CLiCC Webinar II

September 30, 2016

CLiCC Webinar 2
QSAR, Release, Fate & Transport

Mengya Tao, Dingsheng Li, Runsheng Song,
Rucha Thakar, Kendra Garner, Dillon Elsbury

CLiCC Webinar Series

- **Webinar 1, September 14th, 10am - 11am PDT.**
  CLiCC Life-Cycle Inventory module

- **Webinar 2, September 30th, 10am - 11am PDT.**
  CLiCC QSAR, Release, and Fate & Transport modules

- **Webinar 3, October 7th, 10am - 11am PDT.**
  CLiCC Predictive Life Cycle Impact Assessment, Exposure, Toxicity, and Uncertainty modules

All webinars are recorded and
will be available for viewing on clicc.ucsb.edu

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UCSB Team Leadership

Key Team Members


Stefano Cucurachi
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Dingsheng Li
Exposure Module


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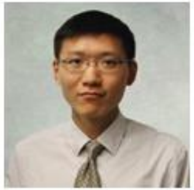
Output Visualization & Pilot Testing


Yiting Ju
Ontology Module


Jeff Frumkin
Chemical Production Module


Runsheng Song
Predictive LCI Module


Kendra Garner
Fate & Transport Module


Mengya Tao
QSAR Module


Yuwei Qin
Uncertainty Module


Dillon Elsbury
Fate & Transport Module


Rucha Thakar
Fate & Transport Module

Webinar 2 Discussion

- QSAR Module (Mengya Tao, PhD Student)
- Release Module (Dr. Dingsheng Li)
- Fate and Transport Module (Dr. Kendra Garner)

QSAR MODULE

Quantitative **S**tructure **A**ctivity **R**elationship

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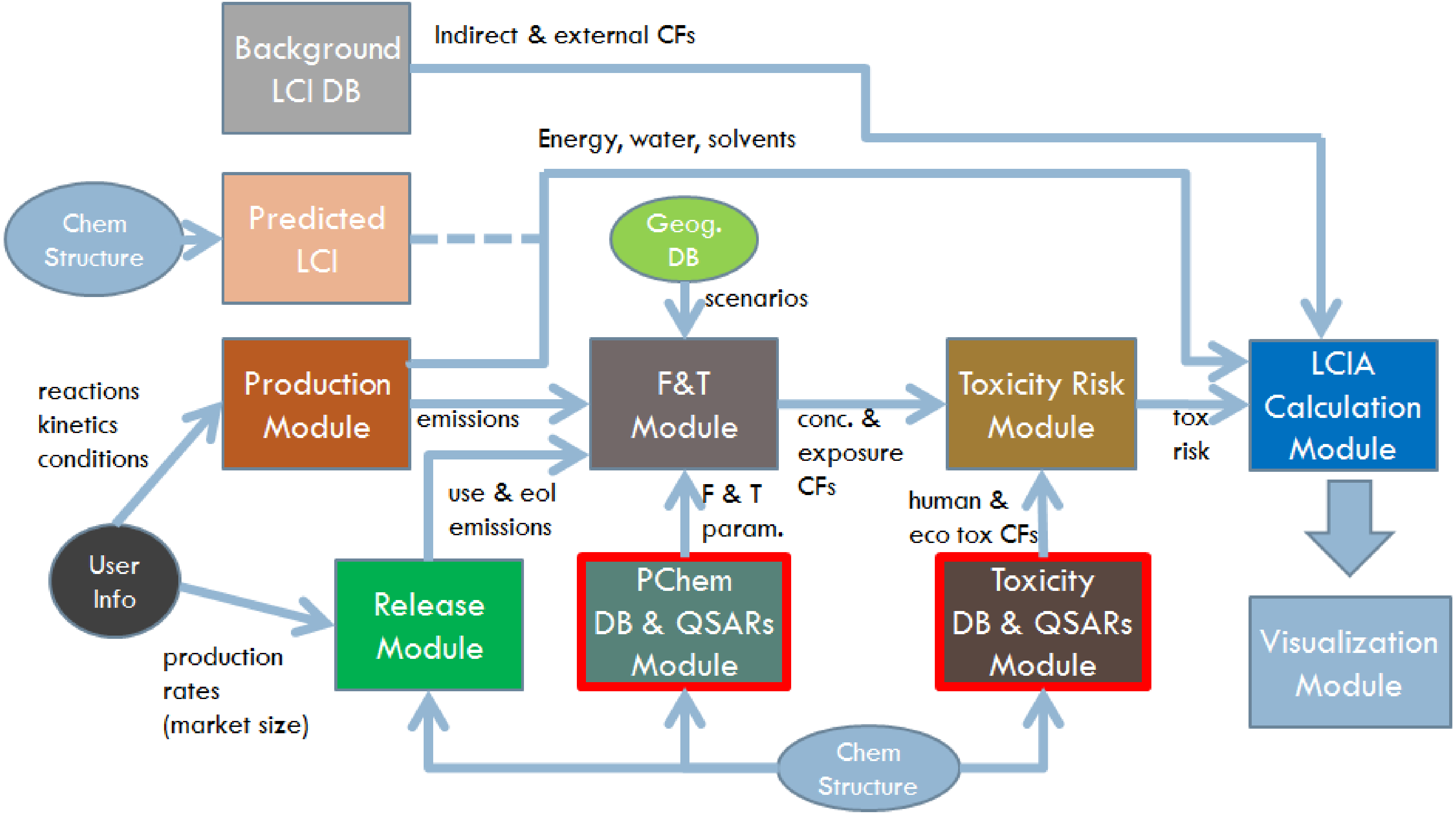
CLiCC Workflow



Overview of QSAR Models

- Goal: Fill in the data gap from available chemical information by QSAR model predictions

- QSARs have been well-developed over the past 50 years and it grows exponentially due to 1) more chemical databases available 2) more advanced statistical techniques

- Assumption: similar chemical structures lead to similar biological activities

QSAR Module Data Sources

	Chemical Databases (Evaluated over 30 sources)	QSAR Tools (Evaluated over 20 tools)
Environmental and Ecotoxicological	PubChem, ChemSpider, ECHA CHEM, ACToR, TOXNET, Enhanced NCI Database Browser, DSSTox, ECOTOX	EPI Suite, T.E.S.T, ECOSAR, VEGA, OpenTox, Demetra, QSAR Toolbox
Human Health Effect	PubChem, ECHA CHEM, ACToR, TOXNET, DSSTox	T.E.S.T, Toxtree, VEGA, Lazar, OpenTox, OncoLogic, QSAR Toolbox

Selected QSAR Tools

- EPI Suite - US EPA
- T.E.S.T - US EPA, Dr. Todd Martin
- VEGA - Istituto di Ricerche Farmacologiche Mario Negri Milano, Dr. Emilio Benfenati & Dr. Alberto Manganaro

Current Endpoints & Prediction Tools

	Endpoint	Unit	Prediction Tool
Physico-chemical and Environmental Fate	Molecular Weight	g/mol	EPI Suite
	Density	g/cm^3	T.E.S.T
	BCF	L/kg wet-wt	EPI Suite, T.E.S.T, VEGA
	Octanol/water partition coefficient (Kow)	unitless	EPI Suite, VEGA
	Organic carbon/water partition coefficient (Koc)	unitless	EPI Suite
	Air/water partition coefficient (Kaw)	unitless	EPI Suite
	Aerosol/air partition coefficient (Koa)	unitless	EPI Suite
	Degradation rate in air (halflife)	h	EPI Suite
	Degradation rate in water (halflife)	h	EPI Suite
	Degradation rate in soil (halflife)	h	EPI Suite
	Degradation rate in sediment (halflife)	h	EPI Suite
	Vapor Pressure	mmHg	EPI Suite, T.E.S.T
	Water Solubility	mg/L	EPI Suite, T.E.S.T
WWTP Process	Total Removal	%	EPI Suite
	Total Biodegradation	%	EPI Suite
	Total Sludge Adsorption	%	EPI Suite
	Total to Air	%	EPI Suite
Ecological Effect	Fish Acute LC50	mg/L	VEGA
	Fathead Minnow LC50 96h	mg/L	T.E.S.T, VEGA
	Daphnia Magna LC50 48h	mg/L	T.E.S.T, VEGA
Human Health Effect	Mutagenicity	Yes/NO	T.E.S.T, VEGA
	Carcinogenicity	Yes/NO	VEGA
	Developmental Toxicity	Yes/NO	T.E.S.T, VEGA
	Estrogen Receptor	Yes/NO	VEGA
	Skin Sensitization	Yes/NO	VEGA
	Oral Rat LD 50	mg/kg	T.E.S.T

Current Endpoint Selection Criteria

Minimum, maximum, arithmetic mean, standard deviation are obtained:

- **Step 1**: **Experimental values**
- **Step 2: VEGA with High reliability/TEST Consensus**
- **Step 3: VEGA with moderate reliability/EPI Suite**
- **Step 4: VEGA with low reliability**

QSAR Example - Phthalic anhydride (CAS 85-44-9)

