GHS Classification Manual

GHS Classification Manual (20 Oct. 2005)

In Japan MSDS are required for approximately 1,500 chemicals which are regulated under the current laws. METI, MHLW and MOE decided to implement classification of these chemicals as a joint project, aiming to help industries issuing MSDS. The results of the projects are not compulsive and allow industries using their own data and classifying chemicals on the basis of their own judgement. Classification results will be publicity available by the end of 2006.
The main objective of this manual is to facilitate the classification of the 1,500 chemicals within the limited time schedule, and to eliminate any different classification results among experts. One of the unique points of the manual is that it allows for users to refer only reliable data sources for the classification of hazards, such as those peer-reviewed by international authorities, and an original scientific paper is not generally used. This enables industries to save their trouble to check the peer review of the international organization in their voluntary classification.

The classification result would be helpful when you consider this manual.
Japanese version is available → http://www.safe.nite.go.jp/ghs/list.html

Chapter 1. Introduction

Chapter 2. Physical and Chemical Hazards

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Chapter 4. Environmental Hazards

Chapter 1. Introduction

[1-1] GHS classification manual

This manual has been prepared so as to provide a set of guidance for the classification of about 1,500 substances – a national project to be undertaken by the Japanese with respect to the implementation of GHS. It should be noted, however, that the manual is designed for provisional classification to be made within a limited time frame and with limited resources, and hence does not provide general rules that should be observed when making GHS-conforming classifications. This manual may be revised as needed, taking classification implementation status and efficiency into account, and based on a consensus of all parties concerned.

[1-2] Classification workflow (pdf files)

Figure 1 GHS Classification Workflow – Physical and Chemical Hazards

Figure 1 GHS Classification Workflow – Health Hazards

Figure 1 GHS Classification Workflow – Environmental Hazards

Chapter 2. Physical and Chemical Hazards

[2-1] Information sources for the classification of physical hazards

The physical properties of substances, particularly the relationship between temperature and physical states, are one of the keys to GHS classification. Information regarding physical hazards such as flammability, explosibility, combustion-supporting properties and explosion limits is also vital. Literature concerning the existing systems used as classification criteria is referred to at the end of this manual.

(2-1-1) Collection of physical properties data

Information regarding physical properties is vital to the GHS classification of gases and low-boiling liquids. This section refers to publications that served as standard references for chemical researchers and engineers throughout the 20th century (1-4), physical data that have been useful in chemical engineering (5,6), and some of the latest information on the physical properties of organic chemicals, including online databases (7-13).

For solids and high-boiling liquids, the information included in the hazard data of the next section would be sufficient because their physical states do not have much of an impact on their hazards.

1) Gmelins Handbuch der Anorganischen Chemie and Gmelin Handbook of Inorganic and Organometallic Chemistry 8th Ed. (1.07 million items)

These works trace their origin back to "Handbuch der theoretischen Chemie," a textbook written by Leopold Gmelin in 1817. The German Chemical Society took over the editing of the textbook in 1921, which later developed into a systematic resource for information on inorganic compounds and organometallic compounds. The 8th edition (from "zinc" with a system number of 32) was published in 1924, with a total of about 300 volumes released in the 20th century. The series was switched to English around 1980, and the latest digitized version comes in CD-ROM format.

2) Beilsteins Handbuch der Organischen Chemie and Beilstein Handbook of Organic Chemistry 4th Ed. (7.05 million items)

These works derive from two volumes of an organic chemistry handbook written by F. K. Beilstein (professor at the Imperial Technical Institute in St. Petersburg) in 1881 and 1882. The 1st to 3rd editions were published by Beilstein; the editing was taken over by the German Chemical Society in 1896. P. Jacobson and B. Prager jointly published the 4th edition in 1918, expanded editions of which were published throughout the 20th century. The 5th edition, published around 1980, was switched to English, and a digitized version in CD-ROM format was released at the end of the 20th century.

3) The Merck Index 13th Ed. (10,250 substances)

A manual for reagents and drugs first published by Merck in 1889

4) Chemical Abstracts

A journal of abstracts originally produced by the American Chemical Society in 1907 and later published by Chemical Publishing (the present Chemical Abstracts Service), this covers worldwide chemical literature and patents in addition to information regarding chemical substances, theoretical chemistry and chemical technologies. Each substance was provided with a CAS number in 1967. It is now offered primarily online, although hard copy is still available.

5) International Critical Tables of Numerical Data, Physics, Chemistry and Technology

Data compiled by the National Research Council under the auspices of the International Research Council and the National Academy of Sciences. A total of 7 volumes were published by McGraw-Hill between 1926 and 1930, and their general index was released in 1933.

6) Bussei Teisu (Property Constants)

A total of 10 volumes – compiled by the Society of Chemical Engineers, Japan – were published by Maruzen between 1963 and 1972. Volume 4, published in 1966, is a general index for volumes 1-3, while no index is available for volumes 5-10.

7) Ullmanns Encyklopaedie der technischen Chemie and Ullmann' s Encyclopedia : Industrial Organic Chemicals

The 4th edition of Ullmann' s Encyclopedia of Industrial Chemistry, which was first published in the 1920s, was published by Verlag Chemie between 1972 and 1984. Volumes 1-7 provide a general introduction, and volumes 8-24, specifics about each substance, while volume 25 is an index. Wiley-VCH published the English version (volumes 1-8) in 1999, focusing on organic base materials and intermediates; the series, coupled with a very concise table of properties, covers major chemical reactions, applications and toxicity, with about 20 descriptions dedicated to each group of substances.

8) Handbook of Physical Properties of Organic Chemicals (about 13,000 substances)

A collection of properties compiled by P.H.Howard and W.M.Meylan (Syracuse Research Corporation) and published by Lewis in 1997, this addresses a total of about 13,000 organic compounds, arranging them in order of CAS number with data on 8 parameters – i.e., melting point, boiling point (including boiling point under reduced pressure), aqueous solubility, octanol/water partition coefficient, vapor pressure, dissociation constant, Henry coefficient, and atmospheric hydroxyl radical reaction rate constant.

9) Chapman and Hall Chemical Data base (442,257 records as of 1997)

A physical and chemical database of organic compounds, originally called “HEILBRON” (a commercial database): http://library.dialog.com/bluesheets/html/bl0303.html

10) HODOC File (Handbook of Data on Organic Compounds) (25,580 substances as of 2002)

A database version of the CRC handbook managed in Japan by the Japan Science and Technology Agency: http://www.cas.org/ONLINE/DBSS/hodocss.html

11) CRC Handbook of Chemistry and Physics

A handbook of physical and chemical properties published by CRC (84th Ed.). Information can be searched by CAS number.

12) Sax's Dangerous Properties of Industrial Materials

A database of dangerous properties published by Wiley (11th Ed.). Data on the reactivity, flammability and explosibility of more than 20,000 substances are listed, searchable by CAS number.

13) Hazardous Substances Data Bank (HSDB)

A database prepared by the National Library of Medicine (NLM) under the Department of Health and Human Services (U.S.), it also contains data on physical and chemical properties, and is searchable online by CAS number (a CD-ROM version is also available).
http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

(2-1-2) Collection of physical and chemical hazard data

Scientific literature focusing on the hazards of chemical substances began to emerge in the latter half of the 20th century. The focus, however, is more on guidelines for emergency measures and hazard prevention than a hazard database, describing ratings in a textbook style, and hence does not serve well for GHS classification of physical hazards. The classification, therefore, will probably be based on approved classification materials referred to in the next section. While the collection of hazard data includes health hazard data, this section refers to those materials containing numerous descriptions of physical hazards. In this sense, they are reference materials for the preparation of MSDSs rather than for GHS classification.

Meanwhile, items 2 and 3, which focus on the mutual reactivity of two substances (a subject not covered by the current GHS), are listed for information only.

1) Hommel, Handbook of Dangerous Goods (1,205 substances)

A German version was compiled by Gunter Hommel and published by Springer-Verlag in 1970, with the text revised from time to time. The 1987 edition was translated by Rokuro Arai; a Japanese version was published in 1991 by Springer-Verlag Tokyo.

2) Bretherick's Handbook of Reactive Chemical Hazards and Dangerous Goods (5th Ed.)

The 1st edition was published in 1975, and the 5th edition, in 1995, by Butterwoth-Heinemann (U.K.). It focuses on reactive chemical hazards. A Japanese version was published in 1998 by Maruzen, with its translation supervised by Shozo Tamura.

3) Kagakuyakuhin no Konshoku Kiken Handbook (Handbook of Reactive Chemical Hazards) (Tokyo Fire Department)

The 1st edition was published in 1980 by Nikkan Kogyo Shimbun under the supervision of Tadao Yoshida and Shozo Tamura, followed by the 2nd edition in 1997. About 520 substances are listed, with their reactive chemical hazards associated with about 10 other substances ranked by degree of severity.

4) Hazardous Chemicals Data Book (G. Weiss) and Solvents Safety Handbook (D. J. De Renzo)

The 2nd edition of the former (covering 1,016 substances) was published in 1986 by Noyes Data Corporation (U.S.), with the latter (covering 335 solvents) spun off. Each substance is listed on one page in a prescribed format, while the latter provides another page (a comparative table with temperatures) for 7 substances. Being U.S. publications, they provide data in Fahrenheit, yards and pounds.

5) Kikenbutsu Data Book (Dangerous Goods Data Book) (Tokyo Fire Department)

A data book edited by the Tokyo Consolidated Fire Prevention Association under the supervision of the Watch Committee of the Tokyo Fire Department, this was first published by Maruzen in 1988, followed by the 2nd edition (covering 290 substances) in 1993.

6) Doroyuso Kikenbutsu no Data Sheet (Road Transport Dangerous Goods Data Sheet) (The Research Institute for Safety Engineering)

A data sheet published by the Research Institute for Safety Engineering in 1991 under the auspices of three Public Highway Corporations. An expanded edition was published later, followed by the 1996 edition (covering 322 substances).

7) Kagakubusshitsu Anzensei Data Book (Chemical Substance Safety Data Book) (The Chemical Substance Safety Information Workshop)

A data book edited by Yoichi Uehara, this was first published by Ohmsha in 1994, followed by the 1997 edition (covers 582 substances).

8) International Chemical Safety Cards

A database developed by the International Programme on Chemical Safety (IPCS), ILO is responsible for classifying physical hazards (firing point, ignition point, explosion limit, etc.), and WHO, health hazards. It comes in 16 different languages, including English, Japanese, Chinese, Korean, German, Italian, French and Russian. Currently, about 1,400 cards are available, each of which can be searched by CAS number.

http://www.ilo.org/public/english/protection/safework/cis/products/icsc/dtasht/index.htm

Japanese version: http://www.nihs.go.jp/ICSC/

9) Fire Protection Guide to Hazardous Materials

Fire Prevention Guidelines drawn up by the National Fire Protection Association (NFPA) of the U.S. The 13th edition is now available, listing data on physical hazards (firing point, ignition point, explosion limit, etc.), each of which can be searched by CAS number.

(2-1-3) Materials based on GHS classification criteria

Classifications based on GHS have yet to be made available. However, laws and regulations (references 1 and 2) with classification based on existing systems can be of use because GHS is based on part of a classification system that has been used in accordance with international agreements (i.e., the United Nations Recommendations on the Transport of Dangerous Goods). References 3 and 4 can be used to supplement the classification, although they are not directly related to GHS classification.

This manual extrapolates the UN GHS classification of physical hazards for the initial discussion of the introduction of GHS. Properly speaking, however, GHS classification should be made in terms of physical and chemical properties, upon which UN classification and numbers should be based.

1) The United Nations Recommendations on the Transport of Dangerous Goods (UNRTDG)

Recommendations made by the UN Committee of Experts on the Transport of Dangerous Goods and the Globally Harmonized System of Classification and Labeling of Chemicals (CETDG/GHS). These are supplemented by GHS recommendations, also made by the committee. It is therefore appropriate that the recommendations on the transport of dangerous goods should be adopted for GHS classification.

The latest edition: Transport of Dangerous Goods, Model Regulations, Rev.13, 2003

For marine transport, the International Maritime Dangerous Goods Code (IMDGC) – issued by the International Maritime Organization (IMO) – is available, with the latest edition published in 2004. This code was adopted for the Regulations for the Carriage and Storage of Dangerous Goods by Ship (hereinafter referred to as the "Dangerous Goods Regulations"), whose 11th edition was published in 2004 by Kaibundo (Japan). Likewise, relevant aviation laws and regulations adopt a classification system based on UNRTDG.

The following publications, although not adopted by GHS, are complementary to the above.

2) The EMS GUIDE: Emergency Response Procedures for Ships Carrying Dangerous Goods

This is in compliance with the 2002 version of the IMDG Code (a Japanese version is not yet available).

3) Emergency Response Guidebook

Guidelines jointly developed by Canada, the U.S. and Mexico for dealing with land transport accidents. A Japanese version was released in 2001 (Emergency Response Guidebook: Application to the Container Yellow Card labeling system, the Japan Chemical Industry Association). Accordingly, Japan's yellow cards are provided with schedule number 111–172.

(2-1-4) Reference materials

The following publications are not directly related to GHS classification, and hence should be considered reference materials.

1) Annex I of Directive 67/548/EEC(EU Annex I)

This annex is a compilation of the labeling of dangerous substances listed on the European Inventory of Existing Commercial Chemical Substances (EINECS) and the labeling based on base-set test results of new chemical substances; it contains qualitative descriptions, which take the form of specific or general warnings.

The classification adopted in Annex I of Directive 67/548/EEC is not based on GHS classification criteria, hence its results are not applicable to GHS classification. A Japanese version was published by JETOC in 2004 (EU: List of Dangerous Substances (7th. Edition)).

2) Guidelines for Providing Information on the Safety of Chemical Substances

These guidelines provide definitions of explosive substances, gases under pressure, flammable liquids, combustible solids/gases, pyrophoric substances, substances that emit flammable gases in contact with water, oxidizing substances, self-reactive substances, and metal corrosives. They were jointly issued by the Ministry of Labour, the Ministry of Health and Welfare and the Ministry of International Trade and Industry on March 26, 1993 as Notice 1.

[2-2] Categories based on physical and chemical lcharacteristics for the classification of physical hazards

(2-2-0) Introduction

GHS physical hazards are grouped into 16 categories, while categories to be assessed can be narrowed down based on the specific characteristics of the substances. Some categories are provided for substances with particular chemical structures. This section gives an overview of these substances to provide an introduction to physical and chemical hazard assessments.

(2-2-1) Gases

Gases are defined as materials whose vapor pressures exceed 300 kPa (absolute pressure) at 50℃, or that evaporate completely at standard atmospheric pressure (101.3 kPa) and a temperature of 20℃, according to GHS1.2. If they are combustible when mixed with air, they are subject to the criteria for judging "combustible/flammable gases." When they contribute to combustion of other substances more than air does, they are categorized as "combustion-supporting/oxidizing gases."

Gases compressed to a pressure of 280 kPa at 20℃ or more for distribution, transportation and storage purposes, or those refrigerated and liquefied are categorized as "gases under pressure." The high-pressure classification does not involve chemical hazards inherent in substances, but is associated with physical hazards attributable to the conditions of substances.

When combustible/flammable gases are used as propellants, aerosols are categorized as "combustible/flammable aerosols." Each aerosol product is tested individually because factors such as the structure of the nozzle are related to combustibility/flammability. (When aerosols contain flammable liquids or combustible solids, they are categorized as "combustible/flammable aerosols," even if inert gases are used as propellants.

(2-2-2) Liquids

Liquids are defined as substances whose vapor pressure is below 300 kPa at 50℃, that do not evaporate completely at standard atmospheric pressure (101.3 kPa) and a temperature of 20℃, and whose melting points or initial melting points are below 20℃ at standard atmospheric pressure (101.3 kPa), according to GHS1.2. Highly viscous or pasty substances and mixtures, whose melting points cannot be determined, are tested according to a prescribed method, using penetrometers (ADR Annex A 2.3.4).

Liquid substances are also tested for their flammability, spontaneous combustibility, self-heating properties, and corrosiveness to metals.

(2-2-3) Solids

Any substances or mixtures that are not categorized as either “liquids” or “gases” are defined as “solids,” according to GHS1.2. Solids include powdery, granular, pasty, aggregated, fibrous and tabular substances. The hazards of powdery substances may vary depending on the size of their particles. For this reason, hazards inherent to specific configurations are assessed, not those inherent to the substance.

Solid substances are also tested for their flammability, spontaneous combustibility, self-heating properties, and corrosiveness to metals.

(2-2-4) Selection of items to be assessed according to chemical structure

When liquids or solids contain certain atomic groups in their molecules, assessment shall be conducted for these groups. When they contain atomic groups with explosive properties (see 2-2-5), they shall be assessed as “explosives” and “self-reactive substances.”

When they do not contain such atomic groups, but groups that are self-reactive (see 2-2-6), they shall be assessed as “self-reactive substances.” When they contain metals or semimetals in their molecules, they shall be assessed as “water-reactive combustible substances.” When they contain oxygen, chlorine or fluorine, they shall be assessed as “oxidizing liquids” or “oxidizing solids,” whereas when these elements are bound only to carbon or hydrogen, they do not need to be assessed.

Organic compounds whose molecules have the “-O-O-“structure, and mixtures containing such organic compounds shall be assessed as “organic peroxides.”

