Organisation de Coopération et de Développement Économiques
Organisation for Economic Co-operation and Development

09-Mar-2010

English - Or. English

ENVIRONMENT DIRECTORATE
JOINT MEETING OF THE CHEMICALS COMMITTEE AND THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY

ENV/JM/MONO(2010)7
Unclassified

Series on Testing and Assessment
No. 119

CLASSIFICATION AND LABELLING OF CHEMICALS ACCORDING TO THE UN GLOBALLY HARMONIZED SYSTEM: OUTCOME OF THE ANALYSIS OF CLASSIFICATION OF SELECTED CHEMICALS LISTED IN ANNEX III OF THE ROTTERDAM CONVENTION

JT03279707

English - Or. English

OECD Environment, Health and Safety Publications

Series on Testing and Assessment

No. 119

CLASSIFICATION AND LABELLING ACCORDING TO THE UN GLOBALLY HARMONIZED SYSTEM: OUTCOME OF THE ANALYSIS OF CLASSIFICATION OF SELECTED CHEMICALS LISTED IN ANNEX III OF THE ROTTERDAM CONVENTION

IOMC

INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS

A cooperative agreement among FAO, ILO, UNEP, UNIDO, UNITAR, WHO and OECD

Environment Directorate

ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT
Paris 2010

Also published in the Series on Testing and Assessment:

No. 1, *Guidance Document for the Development of OECD Guidelines for Testing of Chemicals (1993; reformatted 1995, revised 2006 and 2009)*

No. 2, *Detailed Review Paper on Biodegradability Testing (1995)*

No. 3, *Guidance Document for Aquatic Effects Assessment (1995)*

No. 4, *Report of the OECD Workshop on Environmental Hazard/Risk Assessment (1995)*

No. 5, *Report of the SETAC/OECD Workshop on Avian Toxicity Testing (1996)*

No. 6, *Report of the Final Ring-test of the Daphnia magna Reproduction Test (1997)*

No. 7, *Guidance Document on Direct Phototransformation of Chemicals in Water (1997)*

No. 8, *Report of the OECD Workshop on Sharing Information about New Industrial Chemicals Assessment (1997)*

No. 9, *Guidance Document for the Conduct of Studies of Occupational Exposure to Pesticides during Agricultural Application (1997)*

No. 10, *Report of the OECD Workshop on Statistical Analysis of Aquatic Toxicity Data (1998)*

No. 11, *Detailed Review Paper on Aquatic Testing Methods for Pesticides and industrial Chemicals (1998)*

No. 12, *Detailed Review Document on Classification Systems for Germ Cell Mutagenicity in OECD Member Countries (1998)*

No. 13, *Detailed Review Document on Classification Systems for Sensitising Substances in OECD Member Countries 1998)*

No. 14, *Detailed Review Document on Classification Systems for Eye Irritation/Corrosion in OECD Member Countries (1998)*

No. 15, *Detailed Review Document on Classification Systems for Reproductive Toxicity in OECD Member Countries (1998)*

No. 16, *Detailed Review Document on Classification Systems for Skin Irritation/Corrosion in OECD Member Countries (1998)*

No. 17, *Environmental Exposure Assessment Strategies for Existing Industrial Chemicals in OECD Member Countries (1999)*

No. 18, *Report of the OECD Workshop on Improving the Use of Monitoring Data in the Exposure Assessment of Industrial Chemicals (2000)*

No. 19, *Guidance Document on the Recognition, Assessment and Use of Clinical Signs as Humane Endpoints for Experimental Animals used in Safety Evaluation (1999)*

No. 20, *Revised Draft Guidance Document for Neurotoxicity Testing (2004)*

No. 21, *Detailed Review Paper: Appraisal of Test Methods for Sex Hormone Disrupting Chemicals (2000)*

No. 22, *Guidance Document for the Performance of Out-door Monolith Lysimeter Studies (2000)*

No. 23, *Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures (2000)*

No. 24, *Guidance Document on Acute Oral Toxicity Testing (2001)*

No. 25, *Detailed Review Document on Hazard Classification Systems for Specifics Target Organ Systemic Toxicity Repeated Exposure in OECD Member Countries (2001)*

No. 26, *Revised Analysis of Responses Received from Member Countries to the Questionnaire on Regulatory Acute Toxicity Data Needs (2001)*

No 27, *Guidance Document on the Use of the Harmonised System for the Classification of Chemicals which are Hazardous for the Aquatic Environment (2001)*

No 28, *Guidance Document for the Conduct of Skin Absorption Studies (2004)*

No 29, *Guidance Document on Transformation/Dissolution of Metals and Metal Compounds in Aqueous Media (2001)*

No 30, *Detailed Review Document on Hazard Classification Systems for Mixtures (2001)*

No 31, *Detailed Review Paper on Non-Genotoxic Carcinogens Detection: The Performance of In-Vitro Cell Transformation Assays (2007)*

No. 32, *Guidance Notes for Analysis and Evaluation of Repeat-Dose Toxicity Studies (2000)*

No. 33, *Harmonised Integrated Classification System for Human Health and Environmental Hazards of Chemical Substances and Mixtures (2001)*

No. 34, *Guidance Document on the Development, Validation and Regulatory Acceptance of New and Updated Internationally Acceptable Test Methods in Hazard Assessment (2005)*

No. 35, *Guidance notes for analysis and evaluation of chronic toxicity and carcinogenicity studies (2002)*

No. 36, *Report of the OECD/UNEP Workshop on the use of Multimedia Models for estimating overall Environmental Persistence and long range Transport in the context of PBTS/POPS Assessment (2002)*

No. 37, *Detailed Review Document on Classification Systems for Substances Which Pose an Aspiration Hazard (2002)*

No. 38, *Detailed Background Review of the Uterotrophic Assay Summary of the Available Literature in Support of the Project of the OECD Task Force on Endocrine Disrupters Testing and Assessment (EDTA) to Standardise and Validate the Uterotrophic Assay (2003)*

No. 39, *Guidance Document on Acute Inhalation Toxicity Testing (2009)*

No. 40, *Detailed Review Document on Classification in OECD Member Countries of Substances and Mixtures Which Cause Respiratory Tract Irritation and Corrosion (2003)*

No. 41, *Detailed Review Document on Classification in OECD Member Countries of Substances and Mixtures which in Contact with Water Release Toxic Gases (2003)*

No. 42, *Guidance Document on Reporting Summary Information on Environmental, Occupational and Consumer Exposure (2003)*

No. 43, *Guidance Document on Mammalian Reproductive Toxicity Testing and Assessment (2008)*

No. 44, *Description of Selected Key Generic Terms Used in Chemical Hazard/Risk Assessment (2003)*

No. 45, *Guidance Document on the Use of Multimedia Models for Estimating Overall Environmental Persistence and Long-range Transport (2004)*

No. 46, *Detailed Review Paper on Amphibian Metamorphosis Assay for the Detection of Thyroid Active Substances (2004)*

No. 47, *Detailed Review Paper on Fish Screening Assays for the Detection of Endocrine Active Substances (2004)*

No. 48, *New Chemical Assessment Comparisons and Implications for Work Sharing (2004)*

No. 49, *Report from the Expert Group on (Quantitative) Structure-Activity Relationships [(Q)SARs] on the Principles for the Validation of (Q)SARs (2004)*

No. 50, *Report of the OECD/IPCS Workshop on Toxicogenomics (2005)*

No. 51, *Approaches to Exposure Assessment in OECD Member Countries: Report from the Policy Dialogue on Exposure Assessment in June 2005 (2006)*

No. 52, *Comparison of emission estimation methods used in Pollutant Release and Transfer Registers (PRTRs) and Emission Scenario Documents (ESDs): Case study of pulp and paper and textile sectors (2006)*

No. 53, *Guidance Document on Simulated Freshwater Lentic Field Tests (Outdoor Microcosms and Mesocosms) (2006)*

No. 54, *Current Approaches in the Statistical Analysis of Ecotoxicity Data: A Guidance to Application (2006)*

No. 55, *Detailed Review Paper on Aquatic Arthropods in Life Cycle Toxicity Tests with an Emphasis on Developmental, Reproductive and Endocrine Disruptive Effects (2006)*

No. 56, *Guidance Document on the Breakdown of Organic Matter in Litter Bags (2006)*

No. 57, *Detailed Review Paper on Thyroid Hormone Disruption Assays (2006)*

No. 58, *Report on the Regulatory Uses and Applications in OECD Member Countries of (Quantitative) Structure-Activity Relationship [(Q)SAR] Models in the Assessment of New and Existing Chemicals (2006)*

No. 59, *Report of the Validation of the Updated Test Guideline 407: Repeat Dose 28-Day Oral Toxicity Study in Laboratory Rats (2006)*

No. 60, *Report of the Initial Work Towards the Validation of the 21-Day Fish Screening Assay for the Detection of Endocrine Active Substances (Phase 1A) (2006)*

No. 61, *Report of the Validation of the 21-Day Fish Screening Assay for the Detection of Endocrine Active Substances (Phase 1B) (2006)*

No. 62, *Final OECD Report of the Initial Work Towards the Validation of the Rat Hershberger Assay: Phase-1, Androgenic Response to Testosterone Propionate, and Anti-Androgenic Effects of Flutamide (2006)*

No. 63, *Guidance Document on the Definition of Residue (2006, revised 2009)*

No. 64, *Guidance Document on Overview of Residue Chemistry Studies (2006, revised 2009)*

No. 65, *OECD Report of the Initial Work Towards the Validation of the Rodent Utertrophic Assay - Phase 1 (2006)*

No. 66, *OECD Report of the Validation of the Rodent Uterotrophic Bioassay: Phase 2. Testing of Potent and Weak Oestrogen Agonists by Multiple Laboratories (2006)*

No. 67, *Additional data supporting the Test Guideline on the Uterotrophic Bioassay in rodents (2007)*

No. 68, *Summary Report of the Uterotrophic Bioassay Peer Review Panel, including Agreement of the Working Group of the National Coordinators of the Test Guidelines Programme on the follow up of this report (2006)*

No. 69, *Guidance Document on the Validation of (Quantitative) Structure-Activity Relationship [(Q)SAR] Models (2007)*

No. 70, *Report on the Preparation of GHS Implementation by the OECD Countries (2007)*

No. 71, *Guidance Document on the Uterotrophic Bioassay - Procedure to Test for Antioestrogenicity (2007)*

No. 72, *Guidance Document on Pesticide Residue Analytical Methods (2007)*

No. 73, *Report of the Validation of the Rat Hershberger Assay: Phase 3: Coded Testing of Androgen Agonists, Androgen Antagonists and Negative Reference Chemicals by Multiple Laboratories. Surgical Castrate Model Protocol (2007)*

No. 74, *Detailed Review Paper for Avian Two-generation Toxicity Testing (2007)*

No. 75, *Guidance Document on the Honey Bee (Apis Mellifera L.) Brood test Under Semi-field Conditions (2007)*

No. 76, *Final Report of the Validation of the Amphibian Metamorphosis Assay for the Detection of Thyroid Active Substances: Phase 1 - Optimisation of the Test Protocol (2007)*

No. 77, *Final Report of the Validation of the Amphibian Metamorphosis Assay: Phase 2 - Multi-chemical Interlaboratory Study (2007)*

No. 78, *Final Report of the Validation of the 21-day Fish Screening Assay for the Detection of Endocrine Active Substances. Phase 2: Testing Negative Substances (2007)*

No. 79, *Validation Report of the Full Life-cycle Test with the Harpacticoid Copepods Nitocra Spinipes and Amphiascus Tenuiremis and the Calanoid Copepod Acartia Tonsa - Phase 1 (2007)*

No. 80, *Guidance on Grouping of Chemicals (2007)*

No. 81, *Summary Report of the Validation Peer Review for the Updated Test Guideline 407, and Agreement of the Working Group of National Coordinators of the Test Guidelines Programme on the follow-up of this report (2007)*

No. 82, *Guidance Document on Amphibian Thyroid Histology (2007)*

No. 83, *Summary Report of the Peer Review Panel on the Stably Transfected Transcriptional Activation Assay for Detecting Estrogenic Activity of Chemicals, and Agreement of the Working Group of the National Coordinators of the Test Guidelines Programme on the Follow-up of this Report (2007)*

No. 84, *Report on the Workshop on the Application of the GHS Classification Criteria to HPV Chemicals, 5-6 July Bern Switzerland (2007)*

No. 85, *Report of the Validation Peer Review for the Hershberger Bioassay, and Agreement of the Working Group of the National Coordinators of the Test Guidelines Programme on the Follow-up of this Report (2007)*

No. 86, *Report of the OECD Validation of the Rodent Hershberger Bioassay: Phase 2: Testing of Androgen Agonists, Androgen Antagonists and a 5 α-Reductase Inhibitor in Dose Response Studies by Multiple Laboratories (2008)*

No. 87, *Report of the Ring Test and Statistical Analysis of Performance of the Guidance on Transformation/Dissolution of Metals and Metal Compounds in Aqueous Media (Transformation/ Dissolution Protocol) (2008)*

No.88 *Workshop on Integrated Approaches to Testing and Assessment (2008)*

No.89 *Retrospective Performance Assessment of the Test Guideline 426 on Developmental Neurotoxicity (2008)*

No.90 *Background Review Document on the Rodent Hershberger Bioassay (2008)*

No.91 *Report of the Validation of the Amphibian Metamorphosis Assay (Phase 3) (2008)*

No.92 *Report of the Validation Peer Review for the Amphibian Metamorphosis Assay and Agreement of the Working Group of the National Coordinators of the Test Guidelines Programme on the Follow-Up of this Report (2008)*

No.93 *Report of the Validation of an Enhancement of OECD TG 211: Daphnia Magna Reproduction Test (2008)*

No.94 *Report of the Validation Peer Review for the 21-Day Fish Endocrine Screening Assay and Agreement of the Working Group of the National Coordinators of the Test Guidelines Programme on the Follow-up of this Report (2008)*

No.95 *Detailed Review Paper on Fish Life-Cycle Tests (2008)*

No.96 *Guidance Document on Magnitude of Pesticide Residues in Processed Commodities (2008)*

No.97 *Detailed Review Paper on the use of Metabolising Systems for In Vitro Testing of Endocrine Disruptors (2008)*

No. 98 *Considerations Regarding Applicability of the Guidance on Transformation/Dissolution of Metals Compounds in Aqueous Media (Transformation/Dissolution Protocol) (2008)*

No. 99 *Comparison between OECD Test Guidelines and ISO Standards in the Areas of Ecotoxicology and Health Effects (2008)*

No.100 *Report of the Second Survey on Available Omics Tools (2009)*

No.101 *Report on the Workshop on Structural Alerts for the OECD (Q)SAR Application Toolbox (2009)*

No.102 *Guidance Document for using the OECD (Q)SAR Application Toolbox to Develop Chemical Categories According to the OECD Guidance on Grouping of Chemicals (2009)*

No.103 *Detailed Review Paper on Transgenic Rodent Mutation Assays (2009)*

No.104 *Performance Assessment: Conparsion of 403 and CxT Protocols via Simulation and for Selected Real Data Sets (2009)*

No. 105 *Report on Biostatistical Performance Assessment of the draft TG 436 Acute Toxic Class Testing Method for Acute Inhalation Toxicity (2009)*

No.106 Guidance Document for Histologic Evaluation of Endocrine and Reproductive Test in Rodents (2009)

No.107 *Preservative treated wood to the environment for wood held in storage after treatment and for wooden commodities that are not cover and are not in contact with ground. (2009)*

No.108 *Report of the validation of the Hershberger Bioassay (weanling model) (2009)*

No. 109 *Literature review on the 21-Day Fish Assay and the Fish Short-Term Reproduction Assay (2009)*

No. 110 *Report of the validation peer review for the weanling Hershberger Bioassay and agreement of the working of national coordinators of the test guidelines programme on the follow-up of this report (2009)*

No. 111 *Report of the Expert Consultation to Evaluate an Estrogen Receptor Binding Affinity Model for Hazard Identification (2009)*

No. 112 *The 2007 OECD List of High Production Volume Chemicals (2009)*

No. 113 *Report of The Focus Session On Current And Forthcoming Approaches For Chemical Safety And Animal Welfare (2010)*

No. 114 *Performance Assessment of Different Cytotoxic and Cytostatic Measures for the In Vitro Micronucleus Test (MNVIT): Summary of results in the collaborative trial (2010)*

No. 115 *Guidance Document on the Weanling Hershberger Bioassay in Rats: A Short-term Screening Assay for (Anti) Androgenic Properties (2009)*

No. 118 *Workshop Report on OECD Countries Activities Regarding Testing, Assessment and Management of Endocrine Disrupters Part I and Part II (2010)*

No. 119 *Classification and Labelling of chemicals according to the UN Globally Harmonized System: Outcome of the Analysis of Classification of Selected Chemicals listed in Annex III of the Rotterdam Convention (2010)*

ABOUT THE OECD

The Organisation for Economic Co-operation and Development (OECD) is an intergovernmental organisation in which representatives of 30 industrialised countries in North America, Europe and the Asia and Pacific region, as well as the European Commission, meet to co-ordinate and harmonise policies, discuss issues of mutual concern, and work together to respond to international problems. Most of the OECD's work is carried out by more than 200 specialised committees and working groups composed of member country delegates. Observers from several countries with special status at the OECD, and from interested international organisations, attend many of the OECD's workshops and other meetings. Committees and working groups are served by the OECD Secretariat, located in Paris, France, which is organised into directorates and divisions.

The Environment, Health and Safety Division publishes free-of-charge documents in ten different series: **Testing and Assessment**; **Good Laboratory Practice and Compliance Monitoring**; **Pesticides and Biocides**; **Risk Management**; **Harmonisation of Regulatory Oversight in Biotechnology**; **Safety of Novel Foods and Feeds; Chemical Accidents; Pollutant Release and Transfer Registers; Emission Scenario Documents; and the Safety of Manufactured Nanomaterials.** More information about the Environment, Health and Safety Programme and EHS publications is available on the OECD's World Wide Web site (http://www.oecd.org/ehs/).

This publication was developed in the IOMC context. The contents do not necessarily reflect the views or stated policies of individual IOMC Participating Organizations.

The Inter-Organisation Programme for the Sound Management of Chemicals (IOMC) was established in 1995 following recommendations made by the 1992 UN Conference on Environment and Development to strengthen co-operation and increase international co-ordination in the field of chemical safety. The participating organisations are FAO, ILO, OECD, UNEP, UNIDO, UNITAR and WHO. The World Bank and UNDP are observers. The purpose of the IOMC is to promote co-ordination of the policies and activities pursued by the Participating Organisations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

This publication is available electronically, at no charge.

