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Part II: Toxicity assessment

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Abstract

Aquatic and non-aquatic ecosystems differ with regards to metabolism as well as exposure and uptake routes. Current international and European regulatory criteria for Persistence, Bioaccumulation, and Toxicity (PBT) assessment of chemical substances are mainly based on toxicity and bioaccumulation data in aquatic species. In the literature, there is evidence that several persistent organic chemicals, which are not classified as bioaccumulative and/or toxic in aquatic organisms according to existing criteria, can biomagnify in non-aquatic food chains up to the top predators (including humans) and exert their toxicity. Therefore, the regulatory frameworks may fail to identify a number of substances that are bioaccumulative and/or toxic in non-aquatic organisms and related food chains (exposed through soil and food), but not in aquatic species. Based on these considerations, two reports were prepared on available criteria for non-aquatic organisms within PBT/vPvB frameworks: one on bioaccumulation assessment (Part I) and one on toxicity assessment (Part II). Specifically, the present document illustrates and discusses the outcomes of a regulatory and literature review on available criteria for toxicity assessment in non-aquatic organisms at international and European level (Part II). This report could be used to support an eventual revision of guidance documents, e.g. for REACH (EU Regulation 1907/2006), as well as to promote the harmonisation of regulatory criteria for PBT/vPvB assessment.

Review of available criteria for non-aquatic organisms within PBT/vPvB frameworks

Part II: Toxicity assessment

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Preface

This report has been prepared in the frame of an Administrative Arrangement between the Directorate-General Environment (DG ENV) and the Joint Research Centre (JRC), Institute for Health and Consumer Protection (IHCP) on 'Scientific and technical support to safety assessment of chemicals'. One of the requests of DG ENV was to carry out a review of available criteria for bioaccumulation and toxicity assessment in non-aquatic organisms within current regulatory Persistent Bioaccumulative Toxic (PBT) and very Persistent very Bioaccumulative (vPvB) assessment frameworks.

Based on this request two reports were prepared on available criteria for non-aquatic organisms within PBT/vPvB frameworks: one on bioaccumulation assessment (Part I) (Gottardo et al. 2014) and the present one on toxicity assessment (Part II). An intermediate version of this report on toxicity assessment was circulated to participants of the PBT Expert Group of the European Chemicals Agency (ECHA). Thereafter, the report has been amended, taking into consideration the comments and suggestions of the ECHA PBT Expert Group.

We would like to thank the experts of the ECHA PBT Expert Group and the colleagues from DG ENV, ECHA and the JRC for their useful comments.

Executive Summary

In current international and European legislative frameworks for identification of substances with Persistent Bioaccumulative Toxic and very Persistent very Bioaccumulative (PBT/vPvB) properties and for hazard classification and labelling focus has been largely on the aquatic environment and only to a lesser extent on the non-aquatic environment. However, increased attention has been given to non-aquatic hazard assessment through the 1990s and early 2000s at international level. Criteria for non-aquatic organisms were proposed and discussed under the United Nations (UN) umbrella but have not been developed any further and have not been implemented in the internationally agreed Globally Harmonised System of classification and labelling of chemicals (hereafter referred to as GHS).

From a scientific perspective, environmental hazard assessment should aim to protect the environment as a whole. However, extrapolation of toxicity data from aquatic to non-aquatic organisms, which is often done, is hampered by e.g. possibly different mechanisms of toxicity, routes of exposure, uptake and elimination efficiencies, and metabolic abilities. Moreover, effects of substances with high hydrophobicity and low water solubility may not be detectable through standard acute aquatic toxicity tests. Hazards may instead be identified through prolonged aquatic exposure or through tests with non-aquatic organisms exposed through soil or food. Although hazard data from the aquatic system in general tends to result in a more conservative classification there are exceptions reported in the literature where higher toxicity is observed for the non-aquatic system. As a result, the classification based on toxicity criteria for aquatic organisms may miss some substances that are toxic in non-aquatic food chains. This could speak for the need of development of non-aquatic toxicity criteria for the use in PBT/vPvB assessment.

Based on these considerations, the Joint Research Centre (JRC), Institute for Health and Consumer Protection (IHCP), was asked by the Directorate-General Environment (DG ENV) to prepare a regulatory and literature review on available criteria for toxicity assessment in non-aquatic organisms to support the revision process of the ECHA *Guidance on information requirements and chemical safety assessment. Chapter R.11: PBT assessment* for implementation of the European chemicals legislation (REACH Regulation 1907/2006), as well as to promote the harmonisation of regulatory criteria for PBT/vPvB assessment at European level.

Based on the outcomes of the regulatory and literature review, a preliminary approach on how toxicity data for non-aquatic organisms could be used for non-aquatic toxicity assessment under PBT/vPvB frameworks is presented. Specifically, non-aquatic toxicity cut-off values for PBT/vPvB assessment are derived from available non-aquatic toxicity cut-off values for hazard classification by applying specific factors. However, it is recognised that this is a simplified approach that will require further development and evaluation. Therefore it is suggested to use the increased amount of data on terrestrial toxicity through REACH registration dossiers to further develop, verify and adjust this proposal (e.g. sensitivity to chemicals of aquatic versus non-aquatic organisms, acute-to-chronic extrapolation, applicability of the EqP method, cut-off values expressed as bulk soil concentrations and/or pore water concentrations). Moreover, the impact that the introduction of non-aquatic criteria in a regulatory context may have needs to be analysed in depth.

It should be highlighted that the aim of this document is not to re-open the discussion on non-aquatic criteria for hazard classification. Rather the aim is to collect information and suggest

approaches for the development of non-aquatic toxicity criteria for PBT/vPvB assessment so that, when toxicity data is available for non-aquatic organisms, this information can be used appropriately in the PBT/vPvB assessment. This might be particular useful for chemicals for which non-aquatic data are routinely available (e.g. biocidal and plant protection products).

1 Background and scope

In current international and European legislative frameworks for hazard assessment of chemicals focus has been largely on the aquatic environment and only to a lesser extent on the non-aquatic environment (See Glossary in Annex I). This is also reflected in regulatory criteria for the identification of hazardous substances including those for Persistent, Bioaccumulative and Toxic (PBT) substances as well as very Persistent very Bioaccumulative (vPvB) substances. PBT/vPvB substances are of concern due to their non-degradable nature making it difficult to effectively reduce environmental exposure upon release into the environment. Even if emissions are reduced/eliminated, the slow degradation implies that these substances will persist in the environment for a long period. This, in turn, may lead to transport of the substances over long distances and long-term exposure of organisms. Furthermore, their properties can cause irreversible bioaccumulation and biomagnification through the food web (see Glossary in Annex I).

For substances with high K_{ow} (octanol-water partitioning coefficient) values (see Glossary in Annex I), which indicate potential for bioaccumulation, the solubility in water is expected to be low. This presents a challenge to aquatic toxicity testing as 1) it is difficult to maintain/verify the exposure concentration, 2) for these substances the short exposure period in acute toxicity testing may not be long enough to reach equilibrium partitioning and be sufficiently taken up by the test organism (ECHA 2012), and 3) exposure concentrations may be limited by solubility. For these reasons acute aquatic toxicity tests may not be sufficient to detect any effect (which could possibly be detected by long-term exposure). This does not mean that non-aquatic organisms are necessarily more sensitive on a body residue basis. However, taken as a whole and taking into account the intrinsic properties of PBT/vPvB substances, which hamper aquatic hazard testing, it may speak for the need of development of non-aquatic toxicity criteria allowing for better use of this data in PBT/vPvB assessment.

Several national and international measures are currently in place to reduce the presence of PBT/vPvB substances in the environment. In these conventions, regulations and directives specific criteria for the identification of PBT/vPvB substances are described – in a qualitative or quantitative manner. Regarding quantitative criteria for bioaccumulation and toxicity the focus is mainly on aquatic organisms. Despite regulatory focus on the aquatic environment, increased attention has been given to terrestrial hazards through the 1990s and early 2000s. In a European context Risk phrases (R phrases) were previously included in Annex III of the EU Dangerous Substances Directive (DSD) 67/548/EEC for classification and labelling with respect to both the aquatic (R50-R53[3]) and the non-aquatic environment (R54-R57[4]). The DSD recognises that certain substances may affect non-aquatic environments and defines them as: 'Substances which on the basis of the available evidence concerning their toxicity, persistence, potential to accumulate and predicted or observed environmental fate and behaviour may present a danger immediate or long-term and/or delayed, to the structure and/or functioning of natural ecosystems' other than the aquatic ones. However, despite the DSD explicitly requires that detailed criteria for the non-aquatic environment are

[3] R50: Very toxic to aquatic organisms, R51: Toxic to aquatic organisms, R52: Harmful to aquatic organisms, R53: May cause long-term adverse effects in the aquatic environment.

[4] R54: Toxic to flora, R55: Toxic to fauna, R56: Toxic to soil organisms, R57: Toxic to bees.

elaborated at a later stage, only criteria for the aquatic environment were developed and included in the legal text. The DSD has been repealed by Regulation (EC) 1272/2008 on Classification Labelling and Packaging (CLP) (EC 2008a; EC 2011) in which classification criteria are still only included for aquatic hazards. In preparation of the implementation of the Global Harmonised System on Classification and Labelling of Chemicals (GHS) (UN 2011), and incorporation of the GHS criteria into Community law, a White Paper Working Group was addressing the issue of terrestrial hazard criteria and providing technical assistance to the European Commission. In the document 'Final report - Technical Assistance to the Commission on the implementation of the GHS' it was specified that 'The GHS contains neither hazard classes nor criteria for terrestrial environmental toxicity' (Ökopol 2004). This also implies that the terrestrial R-phrases (R54-57) are not covered by the GHS. It is further specified that 'The White Paper Working Group recommended these hazard classes not to be implemented in the new regulatory system' (Ökopol 2004). Furthermore, the Working Group recommended that the process was to be continued through a cost-benefit study, which resulted in a report on 'Cost and benefit analysis of the development and use of environmental hazard-effects classification criteria for terrestrial organisms' in 2003. This report highlights a number of benefits of the development of hazard criteria for the terrestrial compartments including coherence within the EU regulatory system (to cover both aquatic as well as non-aquatic hazards) and more complete environmental protection (Vega/ERA Consult 2003). However, this did not result in the inclusion of non-aquatic criteria in the CLP Regulation.

International efforts in relation to non-aquatic hazard assessment was summarised in an UN overview report in 2003 (UN 2003). Since then, the UN Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals (UNSCEGHS) decided that work should continue (in the programme of work for the biennium 2005-2006) with regards to development of classification and labelling criteria for terrestrial environmental hazards. However, it would be addressed by an informal working group led by Spain and the UNSCEGHS would be kept informed about their work (UN 2004a). This work resulted in a proposal for 'Classification criteria for the terrestrial environment' in 2006 (UN 2006), which was presented at the 16th session of the UNSCEGHS in December 2008 (UN 2008a). At the meeting there was a lack of consensus regarding the need and priority for further developments of non-aquatic criteria. As a consequence, the topic was not included in the programme of work for the biennium 2009-2010. It was planned that a correspondence working group led by Spain would continue the activities (UN 2008a). However, the criteria proposal has not been developed any further since. Hence, non-aquatic criteria have not been implemented in any of the subsequent revisions of the internationally agreed GHS (last revision: 4th edition, 2011 (UN 2011)).

From a scientific perspective the main arguments for considering non-aquatic hazards in relation to environmental classification are as follows:

- Non-aquatic hazards should be considered in order to protect the environment as a whole.
- Extrapolation of toxicity data from aquatic to non-aquatic is hampered by possibly different mechanisms of toxicity (and metabolism) e.g. for unicellular algae versus vascular plants (Tarazona et al. 2000).
- As described above effects of substances with low water solubility may not be detectable through acute aquatic toxicity tests. Hazards may instead be identified through prolonged aquatic exposure – or through tests with terrestrial organisms exposed through soil or food

(Tarazona et al. 2000)[5]. It has also been proposed that for substances with log K_{ow} > 3 (for non-polar substances) or BCF > 100 exposure via food is relevant (Carbonell et al. 1997).

Although hazard data from the aquatic system in general tends to result in a more conservative classification there are exceptions where higher toxicity is observed for the terrestrial system[6] (Renaud et al. 2004). As a result the classification based on toxicity criteria for aquatic organisms may miss some substances that are toxic in non-aquatic food chains.

Although this document is focused specifically on non-aquatic hazard criteria for PBT/vPvB assessment it is acknowledged that this is closely linked to the debate on non-aquatic hazards in relation to general environmental hazard assessment in classification and labelling frameworks. Accordingly, the present report focuses on reviewing the legislative status of non-aquatic hazard assessment within both PBT/vPvB and classification and labelling frameworks at international and European level and provides some preliminary views on possible incorporation of non-aquatic criteria in the identification of PBT/vPvB substances.

It should be highlighted that the aim of this document is not to re-open the discussion on non-aquatic criteria for hazard classification. Rather the aim is to collect information and suggest approaches for the derivation of non-aquatic toxicity criteria for PBT/vPvB assessment so that, when toxicity data is available for non-aquatic organisms, this information can be used appropriately in the assessment. This might be useful for chemicals for which non-aquatic data are routinely available (e.g. biocidal and plant protection products).

Based on a literature review the scope of this document is to:

- Give an overview of existing qualitative and quantitative environmental (aquatic and non-aquatic) toxicity criteria within the context of PBT/vPvB assessment, which are applied in various European and international regulations, directives and conventions (Section 2);
- Update information contained in the UN/SCEGHS/15/INF.29 review report from 2008 (UN 2008b) on terrestrial criteria for general hazard classification (i.e. not meant for PBT/vPvB assessment) and testing requirements with respect to terrestrial organisms. Additional information is provided to give an overview of criteria for terrestrial toxicity assessment and labelling within various European and international regulations, directives and conventions (Section 3);
- Give an overview of relevant non-aquatic OECD test guidelines and test methods in the European Test Method Regulation (TMR) (EC 2008b) (Section 4); and
- To illustrate and discuss state-of-the-art scientific knowledge and viewpoints regarding toxicity assessment and cut-off criteria for non-aquatic organisms that are used or could be used within PBT/vPvB frameworks and general hazard classification and labelling frameworks (Section 5).