The following table summarizes the above descriptions:

Chapter	Category	Gas	Liquid	Solid	Possibly Covered Chemical Structure
2.1	Explosives	×	○	○	Molecules containing atomic groups with explosive properties (see 2-2-5)
2.2	Combustible/Flammable Gases	○	×	×	
2.3	Combustible/Flammable Aerosols	○	○	○	
2.4	Combustion-supporting/Oxidizing Gases	△	×	×	
2.5	Gases under pressure	○	×	×	
2.6	Flammable Liquids	×	○	×	
2.7	Combustible Solids	×	×	○	(Powdery, granular or pasty substances are assessed)
2.8	Self-reactive Substances	×	○	○	Molecules containing atomic groups with explosive properties or self-reactivity (see 2-2-5 and 2-2-6)
2.9	Pyrophoric Liquids	×	○	×	
2.10	Pyrophoric Solids	×	×	○	
2.11	Self-heating Substances	×	△	○	
2.12	Water-reactive Combustible Substance	×	○	○	Metals or semimetals (e.g., Si, Ge, As, Sb, Bi)
2.13	Oxidizing Liquids	×	○	×	Oxygen, chlorine and fluorine bound to elements other than carbon and hydrogen
2.14	Oxidizing Solids	×	×	○	
2.15	Organic Peroxides	×	○	○	Organic compounds with the “-O-O-“ structure, excluding those whose content of active oxygen (%) is referred to in 2.15.2.1 (a),(b)
2.16	Metal Corrosives	△	○	△	

○: Possibly applicable

×: Not applicable

△: Possibly applicable, but no test method is available

(2-2-5) Atomic groups with explosive properties

“Atomic groups with explosive properties” described in GHS2.1.4.2.2(a) refer to the following:

Unsaturated “-C-C-“ bond	Acetylenes, acetylides, 1,2-dienes
C-metals, N-metals	Grignard reagents, organolithium compounds
Neighboring nitrogen atoms	Azides, aliphatic azo compounds, diazonium salts, hydrazines, sulfonyl hydrazides
Neighboring oxygen atoms	Peroxides, ozonides
N-O	Hydroxylamines, nitrate salts, nitrates, nitro compounds, nitroso compounds, N-oxides, 1,2-oxazoles
N-halogen	Chloramines, fluoroamines,
O-halogen	Chlorates, perchlorates, iodosyl compounds

(UNRTDG: Manual of Tests and Criteria, Appendix 6, Table A6.1)

Substances not containing these atomic groups do not need to be assessed for explosiveness. In addition, “substances containing atomic groups with explosive properties (such as oxygen)” are not considered “explosive,” when their oxygen balance is lower than -200 (GHS2.1.4.2.2(b)).

The oxygen balance of chemical reactions is calculated as follows:

$\mathrm{CxHyOz} + [x + (y/4) - (z/2)].\ O_2 \rightarrow x.\ CO_2 + (y/2).\ H_2O$

The following equation is applicable in this case:

$\text{Oxygen balance} = -1600\ [2.x + (y/2) - z]\ /\ \text{molecular weight}$

Organic materials (or their homogenized mixtures) containing atomic groups with explosive properties are not considered “explosive,” when their decomposition energy is less than 500 J/g, and their decomposition starts at a temperature of less than 500℃. (GHS2.1.4.2.2(c)).

Likewise, inorganic oxidizing substances and their mixtures with organic materials are not considered “explosive,” when their concentration is less than 15% by weight (Receptacle Grade 1 and 2), or less than 30% by weight (Receptacle Grade 3) (GHS2.1.4.2.2(d)).

(2-2-6) Atomic groups with self-reactivity

“Self-reactive atomic groups” described in GHS2.8.4.2(a) refers to the following:

Cross-reacting group	Aminonitriles, haloanilines, organic salts of oxidizing acids
S=O	Halogenated sulfonyl compounds, sulfonyl cyanides, azides
	Sulfonyl hydrazides
P-O	Phosphites

Strained ring	Epoxides, aziridines
Unsaturated bond	Olefins, oxidized cyanides

(UNRTDG: Manual of Tests and Criteria, Appendix 6, Table A6.2)

Substances containing no atomic groups with explosive properties or self-reactivity do not need to be assessed for self-reactivity. Organic materials (or their homogenized mixtures) are not considered "self-reactive," when their estimated SADT value exceeds 75℃, or their decomposition energy is less than 300 J/g GHS2.8.4.2(b)).

[2-3] Classification and specifics of physical hazards

(2-3-1) Explosives

A) GHS classification criteria

The classification criteria set out in UN GHS 2.1.2 can be summarized as follows:

Category 1.1: Substances, mixtures or articles involving a mass explosion hazard

Category 1.2: Substances, mixtures or articles involving a projection hazard, but not a mass explosion hazard

Category 1.3: Substances, mixtures or articles involving a fire hazard and either a minor blast hazard or a minor projection hazard (or both), but not a mass explosion hazard

Category 1.4: Substances, mixtures or articles involving no significant hazard – i.e., substances, mixtures and articles presenting only a minor hazard in the event of ignition or initiation

Category 1.5: Extremely insensitive substances involving a mass explosion hazard

Category 1.6: Extremely insensitive articles involving no mass explosion hazard

Tests shall be performed based on the UNRTDG Manual of Tests and Criteria.

B) Data availability

The performance of explosives depends on their preparation, and data on the explosion performance of each substance are limited.

C) Comparison with previous classification systems

Category 1.1-6 described above follows the definition adopted in UNRTDG2.1.1.4.

D） Information sources classified according to previous systems, and a tentative classification method

The UNRTDG list of dangerous goods is adopted – e.g., Annex 1: Dangerous Goods Regulations.

Unstable explosives: explosive substances and articles, whose transportation is prohibited.

Category 1.1: UNRTDG1.1

Examples

0004	Ammonium picrate (dry or wetted with less than 10% water)
0028	Blasting powder
0072	Cyclotrimethylenetrinitramine (wetted with more than 15% water)
0074	Diazodinitrophenol (wetted with more than 40% water)
0075	Diethyleneglycol dinitrate (with more than 25% desensitizers)
0076	Dinitrophenol (dry or wetted with less than 15% water)
0077	Alkali metal dinitrophenolates (dry or wetted with less than 15% water)
0078	Dinitroresorcinol (dry or wetted with less than 15% water)
0079	Hexanitrodiphenylamine
0113	Guanyl nitrosamino guanylidene hydrazine (wetted with more than 30% water)
0114	Guanyl nitrosamino guanylidene tetrazene (wetted with more than 30% water)
0118	Hexolite (dry or wetted with less than 15% water)
0129	Lead azide (wetted with more than 20% water)
0130	Lead styphnate (with more than 20% water)
0133	Mannitol hexanitrate (wetted with more than 40% water)
0143	Nitroglycerine (with more than 40% desensitizers)
0146	Nitrostarch (dry or wetted with less than 20% water)
0147	Nitrourea
0150	Pentaerythrite tetranitrate (with more than 15% desensitizers or wetted with more than 25% water)
0151	Pentolite (dry or wetted with less than 15% water)

0153	Trinitroaniline
0154	Picric acid (dry or wetted with less than 30% water)
0155	Trinitrochlorobenzene
0207	Tetranitroaniline
0208	Trinitrophenylmethylnitramine
0209	Trinitrotoluene (dry or wetted with less than 30% water)
0213	Trinitroanisole
0214	Trinitrobenzene (dry or wetted with less than 30% water)
0215	Trinitrobenzoic acid (dry or wetted with less than 30% water)
0216	Trinitro-m-cresol
0217	Trinitronaphthalene
0218	Trinitrophenetole
0219	Trinitroresorcinol (dry or wetted with less than 20% water)
0220	Urea nitrate (dry or wetted with less than 20% water)
0222	Ammonium sulfate (with more than 0.2% combustibles)
0224	Barium azide (dry or wetted with less than 50% water)
0226	Cyclotetramethylenetetranitramine (wetted with more than 15% water)
0266	Octolite (dry or wetted with less than 15% water)
0282	Nitroguanidine (dry or wetted with less than 20% water)
0340	Cellulose nitrate (dry or wetted with less than 25% water)
0341	Cellulose nitrate (unmodified or with less than 18% plasticizers)
0385	5-Nitrobenzotriazole
0386	Trinitrobenzene sulfonic acid
0387	Trinitrofluorenone
0390	Tritonal
0392	Hexanitrostilbene
0393	Hexotonal
0394	Trinitroresorcinol (wetted with more than 20% water)
0402	Ammonium perchlorate
0483	Cyclotrimethylenetrinitramine (desensitized)
0484	Cyclotetramethylenetetranitramine (desensitized)

0489	Dinitroglycoluril
0490	Nitrotriazolone
0496	Octonal
0504	1H-tetrazole

Category 1.2: UNRTDG1.2

Substances are included by definition, although UN numbers are issued for articles only.

Category 1.3: UNRTDG1.3.

0161	Smokeless powder
0234	Dinitro-o-cresol sodium salt (dry or wetted with less than 15% water)
0235	Sodium picramate (dry or wetted with less than 20% water)
0236	Zirconium picramate (dry or wetted with less than 20% water)
0342	Nitrocellulose (with more than 25 alcohol)
0343	Nitrocellulose (with more than 18% plasticizers)
0406	Dinitrobenzene
0411	Pentaerythrite tetranitrate (with more than 7% wax)

Category 1.4: UNRTDG1.4.

0407	Tetrazole-1-acetic acid
0448	5-mercaptotetrazole-1-acetic acid

Category 1.5: UNRTDG 1.5.

0331	Blasting powder B

Category 1.6: UNRTDG1.6

None

E) Desensitized explosives (GHS2.1.2.2, Note 2)

Desensitized explosives wetted with water, alcohol, etc. do not fall into the category of “explosives” under GHS; they belong to Class 3 of UNRTDG or are considered part of Category 4.1, while corresponding to substances of NAERG (North American Emergency Response Guidebook) Schedule 113 (flammable solids – toxic wet/desensitized explosives). In addition, these substances are categorized under EmS as F-E (non water-reactive flammable liquids) or S-J (wet explosives and self-heating substances).

(Examples)UNRTDG3*EmS:F-E

1204	Nitroglycerine (alcoholic solution of 1% nitroglycerine)
2059	Nitrocellulose solution (with a concentration of less than 55%)

UNRTDG4.1*NAERG113(UNRTDG4.1*EmS:S-J)

1310	Ammonium picrate (wetted with more than 10% water)
1320	Dinitrophenol (wetted with more than 15% water)
1336	Nitroguanidine (wetted with more than 20% water)
1337	Nitrostarch (wetted with more than 20% water)
1354	Trinitrobenzene (wetted with more than 30% water)
1355	Trinitrobenzoic acid (wetted with more than 30% water)
1356	Trinitrotoluene (wetted with more than 30% water)
1357	Urea nitrate (wetted with more than 20% water)
1571	Barium azide (wetted with more than 50% water)
2555	Nitrocellulose (wetted with more than 25% water)

(2-3-2) Combustible/flammable gases

A) GHS classification criteria

According to Section 2.2.2. of the UN GHS classification, single-component gases belong to Category 1 when they are explosive (combustible) in a mixture of 13% or less by volume with air, or have an explosive (combustible) range of at least 12 percentage points, regardless of their lower explosion limit.

Gases other than those in Category 1 belong in Category 2 when they have an explosive (combustible) range when mixed with air at 20℃ and 1 atmosphere pressure.

Mixed gases are classified according to ISO10156:1996 set out in GHS2.2.5, although Tci values are needed for the components of each combustible/flammable gas.

B) Data availability

Data on the properties of gaseous substances are relatively accessible. Gaseous substances that are combustible/flammable under normal pressure and temperature conditions are all categorized as “combustible/flammable gases.” Single-component gases can be readily classified when data on their combustible range (i.e., explosion limit) are available.

C) Comparison with previous classification systems

The definition of Category 2.1, set out in UNRTDG2.2.2.1, is consistent with the GHS classification and EmS Schedule F-D (Schedule S-U include toxic gases). Combustible/flammable gases fall into Schedules 115, 116, 117, 118, and 119 of NAERG. Gaseous substances categorized as R12 in EU-Annex I belong in Category 1 and Category 2, although no category is defined.

D) Information sources classified according to previous systems, and a tentative classification method

Category 1: UNRTDG2.1 and 2.3 (2.1)

Category 2: Combustible gases other than those in Category 1

“Class 2: Gases” defined in UNRTDG refers only to those that are in a state (compressed or liquefied) conforming to the definition for gases under pressure set out in (2-2-5). According to GHS, meanwhile, combustible/flammable gases include not only high-pressure but also normal-pressure gases.

Examples of Category 1

UNRTDG2.1

1012	Butylene
1036	Ethyl amine
1049	Compressed hydrogen
1978	Propane
2203	Silane
2454	Methyl fluoride
3153	Perfluoro (methyl vinyl ether)

UNRTDG2.3 (2.1)

1053	Hydrogen sulfide
1082	Trifluorochloroethylene
2188	Arsine
2204	Carbonyl sulfide

Example of Category 2

1062	Methyl bromide

(2-3-3) Combustible/flammable aerosols

A) GHS classification criteria

According to Section 2.3.2. of the UN GHS classification, “flammable aerosols” are defined as those aerosols containing components that are considered combustible/flammable, based on the GHS classification criteria for flammable liquids, combustible/flammable gases and combustible solids.

Category 1:

- Aerosols that contain ≧ 85% flammable components and have a combustion heat ≧ 30 kJ/g, or
- Spray aerosols that have an ignition distance≧ 75 cm
- Foam aerosols that have a flame height ≧ 20 cm with a flame duration ≧ 2 seconds, or a flame height≧ 4 cm with a flame duration ≧ 7 seconds

Category 2:

- Spray aerosols that have a combustion heat ≧20 kJ/g and an ignition distance≧15 cm; or in the enclosed space ignition test have a time equivalent ≦ 300 s/m^3 or a deflagration density≦300 g/m^3
- Foam aerosols that have a flame height ≧ 4 cm with a flame duration ≧ 2 seconds

Other

- Aerosols that contain≦ 1% flammable components and have a combustion heat ≦ 20 kJ/g

B) Data availability

Product designers determine the components of aerosols. Aerosol liquids or propellants, when the GHS classification criteria are applicable, shall be categorized and tested as needed, based on the classification system of GHS2.3.4.1.

C) Comparison with previous classification systems

The classification method set out in Special Provision 63 corresponding to UN#1950 (Aerosols) of the UNRTDG3.2.1 Dangerous Goods List is applicable.

D) Information sources classified according to previous systems, and a tentative classification method

Each manufactured product should be tested in accordance with the GHS classification criteria.

(2-3-4) Combustion-supporting/oxidizing gases

A) GHS classification criteria

According to Section 2.4.2. of the UN GHS classification, "combustion-supporting/oxidizing gases" are defined as those gases the sum of whose oxygen equivalent coefficient (Ci) and volume ratio percentage (vol%) exceeds 21.

Oxygen equivalent coefficient (Ci)

Nitrous oxide: 0.6 (categorized as a combustion-supporting/oxidizing gas if more than 35%)

Oxygen: 1 (categorized as a combustion-supporting/oxidizing gas if more than 21%)

Other oxidizing gases: 40 (categorized as a combustion-supporting/oxidizing gas if more than 0.525%)

B) Data availability

Calculation should be performed in accordance with ISO-10156, based on components (GHS2.4.4.2).

C) Comparison with previous classification systems

The definition (UNRTDG2.5.2) of oxidizing substances (Category 5.1) applies only to liquids and solids. Although no classification criteria are available for oxidizing gases, some gases are indexed with 5.1 to indicate their secondary hazard (however, not comprehensive as of 2005); they fall into NAERG Schedule 122 and EmS S-W, on which the selection of oxidizing gases can be based.

All the gases listed below (nitrogen trifluoride and the following) are categorized as "all other oxidizing gases."

D) Information sources classified according to previous systems, and a tentative classification method

Relevant oxidizing gases are those categorized as Category 2.2 (5.1), 2.3 (5.1) and 2.3 (5.1,8) in the third and forth columns of the UNRTDG Dangerous Goods List; some of those categorized as Category 2.2 and 2.3 may belong here even though they do not produce secondary hazards.

For transport of dangerous goods, only those categorized as “gases under pressure” are regulated, while normal-pressure gases are also included in the GHS category because of the absence of such conditions in GHS.

Examples

2.2 (5.1)

1003	Liquid air
1014	Compressed mixtures of carbon dioxide and oxygen
1070	Nitrous oxide
1072	Compressed oxygen
1073	Liquefied oxygen
2201	Liquefied nitrous oxide
2451	Compressed nitrogen trifluoride

2.3 (5.1,8) or 2.3 (5.1)

1045	Compressed fluorine
1067	Nitrogen dioxide
1660	Compressed nitrogen monoxide
1749	Chlorine trifluoride
1975	Mixtures of nitrogen monoxide and nitrogen dioxide
2190	Compressed oxygen difluoride
2421	Dinitrogen trioxide
2548	Chlorine pentafluoride
2901	Bromine chloride
3083	Perchloryl fluoride

(2-3-5) Gases under pressure

A) GHS classification criteria

Section 2.5.2 of the UN GHS classification categorizes gases under pressure as follows:

- Compressed gas: Gases that are completely in the gaseous phase at −50°C (including all gases with critical temperatures below −50°C)
- Liquefied gas: Gases that are partially in the liquid phase at temperatures above −50°C
- High-pressure liquefied gas: Gases with critical temperatures between −50°C and 65°C
- Low-pressure liquefied gas: Gases with critical temperatures above 65°C
- Refrigerated liquefied gas: Gases that are partially in the liquid phase at low temperatures
- Dissolved gas: Gases that dissolve in liquid solvents under pressure

B) Data availability

The data required are vapor pressure at 50℃, physical properties at 20℃ and 1 atmospheric pressure, and critical temperatures (GHS2.5.4.2), all of which are relatively accessible. Physical conditions of gases under pressure, when compressed in cylinders, depend on the design of manufacturers.

