

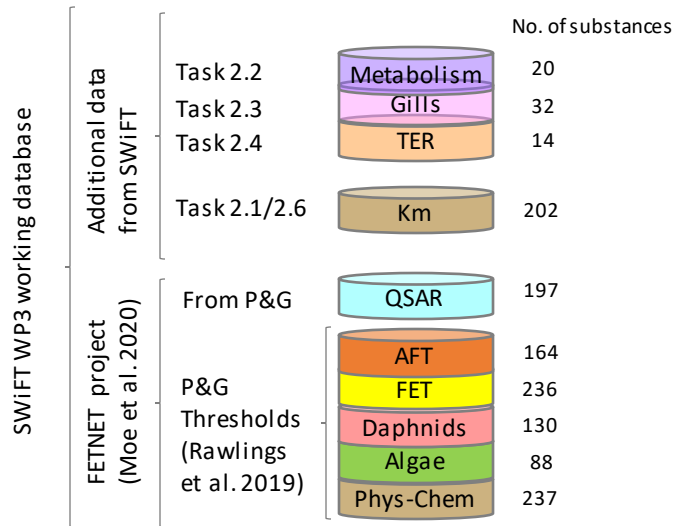
WP3: Development and evaluation of the BN model for replacing AFT

Cefic-LRI ECO51 – SWiFT: Strengthening weight of evidence for FET data to replace acute fish toxicity

Progress meeting 13.10.2021
Jannicke Moe (NIVA)

Current BN model structure and use for WoE

Data sources for current BN model



- Currently expanded by SWiFT WP1 (Kristin Connors)
- Expanded SWiFT database will be used for final revision of BN model November - December 2021

How can our Bayesian Network be used in a WoE approach?

Guidance on the use of the weight of evidence approach in scientific assessments

EFSA Scientific Committee, Anthony Hardy, Diane Benford, Thorhallur Halldorsson, Michael John Jeger, Helle Katrine Knutsen, Simon More, Hanspeter Naegeli, Hubert Noteborn ... See all authors

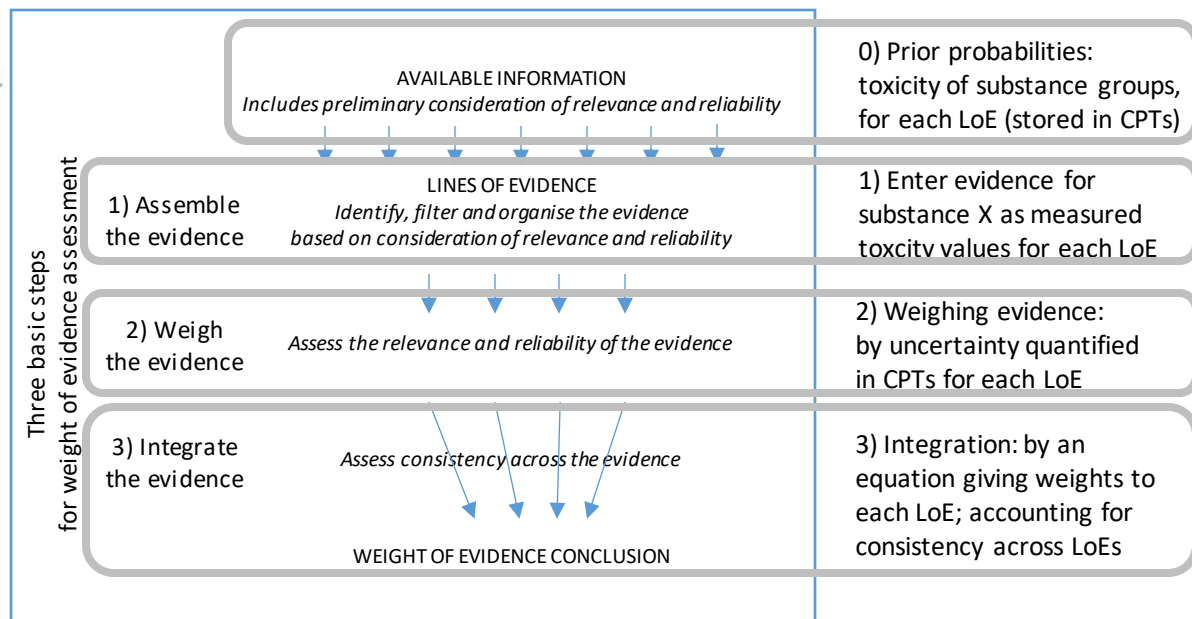
First published: 03 August 2017 | <https://doi.org/10.2903/j.efsa.2017.4971> | Citations: 47

Our BN-WoE should be

- **consistent** with WoE approaches recommended for regulatory frameworks (EFSA, ECHA, US EPA, OECD)
- **quantitative**
- **intuitive**
- **flexible**