Module		Avg	MAX	MIN	Sample Size	SD	Note	Source	Unit
Fate & Transport Module	MD	1.53E+00	1.53E+00	1.53E+00	4	0	exp	TEST	g/cm^3
	MW	1.48E+02	1.48E+02	1.48E+02	1	0	NA	EPI	g/mol
	DegAero	5.13E-03	5.13E-03	5.13E-03	1	0	est	EPI	1/day
	DegAir	4.85E-02	4.85E-02	4.85E-02	1	0	est	EPI	1/day
	DegSSed	5.13E-03	5.13E-03	5.13E-03	1	0	est	EPI	1/day
	DegSed	5.13E-03	5.13E-03	5.13E-03	1	0	est	EPI	1/day
	DegSoil	2.31E-02	2.31E-02	2.31E-02	1	0	est	EPI	1/day
	DegWater	4.62E-02	4.62E-02	4.62E-02	1	0	est	EPI	1/day
	kAerAir	5.97E+07	5.97E+07	5.97E+07	1	0	est	EPI	NA
	kAirWater	6.67E-07	6.67E-07	6.67E-07	1	0	est	EPI	NA
	kOctWater	3.98E+01	3.98E+01	3.98E+01	4	0	exp	VEGA & EPI	NA
	kOrgWater	1.62E+01	2.25E+01	1.00E+01	2	6.23E+00	est	EPI	NA
Release Module	VP	6.80E-07	6.80E-07	6.80E-07	2	6.58E-10	exp	EPI & VEGA	atm
	WS	6.20E+03	6.20E+03	6.20E+03	2	1.59E+00	exp	EPI & VEGA	mg/L
Toxicity Module	BCF	2.43E+00	5.28E+00	5.20E-01	5	2.17E+00	est moderate	VEGA & EPI	L/kg wet-wt
	Orat LD50	1.53E+03	1.53E+03	1.53E+03	3	2.27E-13	exp	TEST	mg/kg
	dmLC50	2.33E+00	3.72E+00	9.48E-01	2	1.39E+00	est low	VEGA	mg/L
	fishLC50	8.32E+01	8.32E+01	8.32E+01	1	0	est good	VEGA	mg/L
	fmLC50	1.92E+01	1.92E+01	1.92E+01	1	0	est moderate	VEGA	mg/L

Module		Avg	# of N	# of P	# of NC	SS	Note	Source
Direct Output	ER	negative	2	0	0	2	est good	VEGA
	carciTox	negative	4	0	0	4	exp	VEGA
	deveTox	negative	1	0	0	1	est	TEST
	mutaTox	negative	5	0	0	5	exp	VEGA & TEST
	skinSensi	negative	1	0	0	1	est good	VEGA

est: estimated

exp: experimental

RELEASE MODULE

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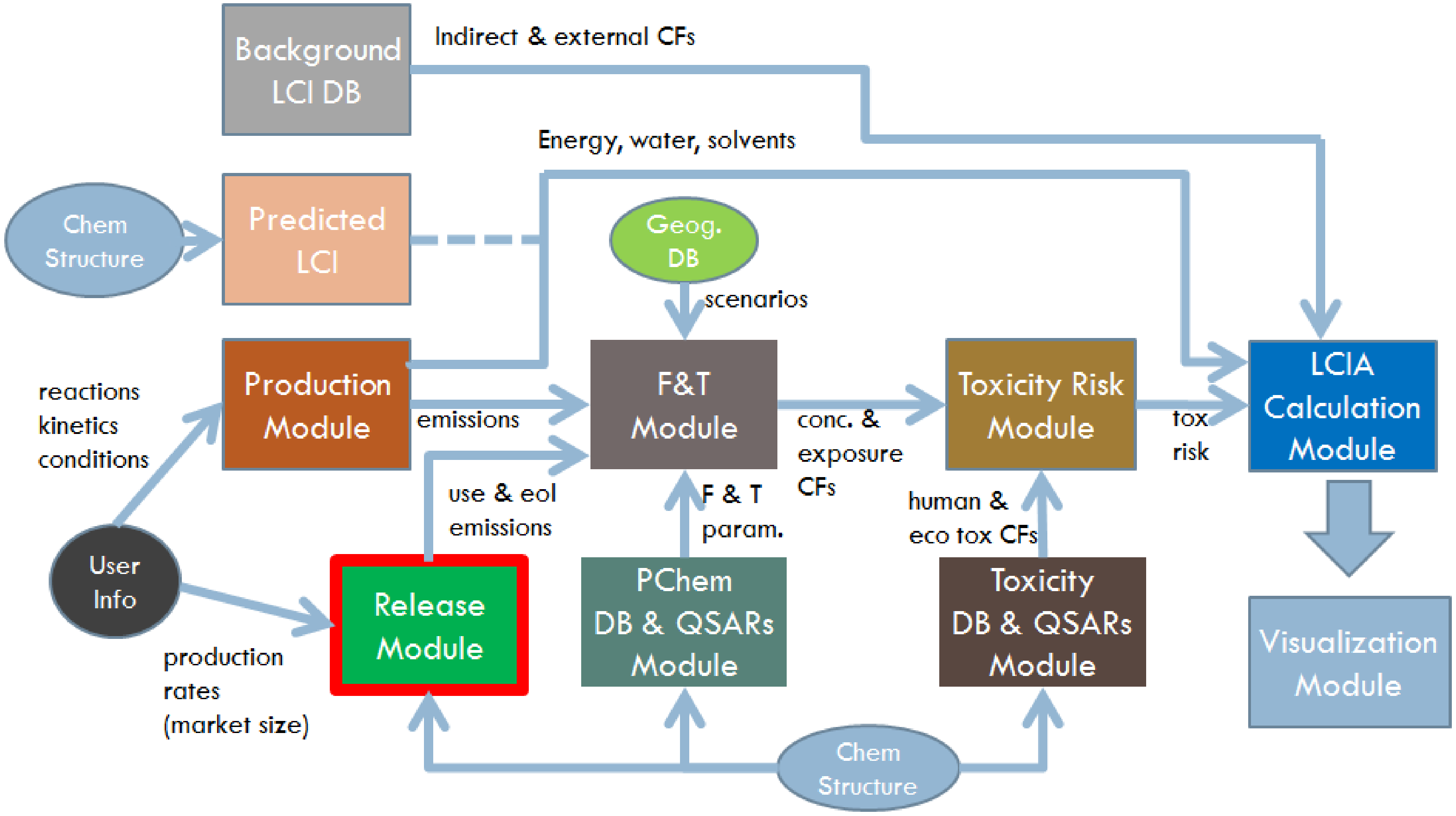
CLiCC Workflow



Sources of Release

- **Outdoor**
  - Point sources: stacks, pipes, etc.
  - Area sources: open burning, runoff, etc.
- **Indoor**
  - Stoves
  - Consumer products

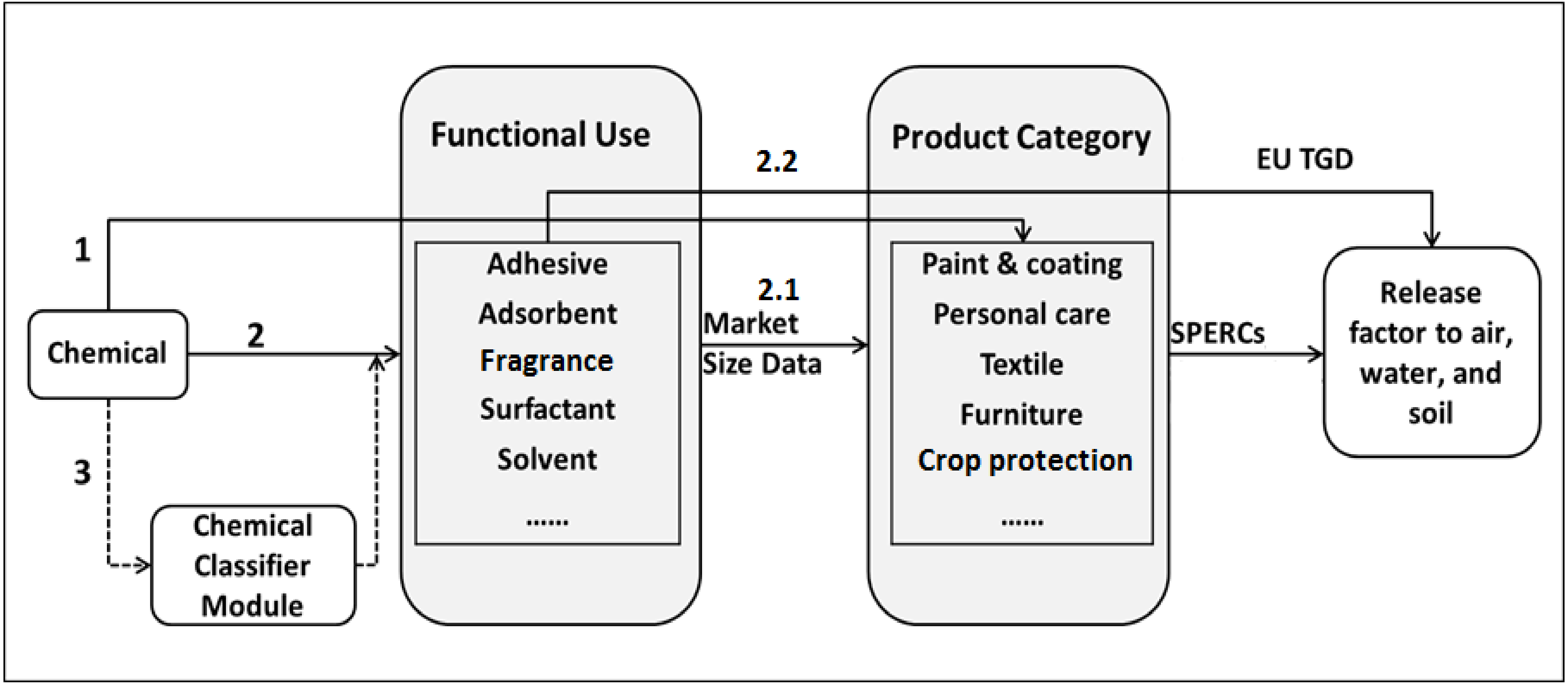
Assessing the release of chemicals from consumer products is most challenging