C) Comparison with previous classification systems

The definition of Class 2 (gas) set out in UNRTDG2.2.1.2 and that of gas in GHS are consistent with “substances that are completely in the gaseous phase at 50℃ and above 300 kPa (absolute pressure) or at 20℃ and 101.3 kPa (normal-pressure). UNRTDG, meanwhile, does not provide a definition of “gases under pressure,” which are newly defined by GHS as “gases with a vapor pressure of more than 280 kPa (absolute pressure) at 20℃.”

D) Information sources classified according to previous systems, and a tentative classification method

This depends on the design selected by the manufacturer. Gases under pressure can be categorized further, with external data incorporated as supplements.

(2-3-6) Flammable liquids

A) GHS classification criteria

Section 2.6.2 of the UN GHS classification categorizes gases under pressure as follows:

Category 1: Flash point < 23°C and initial boiling point ≦ 35°C

Category 2: Flash point < 23°C and initial boiling point > 35°C

Category 3: Flash point ≧ 23 °C and ≦ 60 °C

Category 4: Flash point > 60 °C and ≦ 93 °C

B) Data availability

With the Fire Defense Law mandating such measurements, data are relatively accessible even for mixtures. However, the law requires the "open method" for the measurement of high flash points, which poses a problem around the upper limit of Category 4.

C) Comparison with previous classification systems

In general, Categories 1–3 are in line with Class 3 of UNRTDG.

Category 1 coincides with Class 3I of UNRTDG. (No upper limits are provided for flash points, but no combustible substances have been reported with an initial boiling point of 35°C and below and a flash point of 23°C and above.)

Category 2 = UNRTDG. 3II

Category 3 = UNRTDG. 3III

Category 4 = Non-dangerous goods under UNRTDG

The classification of EU Annex I differs from that of GHS (R12, 11 and 10 only serve as a reference).

D) Information sources classified according to previous systems, and a tentative classification method

Relevant laws and regulations in line with UNRTDG, such as the Dangerous Goods Regulations (Japan), can be applied to Categories 1, 2 and 3, according to the procedures set out in the previous section. Classification, when data are available, can be based on flash points or boiling points.

Examples of Category 1 (UNRTDG 3I)

1093	Acrylonitrile
1131	Carbon disulfide
2481	Ethyl isocyanate

Examples of Category 2 (UNRTDG 3II)

1090	Acetone
1154	Diethylamine
1717	Acetyl chloride

1230	Methanol

Examples of Category 3 (UNRTDG 3III)

1157	Di-isobutyl ketone
2260	Tripropylamine
2529	Isobutyric acid

Examples of Category 4

Divinylbenzene
N-ethylaniline
Ethylene cyanohydrin
Nitrobenzene

(2-3-7) Combustible solids

A) GHS classification criteria

The classification criteria set out in UN GHS 2.7.2 can be summarized as follows (tests shall be performed based on the method described in UNRTDG Manual of Tests and Criteria III 33.2.1):

Substances and mixtures excluding metal powders

Category 1: (a) Wetted zone does not stop fire, with (b) burning time < 45 seconds or burning rate > 2.2 mm/sec.

Category 2: (a) Wetted zone stops fire for at least 4 minutes, with (b) burning time < 45 seconds or burning rate > 2.2 mm/sec.

Metal powders

Category 1: Burning time $\leqq 5$ minutes

Category 2: Burning time > 5 minutes and $\leqq 10$ minutes

B) Data availability

Very few test results on burning rates are available.

C) Comparison with previous classification systems

The definition coincides with that of the Category 4.1 (Flammable solids) of UNRTDG. Category 4.1 also includes "(2-2-8) Self-reactive substances" and "(2-2-1E) Desensitized explosive substances," and hence should be construed along with NAERG.

NAERG Schedules concerned are:

133	Flammable solids
134	Flammable solids - toxicity/corrosiveness
170	Metals (powder, dust, shavings, chips, lathe cuttings, etc.

Combustible solids, along with self-reactive substances, belong to EmS Schedule S-G. Solids indexed with R11 of EU-Annex I are also subject to the classification criteria.

D) Information sources classified according to previous systems, and a tentative classification method

The following substances are covered under UNRTDG (or Japan's Dangerous Goods Regulations):

Category 1 = UNRTDG 4.1 II * NAERG 133, 134 and 170

Category 2 = UNRTDG 4.1 III * NAERG133, 134 and 170

Examples of Category 1

(4.1 II * 133)

1345	Rubber scraps
2989	Lead hydrogen phosphate

(4.1 II * 134)

1868	Decaborane

(4.1 II * 170)

1309	Aluminum powder (for surface coating)

1323	Ferrocerium
1871	Titanium hydride

Examples of Category 2

(4.1 III * 133)

1312	Borneol
1328	Hexamethylenetetramine
2213	Paraformaldehyde
3241	Bronopol
3251	Isosorbide mononitrate

(4.1 III * 134)

None

(4.1 III * 170)

1346	Silicon powder (amorphous)
2878	Sponge titanium (granule or powder)

(2-3-8) Self-reactive substances and mixtures

A) GHS classification criteria

The classification criteria set out in UN GHS 2.8.2 can be summarized as follows:

Self-reactive substances, by definition, do not include the following:

- Explosives, oxidizing liquids and oxidizing solids (mixtures of oxidizing liquids and solids, containing more than 5% combustible organic substances, are examined in accordance with Note 1 of GHS2.8.2.2)
- Organic peroxides
- Those with decomposition energy of less than 300 j/g
- Those whose self-accelerating decomposition temperature (SADT) exceeds 75°C for a 50 kg package

Self-reactive substances and mixtures can be categorized as follows according to the classification criteria of GHS2.8.4:

- Type A: Self-reactive material type A is a self-reactive material that, as packaged for transportation, can detonate or deflagrate rapidly
- Type B: Self-reactive material type B is a self-reactive material that, as packaged for transportation, neither detonates nor deflagrates rapidly, but is liable to undergo a thermal explosion in the package
- Type C: Self-reactive material type C is a self-reactive material that, as packaged for transportation, neither detonates nor deflagrates rapidly and cannot undergo a thermal explosion
- Type D: Self-reactive material type D is a self-reactive material that:
  - (i) Detonates partially, does not deflagrate rapidly and shows no violent effect when heated under confinement
  - (ii) Does not detonate at all, deflagrates slowly and shows no violent effect when heated under confinement; or
  - (iii) Does not detonate or deflagrate at all and shows a medium effect when heated under confinement
- Type E: Self-reactive material type E is a self-reactive material that, in laboratory testing, neither detonates nor deflagrates at all and shows only a low or no effect when heated under confinement
- Type F: Self-reactive material type F is a self-reactive material that, in laboratory testing, neither detonates in the cavitated state nor deflagrates at all and shows only a low or no effect when heated under confinement as well as low or no explosive power
- Type G: Self-reactive material type G is a self-reactive material that, in laboratory testing, does not detonate in the cavitated state, will not deflagrate at all, shows no effect when heated under confinement, nor shows any explosive power. They should be desensitized with diluents (with a boiling point above 150°C) when they are thermally stable (SADT is 60–75°C for a 50 kg package) or liquid mixtures

B) Data availability

Very few measurement data concerning flow charts are available.

Self-reactive substances are rarely handled on their own; they are usually marketed and used in the form of chemical compounds or mixtures, with diluents or stabilizers added. Such compounds and mixtures should be tested individually and classified into Types A–G described above.

C) Comparison with previous classification systems

The flow chart of GHS2.8.4 is identical with the Figure 2.4.1 of UNRTDG.

According to EmS, self-reactive substances that do not require temperature control are classified into Schedules S-G along with combustible solids, and those that require temperature control, into

Schedules S-K; they fall into Schedule 149 and 150 of NAERG.

D) Information sources classified according to previous systems, and a tentative classification method

This applies to chemical substances classified into UNRTDG4.1*NAERG149, 150 by UNRTDG and NAERG.

		Temp. control not required (149)		Temp. control required (150)	
		Liquids	Solids	Liquids	Solids
Type A	=	(Substances whose transport is prohibited)			
Type B	=	UN3221	3222	3231	3232
Type C	=	UN3223	3224	3233	3234
Type D	=	UN3225	3226	3235	3236
Type E	=	UN3227	3228	3237	3238
Type F	=	UN3229	3230	3239	3240
Type G	=	Non-dangerous goods			

Typical examples are shown in the table of UNRTDG2.5.3.2.4 (or Note 1 (2) of the attached Table 1 of the Dangerous Goods Regulations), some of which are listed below. Some can be classified into lower type by inactivation agent.

Examples of Type B

3221	No substances specified
3222	2-diazo-1-naphtol-4(5)-sulphochloride
3231	No substances specified
3232	Azodicarbonamide product B (temperature control required)

Examples of Type C

3223	No substances specified
3224	2,2'-azodiisobutyronitrile (with less than 50% water, paste)
3233	No substances specified
3234	2,2'-azodi (isobutyronitrile)

Examples of Type D

3225	No substances specified
3226	Benzene sulfonyl hydrazide
3235	2,2'-azodi (ethyl-2-methyl propionate)
3236	2,2'-azodi (2,4-dimethyl-4-methoxyvaleronitrile)

Examples of Type E

3227	No substances specified
3228	4- dimethylamino benzene diazonium chloride zinc-1
3237	Mixture of diethylene glycol bis (allyl carbonate) (>88%) and diisopropyl peroxydicarbonate (<12%)
3238	No substances specified

Examples of Type F

3229	No substances specified
3230	No substances specified
3239	No substances specified
3240	No substances specified

GHS is not applicable to those classified as Type G.

(2-3-9) Pyrophoric liquids

A) GHS classification criteria

The classification criteria set out in UN GHS 2.9.2 can be summarized as follows:

Liquids that ignite when added to an inert carrier and exposed to air for five minutes or less, and those that char or ignite a filter paper when exposed to air for five minutes or less; no subcategories available.

B) Data availability

Very few data are available.

C) Comparison with previous classification systems

The definition of pyrophoric liquids set out in GHS2.9.1 is consistent with the description in UNRTDG2.4.3.2.2. As described in UNRTDG 2.4.3.3.1, containers are categorized as Grade I.

According to EmS, pyrophoric liquids are classified in Schedules S-M (Pyrophoric Hazards) along with pyrophoric solids described in 2-2-10, or Schedule S-L (Pyrophoric Water-reactive Substances); they fall into Schedule 135 and 136 (Pyrophoric Substances) of NAERG, which classifies pyrophoric substances and self-heating substances (described in 2-2-11) in the same category.

D) Information sources classified according to previous systems, and a tentative classification method

Category 1 appears to correspond with UNRTDG4.2 I (Liquids). These substances may also have the properties of “water-reactive combustible substances” described in 2-2-12.

Examples of UNRTDG4.2 I

1366	Diethylzinc
1370	Dimethylzinc
1380	Pentaborane
2445	Lithium alkyl
2870	Aluminum borohydride
3053	Magnesium alkyl
3076	Aluminum alkyl hydride
3254	Tributyl phosphane
3255	tert-Butyl hypochlorite

(2-3-10) Pyrophoric solids

A) GHS classification criteria

The classification criteria set out in UN GHS 2.10.2 can be summarized as follows:

Solids that ignite when exposed to air for five minutes or less; no subcategories available. Tests shall be performed based on Method N.2 specified in UNRTDG Manual of Tests and Criteria III 33.3.1.4.

B) Data availability

Very few data are available.

C) Comparison with previous classification systems

The definition of pyrophoric solids set out in GHS2.9.1 is consistent with the description in UNRTDG2.4.3.2.1. As described in UNRTDG 2.4.3.3.1, containers are categorized as Grade I.

According to EmS, pyrophoric solids are classified in Schedules S-M (Pyrophoric Hazards) along with pyrophoric liquids described in 2-2-9, or Schedules S-L (Pyrophoric Water-reactive Substances); they fall into Schedules 135 and 136 (Pyrophoric Substances) of NAERG, which classifies pyrophoric substances and self-heating substances (described in 2-2-11) in the same category.

D) Information sources classified according to previous systems, and a tentative classification method

Category 1 appears to correspond with UNRTDG4.2 I (Solids). These substances may also have the properties of “water-reactive combustible substances” described in 2-2-12.

Examples of UNRTDG4.2 I

1854	Barium alloy
1855	Calcium or calcium alloy
2005	Magnesium diphenyl
2008	Zirconium powder (dry)
2441	Titanium trichloride
2545	Hafnium powder (dry)
2546	Titanium powder (dry)

(2-3-11) Self-heating substances and mixtures

A) GHS classification criteria

The classification criteria set out in UN GHS 2.11.2 can be summarized as follows:

Liquids, solids or mixtures (other than pyrophoric liquids or solids) that, in contact with air and without an energy supply, are liable to self-heating. Tests shall be performed based on Method N specified in UNRTDG Manual of Tests and Criteria III 33.3.1.4.6.

Category 1: Test results on a 25 mm cube sample show positive at 140°C.

Category 2: (a) Test results on a 100 mm cube sample and a 25 mm cube sample show positive and negative, respectively, at 140°C; the substances or mixtures concerned are packaged in a container larger than 3 m^3, or

(b) Test results on a 100 mm cube sample and a 25 mm cube sample show positive and negative, respectively, at 140°C, and those on a 100 mm cube sample show positive at 120°C; the substances or mixtures concerned are packaged in a container larger than 450 liters.

(c) Test results on a 100 mm cube sample and a 25 mm cube sample show positive and negative, respectively, at 140°C, and those on a 100 mm cube sample show positive at 100°C.

B) Data availability

Very few data are available.

C) Comparison with previous classification systems

Of Category 4.2 described in UNRTDG2.4.3.2.3, the definition of self-heating substances is consistent with the classification criteria of GHS2.11.2. Container Grade II and Grade III correspond with Category 1 and Category 2 of GHS, respectively. Category 4.2 also includes pyrophoric solids (2.4.3.2.1) and pyrophoric liquids (2.4.3.2.2). They fall into Schedules 135 and 136 (Pyrophoric Substances) of NAERG.

According to EmS, self-heating substances and mixtures are classified in Schedules S-J (Wet Explosives and Self-Heating Substances), with the former falling into Category 4.1 of UNRTDG, as described in 2-2-1E.

D) Information sources classified according to previous systems, and a tentative classification method

Substances covered are those classified in UNRTDG4.2*EmS: S-J.

Examples of Category 1

UNRTDG4.2II*EmS: S-J

1369	p-nitro-dimethyl aniline
1382	Potassium sulfide (anhydride, or crystalline water<30%)
1384	Sodium dithionite
1385	Sodium sulfide (anhydride, or water of crystallization <30%)
1923	Calcium dithionite
1929	Potassium dithionite

2318	Sodium hydrogen sulfide (water of crystallization <25%)
2940	9-phosphabicyclononane
3341	Thiourea dioxide

Examples of Category 2

UNRTDG4.2III*EmS: S-J

1362	Activated carbon
1363	Copra
1364	Cotton waste (oily)
1365	Raw cotton (wet)
1379	Oil coated paper (carbon paper)
1387	Wool waste (wet)
1386	Seedcake (with vegetable oil)
1857	Textile waste
2002	Celluloid waste
2793	Iron and steel cutting scrap
3174	Titanium disulfide

(2-3-12) Substances and mixtures which, in contact with water, emit flammable gases

A) GHS classification criteria

The classification criteria set out in UN GHS 2.12.2 can be summarized as follows:

Solids, liquids or mixtures that in contact with water become pyrophoric or emit large amounts of flammable/combustible gases.

Category 1: Substances or mixtures that react violently with water at ambient temperatures and are liable to emit flammable gases, or whose generation rates of flammable gases exceed 10 liter/min/kg.

Category 2: Substances or mixtures (other than those classified in Category 1) that react rapidly with water at ambient temperatures and are liable to emit flammable gases, or whose maximum generation rates of flammable gases exceed 20 liter/min/kg.

Category 3: Substances or mixtures (other than those classified as Category 1 or 2) that react slowly with water at ambient temperatures and are liable to emit flammable gases, or whose maximum generation rates of flammable gases exceed 1 liter/min/kg.

B) Data availability

Very few data on gas generation rates are available.

C) Comparison with previous classification systems

The classification criteria of GHS2.12.2 are identical with that of Category 4.3 of UNRTDG; those of EU-Annex VI are also consistent with GHS, although no category is provided.

D) Information sources classified according to previous systems, and a tentative classification method

Relevant laws and regulations in line with UNRTDG, such as the Dangerous Goods Regulations (Japan), are applicable.

Category 1 = UNRTDG 4.3I

Category 2 = UNRTDG 4.3II

Category 3 = UNRTDG 4.3III

Substances specified in UNRTDG 4.2 (4.3) are classified in Category 1 of GHS.

The classification criteria apply to substances specified in R15 of EU-Annex I, although no category is provided.

