SETAC SCIENCE BRIEF

TAKING THE MYSTERY OUT OF TOXICITY TESTING

All materials around us are a mixture of different chemicals, from water and oxygen to chemicals manufactured to address a specific need, such as personal care products (shampoo and soap), pharmaceuticals, cleaning products, food ingredients and additives, building materials, household items (furniture and cookware), and plant protection products (pesticides). Many consumers are concerned about the possible risks posed by chemicals in their lives. While chemicals are an integral part of our world, any chemical can be harmful at some dose. In the toxicity field (study of the effects of chemicals on humans) and the ecotoxicity field (the study of the effects of chemicals on ecological beings), it is well known that "the dose makes the poison." Therefore, it is important to understand the potential toxicity of chemicals to manage them in order to protect human health and the environment.

Approaches used to minimize risk to heath and the environment from chemicals (chemical management approaches) vary depending on the intended use of the chemical and vary from country to country. Most chemical management approaches are based on data obtained from toxicity tests. While there are data from toxicity studies for many chemicals in use, there is a lack of information regarding toxicity of new chemicals entering the market every day, not to mention new chemical mixtures being formed. Also, under some circumstances a chemical that is well known and has been in use for a long time needs to be reevaluated, for example, when there is a new use. These factors create an ongoing need for data from chemical toxicity tests to protect humans and ecosystems.

Traditional ecotoxicity tests are based on studies in ecological organisms. For example, fish are regularly used to evaluate the effects of chemicals found in water. Likewise, rodents have been traditionally used to study potential toxicity of chemicals to humans – a use that clearly led to terms such as "lab rat" to indicate a test subject. However, in the fields of toxicology and ecotoxicology, there is an ongoing effort to identify alternative techniques to animal testing.

All chemicals at high enough doses can be toxic and should be managed to minimize harm.

The 3Rs of Alternatives to Animal Testing

Alternative approaches to animal testing have been often referred to as the "3Rs" for reduction in numbers of animals used; refinement of any procedures to minimize pain, suffering, and distress; and replacement of the use of animals whenever possible. This concept was first described by William Russell and Rex Burch in their 1959 book "The Principles of Humane Experimental Technique."

There are a wide variety of potential alternative approaches to animal testing in ecotoxicity studies, including in silico, in vitro, and even in vivo test methods. A brief overview of these approaches follows.

In Silico Alternatives to Animal Testing

In silico approaches to obtaining toxicity data rely on mathematical or chemical structural models and computer simulations. Examples of such techniques include the use of quantitative structure–activity relationship (QSAR) models, read-across, and scaling and extrapolation models.

QSAR models and read-across approaches are based on the similarity principle and assume that chemicals similar in structure have similar mechanisms of toxicity. Using these techniques, new substances can be screened by comparison for certain characteristics, such as persistence in the environment, carcinogenicity (causing cancer), or teratogenicity (causing birth defects) and, thus, reduce the need for animal testing.

Scaling and extrapolation models are methods used to infer chemical toxicity data for a test species (species A) from data obtained of another species (species B), thereby reducing the need to test each species. These types of models are especially important to protect diverse groups of ecological organisms in the wild (such as birds and mammals) by deducing available toxicity data from species used in laboratories minimizing further animal testing.

Read-across approaches help toxicologists infer toxicity information for one chemical (chemical A) based on toxicity data available for another chemical (chemical B), when chemical B is similar to chemical A in structure and composition.

In Vitro Alternatives to Animal Testing

In vitro techniques refer to studies performed with biological material, not living organisms, outside their normal context in laboratory glassware (test tubes or petri dishes). For example, scientists are using cultured fish cell lines, not live fish, to study the effects of chemicals on fish since the primary interaction between chemicals and fish begins at the cell surface.

In Vivo Alternatives to Animal Testing

In vivo studies are studies performed with living organisms, alternative approaches aim to use fewer animals, younger life stages (such as embryos), and for a shorter duration. One excellent example is a fish embryo test that has increasingly been used instead of a test using juvenile fish.

Looking Forward

While alternatives to animal testing are being developed, obtaining regulatory acceptance of these new approaches remains a major challenge. Scientists continue to promote the advancement of alternatives to animal testing through appropriate stewardship and dialogue with regulators so that they become the norm for generating high-quality ecotoxicity data for chemical management. In the interim, wide use of existing toxicity data could lead to a substantial reduction in the number of animals used in regulatory ecotoxicity testing with cooperation and harmonization of testing at both national and international levels.

Resource

Organisation for Economic Co-operation and Development. Animal Welfare. http://www.oecd.org/chemicalsafety/testing/animal-welfare.htm.

Acknowledgments

SETAC is grateful for the efforts and contributions of those involved in the publication of this document: Barnett Ratter and Tamar Schlekat.

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When referring to this text, please use the following citation: [SETAC] Society of Environmental Toxicology and Chemistry. 2019. Taking the Mystery Out Of Toxicity Testing. Pensacola (FL): SETAC. 2pp.