For this and many other Environment, Health and Safety publications, consult the OECD's World Wide Web site (www.oecd.org/ehs/)

or contact:

OECD Environment Directorate, Environment, Health and Safety Division

2 rue André-Pascal
75775 Paris Cedex 16
France

Fax: (33-1) 44 30 61 80

E-mail: ehscont@oecd.org

FOREWORD

This document presents the results of a pilot exercise to review underlying classification data for a sub-set of chemicals included in Annex III of the Rotterdam Convention. The sub-set of chemicals was classified according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). The review exercise was undertaken by a small group of experts nominated by relevant OECD Task Forces on Hazard Assessment and Harmonisation of Classification and Labelling. Annex 1 is a compilation of available GHS classifications for all chemicals included in Annex III of the Rotterdam Convention. Annex 2 reports the views of experts who participated in the pilot exercise to review underlying data for a sub-set of chemicals. The data supporting the classifications have not been included in Annex 2 due to the size of the file for each chemical.

The Joint Meeting agreed to the declassification of the report on 10 February 2010. This document is published under the responsibility of the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology.

TABLE OF CONTENTS

BACKGROUND

1. At the initiative of Germany in November 2008, an activity was launched to review available GHS classifications for chemicals included in Annex III of the Rotterdam Convention. The aim was initially to share agreed GHS classifications (see Annex 1). Cases where there were consistencies in classification elements are compiled in Annex 1, part 1 of individual chemical tables. However the compilation showed a large number of discrepancies in GHS classifications across countries/regions (see Annex 1, part 2 of individual chemical tables).

2. To further understand possible reasons leading to diverging classification outcomes, the Joint Meeting in June 2009 "supported the activity to collect and review underlying datasets for classifications presenting discrepancies across countries or regions, with the aim of determining the reasons for the different classification outcomes, but stressed that the resulting classifications were not mandatory and should not be presented as such". The results of this activity are reported in Annex 2. The Joint Meeting recommended focusing on a subset of chemicals of interest rather than on all chemicals, for an efficient use of limited resources.

OBJECTIVE OF THE REVIEW

3. The main objective of the review exercise carried out following the compilation of available GHS classifications was to analyse possible reasons leading to diverging classification outcomes of chemicals listed in Annex III of the Rotterdam Convention.

ORGANISATION OF THE WORK

4. In July 2009, the Secretariat invited countries and regions with available GHS classifications for the chemicals included in Annex III of the Rotterdam Convention to provide the underlying datasets which were the basis for the classification, where possible. It appeared that availability of data in an electronic format was a limiting factor for the choice of a subset of chemicals. Only five chemicals had supporting data from the three countries/regions in electronic format. These five chemicals were lindane, methamidophos, methyl parathion, thiomersal and parathion; the first four chemicals were retained to keep the exercise manageable.

5. The review exercise was carried out between September and November 2009. Twenty-three experts from eleven countries or organisations were nominated. Seven experts from France, Japan, New Zealand, Switzerland and the European Commission submitted reviews for four of the chemicals selected. In total, thirteen reviews were completed (see **Table 1** below).

6. One expert from the United States submitted observations, based on a review of the studies referenced in the U.S. Environmental Protection Agency's Re-registration Eligibility Decisions and supporting risk assessments prepared for lindane, methyl parathion and methamidohpos, compared to the classification criteria in the Globally Harmonized System of Classification and Labelling of Chemicals (Rev. 3, © UN, 2009) for health and environmental effects. These observations are reported in the tables in Annex 2.

7. In December 2009, a teleconference was organised with experts to review the results of the analysis and discuss the conclusions of this exercise. Experts had the opportunity to make corrections or add notes to individual tables in Annex 2.

Table 1: overview of the review exercise.

Chemical name	Number of reviews by experts	Number of hazard classes covered
Lindane	3	7
Methamidophos	2	5
Methyl parathion	3	7
Thiomersal	4	11

CONCLUSIONS

8. Overall, the analysis demonstrates that the reasons for diverging classification outcomes are diverse but the difference in datasets used is the main reason identified in the majority of cases. There were in total thirty hazard classes reviewed (seven for lindane, five for methamidophos, seven for methyl parathion, and eleven for thiomersal). For ten of these hazard classes (1/3), the only reason for diverging classifications is the differences in the datasets used. For eight hazard classes, the reason is mainly a difference in the datasets used, but there are other possible reasons as well. For ten hazard classes, the reasons are mixed (different datasets used, interpretation of the data, and application of the classification criteria).

9. From the point of view of experts reviewing the data and from the information available, it would not be too difficult to reconcile differences for at least seven hazard classes: acute oral toxicity for lindane, hazard to the aquatic environment for methamidophos, reproductive toxicity and target organ toxicity for methyl parathion, and sensitization, mutagenicity and carcinogenicity for thiomersal. For other hazard classes, further discussion and a better understanding of information available would be needed.

10. Finally, a number of issues were identified by experts as impediments to take a decision or reconcile differences in classification:

Issues related to the datasets used and data interpretation

- Lack of rationale in the assessment of data available (e.g., why choose rat data rather than rabbit data for acute dermal toxicity? (see Table 1.2 in Annex 2); no information on study quality nor rationale for selecting a study over another); a succinct report documenting the rationale for the classification could improve transparency and communication;

- Issue of clear presentation of the data considered in deriving a classification; lack of details on the studies used to derive a classification;

- Issue of read-across between analogue substances (e.g. EU applied a read-across approach between organic mercury compounds, with a group entry for all organic mercury compounds);

- Issue of expert judgement/weight-of-evidence from classification for skin corrosivity to classification for eye irritation;

- Issue of transparency/communication on the decision taken (or not yet taken, or taken technically but not yet enacted?);

- Use of secondary data/literature which is not always reliable or accurate when the original studies were not available.

Issues not related to the datasets used

- Difference in the application of classification criteria when a range of values is available, e.g., take the lowest value versus take the range and apply statistics (see Table 3.1 in Annex 2);

- Possible issue of terminology in the OECD Test Guidelines regarding the use of "slightly irritating" versus "mildly irritating" (see Table 1.4 in Annex 2);

ANNEX 1

COMPILATION OF GHS CLASSIFICATIONS FOR CHEMICALS INCLUDED IN ANNEX III OF THE ROTTERDAM CONVENTION

BACKGROUND

Annex III of the Rotterdam Convention covers pesticides and industrial chemicals that have been banned or severely restricted for health or environmental reasons by Parties to the Convention. Article 13 of the Convention specifies that chemicals listed in Annex III and chemicals banned or severely restricted in the national territory are, when exported, subject to labeling requirements that ensure adequate availability of information with regard to risks and/or hazards to human health or the environment, taking into account relevant international standards.

SUBMISSIONS

Japan submitted classifications for 49 chemicals; New Zealand submitted classifications for 16 chemicals, and the European Union published in December 2008 a list of GHS classifications for chemicals included in Annex I to Directive (EC) 67/548/EEC [see Regulation (EC) No.1336/2008 of the European Parliament and of the Council of 16 December 2008]. These submissions are deemed sufficiently representative of countries that have implemented the GHS for classification and labeling, based on the survey on the status of implementation completed two years ago (see Monograph No.70 in the OECD Series on Testing and Assessment, Report on preparation of GHS implementation in OECD countries).

This annex is intended to present GHS classification and labelling elements which are identical across submitting countries or regions. For each substance, a table reports classification and labelling elements identical across countries or region.

STATISTICS

Table 1: Statistics on the classifications submitted/available

Number of individual chemicals in Annex III of the Rotterdam Convention		92[1]
Number of chemicals for which classifications were submitted		87[2]
Contributions from:	*EC*	79[2]
	Japan	47
	New Zealand	16

[1] Comprises 45 mercury compounds (organic and inorganic), 1 pesticide formulation composed of 3 active ingredients for which individual classifications were submitted/available, 7 tributyltin compounds, 3 polybrominated biphenyls, 1 polychlorinated biphenyl, 5 forms of asbestos, and 30 individual chemicals.

[2] Comprises 45 mercury compounds available from the EC classification of organic and inorganic mercury compounds.

Number of classifications elements identical across countries/region	118
Number of classification elements differing across countries/region	268

OVERVIEW

Table 2: Overview of substances included in Annex III of the Rotterdam Convention for which classification and labeling were submitted or available from the EC, Japan and New Zealand

Chemical name	**CAS number**	**Classifications received/available**		
		European Commission	**Japan**	**New Zealand**
2,4,5-T and its salts and esters	*93-76-5 (other CAS numbers not specified in the DGD)*	*X*	*X*	
Aldrin	*309-00-2*	*X*	*X*	
Binapacryl	*485-31-4*	*X*	*X*	*X*
Captafol	*2425-06-1*	*X*	*X*	
Chlordane	*57-74-9*	*X*	*X*	
Chlordimeform	*6164-98-3*	*X*	*X*	
Chlorobenzilate	*510-15-6*	*X*	*X*	
DDT	*50-29-3*	*X*	*X*	
Dieldrin	*60-57-1*	*X*	*X*	
Dinitro-ortho-cresol (DNOC) and its salts (such as ammonium salt, potassium salt and sodium salt)	*534-52-1; 2980-64-5; 5787-96-2; 2312-76-7*	*X*	*X*	*X*
Dinoseb* and its salts and esters	*88-85-7*	*X*		
1,2-dibromoethane (EDB)	*106-93-4*	*X*	*X*	*X*
Ethylene dichloride	*107-06-2*	*X*	*X*	*X*
Ethylene oxide	*75-21-8*	*X*	*X*	*X*
Fluoroacetamide	*640-19-7*	*X*	*X*	
HCH (mixed isomers)	*608-73-1*		*X*	
Heptachlor	*76-44-8*	*X*	*X*	
Hexachlorobenzene	*118-74-1*	*X*	*X*	*X*
Lindane	*58-89-9*	*X*	*X*	*X*
Mercury compounds including inorganic mercury compounds, alkyl mercury compounds and alkyloxyalkyl and	For all CAS numbers included, see http://www.pic.int/en/CasNumbers/mercury%20compounds%20CAS%20numbers.pdf	X (7487-94-7) (7439-97-6) (62-38-4) (100-57-2) (55-68-5)	*X* (54-64-8) (21908-53-2) (7487-94-7) (7439-97-6) (1600-27-7)	X (54-64-8) (55-68-5)

Chemical name	CAS number	Classifications received/available		
		European Commission	Japan	New Zealand
aryl mercury compounds			(62-38-4)	
Monocrotophos	6923-22-4	*X*	X	
Parathion	56-38-2	*X*	X	
Pentachlorophenol and its salts and esters	*87-86-5 (other CAS numbers not specified in the Decision Guidance Document)*	*X*	X	*X*
Toxaphene	*8001-35-2*	*X*	X	*X*
Dustable powder formulations containing a combination of : benomyl at or above 7 per cent, carbofuran at above 10 per cent, thiram at or above 15 per cent	*17804-35-2; 1563-66-2; 137-26-8*	*X (17804-35-2) (1563-66-2) (137-26-8)*	*X (17804-35-2) (137-26-8)*	*X (17804-35-2)*
Methamidophos	*10265-92-6*	*X*	*X*	*X*
Phosphamidon	*13171-21-6* (mixture, (E)&(Z) isomers) *23783-98-4* ((Z)-isomer) *297-99-4* ((E)-isomer))	*X*	*X*	
Methyl-parathion	*298-00-0*	*X*	*X*	*X*
Asbestos Crocidolite Actinolite Anthophyllite Amosite Tremolite	 *12001-28-4* *77536-66-4* *77536-67-5* *12172-73-5* *77536-68-6*	*X*	*X*	
Polybrominated biphenyls (PBB) (hexa-) (octa-) (deca-)	 *36355-01-8* *27858-07-7* *13654-09-6*		 *X* *X* *X*	*X*
Polychlorinated biphenyls (PCB)	*1336-36-3 (for other CAS numbers, see* http://www.pic.int/en/CasNumbers/PCB%20CAS%20number.pdf *)*	*X*	*X*	
Polychlorinated terphenyls (PCT)	*61788-33-8*		*X*	
Tetraethyl lead	78-00-2		*X*	X
Tetramethyl lead	75-74-1		*X*	
Tris (2,3-dibromopropyl) phosphate	126-72-7		*X*	
Tributyltin Tributyltin oxide	 56-35-9		 X	

Chemical name	CAS number	Classifications received/available		
		European Commission	Japan	New Zealand
Tributyltin benzoate	4342-36-3			
Tributyltin chloride	1461-22-9		X	
Tributyltin fluoride	1983-10-4		X	
Tributyltin linoleate	24124-25-2			
Tributyltin methacrylate	2155-70-6		X	
Tributyltin naphthenate	85409-17-2		X	

* Only the CAS numbers of parent compounds are listed. For a list of other relevant CAS numbers, reference may be made to the relevant decision guidance document.
(126-72-7)

INDIVIDUAL SUBSTANCE CLASSIFICATION AND LABELLING ELEMENTS

11. For each individual substance table, Part 1 of the table lists the hazard classes for which classifications available were identical across countries/region; Part 2 of the table lists the hazard classes for which there was inconsistency in the classifications available from countries/region, or for which only one country /region submitted a classification and labelling.

12. For the EU classifications, as the GHS was implemented in the EU through Regulation 1272/2008 (CLP), the complete list of classifications made in the classification system set up in Annex I to Directive 67/548/EEC was translated into CLP classifications. Many hazard classes corresponded directly between the two classification systems and there was no need to re-visit the original data upon which the classification was based. However, for physical hazards all classifications were re-evaluated as the new system was very different from the classification system under the Directive 67/548/EEC. For a few hazard classes minimum classifications[3] were used.

2,4,5-T

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 4	Exclamation mark	warning	Harmful if swallowed
Skin corrosion/irritation	Category 2	Exclamation mark	warning	Causes skin irritation
Serious eye damage/irritation	Category 2*	Exclamation mark	warning	Causes serious eye irritation
Specific target organ/systemic toxicity following single exposure	Category 3	Exclamation mark	warning	May cause respiratory irritation
Hazardous to the aquatic environment (acute)	Category 1	Environment	warning	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	warning	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				

[3] Minimum classification: for certain hazard classes, including acute toxicity and STOT repeated exposure, the classification according to the criteria in Directive 67/548/EEC does not correspond directly to the classification in a hazard class and category under this Regulation. In these cases the classification in this Annex shall be considered as a minimum classification. This classification shall be applied if none of the following conditions are fulfilled:
— the manufacturer or importer has access to data or other information as specified in Part 1 of Annex I to Regulation 1272/2008 that lead to classification in a more severe category compared to the minimum classification. Classification in the more severe category must then be applied;
— the minimum classification can be further refined based on the translation table in Annex VII of Regulation 1272/2008when the physical state of the substance used in the acute inhalation toxicity test is known to the manufacturer or importer. The classification as obtained from Annex VII shall then substitute the minimum classification indicated in this Annex if it differs from it.'

- Acute toxicity (dermal) (Japan classified as Category 4, EC did not classify) - Toxic to reproduction (Japan classified as sub-Category 1B, EC did not classify) - Specific target organ/systemic toxicity following repeated exposure (Japan calssified as Category 1, EC did not classify)

* Japan classified as "sub-Category 2A"

Aldrin

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Carcinogenicity	Category 2	Health hazard	Warning*	Suspected of causing cancer
Specific target organ/systemic toxicity following repeated exposure	Category 1	Health hazard	Danger	Causes damage to organs
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning*	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning*	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (oral and dermal) (Japan classified as Category 2, EC classified as Category 3) - Acute toxicity (inhalation) (Japan classified as Category 1, EC did not classify) - Skin corrosion, irritation (Japan classified as Category 3, EC did not classify) - Serious eye dame/eye irritation (Japan classified as sub-Category 2B, EC did not classify) - Germ cell mutagenicity (Japan classified as Category 2, EC did not classify) - Toxic to reproduction (Japan classified as Category 2, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan calssified as Category 1, EC did not classify)				

* the signal word "warning" was only mentioned in the Japanese labeling

Binapacryl

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning*	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning*	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (oral and dermal) (Japan classified as Category 3, EC and New Zealand classified as Category 4) - Toxic to reproduction (EC and New Zealand classified as sub-Category 1B, Japan did not classify)				

* the signal word "warning" was only mentioned in the Japanese labelling

Captafol

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Respiratory/skin sensitizer	Category 1	Health hazard	Warning*	May cause an allergic skin reaction
Carcinogenicity	Category 1B	Health hazard	Danger	May cause cancer
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning*	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning*	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				
- Skin corrosion, irritation (Japan classified as Category 2, EC did not classify) - Serious eye dame/eye irritation (Japan classified as sub-Category 2A, EC did not classify) - Germ cell mutagenicity (Japan classified as sub-Category 1B, EC did not classify) - Specific target organ/systemic toxicity following repeated exposure (Japan calssified as Category 1, EC did not classify) - Acute toxicity (Oral) (WHO classified as Category 5)				

* the signal word "warning" was only mentioned in the Japanese labelling

Chlordane

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 4	Exclamation mark	Warning	Harmful if swallowed
Carcinogenicity	Category 2	Health hazard	Warning	Suspected of causing cancer
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (dermal) (Japan classified as Category 3, EC classified as Category 4) - Skin corrosion, irritation (Japan classified as Category 2, EC did not classify) - Serious eye dame/eye irritation (Japan classified as Category 2, EC did not classify) - Germ cell mutagenicity (Japan classified as Category 2, EC did not classify) - Toxic to reproduction (Japan classified as Category 2, EC did not classify) - Specific target organ/systemic toxicity following single and repeated exposure (Japan calssified as Category 1, EC did not classify)				

Chlordimeform

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (oral and dermal) (Japan classified as Category 3, EC classified as Category 4) - Acute toxicity (inhalation) (Japan classified as Category 4, EC did not classify) - Skin corrosion, irritation (Japan classified as Category 3, EC did not classify) - Serious eye dame/eye irritation (Japan classified as sub-Category 2B, EC did not classify) - Carcinogenicity (EC classified as Category 2, Japan did not classify) - Specific target organ/systemic toxicity following single and repeated exposure (Japan calssified as Category 1, EC did not classify)				

Chlorobenzilate

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 4	Exclamation mark	Warning	Harmful if swallowed
PART 2: OTHER CLASSIFICATIONS				
- Hazardous to the aquatic environment (acute and chronic) (EC classified as Category 1, Japan did not classify)				

DDT

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Carcinogenicity	Category 2	Health hazard	Warning*	Suspected of causing cancer
Specific target organ/ systemic toxicity following repeated exposure	Category 1	Health hazard	Danger	Causes damage to organs
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning*	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning*	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				

- Acute toxicity (oral) (Japan classified as Category 4, WHO and the EC classified as Category 3) - Acute toxicity (dermal) (Japan classified as Category 3, EC did not classify) - Skin corrosion, irritation (Japan classified as Category 2, EC did not classify) - Serious eye dame/eye irritation (Japan classified as sub-Category 2B, EC did not classify) - Germ cell mutagenicity (Japan classified as sub-Category 1B, EC did not classify) - Toxic to reproduction (Japan classified as Category 2, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan calssified as Category 1, EC did not classify)