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[5] At the same time, however, testing of high log K_{ow} substances present other challenges including adsorption to soil particles and organic matter, which in turn influences bioavailability.

[6] The analysis was based on data on substances in the IUCLID database, for 87 substances (out of 2604) data was available that was appropriate for classification according to terrestrial hazards. Of these 87 substances approximately half were identified as pesticides. However, details on specific substances are not included in the paper.

Based on the information that is compiled in the previous sections, Section 6 provides some preliminary proposals regarding PBT/vPvB assessment based on non-aquatic cut-off criteria used in general hazard classification and labelling frameworks. As a first step a procedure for making 'general-hazard-to-PBT/vPvB-hazard' cut-off value extrapolation is presented. This procedure is based mainly on an examination of aquatic cut-off values in existing European legislation (i.e. CLP (general hazard classification) versus REACH (PBT/vPvB classification)). As a second step, and using this extrapolation method, the cut-off values for general non-aquatic hazard classification (compiled from international legislation and scientific literature reported in Section 3) forms the basis for the identification of potential ranges of values for non-aquatic cut-off values for PBT/vPvB assessment. Such cut-off values could eventually be incorporated into the European regulatory frameworks for PBT/vPvB assessment. However, the proposed criteria are based on a simple approach and would require further discussion by experts. In Section 7 current and future initiatives that could provide more information and tools on toxicity in non-aquatic environments are briefly illustrated. Finally, main conclusions are drawn in Section 8.

Annex I explains some expressions used in this report. Annex II contains tables with a complete overview of compiled information on hazard criteria from regulatory frameworks and the peer-reviewed literature. Annex III is a list of relevant international and national bodies. Annex IV contains an overview of relevant European legislation.

2 International and European regulatory criteria for toxicity assessment for PBT/vPvB assessment

Different criteria are used for toxicity assessment in various international and European pieces of legislation within frameworks of PBT/vPvB assessment. An overview of these criteria is given in Annex II Table II.a. Some criteria are quantitative (e.g. cut-off values) while other regulations use qualitative criteria. Quantitative environmental toxicity criteria are in those cases based on toxicity to aquatic organisms only.

Within the European legislative framework the eco-toxicity (T) criterion for PBT/vPvB assessment is a long-term no-observed effect concentration (NOEC) or 10% effect concentration (EC_{10}) value of less than 0.01 mg/L. This is based on toxicity to marine or freshwater organisms. This is the case in both REACH Regulation 1907/2006 (EC 2006) and the Plant Protection Products (PPPs) Regulation 1107/2009 (EC 2009) whereas the Biocidal Products Regulation 528/2012 (EC 2012a) refers to REACH criteria. With regard to the PPPs Regulation 1107/2009, in a DG SANCO Working Document on *'Evidence needed to identify POP, PBT and vPvB properties for pesticides'* it is specified that in the absence of a relevant NOEC value EC_{50} values with an assessment factor of 10 can also be used (EC 2012b). The Classification Labelling Packaging (CLP) Regulation 1272/2008 does not foresee classification and labelling for PBT/vPvB substances.

In the US legislation no specific quantitative toxicity criteria for PBT/vPvB assessment are specified. However, a tiered testing strategy is described in which concerns for P, B and T are taken into account. A screening level tool (PBT Profiler) has been developed under contract to the US Environment Protection Agency (EPA) and highlights substances that may be chronically toxic to fish by use of quantitative criteria, where substances of high concern are those with fish chronic toxicity value < 0.1 mg/L.

In the Canadian legislation (i.e. *"Toxic Substances Management Policy"*), the toxicity criteria for PBT assessment are based on the general definition of toxicity in the Canadian Environmental Protection Act (CEPA) (Environment Canada 1995). For substances on the Domestic Substances List (DSL) under CEPA the determination of 'inherent toxicity' (iT) (for the purpose of categorisation) takes into account the water solubility of the substance (Environment Canada 2003). However, the criteria mentioned in relation to DSL categorisation on the Environment Canada webpage are $L(E)C_{50}$ (50% lethal (effect) concentration) ≤ 1 mg/L for acute and NOEC ≤ 0.1 mg/L for chronic toxicity to aquatic species (algae, invertebrates, fish) (Environment Canada 2006).

In the global treaty 'The Stockholm Convention on Persistent Organic Pollutants' (POP) the toxicity screening criteria are qualitative i.e. if the substance has the 'potential for damage to human health or to the environment' (UN 2009).

In 'The Convention for the Protection of the Marine Environment of the North-East Atlantic' (i.e. the *"OSPAR Convention"*) PBT properties are used to determine if a substance is defined as a Hazardous Substance and for selecting/deselecting substances. The ecotoxicity cut-off values are based on aquatic toxicity i.e. acute $L(E)C_{50}$ ≤ 1 mg/L or long-term NOEC ≤ 0.1 mg/L (OSPAR 2005).

In summary all quantitative cut-off criteria for ecotoxicity for the purpose of PBT assessment are based on aquatic toxicity values. For most international legislation and conventions the specific values are: $L(E)C_{50}$ ≤ 1 mg/L (acute) and NOEC ≤ 0.1 mg/L (long-term). The exception is the European

legislation. Here a long-term NOEC or EC_{10} value ≤ 0.01 mg/L is required for a substance to be classified as PBT, which is a factor 10 lower than the value used in other international legislative frameworks. Hence, the European legislation is less protective from a PBT classification point of view compared to e.g. US and Canadian legislation as well as the UN OSPAR Convention, which all apply more conservative long-term NOEC-based cut-off values.

3 Update of UN review on terrestrial environmental hazards from 2008

In this Section the information in an annex (UN 2008b) to a UN progress report on terrestrial environmental hazards (UN 2008c) from 2008 is reviewed and updated where appropriate. The title of the annex is 'Annex to the progress report on terrestrial environmental hazards: Detailed review of existing classification and labelling systems' and contains a summary of classification systems (and test requirements) for the terrestrial environment. The countries/geographical areas/conventions included in the review are: The Andean Community, Argentina, The Basel Convention, Canada, The European Union, New Zealand, Mexico, and The United States. The information in the review has been checked and possible updates on terrestrial classification systems and legislative bases have been identified. An overview of this update activity can be seen from Annex II Table II.b.

Compared to the information gathered through the UN review (UN 2008b; UN 2008c) in 2008 the only significant change to legislative requirements for classification and labelling frameworks has been the replacement of the DSD 67/548/EEC (EEC 1967) with the CLP Regulation 1272/2008 (EC 2008a; EC 2011). Although the DSD included classification with respect to both the aquatic (R50-R53) and the terrestrial environment (R54-R57), only criteria for the aquatic environment were developed for the CLP Regulation.

The current requirements in the classification systems for countries included in the UN review can be found in Annex II Table II.c, in which the official terrestrial criteria used for general hazard assessment and labelling as well as testing requirements for terrestrial organisms in different pieces of international and European legislation are summarised. In addition to the countries considered in the UN review, information from a few other countries (China, Korea and Japan) was included for comparison.

According to the GHS (UN 2011) chemicals can be classified as hazardous to the environment based on either acute or chronic toxicity to aquatic organisms. In brief, the GHS contains three categories (Cat) for acute aquatic toxicity: Acute Cat I if L(E)C_{50} ≤ 1 mg/L; Acute Cat II if L(E)C_{50} > 1 but ≤ 10 mg/L; and Acute Cat III if L(E)C_{50} > 10 but < 100 mg/L. Chronic toxicity classification takes into account degradability – and to some extend also bioaccumulation (potential). If the classification is based on available NOEC/EC_x data for aquatic organisms, the cut-off values are a factor of 10 or 100 lower (for non-rapidly degradable or rapidly degradable substances, respectively) compared to the cut-off values for acute toxicity classification. Even in the absence of adequate chronic toxicity data a substance can be classified into the chronic categories based on acute toxicity data when combined with a lack of rapid degradability and/or aquatic Bioconcentration Factor (BCF) ≥ 500 L/Kg (or log K_{ow} ≥ 4). This implies that chemicals with 'PBT properties' (toxic, non-rapidly degradable and (potentially) bioaccumulative) will be classified as Chronic Cat I. The GHS also contains a 'Safety net' classification named Chronic Cat IV. This applies to 'Poorly soluble substances, No acute aquatic toxicity up to level of water solubility, lack of rapid degradability and log K_{ow} ≥ 4 (unless scientific evidence shows that classification is unnecessary, e.g. experimental BCF < 500, chronic toxicity > 1 mg/L, evidence of rapid degradation in the environment)' (UN 2011). Substances with vPvB properties will often (though not necessarily always) be classified as Chronic Cat IV.

Other legislations/conventions, which refer to are in line with the GHS criteria include: the Basel Convention as well as Chinese, Korean and Japanese legislation on labelling of chemicals. The legislation in the Andean Community refers to Food and Agriculture Organization (FAO) guidelines

that are based on classification criteria for pesticides as recommended by the World Health Organisation (WHO), for which the next updated version is foreseen to follow the GHS.

In a European context relevant legislation includes REACH, PPPs Regulation, Biocidal Products Regulation and CLP. Only the CLP contains toxicity criteria for classification and labelling and these are for aquatic organisms (EC 2008a). The criteria were initially only based on acute toxicity values but have been amended in 2011 through the 2nd Adaptation To Progress (ATP) (EC 2011) so that Chronic Cat 1, 2, and 3, can be based on adequate chronic data (NOEC or EC_x), with criteria in line with those in the GHS. Also in line with the GHS classification system the CLP includes considerations for degradability and (potential for) bioaccumulation for the Chronic Cat 1, 2 and 3. The toxicity cut-off values can be seen from Annex II Table II.c.

REACH, the PPPs Regulation and the Biocidal Products Regulation do contain data requirements for toxicity testing of non-aquatic organisms. In REACH information on terrestrial toxicity is required for chemicals produced or imported in quantities > 100 tonnes/year if the results of the chemical safety assessment indicate a need for testing but can be waived if terrestrial exposure is unlikely. In the previous PPPs Directive 91/414/EEC (EEC 1991) tests of active substances were required on aquatic organisms (fish, *Daphnia magna*), birds (and other terrestrial vertebrates), arthropods (bees and other non-target arthropods), earthworms, soil non-target micro-organisms, other non-target organisms (flora and fauna, such as plants, mites, *Collembola*, etc.) and biological methods for sewage treatment (according to Annex II and III of PPPs Directive 91/414/EEC). The choice of specific testing depended on the application of the PPP. In 2009 the PPPs Directive 91/414/EEC was repealed by Regulation (EC) No. 1107/2009 (EC 2009). New data requirements were subsequently published as Regulation (EU) No. 283/2013 for active substances (EC 2013a) and Regulation (EU) No. 284/2013 for formulated plant protection products (EC 2013b). Main changes in the new requirements for active substances include tests on an additional aquatic invertebrate in addition to *Daphnia magna*, honey bees and terrestrial wildlife including mammals, reptiles, and amphibians. In addition to the data requirements, two European Commission Communications were published, which list the recommended guidance documents and test guidelines to be followed for each requirement[7]. The Biocidal Products Regulation (EC 2012a) contains information requirements for the preparation of a dossier for an active substance. The ECHA *Guidance on information requirements* describes the testing strategy to be followed for the PBT assessment of biocidal active substances, biocidal products and treated articles, for example if the biocide is directly applied or emitted to soil a soil simulation test is required (ECHA 2013). Some information requirements are included in a Core Data Set (CDS), covering basic data requirements that should be provided by the applicant for all active substances. Moreover, there are requirements for an Additional Data Set (ADS) where the data to be provided for a specific active substance is evaluated based on the CDS taking into account e.g. physical and chemical properties of the substance, existing data, use and exposure patterns. As part of the ADS data requirements, tests on a number of non-aquatic species are included.

The US Pesticides Programs contains ecotoxicity categories for both terrestrial and aquatic organisms including avian, aquatic, wild mammal and non-target insect. Toxicity cut-off values are provided for categorisation into five different categories: *Very highly toxic*, *Highly toxic*, *Moderately toxic*, *Slightly*

[7] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2013:095:0001:0020:EN:PDF
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2013:095:0021:0037:EN:PDF

Toxic and Practically nontoxic. In the legal text of the US Toxic Substances Control Act (TSCA) no specific criteria are mentioned. Instead it refers to *concerns for environmental effects*. In 2003 the US EPA published information on 'TSCA Section 8(e); *Notification of Substantial Risk; Policy Clarification and Reporting Guidance*' (US EPA 2003a). In Part V ('What Constitutes Substantial Risks') the meaning of 'environmental effects' in the context of the TSCA is further clarified.

In New Zealand the classification of chemical substances is legislated through *The Hazardous Substances and New Organisms Act* 1996 (HSNO Act) and the Hazardous Substances (Classification) Regulations 2001. The classification system consists of categories for both terrestrial and aquatic organisms, i.e. for aquatic ecotoxicity, ecotoxicity to the soil environment, ecotoxicity to terrestrial vertebrates and ecotoxicity to terrestrial invertebrates. For the different classes there are up to four hazard categories: A) 'Very Ecotoxic', B) 'Ecotoxic', C) 'Harmful' and D) 'Slightly harmful'. Category D only applies to aquatic and soil ecotoxicity (NZEPA 2012).

In conclusion, as can be seen from Annex II Table II.c criteria for classification and labelling within CLP and GHS are based solely on aquatic organisms. However, data requirements for hazard assessment in European legislation are in some cases also based on effects to other non-target organisms such as e.g. honey bees, soil organisms and birds.