Estimating Release

- **Bottom-up approach**
  - Study the specific type of consumer product and use patterns
  - Need to know the detail information of the ingredients, which may not be available

- **Top-down approach**
  - Linking the chemicals’ functional uses, product categories, and release factors
  - Able to perform screening of many chemicals

Release Framework



Market Size Data (Samples)

Samples of market size data (numbers are not accurate due to confidentiality)

Product categories	Functional uses			
	Solvents	Surfactants	Biocides	Aerosol propellants
Paints & coatings	62.0%	3.0%	13.0%	17.0%
Printing inks	10.0%			
Pharmaceuticals	7.5%			
Cosmetics/Personal Care	3.5%	20.0%	12.0%	35.0%
Adhensives	2.5%			
Construction		4.0%		
Home care		45.0%		30.0%
Industrial & institutional cleaners		4.0%		
Food processing		3.5%		
Oilfield chemicals		4.0%		
Agricultural chemicals		4.0%	18.0%	
Textile		2.5%		
Water treatment			20.0%	
Food & beverage			21.0%	10.0%
Wood preservation			16.0%	
Medical				5.5%
Other	14.5%	10.0%		2.5%

Release Factors Data Sources

- **SPERCs SPecific Environmental Release Categories**
  - Developed by a variety of European trade groups and sector organizations
  - More than 190 SPERCs have been developed in a standardized format by 13 industry sectors
- **EUTGD - European Union Technical Guidance Documents**
  - Mainly for functional use
- **Note that these release factors are for use phase only, mass balance may not add up to 1 - there may be release in disposal phase**

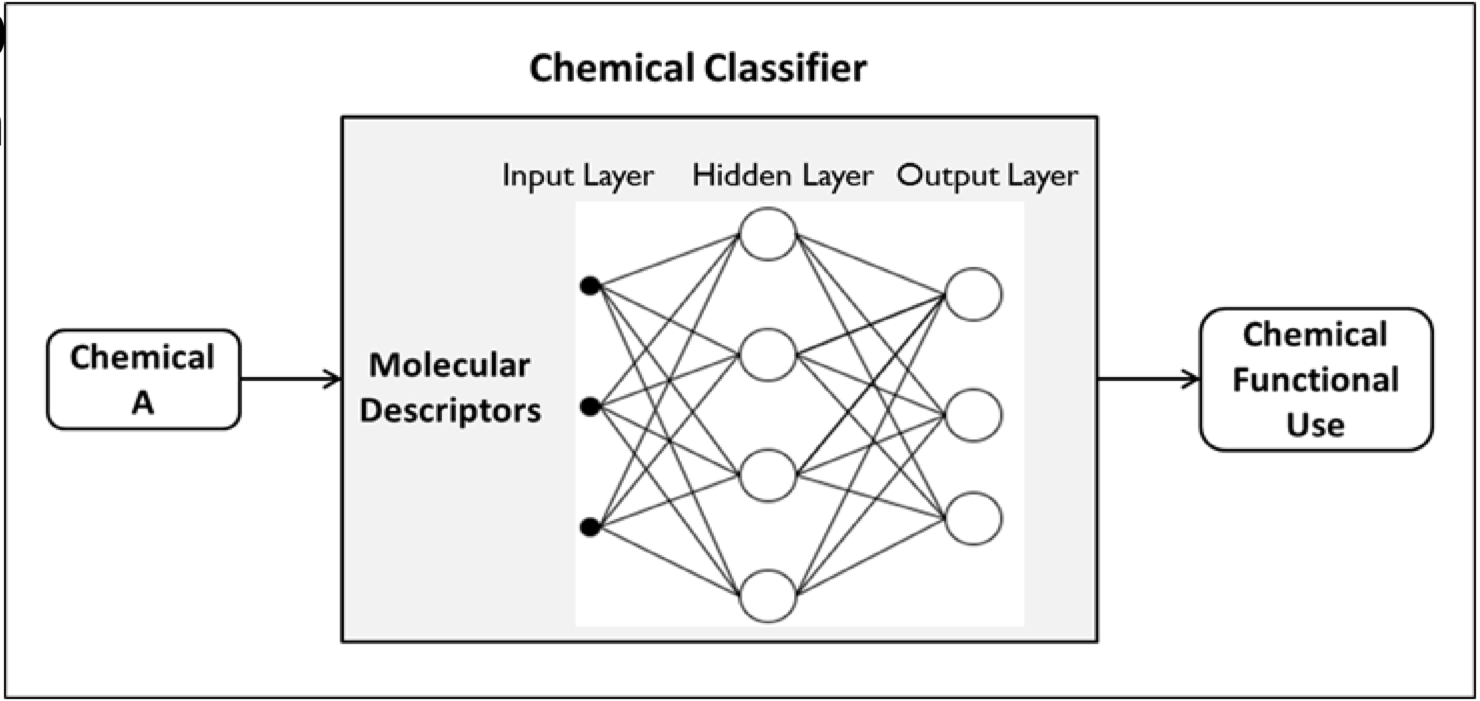
SPERC Data Samples

Samples of SPERC release factor data

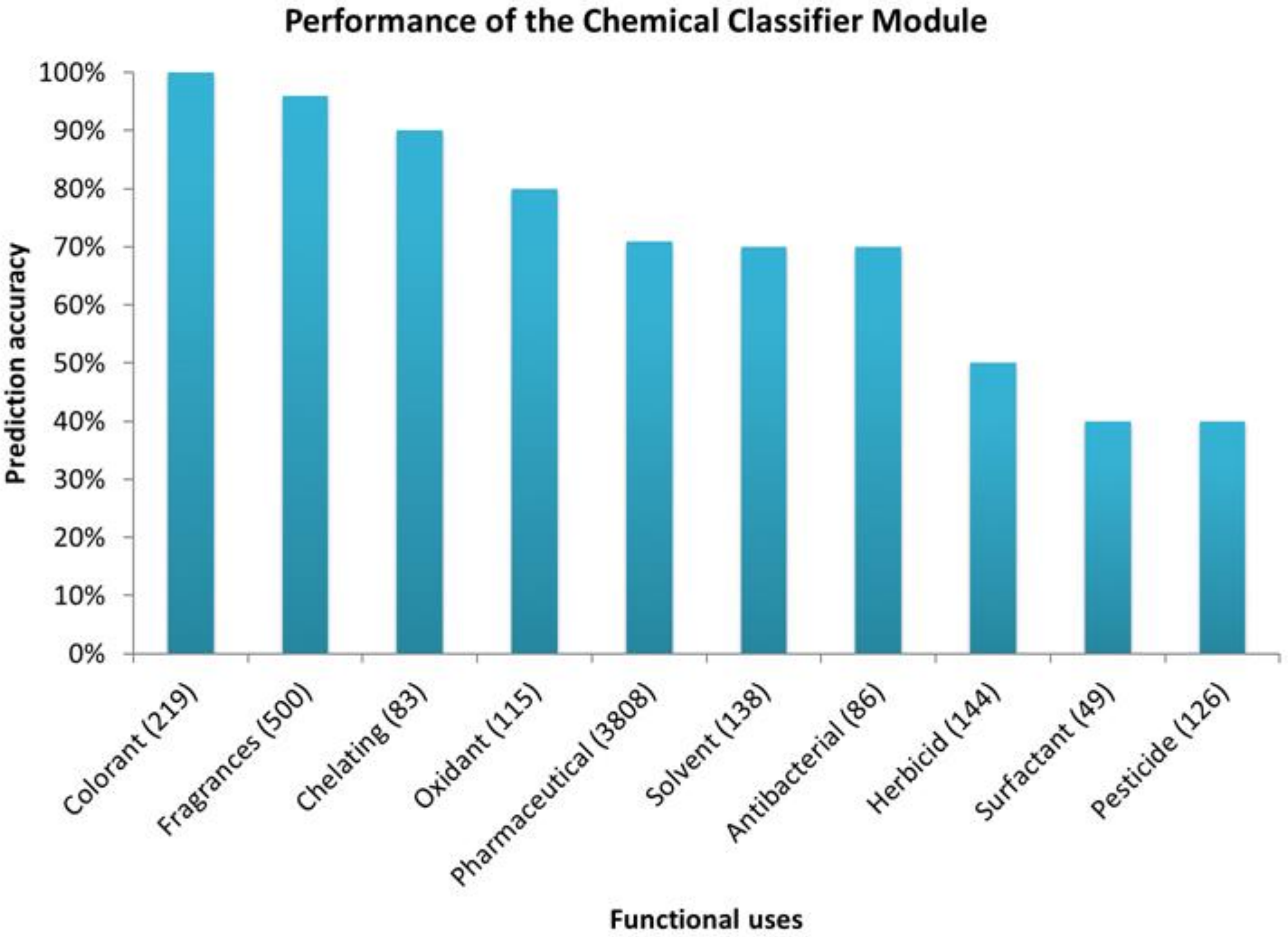
Product Category	SPERC Code	Use Type	Application Type	Indoor/ Outdoor	Closed/ Open System	Physical Property	Release fraction to air	Release fraction to waste water	Release fraction to soil	Release fraction to waste
Hair and Skin Care Products	Cosmetics Europe SPERC 8a.1.a.v2	Wide Dispersive Use	Down the drain	NA	NA	NA	0	1	0	0
	Cosmetics Europe SPERC 8a.1.b.v2	Wide Dispersive Use	Aerosol (Propellants)	NA	NA	NA	1	0	0	0
	Cosmetics Europe SPERC 8a.1.c.v2	Wide Dispersive Use	Aerosol (Non-Propellants)	NA	NA	NA	0	1	0	0
Crop Protection Products	ECPA SPERC 8d.1.v2	All Uses	Solids	Both	NA	NA	0	0	1	0
	ECPA SPERC 8d.2.v2	All Uses	Spray	Both	NA	Vapor Pressure	VP > 0.01 Pa = 1; VP 0.001-0.01 Pa = 0.5; VP 0.0001-0.001 Pa = 0.2; VP 0.00001-0.0001 Pa = 0.1; VP <= 0.00002 Pa = 0.01	0	VP > 0.01 Pa = 0; VP 0.001-0.01 Pa = 0.5; VP 0.0001-0.001 Pa = 0.8; VP 0.00001-0.0001 Pa = 0.9; VP <=0.00001 Pa = 0.99	0

