

## Glossary and Definition of Abbreviations.

This page attempts to provide simple definitions of terms used in this project. These definitions are in the context of this project and are designed for the non-expert to obtain some understanding of the key elements of the projects. These terms have no legal basis and may differ in terminology, wording and meaning from definitions provided elsewhere e.g. Defra, OECD, European Commission, US EPA etc.

This collection of definitions has been compiled from knowledge within the consortium as well as from the reference materials noted at the end of this page. These definitions are for illustration only, it is recommended that they are not used in any formal context as a source of reference.

Term	Simple (Non-Technical) Definition
3Rs	The principles of the 3Rs - Replacement, Refinement and Reduction - were originally developed by Professor William Russell and Rex Burch and are now widely accepted internationally as criteria for humane animal use in research and testing.
Abiotic transformation	The transformation of a chemical that does not involve a biological organism, i.e. a chemical process such as oxidation, hydrolysis etc. This transformation may convert a non-reactive chemical into a reactive chemical, or <i>vice versa</i> .
Acute fish toxicity	The relative lethality of a chemical to fish following short term (e.g. 4 day) exposure.
Alternatives to toxicity testing	<p>These include (possible novel) toxicity tests that may</p> <ul style="list-style-type: none"><li>• eliminate the need for a whole animal (replacement alternative);</li><li>• substantially decrease the number of whole animals used for a particular procedure (reduction alternative);</li><li>• or improve the design and/or efficiency of a test, thereby lessening the distress or discomfort experienced by laboratory animals (refinement alternative).</li></ul> <p>Alternatives include the use of <i>in silico</i>, <i>in chemico</i> and <i>in vitro</i> methods. For successful use they must be properly described, characterised and evaluated and may require a formal process of validation for regulatory purposes.</p>
Analogue and / or category approach	Techniques for grouping “similar” chemicals.
Biotic transformation	The biological transformation of a chemical, for

	instance by metabolism. This transformation may convert a non-reactive chemical into a reactive chemical, or <i>vice versa</i> .
Category formation	The process of forming a group of chemicals – often termed a category – on a rational basis, such as having a similar chemical structure or mechanism of action.
Chemical category	A chemical category is a group of chemicals whose physico-chemical and human health and/or environmental toxicological properties and/or environmental fate properties are likely to be similar or follow a regular pattern as a result of structural similarity (or other similarity characteristic).
DEFRA	Department for Environment Food and Rural Affairs
Excess toxicity (in the context of acute fish toxicity)	It is assumed that for un-ionised, stable and water soluble organic chemicals there is a baseline (or minimum) acute toxicity to aquatic species, such as fish, exerted by narcosis. Should toxicity be significantly greater than that predicted by narcosis, it is termed excess toxicity. There may be many reasons for excess acute aquatic toxicity. It is usually indicative of a mechanism of toxic action other than narcosis. Many mechanisms associated with excess toxicity are electrophilic in nature. Other mechanisms could include metabolism to a more toxic form, receptor mediated and specific toxicities, formation of free radicals etc.
Expert system for predicting toxicity	Any formalised system which enables a user to obtain rational predictions about the toxicity of chemicals.
<i>In chemico</i>	The use of abiotic (non-animal or <i>in vitro</i> ) measurements of the reactivity or other physico-chemical properties of compounds.
<i>In silico</i> methods for toxicity prediction	The use of computer-based methods e.g. databases, (Q)SARs, read-across etc to retrieve or estimate toxicological effects of chemicals. These do not require the testing of a chemical (and hence can be termed non-testing information).
<i>In vitro</i> toxicity tests	Non-animal tests to determine toxicological information.
Integrated Testing Strategy (ITS)	An ITS is an approach that integrates different types of toxicological data and information into a decision-making process for the safety of a chemical. In addition to the information from individual assays, test batteries, and/or tiered test schemes, integrated testing strategies may