The following (NAERG Schedule) are relevant to GHS water-reactive flammability:

135	Pyrophoric substances
138	Water-reactive substances that emit flammable gases
139	Water-reactive substances that emit flammable/toxic gases

Examples of substances to which the classification criteria apply

Category 1 UNRTDG4.3I*NAERG138: Alkali metals and their alloys or hydrides, or amalgams and suspended solids (including alkali earth metals)

1410	Lithium aluminum hydride
1426	Sodium borohydride
1428	Sodium

UNRTDG4.3I*NAERG139: Phosphides and part of silane compounds

1183	Ethyldichlorosilane
1360	Calcium phosphide
1714	Zinc phosphide

Category 2 UNRTDG4.3II*NAERG138: Alkali earth metals, metal carbides and metal silicides

1394	Aluminum carbide
1401	Calcium
2624	Magnesium silicide

UNRTDG4.3II*NAERG139: Phosphides and some silanes

1340	Phosphorus pentasulfide
1395	Aluminum ferrosilicon

Category 3 UNRTDG4.3III*NAERG138: Light metals and metal silicides

1398	Aluminum silicon powder
1435	Zinc scrap

UNRTDG4.3II*NAERG139: Metal silicides

1408	Ferrosilicon

E) Water-reactive substances to which the classification criteria do not apply

The GHS classification criteria do not apply to substances that in contact with water produce nonflammable (often toxic or corrosive) gases or generate heat (along with hazardous splashes). NAERG provides a Schedule, which includes the term “water-reactive.”

137	Water-reactive substances – corrosive to metals such as phosphorus pentoxide and sulfuric acid
144	Oxidants (water-reactive), sodium peroxide
155	Toxic/corrosive to metals (flammable/water-reactive), acetone cyanohydrin
156	Toxic/corrosive to metals (combustible/water-reactive), benzyl chloride
157	Toxic/corrosive to metals (non-combustible/ water-reactive), antimony trichloride
166	Radioactive substances – corrosive to metals such as uranium hexafluoride (water-reactive)

These substances should be treated without regard to “water-reactive combustibility” defined in GHS.

(2-3-13) Oxidizing liquids

A) GHS classification criteria

The classification criteria set out in UN GHS 2.13.2 can be summarized as follows (tests shall be performed based on Method O.2 described in UNRTDG Manual of Tests and Criteria 34.4.2):

Category 1: Substances or mixtures that in 1:1 mixtures (by mass) with cellulose spontaneously ignite; or for which the mean pressure rise time of their 1:1 mixtures (by mass) with cellulose is less than that of a 1:1 mixture (by mass) of 50% perchloric acid and cellulose.

Category 2: Substances or mixtures: whose mean pressure rise time of their 1:1 mixtures (by mass) with cellulose is less than that of a 1:1 mixture (by mass) of 40% aqueous sodium chlorate solution and cellulose; that are not classified in Category 1.

Category 3: Substances or mixtures: whose mean pressure rise time of their 1:1 mixtures (by mass) with cellulose is less than that of a 1:1 mixture (by mass) of 65% aqueous nitric acid and cellulose; that are classified in neither Category 1 nor Category 2.

B) Data availability

Very few data on oxidization tests are available.

C) Comparison with previous classification systems

The classification criteria of GHS2.13.2 are identical with those of Category 5.1 of UNRTDG2.5.2.3.2.

NAERG classifies oxidizing substances (including solids) in Schedules 140, 141, 142, 143 and 144 – which do not serve as guidance for GHS classification. EmS classifies oxidizing liquids and solids in

Schedules S-Q.

D) Information sources classified according to previous systems, and a tentative classification method

Category 1 = UNRTDG-5.1I (Liquids)

Category 2 = UNRTDG-5.1II (Liquids)

Category 3 = UNRTDG-5.1III (Liquids)

Examples of Category 1

1873	Perchloric acid solution (50-72%)
2495	Iodine pentafluoride

Examples of Category 2

2014	Hydrogen peroxide solution (20-40%)
2427	Potassium chlorate solution (classified in Category 3, depending on the concentration)

Example of Category 3

2984	Hydrogen peroxide solution (8-20%)

(2-3-14) Oxidizing solids

A) GHS classification criteria

The classification criteria set out in UN GHS 2.14.2 can be summarized as follows (tests shall be performed based on Method O.1 described in UNRTDG Manual of Tests and Criteria 34.4.1):

Category 1: Substances or mixtures whose mean burning time of their 4:1 or 1:1 mixtures (by mass) with cellulose is less than that of the 3:2 mixture (by mass) of potassium bromate and cellulose.

Category 2: Substances or mixtures: whose mean burning time of their 4:1 or 1:1 mixtures (by mass) with cellulose is less than that of the 2:3 mixture (by mass) of potassium bromate and cellulose; that are not classified in Category 1.

Category 3: Substances or mixtures: whose mean burning time of their 4:1 or 1:1 mixtures (by mass) with cellulose is less than that of the 3:7 mixture (by mass) of potassium bromate and cellulose; that are classified as neither Category 1 nor Category 2.

B) Data availability

Very few data on oxidation tests are available.

C) Comparison with previous classification systems

The classification criteria of GHS2.14.2 are identical with those of Category 5.1 of UNRTDG2.5.2.2.2.

NAERG classifies oxidizing substances (including liquids) in Schedules 140, 141, 142, 143 and 144 – which do not serve as guidance for GHS classification. EmS classifies oxidizing solids and liquids in Schedules S-Q.

D) Information sources classified according to previous systems, and a tentative classification method

Category 1 = UNRTDG-5.1I (Solids)

Category 2 = UNRTDG-5.1II (Solids)

Category 3 = UNRTDG-5.1III (Solids)

Examples of Category 1

1504	Sodium peroxide
2466	Potassium superoxide

Examples of Category 2

1439	Ammonium dichromate
1463	Chromium trioxide (anhydride)
1493	Silver nitrate
1496	Sodium chlorite (solid)
2719	Barium bromate

Examples of Category 3

2067	Ammonium nitrate fertilizers
2469	Zinc bromate

2724	Manganese nitrate
2728	Zirconium nitrate

(2-3-15) Organic peroxides

A) GHS classification criteria

The classification criteria set out in UN GHS 2.15.2 can be summarized as follows:

Organic compounds containing oxygen in the bivalent -O-O- structure are not considered organic peroxides if any of the following applies:

a) For materials containing no more than 1.0% hydrogen peroxide, the available oxygen is less than 1.0%, or

b) For materials containing more than 1.0% but not more than 7.0% hydrogen peroxide, the available oxygen is less than 0.5 percent

For a single organic peroxide, however, the content resulting in 1% active oxygen is given by the following formula, with the formula shown in 2.15.2 converted:

$C = m/16*n(\%)$

In the case of benzoyl peroxide (molecular weight 242.24), the exception rule set out in 2.15.2 is not applicable, regardless of the hydrogen peroxide content, when the active oxygen content exceeds 15.2 % -- and hence tests are required for classification. For peracetic acid (molecular weight 76.06), meanwhile, the active oxygen content exceeds 1% with 4.8% hydrogen peroxide. Other organic peroxides can be calculated in the same manner. In general, the content of hydrogen peroxide does not influence the judgment on the exclusion unless it is very low.

Organic peroxides, based on the classification criteria of GHS2.8.4, fall into each of the following categories:

- Type A: Organic peroxide type A is a material that, as packaged for transportation, can detonate or deflagrate rapidly
- Type B: Organic peroxide type B is a material that, as packaged for transportation, neither detonates nor deflagrates rapidly, but is liable to undergo thermal explosion in the package
- Type C: Organic peroxide type C is a material that, as packaged for transportation, neither detonates nor deflagrates rapidly and cannot undergo thermal explosion
- Type D: Organic peroxide type D is a material that:
    - (iv) Detonates partially, does not deflagrate rapidly and shows no violent effect when heated under confinement
    - (v) Does not detonate at all, deflagrates slowly and shows no violent effect when heated under confinement; or
    - (vi) Does not detonate or deflagrate at all and shows a medium effect when heated under confinement

- Type E: Organic peroxide type E is a material that, in laboratory testing, neither detonates nor deflagrates at all and shows only a low or no effect when heated under confinement
- Type F: Organic peroxide type F is a material that, in laboratory testing, neither detonates in the cavitated state nor deflagrates at all and shows only a low or no effect when heated under confinement as well as low or no explosive power
- Type G: Organic peroxide type G is a material that, in laboratory testing, does not detonate in the cavitated state, will not deflagrate at all, shows no effect when heated under confinement, nor shows any explosive power; they should be desensitized with diluents (with a boiling point above 150°C) when they are thermally stable (SADT is above 60°C for a 50 kg package) or liquid mixtures.

B) Data availability

While the calculation of active oxygen content is easy for those with a basic knowledge of chemistry, that of hydrogen peroxide content requires careful analysis, except where it is added intentionally. Very few data on test results concerning flow charts are available. Organic peroxides are rarely handled on their own; they are usually marketed and used in the form of chemical compounds or mixtures, with diluents or stabilizers added. Such compounds and mixtures should be tested individually and classified as types A-G described above.

C) Comparison with previous classification systems

The flow chart of GHS2.15.2.2 is identical with Figure 2.5.1 of UNRTDG.

D) Information sources classified according to previous systems, and a tentative classification method

Chemical substances covered are those classified in UNRTDG5.2*NAERG147 and 148 by UNRTDG and NAERG.

		Temp. control not required (147)		Temp. control required (148)	
		Liquids	Solids	Liquids	Solids
Type A	=	(Substances whose transport is prohibited)			
Type B	=	UN3101	3102	3111	3112
Type C	=	UN3103	3104	3113	3114
Type D	=	UN3105	3106	3115	3116
Type E	=	UN3107	3108	3117	3118
Type F	=	UN3109	3110	3119	3120
Type G		(Non-dangerous goods)			

Typical examples are shown in the table of UNRTDG2.5.3.2.4 (or Note 3 of the attached Table 1 of the Dangerous Goods Regulations), some of which are listed below. Some can be classified into lower type by inactivation agent.

Examples of Type B

3101	tert-Amyl peroxy-3,5,5-trimethylhexanoate
3102	The correct compound name to be extracted from the table of the Dangerous Goods Regulations
3111	Diisobutyl peroxide (32-35%, diluent B>48%)

3112	Dibenzyl peroxydicarbonate (<87%, water>13%)

Examples of Type C

3103	tert-Amyl peroxybenzoate
3104	Benzoyl peroxide (<77%, water >23%)
3113	tert-Butyl peroxy diethyl acetate
3114	Didecanoyl peroxide

Examples of Type D

3105	Acetyl acetone peroxide (<42%, diluent A >48%, water >8%)
3106	Dilauroyl peroxide
3115	Diacetyl peroxide (<27%, diluent B>73%)
3116	Di-n-nonanoyl peroxide

Examples of Type E

3107	Di-tert-amyl peroxide
3108	Benzoyl peroxide (<52%, paste)
3117	Dipropionyl peroxide (<27%, diluent B >73%)
3118	tert-Butyl peroxy neodecanoate (<42%, stable frozen-water dispersion element)

Examples of Type F

3109	Peracetic acid (with stabilizer)
3110	Dicumyl peroxide (>42%, solid diluent <57%)
3119	Diacetyl peroxydicarbonate (<42%, stable frozen-water dispersion element)
3120	None

(2-3-16) Metal Corrosives

A) GHS classification criteria

GHS2.16.2 defines metal corrosives as substances whose corrosion rates on steel or aluminum exceed 6.25 mm per year at 55°C.

B) Data availability

Very few data on metal corrosion rates are available.

C) Comparison with previous classification systems

The definition provided by GHS is identical to that for metal corrosiveness of Class 8 Pkg III set out in UNRTDG2.8.2.5(c) (ii).

D) Information sources classified according to previous systems, and a tentative classification method

As UNRTDG Class 8 covers both metal corrosiveness and skin corrosiveness, the attached Table 1 of the Dangerous Goods Regulations does not indicate metal corrosiveness. Corrosion tests require metal samples with immaculate surfaces – which makes them very costly. A feasible solution for the moment would be to classify substances commonly known as corrosives as “metal corrosives,” and to label “possible metal corrosive” as such. The GHS classification is based on UNRTDG, which is designed to address the leakage of hazardous substances. Possible hazards associated with the storage and use of such substances (i.e., containers and piping) should therefore be taken into account, even if they are not included in the classification.

Chapter 3. Health Hazards

[3-1] Information useful for classification

Substances shall be classified according to the criteria for classification, obtaining the required data from the information sources specified below.

Major information sources containing a general introduction or databases and their priorities are provided below. Information sources listed under each priority are similar in terms of their credibility and hence have the same priority, although they may vary in terms of the toxicity indices that they cover (for example, IARC specializes in information related to carcinogenicity and mutagenicity). This should not limit the use of reliable and useful information sources other than those listed here (such as JMPR for pesticides). The number of substances referred to in each information source represents an estimate as of October 2004.

For classification, review all of the acquired or accessible evaluation documents specified under Priority 1 to look for information on the relevant substance. If the selected source lacked the required information, check additional sources. If the required information could not be obtained from sources in Priority 1, repeat the process with sources in Priority 2. Information sources in Priority 3 are presented merely for reference and basically do not need to be reviewed.

Priority 1:

Reliable information sources provided by international agencies, governments of major countries, etc. Basically, evaluation documents and books whose primary sources can be traced and whose accuracy can be confirmed wherever necessary.

1-1) “Chemical Substance Hazard Data” (294 substances as of September 2005), prepared by the Chemicals Evaluation and Research Institute, Japan (CERI)

http://www.cerij.or.jp/ceri_jp/koukai/sheet/sheet_indx4.htm

http://www.safe/nite.go.jp/data/sougou/pk_list.html?table_name=hyoka&rank=sheet&sort=cas&page=1

1-2) “Hazard Evaluation” (99 substances as of September 2005, documentation in progress), prepared by the Chemicals Evaluation and Research Institute, Japan (CERI) and the National Institute of Technology and Evaluation (NITE)

http://www.safe.nite.go.jp/data/sougou/pk_search_frm.html?search type=list

1-3) “Initial Risk Evaluation”, prepared by the National Institute of Technology and Evaluation

1-4) "Report on Toxicity Tests of Chemical Substances" (300 substances), prepared by the Liaison Council on the Promotion of Chemical Substances Examination, Ministry of Health, Labour and Welfare

http://www.db.mhlw.go.jp/ginc/html/db1-j.html

1-5) "Chemical Substance Environmental Risk Assessment" Volumes 1, 2 and 3 (as of September 2005), prepared by the Environmental Risk Assessment Office, Ministry of the Environment

http://www/env.go.jp/chemi/risk/index.html

1-6) "SIDS Initial Assessment Report" (180 substances as of November 2004), prepared by OECD

http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html

1-7) "Environmental Health Criteria (EHC)" (No.1-No.231 as of September 2005), prepared by WHO/IPCS

http://www.inchem.org/pages/ehc.html

http://www.who.int/ipcs/publications/ehc/en/index.html

Japanese translation of EHC "Kagaku Busshitsu no Anzensei Hyouka (Environmental Health Criteria) Volumes 1, 2, 3 and 4", planned and edited by Division of Safety Information on Drug, Food and Chemicals, the National Institute of Health Sciences, issued by The Chemical Daily Co., Ltd.

Abridged Japanese translation of EHC: http://www.nihs.go.jp/DCBI/PUBLIST/ehchsg/

1-8) "Concise International Chemical Assessment Documents", prepared by WHO/IPCS
http://www.who.int/ipcs/publication/cicad/pdf/en

Abridged and full translations of CICAD Executive Summary (84 substances as of 2005)

http://www.nihs.go.jp/cicad/cicad2.html

1-9) "ACGIH Documentation of the threshold limit values for chemical substances (7th edition, 2001)" (690 substances), prepared by American Conference of Governmental Industrial Hygienists; and

"TLVs and BEIs" (annually issued by ACGIH)

1-10) “Occupational Toxicants: Critical Data Evaluation for MAK Values and Classification of Carcinogens” Vol. 1-20 (300 substances) prepared by Deutsche Forschungsgemeinschaft (DFG); and

“List of MAK and BAT values” (annually issued by DFG)

1-11) “EU Risk Assessment Report” (Volumes 1-55 as of September 2005), prepared by EU

Accessible at the following website:

http://ecb.jrc.it/existing-chemicals/

“DOCUMENT” tab → “RISK ASSESSMENT”

1-12) “Assessment Report”, prepared by Canadian and Australian governments

“Priority Substance Assessment Reports” (66 substances as of September 2005), prepared by Environment Canada

“Priority Existing Chemical Assessment Reports” (No.1-No.26 as of September 2005), prepared by Australia NICNAS

Both accessible at the following website of the National Institute of Technology and Evaluation, under “Risk assessment target substances specified by various countries”

http://www.safe.nite.go.jp/data/sougou/pk_search_frm.html?search_type=list

1-13) “Technical Report Series” (100 substances) and JACC Report Series, prepared by the European Center for Ecotoxicology and Toxicology of Chemicals (ECETOC)

1-14) Patty’s Toxicology (5th edition, 2001)

1-15) “IARC Monographs Programme on the Evaluation of Carcinogenic Risk to Humans”, prepared by WHO International Agency for Research on Cancer (IARC)

http://monographs.iarc.fr/

or

http://monographs.iarc.fr/htdig/search.html

Only “Summary of Data reported and Evaluation” can be accessed at the above websites. For full text, see IARC publications.