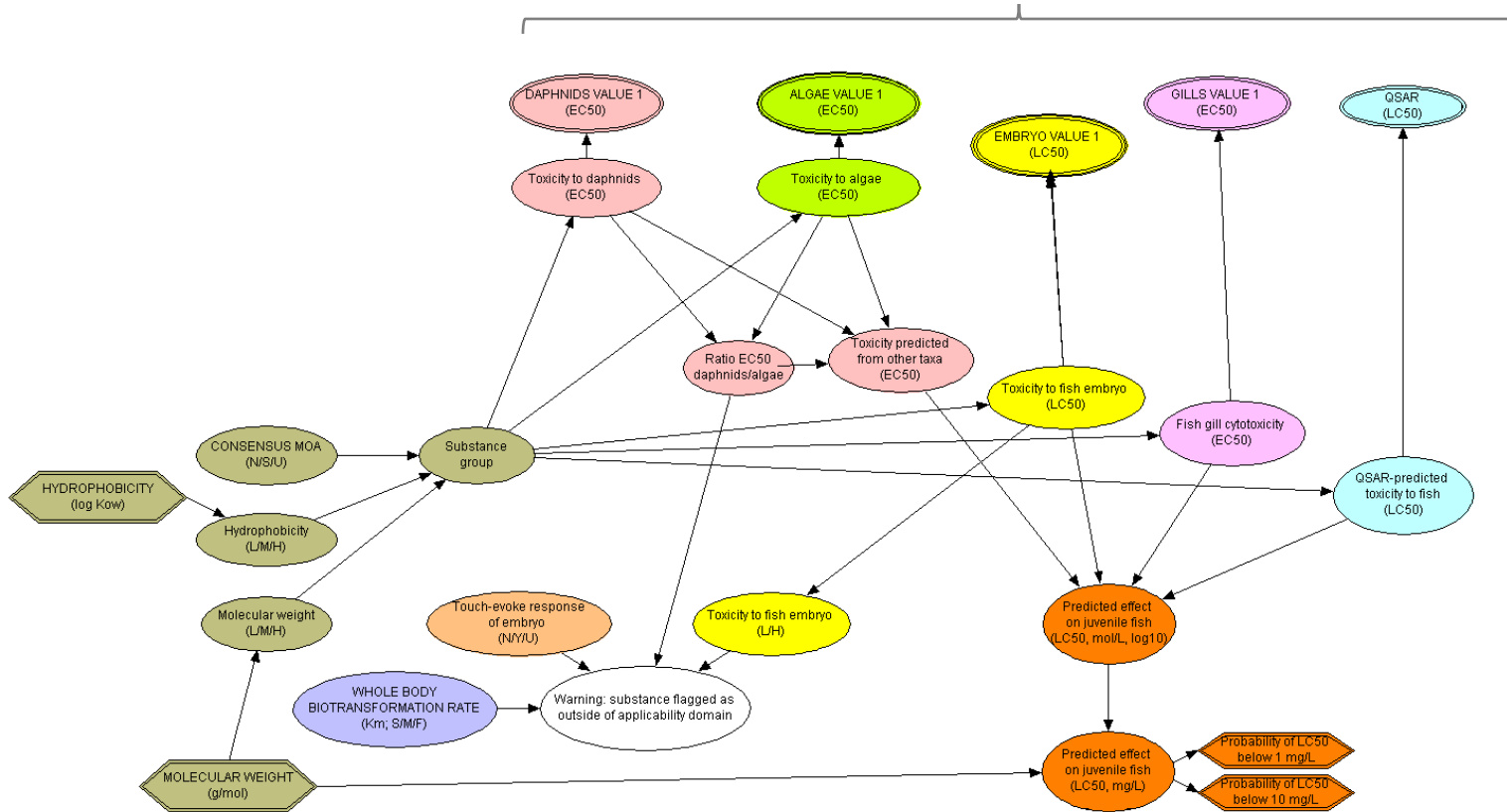
Main steps for WoE assessment (EFSA):

Main steps of our BN model, run for substance X:



Current BN-WoE model

Lines of Evidence

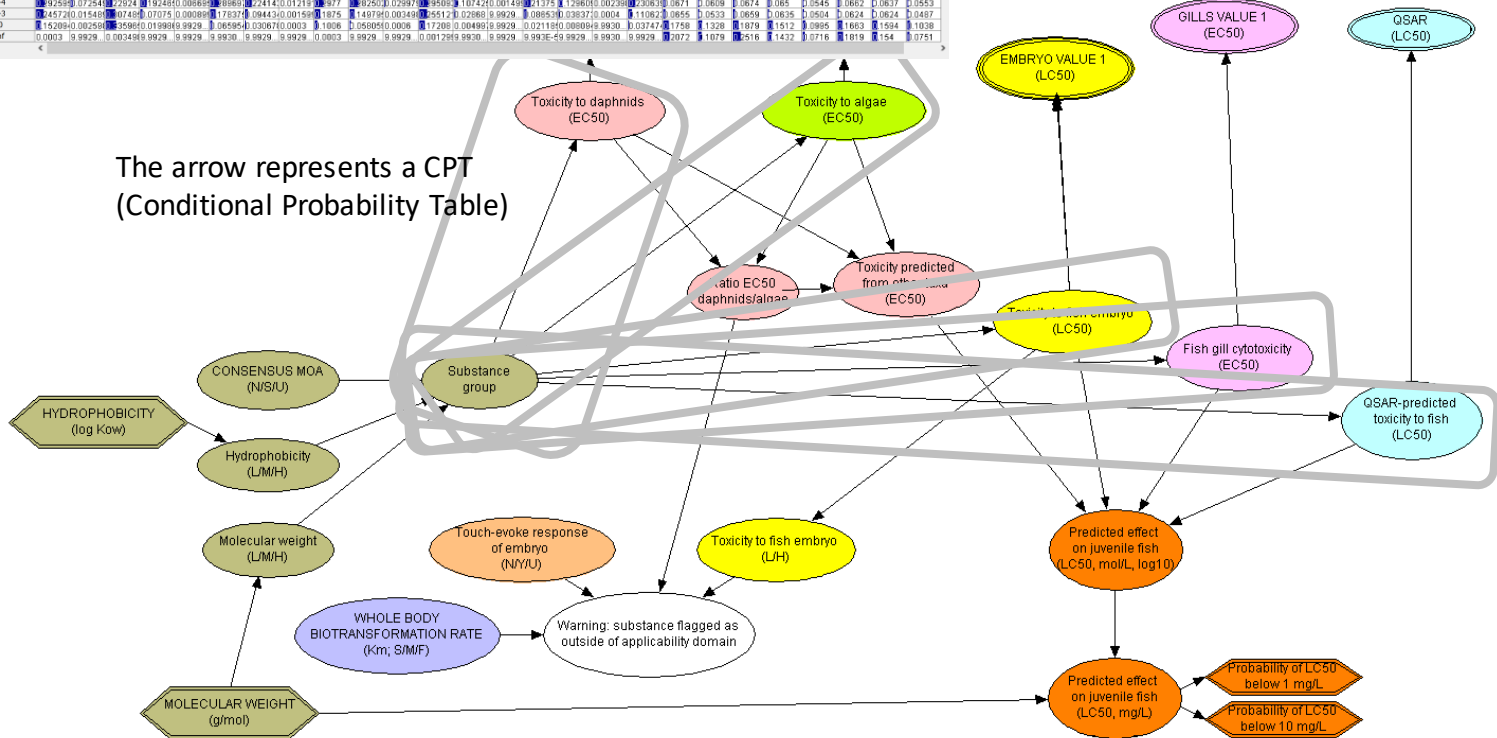


Current BN-WoE model

Lines of Evidence

Substance	LLN	LLS	LLU	LMN	LMS	LMU	LHN	LHS	LHU	MLN	MLS	MLU	MNN	MNS	MMU	MHN	MHS	MMU	MLN	HLS	HLU	HNN	HMS	HMU	HNN	HHS
inf -9	0.9929	0.04317	0.9929	0.00019	0.58410	0.0006	0.00429	0.07150	0.0007	0.00129	0.1449	0.02496	0.000496	0.01886	0.09520	0.00279	0.0337	0.004	0.1939	0.157	0.0729	0.0643	0.093	0.0487		
9 -6	0.09713	0.00230	0.02718	0.00271	0.00310	0.19576	0.00159	0.00176	0.01708	0.22784	0.02979	0.08703	0.0007	0.00092	0.00563	0.00061	0.00038	0.2457	0.185	0.0003	0.1708	0.1985	0.1945	0.1919	0.2007	0.1984
4 -5	0.21295	0.0026	0.00653	0.07733	0.04559	0.08951	0.06193	0.06115	0.124	0.0043	0.10420	0.09726	0.23730	0.01219	0.07776	0.50245	0.20088	0.1779	0.0657	0.0444	0.0626	0.0848	0.0556	0.067	0.0615	0.062
5 -4	0.25950	0.02943	0.2924	0.19248	0.00689	0.08989	0.22414	0.01219	0.197	0.0250	0.02597	0.05005	0.07420	0.00149	0.1375	0.12960	0.00230	0.23630	0.071	0.0609	0.0674	0.085	0.0545	0.0652	0.0637	0.0553
4 -3	0.24570	0.01548	0.07480	0.07074	0.00089	0.17637	0.08430	0.00159	0.1875	0.14978	0.00349	0.05512	0.02888	0.0929	0.08530	0.03837	0.0004	0.11062	0.0655	0.0533	0.0659	0.0635	0.0504	0.0624	0.0624	0.0487
3 -0	0.15289	0.00286	0.05860	0.01998	0.9929	0.08595	0.03067	0.0003	0.1006	0.05899	0.0006	0.17208	0.00496	0.9929	0.02119	0.00099	0.9930	0.03747	0.1758	0.128	0.1879	0.1512	0.0955	0.1663	0.1594	0.1038
0 -inf	0.0003	0.9929	0.00349	0.9929	0.9929	0.9929	0.9929	0.0003	0.9929	0.9929	0.9929	0.00129	0.9929	0.9929	0.9929	0.9929	0.9929	0.9929	0.9929	0.9929	0.9929	0.9929	0.9929	0.9929	0.9929	0.9929

The arrow represents a CPT (Conditional Probability Table)



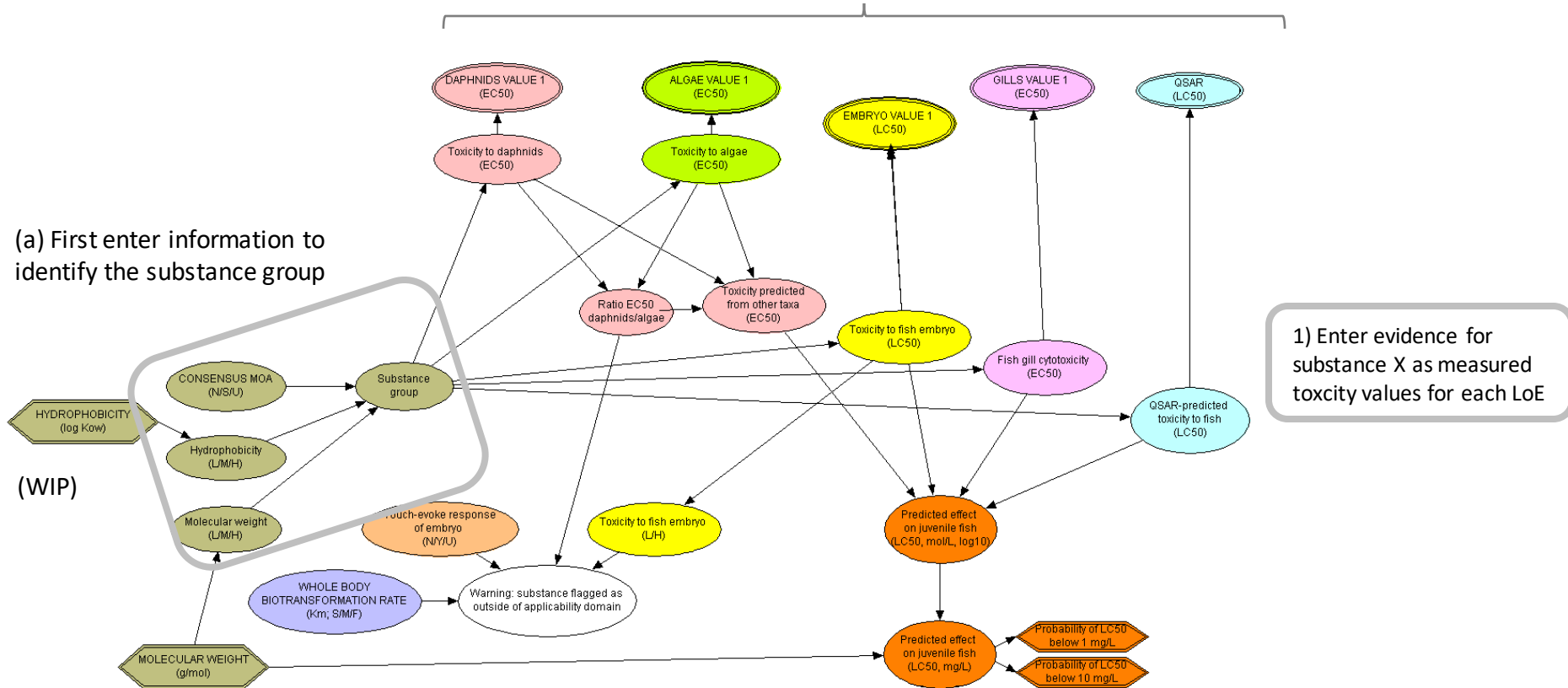
0) Prior probabilities: toxicity of substance groups, for each LoE (stored in CPTs)