* the signal word "warning" was only mentioned in the Japanese labelling

Dieldrin

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (dermal)	Category 1	Skull and crossbones	Danger	Fatal in contact with skin
Specific target organ/systemic toxicity following repeated exposure	Category 1	Health hazard	Danger	Causes damage to organs
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning*	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning*	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (oral) (Japan classified as Category 1, EC classified as Category 3) - Acute toxicity (inhalation) (Japan classified as Category 1, EC did not classify) - Carcinogenicity (EC classified as Category 2, Japan did not classify) - Toxic to reproduction (Japan classified as sub-Category 1B, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan calssified as Category 1, EC did not classify)				

* the signal word "warning" was only mentioned in the Japanese labelling

DNOC

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 2	Skull and crossbones	Danger	Fatal if swallowed
Acute toxicity (inhalation)	Category 2	Skull and crossbones	Danger	Fatal if inhaled
Skin corrosion/irritation	Category 2	Exclamation mark	Danger	Causes skin irritation
Serious eye damage/eye irritation	Category 1	Corrosion	Danger	Causes serious eye damage

PART 2: OTHER CLASSIFICATIONS
- Acute toxicity (dermal) (Japan and New Zealand classified as Category 2, EC classified as Category 1) - Respiratory/skin sensitizer (EC and New Zealand classified as category 1, Japan did not classify) - Germ cell mutagenicity (Japan classified as sub-Category 1B, EC and New Zealand classified as Category 2) - Toxic to reproduction (Japan classified as Category 2, EC and New Zealand did not classify) - Specific target organ/systemic toxicity following single and repeated exposure (Japan calssified as Category 1, EC and New Zealand did not classify) - Hazardous to the aquatic environment (acute and chronic) (EC and New Zealand classified as Category 1, Japan did not classify)

Sodium salt of DNOC and Potassium salt of DNOC

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (oral), EC classified as Category 3) - Acute toxicity (dermal), EC classified as Category 3) - Acute toxicity (inhalation) (EC classified as Category 3,) - Specific target organ/systemic toxicity following repeated exposure, EC classified as Category 2) - Hazardous to the aquatic environment (acute and chronic) (EC and New Zealand classified as Category 1, Japan did not classify)				

Ammonium salt of DNOC

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word*	Hazard satement
-	-	-	-	-
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (oral), EC classified as Category 3) - Acute toxicity (dermal), EC classified as Category 1) - Acute toxicity (inhalation) (EC classified as Category 3,) - Specific target organ/systemic toxicity following repeated exposure, EC classified as Category 2) - Hazardous to the aquatic environment (acute and chronic) (EC and New Zealand classified as Category 1, Japan did not classify)				

Dinoseb

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (oral and dermal) (Japan classified as Category 2, EC classified as Category 3) - Skin corrosion, irritation (Japan classified as Category 1, EC did not classify)				

- Serious eye dame/eye irritation (Japan classified as Category 1, EC classified as Category 2) - Toxic to reproduction (EC classified as sub-Category 1B, Japan classified as Category 2) - Specific target organ/systemic toxicity following single and repeated exposure (Japan calssified as Category 1, EC did not classify) - Hazardous to the aquatic environment (acute and chronic) (EC classified as Category 1, Japan did not classify)

No common classification elements identified across countries.

1,2-dibromoethane

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 3	Skull and crossbones	Danger	Toxic if swallowed
Acute toxicity (dermal)	Category 3	Skull and crossbones	Danger	Toxic in contact with skin
Skin corrosion/irritation	Category 2	Exclamation mark	warning	Causes skin irritation
Serious eye damage/eye irritation	Category 2	Exclamation mark	warning	Causes serious eye irritation
Carcinogenicity	Category 1B	Health hazard	Danger	May cause cancer
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (inhalation) (Japan classified as Category 2, EC and New Zealand classified as Category 3) - Germ cell mutagenicity (Japan classified as Category 2, EC and New Zealand did not classify) - Toxic to reproduction (Japan classified as Category 2, EC and New Zealand did not classify) - Specific target organ/systemic toxicity following single exposure (Japan calssified as Category 1, EC classified as Category 3) - Specific target organ/systemic toxicity following repeated exposure (Japan calssified as Category 2, EC and New Zealand did not classify) - Hazardous to the aquatic environment (acute) (Japan classified as Category 3, EC did not classify, New Zealand classified as Category 2) - Hazardous to the aquatic environment (chronic) (Japan did not classify, EC and New Zealand classified as Category 2)				

Ethylene dichloride

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Flammable liquids	Category 2	Flame	-	Highly flammable liquid and vapour
Acute toxicity (oral)	Category 4	Exclamation mark	Danger*	Harmful if swallowed
Skin corrosion/irritation	Category 2**	Exclamation mark	Danger*	Causes skin irritation
Serious eye damage/eye irritation	Category 2	Exclamation mark	Danger*	Causes serious eye irritation

PART 2: OTHER CLASSIFICATIONS
- Acute toxicity (inhalation) (Japan and New Zealand classified as Category 3, EC did not classify) - Acute toxicity (dermal) (Japan and New Zealand classified as Category 5, EC did not classify***) - Skin sensitizer (New Zealand classified as category 1, EC and Japan did not classify) - Germ cell mutagenicity (Japan and New Zealand classified as Category 2, EC did not classify) - Carcinogenicity (Japan and New Zealand classified as Category 2, EC classified as sub-Category 1B) - Specific target organ/systemic toxicity following single exposure (Japan calssified as Category 1, EC classified as Category 3) - Specific target organ/systemic toxicity following repeated exposure (Japan calssified as Category 1, New Zealand classified as Category 2 and the EC did not classify) - Aspiration hazard (Japan classified as Category 1, EC and New Zealand did not classify) - Hazardous to the aquatic environment (acute) (Japan and EC did not classify, New Zealand classified as Category 3)

* Only the EC indicated a signal word
** Japan classified as "category 2B"
*** Acute toxicity category 5 is not implemented within the EU

Ethylene oxide

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Flammable gas	Category 1	Flame	Danger*	Extremely flammable
Acute toxicity (inhalation)	Category 3	Skull and crossbones	Danger*	Toxic if inhaled
Skin corrosion/irritation	Category 2	-	-	Causes skin irritation
Germ cell mutagenicity	Category 1**	Health hazard	Danger*	May cause genetic effects
Carcinogenicity	Category 1B	Health hazard	Danger*	May cause cancer

PART 2: OTHER CLASSIFICATIONS
- Acute toxicity (oral) (Japan and New Zealand classified as Category 3, EC did not classify) - Serious eye damage/eye irritation (EC and New Zealand classified as Category 2, Japan did not classify) - Respiratory/skin sensitizer (New Zealand classified as Categort 1, Japan and the EC did not classify) - Toxic to reproduction (Japan classified as sub-Category 1B, New Zealand classified as Category 1, and the EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1 and the EC classified as Category 3) - Specific target organ/systemic toxicity following repeated exposure (Japan classified as Category 1, New Zealand classified as Category 2 and the EC did not classify) - Hazardous to the aquatic environment (acute) (New Zealand classified as Category3, Japan and EC did not classify). -Gases under pressure (EC also classified as gas under pressure with the Note: When put on the market gases have to be classified as 'Gases under pressure', in one of the groups compressed gas, liquefied gas, refrigerated liquefied gas or dissolved gas. The group depends on the physical state in which the gas is packaged and therefore has to be assigned case by case.)

* Only the EC indicated a signal word

** Japan and the EC classified as "category 1B"

Fluoroacetamide

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 2	Skull and crossbones	Danger	Fatal if swallowed
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (dermal) (Japan classified as Category 2, EC classified as Category 3) - Acute toxicity (inhalation) (Japan classified as Category 1, EC did not classify) - Toxic to reproduction (Japan classified as Category 2, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan calssified as Category 2, EC did not classify)				

HCH

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-
PART 2: OTHER CLASSIFICATIONS				
Only Japan classified (with the exception of acute oral toxicity where WHO also classified) - Acute toxicity (oral) (Category 3) - Acute toxicity (dermal) (Category 3) - Acute toxicity (inhalation) (Category 3) - Carcinogenicity (Category 2) - Toxic to reproduction (Category 2) - Specific target organ/systemic toxicity following single and repeated exposure (Category 1) - Hazardous to the aquatic environment (acute and chronic) (Category 1).				

Heptachlor

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 3	Skull and crossbones	Danger	Toxic if swallowed
Carcinogenicity	Category 2	Health hazard	Warning*	Suspected of causing cancer
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning*	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning*	Very toxic to aquatic life with long lasting effects

PART 2: OTHER CLASSIFICATIONS
- Acute toxicity (dermal) (Japan classified as category 2, EC classified as Category 3) - Toxic to reproduction (Japan classified as sub-Category 1B, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1, EC did not classify) - Specific target organ/systemic toxicity following repeated exposure (Japan classified as Category 1, EC classified as Category 2)

* the signal word "warning" was only mentioned in the Japanese labelling

Hexachlorobenzene

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Specific target organ/ systemic toxicity following repeated exposure	Category 1	Health hazard	Danger	Causes damage to organs
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning*	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning*	Very toxic to aquatic life with long lasting effects

PART 2: OTHER CLASSIFICATIONS
- Acute toxicity (oral) (New Zealand classified as Category 4, WHO classified as Category 5) - Carcinogenicity (Japan classified as sub-Category 1B, EC classified as sub-Category 1B, New Zealand classified as Category 2) - Toxic to reproduction (Japan classified as sub-Category 1A, New Zealand classified as Category 1, EC did not classify)

* the signal word "warning" was only mentioned in the Japanese labelling

Lindane

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning*	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning*	Very toxic to aquatic life with long lasting effects

PART 2: OTHER CLASSIFICATIONS
- Acute toxicity (oral) (Japan, the EC and WHO classified as Category 3, New Zealand classified as Category 2) - Acute toxicity (dermal) (Japan classified as Category 2, EC classified as Category 4, New Zealand classified as Category 3) - Acute toxicity (inhalation) (Japan and EC classified as Category 4, New Zealand classified as Category 1) - Serious eye damage/eye irritation (Japan classified as sub-Category 2B, EC and New Zealand did not classify) - Carcinogenicity (Japan and New Zealand classified as category 2, EC did not classify) - Toxic to reproduction (New Zealand classified as Category 2+effects on lactation, EC classified effects on lactation and and Japan did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1, EC and New Zealand did not classify) - Specific target organ/systemic toxicity following repeated exposure (Japan and New Zealand classified as Category 1, EC classified as Category 2)

Mercury compounds

Phenylmercuric nitrate (CAS. 55 68-5)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning	Very toxic to aquatic life

Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning	Very toxic to aquatic life with long lasting effects

PART 2: OTHER CLASSIFICATIONS
- Acute toxicity (oral) (New Zealand classified as Category 2, EC classified as Category 3) - Acute toxicity (dermal) (New Zealand classified as Category 2, EC did not classify) - Skin corrosion/irritation (New Zealand classified as sub-Category 1C, EC classified as sub-Category 1B) - Serious eye damage/irritation (New Zealand classified as Category 1, EC did not classify) - Respiratory and skin sensitizer (New Zealand classified as Category 1, EC did not classify) - Toxic to reproduction (New Zealand classified as Category 1, EC did not classify) - Specific target organ/systemic toxicity following repeated exposure (New Zealand classified as Category 1, EC did not classify)

Thiomersal (CAS. 54-64-8)
Comment: In EU this substance is included in the group entry 'organic compounds of mercury with the exception of those specified elsewhere in this Annex' (Index No: 080-004-00-7 in Annex VI to Regulation 1272/2008).

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-

PART 2: OTHER CLASSIFICATIONS
- Acute toxicity (oral) (Japan classified as Category 3, New Zealand and EC classified as Category 2) - Acute toxicity (dermal) (EC classified as Category 1, Japan and New Zealand did not classify) - Acute toxicity (inhalation) (EC classified as Category 2, Japan and New Zealand did not classify) - Skin corrosion/irritation (New Zealand classified as Category 1C) - Serious eye damage/eye irritation (Japan classified as sub-Category 2B, New Zealand classified as Category 1, EC did not classify) - Skin sensitizer (EC did not classify, Japan and New Zealand classified as Category 1) - Germ cell mutagenicity (EC did not classify, Japan and New Zealand classified as Category 2) - Carcinogenicity (Japan and New Zealand classified as category 2, EC did not classify) - Toxic to reproduction (EC did not classify, Japan calssified as sub-Category 1B, New Zealand classificed as Category 1+effects on lactation) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 2, New Zealand and EC did not classify) - Specific target organ/ systemic toxicity following repeated exposure (Japan and New Zealand classified as Category 1, EC classified as Category 2) - Hazardous to the aquatic environment (chronic) (Japan did not classify, New Zealand classified as Category 2, EC classified as Category 1) - Hazardous to the aquatic environment (acute) (Japan and New Zealand did not classify, EC classified as Category 1)

* Only the Japanese labelling had these classification elements

Phenylmercury acetate (CAS. 62-38-4)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Specific target organ/ systemeic toxicity following repeated exposure	Category 1	Health hazard	Danger	Causes damage to organs
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (oral) (Japan classified as Category 2, EC classified as Category 3) - Skin corrosion/irritation (Japan classified as Category 2, EC classified as sub-Category 1B) - Serious eye damage/eye irritation (Japan classified as Category 2, EC did not classify) - Respiratory/skin sensitizer (Japan classified as Category 1, EC did not classify) - Germ cell mutagenicity (Japan classified as Category 2, EC did not classify) - Carcinogenicity (Japan classified as category 2, EC did not classify) - Toxic to reproduction (Japan classified as Category 2, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 2, EC did not classify) - Hazardous to the aquatic environment (acute and chronic) (Japan did not classify and EC claasified as Category 1)				

Mercury monoxide (CAS. 21908-53-2)

Comment: In EU this substance is included in the group entry 'inorganic compounds of mercury with the exception of mercuric sulphide and those specified elsewhere in this Annex' (Index No: 080-002-00-6 in Annex VI to Regulation 1272/2008).

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Specific target organ/systemic toxicity following repeated exposure	Category 2	Exclamation mark*	Health hazard*	May cause damage to organs*
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (oral) (EC classified as Category 2, Japan did not classify) - Acute toxicity (dermal) (EC classified as Category 1, Japan did not classify) - Acute toxicity (inhalation) (EC classified as Category 2, Japan did not classify) - Skin corrosion/irritation (Japan classified as Category 2, EC did not classify) - Serious eye damage/irritation (Japan classified as Category 2, EC did not classify) - Respiratory/skin sensitizer (Japan classified as Category 1, EC did not classify) - Toxic to reproduction (Japan classified as sub-Category 1B, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Category 1) - Hazardous to the aquatic environment (acute and chronic) (EC classified as Category 1, Japan did not classify)				

* only the EC reported these symbol, signal word and hazard statement.

Mercury dichloride (CAS. 7487-94-7)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 2	Skull and crossbones	Danger	Fatal if swallowed
Specific target organ/ systemeic toxicity following repeated exposure	Category 1	Health hazard*	-	Causes damage to organs*
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (dermal) (Japan classified as Category 1, EC did not classify) - Skin corrosion/irritation (Japan classified as Category 2, EC classified as sub-Category 1B) - Serious eye damage/eye irritation (Japan classified as sub-Category 2A, EC did not classify) - Respiratory/skin sensitizer (Japan classified as Category 1, EC did not classify) - Germ cell mutagenicity (Japan classified as Category 2, EC did not classify) - Toxic to reproduction (Japan classified as sub-Category 1B, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1, EC did not classify) - Hazardous to the aquatic environment (acute and chronic) (Japan did not classify and EC claasified as Category 1)				

Mercury (CAS. 7439-97-6)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (inhalation) (Japan did not classify, EC classified as Category 3) - Respiratory/skin sensitizer (Japan classified as Category 1, EC did not classify) - Germ cell mutagenicity (Japan classified as Category 2, EC did not classify) - Toxic to reproduction (Japan classified as sub-Category 1A, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1, EC did not classify) - Specific target organ/systemic toxicity following repeated exposure (Japan classified as Category 1, EC classified as Category 2) - Hazardous to the aquatic environment (acute and chronic) (Japan did not classify and EC claasified as Category 1)				

Mercury diacetate (CAS. 1600-27-7)
Comment: In EU this substance is included in the group entry 'organic compounds of mercury with the exception of those specified elsewhere in this Annex' (Index No: 080-004-00-7 in Annex VI to Regulation 1272/2008).

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 2	Skull and crossbones	Danger	Fatal if swallowed
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (dermal) (EC classified as Category 1, Japan classified as Category 3) - Acute toxicity (inhalation) (EC classified as Category 2, Japan did not classify) - Skin corrosion/irritation (Japan classified as Category 1, EC did not classify) - Serious eye damage/irritation (Japan classified as Category 1, EC did not classify) - Respiratory/skin sensitizer (Japan classified as Category 1, EC did not classify) - Germ cell mutagenicity (Japan classified as Category 2, EC did not classify) - Toxic to reproduction (Japan classified as Category 2, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 2, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1, EC classified as Category 2) - Hazardous to the aquatic environment (acute and chronic) (EC classified as Category 1, Japan did not classify)				

* only the EC reported these symbol, signal word and hazard statement.

Other inorganic mercury compounds included in Annex III of the Rotterdam Convention

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-
PART 2: OTHER CLASSIFICATIONS				
Only the EC classified - Acute toxicity (oral) (Category 2) - Acute toxicity (dermal) (Category 1) - Acute toxicity (inhalation) (Category 2) - Specific target organ/systemic toxicity following repeated exposure (Category 2) - Hazardous to the aquatic environment (acute and chronic) (Category 1)				

Other organic mercury compounds included in Annex III of the Rotterdam Convention

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-
PART 2: OTHER CLASSIFICATIONS				

Monocrotophos

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 2	Skull and crossbones	Danger	Fatal if swallowed
Germ cell mutagenicity	Category 2	Health hazard	Warning*	Suspected of causing genetic defects
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning*	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning*	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (dermal) (Japan classified as Category 2, EC classified as Category 3) - Acute toxicity (inhalation) (Japan classified as Category 1, EC classified as Category 2) - Specific target organ/systemic toxicity following single and repeated exposure (Japan classified as Category 1, EC did not classify)				

* Only the Japanese labellings reported the signal word "warning".

Parathion

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 2	Skull and crossbones	Danger	Fatal if swallowed
Specific target organ/ systemeic toxicity following repeated exposure	Category 1	Health hazard*	-	Causes damage to organs*
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning*	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning*	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (dermal) (Japan classified as Category 1, EC classified as Category 3) - Acute toxicity (inhalation) (Japan classified as Category 1, EC classified as Category 2) - Skin corrosion/irritation (Japan calssified as Category 3, EC did not classify) - Serious eye damage/eye irritation (Japan classified as sub-Category 2B, EC did not classify) - Toxic to reproduction (Japan classified as Category 2, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1, EC did not classify)				

* Only the Japanese labellings reported the signal word “warning”.