	incorporate approaches such as weight-of-evidence and exposure/ population data into the final risk assessment for a substance.
Local Lymph Node Assay (LLNA)	The LLNA is a standard test using mice to determine the capability of a chemical to cause skin sensitisation.
Mechanism of toxic action	The mechanism of toxic action is the molecular sequence of events leading from the absorption of an effective dose of a chemical to the production of a specific toxicological response in the target organ or organism.
Non-reactive compounds	Compounds that will not (readily) form covalent bonds with biological macromolecules. Such compounds are often narcotic in acute aquatic toxicity assays and are often not skin sensitisers.
Non-testing information	Non-testing data can be generated by three main approaches: a) grouping approaches, which include read-across and chemical category formation; (quantitative) structure-activity relationships ((Q)SARs); and c) expert systems.
Quantitative Structure-Activity Relationship (QSAR)	A QSAR is a mathematical model relating one or more quantitative parameters derived from chemical structure to a quantitative measure of a property or activity.
Reactive compounds	Compounds that are able to form covalent bonds with biological macromolecules. Many reactions are that of an electrophile reacting with a nucleophile (but may also include nucleophilic reactions, formation and action of free radicals etc). Reactive compounds are often associated with toxicological endpoints such as elevated acute aquatic toxicity and skin sensitisation.
Reactivity	The capability of a (usually organic) compound to form a covalent bond with a biological macromolecule (e.g. a protein or DNA).
Read-across	A technique of filling data gaps in within a chemical category.
Reasoning	Relates to the level of belief in an isolated event or conclusion with respect to an externally defined set of values.
Reduction (in the context of the 3Rs)	A means of lowering the number of animals used to obtain information of a given amount of precision.
Refinement (in the context of the 3Rs)	Any approach which avoids or minimises the actual or potential pain, distress and other adverse effects experienced at any time during the life of the animals involved, and which enhances their well-being.

Registration, Evaluation, Authorisation and restriction of Chemicals (REACH)	An EU regulatory framework for Registration, Evaluation, Authorisation and restriction of Chemicals (REACH). REACH aims to improve the protection of human health and the environment while maintaining the competitiveness and enhancing the innovative capability of the EU chemicals industry.
Replacement (in the context of the 3Rs)	Any scientific method employing non-sentient material which may, in the history of animal experimentation, replace methods which use conscious living vertebrates.
Risk assessment	The process through which the toxic effects (i.e. the hazard) of exposure to a chemical substance are calculated, and a decision regarding the potential uses of the substances is made.
Skin sensitisation	An allergic reaction on the skin when the subject is re-exposed (or challenged) to a chemical, following an initial exposure (the initiation event). It is an immunological response.
Structure-Activity Relationship (SAR)	A SAR is a qualitative relationships that relates a (sub)structure to the presence or absence of a property or activity of interest. The substructure may consist of adjacently bonded atoms, or an arrangement of non-bonded atoms that are collectively associated with the property or activity.
Toxicological data	Data relating to the harmful (toxicological) effects of chemicals. This may include information from animal, human or non-animal ( <i>in vitro</i> ) tests.
Weight of Evidence	A decision making activity aiming at concluding on toxicity of a substance based on integration of information from different sources and various aspects of uncertainty.

#### References and General Sources of Information to Make these Definitions

- AltTox Forum <http://www.alttox.org/ttrc/emerging-technologies/its/>
- Button WG et al (2003) Using absolute and relative reasoning in te prediction of the potential metabolism of xenobiotics. *J. Chem. Inf. Comp. Sci.* 43: 1371-1377.
- Dearden JC et al (1997) The development and validation of expert systems for predicting toxicity. *ATLA* 25:223-252.
- European Chemical Agency (2008) *Guidance on information requirements and chemical safety assessment. Chapter R.7b: Endpoint specific guidance.* Available from: [http://guidance.echa.europa.eu/docs/guidance\\_document/information\\_requirements\\_en.htm?time=1240135572](http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.htm?time=1240135572)

- European Commission Joint Research Centre, Institute of Health and Consumer Protection, Ex-European Chemicals Bureau  
<http://ecb.jrc.ec.europa.eu/reach/>
- Gerberick F et al (2008) Chemical reactivity measurement and the predictive identification of skin sensitizers. The report and recommendations of ECVAM Workshop 64. ATLA 36: 215-242.