute toxicity (LC50) of chemicals tested in two species

Web-ICE

- internet application containing suite of ICE models
- predict acute toxicity to species, genus or family level
- fish/invertebrate/amphibian; algae; wildlife
- modules for SSD generation, batch T&E taxa prediction
- peer reviewed technical basis (publications, SAP)



Regression models built from standardized toxicity values

- chemical identity/purity; CAS/name curation
- water quality, test conditions, species/life stage

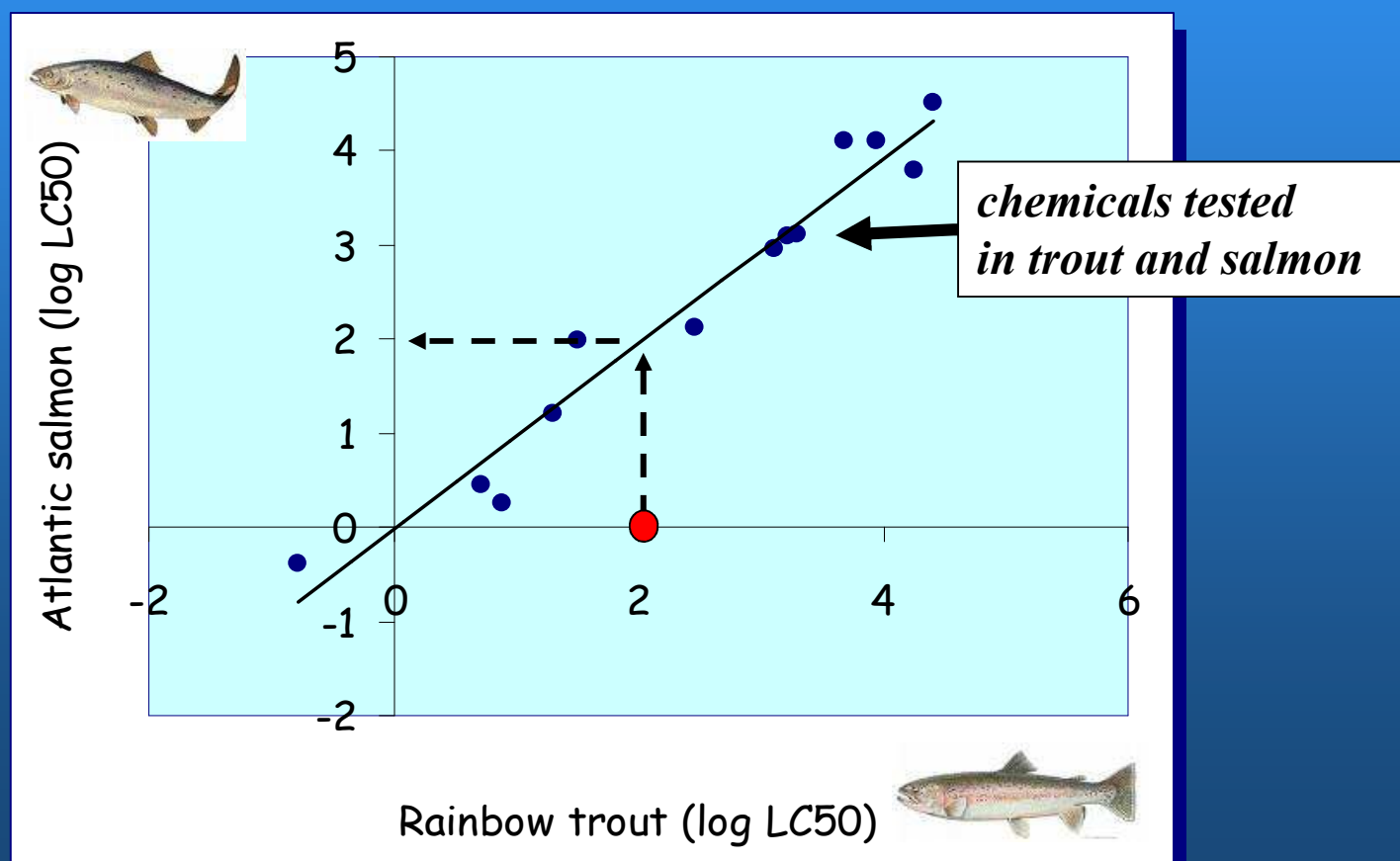
2015 Update

- increased taxa diversity
- change from geomean genus/family level models to minimum toxicity models
- ORD website migration (in progress)

What are ICE models?

Interspecies Correlation Estimation (ICE)

Log-linear models of the relationship between the acute toxicity (LC50) of chemicals tested in two species



Interspecies Correlation Estimation

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You are here: EPA Home » Exposure Assessment » Food Chain » Interspecies Correlation Estimation

Exposure Assessment Models

Web-ICE Home

Aquatic Species
Aquatic Genus
Aquatic Family
Algae Species
Algae Genus
Wildlife Species
Wildlife Family

Species Sensitivity Distributions

Aquatic
Wildlife

Endangered Species

Aquatic
Wildlife

Basic Information

User Manual

Download Model Data

Bibliography



Select taxonomic model for Aquatic or Wildlife

Species Sensitivity Distribution Modules

Endangered Species Modules

Species Sensitivity Distribution Module

ICE Aquatic

ICE Wildlife

Endangered Species Module

ICE Aquatic

ICE Wildlife

Web-ICE Aquatic Data Sources

Acute toxicity: fish, amphibians, and aquatic invertebrates

- ECOTOX
- OPP: ecotox database
- OPPT: PMN, HPV
- OW: AWQC
- USGS (RM grant)
- P&G (CRADA)
- Open literature (T&E, molluscs)