(Source: P&G Thresholds data; later: EnviroTox?)

Current BN-WoE model

Lines of Evidence

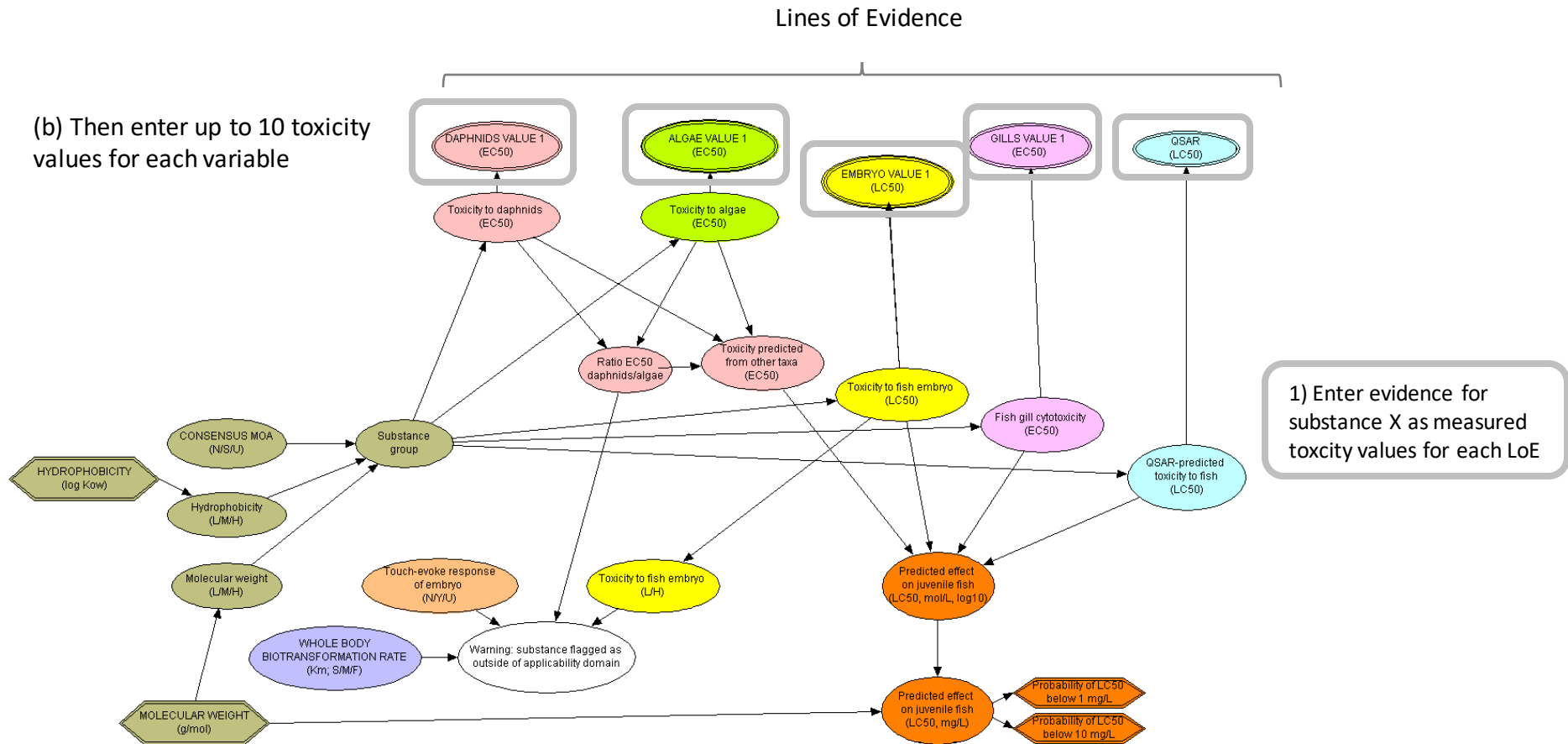
(a) First enter information to identify the substance group