Chemical Classifier Module

- Using Artificial Neural Networks (ANNs) as the modelling basis
- 80
  Ch



Classifier Accuracy



Release Example - Phthalic anhydride

Mainly used as an intermediate in the production of plasticizer

CAS	85-44-9
SMILES	O=C(OC(=O)c1cccc2)c12
Vapor pressure	5.17*10-4 mm Hg at 25 C
Water solubility	6000 mg/L at 25 C
Boiling point	295 C

Release Example

- Pathway 1
  - Product category known as intermediate
  - No release data currently available to proceed

- Pathway 2.1
  - Functional use known as intermediate
  - No market size data to determine product application streams to proceed

Release Example

- Pathway 2.2
  - Functional use known as intermediate
  - Based on EU TGD #55 Others
  - Considering the vapor pressure and solubility
  - Release fraction to air: 0.00075
  - Release fraction to wastewater: 0.1
  - Release fraction to soil: 0.2
  - Release fraction to landfill: 0.69925

Release Example

- Pathway 3
  - Classifier decides it is a pharmaceutical
  - Based on EU TGD #41 Pharmaceutical
  - Release fraction to air: 0
  - Release fraction to wastewater: 0.05
  - Release fraction to soil: 0
  - Release fraction to landfill: 0.95

Fate and Transport for Chemicals

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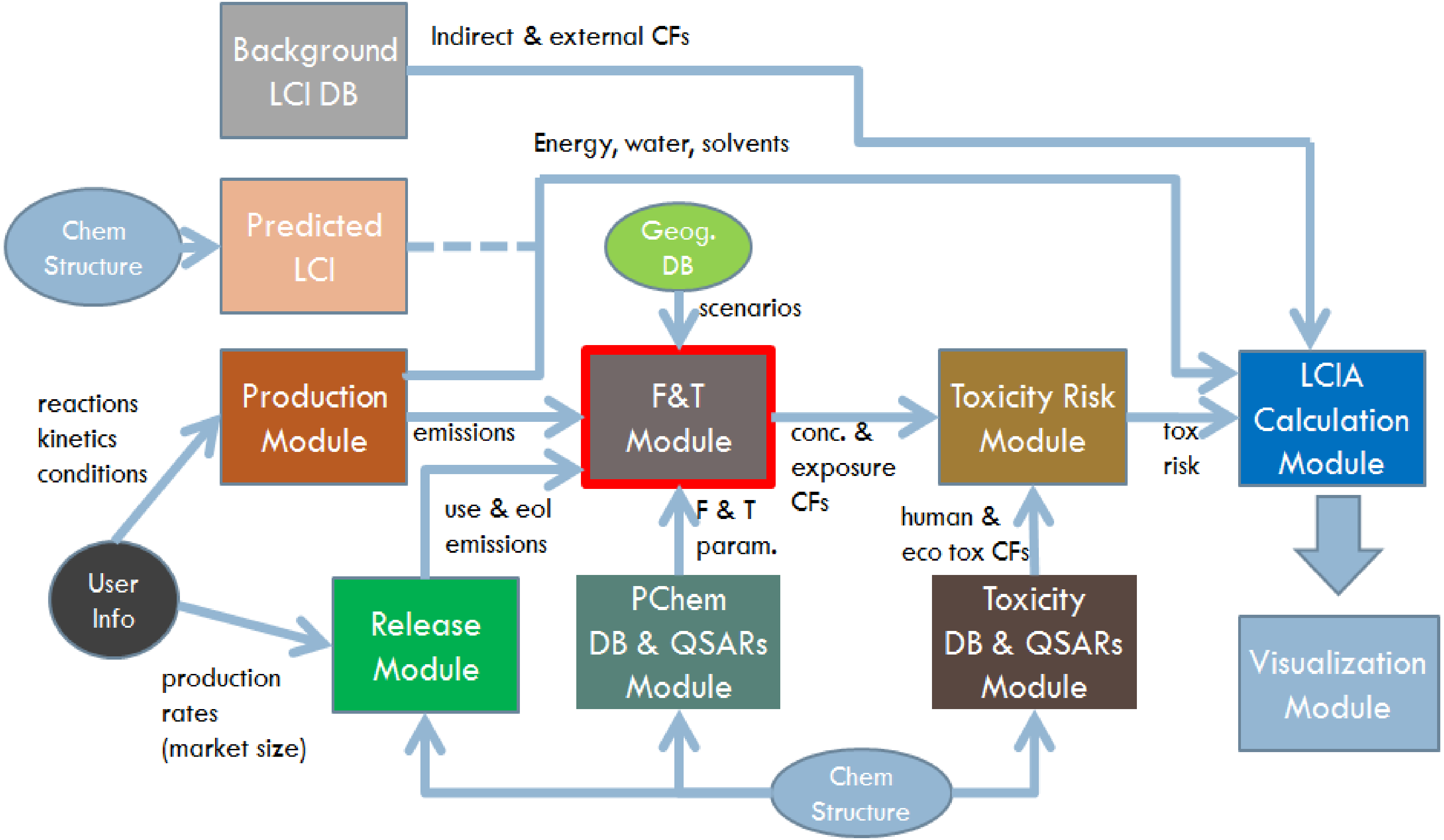
CLiCC Workflow



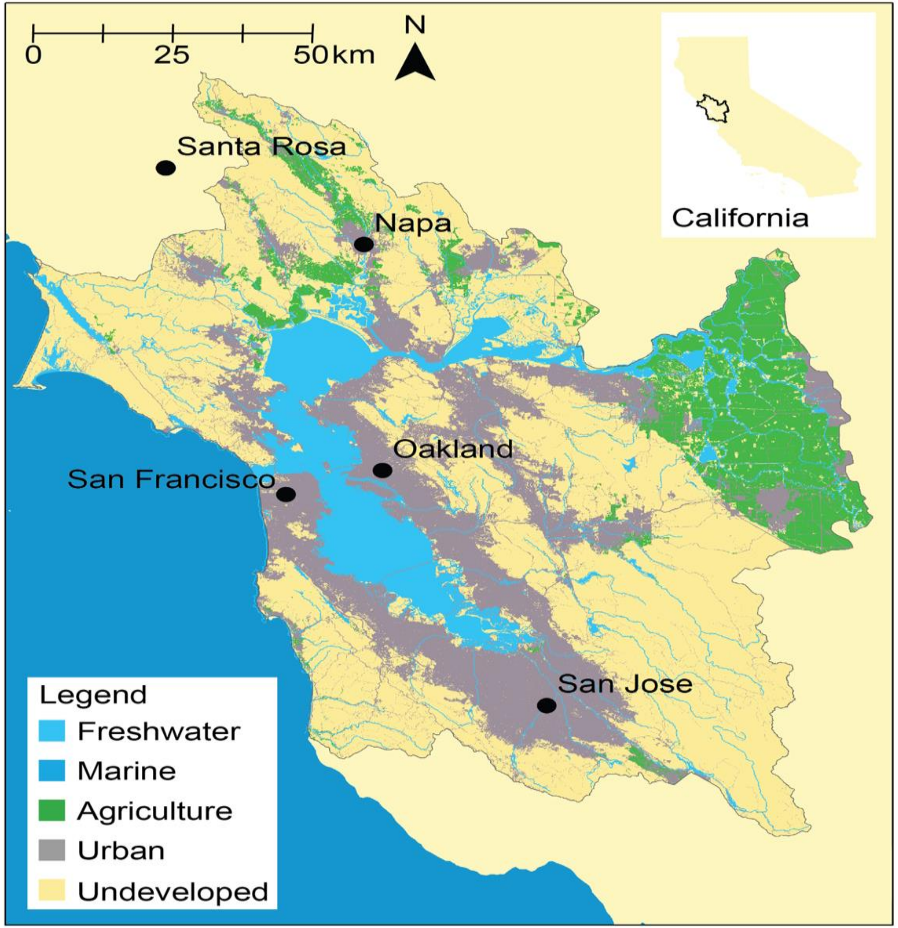
CLiCC Fate & Transport Model	Other Models
• Mass balance model – Non-steady state model	Steady-state
• Predicts time-dependent <u>daily</u> concentrations	Output is average value at steady state
• Uses regionally specific climate data	Low resolution
• Release scenario is fully customizable	Rigid structure