QA/QC:

- centralized data management system
- data transcription thoroughly reviewed
- CAS/chemical curation
- species name consistency
- reviewed each source for quality
- duplicate records removed

	EXPERIMENTAL	LOG	SPECIES	CHEMICAL	GLOCHIDIA LAB	JUVENILE LAB
Metallic stress	(>363, 272)	(>2.6, 2.4)	Lampsis siliquoides	Lead	CERC	CERC
	(>107, 99)	(>2.0, 2.0)	Villosa iris	Mercury	VPI	VPI
	(>247, 19)	(>2.4, 1.3)	Lampsis siliquoides	Cadmium	CERC	CERC
	(>330, 28)	(>2.5, 1.4)	Lampsis cardium	Cadmium	CERC	SU
	(31, 23)	(1.5, 1.4)	Utterbackia imbecilis	Cadmium	JGA	CU
	(10, 11)	(1.0, 1.1)	Lampsis abrupta	Copper	CERC	CERC
	(14, 7.0)	(1.1, 0.84)	Lampsis fasciola	Copper	CERC, Univ. of Guelph, VPI	CERC
	(12, 9.6)	(1.1, 0.98)	Lampsis rafinesquana	Copper	CERC	CERC
	(14, 11)	(1.2, 1.0)	Lampsis siliquoides	Copper	NSU, CERC, Univ. of Guelph	CERC
	(57, 13)	(1.8, 1.1)	Megalania nervosa	Copper	ASU	CERC
Neurotoxic	(23, 25)	(1.4, 1.4)	Utterbackia imbecilis	Copper	JGA	ASU, CERC, CU, UGA
	(11, 7.6)	(1.1, 0.88)	Villosa iris	Copper	CERC	NRNG, CERC
	(411, 200)	(2.6, 2.3)	Actinonasa pectorosa	Zinc	VPI	VPI
	(2779, 182)	(3.4, 2.3)	Lampsis siliquoides	Zinc	CERC	CERC
	(724, 250)	(2.9, 2.4)	Villosa iris	Zinc	VPI	VPI
	(690, 630)	(0.9, 3.8)	Lampsis siliquoides	2-Propanol	NCSU	NCSU
	(390, 375)	(2.6, 2.6)	Utterbackia imbecilis	Nonylphenol	JGA	JGA
	(5900, 7200)	(3.8, 3.9)	Lampsis siliquoides	Glyphosate isopropylamine salt	NCSU	NCSU
	(28750, 10210)	(4.3, 4.0)	Lampsis siliquoides	Propiconazole	NCSU	NCSU
	(680, 30)	(2.7, 1.5)	Lampsis siliquoides	Pyraclostrobin	NCSU	NCSU
Respiratory toxicity	(72, >100)	(1.9, >2)	Lampsis siliquoides	Chlorine	CERC	CERC
	(103, 80)	(2.0, 1.9)	Epiblatia capsaeformis	Chlorine	VPI	VPI
	(1333, 192)	(3.1, 3.0)	Utterbackia imbecilis	Chlorine	JGA	JGA
	(220, 68)	(2.3, 1.8)	Villosa iris	Chlorine	VPI	CERC
	(54425, 389000)	(5.7, 6.6)	Lampsis fasciola	Sodium chloride	NCSU, Univ. of Guelph	NCSU
	(143790, 376769)	(6.2, 6.6)	Lampsis siliquoides	Sodium chloride	CERC, NCSU, Univ. of Guelph	CERC, NCSU
	(276000, 450332)	(6.4, 6.7)	Villosa constricta	Sodium chloride	NCSU	CERC
	(331000, 523000)	(6.5, 6.7)	Villosa delumbis	Sodium chloride	NCSU	NCSU
	(1300, 1156)	(4.1, 4.1)	Lampsis fasciola	Ammonia	CERC	CERC, VPI
	(14763, 16353)	(4.2, 4.3)	Lampsis rafinesquana	Ammonia	CERC	CERC
Other	(19416, 8750)	(4.3, 3.9)	Lampsis siliquoides	Ammonia	CERC	CERC, Purdue Univ.
	(8235, 8441)	(3.9, 3.8)	Utterbackia imbecilis	Ammonia	JGA	CERC, EPA, TVA, UGA
	(7519, 6296)	(3.9, 4.0)	Villosa iris	Ammonia	CERC, VPI	CERC, VPI
	(63614, 66966)	(5.8, 5.8)	Alasmidonta raveneliana	Sodium fluoride	EPA	EPA
	(775751, 517168)	(5.9, 5.7)	Utterbackia imbecilis	Sodium fluoride	EPA	EPA
	(164400, >500000)	(5.2, >5.7)	Lampsis siliquoides	Perfluorooctanoic acid	NCSU	NCSU
	(16100, >500000)	(4.2, >5.7)	Ligumia recta	Perfluorooctanoic acid	NCSU	NCSU
	(15500, 158100)	(4.2, 5.2)	Lampsis siliquoides	Perfluorooctanesulfonic acid	NCSU	NCSU
	(13500, 141700)	(4.1, 5.2)	Ligumia recta	Perfluorooctanesulfonic acid	NCSU	NCSU
	(625, 92)	(2.8, 1.8)	Lampsis siliquoides	Fluoxetine hydrochloride	NCSU	NCSU
Open-ended value	(293, 97)	(2.5, 2.0)	Ligumia recta	Fluoxetine hydrochloride	NCSU	NCSU
	(500, 250)	(2.7, 2.4)	Lampsis siliquoides	Chlorpyrifos	NCSU	NCSU
Multiple Laboratories	(80, 280)	(2.0, 2.4)	Lampsis siliquoides	Chlorothalonil	NCSU	NCSU