Pentachlorophenol

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Skin corrosion/irritation	Category 2	-	-	Causes serious eye irritation
Serious eye irritation/eye damage	Category 2	-	-	Causes serious eye irritation
Carcinogenicity	Category 2	Health hazard	Danger	Suspected of causing cancer
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (oral) (Japan, the EC and WHO classified as Category 3, New Zealand classified as Category 2) - Acute toxicity (dermal) (Japan classified as Category 1, EC classified as Category 3, New Zealand calssified as Category 2) - Acute toxicity (inhalation) (Japan did not classify, EC and New Zealand classified as Category 2) - Toxic to reproduction (Japan classified as sub-Category 1B, EC did not classify, New Zealand classified as Category 2) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1, EC classified as Category 3, and New Zealand did not classify) - Specific target organ/systemic toxicity following repeated exposure (Japan classified as Category 1, New Zealand classified as Category 2 and the EC did not classify) - Hazardous to the aquatic environment (acute and chronic) (Japan did not classify, EC and New Zealand classified as Category 1)				

Toxaphene

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 3	Skull and crossbones	Danger	Toxic if swallowed
Hazardous to the aquatic environment (acute)	Category 1	Environment	-	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	-	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (dermal) (Japan and New Zealand classified as Category 3, EC classified as Category 4) - Acute toxicity (inhalation) (Japan classified as Category 3, EC and New Zealand did not classify) - Carcinogenicity (Japan and EC classified as Category 2, New Zealand did not classify) - Skin corrosion/irritation (Japan classified as Category 3, EC and New Zealand classified as Category 2) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1, EC classified as Category 3, New Zealand did not classify)				

- Specific target organ/systemic toxicity following repeated exposure (New Zealand classified as Category 2)

* Only the Japanese labellings reported the signal word "warning".

Dustable powder formulation containaing: benomyl≥7%, carbofuran≥10%, thiram≥15%
Only classifications and labelling available from countries/region on the active ingredients are listed below. No classification on the formulation itself is available.

Benomyl (CAS. 17804-35-2)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Respiratory/skin sensitizer	Category 1**	Exclamation mark	Warning*	May cause an allergic skin reaction
Germ cell mutagenicity	Category 1***	Exclamation mark	Danger	May cause genetic defects
Toxic to reproduction	Category 1***	Health hazard	Danger	May damage fertility or the unborn child
Hazardous to the aquatic environment (acute)	Category 1	Environment	-	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	-	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (oral) (WHO classified as Category 5) - Skin corrosion/irritation (Japan and New Zealand classified as Category 3, EC classified as Category 2) - Serious eye damage/eye irritation (Japan and the EC did not classify, New Zealand classified as Category 2) - Specific target organ/systemic toxicity following single exposure (Japan did not classify, EC classified as Category 3, New Zealand calssified as Category 2) - Specific target organ/systemic toxicity following repeated exposure (Japan classified as Category 2, EC and New Zealand did not classify)				

* Only the Japanese classifications reported the signal word "warning".
** The EC classified as "sub-Category 1B"
*** Japan and the EC classified as "sub-Category 1B"

Thiram (CAS. 137-26-8)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 4	Exclamation mark	Warning	Harmful if swallowed
Serious eye damae/eye irritation	Category 2*	Exclamation mark	Warning	Causes serious eye irritation

Respiratory/skin sensitizer	Category 1	Exclamation mark	Warning	May cause an allergic skin reaction
Hazardous to the aquatic environment (acute)	Category 1	Environment	-	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	-	Very toxic to aquatic life with long lasting effects

PART 2: OTHER CLASSIFICATIONS

- Acute toxicity (inhalation) (Japan did not classify, EC classified as Category 4)
- Skin corrosion/irritation (Japan classified as Category 3, EC classified as Category 2)
- Germ cell mutagenicity (Japan classified as Category 1, EC did not classify)
- Toxic to reproduction (Japan classified as Category 2, EC did not classify)
- Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1, EC did not classify)
- Specific target organ/systemic toxicity following repeated exposure (Japan classified as Category 1, EC classified as Category 2)

* Japan classified as "sub-Category 2B"

Carbofuran (CAS. 1563-66-2)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION

Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-

PART 2: OTHER CLASSIFICATIONS

Only the EC classified (with the exception of acute oral toxicity where WHO also classified)
- Acute toxicity (oral) Category 2
- Acute toxicity (inhalation) Category 2
- Hazardous to the aquatic environment (acute and chronic) Category1

Methamidophos

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION

Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 2	Skull and crossbones	Danger	Fatal if swallowed

PART 2: OTHER CLASSIFICATIONS

- Acute toxicity (dermal) (Japan and New Zealand classified as Category 2, EC classified as Category 3)
- Acute toxicity (inhalation) (EC classified as Category 2)
- Serious eye dame/eye irritation (Japan classified as ub-Category 2B, EC did not classify, New Zealand classified as Category 2)
- Specific target organ/systemic toxicity following single exposure (Japan classified as Category 2, EC did not classify, New Zealand calssified as Category 1)
- Specific target organ/systemic toxicity following repeated exposure (Japan classified as Category 2, EC and New Zealand did not classify)

- Hazardous to the aquatic environment (acute) (Japan did not classify, EC and New Zealand classified as Category 1)

* Japan classified as "sub-Category 2B"

Phosphamidon

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 2	Skull and crossbones	Danger	Fatal if swallowed
Acute toxicity (dermal)	Category 3	Skull and crossbones	Danger	Toxic in contact with skin
Germ cell mutagenicity	Category 2	Health hazard	Warning*	Suspected of causing genetic defects
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning*	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning*	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (inhalation) (Japan classified as Category 2, EC did not classify) - Serious eye damage/eye irritation (Japan classified as Category 2, EC did not classify) - Specific target organ/systemic toxicity following single and repeated exposure (Japan classified as Category 1, EC did not classify)				

* Only the Japanese labellings reported the signal word "warning".

Methyl-parathion

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (inhalation)	Category 2	Skull and crossbones	Danger	Fatal if inhaled
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning*	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning*	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				
- Flammable liquids (Japan and New Zealand did not classify, EC classified as Category 3) - Acute toxicity (oral) (Japan and EC classified as Category 2, New Zealand classified as Category 1) - Acute toxicity (dermal) (Japan classified as Category 3, EC classified as Category 3, New Zealand				

classified as Category 1) - Skin corrosion/irritation (Japan and New Zealand classified as Category 3, EC did not classify) - Serious eye damage/eye irritation (Japan classified as sub-Category 2, EC did not classify, New Zealand classified as Category 2) - Germ cell mutagenicity (Japan classified as Category 2, EC and New Zealand did not classify) - Toxic to reproduction (Japan and New Zealand classified as Category 2 (+effects on lactation for New Zealand), EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1, EC and New Zealand did not classify) - Specific target organ/systemic toxicity following repeated exposure (Japan and New Zealand classified as Category 1, EC classified as Category 2)

* Only the Japanse classifications reported these labelling elements
** Japan classified as "Category 2B"

Asbestos

Note: In the table below, Japan supplied classifications that apply to Crocidolite (CAS. 12001-28-4) and the EC has classifications that apply to all forms of asbestos listed in Annex III of the Rotterdam Convention.

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Carcinogenicity	Category 1A	Health hazard*	Danger*	May cause cancer*
Specific target organ/systemic toxicity following repeated exposure	Category 1	Health hazard*	Danger*	Causes damage to organs*
PART 2: OTHER CLASSIFICATIONS				
All classifications available were found to be identical.				

*Only the EC reported these labelling elements.

Polybrominated biphenyls

Hexabromo-1,1'-biphenyl (CAS. 36355-01-8)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-
PART 2: OTHER CLASSIFICATIONS				
Only Japan classified - Carcinogenicity (Category 2) - Toxic to reproduction (Category 2)				

Tetrabromo(tetrabromophenyl)benzene (CAS. 27858-07-7)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-

PART 2: OTHER CLASSIFICATIONS
Only Japan classified - Skin corrosion/irritation (Category 2) - Serious eye damage/eye irritation (sub-Category 2B) - Carcinogenicity (Category 2) - Toxic to reproduction (Category 2)

Decabromo-1,1'-biphenyl (CAS. 13654-09-6)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-
PART 2: OTHER CLASSIFICATIONS				
Only Japan classified - Skin corrosion/irritation (Category 3) - Serious eye damage/eye irritation (sub-Category 2B) - Carcinogenicity (Category 2)				

Polychlorinated biphenyls

Chlorodiphenyl (CAS. 1336-36-3)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Hazardous to the aquatic environment (acute)	Category 1	Environment	Warning	Very toxic to aquatic life
Hazardous to the aquatic environment (chronic)	Category 1	Environment	Warning	Very toxic to aquatic life with long lasting effects
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (oral) (Japan classified as Category 4, EC did not classify) - Acute toxicity (dermal) (Japan classified as Category 3, EC did not classify) - Carcinogenicity (Japan classified as sub-Category 1B, EC did not classify) - Toxic to reproduction (Japan classified as Category 1A, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 3, EC did not classify) - Specific target organ/systemic toxicity following repeated exposure (Japan classified as Category 1, EC classified as Category 2)				

Polychlorinated terphenyls

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-
PART 2: OTHER CLASSIFICATIONS				
Only Japan classified - Specific target organ/systemic toxicity following repeated exposure (Category 2)				

Tetraethyl lead

Comment: In EU this substance is included in the group entry 'lead alkyls' (Index No: 082-002-00-1 in Annex VI to Regulation 1272/2008).

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (inhalation)	Category 1	Skull and crossbones*	Danger*	Fatal if inhaled*
Hazardous to the aquatic environment (acute)	Category 1	Environment*	Warning*	Very toxic to aquatic life*
Hazardous to the aquatic environment (chronic)	Category 1	Environment*	Warning*	Very toxic to aquatic life with long lasting effects*
PART 2: OTHER CLASSIFICATIONS				
- Flammable liquid (Japan and New Zealand classified as Category 4, EC did not classify) - Acute toxicity (oral) (Japan and EC classified as Category 2, New Zealand classified as Category 1) - Acute toxicity (dermal) (Japan classified as Category 3, New Zealand classified as Category 1, EC classified as Category 2) - Skin corrosion/irritation (Japan and New Zealand classified as Category 2, EC did not classify) - Serious eye damage/eye irritation (Japan and New Zealand classified as Category 2, EC did not classify) - Specific target organ/systemic toxicity following repeated exposure (Japan and New Zealand classified as Category 1, EC classified as Category 2) - Toxic to reproduction (Japan classified as Category 2, New Zealand classified as Category 1, EC classified as Category 1A)				

*Only Japan reported these classification elements.

Tetramethyl lead

Comment: In EU this substance is included in the group entry 'lead alkyls' (Index No: 082-002-00-1 in Annex VI to Regulation 1272/2008).

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-
PART 2: OTHER CLASSIFICATIONS				
- Flammable liquid (Japan classified as Category 3, EC did not classify)				

- Acute toxicity (oral) (Japan classified as Category 3, EC classified as Category 2) - Acute toxicity (inhalation) (Japan classified as Category 2, EC classified as Category 1) - Acute toxicity (dermal) (EC classified as Category 2) - Toxic to reproduction (EC classified as Category 1A) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1, EC did not classify) - Specific target organ/systemic toxicity following repeated exposure (Japan classified as Category 1, EC classified as Category 2) - Hazardous to the aquatic environment (acute and chronic) (Japan did not classify, EC classified as Category 1)

Tris (2,3-dibromopropyl phosphate)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
-	-	-	-	-
PART 2: OTHER CLASSIFICATIONS				
Only Japan classified - Acute toxicity (Oral) (Category 4) - Germ cell mutagenicity (Category 2) - Carcinogenicity (sub-Category 1B) - Toxic to reproduction (Category 2) - Specific target organ/systemic toxicity following repeated exposure (Category 2) - Hazardous to the aquatic environment (acute and chronic) (Category 2)				

Tributyltin

Comment: In EU the following tributyltin compounds are included in the group entry ' tributyltin compounds, with the exception of those specified elsewhere in this Annex' (Index No: 050-008-00-3 in Annex VI to Regulation 1272/2008).

Tributyltin oxide (CAS. 56-35-9)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 3	Skull and crossbones	Danger	Toxic if swallowed
Skin corrosion/irritation	Category 2	Exclamation mark**	Warning**	Causes skin irritation
Serious eye damage/eye irritation	Category 2*	Exclamation mark**	Warning**	Causes serious eye irritation
Specific target organ/systemic toxicity following repeated exposure	Category 1	Health hazard	Danger	Causes damage to organs

PART 2: OTHER CLASSIFICATIONS
- Acute toxicity (dermal) (Japan classified as Category 3, EC classified as Category 4) - Acute toxicity (inhalation) (Japan classified as Category 2, EC did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 3, EC did not classify) - Hazardous to the aquatic environment (acute and chronic) (EC classified as Category 1, Japan classified as Category 2)

* Japan classified as sub-Category 2A

** Only Japan indicated the “exclamation mark” symbol and the “warning”signal word.

Tributyltin chloride (CAS. 1461-22-9)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 3	Skull and crossbones	Danger	Toxic if swallowed
Skin corrosion/irritation	Category 2	Exclamation mark**	Warning**	Causes skin irritation
Serious eye damage/eye irritation	Category 2*	Exclamation mark**	Warning**	Causes serious eye irritation
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (dermal) (EC classified as Category 4, Japan did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 2, EC did not classify) - Specific target organ/systemic toxicity following repeated exposure (EC classified as Category 1, Japan did not classify) - Hazardous to the aquatic environment (acute and chronic) (EC classified as Category 1, Japan did not classify)				

* Japan classified as sub-Category 2A
** Only Japan indicated the "exclamation mark" symbol and the "warning"signal word.

Tributyltin fluoride (CAS. 1983-10-4)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Serious eye damage/eye irritation	Category 2	Exclamation mark*	Warning*	Causes serious eye irritation
Specific target organ/systemic toxicity following repeated exposure	Category 1	Health hazard	Danger	Causes damage to organs
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (oral) (Japan classified as Category 4, EC classified as Category 3) - Acute toxicity (inhalation) (Japan classified as Category 2, EC did not classify) - Acute toxicity (dermal) (EC classified as Category 4, Japan did not classify) - Skin corrosion/irritation (Japan classified as Category 3, EC classified as Category 2) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1, EC did not classify) - Hazardous to the aquatic environment (acute and chronic) (EC classified as Category 1, Japan did not classify)				

* Only Japan indicated the "exclamation mark" symbol and the "warning"signal word.

Tributyltin naphthenate (CAS. 85409-17-2)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 3	Skull and crossbones*	Danger*	Toxic if swallowed*
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (inhalation) (Japan classified as Category 2, EC did not classify) - Acute toxicity (dermal) (EC classified as Category 4, Japan did not classify) - Skin corrosion/irritation (EC classified as Category , Japan did not classify 2) - Serious eye damage/eye irritation (EC classified as Category 2, Japan did not classify) - Specific target organ/systemic toxicity following single exposure (Japan classified as Category 1, EC did not classify) - Specific target organ/systemic toxicity following repeated exposure (EC classified as Category 1, Japan did not classify) - Hazardous to the aquatic environment (acute and chronic) (EC classified as Category 1, Japan did not classify)				

* Only the EC indicated the symbol, signal word and hazard statement..

Tributyltin methacryalte (CAS. 2155-70-6)

PART 1: CLASSIFICATIONS IDENTICAL ACROSS COUNTRIES/REGION				
Hazard class	Classification	Symbol	Signal word	Hazard satement
Acute toxicity (oral)	Category 3	Skull and crossbones*	Danger*	Toxic if swallowed*
PART 2: OTHER CLASSIFICATIONS				
- Acute toxicity (dermal) (EC classified as Category 4, Japan did not classify) - Skin corrosion/irritation (EC classified as Category , Japan did not classify 2) - Serious eye damage/eye irritation (EC classified as Category 2, Japan did not classify) - Specific target organ/systemic toxicity following repeated exposure (EC classified as Category 1, Japan did not classify) - Hazardous to the aquatic environment (acute and chronic) (EC classified as Category 1, Japan did not classify)				

* Only the EC indicated the symbol, signal word and hazard statement..

ANNEX 2

ANALYSIS OF DATA SETS BY EXPERTS

The following part of the document includes an analysis provided by experts of possible reasons leading to differences in classification outcomes, followed by their proposal to reconcile differences if possible. A table was prepared for each chemical and hazard class, with responses from experts.

LINDANE

Acute toxicity (oral)	**EU: category 3**	**Japan: category 3**	**New Zealand: category 2**	**USEPA[4]: category 3**
Possible reasons leading to differences				
EC Differences in data sets used JP Differences in data sets used: Japan and EC used LD50 obtained in rats. New Zealand used LD_{50} in dogs (40mg/kg) although rat data (76mg/kg) were included in raw data section which would lead classification into Cat. 3. FR Differences in data sets used: NZ classifies lindane based on dog LD_{50}, which is not taken into account neither by Japan or EC. Although Japan (average of LD_{50} values) and EC (source data not specified) methodology is different, it leads to the same classification.				
Proposal to reconcile differences				
EC Most data points would support Category 3 (LD_{50}=50-300 mg/l). However in case the studies in dog and mouse listed by Japan having LD_{50}<50 were evaluated and found to be relevant for the hazard assessment; Category 2 would be the correct classification. The values reported in these two studies are not dramatically lower than other reported values, why it still could be discussed that this is a borderline case in between Category 2 and 3, and it is understandable that the outcome can end up both in Category 2 and 3 depending on the studies considered. To conclude with a correct classification it is necessary to review the dog and mouse study reported by Japan. JP The GHS document give priority to Rat data as for oral acute toxicity (para 3.1.2.3.). Thus, Category 3 is appropriate. FR GHS paragraph 3.1.2.3 specifies that preferred test species for evaluation of acute toxicity by the oral route is the rat. If the tests are all well-performed and if there is a scientific explanation why to use dog data instead of rats, dog data should be taken into account and classification harmonised as category 2 for oral acute toxicity. However, a brief review did not allow finding this explanation. If there is none, rat specie should be used in selecting the most appropriate LD_{50} value. Classification should then be harmonised as category 3. It would be in line with the human data provided by EC.				
Observation from the United States				
Category 3 based on an LD_{50} of 91 mg/kg in female and 88 mg/kg in male rats In addition to differences in data/studies used, reviewers noted that the vehicle used to administer lindane can affect its toxicity (i.e., oily solutions of lindane appear more toxic than water.)				

[4] See paragraph 6 of the document.

Table 1.1: Analysis of data supporting classification for acute toxicity (oral)

Note to Table 1.1: New Zealand used the data from the dog study (LD_{50} =40 mg/kg), but declared that this is not the current practice anymore unless there is specific scientific reason; New Zealand stated that they could align to Category 3. Another expert argued that the most sensitive species should be used, be it a dog or a rat, from a reliable study.