4 OECD Test Guidelines and European Test Methods relevant for toxicity testing on non-aquatic organisms

4.1 OECD Test Guidelines (TGs)

A previous concern in relation to development of terrestrial toxicity criteria has been the lack of standardised test methods. It was pointed out in the 2003 European Commission *Technical Guidance Document on Risk Assessment* that in effect assessment for the terrestrial compartment 'a dataset comprising of toxicity data for primary producers, consumers and decomposers is preferred'; however, 'an internationally accepted set of standardised ecotoxicological tests for hazard assessment of chemicals for the soil compartment' was not available at that time (EC 2003). However, it was concluded already in 2004 by the UNSCEGHS that *"On the basis of the recent OECD efforts for updating and developing new ecotoxicity tests guidelines, it is concluded that it is technically feasible to establish a hazard classification scheme for terrestrial organisms. The terrestrial environmental hazards are to be seen as different from and complementary to aquatic hazards and could produce a different classification scheme"* (UN 2004b). At that time OECD test methods were available for all main taxonomic groups: microorganisms (TGs 216 and 217), plants (TGs 208 and 227), invertebrates (TGs 207, 213, 214, 220 and 222) and vertebrates (birds) (TGs 205 and 206). Furthermore, additional test methods were available e.g. from ISO and the US EPA. Since then, there has been additional progress in this field and Table 1 gives an overview of the currently available OECD test guidelines for non-aquatic toxicity testing. Table 1 also includes information regarding year of adaptation, as well as information on current/future inclusion of the guideline as a Test Method in the EU Test Methods Regulation (TMR) 440/2008 (EC 2008b).

An OECD survey from 2010 shows that 17 OECD member countries (Australia, Austria, Belgium, Canada, Czech Republic, Denmark, France, Germany, Italy, Ireland, Japan, Netherlands, Poland, Slovakia, Slovenia, United Kingdom and United States) have toxicity testing of pollinators as a standard information requirement for registration dossiers for pesticides (OECD 2010a). The test battery includes Acute Honeybee Oral Toxicity (94% of the countries), Acute Honeybee Contact Toxicity (100 %), Field Pollinator Study (59%) and Hive Study (41%). However, there were diverging opinions on whether or not these tests and risk assessment methods are sufficient to assess risks to pollinator adults and brood – especially for potential sub-lethal effects of pesticides on adult and larval honeybees.

Table 1 Overview of OECD Test Guidelines (TGs) for non-aquatic ecotoxicity tests and corresponding Test Methods (TMs) in the European Test Methods Regulation (TMR) (up to May 2014) (EC 2008b). For the OECD TGs for which there is currently no corresponding TMs in the TMR it is indicated through which Adaptation to Technical Progress (ATP) they are expected to be included in the TMR.

OECD Test Guideline No	Name	Year (current version)	Corresponding Test Method in EU Test Methods Regulation (TMR) No 440/2008	To be included through Adaptation to Technical Progress (ATP)
Toxicity to pollinators				
OECD 213	Honeybees, Acute Oral Toxicity Test	1998	C.16. Honeybees – Acute Oral Toxicity Test. This acute toxicity test method is a replicate of the OECD TG 213 (1998).	-
OECD 214	Honeybees, Acute Contact Toxicity Test	1998	C.17. Honeybees – Acute Oral Contact Toxicity Test. This acute toxicity test method is a replicate of the OECD TG 214 (1998).	-
Toxicity to arthropods (including beneficial predators)				
OECD 226	Predatory mite (Hypoaspis (Geolaelaps) aculeifer) reproduction test in soil	2008	-	5th ATP
OECD 228	Determination of Developmental Toxicity of a Test Chemical to Dipteran Dung Flies (Scathophaga stercoraria L. (Scathophagidae), Musca autumnalis De Geer (Muscidae)	2008	-	6th ATP
OECD 232	Collembolan Reproduction Test in Soil	2009	-	5th ATP

Table 1 *(cont.)*

OECD Test Guideline No	Name	Year (current version)	Corresponding Test Method in EU Test Methods Regulation (TMR) No 440/2008	To be included through Adaptation to Technical Progress (ATP)
Toxicity to earthworms				
OECD 207	Earthworm, Acute Toxicity Tests	1984	C.8: Toxicity for Earthworms. Contains reference to OECD 207 but extend of similarity not specified.	-
OECD 220	Enchytraeid Reproduction Test	2004	-	5th ATP
OECD 222	Earthworm Reproduction Test (Eisenia fetida/Eisenia andrei)	2004	-	5th ATP
Toxicity to soil microorganisms				
OECD 216	Soil Microorganisms: Nitrogen Transformation Test	2000	C.21: Soil Microorganisms: Nitrogen Transformation Test. Replicate of OECD TG 216 (2000).	-
OECD 217	Soil Microorganisms: Carbon Transformation Test	2000	C.22: Soil Microorganisms: Carbon Transformation Test (2000). Replicate of OECD TG 217 (2000)	-
Toxicity to terrestrial plants				
OECD 208	Terrestrial Plant Test: Seedling Emergence and Seedling Growth Test	2006	-	5th ATP
OECD 227	Terrestrial Plant Test: Vegetative Vigour Test	2006	-	6th ATP
Toxicity to birds				
OECD 205	Avian Dietary Toxicity Test	1984	-	6th ATP
OECD 206	Avian Reproduction Test	1984	-	6th ATP
OECD 223	Avian Acute Oral Toxicity Test	2010	-	6th ATP

Tests for other bees than honeybees e.g. bumble bees and solitary bees are currently under development within the OECD Pesticide Effects on Insect Pollinators (PEIP) Expert Group that is part of the OECD Working Group Pesticides. This work is in line with the EFSA 'Guidance Document on the risk assessment of plant protection products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees)' (EFSA 2013).

4.2 EU Standardised Test Methods and Test Method Regulation (TMR)

The TMR (EC 2008b) contains EU standardised Test Methods (TMs), which are used for the determination of physico-chemical properties, fate, and hazards of chemical substances. It is updated regularly through the ATPs as required. Three ATPs (2009, 2010 and 2012) were adopted but did not include any TMs on non-aquatic ecotoxicity. The 4th ATP was published in January 2014 (EC 2014). Of relevance to non-aquatic environmental classification, the OECD TG 317 'Bioaccumulation in Terrestrial Oligochaetes' is included as TM. In both the 5th ATP (foreseen to be published after July 2014[8]) and 6th ATP (completion date still to be confirmed) TGs on non-aquatic species are included as specified in Table 1.

As can be seen from Table 1, all non-aquatic OECD TGs will have a corresponding TM in the TMR after the 6th ATP. The conversion of an OECD TG into a TM in the TMR is however not a prerequisite for its acceptance under other European regulations such as PPPs Regulation, Biocidal Products Regulation and REACH. For example, Article 13.3 of REACH already allows for the use of TMs in the TMR or *"other international test methods recognised by the Commission or the Agency as being appropriate"* (EC 2006). Similarly, in the PPPs Regulation there is often reference to other international test methods (e.g. US EPA guidelines) that can be applied where no OECD standard is available.

[8] http://chemicalwatch.com/18807/eu-commission-publishes-updated-reach-test-methods-regulation

5 Literature criteria for toxicity assessment in non-aquatic organisms

This Section contains illustrations and discussions of state-of-the-art scientific knowledge and viewpoints regarding toxicity criteria for non-aquatic organisms. Furthermore, Table 2 includes a summary of cut-off criteria from peer-reviewed literature as well as from the legislation presented in Section 2 and 3.

Table 2 Toxicity cut-off values for environmental terrestrial hazard classification criteria for chemical substances as found in scientific literature, international legislations and official reports. The table contains mainly acute toxicity cut-off values for classification of a substance into acute categories (EC50: 50% Effect Concentration, LD50: 50% Lethal Dose, or LC50: 50% Lethal Concentration). However, for classification of a substance into chronic categories also chronic toxicity cut-off values (NOEC: No-Observed Effect Concentration, NOAEL: No-Observed Adverse Effect Limit) are applied. Measurement units are indicated as reported in the references. Although mg/Kg soil is generally reported in dry weight (dw) this is not always specified.

Organism	Very Toxic/Acute 1/Chronic 1 Category	Toxic/Acute 2/Chronic 2 Category	Harmful/Acute 3/ /Chronic 3 Category	Reference
Soil dwelling invertebrates including earthworms	EC_{50} < 1 mg/Kg soil dw	1 < EC_{50} < 10 mg/Kg soil dw	10 < EC_{50} < 100 mg/Kg soil dw[9]	Carbonell et al. 1997; NZEPA 2012
	EC_{50} ≤ 10 mg/Kg soil	10 < EC_{50} ≤ 100 mg/Kg soil	-	Torstensson et al. 1999
(soil exposure)	EC_{50} < 4 mg/Kg dw			Renaud et al. 2004 (earthworms)
	EC_{50} < 60 mg/Kg dw	-	-	
	EC_{50}/LC_{50}/ER_{50} ≤ 10 mg/Kg dw	10 < EC_{50}/ LC_{50}/ER_{50} ≤ 100 mg/Kg dw	100 < EC_{50}/ LC_{50}/ER_{50} ≤ 1000 mg/Kg dw	UN 2006 (Acute categories)
	NOEC ≤ 1 mg/kg	1 < NOEC ≤ 10 mg/Kg	10 < NOEC ≤ 100 mg/Kg	UN 2006 (Chronic categories)
Foliar invertebrates and pollinators (including bees)	LD_{50} ≤ 1 µg/bee	1 < LD_{50} ≤ 10 µg/bee	10 < LD_{50} ≤ 100 µg/bee	Carbonell et al. 1997; UN 2006; SENASA 1999[10]
	LD_{50} ≤ 2 µg/bee	2 < LD_{50} ≤ 11 µg/bee	LD_{50} > 11 µg/bee	US EPA 2012[11]
	LD_{50} ≤ 2 µg/animal	2 < LD_{50} ≤ 11 µg/animal	11 < LD_{50} ≤ 25 µg/animal	NZEPA 2012 (terrestrial invertebrates in general)

[9] For NZEPA (2012): And Soil DT_{50}> 30 days, otherwise categorised as 'slightly harmful'. Other test methodologies can be used to fulfil the testing requirements for soil effect thresholds.

[10] Categories are: Highly Toxic, Moderately Toxic and Slightly Toxic. At LD_{50} > 100 µg/bee the substance is considered virtually non-toxic

[11] Categories are: Highly Toxic, Moderately Toxic and Practically non-toxic

Table 2 *(cont.)*

Organism	Very Toxic/Acute 1/Chronic 1 Category	Toxic/Acute 2/Chronic 2 Category	Harmful/Acute 3/ /Chronic 3 Category	Reference
Microorganisms	EC_{50} ≤ 1 mg/Kg dw EC_{50} ≤ 1 mg/kg and/or ≥ 50 % of adverse effects at a concentration ≤ 1 mg/Kg dw More than 50% effect at a concentration ≤ 1 mg/Kg dw	1 < EC_{50} ≤ 10 mg/Kg dw 1 < EC_{50} ≤ 10 mg/Kg and/or ≥ 25 but < 50% of adverse at a concentration ≤ 1 mg/Kg dw 30 - 50% effect at a concentration of ≤ 1 mg/Kg dw	10 < EC_{50} ≤ 100 mg/Kg dw[12] 10 < EC_{50} ≤ 100 mg/Kg and/or < 25% of adverse effects at a concentration ≤ 1 mg/Kg dw -	NZEPA 2012 UN 2006 (Chronic categories) Carbonell et al. 1997
Terrestrial plants (soil exposure)	EC_{50}/ LC_{50}/ER_{50} ≤ 10 mg/Kg dw EC_{50} ≤ 1 mg/Kg soil dw	10 < EC_{50}/ LC_{50}/ER_{50} ≤ 100 mg/Kg dw 1 < EC_{50} ≤ 10 mg/Kg soil dw	100 < EC_{50}/ LC_{50}/ER_{50} ≤ 1000 mg/Kg dw 10 < EC_{50} ≤ 100 mg/Kg soil dw	UN 2006 Carbonell et al. 1997
Terrestrial plants (foliar exposure)	EC_{50}/ER_{50} ≤ 10 Kg/ha EC_{50} (biomass or seed germination) ≤ 1 Kg/ha	10 < EC_{50}/ER_{50} ≤ 100 Kg/ha 1 < EC_{50} (biomass or seed germination) ≤ 10 Kg/ha	100 < EC_{50}/ER_{50} ≤ 1000 Kg/ha 10 < EC_{50} (biomass or seed germination) ≤ 100 Kg/ha	UN 2006 Carbonell et al. 1997

[12] NZEPA (2012): And Soil DT_{50}> 30 days, otherwise categorised as 'slightly harmful'. Other test methodologies can be used to fulfil the testing requirements for soil effect thresholds.

Table 2 *(cont.)*

Organism	Very Toxic/Acute 1 /Chronic 1 Category	Toxic/Acute 2 /Chronic 2 Category	Harmful/Acute 3/ /Chronic 3 Category	Reference
Terrestrial vertebrates (birds and mammals) (oral exposure)[13]	LD_{50} ≤ 5 mg/Kg bw	5 < LD_{50} ≤ 50 mg/Kg bw	50 < LD_{50} ≤ 500 mg/Kg bw	UN 2006 (Acute categories)
	NOAEL ≤ 0.5 mg/Kg bw	0.5 < NOAEL ≤ 5 mg/Kg bw	5 < NOAEL ≤ 50 mg/Kg bw	UN 2006 (Chronic categories)
	LD_{50} ≤ 10 mg/Kg (very highly toxic) 10 < LD_{50} ≤ 50 mg/Kg (highly toxic)	50 < LD_{50} ≤ 500 mg/Kg (moderately toxic)	500 < LD_{50} ≤ 5000 mg/Kg (slightly toxic)	US EPA 2012
	LD_{50} ≤ 50 mg/Kg bw	50 < LD_{50} ≤ 500 mg/Kg bw	50 < LD_{50} ≤ 2000 mg/Kg bw	NZEPA 2012
	LD_{50} ≤ 25 mg/Kg bw	25 < LD_{50} ≤ 200 mg/Kg bw	200 < LD_{50} ≤ 2000 mg/Kg bw	Carbonell et al. 1997
Terrestrial vertebrates (birds and mammals) (diet exposure)	LC_{50} ≤ 500 ppm in the diet	500 < LC_{50} ≤ 1000 ppm in the diet	1000 < LC_{50} ≤ 5000 ppm in the diet	NZEPA 2012
	LD_{50} ≤ 50 ppm (very highly toxic) 50 < LD_{50} ≤ 500 ppm (highly toxic)	500 < LD_{50} ≤ 1000 ppm (moderately toxic)	1000 < LD_{50} ≤ 5000 ppm (slightly toxic)	US EPA 2012
Terrestrial vertebrates (air exposure)	$LC_{50, 4h}$ ≤ 0.5 mg/L air	0.5 < $LC_{50, 4h}$ ≤ 2 mg/L air	-	Carbonell et al. 1997

The development of criteria for hazard classification is outside the scope of this paper, which is focused on specific criteria for PBT/vPvB assessment in non-aquatic organisms based on existing and proposed criteria in international and European legislative frameworks as well as scientific literature. Here, however, we provide some general background on available approaches for the development of criteria for non-aquatic hazard classification to be able to critically relate to the criteria in Table 2.

