Weight of Evidence by Conditional Probabilities: A Bayesian Network Model for Predicting Fish Acute Toxicity in Environmental Risk Assessments

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INTRODUCTION

The acute fish toxicity test (AFT; OECD TG 203) is currently required for chemical hazard and risk assessment purposes in many different legislations and regulations. The fish embryo toxicity test (FET; OECD TG 236) has been proposed as an alternative to using juvenile fish to reduce the number of live animals required for hazard and risk assessments of chemicals. However, FET data are not yet accepted as a replacement for AFT data for regulatory purposes such as REACH. The European Chemicals Agency has recommended the development of a Weight of Evidence (WoE) approach for strengthening FET data to predict (juvenile) acute fish toxicity. To meet this challenge, we have developed a Bayesian network (BN) model for using FET data in a probabilistic WoE approach.

In the CEFIC LRI ECO51 project SWiFT (Strengthening Weight of evidence for FET data to replace Acute Fish Toxicity; http://swift.hugin.com), this BN model has been developed with multiple lines of evidence (e.g. fish gill cell-line cytotoxicity assay, neurotoxicity, biotransformation, data on other organisms, read across and in silico predictions), in order to provide more accurate predictions for risk assessments.

METHODOLOGY

A Bayesian network (BN) is a probabilistic graphical model that represents a set of variables and their conditional dependencies via a directed acyclic graph. The purpose of the proposed BN model is to integrate information from large ecotoxicological and physico-chemical datasets, and apply it in a WoE context to predict fish acute toxicity of chemicals from data on fish embryo toxicity tests in combination with other types of information. This BN model was developed from data on fish embryo and juvenile acute toxicity in combination with other information for 237 chemicals, and aims to predict the toxicity interval of each chemical by combining information in four pathways (Figure 1): (i) fish embryo toxicity, (ii) physical and chemical properties, (iii) toxicity to fish from other chemicals in the same category, and (iv) toxicity to other species (algae and Daphnia).

RESULTS

The BN model is freely available via the following link (www.niva.no/swift). Model performance was assessed by running the BN model with input data from a large number of substances and comparing the outcome, i.e. the predicted acute toxicity of selected chemical substances to juvenile fish, to the observed toxicity of the same substances. When the four lines of evidence were given equal weight, the model correctly predicted the most probable acute fish toxicity interval for 80 % of the substances. For the remaining 20 % of the substances, either algae or Daphnia data would have driven the hazard classification as they were more sensitive than the juvenile AFT data.

The weighting of the four lines of evidence has been calibrated to further improve the model performance. As a first step, we have tested a set of five alternative weight combinations: the Embryo line assigned the weights 0 %, 25 %, 50 %, 75 % and 100 %, with the remaining weights equally distributed to the three other lines. Increasing weight to the Embryo line generally resulted in slightly higher precision (i.e. % of correct predictions), as well as higher accuracy (i.e. better balance between over- and underestimation).

DISCUSSION

Regulatory acceptance of animal alternative approaches is challenging. There are many reasons for this including the structure of regulations which vary across the globe and, the dependence on vertebrate data in historical chemical risk assessments. Regulators and scientists will need to possess courage to make decisions when data is less than perfect (which will always be the case) and develop new regulatory inertia in the face of a lack of precedents. Applying a Bayesian Network in a weight of evidence approach for predicting fish acute toxicity is a proven technique for animal alternative approaches. Moreover, the approach we have developed also strengthens the chemical hazard assessment of chemicals per se. Finally, since environmental risk assessment frameworks and chemical legislations are principally employed for the protection of the environment, hazard assessment strategies should be moving away from relying on acute fish toxicity for classification purposes and be more focused on mechanistic/sublethal endpoints to identify chemicals of concern.