Data Standardization

Chemical

- CAS/name curation
- single compound tested; a.i. $\geq 90\%$
- chemical & element specific AWQC normalizations

Species-Specific Test Conditions

- no sed, diet, mixture exposures or phototoxicity results
- ASTM/OCSP standards or equivalent
- temperature (6 °C range); D.O. (>40-60%); Salinity (FW:<1ppt; SW: ≥ 15 ppt)

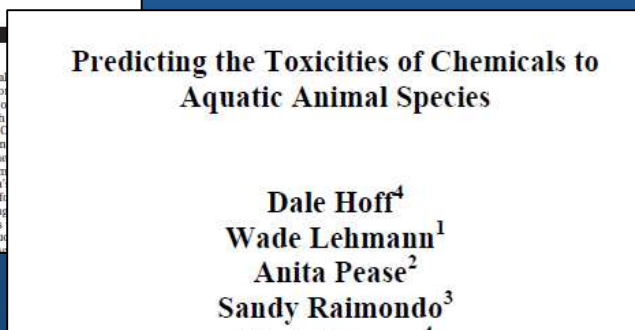
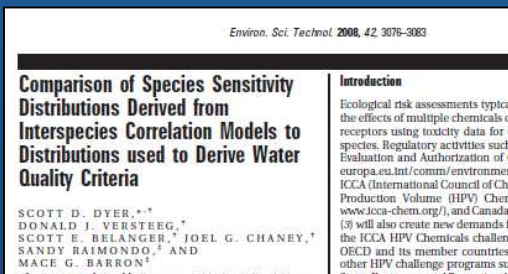
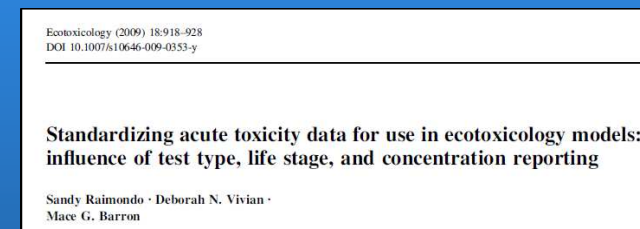
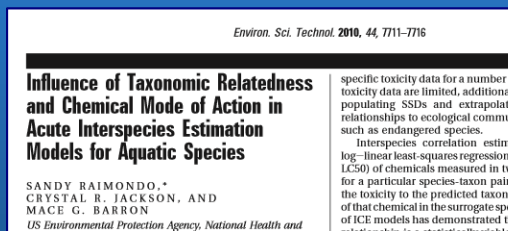
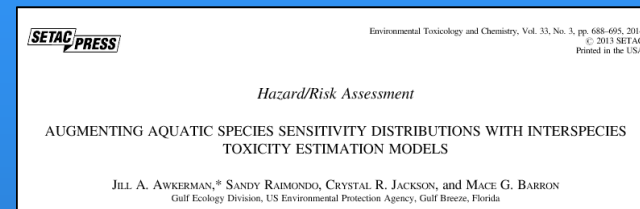
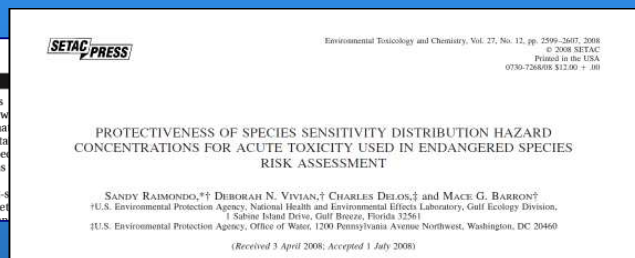
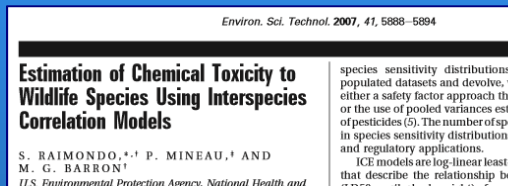
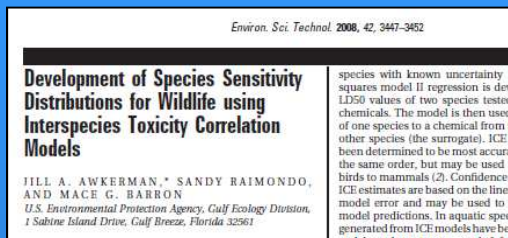
Endpoint = mortality/immobilization

- 24-48 h EC50 – fairy shrimp
- 48h EC/LC50 - daphnids, midges and mosquitoes
- 96h EC/LC50 – fish, amphibians and other invertebrates

Life stage

- fish, decapods: juvenile only
- mollusc: juvenile, spat
- amphibians, insects: immature
- all other species: all life stages except embryo/egg
- T&E listing (ecos.fws.gov/ecos/home.action)

Peer Reviewed ICE Research



Web-ICE 2015 Update (v. 3.3; October)

Increased taxa diversity and expanded T&E:

- new data developed for mussel and fairy shrimp (USGS/FWS collaboration (ms accepted, in prep))
- overall: 1.5x records, 1.8x species, 2x models
- T&E: 1.3x records; 1.5x species, 2x models



Genus and family level changed to minimum toxicity models:

- fit to minimum genus or family value (no longer geomean)

Other updates:

- 2015 User Guidance, Database Documentation, Bibliography
- new MOA specific models (based on MOAtox v. 1.0)

Updated rules of thumb:

- $MSE \leq 0.95$
- $R^2 > 0.6$
- $slope \geq 0.6$
- predicted value CI within 10x

Web-based Interspecies Correlation Estimation

(Web-ICE) for Acute Toxicity: User Manual

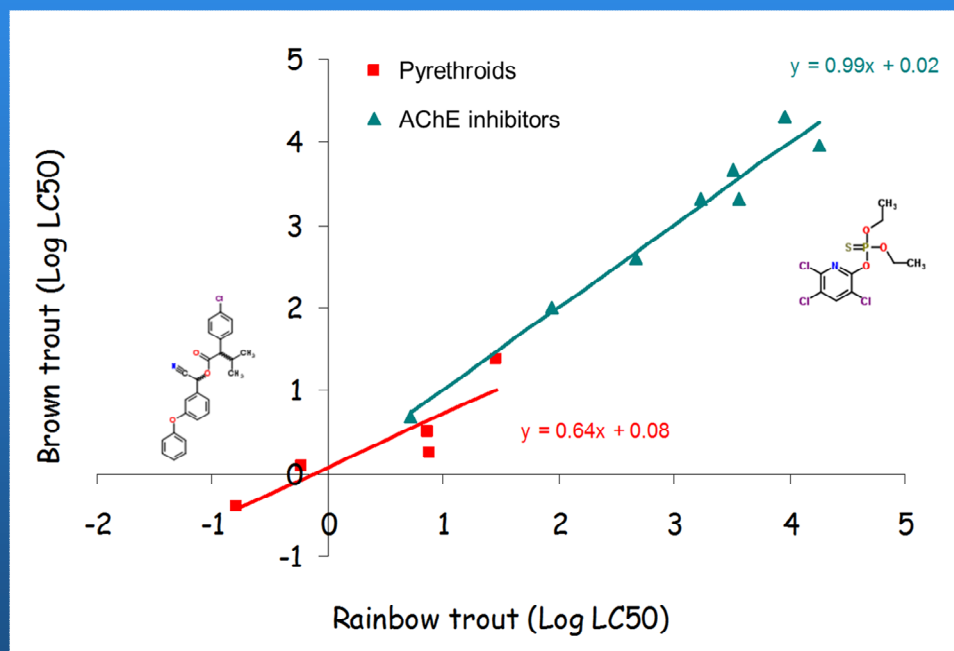
Version 3.3



<http://www.epa.gov/ceampubl/fchain/webice/>

Web-ICE v3.3: Updated MOA-specific models

- standard ICE models have chemicals of mixed mode of action (MOA)
- MOA-specific models developed using MOAtox (Barron et al. 2015)
- improved prediction accuracy for high taxa distance species pairs
- MOA-specific models downloadable via Web-ICE



MOAtox v. 1.0 database

- | | |
|--|---|
| <ul style="list-style-type: none"> • AChE inhibition (285) <ul style="list-style-type: none"> • Carbamate (74) • Organophosphate (211) • Electron transport inhibition (91) <ul style="list-style-type: none"> • Arsenical respiratory inhibition (22) • Oxidative phosphorylation inhibition (14) • Uncoupling oxidative phosphorylation (55) • Iono/Osmoregulatory/Circulatory impairment (51) <ul style="list-style-type: none"> • Anticoagulation (25) • Metallic iono/osmoregulatory impairment (14) • Methemoglobinemia (6) • Other osmoregulatory (6) • Narcosis (465) <ul style="list-style-type: none"> • Ester (48) • Unknown (9) • Nonpolar (347) • Polar (61) | <ul style="list-style-type: none"> • Neurotoxicity (201) <ul style="list-style-type: none"> • Alicyclic GABA antagonism (42) • Diphenyl sodium channel modulation (11) • GABA agonism (16) • nAChR agonism (8) • Other (9) • Pyrazole GABA antagonism (6) • Pyrethroid sodium channel modulation (102) • Sodium channel blocking (3) • Strychnine (4) • Reactivity (111) <ul style="list-style-type: none"> • Acrylate (8) • Alkylation (38) • Carbonyl (13) • Chromate (3) • Cyanate/nitrile (9) • Di/trinitroaromatic (14) • Hydrazine (4) • Other (19) • Phosphide (3) |
|--|---|



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Aquatic Toxicology

journal homepage: www.elsevier.com/locate/aquatox

MOAtox: A comprehensive mode of action and acute aquatic toxicity database for predictive model development

M.G. Barron^{a,*}, C.R. Lilavois^a, T.M. Martin^b

Web-ICE October 2015 Update: increased T&E and taxa diversity

All Species						
Web-ICE Database	Database Attributes			Number of models		
	Records	Species	Chemicals	Species	Genus	Family
v. 3.3 (2015)	8203	314	1501	1544	854	887
v. 3.2 (2013)	5501	180	1266	780	289	374

U.S. Threatened and Endangered Species						
Web-ICE Database	Database Attributes			Number of models		
	Records	Species	Chemicals	Species	Genus	Family
v. 3.3 (2015)	1591	32	492	379	428	547
v. 3.2 (2013)	1272	21	449	230	168	267