In the scientific literature a number of papers and reports are available, which discuss approaches for the development of criteria for non-aquatic hazard classification. In the development of classification criteria for the non-aquatic environment it has been pointed out by Tarazona et al. (2000) that it should follow the scientific concept for hazard classification, already accepted for the aquatic environment, which was summarised by Tarazona et al. (2000) as:

[13] Conversion factors from 'mg/kg bw' to 'ppm in diet' can be found in NZEPA 2012. As examples this factor is 8 for chicken, 10 for young rat, 20 for old rat and 7 for mouse. This means that, in order to obtain a NOEC value rather than a NOEL value, the quoted values have to be divided by this factor.

- The primary criterion is acute toxicity of the substance based on single species toxicity tests under standard conditions to a basis set of three key taxonomic groups, which are given equal weight.
- On the basis of all obtained data the most sensitive species is identified i.e. the lowest E(L)C_{50} value is selected and used for classification.
- Substances are divided into different toxicity clusters where the number and names of clusters may differ. An example is 'very toxic', 'toxic', 'harmful', 'not classified'. The division is done based on cut-off values increasing in magnitude e.g. E(L)C_{50} < 1, 1-10, 10-100, > 100 mg/L.
- Additionally fate properties, such as bioaccumulation and persistency, can be included in the classification considerations. Tarazona and Vega (2002) propose a holistic approach which includes exposure based testing.

This concept for hazard classification, as described above, can also be applied in a reverse manner: on the basis of experimental test results a reference toxicity range for selected substances and organisms can be obtained. Classification criteria can then be established from the reference toxicity range through e.g. statistical procedures.

The same concept is considered to apply for non-aquatic hazard classification, for which the following approaches have been suggested for determining appropriate cut-off criteria (Renaud et al. 2004; Tarazona et al. 2000; EC 2001):

- **Assessment Factor.** Based on mean EC_{50} values for a set of chemical substances for selected (groups of) organisms. This mean value is then divided by a factor (e.g. 100) to account for uncertainty (Renaud et al. 2004; EC 2001).
- **Species sensitivity distributions/statistical extrapolation.** Based on a total number of chemicals a fixed percentage/percentile is chosen (e.g. the most toxic 10% based on the distribution of the L(E)C_{50} values for the most sensitive species) and these are classified as 'very toxic'. On this basis cut-off criteria are established for different toxicity clusters (Renaud et al. 2004; EC 2001).
- **Extrapolation of aquatic criteria to the terrestrial compartment.** Based on comparison of distribution curves for aquatic and terrestrial toxicity values for different taxonomic groups Euclidean distances are calculated. By multiplying the aquatic cut-off values by the Euclidian distances for individual taxonomic groups and exposure routes cut-off values for the terrestrial environment can be calculated (as done by EC 2001). Another approach is to calculate soil criteria from aquatic criteria using the equilibrium partitioning (EqP) method, but is has been described as a method with high uncertainty when applied to organic substances and metals. This can result in both an under- and overestimation of non-aquatic toxicity but may still be a useful tool depending on the amount and quality of the available data on non-aquatic toxicity (van Beelen et al. 2003). For example, based on a species sensitivity distribution for ecotoxicity of PAHs to species in different environmental compartments it has been concluded that the EqP method worked well for the investigated PAHs. Based on internal residues no difference in sensitivity was observed between the organisms from the following different compartments: water (marine and fresh), sediment (marine and fresh) and soil (Verbruggen 2012).

It should be noted that the resulting criteria, when determined by these methods, will hence depend on the dataset on which the criteria are established. It was also concluded by the UNSCEGHS in 2004 that 'efforts for compiling a large database including as many substances, chemicals structures and chemicals categories as possible, would be highly valuable for the further development of criteria for terrestrial hazard classification'.

In a European legislative context, several Member States agreed on a common proposal of classification criteria for the terrestrial environment at a meeting held in Vienna in 2000. The agreed criteria at that time were based on acute toxicity (LC_{50} or EC_{50}) for soil-dwelling organisms (including earthworms and plants) and three hazard classes defined by cut-off values of increasing magnitude i.e. 'very toxic' if $L(E)C_{50} \leq 10$ mg/Kg_{dw}, 'toxic' if $L(E)C_{50}$ in the range 10-100 mg/Kg_{dw} and harmful if $L(E)C_{50}$ in the range 100-1000 mg/Kg_{dw} (ECB 2000). However, this proposal has not been further discussed and implemented. Hence, these criteria are not included in Table 2.

As described in Section 1, criteria for the terrestrial environment were addressed by a White Paper Working Group in preparation of the implementation of the GHS and incorporation of the GHS criteria into Community law. The working group recommended that criteria for the terrestrial environment were not to be implemented in the new regulatory system (i.e. the CLP) but that the process was to be continued though a cost-benefit study. On the basis of specific criteria proposals from Member States such a study was performed in collaboration with JRC and ECB, which resulted in a report on 'Cost and benefit analysis of the development and use of environmental hazard-effects classification criteria for terrestrial organisms' (Vega/ERA Consult 2003). The report contains annexes with the Member State proposals for development of criteria for different terrestrial compartments (i.e. Swedish, Austrian, Spanish, Nordic and German proposals). The German proposal by Feibicke et al. (1999) include what they describe as first proposals, which need *"further adjustment and critical verification e.g. by comparing the frequency distributions of aquatic and terrestrial data sets"* (in: Vega/ERA Consult 2003 - Annex V). Hence, these criteria are not included in Table 2. The Nordic proposal is taken from a report by Torstensson et al. (1999) and cut-off values for toxicity to soil organisms are based on 1) likely concentrations of chemicals in the soil and 2) a comparison between aquatic and terrestrial toxicity. The proposed cut-off values are included in Table 2. A very detailed proposal was made by Spain. A report by Carbonell et al. (1997) provides the scientific basis for the proposal and is the outcome of a workshop for Spanish experts on terrestrial classification criteria. The proposal is based on terrestrial R-phrases in line with the (now repealed) DSD (i.e. R54-R56: very toxic/toxic/harmful to terrestrial environment and R57: may cause long term and/or widely spread adverse effects in the terrestrial environment). The proposed toxicity classification criteria are based on soil exposure, air/contact/deposition exposure and oral exposure for plants, microorganisms, invertebrates and vertebrates. The duration and distribution of effects is based on biodegradability and mobility properties of the substance. The proposed toxicity criteria are included in Table 2.

The criteria proposed by Carbonell et al. (1997) and (Torstensson et al. 1999) were examined by Renaud et al. (2004), who criticized them for being based on relatively limited datasets. Renaud et al. (2004) then went on to develop new criteria for terrestrial hazard classification, which were based on data for earthworm toxicity for either 313, 157, 126 or 72 substances (criteria were compared for the different approaches), most of which were agricultural pesticides, with different modes of toxic action. Also these are included in Table 2. It was furthermore concluded in the paper that **classification based on aquatic data is in general a conservative approach**. This was based on data

for approximately 87 substances, for which terrestrial toxicity data (soil invertebrates and plants) was available and which had already been classified in terms of their aquatic toxicity. However, there are some exceptions where a more severe classification would be given based on terrestrial toxicity data. A general issue in relation to classification based also on terrestrial toxicity data is the lack of appropriate data for many substances. This may have been improved through REACH registrations and consequential increased ecotoxicity data availability from the registration dossiers. However, this is something that requires further investigations.

As described in Section 1, besides from their contributions in a European context, Spain also had a leading role in the international efforts to develop terrestrial hazard criteria. A working group under the UN Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals (UNSCEGHS), led by Spain, developed in 2006 a proposal on 'Classification criteria for the terrestrial environment' (UN 2006). The proposal was presented at the 16th session of the UNSCEGHS in December 2008. However, the criteria proposal has not been developed any further since. The criteria are included in Table 2.

6 Preliminary proposals for non-aquatic toxicity criteria in the framework of PBT/vPvB assessment

Based on the compiled information, this section provides some preliminary proposals regarding new criteria for non-aquatic organisms for the identification of toxic substances in the framework of PBT/vPvB assessment and possible incorporation into European legislative frameworks.

In European legislation aquatic toxicity cut-off values for PBT assessment are based on NOEC/EC_{10} values[14]. Following a 2011 amendment to the CLP, cut-off values of chronic categories for environmental hazard classification are based on a combination of chronic NOEC or EC_x values and acute E(L)C_{50} values (See Annex II Table II.c). Different chronic NOEC or EC_x values are applied as cut-off values depending on the degradability of the substance, with the lowest one (for Chronic Cat 1) of chronic NOEC or $EC_x \leq 0.01$ mg/L. This cut-off value corresponds to the toxicity criteria used for identification of PBT substances under REACH. When adequate chronic toxicity data is not available, a substance can also be classified as Chronic Cat 1 based on L(E)$C_{50} < 1$ mg/L in combination with non-rapid degradability and/or BCF ≥ 500 (or, if absent, log $K_{ow} \geq 4$).

In order to establish cut-off values for PBT assessment of substances in non-aquatic organisms based on available criteria for non-aquatic hazard classification (as summarised in Table 2) one approach could be to simply apply a 'L(E)C-to-NOEC extrapolation factor'. Hereby a correlation could be established between cut-off criteria for hazard classification and corresponding cut-off criteria for toxicity assessment under PBT/vPvB frameworks. **It is acknowledged that this is a simple approach and would potentially require further development.**

In European legislation the following aquatic toxicity cut-off criteria are applied for the highest hazard classification category and for identification of PBT substances:

Hazard classification Acute Cat 1:	L(E)$C_{50} < 1$ mg/L	EC 2011
Hazard classification Chronic Cat 1:	Chronic NOEC/$EC_x < 0.1$ mg/L	EC 2011
PBT assessment Toxicity criteria:	Long-term NOEC/$EC_{10} < 0.01$ mg/L	EC 2006; 2009

Hence the long-term NOEC/EC_{10} value used for PBT assessment under REACH (EC 2006) and PPPs Regulation (EC 2009) is 100 times lower than the L(EC)$_{50}$ value and 10 times lower than the chronic NOEC/EC_x that are used for hazard classification in the CLP (EC 2011). It is noted that the cut-off criteria for general hazard classification in the CPL (EC 2011) (Chronic NOEC/$EC_x < 0.1$ mg/L) correspond with the criteria in Canadian and US legislation as well as the OSPAR Convention (substances with high toxicity: NOEC/$EC_{10} < 0.1$ mg/L). These legislations also include the possibility

[14] However, it should be noted that in ECHA guidance it is described how short-term toxicity can be used as an indicator for whether the T criterion is fulfilled. See Annex I Table I.a.

to classify a substance as PBT based on acute L(E)C_{50} values ≤ 1 mg/L. Hence, based on applied practices, a pragmatic conclusion can be drawn that **a factor of 10 is applied between NOEC/EC_{10} for general hazard classification and NOEC/EC_x for PBT assessment.** Furthermore there is **a factor of 100 between and L$(EC)_{50}$ used for general hazard classification and NOEC/EC_x for PBT assessment.** In the following an assumption will be made that these factors can be applied to convert between acute and chronic cut-off values for non-aquatic toxicity. **It is however acknowledged that this is a very simplified approach which may require further development.** Based on cut-off values for hazard classification (Table 2) potential approximate ranges of non-aquatic cut-off values for toxicity assessment under PBT/vPvB frameworks are presented below (Table 3).

It is noted that, based on the information presented in the previous chapters, there seems to be a need for further investigations of appropriate cut-off values for classification of hazard to the terrestrial environment. As can be seen from Table 2, there are some disagreements on appropriate values found in scientific literature, international legislations and official reports. The difference within one organism group and one exposure route is up to a factor of 60 but generally equal or below a factor of 10. The preliminary proposal presented below is made under the assumption that the values in Table 2 cover the likely range of toxicity cut-off values.

It should further be noted that in Canadian, US, and UN (OSPAR) legislation there is only a factor of 10 between the NOEC value used for PBT assessment and the L(E)C_{50} value used for hazard classification. This corresponds to a more conservative toxicity cut-off value for PBT classification and hence potential higher protection of the environment. For this reason, a more conservative range for T cut-off values has also been calculated by dividing the acute toxicity cut-off value for the highest hazard category by 10 (Table 3). **In the end, the choice of applying a certain factor to cut-off values for hazard classification will have a high impact on the resulting cut-off value for PBT assessment and should therefore receive further attention.**

Table 3 Potential ranges of non-aquatic chronic cut-off values (NOEC) for PBT classification based on available non-aquatic cut-off values for hazard classification (most toxic category) (See Table 2). Cut-off values for PBT assessment are calculated by application of a factor of 100 (or the more conservative value of 10) to acute toxicity cut-off criteria or a factor of 10 to chronic toxicity cut-off criteria for hazard classification. NOEC = No-Observed Effect Concentration; EC50 = 50% Effect Concentration; LC50 = 50% Lethal Concentration; LD50 = 50% Lethal Concentration; NOAEL = No-Observed Adverse Effect Limit.