1-16) US-EPA Integrated Risk Information System (IRIS): http://www.epa.gov/iris/

1-17) U.S. National Toxicology Program (NTP): http://ntp-server.niehs.nih.gov/

● NTP Database Search Home Page:

http://ntp-apps.niehs.nih.gov/ntp_tox/index/cfm

[For Standard Toxicology & Carcinogenesis Studies, Reproductive Studies, Developmental Studies, Immunology Studies, Genetic Toxicity Studies] or

http://ntp-server.niehs.nih.gov/ → Study Results & Research Projects → Study Data Searches

● Report on Carcinogens:

http://ntp-server.niehs.nih.gov/ → Public Health → Report on Carcinogens → 11th RoC (The 11th RoC contains 246 entries, 58 of which are listed as known to be human carcinogens and with the remaining 188 being listed as reasonably anticipated to be human carcinogens.) or

http://ehp.niehs.nih.gov/roc/toc10.html

or

http://ehp.niehs.nih.gov/ntp/docs/ntp.html

● Carcinogenicity Technical Reports

http://ntp-server.niehs.nih.gov/ → Study Results & Research Projects → NTP Study Reports (reports/abstracts of tests including carcinogenicity tests) → Long-term → TR1-TR533 (Reports on carcinogenicity)

1-19) "Recommendations for allowable concentrations (2004)", Journal of Occupational Health Vol. 46, p124-148, 2004, prepared by Japan Society for Occupational Health

Evaluation documents prepared by WHO including EHC, CICAD and IARC can be searched collectively and accessed at website (1) below. Website (2) is linked to risk assessment documents in Japan, U.S and other countries, including those prepared by international agencies.

(1) http://www.inchem.org/

(2) http://www.safe.nite.go.jp/data/sougou/pk_search_frm.html?search_type=list

Priority 2:

Database etc. of primary sources.

2-1) “RTECS” (156,000 substances), prepared by National Institute of Occupational Safety and Health (NIOSH)

2-2) “International Chemical Safety Cards” (1,400 substances), prepared by WHO/IPCS

Although this source is reviewed worldwide and has high credibility, due to the lack of a cited reference list, it is listed under Priority 2 instead of Priority 1.

http://www.ilo.org/public/english.protection/safework/cis/products/icsc/dtasht/index.htm

“Japanese version of IPCS card”: http://www.nihs.go.jp/ICSC/

2-3) “International Uniform Chemical Information Database (IUCLID)” (2,000 substances); and

IUCLID CD-ROM (Updated version, Edition 2-2000) (2,600 substances), prepared by EU European Chemicals Bureau (ECB)

IUCLID data can be downloaded from the following website:

_http://exb.jrc.it/esis.php?PGM=hpv&DEPUIS=autre

2-4) Annex I of EU 7th Amendment to Council Directive (Latest edition: 29th Directive adapting to Council Directive):

Classification results in Annex I (7,400 substances) can be searched at the European Chemicals Bureau (ECB) “SEARCH CLASSLAB”

http://ecb.jrc.it/classification-labelling/

2-5) HSDB: Hazardous Substance Data Bank

http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

2-6) ATSDR: Toxicological Profile

http://www.atsdr.cdc.gov/toxpro2.html

2-7) Hazardous Substance Fact Sheet (New Jersey Department of Health and Senior Services):

http://www.state.nj.us/health/eoh/rtkweb/rtkhsfs.html

2-8) Sittig’s Handbook of Toxic and Hazardous Chemicals and Carcinogens (4th edition, 2002)

2-9) German Chemical Society - Advisory Committee on Existing Chemicals of Environmental Relevance: “BUA Report” (230 substances, but full report is not available at the website)

2-10) Dreisbach’s Handbook of Poisoning (13th edition, 2002)

Priority 3:

Databases for searching and accessing the primary literature. Basically, these databases do not need to be reviewed. Hazard information for individual products that are available from existing MSDSs etc. should not be used for GHS classification of health hazards.

3-1) Document database (search for primary literature)

● Pub-Med/NLM (original literature search)

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi

● NLM TOXNET (on-line search including TOXLINE (original literature search))

http://toxnet.nlm.nih.gov/index.html

● JICST Scientific and technical (medical) literature file (JOIS on-line search)

http://pr.jst.go.jp/db/db.html

3-2) Integrated database of chemical substances

● "Chemical Risk Information Platform" by National Institute of Technology and Evaluation

http://www.safe.nite.go.jp/japan/db/html

● GESTIS-database of hazardous substances (BIA)

http://www.hvbg.de/e/bia/fac/stoffdb/index.html

● "WebKis-Plus Chemicals Database" by National Institute for Environmental Studies

http://w-chemdb.nies.go.jp/

Priorities Where Conflicting Data Exist

The following shall be given a high priority:

1. Data verified by credible agencies, such as those derived from the materials specified in “Priority 1”
2. Data that are deemed reliable, such as those obtained by GLP-conforming laboratories or those whose scientific basis is available and verified
3. Data obtained from other information sources, such as those derived from the materials specified in “Priority 2” and “Priority 3”
4. Latest data (where conflicting data of the same priority are available) or data derived from reliable publications
5. Finally, conservative data shall be adopted, excluding measurement values that are considered abnormal when compared with other relevant data. When classification results based on conflicting data belong to several hazard categories, that supported by the largest amount of data shall be adopted.

[3-2] Classification of health hazards

(3-2-1) Acute toxicity

A) Classification criteria

	Category 1	Category 2	Category 3	Category 4	Category 5
Oral (mg/kg) note (a)	5	50	300	2000	5000 see detailed criteria in note (f)
Dermal (mg/kg) note (a)	50	200	1000	2000	
Gases (ppm) see: notes (a), (b)	100	500	2500	5000	
Vapors (mg/L) see: notes (a), (b), (c), (d)	0.5	2.0	10	20	
Dusts and Mists (mg/L) see: notes (a), (b), (e)	0.05	0.5	1.0	5	

Notes

(a) Acute toxicity values are expressed as LD_{50} (oral, dermal), LC_{50} (inhalation) or acute toxicity estimate (ATE) values.

(b) Gas concentrations are expressed in parts per million by volume (ppmV). Inhalation cut-off values in the table are based on 4-hour test exposures. The existing inhalation toxicity data obtained from 1-hour exposures should be converted by dividing it by a factor of 2 for gases and vapors and 4 for dusts and mists.

(c) It is recognized that saturated vapor concentration may be used as an additional consideration by some regulatory systems to provide for specific health and safety protection. (e.g. United

Nations Recommendations for the Transport of Dangerous Goods).

(d) For some chemicals, the test atmosphere may not just be a vapor but may consist of a mixture of liquid and vapor phases. For other chemicals, the test atmosphere may consist of a vapor which is substantially a gaseous phase. In the latter case, classification should be based on ppm as follows: Category 1 (100 ppm), Category 2 (500 ppm), Category 3 (2500 ppm), Category 4 (5000 ppm). The terms "dusts", "mists" and "vapors" are defined as follows:

Dusts: Solid particles of a substance or a mixture that float in a gas (usually air).

Mists: Liquid droplets of a substance or a mixture that float in a gas (usually air)

Vapors: Gaseous substances or mixtures released from a liquid or solid.

Generally, dusts are formed through a mechanical process, while mists are formed through condensation of supersaturated vapors or physical shearing of liquids. Dust and mist particles are generally smaller than 1 μm but can range up to about 100 μm.

(e) The values for dusts and mists should be reviewed to adapt to any future changes to OECD Test Guidelines made due to technical limitations in generating, maintaining and measuring concentrations of dusts and mists in respirable forms.

(f) Criteria for Category 5 are intended to enable the identification of substances which have relatively low acute toxicity but which, under certain circumstances, may present a danger to vulnerable populations. These substances are anticipated to have an oral or dermal LD_{50} value in the range of 2000–5000 mg/kg and equivalent doses for inhalation. The specific criteria for Category 5 are:

(i) The substance is classified in this category if reliable evidence that indicates the LD_{50} (or LC_{50}) to be in the range of Category 5 values is already available or if other animal studies or toxic effects in humans indicate a concern for acute effects on human health.

(ii) The substance is classified in this category if assignment to a more hazardous category can be ruled out through extrapolation, estimation or measurement of data, and:

- if reliable information indicating significant toxic effects in humans is available; or
- if any mortality is observed when tested up to Category 4 values by oral, inhalation or dermal routes; or
- where expert judgment confirms significant clinical signs of toxicity (except for diarrhea, piloerection or an ungroomed appearance) when tested up to Category 4 values; or
- where expert judgment confirms reliable information indicating the potential for significant acute effects from other animal tests.

B) Data availability

・Data availability can be summarized as follows according to the status and exposure routes of the substances.

	Gases	Liquids	Solids
Oral	N.A.	Abundant	Abundant
Dermal	Extremely rare	Relatively abundant	Extremely rare
Inhalation	Abundant	Rare (vapors, mists)	Rare (dusts)

・Classification should be performed based on the toxicity values reported in a form available for classification.

C) Priorities where conflicting data exist

The following shall be given a high priority:

1. Data verified by credible agencies, such as those derived from the materials specified in “Priority 1”
2. Data that are deemed reliable, such as those obtained by GLP-conforming laboratories or those whose scientific basis is available and verified
3. Data obtained from other information sources, such as those derived from the materials specified in “Priority 2” and “Priority 3”. Despite its large quantity of data, the priority of RTECS should be determined according to criteria 4 and 5, since credibility of the data has not been verified by NIOSH, its editorial agency.
4. Latest data (where conflicting data of the same priority are available) or data derived from reliable publications
5. Finally, conservative data shall be adopted, excluding measurement values that are considered abnormal when compared with other relevant data. When classification results based on conflicting data belong to several hazard categories, those with the largest amount of supporting data shall be adopted.

D) Comparison with previous classification systems

・There is no system with complete correspondence.

・EU-Annex I can be referred to as a rough guide but does not correspond completely.

<table>
<tr><th colspan="2">Category</th><th>1</th><th>2</th><th>3</th><th>4</th><th>5</th></tr>
<tr><td rowspan="2">(Oral)
mg/kg</td><td>GHS</td><td>5</td><td>50</td><td>300</td><td>2000</td><td>5000</td></tr>
<tr><td>EU-R phrase</td><td colspan="2">R28 25</td><td>R25 200</td><td>R22 2000</td><td></td></tr>
<tr><td rowspan="2">(Dermal)
mg/kg</td><td>GHS</td><td>50</td><td>200</td><td>1000</td><td>2000</td><td>5000</td></tr>
<tr><td>EU-R phrase</td><td>R27 50</td><td colspan="2">R24 400</td><td>R21 2000</td><td></td></tr>
<tr><td rowspan="2">(Inhalation)
mg/kg</td><td>GHS</td><td>0.5</td><td>2.0</td><td>10</td><td>20</td><td></td></tr>
<tr><td>EU-R phrase</td><td>R26 0.5</td><td>R23 2.0</td><td colspan="2">R20 20</td><td></td></tr>
</table>

・UNRTDG Class 6.1 is not categorized by the exposure route.

E) Instructions

・Note that units for inhalation toxicity vary depending on the form of the inhaled substance. Classification should be performed on the basis of the values for gases (ppm) if the test atmosphere consists of a gaseous phase including vapor which is substantially a gaseous phase, values for vapors (mg/L) if the test atmosphere consists of a liquid with a relatively low boiling point and values for mists (mg/L) for other cases.

(reference) Conversion of ppm and mg/L units (under 1 atm at 25℃)

$(\text{ppm}) = \{(\text{mg/L}) \times 24.45 \times 10^{3}\} / \text{molecular weight}$

$(\text{mg/L}) = \{(\text{ppm}) \times \text{molecular weight} \times 10^{-3}\} / 24.45$

・Doses higher than 2000 mg/kg are not used in recent oral and dermal toxicity tests; therefore, data corresponding to Category 5 can be found only in old reports. For classification based on recent test reports, the data must be examined to check whether any mortality was observed in the test animals or whether information indicating acute toxicity effects is available.

・Criteria for Category 5 for inhalation toxicity are not presented and only defined as doses equivalent to the range of 2000–5000 mg/kg by the oral or dermal route. Whether a substance belongs to Category 5 should be judged on the basis of the notes for “A) Classification criteria”. Category 5 is originally intended to identify chemicals which have relatively low acute toxicity but which, under certain circumstances, may present a danger to vulnerable populations. If the data suggest such a risk, the substance should be classified as Category 5.

(3-2-2) Skin corrosion/irritation

A) Classification criteria

Category Corrosive	Corrosive subcategories	Corrosive in ≧1 of 3 animals	
(applies to authorities not using subcategories)	(only applies to some authorities)	Exposure period	Observation period
corrosive	1A	≦3 minutes	≦1 hour
	1B	>3 minutes – ≦1 hour	≦14 days
	1C	> 1 hour – ≦4 hours	≦14 days

Category	Criteria
Irritant (Category 2) (Applies to all regulatory authorities)	(1) Values of ≧2.3 – <4.0 for erythema/eschar or for edema in at least 2 of 3 tested animals from grading at 24, 48 and 72 hours after patch removal or, if reactions are delayed, from grading on 3 consecutive days after the onset of skin responses; or (2) Inflammation that persists to the end of the observation period, normally 14 days, in at least 2 animals, particularly taking into account alopecia (in limited area), hyperkeratosis, hyperplasia and scaling; or (3) In some cases where there is pronounced variability of response among animals and where very definite positive effects that are related to chemical exposure but are less than the criteria above are observed in a single

	animal.
Mild irritant (Category 3) (only applies to some regulatory authorities)	Values of ≧1.5 – <2.3 for erythema/eschar or for edema in at least 2 of 3 tested animals from grading at 24, 48 and 72 hours after patch removal or, if reactions are delayed, from grading on 3 consecutive days after the onset of skin responses (when not included in the irritant category above).

B) Data availability

・The definitions of the categories are based on irritation test results, but there are few data books that contain specific Draize scores to which GHS criteria can be applied. Classification of substances into subcategories (1A, 1B, 1C) under Category 1 cannot be performed without specific data.

(OECD has proposed a test method guideline 435 (in vitro membrane barrier test) for classifying into skin corrosion categories (1A, 1B, 1C).)

・If an appropriate information source based on data cannot be obtained easily, classification can be performed based on comments related to skin corrosion/irritation, such as Severe, Moderate and Mild, in test reports or existing MSDSs.

・Classification can be performed based on R-Phrases (R34, R35, R38, R36/37, R36/38, R37/R38, R36/37/38) related to skin corrosion/irritation in Annex I of EU 7th Amendment to Council Directive.

C) Priorities where conflicting data exist

The following shall be given a high priority:

1. Data that are verified by credible agencies, such as those derived from the materials specified in “Priority 1”, and contain descriptions of skin corrosion/irritation.

2. Data that are deemed reliable, such as those obtained by GLP-conforming laboratories or those whose scientific basis is available and verified

3. Data obtained from other information sources, such as those derived from the materials specified in “Priority 2” and “Priority 3”.

4. Latest data (where conflicting data of the same priority are available) or data derived from reliable literatures

5. Finally, conservative data shall be adopted, excluding measurement values that are considered abnormal when compared with other relevant data. When classification results based on conflicting data belong to several hazard categories, those with the largest amount of supporting data shall be adopted.

D) Comparison with previous classification systems

・Substances classified as Corrosive (C) with R34 or R35 in EU-Annex I correspond to Category 1.

・Substances classified as Irritant (Xi) with R38 or combination R-Phrases relevant to R38 (R36/38, R37/R38, R36/37/38) in EU-Annex I correspond to Category 2.

E) Instructions

・Substances evaluated as “Severe”, “Moderate” and “Mild” for skin corrosion and irritation in test reports roughly correspond to Category 1, Category 2 and Category 3, respectively. However, Category 1 includes substances that cause irreversible lesions (such as necrosis) during the observation period in skin corrosion/irritation tests. A substance marked “Severe” but inducing no irreversible lesion is classified as category 2.

・In terms of physicochemical properties, substances described as strong acids (pH≦2) or strong bases (pH≧11.5) are classified as Category 1.

(3-2-3) Serious eye damage/eye irritation

A) Classification criteria

An eye irritant Category 1 (irreversible effects on the eye) is a material that produces:

- at least in one animal, effects on the cornea, iris or conjuctiva that are not expected to reverse or have not fully reversed within an observation period of (normally) 21 days;

and/or

- at least in 2 of 3 tested animals, a positive response of:

corneal opacity ≧ 3 and/or

iritis > 1.5,

calculated as the mean score following grading at 24, 48 and 72 hours after application of the test material.

An eye irritant Category 2A (irritating to eyes) is a material that produces:

– at least in 2 of 3 tested animals, a positive response of:

corneal opacity ≧ 1 and/or

iritis ≧ 1 and/or

conjunctival redness ≧ 2 and/or

conjunctival edema ≧ 2,

calculated as the mean score following grading at 24, 48 and 72 hours after application of the test material, and

– which fully reverses within an observation period of (normally) 21 days.

Within this category, an eye irritant is considered to be "Mildly irritating to eyes" (Category 2B) when the effects listed above are fully reversible within 7 days of observation.

B) Data availability

・The definitions of the categories are based on eye irritation test results, but there are few data sources that contain specific Draize scores to which GHS criteria can be applied.

・Generally, no animal testing for eye irritation is undertaken for a skin-corrosive substance. If eye irritation test data are not available for a skin-corrosive substance, it is classified as a substance causing severe eye damage (Category 1).

・If appropriate information sources based on data cannot be obtained easily, classification can be performed on the basis of the comments related to eye damage/irritation, such as "Severe", "Moderate" and "Mild", in test reports or existing MSDSs.

・Classification can be performed based on R-Phrases (R36, R41, R36/37, R36/38, R36/37/38) related to severe eye damage/eye irritation in Annex I of EU 7th Amendment to Council Directive.