Acute toxicity (dermal)	**EU: category 4**	**Japan: category 2**	**New Zealand: category 3**	**USEPA: category 2**
Possible reasons leading to differences				
EC	Differences in data sets used and differences in interpretation of data			
JP	Differences in data sets used: Japan used rabbit data. New Zealand and EC used rat.			
FR	Differences in data sets used: No indication is given regarding the data used by EC to determine the dermal LD_{50} in rats. Its value is close to the one defined by NZ (respectively 1000 mg/kg bw and 900 mg/kg bw). Data provided by NZ do not allow either to understand where the LD_{50} comes from. Japan uses rabbit value for LD_{50} determination.			
Proposal to reconcile differences				
EC	A better understanding both of the totally available database, and how the calculations were made is necessary to conclude on which classification is correct.			
JP	As for dermal acute toxicity, both rat and rabbit data are appropriate to use. However, data from more sensitive species should be used unless there is clear evidence suggesting such data are species-specific and not applicable for humans. Cat. 2 is appropriate.			
FR	If the rabbit study is well-performed and based on GHS paragraph 3.1.2.3, rat or rabbit are preferred for evaluation of acute dermal toxicity. Therefore, LD_{50} value should be based on rabbit data and classification should be harmonised as category 2.			
Observation from the United States				
	Borderline classification of Category 2 based on an LD_{50} of 900 mg/kg in female and 1000 mg/kg in male rabbits.			

Table 1.2: Analysis of data supporting classification for acute toxicity (dermal)

Note from New Zealand to Table 1.2: New Zealand has classified as Acute toxicity (dermal) Category 3 even though the standard practice was to use the lowest LD_{50} value. The following study that was part of the raw data set was not used for classification in an attempt to harmonise the classification.
LD_{50} Rabbit skin 50 mg/kg [Lewis, R.J. Saxs Dangerous Properties of Industrial Materials. 9th ed. Volumes 1-3. New York, NY: Van Nostrand Reinhold, 1996.339]
In this case expert judgement was used and not just the lowest classification. All the data was from secondary sources with no information on the reliability of the studies.

Acute toxicity (inhalation)	**EU: category 4**	**Japan: category 4**	**New Zealand: category 1**	**USEPA: category 4**
Possible reasons leading to differences				
EC Differences in data sets used JP Differences in data sets used: Japan and EC use the same data 1.6 mg/l (16000mg/m3). New Zealand adopted very small value, i.e. 0.002 mg/l. FR Differences in datasets used and differences in the interpretation of the data: Reference study used is different: - Japan and EU use the DFGOT study setting the LC_{50} value at 1.6mg/L. NZ uses the study performed by Ullman & Mohler (1986) setting the LC_{50} value at 0.002mg/L. It is wondering if a typing error occurred in NZ file as the reference cited (Ullman et Mohler, 1986) indicates that the acute 4-h LC_{50} was found to be about 1600 mg/m3 for animals of each sex and the LD_{50} proposed is 0.002mg/L. To be confirmed by checking references.				
Proposal to reconcile differences				
EC The data used by New Zeeland to conclude with classification for the inhalation route in Category 1, seems to be outstanding, and it would be desirable to look into the study, prior concluding that the Category 4 classification applied by Japan and EU is not correct. JP The reliability of the reported value 0.002mg/l adopted by New Zealand should be reconfirmed by checking its original report, and if this value is reliable, Cat. 1 shall be appropriate. All other reported values are not so small, thus there might be a mistake. FR If it is confirmed that the same dataset is used, LC_{50} was found to be about 1600 mg/m3 or 1.6mg/L. Based on GHS criteria for dust/mist, classification should be harmonised as category 4.				
Observation from the United States				
Category 4 based on an LC_{50} of 1.56 mg/l in rats (both sexes). The value cited by NZ appears to be an outlier. Note that mandatory language ("shall") is not consistent with the GHS' status as a voluntary agreement and its reliance on a criteria-based approach that does not establish any international classifying body.				

Table 1.3: Analysis of data supporting classification for acute toxicity (inhalation)

Note from New Zealand to Table 1.3: The LD_{50} of 0.002 mg/L was used by New Zealand to classify as Acute toxicity (inhalation) Category 1. New Zealand indicated that secondary literature was used in the absence of the original studies, and recognised that reliability of information might be an issue.

Eye irritation	**EU: ----**	**Japan: category 2B**	**New Zealand: -----**	**USEPA: category 2B**
Possible reasons leading to differences				
EC Differences in data sets used JP Differences are coming from interpretation of "mildly irritating or slightly irritating". FR ---------				

Proposal to reconcile differences	
EC	It would again be necessary to compare the data available, to decide whether no classification or Category 2B would be correct. EU not classifying based on no data, can be concluded as disregarded.
JP	Wording for dermal irritation test results (slightly, mildly, or severely) should officially be defined based on AOI or PII values in the OECD test guidelines. However, it is inevitable to results in different classification because GHS allows using old test data and existing classification.
FR	Without access to full report, it is difficult to state if the diverging classification is due to different data sets used or to divergent interpretation of the same data set. Consequently, it is impossible to state for a classification or another.
Observation from the United States	
	Borderline Category 2B based on rabbit study showing no corneal involvement and irritation clearing after 24 hrs. The GHS does give scores for Category 2 eye irritants; the only stated difference between 2A and 2B is the time it takes for the effects to reverse (within 21 days, v. within 7 days of observation.) Some classifiers may have concluded that clearing within 24 hrs warranted a "not classified" conclusion. (EPA currently has a category for minimal effects that clear within 24 hrs, so how to adapt this to GHS would be an issue for us.)

Table 1.4: Analysis of data supporting classification for eye irritation

Carcinogenicity	**EU: -----**	**Japan: category 2**	**New Zealand: category 2**	**USEPA: -------**
Possible reasons leading to differences				
EC	Differences in data sets used and differences in application of the classification criteria			
JP	It seems that EC has not reached its final agreement on classification. Thus, "not classified" is not appropriate for such cases.			
FR	Difficult to state because EU did not provide the exact set of data used. (Austrian comments provided concern reproductive toxicity).			
Proposal to reconcile differences				
EC	Probably border case in between Category 2 and no classification. However it would be necessary to re-visit the complete dataset, and it should be noted that the IARC evaluation leading Category 2B was made in 1991 and the EU evaluation in 2001. At least according the EU experts the complete database in 2001 did no longer support the IARC recommendation. However it should be noted that the EU experts on carcinogenicity also for other substances looking into the same database as IARC not always arrived to the same classification. This was usually not because of the different findings but the considered relevance of certain tumours in rat or mouse to man. This would be interpreted as differences in the application of criteria.			
JP	"Not yet classified" should be used instead of "not classified" if final agreement has not been reached within a party because the latter indicates that the substance is not carcinogenic. We needs scientific evidences for classification.			

FR	Based on data provided by NZ, it appears that lindane increases tumour incidence, at least under specific conditions (strain, sex, phenotype…) providing limited evidence of carcinogenicity. Finally, harmonisation with other existing classifications would be another reason why lindane should be classified as carcinogen category 2.
Observation from the United States	
	Not classified based on data base updated since the IARC classification. EPA had regulated lindane as a "probable/possible human carcinogen" pending receipt of further studies, which were required due to serious deficiencies associated with all studies then available. Additional data have since been provided and are suggestive, but not sufficient to assess human carcinogenic potential. This conclusion was based on an increased incidence of benign lung tumors in female mice only. To propose use of the phrase "not yet classified"seems to confuse the issue and could be used for any hazard class for which there is no, or insufficient, data. Such a phrase implies that classification is going to happen at some unspecified future time, when this is not the case. We have much more data on these chemicals than we have on the vast majority of chemicals.

Table 1.5: Analysis of data supporting classification for carcinogenicity

Reproductive toxicity	**EU: effects on lactation**	**Japan: ----**	**New Zealand: category 2+ effects on lactation**	**USEPA: category 2**
Possible reasons leading to differences				
EC	Differences in data sets used and differences in application of the classification criteria			
JP	It seems that EC has not reached its final classification. Thus, "not classified" is not appropriate for such cases.			
FR	Differences in datasets used and differences of interpretation of the data: It seems plausible that different data set were used also it is difficult to have a clear picture with the data provided. Part of the discrepancy comes from the interpretation of the data. Information available show for example that NZ conclude from the study performed by Fröhberg & Bauer (1972b) that no NOAEL could be identified for developmental toxicity as a decreased number of live fetuses per dam was seen at the lowest dose tested whereas the NOAEL for maternal toxicity was 12 mg/kg bw per day. From the same study, EHC 124 (one of the report used by Japan for not classifying lindane as reprotoxic) stated that only at high dose, when increased maternal mortality (48%) and reduced body weight gain were observed, foetal mortality was increased and fetal weights were decreased. The treatment had no effect on the number of implantations per dam, the percentages of early and late resorptions, the number of runts or the malformation rate. Austrian evaluation (in respond to EU one) led to maternal and foetal NOAEL at 12 mg/kg.			
Proposal to reconcile differences				
EC	In might again be a border case in between Category 2 and no classification. However besides that there might be differences in the data used (evaluations done at quite different points in time, as for the carcinogenicity), but here it might also be a difference in the interpretation of the criteria, i.e. how to interpret findings at high maternal toxicity. EU classified for effects at lactation, which might not have been considered by the other countries.			
JP	"Not yet classified" should be used instead of "not classified" if final agreement has not been reached within a party. We need scientific evidences for classification. Could non-reproductive			

toxicant affect on or through lactation?

FR It is difficult to state the reproductive toxicity classification with the level of details provided.

- First step would be to agree on the relevant studies: King (1991), Fröhberg & Bauer (1972b) and Palmer & Neuff (1971b) seems to be accepted as following guideline requirement. For all the other studies, confidence in the data is not provided.
- Precise review on raw data should be performed. In particular, a consensus on when maternal toxicity arise and the statistical significance of observed effect on offspring.
- Finally, pertinence of some maternal toxicity signs should be evaluated: is the tachypnoea and lethargy described in the Palmer & Neuff study a sign of more important general toxicity (if these signs could be linked to mechanistic action of lindane) or is it weak effects that seems to have no direct linked with reduced pregnancy rate, reduced viable fetuses and increased incidence of fetuses with 13 ribs.

Reasons for classification on lactation (NZ and EU) or not (Japan) are not specified. Therefore, it is difficult to state on that point with the data provided.

Observation from the United States

Category 2 and effects on lactation based on developmental neurotoxicity in rats.

EPA found a maternal toxicity Lowest Observed Adverse Effect Level (LOAEL) of 120 ppm (13.7 mg/kg/day) based on decreased body weight gain, decreased food consumption, and increased reactivity; and a maternal toxicity No Observed Adverse Effect Level (NOAEL) of 50 ppm (5.6 mg/kg/day). The offspring LOAEL is 50 mg/kg/day, based on reduced pup survival, decreased body weights and body weight gains during lactation, increased motor activity and decreased motor activity habituation. The offspring NOAEL is 10 ppm (1.2.mg/kg/day). At the time of the review, this study was missing laboratory validation studies and had fewer than the required number of animals at the highest dose level. In another two generation reproduction study, offspring also demonstrated increased susceptibility to lindane. The LOAEL for reproductive toxicity is 150 ppm (13.05 mg/kg/day) based on reduced pup body weights, decreased viability in both generations, and delayed maturation of pups; the NOAEL is 20 ppm, (1.71. mg/kg day). Classification appears warranted.

A toxicant that has no other reproductive effects could have effects via lactation (e.g., by affecting the nursing infant's nervous system). Again, use the the phrase "not yet classified" would be problematic. [Significant new data are not anticipated?]

Table 1.6: Analysis of data supporting classification for reproductive toxicity

Target organ toxicity	**EU**	**Japan**	**New Zealand**	**US EPA**
single exposure	--------	**Category 1**	---------	---------
Repeated exposure	**Category 2**	**Category 1**	**Category 1**	**Category 1**

Possible reasons leading to differences

EC Differences in data sets used.

JP Differences in data sets used. Between Japan and New Zealand, there are several differences as for targeted organs. This is coming from the differences of data sets they used. It seems that EC has not reached to its final classification. Thus, "not classified" is not appropriate for such cases.

FR Single exposure:
Differences in data sets used and difference in interpretation of the classification criteria:
It seems probable that Japan classifies lindane for STOT-SE based on the effects described in the acute studies also no doses are provided in the document. If the endpoint was considered and excluded or not by EU and NZ is not specified in the document.
It is unusual to set different categories of classification for different organs as Japan did.
Repeated exposure:
It is probable that EU did not use the same data set than Japan and NZ. In particular, why EU does not consider effects on liver (and kidney, also it might be species specific) is not described.

Proposal to reconcile differences

EC Mainly different data sets have been used. EU ending up with classification for STOT Repeated Exposure in Category 2 made their evaluation in 2001, and several of the studies reported by the other countries are from a later date (Japan and New Zealand ended up in Category 1)

JP "Not yet classified" should be used instead of "not classified" if final consensus has not been reached within a party. I think EC has clear evidence of neurotoxicity (Cat. 1) of this substance as described in the last few lines of the supporting information section. If this type of information is ignored, it would be difficult to reach international harmonization of classification results.

FR Single exposure:
In order to reconcile the diverging data, it could be interesting to dig on human data and have more information on the animal data used by Japan.
Repeated exposure:
If there is no scientific explanation why liver effects were not taken into account, this should be taken into account and STOT-RE harmonised as category 1.

Observation from the United States

Specific Target Organ Toxicity—Single Exposure
Not classified based on animal data.
All data are based on more than one dose. In a short term study, for example, clinical signs did not begin until day 14.
There have been human incident/poisoning reports, as there are for most toxic chemicals. Any chemical that is Category 1-2 for acute oral toxicity can seriously poison or kill. At the time the GHS was being developed, it was thought that single exposure STOT would very rarely be used. The example cited was methanol and blindness. Both STOT hazard classes were designed to cover effects not covered in the other GHS hazard classes.

Specific Target Organ Toxicity—Repeated Exposure
Category 1
I suspect everyone agrees that lindane primarily affects the nervous system; it also appears to EPA to cause renal and hepatic toxicity. The EU's lower classification may be based on reference to the "guidance values" in the chapter, i.e., the exposure/dose at which effects are considered to be significant. EPA found a LOAEL of 20 mg/kg/day (rat acute neurotoxicity study, using increased grip strength, decreased grooming behavior and motor activity as endpoints) and 4.81 mg/kg/day (rat chronic feeding and carcinogenicity study, using periacinar hepatocyte hypertrophy, increased liver/spleen weight, and decreased platelets as endpoints).
While the lower of these two LOAELs is clearly covered by the Category 1 "guidance value," experts may not agree on when/which of the effects (endpoints) are significant. It may take experience using the criteria and further discussion among experts who are more expert in these particular effects to resolve these kinds of differences.

Table 1.7: Analysis of data supporting classification for target organ toxicity

Note to Table 1.7: New Zealand indicated that most of the time classification is meant to apply to repeat dose toxicity, and that on rare cases where there is sufficient information, a classification may also be derived for single dose toxicity; this is due to the fact that the national classification system was implemented in 2001 in New Zealand, before the GHS was agreed.

METHAMIDOPHOS

Acute toxicity (dermal)	**EU: category 3**	**Japan: category 2**	**New Zealand: category 2**	**US EPA: category 2**
Possible reasons leading to differences				
JP	Different data sets were used among 3 parties. Supporting data from EU include two 24h-exposure experiments. One is rat data (108-162 mg/kg bw.) and the other is rabbi data (69.1-122.2 mg/kg bw.), both suggesting category 2 classification. Other data from EU are based upon exposure period other than 24hs. According to OECD TG for dermal acute toxicity testing, 24h exposure data should be used for the classification with higher priority.			

Proposal to reconcile differences
JP Priority should be given to dataset obtained by using standard experimental conditions as described in OECD TGs.
Observations from the United States
Category 2 based on an LD_{50} of 118 mg/kg in rabbits.

Table 2.1: Analysis of data supporting classification for acute toxicity (dermal)

Acute toxicity (inhalation)	**EU: category 2**	**Japan: ------**	**New Zealand: category 2**	**USEPA: category 2**
Possible reasons leading to differences				
JP Different data sets were used among 3 parties, however, resulting in the same classification, Category 2.				
Proposal to reconcile differences				
JP ----------				
Observations from the United States				
Category 2 based on LC_{50} values of 0.052-0.128 mg/l in rats. It looks like there is no difference in classification after all—maybe a reporting error/omission in the previous paper.				

Table 2.2: Analysis of data supporting classification for acute toxicity (inhalation)

Eye irritation	**EU: -----**	**Japan: category 2B**	**New Zealand: category 2**	**US EPA: category 1 or 2**
Possible reasons leading to differences				
JP Differences in interpretation of the data: No definite test scores. Interpretation of wording "mildly" or "slightly" irritating resulted in different classification between Japan and EU. However, the information from New Zealand, corneal opacity and pannus, would be a good evidence for classify this substance into category 2.				
Proposal to reconcile differences				
JP ----------				
Observations from the United States				
Category 1 or 2 based on corneal opacity and pannus in 2/6 rabbits for 10 days post-treatment. One death. EPA has classified methamidaphos as Category 1, corrosive, under our current system. Would need to pull the actual study data and review to see if data indicate clearing within 21 days and/or check opacity scores against GHS criteria. Definitely not considered "mild"!				

Table 2.3: Analysis of data supporting classification for eye irritation

Target organ toxicity	EU	Japan	New Zealand	USEPA
single exposure	--------	Category 2	---------	----------
Repeated exposure	--------	Category 2	Category 1	Category 1

Possible reasons leading to differences

JP Differences in the interpretation of the data:
According to the described in the GHS document paragraph 3.9.2.7.3 (b), significant functional changes in the central or peripheral nervous systems, or other organ systems, including signs of central nervous depression …, symptoms due to ChE inhibition should be considered as enough evidence for supporting classification. Nervous system effects have been observed both in humans and animals, thus, this substance should be classified in Category 1 (nervous system). Guidance values should not be used for human cases. Data from New Zealand indicates that the effects should not be considered as reversible.
Unfortunately, Japanese classifier failed to obtain relevant information from "the priority 1 data source" listed in the Japanese "GHS classification manual", and thus assigned category 2 for this substance based upon information from RTECS, HSDB, and ICSC(J), i.e. priority 2 data source, according to the Japanese local rule.

Proposal to reconcile differences

JP ----------

Observations from the United States

Specific Target Organ Toxicity—Single Exposure
Not classified based on animal data. Possibly Category 1 based on human incident data.
There have been human incident/poisoning reports, as there are for most toxic chemicals. Any chemical that is Category 1-2 for acute toxicity can seriously poison or kill. At the time the GHS was being developed, it was thought that single exposure STOT would very rarely be used. The example cited was methanol and blindness. Both STOT hazard classes were designed to cover effects not covered in the other GHS hazard classes.

In this case, however, EPA's incident analysis concluded that "Organophosphate-induced delayed neuropathy in seriously poisoned cases, intermediate syndrome, and chronic neurobehavioral effects have been directly linked to poisoning from methamidophos." The issue of how the STOT single exposure hazard class should be interpreted in light of such findings warrants further discussion in GHS fora.

Specific Target Organ Toxicity—Repeated Exposure
Category 1
In rats, the cholinesterase inhibition Lowest Observed Effect Level (LOEL) is 2 ppm (.0.1 mg/kg/day, lowest dose tested), based on brain, plasma and erythrocyte ChE inhibition. In dogs, The ChE LOEL is 2 ppm (.0.05 mg/kg/day, lowest dose tested), based on brain, plasma and erythrocyte ChE inhibition. In addition, as noted above, human incident data support classification.