Organism	T cut-off value range (NOEC) calculated from acute toxicity cut-off criteria for hazard classification ($EC_{50}/LC_{50}/LD_{50}/ER_{50}$) Factor of 100 applied	T cut-off value range (NOEC) calculated from acute toxicity cut-off criteria for hazard classification ($EC_{50}/LC_{50}/LD_{50}/ER_{50}$) Factor of 10 applied	T cut-off value range (NOEC) calculated from chronic toxicity cut-off criteria for hazard classification (NOEC/NOAEL) Factor of 10 applied
Soil dwelling invertebrates incl. earthworms (soil exposure)	≤ 0.01 to ≤ 0.6 mg/Kg (dw)	≤ 0.1 to ≤ 6 mg/Kg (dw)	≤ 0.1 mg/Kg
Foliar invertebrates and pollinators (incl. bees)	≤ 0.01 to 0.02 µg/bee	≤ 0.1 to 0.2 µg/bee	
Microorganisms	≤ 0.01 mg/Kg (dw)	≤ 0.1 mg/Kg (dw)	
Terrestrial plants (soil exposure)	≤ 0.01 to ≤ 0.1 mg/Kg dw	≤ 0.1 to ≤ 1 mg/Kg dw	
Terrestrial plants (foliar exposure)	≤ 0.01 to ≤ 0.1 Kg/ha	≤ 0.1 to ≤ 1 Kg/ha	
Terrestrial vertebrates (birds and mammals) (oral exposure)	≤ 0.05 to ≤ 0.5 mg/Kg bw (≤ 0.4 to ≤ 4 ppm in food for chicken; ≤ 1 to ≤ 10 ppm in food for rat[15])	≤ 0.5 to ≤ 5 mg/Kg bw (≤ 4 to ≤ 40 ppm in food for chicken; ≤ 10 to ≤ 100 ppm in food for rat[16])	≤ 0.05 mg/Kg bw (≤ 0.4 ppm in food for chicken; ≤ 1 ppm in food for rat)
Terrestrial vertebrates (birds and mammals) (diet exposure)	≤ 5 ppm in food	≤ 50 ppm in food	
Terrestrial vertebrates (air exposure)	≤ 0.05 mg/L air	≤ 0.5 mg/L air	

[15] Conversion factors from 'mg/Kg bw' to 'ppm in diet' can be found in NZEPA (2012). As examples this factor is 8 for chicken, 10 for young rat, 20 for old rat and 7 for mouse. This means that, in order to obtain a NOEC value rather than a NOEL value, the quoted values have to be divided by this factor.

[16] Conversion factors from 'mg/Kg bw' to 'ppm in diet' can be found in NZEPA (2012). As examples this factor is 8 for chicken, 10 for young rat, 20 for old rat and 7 for mouse. This means that, in order to obtain a NOEC value rather than a NOEL value, the quoted values have to be divided by this factor.

With regards to the NOEC cut-off criteria for terrestrial vertebrates (oral exposure, chicken: ≤ 0.4 to ≤ 4 ppm in food; and diet exposure: ≤ 5 ppm in food) it should be noted that it is specified in the ECHA Guidance Document R.11 that a NOEC < 30 mg/kg food in a long-term bird study (sub-chronic or chronic toxicity or toxic for reproduction) should be *"considered as strong indicator for fulfilling the T criterion"* for PBT/vPvB assessment under REACH (ECHA 2012). Although it should be kept in mind that this is a screening criterion and not a criterion for definitive assignment[17], this value is still 6-75 times higher than the NOEC values identified through the approach applied in this paper. This indicates that **the proposed ranges for T criteria for vertebrates in Table 3 seems less protective than what is currently suggested in the ECHA Guidance Document. This should be taken into consideration in any further potential development of such criteria, and could call for the use of the more protective end of the range.**

Another issue for further discussions is the **expression of non-aquatic toxicity values as bulk soil concentrations versus pore water concentrations**. Terrestrial invertebrates and microorganisms as well as most plants are exposed to chemicals in the soil via pore water. PBT/vPvB substances often have hydrophobic properties and toxicity may therefore be masked by a very strong sorption to the soil. This would mean that EC values expressed in bulk soil concentration may be high although it is only a very small fraction that is actually bioavailable (assuming mainly/solely hydrophobic uptake) and causing adverse effects. Also this is an issue that needs further examination.

[17] The difference between screening criteria and criteria for definitive assignment is a factor of 10 for aquatic toxicity in the PBT assessment guidance under REACH in R.11.1.3.3 (ECHA 2012) (Table 11-4).

7 Proposals for future initiatives

As mentioned by Renaud et al. (2004) the majority of available information on effects of chemicals on non-aquatic species has previously been focused on pesticides and veterinary medicines. Based on a more extensive dataset becoming available through REACH registration dossiers further work could be considered in relation to examination of data with the purpose of:

- Investigation of sensitivity of terrestrial versus aquatic organism
  Examine **if criteria based on aquatic organisms provide sufficient protection of the environment as a whole, including the non-aquatic organisms. This also includes further investigations of the applicability of the EqP method**.

- Investigation of appropriate hazard classification criteria for the terrestrial environment
  Taking into account the **availability of new data on non-aquatic organisms through the registration dossiers submitted so far under REACH. This can be done e.g. by the use of Chemicals Sensitivity Distributions**[18].

- Investigation of whether, for non-aquatic toxicity criteria for PBT assessment, cut-off values should be expressed **as bulk soil concentrations and/or as pore water concentrations**. Also **prioritisation of exposure routes** could be investigated.

For this purpose the work of the CSTEE, OECD, UNSCEGHS and a number of other documents related to non-aquatic environmental hazards may provide a starting point. This includes for example the following documents: 'Overview of historical and current work in OECD on Terrestrial Hazard Assessment' (UN 2003); 'Issues to be addressed to develop the classification and labelling for terrestrial environmental hazards' (UN 2004c); 'Classification criteria for the terrestrial environment' (UN 2006); 'Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE) Opinion on the Available Scientific Approaches to Assess the Potential Effects and Risks of Chemicals on Terrestrial Ecosystems' (EC 2001); and ECETOC TR 084 'Scientific Principles for Soil Hazard Assessment of Substances' (ECETOC 2002). Finally, on this basis further work could be carried out to develop new proposals for non-aquatic toxicity cut-off values for PBT assessment. This may also require **investigations of appropriate factors to be applied for extrapolation from short-term to long-term (acute-to-chronic) cut-off values.**

[18] To establish non-aquatic criteria for hazard classification a procedure could be considered, which reflects the specific level of toxicity for substances with PBT properties rather than the entire body of non-aquatic data contained in REACH registration dossiers.

8 Conclusions

Limited information is available regarding the sensitivity of aquatic versus terrestrial organisms to chemical substances. Hazard criteria based on aquatic organisms is by some Authors in the scientific literature considered to provide a conservative classification. On the other hand for some substances higher toxicity has been observed for the terrestrial compartment. At the same time the aquatic and non-aquatic ecosystems differ with regards to mechanisms of toxicity and metabolism as well as exposure and uptake routes. Especially for substances with low water solubility toxic effects may not be detectable through acute aquatic toxicity tests whereas prolonged aquatic exposure and/or tests with terrestrial organisms exposed through soil or food may result in toxic effects. However, current toxicity criteria in European legislation on PBT assessment (e.g. REACH) are based on toxicity in aquatic species. The same applies to legislation for classification and labelling (i.e. CLP Regulation) where hazard classification is based only on aquatic toxicity. Some Authors see this as an incomplete environmental protection.

In order to fill this gap some Authors have proposed new criteria for non-aquatic hazard classification, including a complete classification scheme for the terrestrial environment developed by a Spanish-led working group under the UNSCEGHS. The main reason why this proposal never led to actual implementation of terrestrial criteria in the GHS, and why the discussion has not progressed since, seems to be due to lack of priority and consensus among UN Member States.

In this document a preliminary approach on how the available criteria for non-aquatic hazard classification could further be applied to toxicity assessment under the PBT/vPvB framework is presented. Based on the observation that aquatic NOEC/EC10 cut-off values for PBT/vPvB assessment e.g. under REACH is 10-fold lower than the NOEC/EC10 cut-off values used under CLP/GHS and 100-fold lower than the LC50 cut-off values used under CLP/GHS, **non-aquatic NOEC/EC10 cut-off values for PBT/vPvB assessment are derived by dividing the available non-aquatic NOEC/EC10 or LC50 cut-off values for hazard classification by a factor of 10 or 100, respectively.**

It is however acknowledged that this is a very simplified approach that may require further development and evaluation. In case of a revitalisation of the work on criteria for non-aquatic hazard classification, **the increased amount of data on terrestrial toxicity through REACH registration dossiers could be used to further develop, verify and adjust criteria proposals**. Specifically, the **sensitivity to chemicals of non-aquatic versus aquatic organisms could be more deeply examined** to better understand if criteria based on aquatic organisms provide sufficient protection of the environment as a whole, including the non-aquatic organisms. This would also include **further evaluation of the applicability of acute-to-chronic extrapolation and the EqP method**. Moreover, REACH data could be used **to investigate the appropriateness of criteria for non-aquatic hazard classification e.g. under GHS/CLP**. Finally, the possibility that cut-off values for non-aquatic toxicity under PBT/vPvB assessment could be **expressed as bulk soil concentrations and/or as pore water concentrations** needs to be analysed.

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10 Annexes

10.1 Annex I - Glossary

Note: this list explains expressions used in this report, some of them are common in scientific literature, but not necessarily defined in legal texts.

Non-aquatic organisms

This term refers to all organisms that occur and live in terrestrial environments and are air-breathing, including top predators and humans. In the context of this report, the expression 'non-aquatic organisms' is preferred to other terms used in the literature, such as 'terrestrial organisms', 'soil organisms' and 'air-breathing organisms', as it more clearly encompasses humans as part of the food web.

Persistent Bioaccumulative Toxic/very Persistent very Bioaccumulative (PBT/vPvB)

PBT substances are substances that are persistent, bioaccumulative and toxic while vPvB substances are characterised by high persistence and high tendency to bioaccumulate but not necessarily proven toxicity (ECHA 2012). Because of their very low degradability, PBT/vPvB substances tend to remain in the environment for a long time and may accumulate and magnify in organisms' tissues including top predators and humans. The accumulation of PBT/vPvB substances is difficult to reverse as the reduction or cessation of release into the environment will not necessarily result in a decrease in the concentration level (ECHA 2012). Moreover, the effects of such an accumulation over extended periods are not possible to predict though laboratory testing (ECHA 2012).

Bioconcentration

Bioconcentration is the increase in concentration of a substance in or on an organism (or specified tissue) relative to the concentration of the substance in the test medium (OECD 2012). For aquatic organisms, bioconcentration is the net accumulation of a chemical in an organism that results from direct contact with water only, such as through gill membranes or other external surfaces (US EPA 2003b; 2007). Bioconcentration excludes chemical accumulation from other exposure routes and sources such as ingestion of organisms and sediment (US EPA 2008). Although not routinely defined for terrestrial (air-breathing) organisms, an analogous measure of bioconcentration would be the net accumulation of a chemical that results from direct contact with air or soil only, such as through respiration or dermal uptake (US EPA 2008). In the OECD Test Guideline 317 (OECD 2010b), bioconcentration in terrestrial Oligochaetes is defined as the increase in concentration of a substance in or on an organism relative to the concentration of the substance in the surrounding medium. The increase in concentration is due to the uptake of the substance exclusively from the surrounding medium via both the body surface and ingested soil.

Bioaccumulation

Bioaccumulation is the net accumulation of a chemical in an organism from all possible exposure routes (respiration, diet, dermal) and sources (water, soil/sediment, air and diet) (Spacie et al. 1995; US EPA 2003b; 2007). Bioaccumulation results from both bioconcentration and biomagnification processes (OECD, 2010).

Biomagnification

Biomagnification can be defined as the increase in concentration of a substance in or on an organisms (or specified tissue) relative to the concentration of the substance in the food (OECD 2012). The increase in concentration may occur along a series of predator-prey associations in a food web, primarily through the mechanism of dietary accumulation (trophic transfer) (US EPA 2008).

Steady State

The steady state is defined as the equilibrium between the uptake and elimination processes that occur simultaneously during the exposure phase (OECD 2010b). The steady state is reached by a system when rates of chemical movement between phases and reactions within phases are constant so that concentrations of the chemical in the phases of the system are unchanged over time (US EPA 2008). A system at steady state is not necessarily at equilibrium; steady-state conditions often exist when some or all of the phases of the system have different activities or fugacities for the chemical (US EPA 2008).

Octanol-water partitioning coefficient (K_{ow}) [unitless]

Ratio of the chemical concentrations in 1-octanol (C_o) and water (C_w) in an octanol–water system that has reached a chemical equilibrium: $K_{ow} = C_o/C_w$ (OECD 1995; 2004; 2006; Gobas et al. 2009).

10.2 Annex II - Tables compiling information on hazard criteria from international and European regulatory frameworks and the peer-reviewed literature

Table II.a. Summary of official criteria used for PBT assessment in different pieces of international and European legislation.