Web-ICE October 2015 Update: prediction accuracy; all species models

Cross-validation results; n>3		Percentage within prediction category				
	Taxonomic Distance	Significant Models (N)	5-fold	10-fold	50-fold	>50-fold
genus	1	444	95	4	1	0
family	2	1144	92	6	2	0
order	3	430	87	11	3	0
class	4	5734	77	10	10	3
phylum	5	1658	62	14	16	8
kingdom	6	8006	55	15	19	11

Genus and Family Level Minimum Models

Web-ICE v3.3

Genus and Family Level Models:

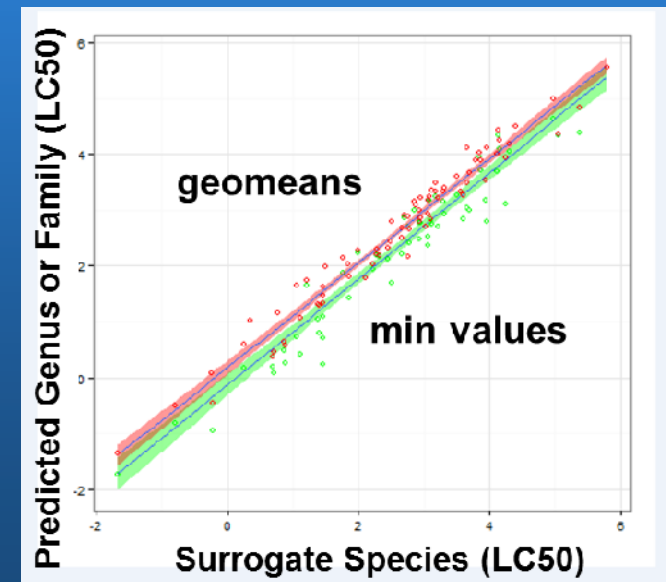
- used when species-specific ICE models not available
- need to be protective of T&E species within the Genus or Family
- previous ICE models (v. 3.2) based on geomean had limited conservatism
- min models in Web-ICE (v. 3.3)

What are minimum toxicity models:

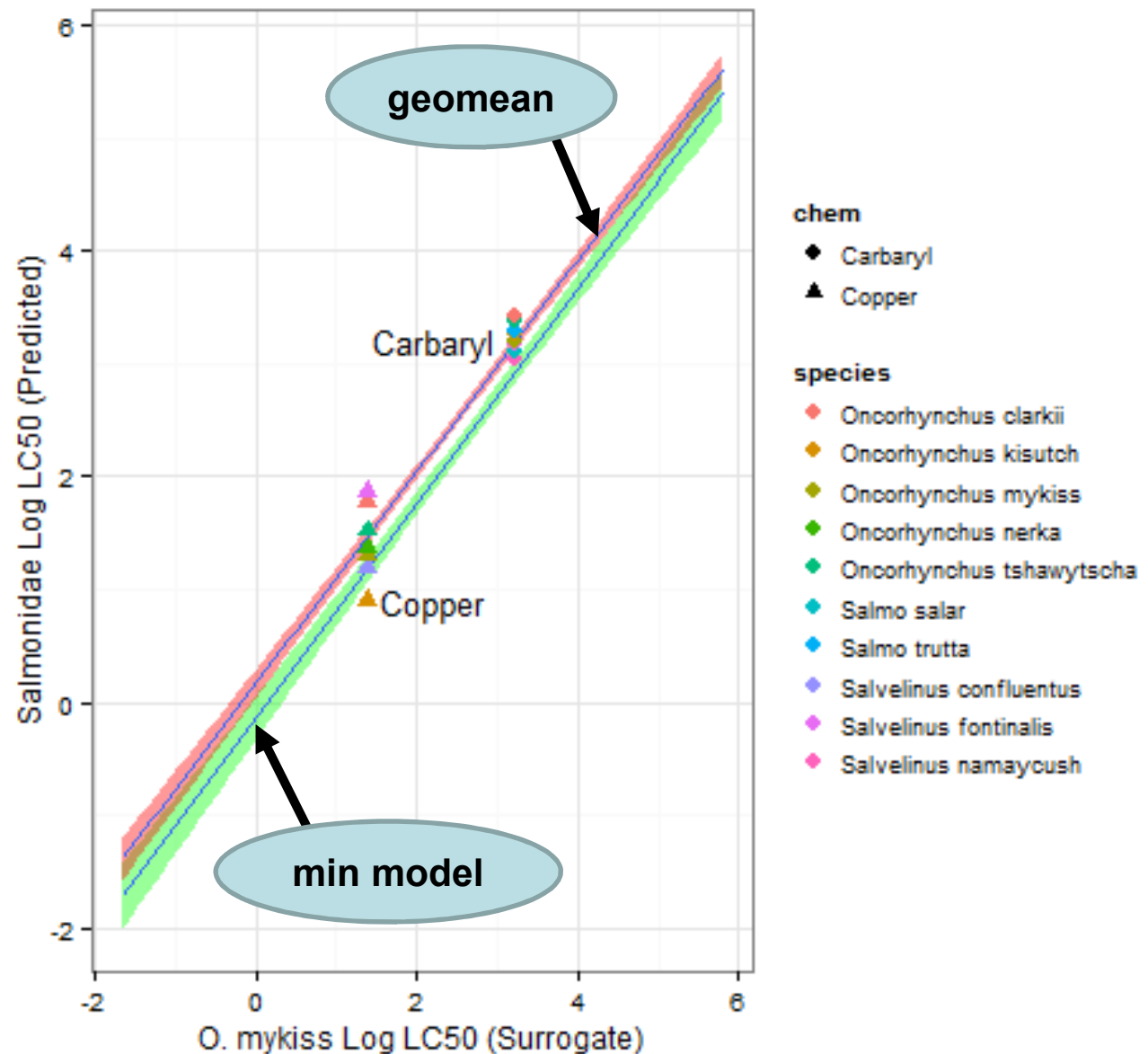
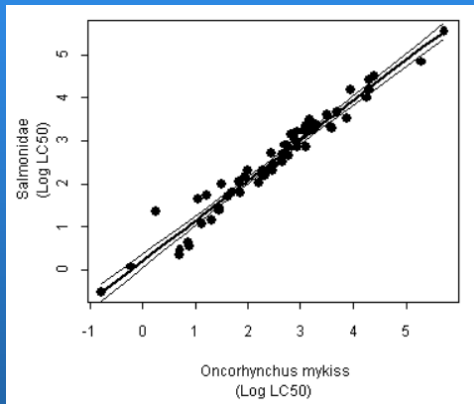
- use lowest observed LC50 for the predicted taxa (rather than geomean)
- objective is to provide more conservative estimate of toxicity to taxa containing listed species