Table 2.4: Analysis of data supporting classification for target organ toxicity

Hazardous to the aquatic environment	EU: category 1	Japan: ---------	New Zealand: category 2
Possible reasons leading to differences			

JP ----------

CH Differences in data sets used.

Acute:

(JP) No classification due to lack of information.

(NZ) **FISH:**
Estuarine/Marine Water:
96-hr LC_{50} 5.6 mg/L (species: *Cyprinidon variegatus*, Sheepshead minnow);
Freshwater:
96-h LC_{50} 25 mg/L (species: *Oncorhynchus mykiss*, Rainbow trout) [Larkin, 1983; USEPA REDS doc], and approximately 100 mg/L (species: *Carassius auratus*, Goldfish, and *Cyprinus carpio*, Carp) [HSG 79, 1993];
96-h LC_{50} 51 mg/L (species: *Salmo gairdneri*, Rainbow trout), Conditions of bioassay not specified [Hartley, D. and H. Kidd (eds.). The Agrochemicals Handbook. 2nd ed. Lechworth, Herts, England: The Royal Society of Chemistry, 1987.,p. A265/Aug 87; HSDB];
96-h LC_{50} 34 mg/L (species: *Lepomis macrochirus*), GLP, analytical monitoring, Test cond. 20°C [Bayer AG, unpublished report, IUCLID 2000];
96-h LC_{50} 47.7 mg/L (species: *Leuciscus idus melanotus*), GLP, analytical monitoring, Test cond. 21°C [Bayer AG, unpublished report, IUCLID 2000];
96-h LC_{50} 40 mg/L (species: *Oncorhychus mykiss*, Rainbow trout), GLP, analytical monitoring, Test cond. 16°C [Bayer AG, unpublished report, IUCLID 2000];
Assumption: All data in ECOTOX was for formulations. NB Methamidophos technical used in products registered in NZ is 70-75% pure [JN]
CRUSTACEA:
Estuarine/Marine Water:
96-h LC_{50} 0.0002 mg/L (species: *Macrobrachium rosenbergil*, Palaemonid prawn larvae) [Juarez LM, Sanchez J; Bull Environ Contam Toxicol 43 (2): 302-9 (1989), HSDB]
Freshwater:
21-d NOEC 0.026 mg/L, LOEC 0.046 (species: *Daphnia magna*), endpoint: reproduction, GLP, analytical monitoring, Test cond. 20°C [Bayer AG, unpublished report, IUCLID 2000];
ALGAE:
96-h EC_{50} >178 mg/L (species: *Scenedesmus subspicatus*), endpoint: growth rate, analytical monitoring, Test cond. 23°C [Bayer AG, unpublished report, IUCLID 2000];
OTHER:
96-h EC_{50} 0.039 mg/L (species: Oyster) [USEPA OPP REDS document – methamidophos, USEPA]

(EC) No data and no rationale for the classification has been provided.

Chronic:

(JP) No classification due to lack of information.

(NZ) **FISH**
Estuarine/Marine Water:

96-hr LC_{50} 5.6 mg/L (species: *Cyprinidon variegatus*, Sheepshead minnow) [Larkin, 1983; USEPA REDS doc];
Freshwater:
21-d LC_{50} 18.7 mg/L (species: *Oncorhychus mykiss*, Rainbow trout), GLP, analytical monitoring, Test cond. 15°C [Bayer AG, unpublished report, IUCLID 2000];
CRUSTACEA:
Estuarine/Marine Water:
96-h LC_{50} 0.0002 mg/L (species: *Macrobrachium rosenbergil*, Palaemonid prawn larvae) [Juarez LM, Sanchez J; Bull Environ Contam Toxicol 43 (2): 302-9 (1989), HSDB]
Freshwater:
21-d NOEC 0.026 mg/L, LOEC 0.046 (species: *Daphnia magna*), endpoint: reproduction, GLP, analytical monitoring, Test cond. 20°C [Bayer AG, unpublished report, IUCLID 2000];
ALGAE:
96-h EC_{50} >178 mg/L (species: *Scenedesmus subspicatus*), endpoint: growth rate, analytical monitoring, Test cond. 23°C [Bayer AG, unpublished report, IUCLID 2000];
OTHER:
96-h EC_{50} 0.039 mg/L (species: Oyster) [USEPA OPP REDS document – methamidophos, USEPA]
BIODEGRADATION
Under aerobic conditions in biologically active waters methamidophos undergoes very rapid and thorough degradation. In studies under anaerobic conditions methamidophos was metabolized very rapidly, too. [Bayer AG, unpublished report, IUCLID 2000].
Although the environmental fate database for methamidophos is not complete, supplemental information from upgradable laboratory studies indicate that methamidophos is not persistent in aerobic environments but may be persistent in anaerobic aquatic environments where it will be associated with the aqueous phase. No acceptable data are available on the behavior of methamidophos under field conditions, but information from acceptable terrestrial field dissipation studies for acephate indicate that methamidophos is not persistent. [USEPA OPP REDS document – methamidophos, USEPA]
AQUATIC FATE: A Henrys Law constant of 8.682X10-10 atm-cu m/mole at 25 deg C(1) can be calculated for methamidophos A water solubility greater than 2000 ppm at 20 deg C(2) has been reported for methamidophos. Based on the Henrys Law constant, volatilization half-lives of 91 and 998 years can be calculated for methamidophos in a model river (1 m depth, 1 m current velocity, 3 m wind speed) and a model lake, respectively(3). A calculated Koc of 3.848(4) indicates that adsorption of methamidophos to sediment will not be an important fate process (SRC). Based on a calculated log Kow of -0.93(5), an estimated BCF of 0.33(3) can be calculated, which indicates the bioconcentration of methamidophos in aquatic organisms is not an important fate process (SRC). [(1) Meylan WM, Howard, PH; Environ Toxicol Chem 10: 1283-93 (1991) (2) WorthingCR, Walker SB, eds; The Pesticide Manual 8th ed.; Suffolk, England: Lavenham Press Ltd (1987) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-15 to 15-32, 5-4 (1990) (4) Meylan WM et al; Environ Sci Technol 26: 1560-7 (1992) (5) Meylan WM, Howard PH; Group Contribution Method for Estimating Octanol-Water Partition Coefficients. SETAC Meeting Cincinnati, OH Nov 8-12 (1992), HSDB]

(EC) No data and no rationale for the classification has been provided.

Proposal to reconcile differences

JP Acute:
Japan's outcome is the same as proposed.
This chemical has been classified to Category 1 based on the toxicity of 48hEC50=0.026 mg/L (Daphnia magna), which is one of the data provided.

	Chronic: Japan's outcome is the same as proposed. This chemical has been classified as Chronic Category 1 based on acute toxicity less than 1 (0.1) mg/L, and not rapidly degradation (estimated by BIOWIN) however this chemical has limited potential for bioaccumulation. Japan will revise to classify of this chemical based on data of chronic toxicity e.g. 21 d NOEC=0.026 mg/L which is provided, according to the3rd version of GHS manual.
CH	Category Acute 1 The data provided by NZ for crustacean support the EC and NZ classification as category 1 for acute aquatic toxicity (96-hr LC_{50} in fish <1 mg/L). This is also supported by many other data that can be retrieved in the ECOTOX database for freshwater and marine crustacean. Category Chronic 2 The data provided by NZ for crustacean (Daphnia magna) and Oyster support the classification as category 2 for chronic aquatic toxicity (Chronic NOEC or EC_x <0.1 mg/L for rapidly degradable substances for which adequate chronic toxicity data are available). This is supported by many other aquatic toxicity data that can be retrieved in the ECOTOX database for freshwater and marine crustacean. The information provided by the Bayer company in IUCLID 2000 states "Under aerobic conditions in biologically active waters methamidophos undergoes very rapid and thorough degradation. In studies under anaerobic conditions methamidophos was metabolized very rapidly, too." The US-EPA concluded in the OPP REDS document – methamidophos "Although the environmental fate database for methamidophos is not complete, supplemental information from upgradable laboratory studies indicate that methamidophos is not persistent in aerobic environments but may be persistent in anaerobic aquatic environments where it will be associated with the aqueous phase." According to the Pesticide Product Database of the University of Hertfordshire, UK (http://sitem.herts.ac.uk/aeru/footprint/en/Reports/453.htm#0), methamidophos has an aqueous hydrolysis half-life DT50 of 5 days at 20°C and pH7, a water-sediment Half-life of 23.5 days and a water phase only half-life of 16 days. Half-lives for aerobic degradation in soil are reported to be about 4 days. The substance has a high solubility in water (around 200 g/L), a log K_{ow} of -0.80, a Henry's law constant at 20°C of $1.1x10^{-9}$ (dimensionless). A BCF of 3.16 L/kg wet-wt is calculated by EPIWEB v4.0. It can be concluded that methamidophos is not readily biodegradable. However, it can be expected that the substance is not persistent, but is inherently biodegradable. Methamidophos has no potential to bioaccumulate.
Observations from the United States	
	Category 1 based on toxicity to freshwater and marine and estuarine invertebrates (daphnia, freshwater prawn, blue prawn all have LC 50 < 1) EPA did not classify for chronic aquatic toxicity.

Table 2.5: Analysis of data supporting classification for hazard to the aquatic environment

METHYL PARATHION

Acute toxicity (oral)	**EU: category 2**	**Japan: category 2**	**New Zealand: category 1**	**US EPA: category 1 or 2**
Possible reasons leading to differences				
NZ Differences in the application of the classification criteria: Both Japan and the EU used a range of LD_{50} values to determine classification category. New Zealand used lowest data point because the range covers two classifications. Cannot tell what data Japan or the EU used. In the case of Japan only a statistic value was given. For the EU only a range was given. JP Differences in the datasets used: There are so many LD50 data ranged from 2.9-62 mg/kg in rats. FR Differences in the interpretation of the data and differences in the application of the classification criteria: The conclusion in Japan is based on the statistical calculation of LD50 in rats using pooling of studies whereas the conclusion in New-Zealand is based on the lowest value available among valid, well-performed tests. The conclusion in Europe seems to be based on the conversion of the classification obtained according to the previous regulation. "Very toxic" has been converted into cat. 2 as proposed by the translation table of the European CLP regulation. However, in this case, direct conclusion on the basis of the data would have been Cat. 1 as conclusion based on the lowest relevant data is generally recommended.				
Proposal to reconcile differences				
NZ A discussion on application of classification criteria is required. The EU approach raises the question of if a range is used then what would be used for mixture calculation? Of Japan's approach it needs to be questioned, is the statistical calculation is valid? New Zealand uses a conservative approach that takes the lowest value. JP Total 15 rat oral LD5s data in EHC, ATSDR, and JMPR (counted separately by sex in some cases) : 2 for < 5mg/kg, 12 for 5-25 mg/kg, 1 for 62 mg/kg. Almost all data were in the range of category 2. Therefore, category 2 (5-50 mg/kg) will be suitable. FR Statistical analysis based on a pool of studies is not considered relevant to conclude as it will mix results obtained from different strains and in different experimental settings. Unless there are reasons to think that some data are not of good quality or that the sensitivity identified in some strains or sexes is not relevant for humans, the lowest relevant LD50 value obtained should be used to conclude on classification. In this case category 1 is warranted.				
Observations from the United States				
Category 1 or 2 based on an LD_{50} range of 4.5-24 mg/kg. From a hazard communication/labeling perspective, it makes no difference whether the classification is Category 1 or Category 2: the label elements are the same. I understand that the distinction between Category 1 and Category 2 was included in the GHS to accommodate packing group issues in the transport sector?				

Table 3.1: Analysis of data supporting classification for acute toxicity (oral)

Acute toxicity (dermal)	**EU: category 3**	**Japan: category 3**	**New Zealand: category 1**	**USE PA: category 1**
Possible reasons leading to differences				
NZ Differences in the datasets used and differences in the application of the classification criteria: The Japanese data are not clear. New Zealand and the EU have similar data but New Zealand has study data with a lower value, therefore a higher classification. Japan and the EU consider ranges whereas New Zealand takes the conservative approach by using the lowest value. JP Differences in data sets used. There are so many LD50 data ranged from 44-483 mg/kg in rats and 300->2000 mg/kg in rabbit. FR Differences in the datasets used, differences in the interpretation of data and differences in the application of the classification criteria: The key study used by New-Zealand was not considered by Europe. The conclusion in Japan is based on the statistical calculation of LD50 in rats using pooling of studies whereas the conclusion in New-Zealand is based on the lowest value available among valid, well-performed tests. The conclusion in Europe seems to be based on the conversion of the classification obtained according to the previous regulation. "Toxic" has been converted into cat. 3 as proposed by the translation table of the European CLP regulation. However, in this case, direct conclusion on the basis of the data would have been Cat. 2.				
Proposal to reconcile differences				
NZ A discussion on application of classification criteria is required. The EU approach raises the question of if a range is used then what would be used for mixture calculation? Of Japan's approach it needs to be questioned, is the statistical calculation valid? New Zealand uses a conservative approach that takes the lowest value. JP Total 8 rat dermal LD50 data in EHC, ATSDR, and JMPR (counted separately by sex in some cases): 2 for 40-50 mg/kg, 4 for 63-120 mg/kg, 2 for 481(M)-483(F) mg/kg. 2 rabbit dermal LD50 data in EHC and IUCLID: 1 for 300 mg/kg, 1 for >2000 mg/kg. Rat data should be used for classification due to more sensitive. Almost data were in the range of category 2 (50-200 mg/kg). Therefore, category 2 will be suitable. Note: If most recent data will be used, which cited in JMPR (might be more reliable due to GLP study), rat dermal LD50 is ca. 480 mg/kg. This suggests category 3 (200-1000 mg/kg). FR Same comment as for oral acute toxicity. In this case classification in category 2 is proposed based on the range of LD50 that is only marginally below the cut-off for classification in category 1.				
Observations from the United States				
Category 1 based on an LD_{50} of 6 mg/kg in rats. Note that the GHS states that rabbits are the preferred species for classification in this case (not clear if EU is using rats or rabbits), and already includes guidance on conservative/protective values to be used when data from studies that give ranges instead of point values are used to classify *mixtures*.				

Table 3.2: Analysis of data supporting classification for acute toxicity (dermal)

Skin corrosion/irritation	**EU: -----**	**Japan: category 3**	**New Zealand: category 3**	**US EPA: -------**
Possible reasons leading to differences				
NZ Differences in the datasets used: For the EU no data are given. The data sets used by New Zealand and Japan agree. JP Differences in the datasets used. FR The discrepancy in classification may be explained from the absence of category 3 implemented in Europe.				
Proposal to reconcile differences				
NZ Category 3. Data exists to show skin irritation should be considered. JP In a recent (interim) review by APVMA (former NRA, cited by New Zealand) in Australia in Mar 1999 (http://www.apvma.gov.au/chemrev/downloads/parathionmethyl_tox.pdf), the descriptions are as follows: In dermal irritation studies in rabbits, undiluted technical parathion-methyl induced slight erythema (score, 1-2) and edema (incidence, 1/6) and these signs resolved by 48 h post treatment. Technical parathion-methyl (with a 4-h contact time) is classified as a slight skin irritant (Cuthbert & Carr, 1986a). Parathion methyl instilled into the conjunctival sac was judged to be slightly irritating to the eye (Cuthbert & Carr, 1986a). The response of irritation did not seem to reach to category 3 by GHS criteria. Therefore, "not classified" will be suitable. FR Available data don't give many numerical results that can be compared to the criteria to conclude on classification. Effects are clearly reversible. The most informative reported study mentions "Very slight-moderate erythema was noted at 1h and 24h and 1/6 rabbits showed slight edema at 1h only". Therefore, mean value for edema grading at 24, 48 and 72h equals zero for each animal and mean value for erythema grading at 24, 48 and 72h cannot exceed 1 in any animal (assuming a 24h grading of 1 to 3 and absence of effect thereafter). No classification should therefore apply according to the criteria.				
Observations from the United States				
Not classified. Data summary indicates a maximum score of 2, and 0.5 at 72 hours. Under the current EPA system, no pictogram, signal word or hazard statement is required. Point 3 in summary document argues for no classification. Agree that EU classification may have been based on policy decision not to include Category 3 in its GHS implementation scheme.				

Table 3.3: Analysis of data supporting classification for skin corrosion/irritation

Eye irritation	**EU: ------**	**Japan: category 2**	**New Zealand: category 2**	**US EPA: category 2B**
Possible reasons leading to differences				
NZ Differences in the datasets used: The EU does not use any data. The data used by New Zealand and Japan agree. New Zealand only has one Category 2 classification, meaning that eye irritation is not divided into two categories. JP Differences in the datasets used.				

FR	----------
Proposal to reconcile differences	
NZ	Category 2B. Data exists to show eye irritation should be considered.
JP	In a recent (interim) review for micro-encapsulated formulation (CS 450 g/L) by APVMA (former NRA, cited by New Zealand) in Australia in Mar 1999 (http://www.apvma.gov.au/chemrev/downloads/parathionmethyl_tox.pdf), the descriptions are as follows: Minimal dermal irritation (grade 1 erythema) was recorded at 1 and 24 h in some rabbits (2/6) and slight ocular effects were observed at 1 h. However, this is for apecial formulation of the compound and treatment length was short. It is difficult to classify due to shortage of information.
FR	Available data don't give many numerical results that can be compared to the criteria to conclude on classification. Effects are clearly reversible. The most informative reported study mentions "Slight redness was noted in all animals at 1 h and persisted in 1 rabbirt at 24 h. All eyes had returned to normal by 48h". Therefore, mean value for corneal opacity, iritis and chemosis grading at 24, 48 and 72h equals zero for each animal and mean value for conjunctival redness grading at 24, 48 and 72h cannot exceed 0.33 in any animal (assuming a 24h grading of 1 and absence of effect thereafter in 1 animal only). No classification should therefore apply according to the criteria.
Observations from the United States	
	Borderline Category 2B based on rabbit study showing irritation clearing after 7 days. EPA review summary did not include scores in tables, so more detailed analysis of the data would be required to see if "not classified" would be the appropriate conclusion.