Model Capabilities

- Traditional Fate and Transport Models also only accurately predict fate for organic chemicals
  - Different types of chemicals are subject to different biogeochemical processes
- We have separate models for:
  - Organic Chemicals
  - Nanomaterials
  - Inorganics including metals (In Development)
  - Polymers (In Development)

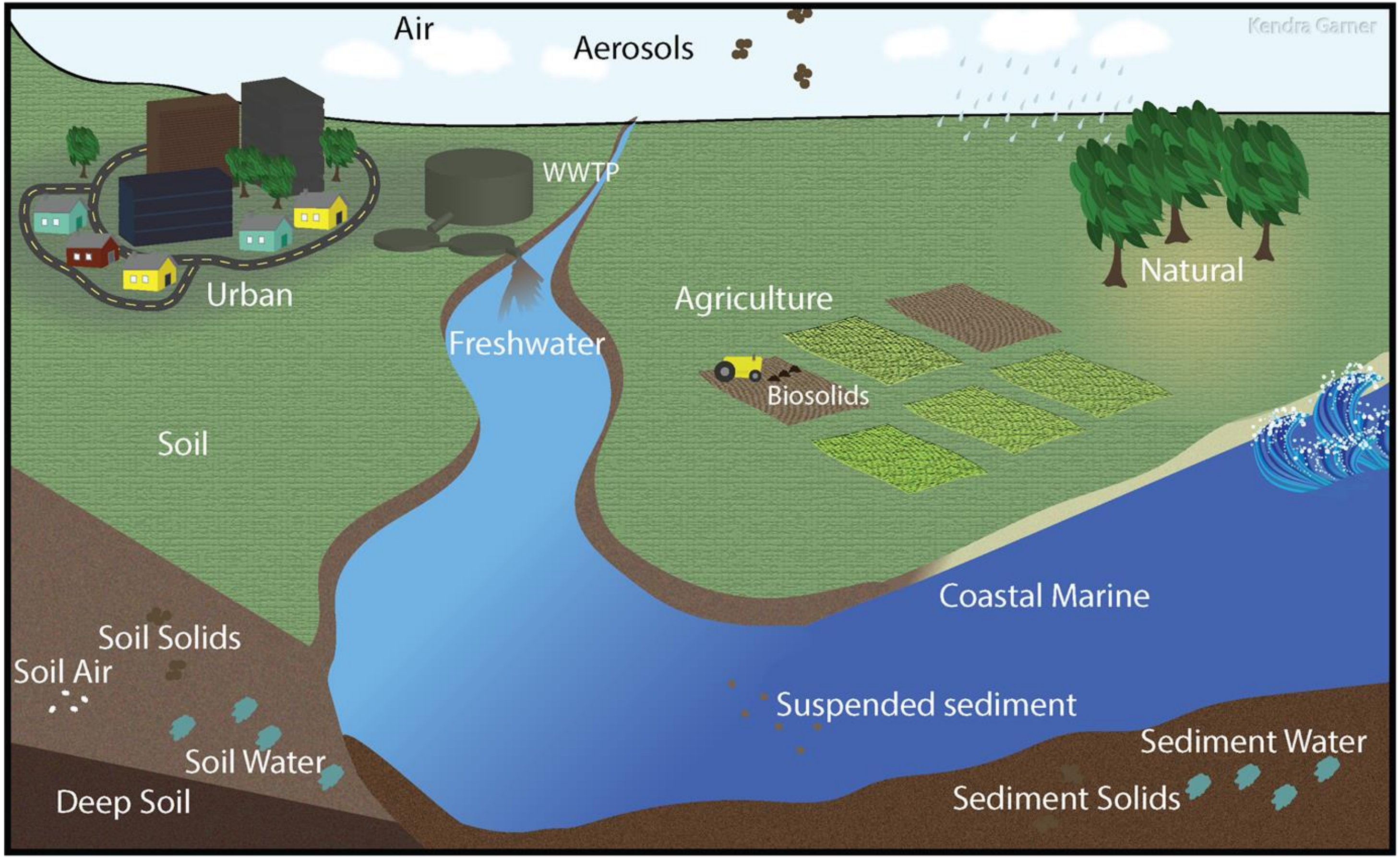
Each location is unique

- Hydro-Climatic conditions
  - Rainfall
  - Wind speed
  - Temperature
  - Surface water flow
- Land Use Types
  - Urban land
  - Agricultural land
  - Natural land
  - Freshwater
  - Seawater
- Population

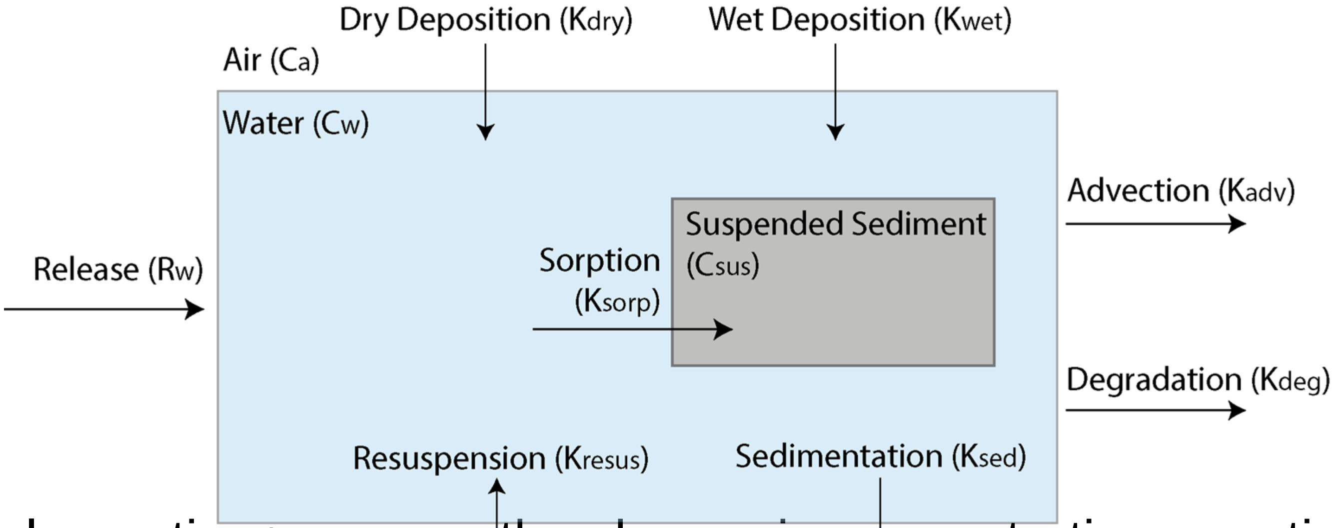


Sample geographical region:
San Francisco, CA

Conceptual Environment



Each environmental compartment is a box which can gain or lose mass



Differential equations express the change in concentration over time in each compartment

$$\triangle C_i(t) = R_i\,(t) + \Sigma(k_{in} * C_{in}(t)) - \Sigma(k_{out} * C_i(t))$$

26 Compartments

Land use patterns change the properties of soil and release quantities

Some products are disproportionately used only in only some regions
ex. pesticides, paints

Sludge from WWTPs (biosolids) is applied to only 5% of agricultural soils

Air Air Aerosols	**Urban Soil** Urban Soil Solids Urban Soil Water Urban Soil Air Urban Deep Soil
Freshwater Freshwater Column Freshwater Suspended Freshwater Sediment Solids Freshwater Sediment Water	**Natural Soil** Natural Soil Solids Natural Soil Water Natural Soil Air Natural Deep Soil
Seawater Seawater Column Seawater Suspended Sediment Seawater Sediment Solids Seawater Sediment Water	**Agricultural Soil** Agricultural Soil Solids Agricultural Soil Water Agricultural Soil Air Agricultural Deep Soil

26 Compartments

Freshwater and marine water (and their benthic regions) are distinct ecosystems. Chemical releases have different impacts on different species

Land-locked regions will not have a marine compartment

Release of treated water from WWTP to water bodies varies depending on the WWTP locations

Air Air Aerosols	**Urban Soil** Urban Soil Solids Urban Soil Water Urban Soil Air Urban Deep Soil
Freshwater Freshwater Column Freshwater Suspended Freshwater Sediment Solids Freshwater Sediment Water	**Natural Soil** Natural Soil Solids Natural Soil Water Natural Soil Air Natural Deep Soil
Seawater Seawater Column Seawater Suspended Sediment Seawater Sediment Solids Seawater Sediment Water	**Agricultural Soil** Agricultural Soil Solids Agricultural Soil Water Agricultural Soil Air Agricultural Deep Soil