How min models derived:

- fit to minimum measured species toxicity value within the predicted taxa (genus or family)
- no longer geomean



Trout-Salmonidae Family Level Models



Web-ICE Prediction to Listed Taxa using Min Models

Case Study based on San Francisco Delta (Hoogeweg et al. 2012*):

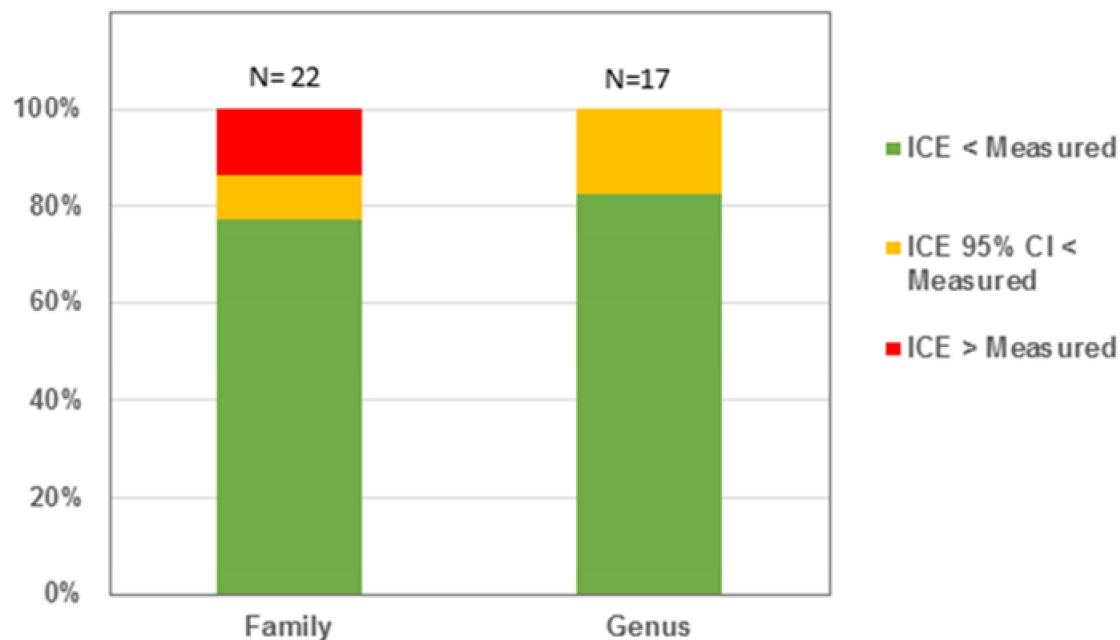
- 13 priority chemicals
- 5 Families containing listed species
- toxicity predicted to Genus and Family level using Web-ICE (v. 3.3) min models
- selected best model for each species:chemical pair using new rules of thumb
- determined percentage of ICE predicted value protective of listed species

Case Study Chems

ATRAZINE
Carbaryl
Chlorpyrifos
COPPER
Cypermethrin
Diazinon
Fipronil
GLYPHOSATE
Imidacloprid
Malathion
Methomyl
Permethrin
Thiobencarb

Case Study Taxa

Acipenseridae
Branchinectidae
Ranidae
Salmonidae
Unionidae



**Pesticide Regulation and the Endangered Species Act Chap 22. ACS Symposium Series Vol. 1111

Augmenting species diversity

Comparison of Web-ICE v. 3.3 (2015) and 3.2 (2013)

- selected 10 representative surrogates (e.g., standard test species)
- determined number of models predicting to specific taxa groups

Surrogate
Americamysis bahia
Ceriodaphnia dubia
Cyprinodon variegatus
Daphnia magna
Hyalella azteca
Ictalurus punctatus
Lampsilis siliquoidea
Lepomis macrochirus
Oncorhynchus mykiss
Pimephales promelas

Total Freshwater Web-ICE Species Models	1985 Freshwater Taxa Requirements (# models predicting to:)							
	salmonid species	any non- salmonid fish species	amphibian species	planktonic crustaceans (cladocern, copepods)	benthic crustaceans (ostracod, isopod, amphipod, crayfish, decapods)	insects	non- arthropoda or chordata (rotifer, annelid)	molluscs
v3.3	49	115	17	29	53	34	8	58
v3.2	34	79	3	15	21	21	1	0