Table 3.4: Analysis of data supporting classification for eye irritation

Mutagenicity	**EU: -------**	**Japan: category 2**	**New Zealand: ------**	**USEPA: ----------**
Possible reasons leading to differences				
NZ	Differences in the application of the classification criteria: New Zealand has interpreted ATSDr data as inconclusive whereas Japan has interpreted it as category 2. The data source the EU used is not indicated.			
JP	Differences in datasets used.			
FR	Difference in interpretation of the data seems to be the probable cause for diverging classification.			
Proposal to reconcile differences				
NZ	Discussion required on interpretation of data.			
JP	There are conflicting results on genotoxicity on this compound. In a recent (interim) review by APVMA (former NRA, cited by New Zealand) in Australia in Mar 1999 (http://www.apvma.gov.au/chemrev/downloads/parathionmethyl_tox.pdf), the descriptions are as follows: Published reviews of gene mutation assays (Wildemauwe et al, 1983) and short-term genotoxicity tests (Waters et al, 1980) concluded that parathion-methyl was not genotoxic, while the EHC Monograph No. 145 (IPCS, 1993) observed that parathion-methyl had produced positive results in many *in vitro* assays, but equivocal results in *in vivo* studies. There is no unequivocal evidence, particularly from recent work, that parathion-methyl is a genotoxin. Conclusion by ATSDR (2001) is as follows: The available evidence is inconclusive, and no determination regarding the potential			

	genotoxic risks of methyl parathion exposure for humans can be made. Conclusion by old IARC (vol 30, 1983) is as follows: There is sufficient evidence that methyl parathion is mutagenic in a variety of cellular systems, but insufficient evidence that it is mutagenic in mammals. After this review, several positive findings in vivo have been published. Based on the review from APVMA and ATSDR, "not classified" will be suitable due to no unequivocal positive result in vivo.
FR	Human data are considered to have important limitations in terms of small size, characterisation of exposure and potential co-exposures and are not sufficient to support the classification. Available data in *in vivo* studies in animals result in both positive and negative outcomes. The level of details presented here and in the ATSDR Toxicological Profile (2001) are not sufficient to decide based on the quality and on the design (e.g. doses, harvest time) of the studies, which studies should be given a more important weight. Conclusion on classification can therefore not be proposed.
Observations from the United States	
	Not classified based on data base showing a lack of mutagenic activity.

Table 3.5: Analysis of data supporting classification for mutagenicity.

Reproductive toxicity	**EU: -------**	**Japan: category 2**	**New Zealand: category 2 + effects on lactation**
Possible reasons leading to differences			
NZ	Differences in the application of the classification criteria: It is not clear which specific studies were used by Japan for their classifications. The EU NOELs for developmental reproduction were very low but no classification was assigned.		
JP	Differences in the interpretation of the data: Japan did not focus on lactation effect in the project.		
FR	Differences in data sets used and differences in the interpretation of the data: Japan only referred directly to one study but they mention reviews from ATSDR and JMPR. Taking into account these reviews the data set used by Japan and New Zealand seems relatively similar. The key studies selected by Japan and New-Zealand for reproductive toxicity are different. Both Japan and Europe conclude that methyl parathion has a developmental effect in presence of maternal toxicity but the interpretation of the severity of maternal toxicity and its relationship with effects on development differs.		
Proposal to reconcile differences			
NZ	New Zealand, EU and Japan all have data to support Category 2. New Zealand and the EU have data to support lactation. It is unclear why the EU does not classify when the data meets the criteria.		
JP	In a recent (interim) review by APVMA (former NRA, cited by New Zealand) in Australia in Mar 1999 (http://www.apvma.gov.au/chemrev/downloads/parathionmethyl_tox.pdf), following summary has been made on reproductive and developmental toxicity: In a three-generation reproduction study using Wistar rats up to 50 ppm in the diet, the NOEL for reproductive effects was set at 2 ppm (0.2 mg/kg bw/day) based on reduced pup survival at the next higher dose tested (10 ppm). In a GLP study, parathion-methyl at doses up to 3 mg/kg bw/day were administered to female rats on days 6 to 15 post-coitum. Fetal growth retardation with attendant ossification anomalies were observed at the 2 highest doses tested namely, 1 and 3 mg/kg bw/day. Therefore, the maternal NOEL is 1 mg/kg bw/day and the feto/embryotoxicity NOEL is 0.3 mg/kg bw/day. The reviews from EHC, JMPR, ATSDR, and APVMA suggest embryo toxicity of this compound. Therefore, category 2 will be		

suitable.
APVMA summarised that "A three-generation reproduction study using Wistar rats fed on parathion-methyl up to 50 ppm in the diet revealed reduced pup survival during lactation at all doses tested. This outcome suggests parathion-methyl is secreted into milk." However, it might be not definitive evidence of lactation effect. So, lactation effect may be not suitable.

FR Available data show that methyl parathion does not induce developmental effects in rabbit teratogenicity studies. In rats, several studies report adverse effects on fetus or pups at doses inducing maternal toxicity. Although it is unlikely that a slight decrease of maternal body weight gain accompanied with clinical signs can explain observation of resorptions (Gupta 1984) the absence of information on the severity and intensity of both maternal and developmental effects in these studies make it difficult to conclude on the potential relationship between these effects.
In 2 studies, however, developmental effects were observed in absence of maternal toxicity according to the data presented: in the 3-generation study (Löser, Eiben 1982) a decrease in pup survival was observed at the median dose whereas decrease in maternal body weight occurred only at the high dose. In one of the rat teratogenicity study (Becker 1991) fetal growth retardation was observed at the median dose in absence of a maternal effect.
On this basis, classification in category 2 is warranted although more information is needed on the different studies to have a definite position.

Table 3.6: Analysis of data supporting classification for reproductive toxicity

Target organ toxicity	**EU**	**Japan**	**New Zealand**
single exposure	--------	**Category 1**	---------
Repeated exposure	**Category 2**	**Category 1**	**Category 1**
Possible reasons leading to differences			
NZ Differences in the datasets used and differences in the application of the classification criteria: It is unclear what data Japan used. There are some differences in the data used by New Zealand and the EU. Dermal information is the same. Differences in interpretation of "significant effects in humans" vs "harmful to human health" seem to be crux of the differences.			
JP Differences in the datasets used: No human data was used in EC.			
FR Differences in datasets used: STOT-single: no acute data reported by the European Commission. STOT-repeated: The different datasets are consistent although they differ a lot in the level of details available. Differences in the interpretation of the data: STOT-single: not possible to say. Rationale for classification for STOT-single was presented only by Japan. However, similar conclusion by Japan and New-Zealand indicate a similar analysis of the database. STOT-repeated: in all cases, inhibition of cholinesterase activity and its adverse consequences are identified as the critical effects of methyl parathion. Differences in the application of the classification criteria: STOT-single: not possible to say. Rationale for classification for STOT-single was presented only by Japan. However, similar conclusion by Japan and New-Zealand indicate a similar analysis of the criteria.			

	STOT-repeated: the conclusion by Japan is based on the dose inducing the critical effect whereas supporting documentation from the European Commission only provides NO(A)EL.
Proposal to reconcile differences	
NZ	To come to reconciliation it would be of value for the EU to provide details as to why the retinal changes, peripheral neuropathy and inhibition of cholinesterase are not considered "significant" for humans. This may be based on mechanism of action, degree of cholinesterase inhibition, inhibition only being confined to plasma cholinesterase or other reasons.
JP	Based on the human findings/experiences and mode of action of this compound, nerve system should be assigned as target organ category 1.
FR	STOT-single: available data on acute toxicity of methyl parathion indicate that it induces effect in humans. However, it is based on case reports of fatal intoxications. These effects are therefore already taken into account by the acute toxicity classification of methyl parathion in category 1. In the same way, acute animal data indicate cholinergic effects in the range of dose inducing lethality and a classification for STOT-single is therefore not warranted. STOT-repeated: inhibition of cholinesterase activity was accompanied by histological evidence of neuronal degeneration at doses triggering classification in category 1 (Daly, 1992). Classification in category 1 is therefore indicated.

Table 3.7: Analysis of data supporting classification for target organ toxicity

MERCURY COMPOUND: THIOMERSAL

Note applicable to Tables 4.1 to 4.11:
The European system used a group entry for all organic mercury compounds in the absence of data on individual organic mercury substance.

Acute toxicity (oral)	**EU: category 2**	**Japan: category 3**	**New Zealand: category 2**
Possible reasons leading to differences			
NZ	Differences in data sets used: Japan uses different data to that used by the EU and New Zealand. The EU has lower LD_{50} values than New Zealand, 16-40 mg/kg and 40-91 mg/kg respectively, but both are classified as Category 2. Japan has a LD_{50} of 75 and a Category 3 classification. Category 2 covers the following range 5-50 mg/kg New Zealand data was for ethylmercury; Japan did not define the substance they classified on; One EU study was on methylmercury, the other just gave mercury content but does not state the form.		
CH	Differences in datasets used: (J) LD50 rat 75 mg/kg [Pesticide Chemicals Official Compendium (PCOC), Association of the American Pesticide Control Officials, Incorporated, Topeka, Kansas, 1966, pp. 1130-1131(aus RTECS 2004)] (NZ) US National Toxicology Program report (1991). Executive summary of safety and toxicity information:((0-carboxyphenyl)thio) ethylmercury sodium salt (CAS no. 54-64-8): LD50 rat 40 mg/kg [Original study? (Lin et al?)]. Additional evidence: reports on human toxicity as a result of accidental injection or oral ingestion of high doses, causing death or symptoms of severe organic mercury poisoning. (EC) (1) Yasutake et al (1991): mice single dose (methyl-Hg): LOAEL male 16 mg Hg/kg: 4/6 male		

	died (decreased renal function); LOAEL female 40 mg/kg Hg/kg: 4/6 female died [no LD50 calculated, but: LOAEL male und female in Cat. 2 . Highest Dose tested in Cat.2 shows more than 50% mortality]. (2) Lin et al, 1975: 25 mg methylmercury/kg bw in adult rats; 40 mg methylmercury/kg bw in young rats
JP	Differences in data sets used and differences in the interpretation of the data: RTECS, HSDB, ChemID Plus and SAX describe LD50 rat oral is 75 mg/kg. Rat LD50 40 mg/kg as unreported route is mentioned in RTECS and ChemID Plus. The web page (http://ntpserver.niehs.nih.gov/htdocs/Chem_background/ExecSumm/Thiomersal) is not found for US NTP report 1991 from New Zealand, but report 2001 is in the other NTP site (http://ntp.niehs.nih.gov/ntp/htdocs/Chem_Background/ExSumPdf/Thimerosal.pdf). However, no information is avairable on rat oral LD50 in it. In EC evaluation, 25 mg methylmercury/kg bw is equivalate 47 mg thiomersal/kg in adult rats (thiromersal MW 404.8, methylmercury MW 215.6). 40 mg methylmercury/kg bw is equivalate 75 mg thiomersal/kg in young rats. Difinitions of adult and young are unclear. If these data will be merged, LD50 will be more than 50 mg thiomersal /kg.
Proposal to reconcile differences	
NZ	Category 2. It is assumed that since the Japanese data source is RTECS that the choice of LD_{50} was not based on the quality of data i.e., that it met the test guidelines and was done under GLP. Taking a precautionary approach the lowest available values should be used where it cannot be shown that the data for a higher category is not of a sufficient quality.
CH	Category 2: The data presented by NZ and EC support this classification (LD50<50mg/kg bw).
JP	No clear data source of LD50 rat oral 40 mg/kg was found in thiomersal itself. Almost information sources cite 75 mg/kg as rat oral LD50. Therefore, data suggests that category 3 will be suitable.

Table 4.1: Analysis of data supporting classification for acute toxicity (oral)

Acute toxicity (dermal)	**EU: category 1**	**Japan: -------**	**New Zealand: -------**
Possible reasons leading to differences			
NZ	For New Zealand and Japan there are no data available. The EU has no direct quantitative data but have used expert judgement based on data from other organic mercury substances.		
CH	Differences in datasets used and differences in the application of the classification criteria: (J) (NZ): no data = not classified (EC) Available information on absorbtion (mouse/ occupational case study) has been considered. (EC) no test data available for dermal exposure route. However, organic mercury compounds were classified as **Cat.1** (ATE < 50 mg/kg bw) in a weight of evidence approach. The known acute toxicity of organic mercury together with information on high absorption rates (e.g. phenylmercuric acetate; dimethylmercury) was taken into account for classification.		
JP	Differences in interpretation of the data: EC assigns category 1 based on the information from organic mercuries. Thiomaersal will be absorbed through the skin, resulting in death. However, category 1 (<50 mg/kg for skin) will be overestimate. Because, LD50 rat subcutaneous is 98 mg/kg, and LD50 mouse iv or sc is 45 mg/kg or		

66 mg/kg, respectively. These data might suggest dermal LD50 will be more then 50 mg/kg (category 2 or more).

Proposal to reconcile differences

NZ Further discussion required with respect to expert judgement and how this is applied. Also discussion on how to use "read-across" would be of value.

CH ----------

JP HSDB describes "Ten of 13 infants exposed to (repeated) topical applications of a thiomerosal tincture 0.1% for the treatment of exomphalos died." RETCS reports 60 mg/kg/4W intermittent (route: intraaural) as LDLo (lowest published lethal dose) in child. Based on this information, category 2 will be suitable, though sufficient review of original paper(s) will be needed.

Table 4.2: Analysis of data supporting classification for acute toxicity (dermal)

Acute toxicity (inhalation)	**EU: category 2**	**Japan: ---------**	**New Zealand: ---------**

Possible reasons leading to differences

NZ For New Zealand and Japan there are no data available. The EU has used data from human and animal studies on organic mercury substances, the animal data are quantitative but do not follow std OECD test guideline and only limited information is available. There is no information regarding the reliability of the data used by the EU.

CH Differences in datasets used and differences in the application of the classification criteria:

(J), (NZ): no data = not classified
(EC) Available information from case studies (occupational exposure) has been considered.

(EC) no test data available for inhalation. However, organic Hg-Compounds were classified as **Cat.2** in a weight of evidence approach. Although no studies on absorption of organic mercury by inhalation are available, case studies of occupational exposure (e.g. diethylmercury vapour, unspecified alkyl mercury compounds) provide indirect evidence that organic mercury, that is known to be acute toxic, is absorbed readily through the lung.

JP Difference in the interpretation of the data:

EC assigns category 2 based on human experience and animal data with organic mercury (not thiomersal). Human experience is not lethal data. Animal data show LD50-like values (27-28 mg/m3 Hg0 vapour) which might be equivalent to 55 mg/m3 thiomersal. Thiomersal will be absorbed by inhalation, causing toxic effect including death. However, It is difficult to estimate LD50 value because of different vapour pressure, absorption, and toxicity, etc between thiomersal and other organic mercury compounds.

Proposal to reconcile differences

NZ Further discussion required with respect to expert judgement, how this is applied and assessing quality of data.

CH ----------

JP There is no data on this specific compound. However, some regulatory bodies (eg., ACGIH, NIOSH) will regard thiomersal as a mercury (organo) alkyl compound. NIOSH established 2 mg Hg/m3 as IDLH (Immediately Dangerous to Life or Health) for mercury (organo) alkyl compounds, based on lethal information from organo alkyl mercuries (http://www.cdc.gov/niosh/idlh/merc-hg.html). For hazard communication in regulatory purpose, category 2 will be suitable like a classification by EC.

Table 4.3: Analysis of data supporting classification for acute toxicity (inhalation)

Skin corrosion/irritation	**EU: -------**	**Japan: -------**	**New Zealand: category 1C**
Possible reasons leading to differences			
NZ Differences in datasets used: No data are available for Japan and the EU. New Zealand has used data from a reliable reference source in conjunction with data from other sources and made an expert judgement based on weight-of-evidence.			
CH Differences in datasets used: (J), (EC): no data = not classified (NZ): Pesticide Chemicals Official Compendium (PCOC), Association of the American Pesticide Control Officials, Incorporated, Topeka, Kansas, 1966, pp. 1130-1131. The dry powder of ((o-carboxyphenyl)thio) ethylmercury sodium salt is reportedly caustic and has produced a chemical burn on skin contact. Prolonged contact with a 5% solution of ((o-carboxyphenyl)thio) ethylmercury sodium salt has produced marked irritation. Concentrations less than 1% ((o-carboxyphenyl)thio) ethylmercury sodium salt should cause little or no reaction. = Cat. 1C			
JP Differences in the interpretation of the data: Human experiences provided from New Zealand are difficult for evaluation. An experience from a patient might be due to the action of thiomersal on aluminium. Report of the Association of the American Pesticide Control Officials was shortage of information (e.g., no information of number of people applied, vehicle used, duration of application, degree of reaction).			
Proposal to reconcile differences			
NZ ---------- CH Weight of evidence issue. JP ----------			

Table 4.4: Analysis of data supporting classification for skin corrosion/irritation

Eye irritation	**EU: ----------**	**Japan: category 2B**	**New Zealand: category 1**
Possible reasons leading to differences			
NZ Differences in datasets used: Japan uses different data to that used by New Zealand. As with skin classification New Zealand used a reliable reference source and expert judgement based on a weight-of-evidence. Part of the weight-of-evidence approach was to consider the skin classification; unless reliable data are available to the contrary, a substance which is a skin corrosive should also be classed as an eye corrosive. This is in-line with the OECD tiered approach to assessment of skin and eye irritation/corrosion.			
CH Differences in datasets used: (J) Qualitative description "mild irritant" from RTECS 2004 (EC): no data = not classified (NZ): Pesticide Chemicals Official Compendium (PCOC), Association of the American Pesticide Control Officials, Incorporated, Topeka, Kansas, 1966, pp. 1130-1131. The dry powder of ((o-carboxyphenyl)thio) ethylmercury sodium salt is reportedly caustic and has produced a chemical			

	burn on skin contact. Prolonged contact with a 5% solution of ((o-carboxyphenyl)thio) ethylmercury sodium salt has produced marked irritation. Concentrations less than 1% ((o-carboxyphenyl)thio) ethylmercury sodium salt should cause little or no reaction. = Cat. 1C
JP	Differences in datasets used: Classification was made based on the rabbit data (RTECS) in Japan. RTECS describes standard eye draize test was mild in rabbit using a dose of 8 ug. No further information is avairable (application time, vehicle, definition of "mild"). On the other hand, the classification was from the classification in skin irritation in New Zealand.
Proposal to reconcile differences	
NZ	----------
CH	• Information from PCOC (NZ): Weight of evidence issue • Qualitative Description "mild irritant"from RTECS (J) is not necessarally linked to the GHS classification terminology" for Cat.2B.
JP	Based on the limited animal data, thiomersal will cause eye irritation. Though it is unclear whether the degree will meet the criteria of category 2B or not, category 2B might be useful for hazard communication.

Table 4.5: Analysis of data supporting classification for eye irritation

Note to Table 4.5: New Zealand applied a read-across from the skin irritation classification to classify for the eye irritation.

Respiratory/skin sensitization	**EU: -------**	**Japan: category 1**	**New Zealand: category 1**

Possible reasons leading to differences

NZ Differences in datasets used: No data are given for the EU. The lack of data leads to no classification. Japan and New Zealand information indicates sensitization in humans

CH skin sensitization:
Differences in datasets used: (J): DFGOT vol.15(2001), there were several reports which showed skin sensitization in human and guinea pig.
(NZ): Because ((o-carboxyphenyl)thio) ethylmercury sodium salt has been found to be a common cause of allergic contact sensitization in the United States, the North American Contact Dermatitis Research Group (NACDG) has introduced ((o-carboxyphenyl)thio) ethylmercury sodium salt in the "standard" or "screening" patch test tray [Fisher, 1981]. In their 1972 study, the NACDG patch tested 1200 subjects in North America with 16 allergens. ((o-Carboxyphenyl)thio) ethylmercury sodium salt was found to be one of the seven most common sensitizers [NACDG, 1973]. Furthermore, it has been reported that ((o-carboxyphenyl)thio) ethylmercury sodium salt is one of the most common sensitizers in children because of its widespread use in topical medication [Fisher, 1981]. The significance of positive patch test reactions to ((o-carboxyphenyl)thio) ethylmercury sodium salt is uncertain because many individuals with hypersensitivity demonstrated by patch tests do not have clinically detectable reactions to ((o-carboxyphenyl)thio) ethylmercury sodium salt-containing products [Cox et al., 1988].
(EC): no data presented

JP Differences in the interpretation of the data.