1) Enter evidence for substance X as measured toxicity values for each LoE

Current BN-WoE model

(b) Then enter up to 10 toxicity values for each variable

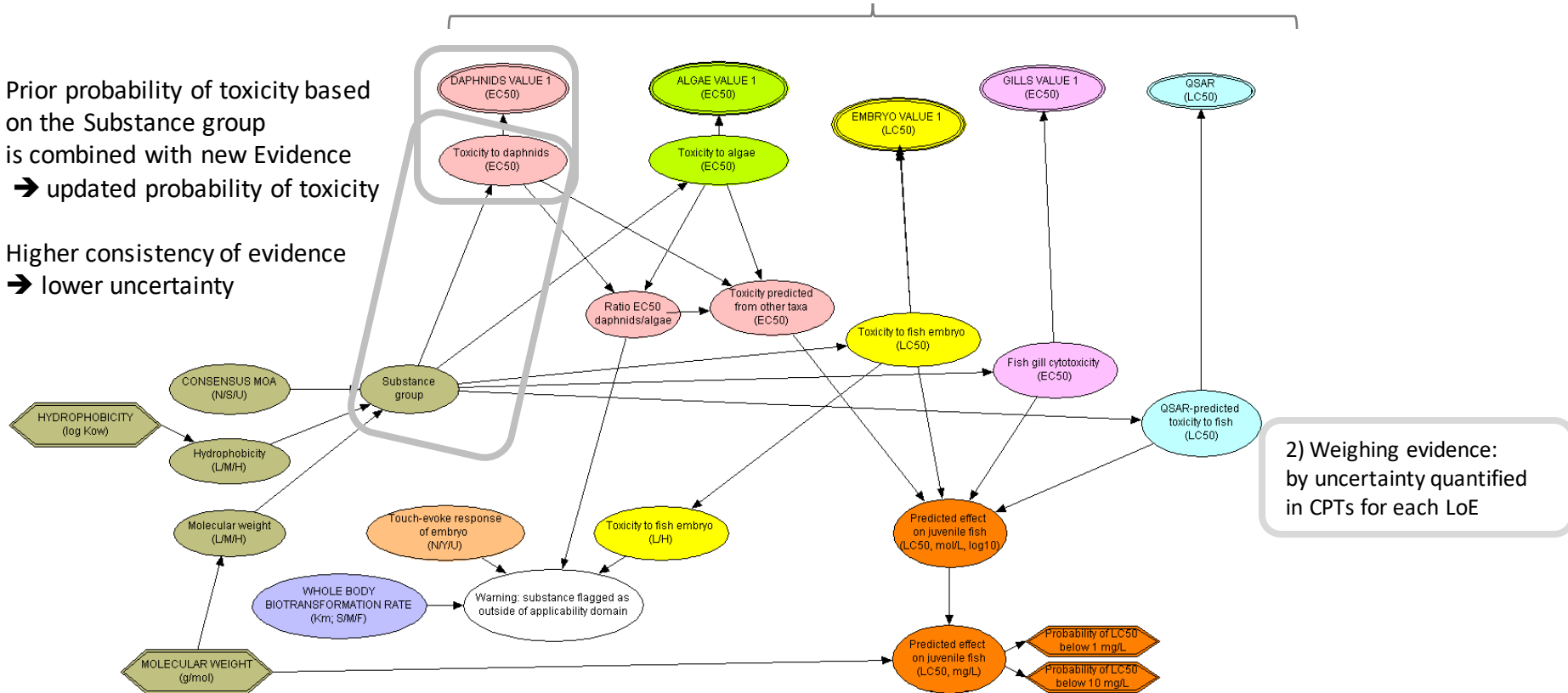


Current BN-WoE model

Lines of Evidence

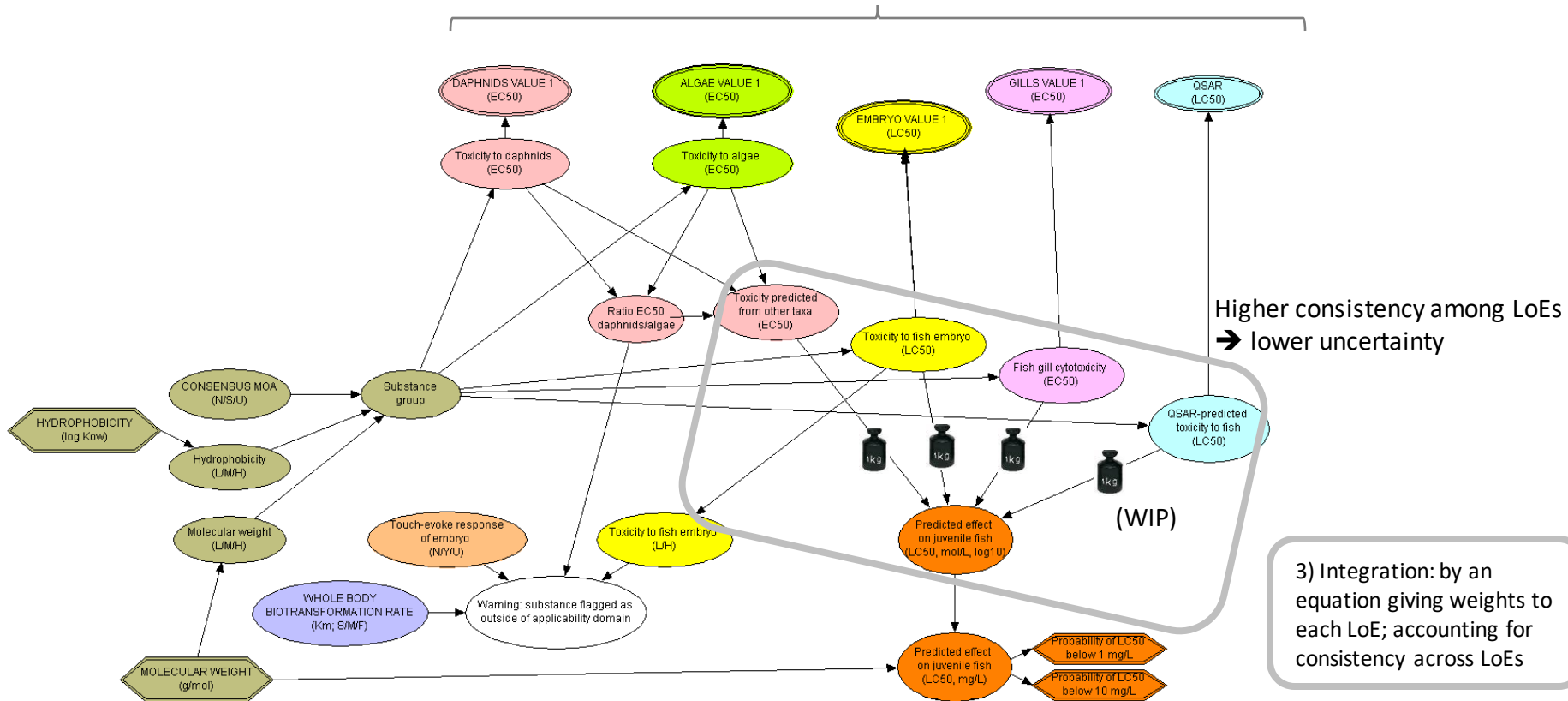
Prior probability of toxicity based on the Substance group is combined with new Evidence → updated probability of toxicity