Customizable Release Scenarios

Consistent (Constant)

Toothpaste

Seasonal

Pesticide, sunscreen

Sporadic

occurring at irregular intervals or only in a few places; scattered or isolated

- Increasing/decreasing with time
  - ENMs, CFCs

Single Event

Accidental chemical spill

Release to freshwater or marine based on WWTP locations

Based on urban planning

Case Study: Phthalic Anhydride in San Francisco

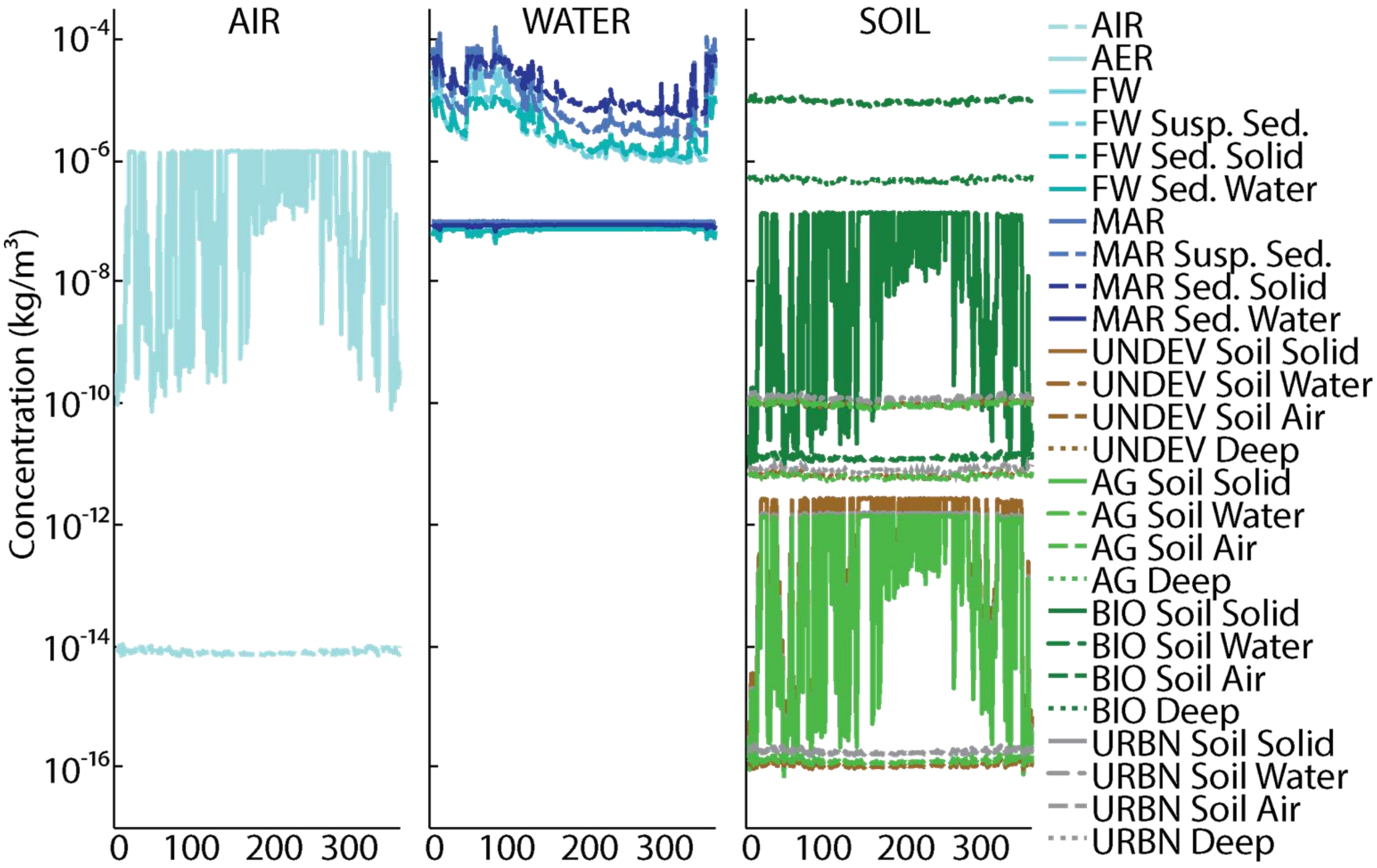
Information Provided by CLiCC Modules (or User)

- Chemical Properties from QSARS Module
- Release Ratios from Release Module

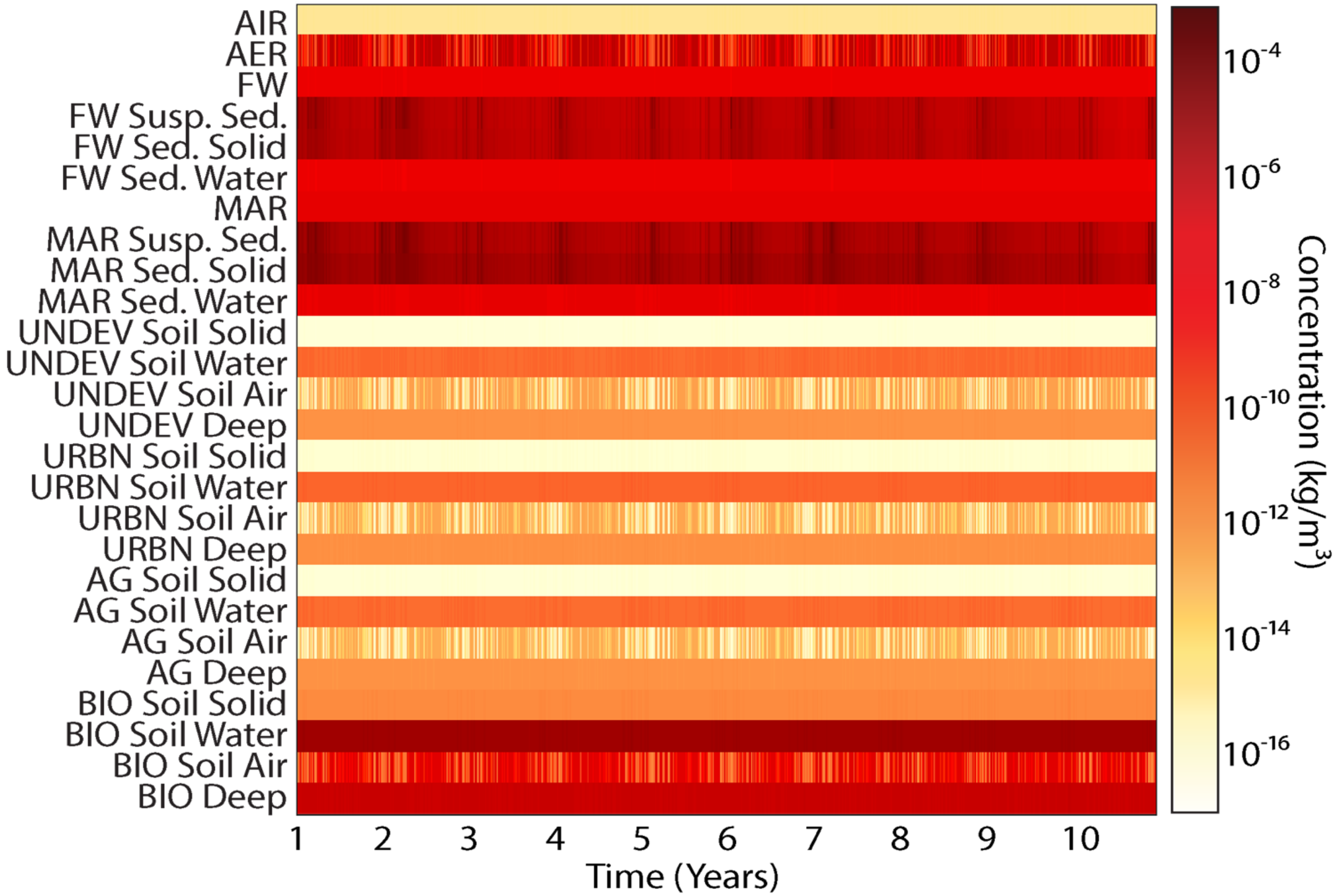
Direct Model Input

- Background concentrations assumed zero
- Use mass/volume of chemical 100 kg/day
  - 0.075 kg/day to Air
  - 20 kg/day to agricultural soils through biosolids application