Proposal to reconcile differences

NZ Contact sensitization: Category 1
Evidence in humans that thiomersal is a dermal sensitizer and therefore should be considered as such even though test data using test guidelines is not available. Exploration of what criteria are used when assessing whether a data source is reliable or not would be of value.

CH **Cat.1:** According to the GHS (3.4.2.2.2.1) positive data from patch testing, normally obtained in more than one dermatology clinic provide sufficient evidence for classification (High sensitization rates demonstrated).

JP The German evaluation concuded that “Thiomersal has a pronounced sensitization potential which is mainly the result of its use as a preservative in vaccines; in most cases this leads to only latent asymptomatic sensitization. Clinically relevant contact allergy can also develop, however, after topical use. Positive results in more or less valid experiments with animals also confirm its sensitization capacity. Thiomersal is therefore designated with “Sh”.” (DFG Occupational Toxicant, vol. 15, 2001). Recent publication from Canada mentioned that “Of 2252 subjects patch-tested for thiomersal, positive reactions were observed in 102 individuals (4.53%) (Freiman et al., 2003). The authors concluded that “In agreement with previous reports, we conclude that even though positive reactions to thiomersal are frequent, very few seem to be clinically relevant.” (Freiman et al., Patch testing with thiomersal in a Canadian center: an 11-year experience, Am J Contact Dermat. 14, 138-143, 2003).
Based on the above evaluation, category 1 will be suitable for skin sensitization.

Note: National Advisory Committee on Immunization in Canada recommended that “A previous

episode of anaphylaxis attributed to thiomersal is an absolute contraindication to the use of thiomersal-containing vaccines. While at least one such event has been described, the link to thiomersal was not proven. Prior history of erythema multiforme, Stevens-Johnson syndrome or toxic epidermal necrolysis from thiomersal exposure would also be an absolute contraindication to future exposure. Thiomersal has never been reported to cause such reactions. If there is a documented history of a delayed hypersensitivity reaction to thiomersal (as manifest by a large local reaction or an eczematous rash) or a positive patch test reaction to thiomersal, immunization with thiomersal-containing vaccines can proceed, but individuals should be advised that long-lasting local or systemic cutaneous reactions can occur. They should report any reaction of concern following immunization so that it can be managed appropriately." (Can Commun Dis Rep. 33, 1-13, 2007, http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/07pdf/acs33-06.pdf).

Table 4.6: Analysis of data supporting classification for respiratory skin sensitization

Mutagenicity	**EU: category 1**	**Japan: category 2**	**New Zealand: category 2**
Possible reasons leading to differences			
NZ	The EU has proposed Category 2, which has not yet been accepted. If accepted it will bring the EU into agreement with Japan and New Zealand.		
CH	No diverging outcomes. According to the supporting documentation of the EC a proposal for classification as Cat.2 has been already agreed at the technical level (hand over to ECHA, decision pending).		
JP	Differences in datasets used: Data from Japan is for thiomersal itself, but not from New Zealand and EC (for alkyl mercury). "A in vivo small core examination" in Japan should be read "a in vivo micronucleus test".		
Proposal to reconcile differences			
NZ	Category 2 Japan and New Zealand have assigned Category 2. EU has proposed a classification equivalent to Category 2. Thus there is agreement on classification at a technical level. Only require legal change to be implemented.		
CH	Category 2		
JP	NTP 2001 report mentioned that "Thimerosal was evaluated in *in vivo* studies on chemically induced aneuploidy in mouse bone marrow and spermatocytes in the context of laboratory validation studies sponsored by the European Community. Thimerosal dosing resulted in a weakly positive effect in the mouse micronucleus assays conducted in one of the participating laboratories (Marrazzini 1994). However, no effect was observed in the mouse micronucleus assay conducted at the other laboratories participating in the validation testing (Leopardi 1993; Miller 1992; Adler 1993). Thimerosal produced no chromosomal aberrations in mouse somatic and germinal cells at any of the laboratories involved in these studies. Based upon these results, thimerosal was not classified as an aneugen. The literature search did not locate any publications where thimerosal was assessed in any other genetic toxicology test." (http://ntp.niehs.nih.gov/ntp/htdocs/Chem_Background/ExSumPdf/Thimerosal.pdf) However, ECETOC task force on aneuploidy concluded that results from micronucleus test in vivo were inconclusive (Aaardema et al., Mutat Res., 410, 3-79, 1998). In addition, there is another paper		

that showed weak positive effect in mouse bone marrow micronucleus test (appeared in RTECS; Gudi et al., Environ. Mol. Mutagen., 20, 106-116, 1992). Positive effects reported by Marrazzini 1994 and Gude 1992 were weak and their route of administration was ip injection. The results are supported by positive in vitro micronucleus test.

It might be better for regulatory purpose that inorganic and organic mercury compounds will be somatic cell mutagen (GHS category 2), based on the comments from New Zealand and EC, though data are limited. At least, thiomersal will be category 2, though the data are inconsistent.

Table 4.7: Analysis of data supporting classification for mutagenicity

Carcinogenicity	**EU: -------**	**Japan: category 2**	**New Zealand: category 2**
Possible reasons leading to differences			
NZ The EU has proposed Category 2, which has not yet been accepted. If accepted it will bring the EU into agreement with Japan and New Zealand.			
CH No diverging outcomes. According to the supporting documentation of the EC a proposal for classification as Cat.2 has been already agreed at the technical level (hand over to ECHA, decision pending).			
JP Differences of interpretation of the data: RETCS mentions as follows: Tumrigenic effects, Rat, TDLo-Route: Subcutaneous; Dose: 104 mg/kg/1Y intermittent (1971), Toxic effects: Tumorigenic-Neoplastic by RTECS criteria, Uterine tumors, Tumors at site of application. NTP 2001 report mentions as follows: In the previously discussed toxicology and carcinogenesis study of chemicals found in vaccines, (Mason 1971) Fischer rats were subcutaneously injected twice-weekly with thimerosal at doses ranging from 30 to 1000 ⌈g /kg for 1 year. Control rats were either untreated (negative control), or treated with nickel which is known to induce local inflammatory reactions (positive control). Animals were weighed weekly and autopsied at either 12 or 18 months after initial injection. All animals with spontaneous deaths, moribund, or with gross organ pathology had organs examined histologically as well as those chosen for routine examination. Histological observations included findings of lung tumors at a similar incidence to negative controls or at lower incidence than positive controls. Thimerosal-injected animals demonstrated a dose-related inhibition of spontaneous interstitial cell tumors of the testicles. At the highest dose, 4 of 27 male rats developed interstitial cell tumors; this was a decrease from 100% in control animals to 14.8% ($p < 0.01$). (http://ntp.niehs.nih.gov/ntp/htdocs/Chem_Background/ExSumPdf/Thimerosal.pdf)			
Proposal to reconcile differences			
NZ Category 2 Japan and New Zealand have assigned Category 2. EU has proposed a classification equivalent to Category 2. Thus there is agreement on classification at a technical level. Only require legal change to be implemented.			
CH Category 2.			
JP Methylmercury was claqssified in Group 2B by IARC. Though thiomersal is ethylmercury compound, GHS category 2 will be better based on the expansion of IARC classification.			

Table 4.8: Analysis of data supporting classification for carcinogenicity

Reproductive toxicity	**EU: -------**	**Japan: category 1B**	**New Zealand: category 1 + effects on lactation**

Possible reasons leading to differences

NZ Differences in datasets used: Japan and New Zealand have based their Category 1 classification on the '*mercury and mercury compounds*" listing in Cal EPA as reproductive treatments.
The EU have reviewed study data but it isn't clear what they are proposing.

Japan and New Zealand used the same source which is based on information on a variety of mercury forms. EU data appears to be methylmercury only.

CH Lactation:
Differences in datasets used:
(J) not classified
(NZ) : Ilback N-G. Toxicology Letters, Vol. 58, No. 2, pages 149-158, 33 references, 1991. "The authors conclude that prenatal or lactational exposure to methylmercury adversely affects immune system development in newborn rats. " [TOXLINE]
(EC): data on migration into breast milk (several studies). Evidence of damage to the central nervous system was found in children exposed to methyl-mercury through the breast milk (Amin-Zaki et al., (1979)

Reproductive toxicity: No diverging outcomes. According to the supporting documentation of the EC a proposal for classification as Cat.1 (development) has been already agreed at the technical level (hand over to ECHA, decision pending).

JP Differences in datasets used:

Lactation effect was not considered in the classification by Japan (out of target in the project).

Proposal to reconcile differences

NZ Japan and New Zealand agree. EU appears to be undecided so no comment can be made.

CH **Cat. 1** (consensus)
Effects on Lactation: data presented by NZ and EC

JP Thiomersal showed embryo and fetal lethality in rat or rabbit administered 6-18D of pregnancy by ip injection or ocular application. There were no teratological effects observed (RTECS). In addition to this finding, there are several evidence of reproductive effects by mercury and mercury compounds including alkyl mercury (see documentation from New Zealand and EC).

In a cohort study, there is no convincing evidence that early exposure to thiomersal-containing vaccines had any deleterious effect on neurologic or psychologic outcome (Heron et al., 2004, http://pediatrics.aappublications.org/cgi/reprint/114/3/577 ; Thompson et al., N Engl J Med., 357, 1281-1292, 2007). National Advisory Committee on Immunization in Canada concluded that the weight of evidence to date clearly refutes an association between thimerosal and neurodevelopmental disorders (Can Commun Dis Rep. 33, 1-13, 2007, http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/07pdf/acs33-06.pdf). However, the scientific evidence is not yet sufficiently strong to provide the same level of assurance for thiomersal-containing vaccines for use in pregnant women or the premature or low birth weight infant (Clemment, Vaccine, 22, 1854-1861, 2004). Recent report from meeting of global advisory committee on vaccine safety mentioned that GACVS remains of the view that there is no evidence supporting any change in WHO's recommendations for thiomersal-containing vaccines and the vaccination of low-birth-weight infants where indicated (Weekly

epidemiological record, 83, 285-292, 2008, http://www.who.int/wer/2008/wer8332.pdf). Therefore, category 2 will be suitable for thiomersal in GHS reproductive toxicity. (Note. This is a hazard classification for thiomersal itself, not for thiomersal-containing vaccines).

Assignment of effect on lactation will be suitable, based on the documentation from EC.

Table 4.9: Analysis of data supporting classification for reproductive toxicity

Target organ toxicity	**EU**	**Japan**	**New Zealand**
single exposure	--------	**Category 2**	---------
Repeated exposure	**Category 2**	**Category 1**	**Category 1**
Possible reasons leading to differences			
NZ Differences in datasets used and differences in application of the classification criteria: Japan and New Zealand have based their classification on limited data. The EU has a number of studies using different species and routes that have been reviewed. The differences in classification appear to be due to different calling levels for "significant toxicity" and "harmful to human health" Japan doesn't indicate whether data are actually for Thiomersal or other organic mercury based substance(s). New Zealand used data for ethyl and methyl mercury to classify. EU information indicates mercury but not what form.			
CH Differences in datasets used: Single exposure: (J) The substance was classified as Category 2 (blood system, kidneys, central nervous system, skin) based on the reports (2 cases) concerning humans in HSDB(2004). (NZ) and (EC): did not classify (no data presented) Repeated exposure: (J) In ACGIH-TLV (2004) it is supposed that repeated exposure of alkyl mercury compounds has effects on the central nervous system. (NZ) Magos et al 1985 Archives of Toxicology, Vol. 57, No. 4, pages 260-267: five daily doses of 8.0 milligrams per kilogram (mg/kg) methylmercuric-chloride (115093) or 8.0 or 9.6mg/kg ethylmercuric-chloride. Selected animals were killed 3 or 10 days after the last dose, and blood, brain, and kidney total mercury (the sum of inorganic and organic mercury), inorganic mercury (7439976), and organic mercury concentrations were determined. Brain, spinal cord, and renal tissue were examined for histopathological changes. Both compounds caused body weight loss and coordination disorders. On an equimolar basis, ethylmercury caused significantly greater weight losses; however, ethylmercury caused less severe coordination disorders. The concentration of total mercury and organic mercury was higher in the blood of ethylmercury treated rats and in the brain and kidney of methylmercury treated rats. The proportion of inorganic mercury was higher after ethylmercury treatment. The 9.6mg/kg dose of ethylmercury caused higher blood and brain total mercury concentrations than the 8.0mg/kg dose, but did not increase the kidney concentration above that from the 8.0mg/kg dose. The effects of methylmercury and ethylmercury on the dorsal root ganglia were similar. Methylmercury caused more extensive damage in the granular layer of the cerebellum. (EC): Fowler 1972: Rat; 0.08 mg Hg/kg bw as methyl mercury (diet); 12 wk; Renal effects: ultrastructural changes (cytoplasmic masses containing ribosomes and bundles of smooth			

endoplasmic reticulum) in kidney proximal tubule cells of female rats, despite the normal appearance of the glomeruli at light microscope.
Mitsumori 1981: Mouse (ICR); 3.1 mg Hg/kg bw (diet); 26 wk; Increased mortality in both males and females.
Hirano 1986: Mouse; 0.6 mg Hg/kg bw (diet); 26 wk; Renal effect: degeneration of the proximal tubules characterised by nuclear swelling and vacuolation of the cytoplasm.
Mitsumori 1990: Mouse (B6C3F1); 104 wk; 0.13 mg Hg /kg bw (diet): epithelial cell degeneration and interstitial fibrosis in kidney, with on-going regeneration of the tubules present
Hirano 1986: Mouse, 0.11 mg Hg/kg bw; 104 wk; Epithelial cell degeneration and interstitial fibrosis in kidney

JP Differences in datasets used and differences in interpretation of the data:

Animal data and/or human findings.

Based on information from alkyl mercury or not.

Proposal to reconcile differences

NZ Without information on which form of mercury Japan and EU used it is not possible to put forward a proposal.

CH single exposure: weight of evidence issue
repeated exposure: **Cat.1**: the presented supporting information shows severe effects at low doses (the Cat. 2 EC-classification is listed as a minimum classification(*) in the CLP-Regulation 1272/2008).

JP ----------

Table 4.10: Analysis of data supporting classification for target organ toxicity

Hazardous to the aquatic environment	**EU**	**Japan**	**New Zealand**
Acute	**Category 1**	**----------**	**---------**
Chronic	**Category 1**	**----------**	**Category 2**

Possible reasons leading to differences

NZ Differences in datasets used: Japan and the EU have no data. New Zealand has used a study from the USEPA ecotox database.

CH Differences in datasets used:

Acute
(JP) No classification due to lack of data
(NZ) Key study for acute toxicity: **48-hr LC_{50} in fish 2.13 mg/L** (Species: Lake trout *Salvelinus namaycush***)**; 48-hr LC_{50} in fish 5.65 mg/L (Species: Channel catfish *Ictalurus punctatus*); Assumption: No 96-hr LC_{50} data available, therefore we have used 48-hr fish; data source: ECOTOX; reference: Willford, W.A. (1966) Toxicity of 22 Therapeutic Compounds to Six Fishes. Source: Invest.Fish Control No.18, Resourc.Publ.No.35, Fish Wildl.Serv., Bur.Sport Fish.Wildl. U.S.D.I., Washington, DC :10 p.
(EC) No data and no rationale for the classification have been provided. From the summary record from the meeting 13 - 15 March 1996 of the Commission Working Group on the Classification and Labelling of dangerous substances: Environmental Effects, it can be concluded that Thiomersal was classified together with mercury, inorganic mercury

compounds and other organic mercury compounds in a category.

Chronic

(JP) No classification due to lack of data

(NZ) mentioned, that no data on chronic aquatic toxicity is available. However the data from the acute 48-hr fish test is provided:
Key study for acute toxicity: **48-hr LC_{50} in fish 2.13 mg/L** (Species: Lake trout *Salvelinus namaycush***)**; 48-hr LC_{50} in fish 5.65 mg/L (Species: Channel catfish *Ictalurus punctatus*); Assumption: No 96-hr LC_{50} data available, therefore we have used 48-hr fish; data source: ECOTOX; reference: Willford, W.A. (1966) Toxicity of 22 Therapeutic Compounds to Six Fishes. Source: Invest.Fish Control No.18, Resourc.Publ.No.35, Fish Wildl.Serv., Bur.Sport Fish.Wildl. U.S.D.I., Washington, DC :10 p.
Aquatic fate – Bioaccumulation: Thiomersal is considered to be bioaccumulative based on data for mercury and methylmercury. It is assumed that "ethylmercury (degradation product of thimerosal) behaves in a similar manner to methylmercury."
Biodegradation: No data on biodegradation is provided. However it is stated: "Thimerosal is 49% mercury by weight - for purposes of assigning persistence, assume persistence as for other mercury compounds."

(EC) No data and no rational for the classification have been provided.

JP No data available on thiomersal itself.

Proposal to reconcile differences

NZ New Zealand used a secondary data source and expert judgement for classification. The actual test data should be reviewed before a proposal can be made.-

CH Category Acute 1 (by weight of evidence)
No 96-hr acute toxicity data for fish are available. However, data presented by NZ support the EC classification as category 1 for acute aquatic toxicity (96-hr LC_{50} in fish < 1 mg/L), assuming that a 96-hr exposure of the fish may cause an increase in mortality, compared to 48-hr exposure. It should also be noted that the test concentrations in all fish tests were nominal (not measured) in a static test system. There is no data on acute or chronic toxicity for aquatic invertebrates and algae available for Thiomersal.

Category Chronic 1 (by weight of evidence)
There is no data on chronic aquatic toxicity available for Thiomersal. In aqueous solutions Thiomersal is present as cation and has a high water solubility (approx. 1 g/L; reference: O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 1659). Because of its ionic nature, Thiomersal is not expected to bioaccumulate. Although there is no data on biodegradation available, Thiomersal is not considered to be persistent under environmental conditions. It can be degraded to the cationic ethylmercury and thiosalicylic acid. Ethylmercury may be reduced to metallic mercury in the environment. Therefore, it is concern that Thiormersal can be transformed under environmental conditions to inorganic mercury and ethyl- and eventually also methylmercury.

JP Classification not possible will be better due to no data on this specific compound. It is difficult to estimate quantitative value.

JP Japan keeps the conclusion that this chemical cannot be classified due to lack of relevant data.
As far as aquatic toxicity there are no data to be used for classification however one fish toxicity data was provided from New Zealand.

Table 4.11: Analysis of data supporting classification for hazard to the aquatic environment