Total Salt Water Web-ICE Species Models	Salt Water Taxa (# models predicting to:)				
	fish	arthropods	echinoderms	molluscs	polychaetes, oligochaetes
v3.3	25	24	0	8	2
v3.2	16	12	1	6	0

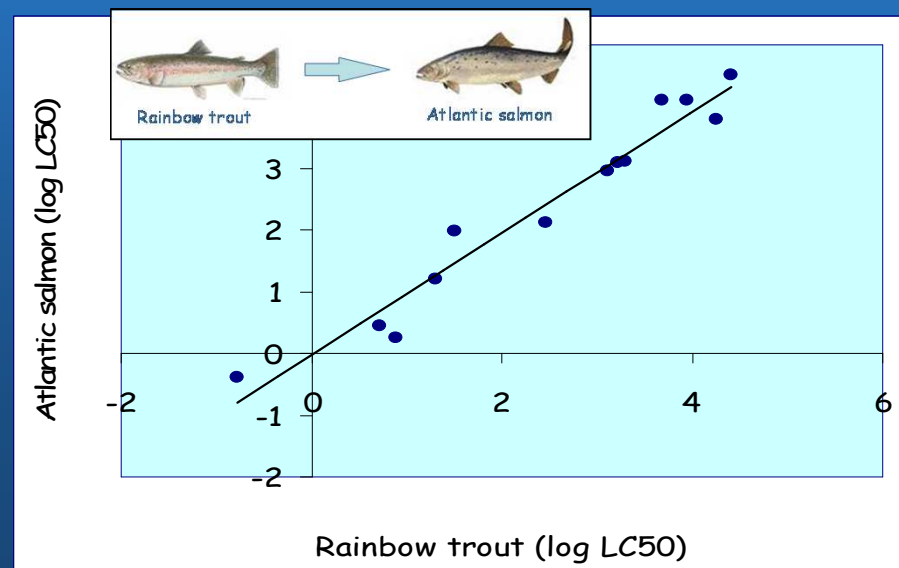
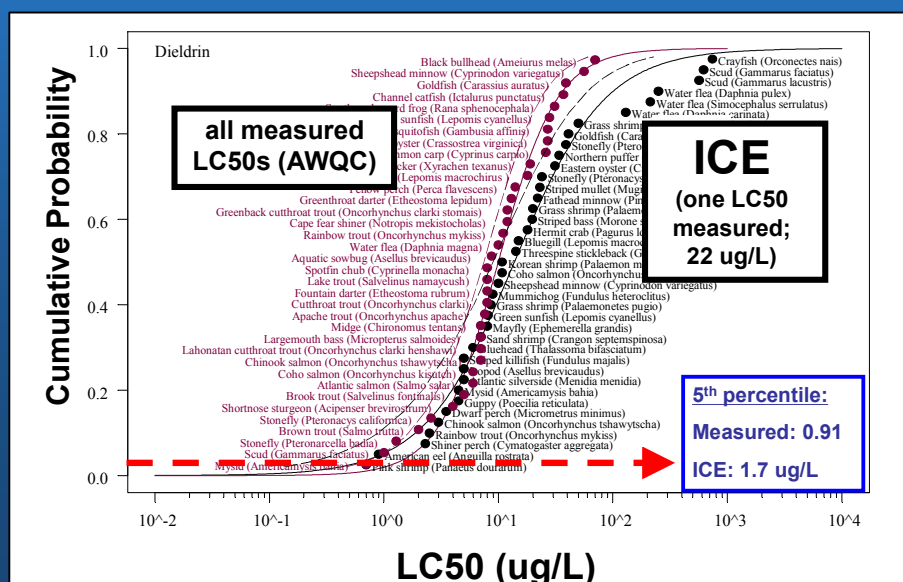
Estimating Taxa Toxicity using Web-ICE

Direct toxicity estimation:

- estimation at species, genus, or family level
- model statistics/uncertainty
- cross validation, taxonomic distance
- single surrogate or multiple surrogates (best estimate)

SSD approach:

- Hazard Concentration (HC1, HC5)
- single surrogate or multiple surrogates (augmentation)



SSD Approach

Rare species similar sensitivity as non-listed species

- species composition affects HC5 more than geography/habitat of assemblage

Raimondo et al. 2008

- HC5s and HC1s lower than 97 and 99.5% of listed species LC50s
- HC5s less than levels derived from 10x safety factors for rainbow trout
- SSD generally protective of listed species



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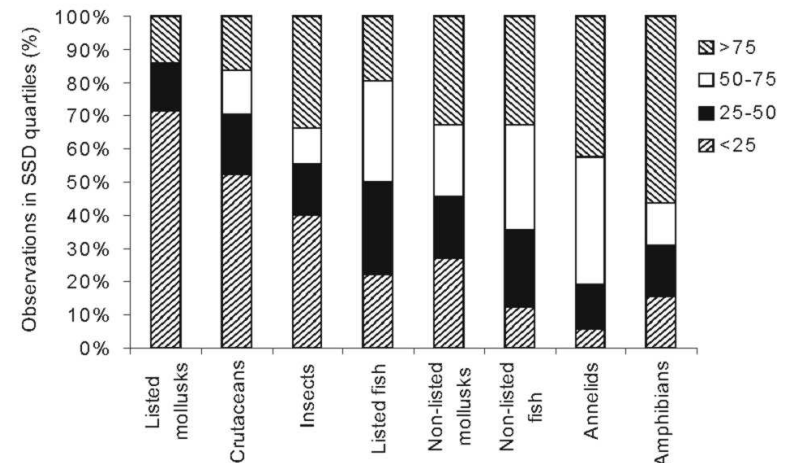
PROTECTIVENESS OF SPECIES SENSITIVITY DISTRIBUTION HAZARD CONCENTRATIONS FOR ACUTE TOXICITY USED IN ENDANGERED SPECIES RISK ASSESSMENT