Higher consistency of evidence → lower uncertainty



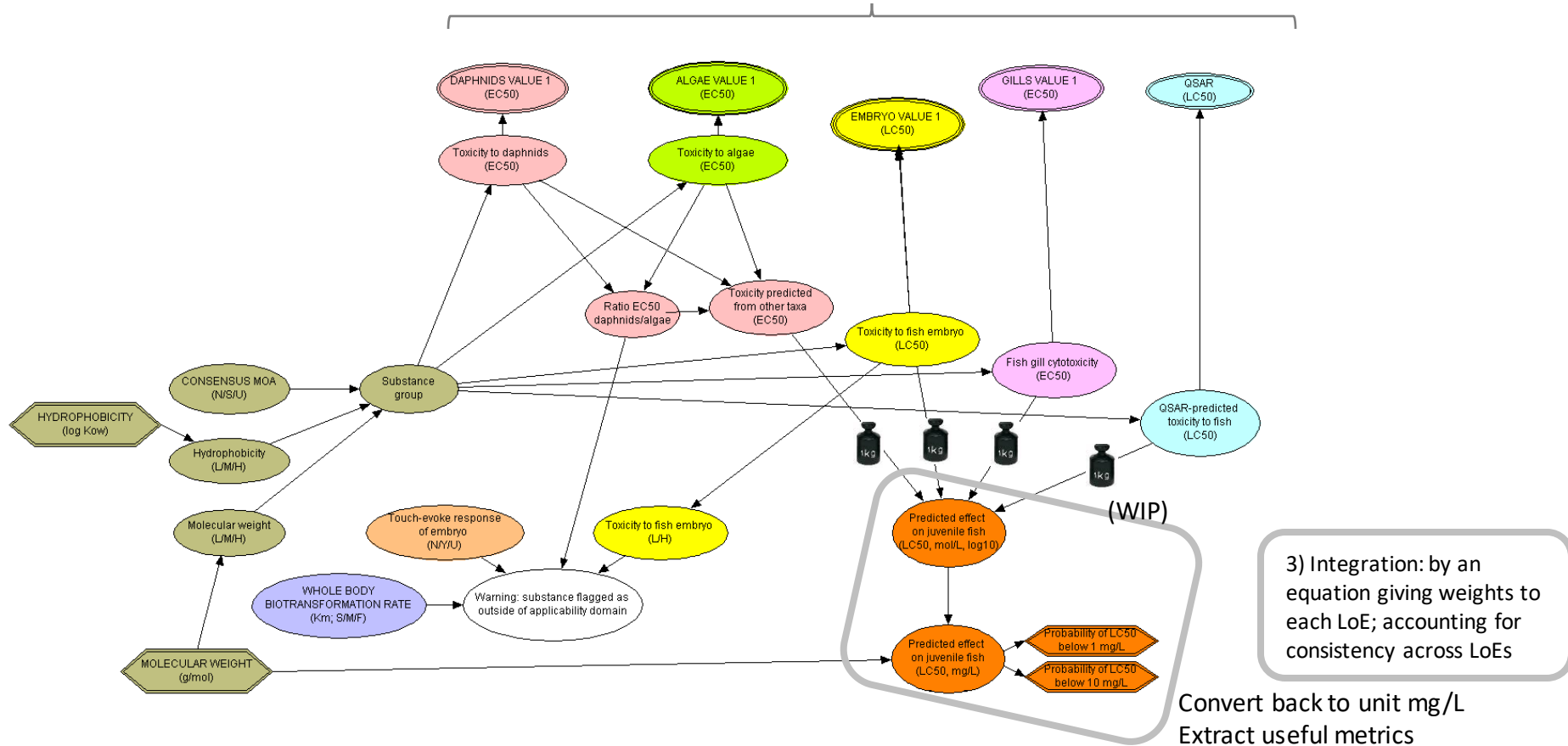
Current BN-WoE model

Lines of Evidence



Current BN-WoE model

Lines of Evidence



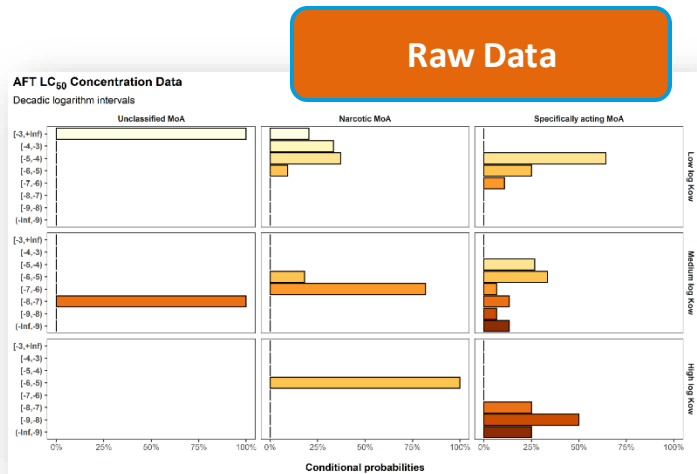
New developments
March – October 2021
&
Ongoing work
October - December 2021