Regulation	Criteria for toxicity (T) assessment	Country/Area/ Organisation
Regulation (EC) No 1907/2006 (REACH) (Annex XIII) (EC 2006)	A substance fulfils the toxicity criterion (T) for PBT assessment in any of the following situations:	EU
Ecotoxicity	(a) the long-term no-observed effect concentration (NOEC) or EC10 for marine or freshwater organisms is less than 0.01 mg/L;	
Mammalian toxicity	(b) the substance meets the criteria for classification as carcinogenic (category 1A or 1B), germ cell mutagenic (category 1A or 1B), or toxic for reproduction (category 1A, 1B, or 2) according to Regulation EC No 1272/2008;	
	(c) there is other evidence of chronic toxicity, as identified by the substance meeting the criteria for classification: specific target organ toxicity after repeated exposure (STOT RE category 1 or 2) according to Regulation EC No 1272/2008.	
Guidance on information requirements and chemical safety assessment. Chapter R.11: PBT Assessment (ECHA 2012)	**NB!** It should be mentioned that according to ECHA Guidance on PBT assessment, short-term toxicity can be used as an indicator for whether the T criterion is fulfilled as follows:	
	Short-term aquatic toxicity (algae, daphnia, fish): EC50 or LC50 < 0.01 mg/L → T, criterion considered to be definitely fulfilled	
	Short-term aquatic toxicity (algae, daphnia, fish): EC50 or LC50 < 0.1 mg/L → T (Screening assignment)	
	Avian toxicity (subchronic or chronic toxicity or toxic for reproduction) → NOEC < 30 mg/Kg food → T (Screening assignment)	

Table II.a. *(cont.)*

Regulation	Criteria for toxicity (T) assessment	Country/Area/ Organisation
Plant Protection Products (PPPs) Regulation (EC) No 1107/2009 (EC 2009) Ecotoxicity Mammalian toxicity	An active substance, safener or synergist fulfils the toxicity criterion for PBT assessment where: - the long-term no-observed effect concentration for marine or freshwater organisms is less than 0.01 mg/L, - the substance is classified as carcinogenic (category 1A or 1B), mutagenic (category 1A or 1B), or toxic for reproduction (category 1A, 1B or 2) pursuant to Regulation (EC) No 1272/2008, or - there is other evidence of chronic toxicity, as identified by the classifications STOT RE 1 or STOT RE 2 pursuant to Regulation (EC) No 1272/2008.	EU
Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures (CLP), amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (EC 2008a)	"Subject to developments at UN level, the classification and labelling of persistent, bioaccumulative and toxic (PBT) and very persistent and very bioaccumulative (vPvB) substances should be included in this Regulation at a later stage." (L 353/7. (75))	EU
Standard Operating Procedures for the Biocides Technical Meeting of Directive 98/8/EC (Fifth Version June 2013) (EC 2013c)	"Active substances used in biocidal products may be identified as Persistent, Bioaccumulative and Toxic (PBT) or Very Persistent and Very Bioaccumulative (vPvB) according to the criteria of Annex XIII of the REACH Regulation (EC) 1907/2006".	EU
Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products (EC 2012a).	"Active substances used in biocidal products may be identified as Persistent, Bioaccumulative and Toxic (PBT) or Very Persistent and Very Bioaccumulative (vPvB) according to the criteria of Annex XIII of the REACH Regulation (EC) 1907/2006".	EU

Table II.a. *(cont.)*

Regulation	Criteria for toxicity (T) assessment	Country/Area/ Organisation
Guidance on Information Requirements Regulation (EU) No 528/2012 Concerning the Making Available on the Market and Use of Biocidal Products (BPR) Version 1.0, July 2013 ECHA 2013)	According to the Biocidal Products Regulation active substances shall not be approved if they meet the criteria for being persistent, bio-accumulative and toxic (PBT) or very persistent and very bio-accumulative (vPvB) in accordance with Annex XIII of REACH Regulation (EC) No 1907/2006. Depending on the conditions of use, a testing strategy is proposed for the environmental compartments which are directly or indirectly exposed.	EU
New chemicals program (NCP) -Toxic Substances Control Act (TSCA) – Chemical categories (US EPA 2010)	The New Chemicals Program (NCP) specifies quantitative criteria for P & B. No quantitative value is specified for toxicity. Instead it is specified to "Develop toxicity data where necessary, based upon various factors, including concerns for P, B, other physical/chemical factors, and toxicity". Toxicity testing is included as a Tier 3 of the General Testing Strategy to establish PBT status of a substance:	US
Human health toxicity	Combined repeated dose oral toxicity with the reproductive /developmental toxicity screening test (OECD No. 422) in rats. Other health testing will be considered where appropriate.	
Chronic environmental Toxicity	Fish (rainbow trout) and daphnids should be tested according to Harmonized Test Guideline 850.1400 (same as OECD 210) and Harmonized Test Guideline 850.1300 (same as OECD 202), respectively.	
Additional	Additional testing to evaluate other biota (e.g., avian, sediment dwelling organisms) or other effects (e.g., endocrine disrupting potential) will be considered where appropriate.	
Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances, Part I (US EPA 1999)	Toxicity testing also to be done in lower tiers where needed on a case-specific basis.	

Table II.a. *(cont.)*

Regulation	Criteria for toxicity (T) assessment	Country/Area/ Organisation
PBT Profiler Version 2.000 (Updated September 2012) (PBT Profiler 2012) Developed by the Environ mental Science Centre under contract to the Office of Chemical Safety and Pollution Prevention, US EPA	The PBT Profiler is a screening-level tool to be used when no data are available. The tool highlights substances that may be chronically toxic to fish by use of the following criteria: Low concern: fish chronic toxicity value: > 10 mg/L. Moderate concern: fish chronic toxicity value: 0.1 - 10 mg/L. High concern: fish chronic toxicity value: < 0.1 mg/L Criteria developed in EPA's New Chemical Program [Clements, R. G.; Nabholz, J. V.; Johnson, D. E.; and Zeeman, M. G. The Use of Quantitative Structure-Activity Relationships (QSARs) as Screening Tools in Environmental Assessment. Environmental Toxicology and Risk Assessment, 2nd Vol., edited by J.W. Gorsuch, F. J. Dwyer, C. G. Ingersoll, and T. W. LaPoint, pp 555-570. ASTM STP 1216. Philadelphia: American Society for Testing and Materials, 1993]	US
Toxic Substances Management Policy (Environment Canada 1995) Canadian Environmental Protection Act (CEPA) (Government of Canada 1999) - As explained by Environment Canada (2012)	Criteria for the identification of Track 1 substances ("persistent, bioaccumulative, toxic and primarily the result of human activity and which is to be targeted for virtual elimination from the environment") is presented and it is stated that "for the purposes of this policy, a substance is considered toxic if it meets or is equivalent to the definition of "toxic" found in the Canadian Environmental Protection Act (referred to as "CEPA-toxic")" "CEPA 1999 uses the term "inherently toxic" (iT) for the categorization of substances on the Domestic Substances List, but does not define it. The definition and interpretation of inherently toxic to non-human organisms is currently under development. Environment Canada has a proposed working definition which will take into consideration the knowledge acquired from the pilot project and which will be subject to consultation before adoption". DSL Categorization under CEPA 1999 Section 73: Ecological Categorization Criteria and Process Criteria for acute and chronic toxicity to aquatic species (algae, invertebrates, fish) Exposure Duration — Criteria Acute — $L(E)C_{50} \leq 1$ mg/L Chronic — NOEC ≤ 0.1 mg/L	Canada

Table II.a. *(cont.)*

Regulation	Criteria for toxicity (T) assessment	**Country/Area/ Organisation**
Guidance Manual for the Categorization of Organic and Inorganic Substances on Canada's Domestic Substances List: Determining Persistence, Bioaccumulation Potential, and Inherent Toxicity to Non-human Organisms (Environment Canada 2003)	"The determination of iT includes consideration of the solubility of the parent substance in water, the stability of the dissolved form, and the aquatic toxicity of the parent substance and/or its constituent parts as interpreted from bioassay data. A tiered approach of combining solubility and toxicity data will be used to determine if a substance meets the criteria for iT. Such an approach is necessary, because many of the solubility values are qualitative, whereas the toxicity values are quantitative. Where both the solubility and toxicity values are quantitative, a parent substance will be categorized IN if it meets the following conditions: 1. water solubility of parent substance is greater than pivotal acute toxicity value, L(E)C_{50}, and 2. moiety of concern has a pivotal acute toxicity value, L(E)C_{50}, of less than or equal to the criteria threshold of 1 mg/L for acute aquatic toxicity. Where only qualitative solubility data are available, a parent substance will be categorized IN if it meets the following conditions: 1. water solubility of parent substance is greater than or equal to 1 mg/L and 2. moiety of concern has a pivotal acute toxicity value, L(E)C_{50}, of less than or equal to the criteria threshold of 1 mg/L for acute aquatic toxicity." *Environment Canada:* *"The iT value of 1 mg/L is not official or even a regulatory criteria. It was used only for the purpose of Categorization"* (*Environment Canada Personal communication (2012)*	Canada
The Stockholm Convention on Persistant organic pollutants (POPs) (UN 2009)	In Annex D "Information Requirements and screening criteria" the following text concerns toxicity: Adverse effects: (i) Evidence of adverse effects to human health or to the environment that justifies consideration of the chemical within the scope of this Convention; or (ii) Toxicity or ecotoxicity data that indicate the potential for damage to human health or to the environment.	UN

Table II.a. *(cont.)*

Regulation	Criteria for toxicity (T) assessment	Country/Area/ Organisation
The Convention for the Protection of the marine Environment of the North-East Atlantic (the 'OSPAR Convention') 05/21/1-E, Annex 7 (OSPAR 2005)	The intrinsic properties of individual substances, specifically whether they are persistent (P), toxic (T) or liable to bioaccumulate (B), determine whether they fall within the definition of hazardous substances given in the OSPAR Strategy with regard to Hazardous Substances. These three intrinsic properties (PTB criteria) have been used, along with cut-off values for each, as the criteria for selecting substances in the Initial Selection Procedure of the Dynamic Selection and Prioritisation Mechanism. The criteria are also used for selection of new substances (c.f. Agreement for Further Work in relation to the DYNAMEC Mechanism, reference number: 2005-8), as well as for deselecting substances. The toxicity cut-off are as follows: Taq: acute L(E)C_{50} ≤ 1 mg/L, long-term NOEC ≤ 0.1 mg/L or Tmammalian: CMR or chronic toxicity	North-East Atlantic
Ecotoxicity Mammalian toxicity		

A report entitled 'Background Information Summary of Listing Processes for Persistent, Bioaccumulative, and Toxic Chemicals: Final Report' (Parametrix 2008) has been prepared for the Oregon Association of Clean Water Agencies. An Appendix to this document gives a general overview on different PBT Ranking Schemes including information on toxicity criteria, corresponding to some of the information found in Table II.a.

Table II.b. Update of the "Annex to the progress report on terrestrial environmental hazards: Detailed review of existing classification and labelling systems" (UN 2008b)

	Current Legal requirements	Legal requirements in 2008 (basis of UN/SCEGHS/15/INF. 29)	Chemical groups covered	Comments and remarks	Significant changes to env. classifi-cation (2008 to 2012)
Andean Community	Decision 767/2011: Modifications of 436/1998. Consolidated version. Manual Técnico: Resolucion 630/2002	Decision 436/1998: Norma Andina para el Registro y Control de Plaguicidas Químicos de Uso Agrícola. Manual Técnico: Resolucion 630/2002	Pesticides	Latest toxicological classification of pesticides recommended by the WHO should be applied Technical guidance has not been updated	N
Argentina	Resolution 302/2012: Modification of 350/1999	Resolutions No. 350/1999 (and 816/2006)	Phytosanitary products	Resolution 302/2012 involves changes to human health toxicity classification criteria but no changes to ecotoxicity criteria have been identified	(N)
Basel Convention	Current version from: January 2011 (Last amended in 1998). Interim guidelines on the hazardous characteristic H12-Ecotoxic (2003)	Last amended in 1998 Interim guidelines on the hazardous characteristic H12-Ecotoxic (2003)	Hazardous Wastes	Technical guidance has not been updated. Follows GHS criteria from 2001 revision..	N
Canada	Pest Control Products Act Last amended on June 28, 2006. Current to June 27, 2012.	Pest Control Products Act Last amended on June 28, 2006	Pesticides	(No changes identified)	(N)

Table II.b. *(cont.)*

	Current Legal requirements	Legal requirements in 2008 (basis of UN/SCEGHS/15/INF. 29)	Chemical groups covered	Comments and remarks	Significant changes to env. classifi-cation (2008 to 2012)
EU	Regulation (EC) 1272/2008 on classification, labelling and packaging (CLP) (amended 2011)	Dangerous Substances Directive 67/548/EEC	Chemicals and mixtures (including substances used in biocides, and plant protection products)	Although the Directive 67/548/EEC included classification with respect to *both* the aquatic (R50-R53) *and* the terrestrial environment (R54-R57), only criteria for the aquatic environment were developed for the CLP Regulation.	Y
New Zealand	Hazardous Substances (Classification) Regulations, 2001 Hazardous substances and New Organisms Act (HSNO), 1996 Thresholds and Classifications Under the Hazardous Substances and New Organisms Act 1996, 2012 (originally published in 2008)	Hazardous Substances (Classification) Regulations, 2001 Hazardous substances and New Organisms Act (HSNO), 1996 User Guide to HSNO Threshold and Classifications	Hazardous substances	No newer versions or amendments identified Guidance was updated in 2008 after the time of issuing of the UN/SCEGHS/15/INF.29	N Y
Mexico	Norma Oficial Mexicana NOM-052-SEMARNAT-2005 (2006)	Norma Oficial Mexicana NOM-052-SEMARNAT-2005 (2006)	Dangerous waste	No newer versions or amendments identified	N
USA	Toxic Substances Control Act (as Amended Through P.L. 107–377, December 31, 2002).	Toxic Substances Control Act (as Amended Through P.L. 107–377, December 31, 2002).	Pesticides and other chemicals	No newer versions or amendments identified	N

Table II.c. Summary of official criteria used for *hazard assessment* and labelling as well as testing requirements for non-aquatic organisms in different pieces of international and European legislation.

Regulation	Criteria for hazard assessment and testing requirements for non-aquatic organisms	Country /Area/Body
Globally Harmonised System (GHS) (4^{th} Edition) (UN 2011)	Acute Cat. I: Acute aquatic $L(E)C_{50} \leq 1$ mg/L (may be subdivided to include a lower band ≤ 0.01 mg/L for some regulatory systems) Acute Cat. II: Acute aquatic $L(E)C_{50}$ >1 but ≤ 10 mg/L Acute Cat. III: Acute aquatic $L(E)C_{50}$ >10 but < 100 mg/L (may be extended beyond 100 mg/L for some regulatory systems) **For non-rapidly degradable substances[19] for which adequate chronic data is available** Chronic Cat. I: Chronic aquatic NOEC/$EC_x \leq 0.1$ mg/L Chronic Cat. II: Chronic aquatic NOEC/$EC_x \leq 1$ mg/L **For rapidly degradable substances for which adequate chronic data is available** Chronic Cat. I: Chronic aquatic NOEC/$EC_x \leq 0.01$ mg/L Chronic Cat. II: Chronic aquatic NOEC/$EC_x \leq 0.1$ mg/L Chronic Cat. III: Chronic aquatic NOEC/$EC_x \leq 1$ mg/L **Substances for which adequate chronic data is not available** Chronic Cat. I: Acute aquatic $L(E)C_{50} \leq 1$ mg/L and lack of rapid degradability and/or BCF ≥ 500 (or log $K_{ow} \geq 4$)[20] Chronic Cat. II: Acute aquatic $L(E)C_{50} > 1$ but ≤ 10 mg/l and lack of rapid degradability and/or BCF ≥ 500 (or log $K_{ow} \geq 4$) Chronic Cat. III: Acute aquatic $L(E)C_{50} > 10$ but ≤100 mg/l and lack of rapid degradability and/or BCF ≥ 500 (or log $K_{ow} \geq 4$) **"Safety net" classification** Chronic Cat. IV**:** Poorly soluble substances, No acute aquatic toxicity up to level of water solubility, lack of rapid degradability and log $K_{ow} \geq 4$ (unless scientific evidence shows that classification is unnecessary e.g. experimental BCF < 500, chronic toxicity > 1 mg/L, evidence of rapid degradation in the environment).	UN

[19] I.e. lack of ready biodegradability or no evidence of rapid degradation. If no data is available the substance should be considered not rapidly degradable.