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Web-ICE SSDs vs measured



Single surrogate ICE generated SSDs

- 55 AWQC chemicals (Dyer et al. 2008)
- HC5s within 10x of measured
- within taxa surrogates (fish to fish; invert to invert)

Multiple surrogates

- augment species diversity
- > 90% within 5 fold (Awkerman et al. 2014)
- accuracy affected by species composition, MOA

Environ. Sci. Technol. **2008**, *42*, 3076-3083

Comparison of Species Sensitivity Distributions Derived from Interspecies Correlation Models to Distributions used to Derive Water Quality Criteria

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MACE G. BARRON[‡]

Introduction

Ecological risk assessments typically require characterizing the effects of multiple chemicals on a diversity of ecological receptors using toxicity data for only a limited number of species. Regulatory activities such as REACH (Registration, Evaluation and Authorization of Chemicals) (1, 2; <http://europa.eu.int/comm/environment/chemicals/reach.htm>), ICCA (International Council of Chemical Associations) High Production Volume (HPV) Chemicals Challenge (<http://www.icca-chem.org/>), and Canada's Domestic Substance List (3) will also create new demands for toxicity data. Note that the ICCA HPV Chemicals challenge is in cooperation with OECD and its member countries which then also include other HPV challenge programs such as those of the United

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Hazard/Risk Assessment

AUGMENTING AQUATIC SPECIES SENSITIVITY DISTRIBUTIONS WITH INTERSPECIES TOXICITY ESTIMATION MODELS

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Web-ICE v3.3 SSD Generator



United States Environmental Protection Agency

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Interspecies Correlation Estimation

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Species Sensitivity

Calculates hazard level confidence interval

Surrogate Species: Fathead minnow (Lepomis macrochirus), Daphnid (Daphnia magna), Sheepshead minnow (Cyprinodon variegatus)

Input Toxicity: 150, 125, 75, 100 µg/L

HCS 8.54 µg/L 95% Confidence Interval: 1.49 – 21.20

Data Filters (Upper and Lower Limits)

Filter

	Lower	Upper		Lower	Upper
Degrees of Freedom (N-2)			Cross-validation Success (%)		
R2			Taxonomic Distance		
p-value			Slope		
Mean Square Error (MSE)			Intercept		

Provide Copy-friendly Output for Selected Data Provide Copy-friendly Output for All Data

Common Name	Scientific Sort	Estimated Toxicity Sort	95% Confidence Intervals Sort	Surrogate Sort	Degrees of Freedom (N-2) Sort	R2 Sort	p-value Sort	Mean Square Error (MSE) Sort	Cross-validation Success (%) Sort	Taxonomic Distance Sort	Slope Sort	Intercept Sort
☒ Amphipod	Gammarus pseudolimnaeus											
☐ Amphipod	Gammarus	54.62	14.45 – 206.39	Daphnid (Daphnia magna)	11	0.77	0.0000	0.87	53.84	5	1.01	-0.16
☐ Amphipod			6.29 – 53.71	Bluegill (Lepomis macrochirus)	15	0.82	0.0000	0.75	64.70	6	1.07	-0.99
☐ Amphipod			1.27 – 10.87	Fathead minnow (Pimephales promelas)	7	0.93	0.0000	0.28	77.77	6	1.26	-2.17
☒ Apache trout	Oncorhynchus mykiss	40.06	13.50 – 118.84	Fathead minnow (Pimephales promelas)	3	0.92	0.0083	0.10	80.00	4	1.00	-0.57
☒ Atlantic salmon	Salmo salar											
☐ Atlantic salmon	Salmo salar	51.05	28.00 – 90.00						100.00	4	1.12	-0.64
☐ Atlantic salmon	Salmo salar	39.18	5.00 – 20.00						66.66	4	1.15	-0.91
☒ Black bullhead	Ameiurus melas											
☐ Black bullhead	Ameiurus melas	456.09	94.09 – 2180.00	Bluegill (Lepomis macrochirus)	9	0.65	0.0024	0.98	63.63	4	0.88	0.81

Unclick boxes to exclude species

Simultaneously calculates toxicity & confidence intervals from all available models

Summary



- NRC (2013) recommended ICE models as alternative to generic safety factors
- Web-ICE platform: data, models, modules for SSDs and T&E extrapolation
 - models for 250 U.S. federally listed T&E; 120 surrogate species
 - most models predict to genus and family
 - mollusc models expand family level predictions to 87 unionids
 - SSD generation additional approach for T&E protective levels
- peer reviewed technical basis (journal articles; FIFRA Science Advisory Panel)
- Web-ICE toxicity estimates and ICE-SSD HCs demonstrated high accuracy for closely related taxa (within same order)
- Web-ICE toxicity extrapolation: increase taxa diversity in SSDs for development of AWQC with reasonable uncertainty

QUESTIONS?



www.epa.gov/ceampubl/fchain/webice/