C) Priorities where conflicting data exist

The following shall be given a high priority:

1. Data that are verified by credible agencies, such as those derived from the materials specified in "Priority 1", and contain descriptions of severe eye damage/eye irritation.

2. Data that are deemed reliable, such as those obtained by GLP-conforming laboratories or those whose scientific basis is available and verified

3. Data obtained from other information sources, such as those derived from the materials specified in "Priority 2" and "Priority 3".

4. Latest data (where conflicting data of the same priority are available) or data derived from reliable publications

5. Finally, conservative data shall be adopted, excluding measurement values that are considered abnormal when compared with other relevant data. When classification results based on conflicting data belong to several hazard categories, those with the largest amount

of supporting data shall be adopted.

D) Comparison with conventional classification systems

・Substances classified as R41 (severely damaging the eye) in EU-Annex I correspond to Category 1.

・Substances classified as R36 (irritating to the eye) or combination R-Phrases relevant to R36 (R36/37, R36/R38, R36/37/38) in EU-Annex I correspond to Category 2.

E) Instructions

・Substances evaluated as “Severe”, “Moderate” and “Mild” for skin corrosion and irritation in test reports roughly correspond to Category 1, Category 2A and Category 2B, respectively. However, Category 1 includes substances that cause irreversible effects to cornea, iris, etc. during the observation period in eye damage/irritation tests. A “Severe” substance inducing no irreversible lesion is classified as category 2A.

(3-2-4) Respiratory or skin sensitization

A) Classification criteria

Respiratory sensitizers

Substances shall be classified as respiratory sensitizers (Category 1) in accordance with the following criteria:

・There is evidence in humans that the substance can induce specific respiratory hypersensitivity, or

・Positive results are obtained from appropriate animal tests.

Skin sensitizers

Substances shall be classified as contact sensitizers (Category 1) in accordance with the following criteria:

・There is evidence that the substance can induce sensitization by skin contact in a substantial number of humans, or

・Positive results are obtained from appropriate animal tests.

B) Data availability

・Classification is performed based on the weight of evidence for respiratory or skin sensitization. Information related to sensitization is very seldom in the published literature.

・A single category each is adopted for classification of respiratory sensitization and skin sensitization, i.e. whether the substance induces sensitization (Category 1) or not (Not classified). The precautionary word used for skin sensitization Category 1 is “Warning”, while the word for respiratory sensitization Category 1 is “Danger”, since the latter is considered to produce more serious effects on human health.

C) Priorities where conflicting data exist

The following shall be given a high priority:

1. Data that are verified by credible agencies, such as those derived from the materials specified in “Priority 1”, and contain descriptions of respiratory or skin sensitization. If appropriate information sources based on data cannot be obtained easily, classification can be performed based on EU-Annex I: R42・R43・R42/43, “Recommendations for allowable concentrations: Airway Sensitization・Skin Sensitization” by Japan Society for Occupational Health, “TLVs: SEN or Sensitization substance” by ACGIHs or “MAK list: Sensitization substances (Sa, Sh, Sah)” by DFG.

2. Data that are deemed reliable, such as those obtained by GLP-conforming laboratories or those whose scientific basis is available and verified.

3. Data obtained from other information sources, such as those derived from the materials specified in “Priority 2” and “Priority 3”.

D) Comparison with previous classification systems

・Among R-Phrases in EU-Annex I, those related to sensitization are R42 (may cause sensitization by inhalation), R43 (may cause sensitization by skin contact) and R42/43 (may cause sensitization by inhalation and skin contact).

・“Recommendations for allowable concentrations” by Japan Society for Occupational Health contains a list of substances identified as sensitizers. Sensitizers are marked “SEN” and “Sa・Sh・Sah” in ACGIH TLV list and DGF MAK list, respectively. Each of the lists contains only a few substances.

E) Instructions

・Classification should be performed on the basis of any description concerning sensitivity found in test reports, reviews, evaluations, etc.

・R42 and R42/43 in EU-Annex I and "Airway Sensitization" in "Recommendations for allowable concentrations" by Japan Society for Occupational Health correspond to respiratory sensitization Category 1. R43 and R42/43 in EU-Annex I and "Skin sensitization" in "Recommendations for allowable concentrations" by Japan Society for Occupational Health correspond to skin sensitization Category I. SEN substances specified by ACGIH correspond to either respiratory sensitization or skin sensitization, according to the information provided in the ACGIH Documentation.

(3-2-5) Germ cell mutagenicity

A) Classification criteria

Category 1: Chemicals known or considered to induce heritable mutations in human germ cells.

Category 1A: Chemicals known to induce heritable mutations in human germ cells

Criterion: Positive evidence from human epidemiological studies.

Category 1B: Chemicals which should be regarded as inducing heritable mutations in human germ cells.

Criteria:

- Positive result(s) from in vivo heritable germ cell mutagenicity tests in mammals; or

- Positive result(s) from in vivo somatic cell mutagenicity tests in mammals in combination with some evidence that the substance has potential to induce mutations in germ cells. This supporting evidence may, for example, be derived from in vivo germ cell mutagenicity/genotoxic tests or by demonstrating the ability of the substance or its metabolite(s) to interact with the genetic material of germ cells; or

- Positive results showing mutagenicity in human germ cells without evidence of transmission to the progeny; for example, an increase in the frequency of aneuploidy in sperm cells of exposed human subjects.

Category 2: Chemicals which have the potential to induce heritable mutations in human germ cells

Criteria: Positive results obtained from mammalian tests and/or, in some cases, from the following in vitro experiments:

- in vivo somatic cell mutagenicity tests in mammals; or

- other in vivo somatic cell genotoxicity tests which are supported by positive results from in vitro mutagenicity tests.

Note:

- Chemicals which were positive in in vitro mutagenicity tests in mammals and which also show a chemical-structure activity relationship to known germ cell mutagens should be considered for classification as Category 2 mutagens.

B) Data availability

・Results from several mutagenicity tests including in vitro tests are reported for many chemicals, but results from in vivo tests using mammalian germ cells are rare. Expert judgment is required for judging mutagenicity in human germ cells based on the large amount of data obtained from several in vitro and in vivo tests.

・The "Decision Logic 3.5.1" in GHS 3.5.5.1 starts with the question, "are there data on the mutagenicity of the substance?". The phrase "data on mutagenicity" basically refers to all data obtained from in vitro or in vivo mutagenicity/genotoxicity tests that are generally used. Expert support is required for judging the mutagenicity from the conflicting results obtained from several tests.

・For classification based on mutagenicity test data, substances with positive evidence from human epidemiological studies are classified as Category 1A. To date, no such substance has been identified.

・Substances with positive evidence from several tests including in vivo mutagenicity tests using germ cells and that should be regarded as inducing genetic mutations or chromosome aberrations in human germ cells are classified as Category 1B.

These include substances showing positive result(s) in in vivo heritable mutagenicity tests in mammalian germ cells (rodent dominant lethal mutation test, mouse heritable translocation assay, mouse specific locus test, etc.), or positive result(s) in in vivo mutagenicity tests in mammalian somatic cells (mammalian bone marrow chromosome aberration test, mammalian erythrocyte micronucleus test, mouse spot test, etc.) in combination with some evidence that the substance has potential to induce mutations in germ cells (for example, positive results in mammalian spermatogonial chromosome aberration test, spermatid micronucleus assay, sister chromatid exchange analysis in spermatogonia, unscheduled DNA synthesis (UDS) test in testicular cells, or evidence of exposure of germ cells to the active substance or its metabolite(s)), or positive results showing mutagenicity in human germ cells without evidence of transmission to progeny (for example, an increase in the frequency of aneuploidy in sperm cells of exposed human subjects).

・Substances which have the potential to induce genetic mutations or chromosome aberrations in human germ cells based on other information are classified as Category 2.

These include substances having positive evidence from in vivo somatic cell mutagenicity tests in mammals (mammalian bone marrow chromosome aberration test, mammalian erythrocyte micronucleus test, mouse spot test, etc.), or positive results in in vivo somatic cell genotoxicity tests (in vivo liver unscheduled DNA synthesis (UDS), mammalian bone marrow sister chromatid exchanges (SCE), etc.) which are supported by positive results from in vitro mutagenicity tests (in vitro mammalian chromosome aberration test, in vitro mammalian cell genetic mutation test, bacterial reverse mutation test). Substances which only have positive results from in vitro mammalian mutagenicity tests but show (strong) structural analogy with known germ cell mutagens (Category 1A or 1B) should also be classified as Category 2.

・Test data serving as basis for classification in GHS 3.5.2

(1) Examples of in vivo heritable mutagenicity tests in germ cells are;

Rodent dominant lethal mutation test (OECD 478)

Mouse heritable translocation assay (OECD 485)

Mouse specific locus test

(2) Examples of in vivo somatic cell mutagenicity tests are:

Mammalian bone marrow chromosome aberration test (OECD 475)

Mouse spot test (OECD 484)

Mammalian erythrocyte micronucleus test (OECD 474)

(3) Examples of mutagenicity/genotoxicity tests in germ cells are:

(a) Mutagenicity tests:

Mammalian spermatogonial chromosome aberration test (OECD483)

Spermatid micronucleus assay

(b) Genotoxicity tests:

Sister chromatid exchange (SCE) analysis in spermatogonia

Unscheduled DNA synthesis test (UDS) in mammalian testicular cells

(4) Examples of in vivo genotoxicity tests in somatic cells are:

Liver unscheduled DNA synthesis (UDS) in vivo (OECD 486)

Mammalian bone marrow sister chromatid exchange (SCE) test

(5) Examples of in vitro mutagenicity tests are:

In vitro mammalian chromosome aberration test in mammalian cultured cells (OECD 473)

In vitro mammalian cell gene mutation test (OECD 476)

Bacterial reverse mutation test (OECD 471)

C) Priorities where conflicting data exist

(1) Data concerning mutagenicity tests are relatively abundant, and the data concerning mutagenicity in human germ cells (in vivo tests rather than in vitro, tests using human cells rather than mammalian cells, tests using germ cells rather than somatic cells) shall be given a high priority.

(2) As can be seen from the classification criteria described in the GHS document (see B), generally, positive results from in vitro mutagenicity tests alone do not serve as a basis for classification to Category 2. Similar attention should be paid to results from in vivo mutagenicity tests in drosophila. Some test reports may contain several negative or positive results, and classification based on only some of the positive results needs to be verified.

D) Comparison with previous classification systems

・The concept of GHS classification for germ cell mutagenicity basically agrees with that for Mutagenicity Categories 1, 2 and 3 in EU-Annex I.

E) Instructions

・Mutagens classified as Category 1 with R46 in EU-Annex I correspond to Category 1A.

(To date, no such substance has been identified.)

Mutagens classified as Category 2 with R46 in EU-Annex I correspond to Category 1B.

Mutagens classified as Category 3 with R68 in EU-Annex I correspond to Category 2.

・Classification should be performed on the basis of data derived from appropriate information sources, but (germ cell) mutagenicity classifications established by the EU and the German MAK committee should also be helpful.

(3-2-6) Carcinogenicity

A) Classification criteria

Category 1: Known or presumed human carcinogens

The placement of a chemical in Category 1 is done on the basis of epidemiological and/or animal data. Individual chemicals may be further subdivided into:

Category 1A: chemicals known to have carcinogenicity in humans; classification is mainly based on human evidence.

Category 1B: chemicals presumed to have carcinogenicity in humans; classification is mainly based on animal evidence.

Based on the strength of the evidence together with additional considerations, such evidence may be derived from human studies that establish a causal relationship between human exposure to the chemical and the development of cancer (known human carcinogen). Alternatively, evidence may be derived from animal experiments for which sufficient evidence exists to demonstrate animal carcinogenicity (presumed human carcinogen). In addition, on a case-by-case basis, scientific judgment may warrant a decision of presumed human carcinogenicity for chemicals with limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals.

Classification: Category 1 (A and B) Carcinogen

Category 2: Suspected human carcinogens

The placement of a chemical in Category 2 is done on the basis of evidence which is obtained from human and/or animal studies but is not sufficiently convincing to classify the chemical as Category 1. Based on the strength of evidence together with additional considerations, such evidence may be derived either from limited evidence of carcinogenicity in human studies or from limited evidence of carcinogenicity in animal studies.

Classification: Category 2 Carcinogen

B) Data Availability

・Descriptions of carcinogenicity are found frequently in hazard-related reviews or data collections. Several organizations have reported ranking of carcinogenicity, which should be useful for classification (WHO International Agency for Research on Cancer (IARC), classification results in Annex I of EU 7th Amendment to Council Directive, National Toxicology Program (NTP), carcinogens in “Recommendations for allowable concentrations” by Japan Society for Occupational Health, carcinogenicity notes in “TLV and BEIs” by ACGIH, US-EPA Integrated Risk Information System (IRIS), carcinogenicity notes in “List of MAK and BAT values” by German DFG, etc., see [3-1]).

C) Priorities where conflicting data exist

The following shall be given a high priority:

1. Data verified by credible agencies, such as those derived from the materials specified in “Priority 1”. Evaluation by IARC and EU represents a consensus of many expert opinions and therefore shall be given a high priority. Refer to any information released by Japan Society for Occupational Health, US-EPA, US-NTP, ACGIH or German DGF, which is given the next priority.

2. Data that are deemed reliable, such as those obtained by GLP-conforming laboratories or those whose scientific basis is available and verified.

3. Data obtained from other information sources, such as those derived from the materials specified in “Priority 2” and “Priority 3”.

D) Comparison with previous classification systems

・The concept of the GHS classification for carcinogenicity agrees with those of the IARC classification and the EU-Annex I classification.

E) Instructions

・For classification based on carcinogenicity test data, substances known to be carcinogenic in humans are classified as Category 1A. Substances presumed to be carcinogenic in humans from evidence mostly derived from animal tests are classified as Category 1B. Other substances suspected to be carcinogenic in humans are classified as Category 2.

・The GHS classification categories are substantially identical to those in conventional classification systems. GHS categories correspond to the following conventional categories:

Category 1A: IARC・Group 1, Japan Society for Occupational Health・Group 1, substances classified as Category 1 with R45 and R49 in EU-Annex I, US-EPA A, US-NTP A, ACGIH A1.

Category 1B: IARC・Group 2A by, Japan Society for Occupational Health・Group 2A, substances classified as Category 2 with R45 and R49 in EU-Annex I, US-EPA B1, US-NTP B, ACGIH A2

Category 2: IARC・Group 2B, Japan Society for Occupational Health/・Group 2B, substances classified as Category 3 with R40 in EU-Annex I, US-EPA B2, ACGIH A3

(3-2-7) Reproductive toxicity

A) Classification criteria

Category 1: Known or presumed human reproductive toxicant

This category includes substances which are known to produce adverse effects on reproductive function and capacity or on development in humans or for which there is evidence from animal studies, possibly supplemented with other information that strongly suggests that the substance has the potential to interfere with reproduction in humans. For regulatory purposes, the substances can be further classified on the basis of whether the evidence for classification is primarily from human data (Category 1A) or from animal data (Category 1B).

Category 1A: Substances known to have reproductive toxicity to humans

Placing a substance in this category is mainly based on evidence from humans.

Category 1B: Substances presumed to have reproductive toxicity to humans

Placing a substance in this category is mainly based on evidence from experimental animals. Data from animal studies should provide clear evidence of adverse effects on reproductive function and capacity or on development in the absence of other toxic effects. If the substance has other toxic effects, its adverse effect on reproduction should not be considered as a secondary non-specific consequence of the other toxic effects. However, when there is mechanistic information that raises doubt about the relevance of the effects for humans, classification in Category 2 may be more appropriate.

Category 2: Suspected human reproductive toxicant

This category includes substances for which there is some evidence from humans or experimental animals, possibly supplemented with other information, of adverse effects on reproductive function and capacity or on development in the absence of other toxic effects or substances which have, together with other toxic effects, adverse effects on reproduction that is not considered as secondary non-specific consequences of the other toxic effects but whose evidence is not sufficiently convincing to place the substance in Category 1. For instance, deficiencies in the study may make the quality of evidence less convincing; in such a case, Category 2 could be the more appropriate classification.

Effects on or via lactation

Effects on or via lactation are allocated to a separate single category. It is recognized that, for many substances, there is no information on the potential to cause adverse effects on infants via lactation. However, substances that are absorbed by women and have been shown to interfere with lactation or which may be present (including metabolites) in breast milk in amounts sufficient to raise concern about the health of a breastfed child, should be classified here to indicate this property, namely, hazardous to breastfed babies. This classification can be assigned on the basis of:

(a) results from absorption, metabolism, distribution and excretion studies that suggest the presence of the substance at a potentially toxic level in breast milk; or

(b) results of one- or two-generation studies in animals which provide clear evidence of adverse effects on the offspring or the quality of breast milk due to the transfer of the substance to the breast milk; or

(c) human evidence indicating a hazard to babies during the lactation period.

B) Data availability

・Evaluation of reproductive toxicity has been reported in "Chemical Substance Hazard Data" prepared by CERI, EHC, ECETOC, SIDS, etc.

・A large amount of data are available from reports on reproductive toxicity, but whether they meet the criteria must be checked by experts by tracing back to their original publication.

C) Priorities where conflicting data exist

The following shall be given a high priority:

1. Data verified by credible agencies, such as those derived from the materials specified in "Priority 1".
2. If appropriate information sources based on data cannot be obtained easily, classification is performed based on the evaluation by the EU, the only organization performing evaluation on reproductive toxicity.
3. Data that are deemed reliable, such as those obtained by GLP-conforming laboratories or those whose scientific basis is available and verified.
4. Data obtained from other information sources, such as those derived from the materials specified in "Priority 2" and "Priority 3".