[20] The potential to bioaccumulate can only be estimated from log K_{ow} when this it considered being an appropriate descriptor of the bioaccumulation potential of the substance. Measured BCF (and K_{ow}) values have priority over estimated values.

Table II.c. *(cont.)*

Regulation	Criteria for hazard assessment and testing requirements for non-aquatic organisms	Country /Area/Body
Basel convention	In the 'Interim guidelines on the hazardous characteristic H12-Ecotoxic' (UNEP 2003) it is stated that "criteria for ecotoxic hazard should be based on the properties of the substances in the waste such as toxicity, degradability and ability to bioaccumulate in line with the internationally agreed classification (OECD 2001)". Hence the criteria for ecotoxicity are in line with the GHS criteria. In the document it is further recommended "not to include classification of chemicals based on terrestrial toxicity". However, in the **evaluation of mixtures of hazardous substances "i**t is proposed that the test strategy includes batteries of tests representing both the terrestrial and aquatic environments" (UNEP 2003).	UN
Regulation (EC) No 1907/2006 (REACH) (EC 2008b)	Data on environmental hazards "shall include relevant available data on aquatic toxicity, both acute and chronic for fish, crustaceans, algae and other aquatic plants. In addition, toxicity data on soil micro- and macro-organisms and other environmentally relevant organisms, such as birds, bees and plants, shall be included when available." Information requirements are based on tonnage and information on terrestrial toxicity is required for chemicals produced or imported in quantities above 100 tonnes / annum. However "These studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely. In the absence of toxicity data for soil organisms, the equilibrium partitioning method may be applied to assess the hazard to soil organisms. The choice of the appropriate tests depends on the outcome of the chemical safety assessment. In particular for substances that have a high potential to adsorb to soil or that are very persistent, the registrant shall consider long-term toxicity testing instead of short-term." For chemicals with a tonnage above 1000 tonnes / annum, regarding terrestrial toxicity, "Long-term toxicity testing shall be proposed by the registrant if the results of the chemical safety assessment according to Annex I indicates the need to investigate further the effects of the substance and/or degradation products on terrestrial organisms. The choice of the appropriate test(s) depends on the outcome of the chemical safety assessment. These studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely". **The legislation does not contain specific criteria for environmental hazards except for those stated in Annex XIII specifically for PBT assessment (see above) and reference to CLP (see below). The same criteria are used to decide if a Chemical Risk Assessment has to be performed. The basic tool used in the decision making is the PEC/PNEC ratio.**	EU

Table II.c. *(cont.)*

Regulation	Criteria for hazard assessment and testing requirements for non-aquatic organisms	Country /Area/Body
Plant Protection Products (PPPs) Regulation EC No 1107/2009 (EC 2009) and related data requirements in Regulation (EU) No 283/2013 and 284/2013 (EC 2013a; EC 2013b)	New data requirements are published as Regulation (EU) No 283/2013 for active substances (EC 2013a) and 284/2013 for formulated plant protection products (EC 2013b). Tests of active substances are required on aquatic organisms (fish, Daphnia magna, and an additional aquatic invertebrate), birds (and other terrestrial vertebrates including terrestrial wildlife e.g. mammals, reptiles, and amphibians), arthropods (bees and honeybees), earthworms, soil non-target micro-organisms, other non-target organisms (flora and fauna, such as plants, mites, collembola etc.) and biological methods for sewage treatment. In addition to the data requirements, two European Commission Communications were published that list the recommended guidance documents and test guidelines to be followed for each requirement. Furthermore (according to EC 2009): "An active substance, safener or synergist shall be approved only if it is established following an appropriate risk assessment on the basis of Community or internationally agreed test guidelines, that the use under the proposed conditions of use of plant protection products containing this active substance, safener or synergist: — will result in a negligible exposure of honeybees, or — has no unacceptable acute or chronic effects on colony survival and development, taking into account effects on honeybee larvae and honeybee behaviour."	EU
Directive 98/8/EC (Biocidal Products) (EC 1998)	ANNEX IIIA: Additional data for active substances include: - Acute toxicity test on one other, non-aquatic, non-target organism - If the results of the ecotoxicological studies and the intended use(s) of the active substance indicate a danger for the environment then the tests described in Sections XII and XIII shall be required These tests include tests on both aquatic and terrestrial organisms as well as birds.	EU

Table II.c. *(cont.)*

Regulation	Criteria for hazard assessment and testing requirements for non-aquatic organisms	Country /Area/Body
Replaced by Regulation (EU) No 528/2012 (Biocidal Products) (EC 2012a)	An annex to the regulation contains the information requirements for the preparation of a dossier for an active substance. Some information requirements are included in a Core Data Set (CDS), covering basic data requirements that should be provided by the applicant for all active substances. In addition there are requirements for an Additional Data Set (ADS) where the data to be provided for a specific active substance is evaluated based of the CDS taking into account e.g. physical and chemical properties of the substance, existing data, use and exposure patterns. As part of the ADS data requirements tests on a number of non-aquatic species is included: 9.1.8. Effects on any other specific, non-target organisms (flora and fauna) believed to be at risk 9.1.9. Studies on sediment- dwelling organisms 9.1.10. Effects on aquatic macrophytes 9.2. Terrestrial toxicity, initial tests 9.2.1. Effects on soil micro-organisms 9.2.2. Effects on earthworms or other soil- dwelling non-target invertebrates 9.2.3. Acute toxicity to plants 9.3. Terrestrial tests, long term 9.3.1. Reproduction study with earthworms or other soil-dwelling non-target invertebrates 9.4. Effects on birds 9.4.1. Acute oral toxicity 9.4.2. Short-term toxicity — eight-day dietary study in at least one species (other than chickens, ducks and geese) 9.4.3. Effects on reproduction (For endpoint 9.4.3 the study does not need to be conducted if: — the dietary toxicity study shows that the LC50is above 2 000 mg/kg) Some specific indications for inclusion of ADS data are in some cases included in Column 1. However this is not the case for any of the non-aquatic tests.	EU

Table II.c. *(cont.)*

Regulation	Criteria for hazard assessment and testing requirements for non-aquatic organisms	Country /Area/Body
	No specific criteria are given. The regulation gives a description of 'substance of concern': — a substance classified as dangerous or that meets the criteria to be classified as dangerous according to Directive 67/548/EEC, and that is present in the biocidal product at a concentration leading the product to be regarded as dangerous within the meaning of Articles 5, 6 and 7 of Directive 1999/45/EC, or — a substance classified as hazardous or that meets the criteria for classification as hazardous according to Regulation (EC) No 1272/2008, and that is present in the biocidal product at a concentration leading the product to be regarded as hazardous within the meaning of that Regulation, — a substance which meets the criteria for being a persistent organic pollutant (POP) under Regulation (EC) No 850/2004, or which meets the criteria for being persistent, bio-accumulative and toxic (PBT) or very persistent and very bio-accumulative (vPvB) in accordance with Annex XIII to Regulation (EC) No 1907/2006; (i.e. REACH) **The basic tool to be used in the environmental risk characterisation is the PEC/PNEC ratio.**	EU
Regulation (EC) No 1272/2008 (CLP) on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (EC 2008a) As amended by Commission Regulation (EU) No 286/2011 of 10 March 2011	**Acute Category 1:** 96 hr LC_{50} (for fish): ≤ 1 mg/L and/or 48 hr EC_{50} (for crustacean): ≤ 1 mg/L and/or 72 or 96 hr ErC_{50} (for algae or other aquatic plants) ≤ 1 mg/L. **Chronic Category 1:** Chronic NOEC or EC_x (for fish): ≤ 0.1 mg/L and/or Chronic NOEC or EC_x (for crustacea): ≤ 0.1 mg/L and/or Chronic NOEC or EC_x (for algae or other aquatic plants): ≤ 0.1 mg/L. For ***non-rapidly degradable substances*** for which there are adequate chronic toxicity data available. Chronic NOEC or EC_x (for fish): ≤ 0.01 mg/L and/or Chronic NOEC or EC_x (for crustacea): ≤ 0.01 mg/ L and/or Chronic NOEC or EC_x (for algae or other aquatic plants): ≤ 0.01 mg/L. For ***rapidly degradable substances*** for which there are adequate chronic toxicity data available. 96 hr LC_{50} (for fish): ≤ 1 mg/L and/or 48 hr EC_{50} (for crustacean): ≤ 1 mg/L and/or 72 or 96 hr ErC_{50} (for algae or other aquatic plants): ≤ 1 mg/L and/or For substances for which ***adequate chronic toxicity data are not available*** and where the substance is ***not rapidly degradable and/or the experimentally determined BCF ≥ 500*** (or, if absent, the log K_{ow} ≥ 4).	

Table II.c. *(cont.)*

Regulation	Criteria for hazard assessment and testing requirements for non-aquatic organisms	Country /Area/Body
	<u>Chronic Category 2:</u> Chronic NOEC or EC_x (for fish): > 0.1 to ≤ 1 mg/L and/or Chronic NOEC or EC_x (for crustacea): > 0.1 to ≤ 1 mg/L and/or Chronic NOEC or EC_x (for algae or other aquatic plants): > 0.1 to ≤ 1 mg/L For ***non-rapidly degradable substances*** for which there are adequate chronic toxicity data available. Chronic NOEC or EC_x (for fish): > 0.01 to ≤ 0.1 mg/L and/or Chronic NOEC or EC_x (for crustacea): > 0.01 to ≤ 0.1 mg/L and/or Chronic NOEC or EC_x (for algae or other aquatic plants): > 0.01 to ≤ 0.1 mg/L For ***rapidly degradable substances*** for which there are adequate chronic toxicity data available. 96 hr LC_{50} (for fish): >1 to ≤ 10 mg/L and/or 48 hr EC_{50} (for crustacean): >1 to ≤ 10 mg/L and/or 72 or 96 hr ErC_{50} (for algae or other aquatic plants) >1 to ≤ 10 mg/L For substances for which ***adequate chronic toxicity data are not available*** and where the substance is ***not rapidly degradable and/or the experimentally determined BCF ≥ 500*** (or, if absent, the log K_{ow} ≥ 4).	
	<u>Chronic Category 3:</u> Chronic NOEC or EC_x (for fish): > 0.1 to ≤ 1 mg/L and/or Chronic NOEC or EC_x (for crustacea): > 0.1 to ≤ 1 mg/L and/or Chronic NOEC or EC_x (for algae or other aquatic plants): > 0.1 to ≤ 1 mg/L For ***rapidly degradable substances*** for which there are adequate chronic toxicity data available. 96 hr LC_{50} (for fish): > 10 to ≤ 100 mg/L and/or 48 hr EC_{50} (for crustacean): > 10 to ≤ 100 mg/L and/or 72 or 96 hr ErC_{50} (for algae or other aquatic plants) > 10 to ≤ 100 mg/L For substances for which ***adequate chronic toxicity data are not available*** and where the substance is ***not rapidly degradable and/or the experimentally determined BCF ≥ 500*** (or, if absent, the log K_{ow} ≥ 4). **'Safety net' classification, <u>Chronic Category 4:</u>** Cases when data do not allow classification under the above criteria but there are nevertheless some grounds for concern. This includes, for example, poorly soluble substances for which no acute toxicity is recorded at levels up to the water solubility (note 4), and which are not rapidly degradable in accordance with section 4.1.2.9.5 and have an experimentally determined BCF ≥ 500 (or, if absent, a log Kow ≥ 4), indicating a potential to bioaccumulate, which will be classified in this category unless other scientific evidence exists showing classification to be unnecessary. Such evidence includes chronic toxicity NOECs > water solubility or > 1 mg/L, or other evidence of rapid degradation in the environment than the ones provided by any of the methods listed in Section 4.1.2.9.5.	

Table II.c. *(cont.)*

<table>
<tr><th>Regulation</th><th>Criteria for hazard assessment and testing requirements for non-aquatic organisms</th><th>Country /Area/Body</th></tr>
<tr><td>Pesticide Programs. 40 CFR Parts 150 -189</td><td>Ecotoxicity Categories for Terrestrial and Aquatic Organisms
(as used by the US EPA Office of Pesticide Programs (US EPA 2012)).

<table><tr><th>Toxicity Category</th><th>Avian: Acute OralConc. (mg/Kg)</th><th>Avian: Dietary Conc. (ppm)</th><th>Aquatic Organisms: Acute Conc. (ppm)</th><th>Wild Mammals: Acute Oral Conc. (mg/ Kg)</th><th>Non-Target Insects: Acute Conc. (µg/bee)</th></tr><tr><td>very highly toxic</td><td>< 10</td><td>< 50</td><td>< 0.1</td><td>< 10</td><td></td></tr><tr><td>highly toxic</td><td>10-50</td><td>50-500</td><td>0.1-1</td><td>10-50</td><td>< 2</td></tr><tr><td>moderately toxic</td><td>51-500</td><td>501-1000</td><td>> 1-10</td><td>51-500</td><td>2-11</td></tr><tr><td>slightly toxic</td><td>501-2000</td><td>1001-5000</td><td>> 10-100</td><td>501-2000</td><td></td></tr><tr><td>practically nontoxic</td><td>> 2000</td><td>> 5000</td><td>> 100</td><td>> 2000</td><td>> 11</td></tr></table></td><td>US</td></tr>
<tr><td>Toxic Substances Control Act of 1976, As Amended Through P.L. 107–377, December 31, 2002

Section 8(e)</td><td>No specific criteria are mentioned in the legal text. Regarding reporting of information it is specified in Sec. 8(e) that "The Administrator may require (…) maintenance of records and reporting" of e.g. "All existing data concerning the environmental and health effects of such substance or mixture"

In 2003 the US EPA published information on "TSCA Section 8(e); Notification of Substantial Risk; Policy Clarification and Reporting Guidance". From Part V ("What Constitutes Substantial Risks") it is further understood that environmental effects are related to:

- Pronounced bioaccumulation (incl. BCF > 5000 in fish or Kow > 25,000) in combination with potential for widespread exposure and adverse effect.