1) Refinement of prior probability distributions

- Used hierarchical Bayesian regression model to set conditional probability tables (priors)
- Incorporating all known sources of uncertainty

Ongoing:

- Re-do with larger dataset (EnviroTox)



Jannicke Moe

Regulating a SWiFT Transition

A Bayesian Network as Weight-of-Evidence Approach to Replace the AFT With the FET

Raoul Wolf, Scott Belanger, Thomas Braunbeck, Kristin Connors, Michelle Embry, Anders Madsen, Jannicke Moe, Kristin Schirmer, Stefan Scholz, Adam Lillicrap

raoul.wolf@niva.no

SETAC Europe 2021 | SETAC Europe 31st Annual Meeting




13.10.2021


13

2) Refinement of BN structure and evaluation

- Explored alternative scenarios for weighting of lines of evidence
- Compared predicted and observed AFT (toxicity to juvenile fish)



SETAC EUROPE 2021
3-6 MAY 2021 | VIRTUAL CONFERENCE










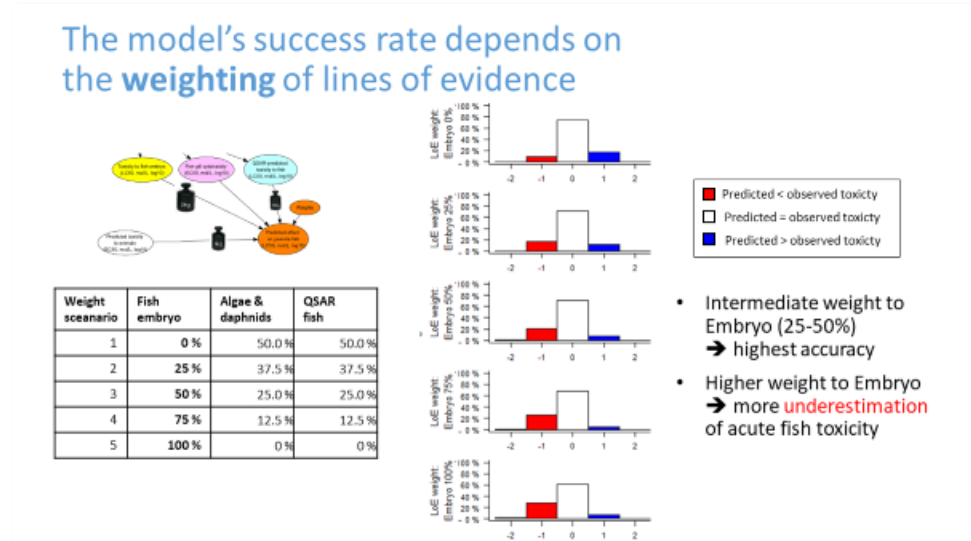
Weight of Evidence by Conditional Probabilities: A Bayesian network model for predicting fish acute toxicity based on fish embryo testing

[Jannicke Moe](#), Anders L. Madsen, Raoul Wolf, Kristin A. Connors, Jane M. Rawlings,
 Scott E. Belanger, Wayne G. Landis, T. Braunbeck, M. Embry, K. Schirmer, S. Scholz, Adam D. Lillicrap

Session 4.01: Artificial Intelligence Approaches in Environmental Risk Assessment:
 Bayesian Networks, Machine Learning and Predictive Modelling

Presentation ID: 4.01.08



2) Refinement of BN structure and evaluation

Recent:

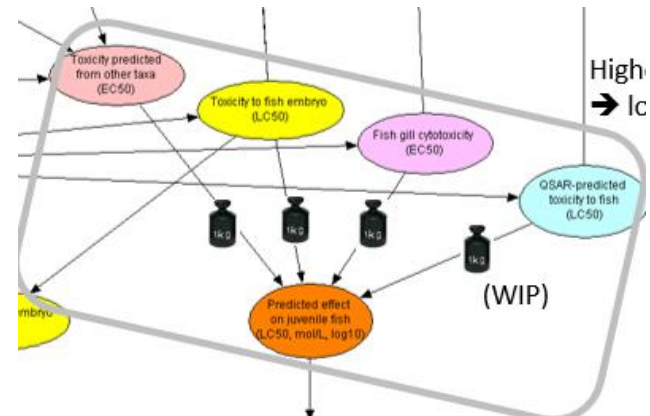
- All expert-based CPTs are replaced by equations
- Integration step: weights calibrated by linear regression

AFT = 35% FET + 30% Algae & Daphnids + 25% Gills + 10% QSAR

- Testing: Calibrated model does not yet perform better than the initial scenarios

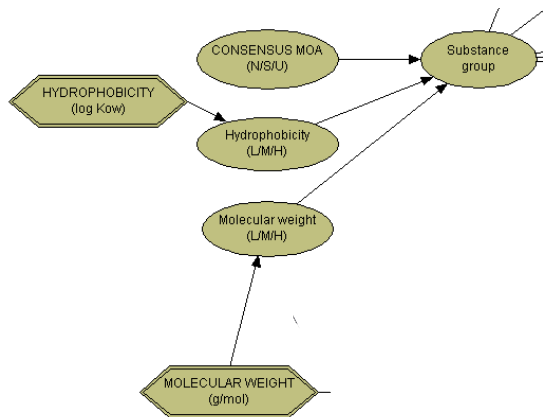
Ongoing:

- Refine method for calibrating weights
- Refine method for model evaluation
 - Consider training vs. testing data
 - Cross-validation?
- Aim: finalise BN by end of December 2021



3) Definition of Substance group

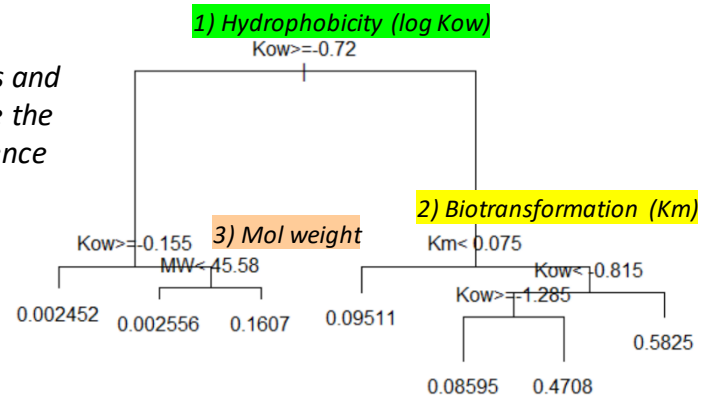
- Prior probabilities of toxicity for each substance group are stored in the BN
- Currently defined by 3 variables:
 - Consensus MOA
 - Molecular weight
 - Hydrophobicity (log Kow)



Ongoing:

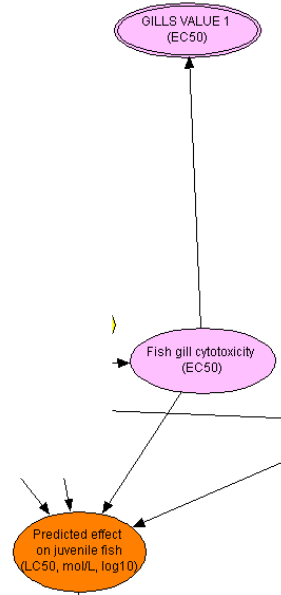
- Use Whole body fish biotransformation rate (Km) as alternative variable?
- Explore relationship & thresholds between AFT and all candidate components of substance group
- Method: Regression tree analysis
- Re-do with larger dataset: EnviroTox

Which variables and thresholds have the strongest influence on AFT values?



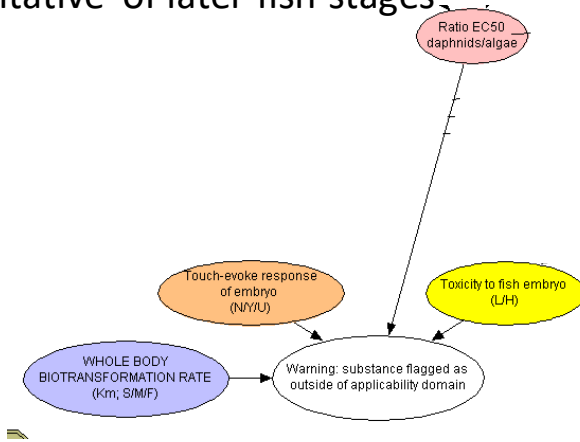
4) Inclusion of Gill cytotoxicity as a LoE

- EC50 data for 32 substances are included in the BN as a separate Line of Evidence
- Included in the integration



5) «Warning node»

- Purpose:
identify substances for which the BN predictions may not be reliable
- Reasoning:
response of fish embryo may not be representative of later fish stages



Current criteria to trigger a warning:

- Fish embryo toxicity = Low
- Daphnia/algae toxicity ratio = High
- **Touch-evoke response** = Yes / Unmeasured
- Biotransformation rate = Fast

Ongoing work:

- Refine Embryo toxicity criterion (< Daphnia & Algae toxicity)
- Include **Metabolic activity** (embryo vs. juvenile fish) as alternative variable?

6) Define the applicability domain of the BN

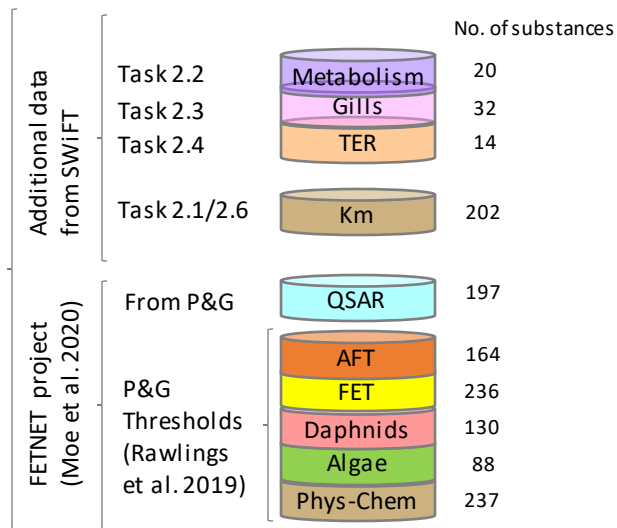
Criteria for exclusion from the applicability domain:

- 1) "Warning node": substances with certain combination of toxicity values and other properties
 - 2) Substances without QSAR values: metals
 - 3) ... [to be continued]
- Applicability domain is a scientific decision, not a technical issue
 - Criteria must be defined in the Technical user manual (task 4.2) and the Guidance document for stakeholders (task 5.3)

Data sources for BN development and evaluation

Data sources for current BN model

SWiFT WP3 working database



- Currently expanded by SWiFT WP1 (Kristin Connors)
- Expanded SWiFT database will be used for final revision of BN model November - December 2021