D) Comparison with previous classification systems

・The concept of the GHS classification for reproductive toxicity agrees with that of the EU-Annex classification.

E) Instructions

・For classification based on reproductive toxicity test data, substances known to have reproductive toxicity to humans is classified as Category 1A. Substances presumed to have reproductive toxicity to humans from evidence mostly derived from animal tests are classified as Category 1B. Other substances suspected to have reproductive toxicity to humans is classified as Category 2.

・Substances classified in Category 1 with R60 and R61 in EU-Annex I correspond to Category 1A.

Substances classified in Category 2 with R60 and R61 in EU-Annex I correspond to Category 1B.

Substances classified in Category 3 with R62 and R63 in EU-Annex I correspond to Category 2.

・Substances classified with R64 (may cause harm to breastfed babies) in EU-Annex I correspond to "additional category for effects on or via lactation" and therefore should carry the hazard statement "may cause harm to breast-fed children".

(3-2-8&9) Specific Target Organ/Systemic Toxicity (Single/Repeated Exposure)

A) Classification Criteria

Specific target organ/systemic toxicity (single exposure)

Category 1: Substances that have produced significant toxicity in humans or that, on the basis of evidence from studies in experimental animals, can be presumed to have the potential to produce significant toxicity in humans following a single exposure

Placing a substance in Category 1 is done on the basis of:

・reliable and good-quality evidence from human cases or epidemiological studies; or

・observations from appropriate studies in experimental animals in which significant and/or severe toxic effects on human health were produced at generally low exposure levels.

Category 2: Substances that, on the basis of evidence from studies in experimental animals, can be presumed to have the potential to harm human health following a single exposure

Placing a substance in Category 2 is done on the basis of observations from appropriate studies in experimental animals in which significant toxic effects on human health were produced at generally moderate exposure levels.

In exceptional cases, human evidence can also be used to place a substance in Category 2.

Category 3: Transient effects on specific organs

There are specific organ effects for which a substance or mixture may not meet the criteria for Categories 1 or 2 indicated above. These are effects that adversely alter human function for a short duration after exposure and from which humans may recover in a reasonable period with no significant residual structural or functional alteration. This category includes narcotic effects and respiratory tract irritation.

Note: For the above categories, the specific target organ/system that has been primarily affected by the classified substance may be identified, or the substance may be identified as a general systemic toxicant. Attempts should be made to determine the primary target organ of toxicity and to classify substances accordingly, e.g. as hepatotoxicants, neurotoxicants, etc. One should carefully evaluate the data and, wherever possible, exclude secondary effects. For example, hepatotoxicants can produce secondary effects in the nervous or gastro-intestinal system.

Specific target organ/systemic toxicity (repeated exposure)

Category 1: Substances that have produced significant toxicity in humans or that, on the basis of evidence from studies in experimental animals, can be presumed to have the potential to produce significant toxicity in humans following repeated exposure

Placing a substance in Category 1 is done on the basis of:

・reliable and good-quality evidence from human cases or epidemiological studies; or

・observations from appropriate studies in experimental animals in which significant and/or severe toxic effects on human health were produced at generally low exposure concentrations.

Category 2: Substances that, on the basis of evidence from studies in experimental animals, can be presumed to harm human health following repeated exposure

Placing a substance in Category 2 is done on the basis of observations from appropriate studies in experimental animals in which significant toxic effects on human health were produced at generally moderate exposure concentrations.

In exceptional cases, human evidence can also be used to place a substance in Category 2.

Note: For both categories, the specific target organ/system that has been primarily affected by the classified substance may be identified, or the substance may be identified as a general systemic toxicant. Attempts should be made to determine the primary target organ of toxicity and to classify substances accordingly, e.g. as hepatotoxicants, neurotoxicants, etc. One should carefully evaluate the data and, wherever possible, exclude secondary effects. For example, hepatotoxicants can produce secondary effects in the nervous or gastro-intestinal system.

B) Data availability

・Sufficient information for classification cannot be obtained from the brief descriptions in existing MSDSs. A literature search should be conducted to obtain solid information from reviews or primary information concerning toxicity.

・Substances classified with R39 (danger of very serious irreversible effects), R48 (danger of serious damage to health by prolonged exposure) or combination R-Phrases relevant to R39 or R48 have risk of causing specific organ/systemic toxicity (single/repeated exposure).

C) Priorities where conflicting data exist

The following shall be given a high priority:

1. Data verified by credible agencies, such as those derived from the materials specified in “Priority 1”.

2. If appropriate information sources based on data cannot be obtained easily, classification can be performed based on the evaluation by the EU (R−39, R−48), the only organization performing evaluation on specific target organ/systemic toxicity.

3. Data that are deemed reliable, such as those obtained by GLP−conforming laboratories or those whose scientific basis is available and verified.

4. Data obtained from other information sources, such as those derived from the materials specified in “Priority 2” and “Priority 3”.

D) Comparison with previous classification systems

・The concept of this classification is new to our country and has no corresponding system.

E) Instructions

・If information concerning specific, non−lethal, specific organ/systemic toxicity arising from a single or repeated exposure is obtained, whether the toxicity is significant to human health should be determined through expert judgment.

・The relevant route of exposure by which the classified substance has produced damage should be identified.

・Examples of toxic effects in humans or experimental animals that must be taken into consideration in the classification of specific organ/systemic toxicity are provided below (GHS United Nations Recommendations 3.8.2.1.7 and 3.9.2.7):

- Disease resulting from single exposure;

- Disease or death resulting from repeated or prolonged exposure. The disease or death may result, even at relatively low doses/concentrations, due to bioaccumulation of the substance or its metabolites or due to the overwhelming of the detoxification process by repeated exposure;

- Significant functional changes in the central or peripheral nervous systems or other organ systems which are not transient in nature, including signs of central nervous system depression and effects on special senses (e.g. sight, hearing and sense of smell);

- Any consistent and significant adverse change in clinical biochemistry, hematology or urinalysis parameters;

- Significant organ damage that may be noted at necropsy or subsequently observed or confirmed at histopathological examination;

- Multifocal or diffuse necrosis, fibrosis or granuloma formation in vital organs with regenerative capacity;

- Morphological changes that are potentially reversible but provide clear evidence of marked organ dysfunction;

- Evidence of marked cell death (including cell degeneration and reduced cell number) in vital organs incapable of regeneration.

・Toxic effects listed below are assessed separately in the GHS and are therefore not included in specific organ/systemic toxicity.

- Acute lethality/toxicity (3-2-1)
- Skin corrosivity/irritation (3-2-2)
- Serious eye damage/eye irritation (3-2-3)
- Skin and respiratory sensitization (3-2-4)
- Germ cell mutagenicity (3-2-5)
- Carcinogenicity (3-2-6) and
- Reproductive toxicity (3-2-7)

・Criteria for specific organ/systemic toxicity (single exposure) Category 3 “Respiratory Tract Irritation” are (GHS United Nations Recommendations 3.8.2.2.1):

- Respiratory tract irritation includes effects (characterized by localized redness, edema, pruritus or pain) that disturb the function with symptoms such as cough, pain, choking and breathing difficulty. The evaluation is recognized as being primarily based on human data.
- Subjective human observations could be supported by objective measurements of clear respiratory tract irritation (RTI) (e.g. electrophysiological responses, biomarkers of inflammation in nasal or bronchoalveolar lavage fluids).
- The symptoms observed in humans should be typical of those that would be produced in the exposed population rather than being an isolated idiosyncratic response triggered only in individuals with hypersensitive airways.
- Ambiguous reports simply of “irritation” should be excluded, as this term is commonly used to describe a wide range of sensations including smell, unpleasant taste, tickling sensation and dryness, which are outside the scope of this classification endpoint.
- Currently, there is no validated animal test that clearly deals with RTI, but useful information may be obtained from single and repeated inhalation toxicity tests. For example, animal studies may provide useful information in terms of clinical signs of toxicity (breathing difficulty, rhinitis, etc.) and histopathology (e.g. hyperemia, edema, minimal inflammation, thickened mucous layer) which are reversible and may reflect the characteristic chronic symptoms described above.
- This special classification would be made only when more severe organ/systemic effects including the respiratory system are not observed.

・Criteria for specific organ/systemic toxicity (single exposure) Category 3 “Narcotic Effects” are (GHS United Nations Recommendations 3.8.2.2.2):

- Central nervous system depression including narcotic effects in humans such as drowsiness, narcosis, reduced alertness, loss of reflexes, lack of coordination and vertigo. These effects can also be manifested as severe headache or nausea and can lead to reduced judgment, dizziness, hypersensitivity, fatigue, impaired memory function, deficits in perception and coordination, retarded reaction or sleepiness.
- Narcotic effects observed in animal studies including lethargy, lack of coordination righting reflex, narcosis and ataxia. If these effects are not transient in nature, they

should be considered for classification in category 1 or 2.

(3-2-10) Aspiration hazards

A) Classification criteria

Categories	Decision criteria
Category 1: Chemicals known to cause human aspiration toxicity hazards or to be regarded as if they cause human aspiration toxicity hazard	A substance is classified as Category 1: (a) based on reliable and good-quality human evidence (see note 1); or (b) if it is a hydrocarbon and has a kinematic viscosity of $\leqq$20.5 mm^2/s measured at 40℃.
Category 2: Chemicals which cause concern owing to the presumption that they cause human aspiration toxicity hazard	A substance is classified as Category 2 on the bases of existing animal studies and expert judgment that takes into account surface tension, water solubility, boiling point, and volatility, substances, other than those classified in Category 1, which have a kinematic viscosity of $\leqq$14 mm^2/s or less, measured at 40℃ (see Note 2).

Note 1: Examples of substances included in Category 1 are certain hydrocarbons such as turpentine and pine oil.

Note 2: Taking this into account, some authorities would consider the following substances to be included in this category: n-primary alcohols composed of at least 3 carbon atoms but not more than 13; isobutyl alcohol and ketones composed of no more than 13 carbon atoms.

B) Data availability

・Aspiration hazards is a severe acute effect that induces chemical pneumonitis or lung injuries of various severity after aspiration, or death. The term “aspiration” refers to invasion of a liquid or solid chemical into the trachea or the lower respiratory tract, either directly through the mouth or the nasal cavity or indirectly through vomiting.

・Although some methodologies for determining aspiration hazards in animals exist, none has been standardized. Positive evidence from animal tests merely serves as a guideline for the potential to induce effects classified as aspiration hazards in humans.

C) Priorities where conflicting data exist

The following shall be given a high priority:

1. Data that are verified by credible agencies, such as those derived from the materials specified in “Priority 1”, and containing descriptions of skin corrosion/irritation.

2. Data that are deemed reliable, such as those obtained by GLP-conforming laboratories or those whose scientific basis is available and verified

3. Data obtained from other information sources, such as those derived from the materials specified in “Priority 2” and “Priority 3”.

4. Latest data (where conflicting data of the same priority are available) or data derived from

reliable publications

D) Comparison with previous classification systems

・The concept of this classification is new and therefore has no corresponding system.

E) Instructions

・A review of medical literature on chemical aspiration revealed that some hydrocarbons (petroleum distillates) and certain chlorinated hydrocarbons display aspiration hazards in humans. Primary alcohols and ketones have been shown to pose an aspiration hazard only in animal studies.

Examples of substances included in Categories 1 and 2 are listed in Notes 1 and 2 in "A) evaluation criteria".

・The classification criteria refer to kinematic viscosity. The following provides the conversion between viscosity and kinematic viscosity.

Viscosity (mPas) / Density (g/cm^3) = Kinematic viscosity (mm^2/s)

Chapter 4. Environmental Hazards

[4-1] Classification of environmental hazards

As of January 2005, the GHS classification criteria for environmental hazards provide only for "aquatic environmental hazards," which are addressed in Section 4.1 of the UN GHS classification. In addition, Annex 9 (Guideline on Hazards to the Aquatic Environment) and Annex 10 (Guidance on Transformation/Dissolution of Metals and Metal Compounds) should be referred to.

(4-1-1) Aquatic environmental hazards

A) GHS classification criteria

The classification criteria set out in UN GHS 4.1.2 can be summarized as follows:

Category: Acute 1
- 96 hr LC50 (for fish) ≦1 mg/l and/or
- 48 hr EC50 (for Crustacea) ≦1 mg/l and/or
- 72 or 96 hr ErC50 (for algae or other aquatic plants)≦1 mg/l

Category: Acute 2
- 1mg/l < 96 hr LC50 (for fish) ≦10 mg/l and/or
- 1mg/l < 48 hr EC50 (for Crustacea) ≦10 mg/l and/or
- 1mg/l < 72 or 96hr ErC50 (for algae or other aquatic plants) ≦10 mg/l

Category: Acute 3
- 10mg/l < 96 hr LC50 (for fish) ≦100 mg/l and/or
- 10mg/l < 48 hr EC50 (for Crustacea)≦100 mg/l and/or
- 10mg/l < 72 or 96 hr ErC50 (for algae or other aquatic plants≦100 mg/l

Category: Chronic 1
Those classified as Acute 1, not readily degradable, and/or the logKow ≧ 4 (unless the experimentally determined BCF < 500).

Category: Chronic 2
Those classified as Acute 2, not readily degradable, and/or the logKow≧ 4 (unless the experimentally determined BCF <500), unless the chronic toxicity NOEC > 1 mg/l.

Category: Chronic 3
Those classified as Acute 3, not readily degradable, and/or the logKow ≧4 (unless the experimentally determined BCF <500), unless the chronic toxicity NOEC > 1 mg/l.

Category: Chronic 4
Poorly soluble substances for which no acute toxicity is recorded at levels up to the water solubility, and which are not readily degradable and have a logKow ≧ 4, unless an experimentally determined BCF < 500, or a chronic toxicity NOEC > 1 mg/l.

B) Data availability
The better part of classification data (Priority 1 and Priority 2) on acute aquatic toxicity, bioaccumulation properties (distribution coefficient), degradability (biological or non-biological), and chronic aquatic toxicity can be obtained through the Internet. Data on water solubility should also be collected, as they are required for classification.

Classification results in Annex I of EU Directive 67/548/EEC, which are almost consistent with the GHS classification, are available. However, they cannot be used as-is for GHS classification since there are discrepancies in the criteria for chronic aquatic toxicity, and information on their scientific basis is hard to obtain.

C) Information sources for the classification of environmental hazards
(1) Information sources of data on aquatic environmental hazard tests (those of agrochemicals are being identified).
Priority 1
Reliable information sources developed by international agencies or the governments of major countries (original articles should be referred to for those whose reliability needs to be verified, and those that are considered unreliable should not be adopted).

1-1) Tests for the Ecological Effects of Chemical Substances (Ministry of the Environment) (369 substances as of Sep. 2005)
http:/www.env.go.jp/chemi/sesaku/seitai.html

1-2) Environmental Risk Assessments for Chemical Substances, Vols. 1, 2 and 3 (Environmental Risk Assessment Office, Ministry of the Environment) (as of Sep. 2005)
http://www.env.go.jp/chemi/risk/index.html

1-3) OECD: SIDS Report (SIDS Initial Assessment Report) (180 substances as of Nov. 2004)
http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html

1-4) WHO/IPCS: Environmental Health Criteria (EHC), No.1-231 (as of Sep. 2005)
http://www.inchem.org/pages/ehc.html

http://www.who.int/ipcs/publications/ehc/en/index.html

EHC Japanese version: Safety Assessments for Chemical Substances, Vols. 1, 2 and 3
Edited by the National Institute of Health Science (Division of Safety Information on Drugs, Food and Chemicals) and the Chemical Daily Co., Ltd.
EHC concise Japanese version: http://www.nihs.go.jp/DCBI/PUBLIST/ehchsg/

1-5) WHO/IPCS: Concise International Chemical Assessment Documents, No.1-66 (as of 2004)
http://www.inchem.org/pages/cicads.html

http://www.who.int/ipcs/publications/cicad/en/index.html

Concise and complete Japanese versions of CICAD Executive Summary (84 substances as of 2005)
http://www.nihs.go.jp/cicad/cicad2.html

1-6) EU Risk Assessment Report, Vols. 1-55 (as of Sep. 2005)
http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/

1-7) Assessment Report (Ministry of the Environment, Canada) (66 substances as of Sep. 2005)
http://www.ec.gc.ca/substances/ese/eng/psap/psap.cfm

1-8) NICNAS (National Industrial Chemicals Notification and Assessment, Australia), No.1-26 (as of Sep. 2005)
Australia NICNAS: Priority Existing Chemical Assessment Report
http://www.nicnas.gov.au/publications/CAR/PEC/default.asp

1-9) European Center for Ecotoxicology and Toxicology of Chemicals (ECETOC): Technical Report Series (100 substances), TR91 (Aquatic Hazard Assessment II) *
*Caution must be taken when using the data since some parts have been lost, presumably due to data conversion.
http://www.ecetoc.org/content/default.asp?pageid=22

1-10) WHO/FAO Pesticide Data Sheets
http://www.inchem.org/pages/pds.html

1-11) Chemical Substance Safety (Hazard) Data (Chemicals Evaluation and Research Institute, Japan) (294 substances as of Sep. 2005)
http://www.cerij.or.jp/ceri_jp/koukai/sheet/sheet_indx4.htm

http://www.safe.nite.go.jp/data/sougou/pk_list.html?table_name=hyoka&rank=sheet&sort=cas&page=1

1-12) Hazard Evaluation Report (Chemicals Evaluation and Research Institute, Japan, and National Institute of Technology and Evaluation) (99 substances as of Sep. 2005, compilation underway)
http://www.safe.nite.go.jp/data/sougou/pk_list.html?table_name=hyoka

Priority 2
Information sources whose reliability has yet to be assessed; data authenticity needs to be verified.