Comparison between Compartments for Phthalic Anhydride in San Francisco



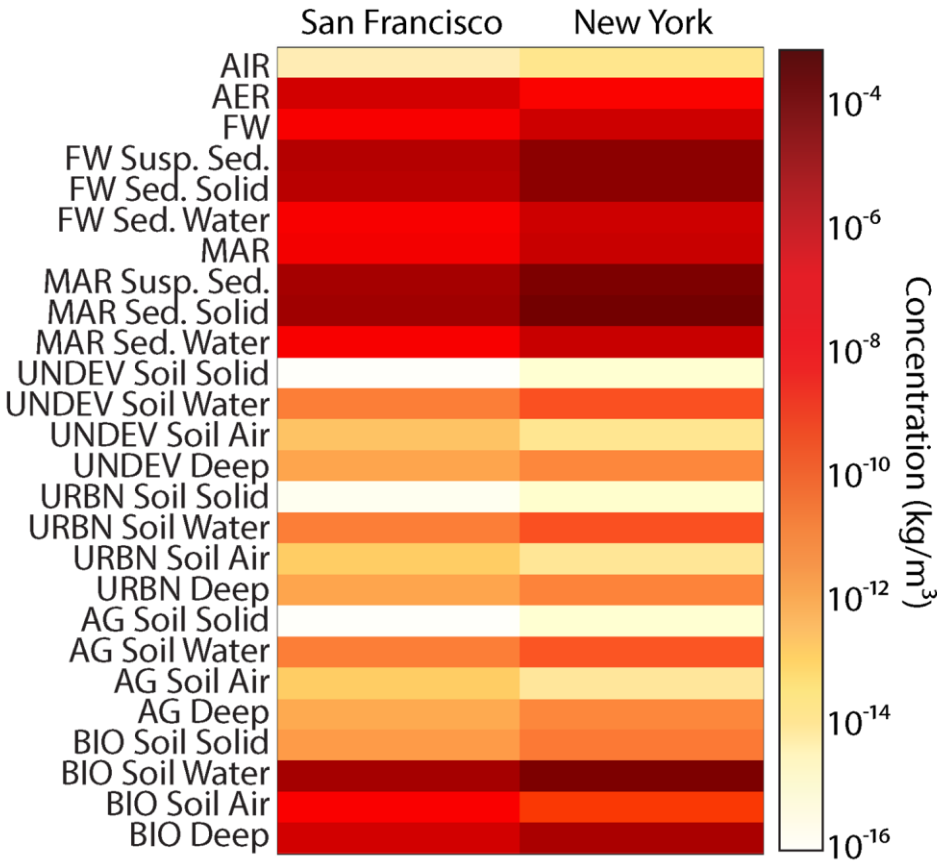
Long Term Variability - Phthalic Anhydride



Comparison between Regions

New York:

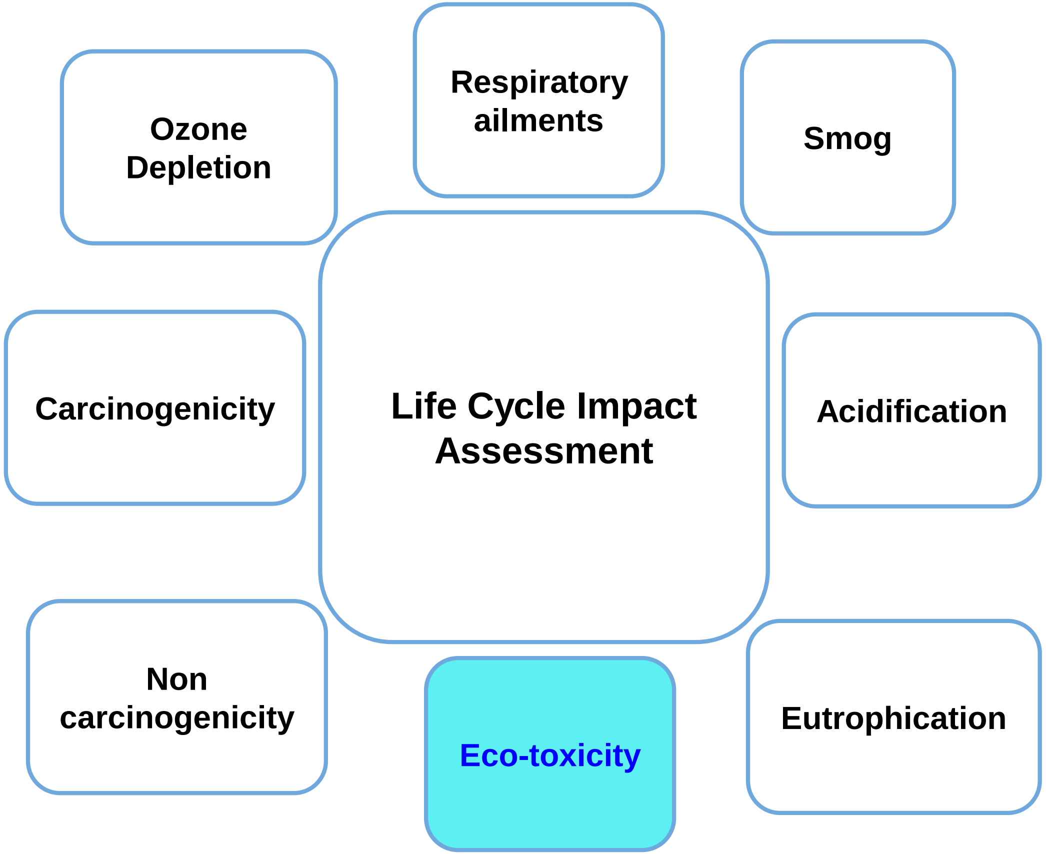
- smaller region
- higher population density
- very high impervious areas and urban land
- has much more precipitation



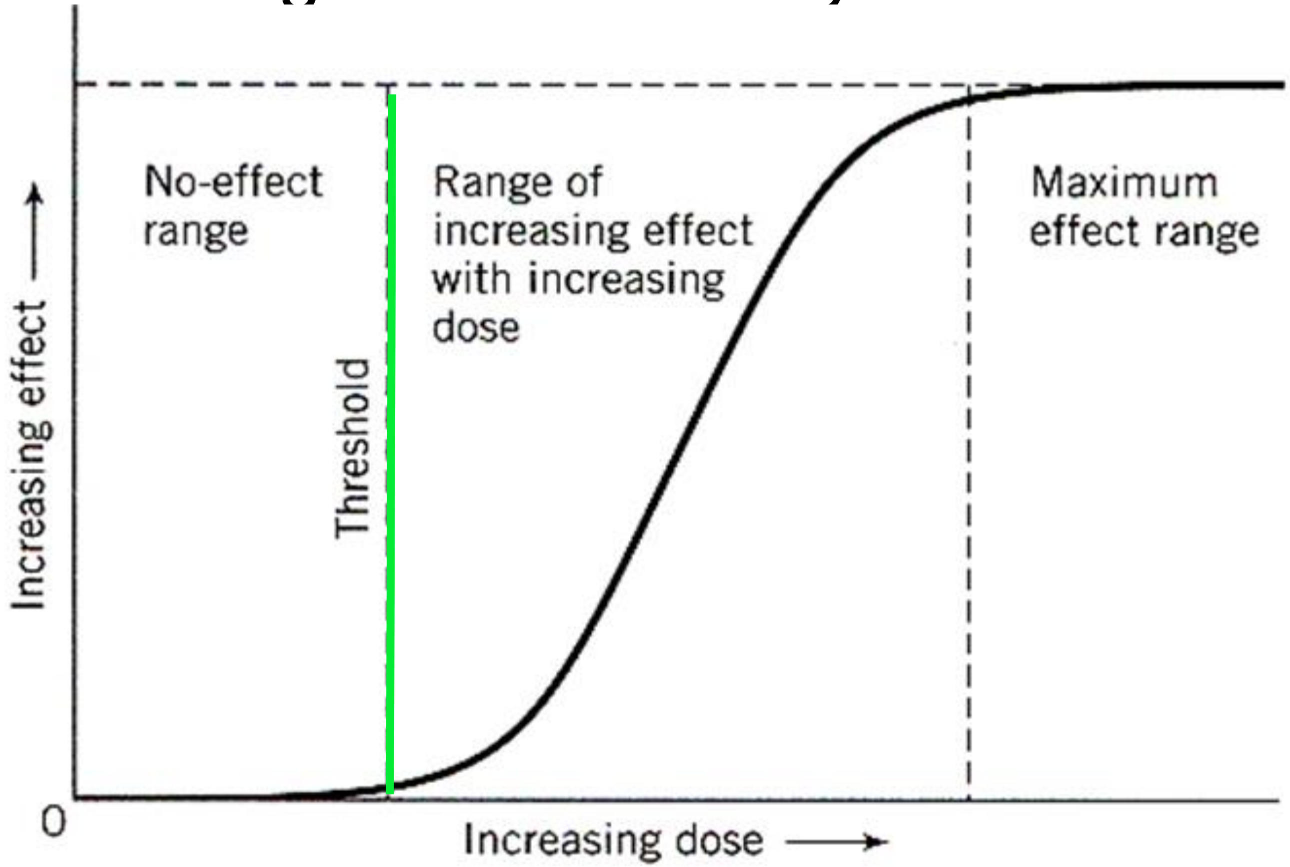
Relating chemical presence to impacts

- Life Cycle Impact Assessment is the “so what” stage of the LCA

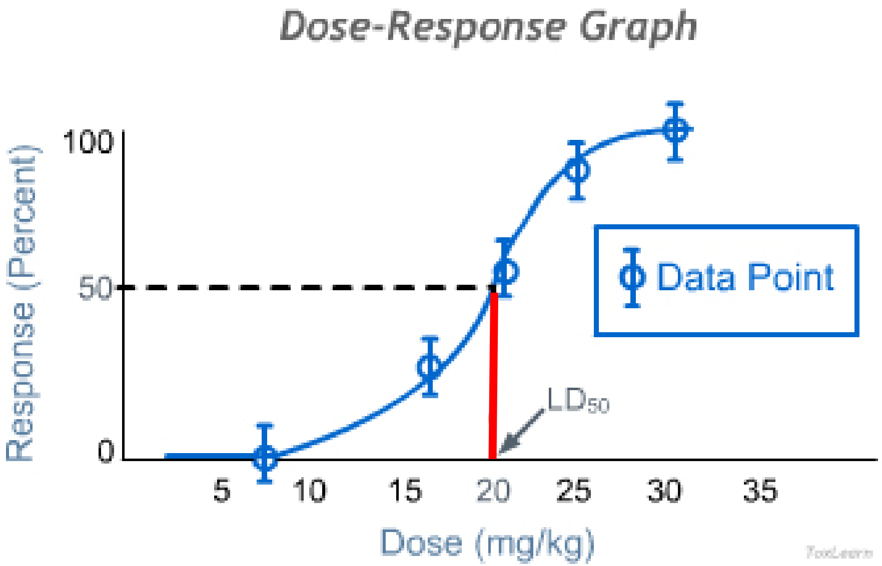
- EcoToxicity can be further understood as:
  Freshwater aquatic ecotoxicity
  marine aquatic ecotoxicity
  freshwater sediment ecotoxicity
  marine sediment ecotoxicity
  terrestrial ecotoxicity
  human toxicity