- Non-trivial adverse effects of a chemical known to bioaccumulate or to be widespread in environmental media

- Ecologically significant changes in species' interrelationships (due to e.g. changes in behaviour, growth, survival, etc.of a population that in turn affect other species' behavior, growth, or survival

- Chemicals with transformation or degradation product that cause an unacceptable risk as defined above.(US EPA 2003a)</td><td>US</td></tr>
</table>

Table II.c. *(cont.)*

Regulation	Criteria for hazard assessment and testing requirements for non-aquatic organisms	Country /Area/Body
Pest Control Products Act, 2002. Last amended on June 28, 2006. Current to June 27, 2012	"Before pesticides are marketed, Health Canada evaluates scientific data submitted by pesticide companies in support of a registration to ensure that the pesticides are of acceptable health and environmental risk, and of value to Canada, in accordance with the Pest Control Products Act (PCPA)." (Government of Canada 2010) GHS is expected to be implemented into the the Canadian regulation on Pest Control Products. However, "discussions are occurring but the consultations are not complete" (Canadian Center for Occupational Health and Safety 2012).	Canada
Decision 767/2011. Modifications of 436/1998: Norma Andina para el Registro y Control de Plaguicidas Químicos de Uso Agrícola Consolidated version). (La Comisión de la Cominidad Andina 2011)	"Artículo 46.- Para los ensayos y estudios ecotoxicológicos, se tomarán en consideración las Directrices de FAO sobre "Criterios Ecológicos para el Registro de Plaguicidas" y cuando se estime conveniente se podrán utilizar como referencia otros métodos reconocidos por organismos internacionales." **Translation:** Article 46. - For ecotoxicological tests and studies the FAO Guidelines on "Ecological Criteria for Registration of Pesticides" will be taken into consideration and when deemed appropriate reference may be used other methods recognized by international organizations. The FAO document "Guidelines on good labelling practice for pesticides" was last updated in 1995 but is currently under revision by the FAO/WHO Joint Meeting on Pesticide Management (JMPM) (FAO 2012). The current version of the guidelines refers to WHO Recommended Classification of Pesticides (FAO 1995). The WHO guidelines were last updated in 2009 and aligned with the GHS criteria. However the guidelines only cover human health hazards (WHO 2009). Also, on the 5rd JMPM meeting in 2011 it was concluded, regarding the updated version of the FAO guidelines, "that the GHS be given preference as the basis for hazard communication on the pesticide label" (FAO 2011). Hence pesticide labelling will be based hazard criteria stipulated by the GHS and the GHS criteria are expected to have an increasingly important role also in the context of the Andean Community pesticide regulation.	Andean Community
The Hazardous Substances and New Organisms (HSNO) Act, 1996 (ERMA NZ 2001)	The Hazardous Substances and New Organisms (HSNO) Act contains four ecotoxicity subclasses, for which a substance can be classified : Subclass 9.1: aquatic ecotoxicity. Subclass 9.2: ecotoxicity to the soil environment Subclass 9.3: ecotoxicity to terrestrial vertebrates Subclass 9.4: ecotoxicity to terrestrial invertebrates	New Zealand
Hazardous Substances (Classification) Regulations, 2001 (Government of New Zealand 2001)	Schedule 6 to the Hazardous Substances (Classification) Regulations 2001 contains classification criteria for subclasses 9.1-9.4, divided into four hazard levels: A) very ecotoxic, B) ecotoxic, C) harmful and D) slightly harmful. In hazard classification the basic consideration is acute ecotoxicity (Subclasses 9.1-9.4). For subclass 9.1. and 9.2. also degradability of the substance is taken into consideration. In the case of Subclass 9.1. (potential) bioaccumulation is an additional criteria for classification. An overview of the classification criteria for single component substances, based on the Thresholds and Classifications guidance document as well as the Hazardous Substances (Classification) Regulations (2001), is seen below.	

Table II.c. *(cont.)*

Regulation	Criteria for hazard assessment and testing requirements for non-aquatic organisms					Country /Area/Body
Guidance: Thresholds and Classifications Under the Hazardous Substances and New Organisms Act 1996, 2012 (originally published in 2008) (NZEPA 2012)		Aquatic (9.1)	Soil (9.2)	Terrestrial vertebrate (9.3)	Terrestrial invertebrate (9.3)	
	Very Ecotoxic (A)	Acute L(E)C50 ≤ 1mg/L.	Acute L(E)C50 ≤ 1 mg/Kg	LD50 ≤ 50 mg/kg bw (oral or dermal) or LC50 ≤ 500 ppm (diet).	LD50 < 2 µg/ animal	
	Ecotoxic (B)	1 < Acute L(E)C50 ≤ 10 mg/L. Chronic NOEC ≤ 1 mg/L or unknown. Not rapidly degradable and/or bioaccumulative.	1 < Acute L(E)C50 ≤ 10 mg/Kg	50 < LD50 ≤ 500 mg/Kg bw (oral or dermal) or 500 < LC50 ≤ 1000 ppm (diet).	2 < LD50 ≤ 11 µg/ animal	
	Harmful (C)	10 < Acute L(E)C50 ≤ 100 mg/L. Chronic NOEC ≤ 1 mg/L or unknown. Not rapidly degradable and/or bioaccumulative.	10 < Acute L(E)C50 ≤ 100 mg/Kg and Soil DT50 > 30 days	500 < LD50 ≤ 2000 mg/Kg bw (oral or dermal) or 1000 < LC50 ≤ 5000 ppm (diet) or a chronic MATC 100 ppm (diet), but which does not meet the criteria for classifications 9.3A or 9.3B.	11 < LD50 ≤ 25 µg/ animal	
	Slightly harmful (D)	1 < Acute L(E)C50 ≤ 100 mg/L. Chronic NOEC > 1 mg/L. Not rapidly degradable and/or bioaccumulative. Or 10 < Acute L(E)C50 ≤ 100 mg/L. Chronic NOEC ≤ 1 mg/L or unknown. Rapidly degradable, not bioaccumulative. Or Acute L(E)C50 > 100 mg/L. Chronic NOEC ≤ 1 mg/L or unknown. Not rapidly degradable and/or bioaccumulative.	10 < Acute L(E)C50 ≤ 100 mg/Kg Soil DT50 < 30 days			
	Not classified as hazardous	Acute L(E)C50 > 100 mg/L. Chronic NOEC > 1 mg/L. Rapidly degradable, not bioaccumulative. If intended for biocidal use case 9.1D applies.	Acute L(E)C50 > 100 mg/Kg	LD50 > 2,000 mg/Kg bw (oral or dermal); or LD50 > 5,000 ppm (diet); or a chronic MATC > 100 ppm (diet).	LD50 > 25 µg/ animal	

Table II.c. *(cont.)*

Regulation	Criteria for hazard assessment and testing requirements for non-aquatic organisms	Country /Area/Body
Regulations on the Safe Management of Hazardous Chemicals. Decree 591 of the State Council of China. Last revision of March 2011 The Measures on Environmental Administration of New Chemical Substances. MEP Decree No. 7 Last amended in 2010	Contains requirement for labelling of hazardous chemical substances according to GHS hazard criteria Contains requirement for labelling of new chemical substances according to GHS In addition there are "Safety rules for classification, precautionary labelling and precautionary statements of Chemicals". These consist of 26 national standards (GB 20576/2006 to GB 20602/2006) and follows the GHS classification criteria for environmental hazards (based on GHS 1st Edition, 2003). (Based on information from Liang (2012) and CIRS (2012)).	China
Occupational Safety & Health Act, Act No. 4220, Jan. 13, 1990. Last amended in 2009 (by Act no. 9796) Toxic Chemicals Control Act. latest revised version (Act No.895) March 2008	Contains requirements for classification and labelling of chemicals according to GHS hazard criteria. Contains requirements for classification and labelling of toxic chemicals according to GHS hazard criteria. There are additional standards that contain requirements for classification and labelling of chemicals i.e. Public Notice No 2008-26 and MoL Notice No 2012-14 (Based on information from Liang (2012) and CIRS (2012)).	Korea

Table II.c. *(cont.)*

Regulation	Criteria for hazard assessment and testing requirements for non-aquatic organisms	Country /Area/Body
Industrial Safety and Health Law Law (ISHL) No. 57 of June 8, 1972. Latest Amendments: Law No. 25 of May 31, 2006	Contains requirement for classification and labelling according to GHS criteria for ISHL listed substances(~640 substances);	Japan
Chemical Substances Control Law (CSCL) of 16 April 1974. Last amended on May 20, 2009	Contains requirement for labelling of Class II Specified Chemical Substances. Furthermore through the Pollutant Release and Transfer Register MSDS is required for over 400 substances. Also the Poisonous and Deleterious Substances Control Law (PDSCL) required an MSDS for more than 300 substances. These legislations do not mention GHS. However GHS SDS and labels are recommended. Additional standards include those for: GHS classification (JISZ7252), MSDS (JISZ7250), Labelling (JISZ7251) and SDS+Labellling (JISZ7253) (to replace JISZ7250 and JISZ7251 in 2012). (Based on information from Liang (2012) and CIRS (2012)).	

10.3 Annex III - Relevant international and national bodies

International:

- OSPAR (The Convention for the Protection of the marine Environment of the North-East Atlantic,) http://www.ospar.org/
- UNECE LRTAP (Convention on Long-range Transboundary Air Pollution), http://www.unece.org/env/lrtap
- UNEP POP (The Stockholm Convention on Persistent Organic Pollutants (POPs)), http://chm.pops.int/
- UNEP (The Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal) http://www.basel.int/
- HELCOM (Baltic Marine Environment Protection Commission), http://www.helcom.fi/
- OECD (e.g. OECD Pesticide Assessment and Testing project) http://www.oecd.org/document/10/0,3343,en_2649_34383_31951370_1_1_1_1,00.html

National/regional for which information is included in the UN/SCEGHS/15/INF.29 review report on terrestrial environmental hazards:

- US EPA (United States Environmental Protection Agency), http://www.epa.gov/
- Environment Canada http://www.ec.gc.ca/
- Andean Community http://www.comunidadandina.org/
- Argentina http://www.ambiente.gov.ar/
- New Zealand http://www.epa.govt.nz/
- Mexico http://www.semarnat.gob.mx/
- European Commission http://ec.europa.eu/

10.4 Annex IV - Relevant European legislation

Table III. Relevant European legislation in relation to toxicity criteria for PBT assessment

Regulation (EC) No 1272/2008 (CLP) (Hazard based) (amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006)	http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:1355:en:PDF
Regulation (EC) No 1907/2006 (REACH) (New & Existing chemicals) (Risk based) (repealing Regulation 793/93/EEC)	http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=oj:l:2006:396:0001:0849:en:pdf
Regulation (EU) No 528/2012 (Biocides) (Risk based)	http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:167:0001:0123:EN:PDF SOP (Fifth Version June 2013): http://ihcp.jrc.ec.europa.eu/our_activities/public-health/risk_assessment_of_Biocides/doc/TNsG/SOP_TM_BPD_FIFTH_VERSION_2013.pdf
Regulation 1107/2009 (Plant Protection Products) (Risk based) (repealing Directive 91/414/EEC)	http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:309:0001:0050:EN:PDF
Directive 2000/60/EC (Water Framework Directive) (Risk based) Directive 2008/105/EC on Environmental Quality Standards (EQSD) List of priority substances which present a significant risk to or via the aquatic environment. Amendment, proposal COM(2011) 876 final:	http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2000:327:0001:0072:EN:PDF http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32008L0105&from=EN http://ec.europa.eu/environment/water/water-dangersub/pdf/com_2011_876.pdf

10.5 Annex V - Abbreviations

ADS	Additional Data Set
ATP	Adaptation to Technical Progress
BCF	Bioconcentration Factor
CDS	Core Data Set
CEPA	Canadian Environmental Protection Act
CLP	Classification Labelling Packaging
CSTEE	Scientific Committee on Toxicity, Ecotoxicity and the Environment
DG SANCO	Directorate-General for Health and Consumers
DSD	Dangerous Substances Directive
DSL	Domestic Substances List
EC	European Commission
EC_{10}	Effect Concentration at 10%
EC_{50}	Effect Concentration at 50%
ECB	European Chemical Bureau
ECHA	European Chemicals Agency
EFSA	European Food Safety Agency
EqP	Equilibrium Partitioning
EU	European Union
FAO	Food and Agriculture Organisation
GHS	Globally Harmonised System
HSNO	Hazardous Substances and New Organisms
ISO	International Standardisation Organisation
iT	inherent (eco)toxicity
IUCLID	International Uniform ChemicaL Information Database

JRC-IHCP	Joint Research Centre's Institute for Health and Consumer Protection
K_{ow}	octanol-water partitioning coefficient
LC_{50}	Lethal Concentration at 50%
LD_{50}	Lethal Dose at 50%
NOAEL	No Observed Adverse Effect Level
NOEC =	No Observed Effect Concentration
OECD	Organisation for Economic Cooperation and Development
OSPAR	Convention for Protection of the marine Environment of the North-East Atlantic
PAHs	Polycyclic Aromatic Hydrocarbons
PBT	Persistent Bioaccumulative Toxic
PEIP	Pesticide Effects on Insect Pollinators
POP	Persistent Organic Pollutant
PPP	Plant Protection Product
REACH	Registration Evaluation Authorisation and Restriction of Chemicals
T	(Eco)toxicity
TG	Test Guideline
TM	Test Method
TMR	Test Methods Regulation
TSCA	Toxic Substances Control Act
UN	United Nations
UNSCEGHS	United Nations Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals
US	United States
US EPA	United Stated Environmental Protection Agency
vPvB	very Persistent very Bioaccumulative
WHO	World Health Organisation

European Commission
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