2-1) AQUIRE (Aquatic Toxicity Information Retrieval) (7,200 substances as of March 2004)
A database of chemical substances and their aquatic toxicity, developed by the EPA in 1981
http://www.cas.org/ONLINE/DBSS/aquiress.html

http://w-chemdb.nies.go.jp/aquire/aquire.htm

2-2) HSDB (Hazardous Substance Data Bank) (4,810 Records)
A database developed by the U.S. National Library of Medicine
http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

2-3) EU European Chemicals Bureau (ECB)
ESIS: European chemical Substances Information System

International Uniform Chemical Information Database (IUCLID DS)
IUCLID CD-ROM (Edition 2 - 2000) (2,604 substances)
http://ecb.jrc.it/esis/esis.php?PGM=ein

2-4) EU European Chemicals Bureau (ECB)
The N-CLASS Database on Environmental Hazard Classification (7,869 substances as of Nov. 2004)
A database jointly developed by ECB and the Nordic Council of Ministers - which provides information on EU dangerous goods N (R50-53)
http://www.kemi.se/nclass/

2-5) German Chemical Society: Advisory Committee on Existing Chemicals of Environmental Relevance “BUA Report” (240 substances)
The full version of the report is not available on the website. Caution must be taken when using the data in BUA Report, since they are not fully reviewed.
http://www.hirzel.de/bua-report/

Requirements for data to be collected and adopted
1) Data on acute aquatic toxicity tests
(Requirements for data to be collected)
Tests shall be conducted using fish, crustacea and algae (or other aquatic plants) - specifically, organisms recommended by OECD Test Guidelines and ASTM Standard Test Methods, or organisms that belong to the same genera as those recommended by OECD Test Guidelines and ASTM Standard Test Methods.

The exposure time and endpoint are as follows:
Fish: 96 hr. LC50 (lethal)
Crustacea:
Daphnia: 24 or 48 hr, EC50 (immobile), LC50 (lethal)
Decapoda, Amphipoda, Mysidacea: 24, 48 or 96 hr, EC50 (immobile), LC50 (lethal)
Algae (or other aquatic plants):
Algae: 72 or 96 hr, ErC50 (growth inhibited), EC50 (growth inhibited)
Other aquatic plants (Lemna): 7 or 14 days, ErC50 (growth inhibited), EC50 (growth inhibited)

“Endpoint TLm” and “IC50” shall be treated the same as “Fish LC50” and “Crustacea and Algae EC50,” respectively.

(Requirements for data to be adopted)
In principle, aquatic environment hazard data shall not be used for the classification when they are derived from concentrations above the water solubility. Descriptions in GHS Annex 9 on “substances that are difficult to test” should be referred to when handling unstable (hydrolytic) substances (hazardous properties of degradation products), poorly soluble substances (toxicity levels above the water solubility), etc. (For instance, the toxicity of hydrolysates shall be construed as that of test substances (parent substances) when the better part of the test substances are hydrolyzed during the test and their hydrolysates present aquatic environmental hazards. For details concerning the handling of degradation products, refer to Section A9.2.6.3 of Annex 9.) In such cases, however, it should be noted that the classification is based on the toxicity of hydrolysates.

In principle, data conforming to GLP or, where no definite descriptions are available, data that are considered reliable by experts in view of the test conditions concerned shall be adopted. When specific data appear to be in a gray zone, final judgment on whether or not to adopt them shall be rendered by experts.

For each species of organism, refer to the following. Data of Priority 1 without proof that their acquisition conformed to the guidelines described below shall be used on condition that species, exposure time, and endpoint are consistent with those specified in the guidelines.

Fish

For tests using fish, data on 96 hour LC50 based on OECD Test Guidelines 203 or equivalent shall be used.

Crustacea
For tests using crustacea, data on 48 hour EC50 obtained based on OECD Test Guidelines 202 (for acute toxicity tests on Daphnia) or equivalent shall be adopted. However, data on 24 hour EC50 based on former OECD Test Guidelines 202 may be adopted when those on 48 hour EC50 are not available. For tests using Mysidacea or other species, data on 96 hour LC50 based on US EPA850.1035 (for acute toxicity tests on Mysidacea) or equivalent shall be adopted. When such data are not available, data on 24 or 48 hour LC50 may be adopted. In addition, final judgment on how to deal with data of Priority 2 shall be rendered by experts.

Algae (or other aquatic plants)
Algae:
For tests using algae, data on 72 or 96 hour EC50 based on OECD Test Guidelines 201 or equivalent shall be adopted. While rate-based ErC50 has a higher priority than area-based EbC50, any data shall be adopted on a provisional basis when the categories to which they belong are not yet determined. In addition, rate-based data such as those on 24-48 hour ErC50 shall be taken into account when those on 72 or 96 hour EC50 are not available. For algae, the maximum exposure time shall be set at 96 hours, as longer exposure time produces no useful data.

Other aquatic plants:
For tests using other aquatic plants, data on acute EC50 based on provisional OECD Test Guidelines or US EPA 850.4400 may be adopted. While rate-based ErC50 has a higher priority than area-based EbC50, data shall be adopted on a provisional basis when categories to which they belong are not yet determined. Data based on an exposure time of 7 days shall be prioritized over those based on an exposure time of 14 days for both ErC50 and EbC50.

2) Data on chronic aquatic toxicity tests
The current GHS classification of chronic aquatic toxicity does not agree with the classification based on data on chronic aquatic toxicity. For the time being, therefore, data on chronic aquatic toxicity shall be used as a benchmark for judging whether NOECs exceed 1 mg/l. (Reliable data based on an exposure time longer than that of the tests described below, if any, shall be taken into account.) When NOECs exceed 1 mg/l, the following descriptions (requirements for data to be adopted) should be referred to in determining whether this can be used as a basis to rule out its chronic aquatic toxicity. Substances shall not be considered chronically toxic in the aquatic environment when NOECs above 1mg/l are confirmed in any species that serve as a basis for indicating their chronic aquatic toxicity, or in species with sensitivity similar to that of the said species. (For instance, when the acute toxicity values for both Oryziatidae and Daphnia are classified as Acute 2 and, at the same time, are classified as Chronic 2 because of their high degradability and bioaccumulativity, the substances concerned shall not be excluded from Chronic 2 unless their NOECs exceed 1mg/l for both Oryziatidae and Daphnia.

(Requirements for data to be collected)
Tests shall be conducted using fish, Crustacea and algae (or other aquatic plants) - specifically, organisms recommended by OECD Test Guidelines and ASTM Standard Test Methods, or organisms that belong to the same genera as those recommended by OECD Test Guidelines and ASTM Standard Test Methods.

The exposure time and endpoint are as follows:
Fish: 28 days or more, NOEC - hatching success rates, growth (length and weight development), spawning success rates and survival rates
Crustacea: 7 days or more, NOEC - the period up to the first spawning, the number of eggs per female, growth rates and survival rates
Algae (or other aquatic plants):
Algae: 72 or 96 hours, NOEC (growth inhibited)
Other aquatic plants: No chronic toxicity tests (those officially approved for use in classification) are available at this time.

(Requirements for data to be adopted)
In principle, aquatic environment hazard data shall not be used for classification when the toxic level exceeds the water solubility of the compound. Descriptions in GHS Annex 9 on “substances

that are difficult to test" should be referred to when handling unstable (hydrolytic) substances (hazardous properties of degradation products), poorly soluble substances (toxicity levels above the water solubility), etc. (For instance, the toxicity of hydrolysates shall be construed as that of test substances (parent substances) when the better part of the test substances are hydrolyzed during the test and their hydrolysates have aquatic environmental hazards. For details concerning the handling of degradation products, refer to Section A9.2.6.3 of Annex 9.) In such cases, however, it should be noted that the classification is based on the toxicity of hydrolysates.

In principle, data conforming to GLP or, where no definite descriptions are available, data that are considered reliable by experts in view of the test conditions concerned shall be adopted. When specific data appear to be in a gray zone, final judgment on whether or not to adopt them shall be rendered by experts.

For each species of organisms, refer to the following. Of the data of Priority 1, those without proof that their test results conform to the guidelines described below shall be adopted on condition that species, exposure time, and endpoint are consistent with those specified in the guidelines.

Fish:
Chronic or long-term toxicity tests using fish shall be conducted based on OECD Test Guidelines 210 (Fish Early Life Stage), US EPA 850.1500 (Fish Life Cycle) or equivalent (one- or two-generation tests). Test results based on OECD Test Guidelines 210, though designed for sub-chronic toxicity, may serve as data on chronic aquatic toxicity as they effectively represent chronic toxicity.

The appendix of OECD Test Guidelines 210 defines exposure time for each species (e.g., up to 30 days - or 28 days at minimum - after hatching, for Oryziatidae), while US EPA 850.1500 (Fish Life Cycle) provides no such definitions. For data that need to be verified, therefore, the exposure time adopted shall be considered appropriate on condition that OECD Test Guidelines 210, US EPA 850.1500 (Fish Life Cycle) or equivalent are followed in the testing.

Endpoint in this case concerns hatching success rates, growth (length and weight development), spawning success rates and survival rates.

Crustacea:
Chronic toxicity tests using Crustacea shall be conducted based on OECD Test Guidelines 211 (Daphnia reproduction), US EPA OPPTS 850.1035 (chronic toxicity for Mysidacea) or equivalent (NOECs of 21 days for Daphnia, NOECs of 7 days or more for Ceriodaphnia).

Endpoint in this case concerns the period up to the first spawning, the number of eggs per female, growth rates and survival rates.

Algae (or other aquatic plants)
Algae:
In principle, NOECs based on OECD Test Guidelines 201 (alga growth inhibition tests, 72 or 96 hours) shall not be used as a basis for exclusion from chronic aquatic toxicity, as they are not designed for long-term tests - except where the classification of acute aquatic toxicity is based on tests results on a single species of alga or another aquatic plant, and NOECs exceed 1 mg/l for other species of algae.

In principle, growth inhibition (NOECs) based on the growth rate method shall be used as endpoint; NOECs may be used on a provisional basis when the method involved cannot be identified.

Other aquatic plants:
Priority 2 shall be adopted since no officially approved methods are available for testing long-term chronic aquatic toxicity. Judgment of exclusion from chronic aquatic toxicity shall be rendered by experts.

(2) Information sources of data on bioaccumulativity and degradability (those of agrochemicals are being identified)

Priority 1
Reliable information sources developed by international agencies or the governments of major

countries

1-1) Existing Chemical Substances Safety Evaluation Data
http://www.safe.nite.go.jp/japan/kizon/KIZON_start_hazkizon.html

1-2) PHYSPROP Database (SRC, 2005)
PHYSPROP Database (Demo)
http://www.syrres.com/esc/physdemo.htm

The information sources of Priority 1 described earlier may be referred to, when data cannot be obtained from these two information sources.

Priority 2
Information sources whose reliability has yet to be assessed; data authenticity needs to be verified.

2-1) AQUIRE (Aquatic Toxicity Information Retrieval) (7,200 substances as of March 2004)
A database of chemical substances and their aquatic toxicity, developed by EPA in 1981
http://www.cas.org/ONLINE/DBSS/aquiress.html

http://w-chemdb.nies.go.jp/aquire/aquire.htm

2-2) HSDB (Hazardous Substance Data Bank) (4,810 Records)
A database developed by the U.S. National Library of Medicine
http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

2-3) EU European Chemicals Bureau (ECB)
ESIS: European chemical Substances Information System
International Uniform Chemical Information Database (IUCLID DS)
IUCLID CD-ROM (Edition 2 - 2000) (2,604 substances)
http://ecb.jrc.it/esis/esis.php?PGM=ein

2-4) logKow
2-4) logKow estimation software (KOWWIN, CLOGP)
http://www.syrres.com/esc/est_kowdemo.htm

http://www.biobyte.com/bb/prod/clogp40.html

Requirements for data to be adopted
Data on bioaccumulativity (BCF, logKow) and degradability (biodegradability, hydrolytic properties, etc.) shall be based on the test methods specified by the Chemical Substances Control Law (Law Concerning the Examination and Regulation of Manufacture, etc of Chemical Substances), OECD Test Guidelines, ASTM Standard Test Methods, etc. In principle, data conforming to GLP or, where no definite descriptions are available, data that are considered reliable by experts in view of the test conditions concerned shall be adopted.

1) Bioaccumulativity data
For bioaccumulativity data, measured BCFs in fish (degradability of existing chemical substances by microorganisms, data on concentrations in fish, etc.), if any, shall be prioritized over other data. However, results based on the properties of low concentrations, etc. may not be adopted as-is. Measured logKows may serve as a benchmark when measured BCFs are not available. In addition, logKows may be estimated with established methods such as QSAR when measures logKows are not available or considered unreliable.

Results of the following tests or equivalent may be adopted:
- OECD Test Guidelines 305 and the former OECD Test Guidelines 305 A-D (BCF)
- OECD Test Guidelines 107 and 117 (Kow)

Tests results (Kow) based on OECD Test Guidelines 123 (Draft) or equivalent may be adopted when the results described above are not available, provided that expert insight and judgment are then sought.

2) Degradability data
Both biotic and abiotic degradability (such as hydrolysis) shall be taken into account. Substances are considered "readily degradable" when they degrade biotically or abiotically in the aquatic environment by > 70% in 28 days, or tests based on oxygen depletion or carbon dioxide generation > 60% of theoretical maxima. Substances judged to be "readily degradable" based on the Chemical Substances Control Law (the Existing Chemical Substance Evaluation) may be considered "readily degradable" under the GHS classification. However, other degradability data should be taken into account when applying evaluation results of "slow degradability" to the GHS classification. Meanwhile, "rapid degradability" of substances may be taken into account when their hydrolysates are not toxic in the aquatic environment.

Tests results based on OECD Test Guidelines 301 A-F (Degradability Tests) or equivalent may be adopted.

Results of the following tests or equivalent may be adopted when the results described above are not available, provided that expert insight and judgment are then sought.
- OECD Test Guidelines 302A, 302B, 302C, 303A, 303B, 304A, 306, 307, 308 and 309
- OECD Test Guidelines 310 (Draft) and 311 (Draft)

D) Priority when conflicting data exist
(1) When data of Priority 1 are available:
1) In principle, data on the safe side shall be adopted (i.e., the lowest concentration available for data on aquatic environmental hazards, the highest value available for data on bioaccumulativity, and the lowest value available for data on degradability). When four or more data sets are available for the same life stage, condition, and test period of the same species, however, their geometric average shall be adopted as data representing the species.
2) When one datum deviates substantially from others, it is recommended that original articles should be referred to and the reliability of the data should be verified. When verifying data, moreover, it should be ascertained that the information sources consulted are the latest available.

(2) When data of Priority 1 are absent:
1) Data collected from other information sources (such as those specified in Priority 2), those that are considered reliable (GLP-conforming data, or those whose backup data are presented and assessed) shall be adopted. When data appear to be in a gray zone, final judgment on whether or not to adopt the data shall be rendered by experts.
2) When adopting the data, it should be ascertained that the latest available evaluation materials, database, and reliable literature are referred to.
3) Of data that are considered relatively reliable by experts, those on the safe side shall be adopted (i.e., the lowest concentration available for data on aquatic environmental hazards, and the highest value available for data on bioaccumulativity). When four or more data sets are available for the same life stage, condition, and test period of the same species, however, their geometric average shall be adopted as data representing the species.

E) Comparison with previous classification systems
The definitions of EU Annex VI 5.2.1 are almost consistent with the GHS classification.

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

Based on consideration of the four "R" categories described above, each category can be extrapolated as follows:

Category Acute 1 = EU-R50 (and R50/53)
Category Acute 2 = EU-R51 (and R51/53)
Category Acute 3 = EU-R52 (and R52/53)
Category Chronic 1 ≒ EU-R50/53
Category Chronic 2 ≒ EU-R51/53

Category Chronic 3 ≒ EU-R52/53

The definitions of R50, R51 and R52 correspond to those of Acute 1, Acute 2 and Acute (GHS classification). However, the former differ from the latter in that Crustacea refers to Daphnia only, and that the testing time for algae is fixed at 72 hours. The requirements for R53 (i.e., logKow ≧ 3.0 or BCF > 100) are slightly more lenient compared to GHS. Moreover, public test data for establishing a scientific basis are insufficient, and some of them appear to have been evaluated based on structure-activity relationships, or test data on similar substances. Data on biodegradability and bioaccumulativity should therefore be assessed. At the same time, caution must be taken when referring to the “R” categories, because they are amended from time to time; they should remain a reference for the classification.

Most of the substances categorized as “toxic in the aquatic environment” in Annex 1 of EU Directive 67/548/EEC are ELINCS substances (which can only be produced and imported by registered companies). Information on EINECS substances for general use is relatively limited except for agrochemicals.

In Japan, the classification of chemical substances concerns Class 1-2 Specified Chemicals and Class 1-3 Controlled Chemicals (under the Chemical Substances Control Law); and fish acute toxicity A-D for agrochemical registry data (under the Agricultural Chemicals Control Law). These categories, however, are not consistent with the GHS classification, and hence are of no use at this time.