Understanding **Acute** Toxicity from F&T results



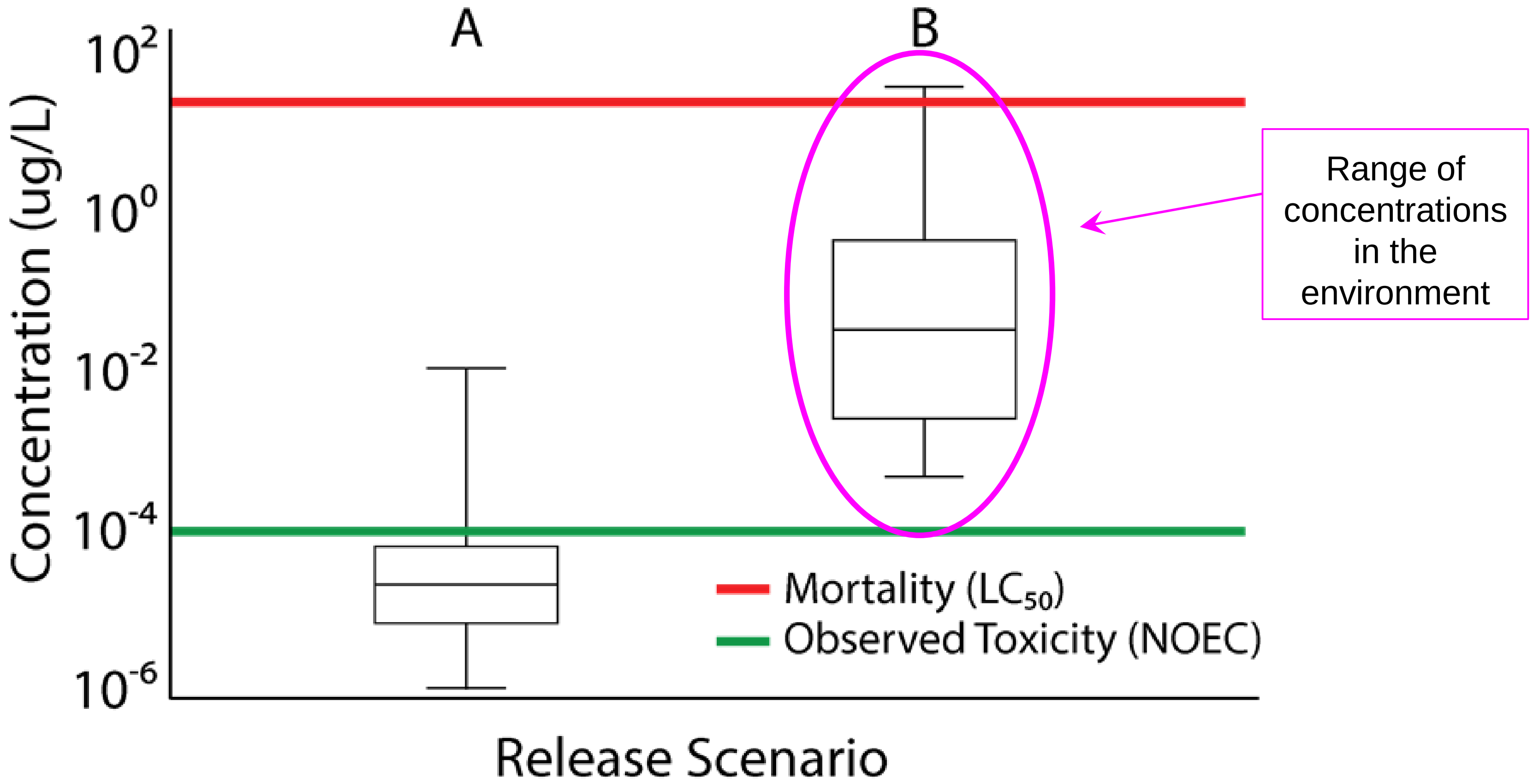
If the examined effect is death...



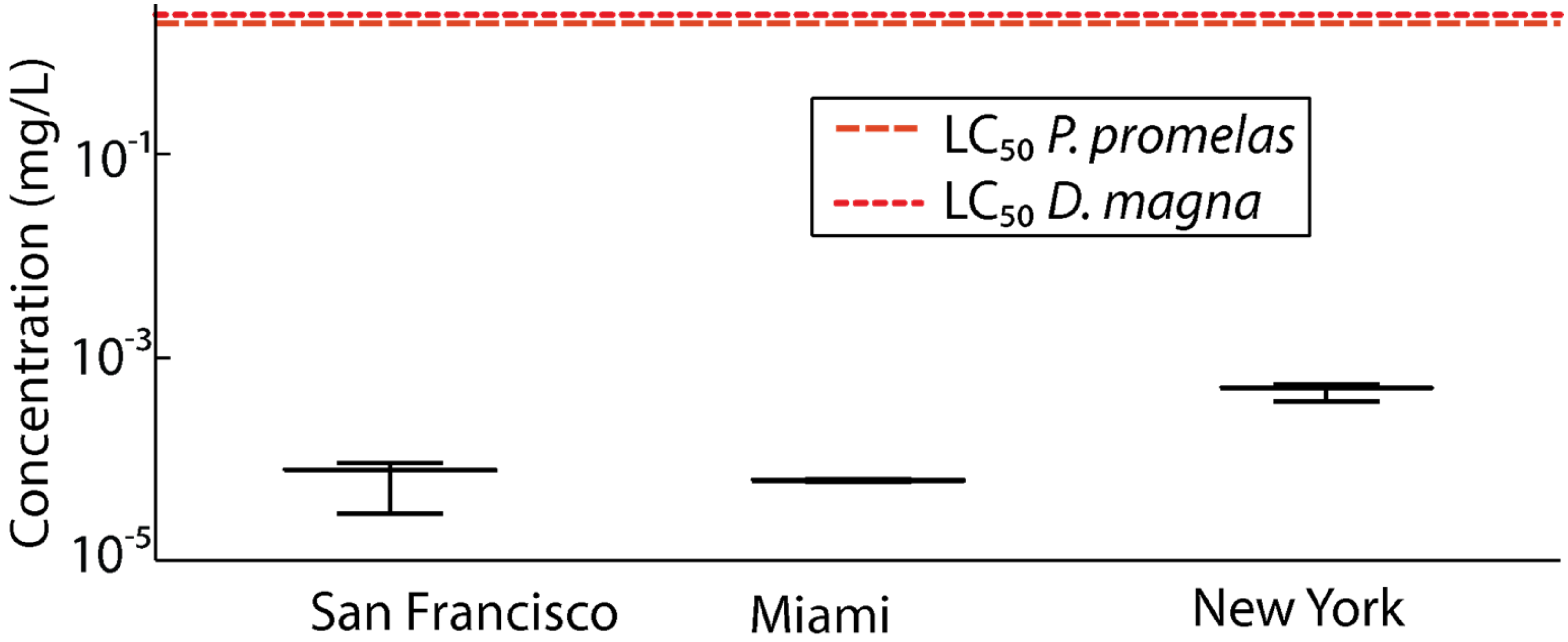
"mg/kg" refers to the amount of the chemical in milligrams per kilogram of body weight of the subject

https://toxlearn.nlm.nih.gov/htmlversion/module1.html

Sample Results - Understanding Toxicity



Phthalic Anhydride



Limitations of the Fate and Transport Model

Limitations

- Limited by data availability and uncertainty
  - What does this mean for such studies in other parts of the world?
  - Chronic toxicity and phytotoxicity information is rarely available
- Assumptions about environmental parameters
  - Difficult to determine if the model is it too simple or too complex
  - Lakes and groundwater are more complex - not YET modelled in CLiCC
- Model Validation
  - Chemical concentrations in all compartments are difficult to measure
  - Limited observed data points (single observation)

Thank you for your patience

Any questions can be directed to module experts
or clicc@list.bren.ucsb.edu

Next CLiCC webinar will be held on October 7, 2016,
10 - 11 am, PDT