Science memo for reassessment of methyl bromide

APP203660

Substance database ID: 1479 & 3523

SEPTEMBER 2019

Environmental Protection Authority
Te Mana Rauhī Taiao

New Zealand Government

Executive summary

Stakeholders in Methyl Bromide Reduction Incorporated (STIMBR) applied for the reassessment of methyl bromide under section 63 of the Hazardous Substances and New Organisms Act ("the Act").

STIMBR asked for the approval of methyl bromide (HSR001635) to be reassessed to make changes to that approval to amend the recapture and associated buffer zone controls.

Their reassessment application was received on 9 April 2019, and the Environmental Protection Authority ("EPA") decided that the application would be progressed as a publicly notified, modified reassessment in accordance section 63A of the Act.

The applicant submitted reviews of information about the hazard classifications regarding harm to human health and the risks to the environment.

The EPA has evaluated this information and recommends that the human health and environmental classifications be amended to: 6.1C(O), 6.1C(I), 6.1E(resp), 8.2C, 8.3A, 6.6B, 6.8B, 6.9A, 9.1A, 9.2A, 9.3B, 9.4A.

The potential addition of the respiratory irritation classification 6.1E(resp) and the potential revision of the acute oral classification by inhalation (6.1B to 6.1C), are the only proposed changes to the current classification.

The EPA is not aware of significant new information that would change the conclusions of the 2010 reassessment of methyl bromide in relation to risks to the environment.

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1. Introduction/Background

1.1. This application is to reassess methyl bromide (CAS number 74-83-9) so as to make changes to its approval (HSR001635) to amend the recapture and associated buffer zone controls.

1.2. In support of their application, the applicant has provided two documents reviewing the hazard classifications regarding i) harm to human health and ii) the environment, that had been originally assigned to methyl bromide following the 2009 reassessment of the susbtance (application number HRC08002). These documents are as per below:

i. Review the 6 and 8 classifications contained in Dr Martin Edward's report; Appendix D of the ERMA chief executive reassessment of methyl bromide – Dr Lynne Chapham

ii. Methyl Bromide – Consideration of environmental fate and ecotoxicity data available since NZ EPA reassessment of methyl bromide in 2009 – 14 August 2018 – Australian Environment Agency Proprietary Limited (Australian Environment Agency)

1.3. In this document, the EPA has reviewed the information contained in these two documents and provided some conclusions related to the human health and environmental hazard classifications of methyl bromide.

1.4. The current flammability (2.1.1B) classification of methyl bromide was not reviewed as part of this document.

2. Review of human health classification of Methyl Bromide

Introduction

2.1. The document: "*Review the 6 and 8 classifications contained in Dr Martin Edward's report; Appendix D of the ERMA chief executive reassessment of methyl bromide*" by Dr Lynne Chapham provided the following objectives:

- "*Comment on the reliability and robustness of the studies used to assign the HSNO classifications 6 and 8 for methyl bromide as part of the ERMA 2010 Chief Executive iniitiated reassessment of methyl bromide*
- *Provide comment on any relevant information that has arisen since the 2010 reassessment which may impact on the HSNO Class 6 and 8 hazard classifications for methyl bromide*
- *Provide an overall conclusion on whether or not there is new and substantive toxicology knowledge which indicate a review of the toxicology should be undertaken by New Zealand EPA, as part of any future reassessment*."

2.2. With this document, the EPA has taken a similar approach, so as to provide a comparison between the applicant and the EPA's findings.

2.3. A comparison of: i) the current EPA classification applicable to methyl bromide (HSR001635), ii) the position proposed by the applicant, and iii) the EPA's views based on this current review, is presented in Table 1.

2.4. The EPA has taken into account classification for methyl bromide assigned by other regulators worldwide, notably the European Union (EU) Global Harmonized System (GHS) classification for methyl bromide according to the Classification, Labelling and Packaging (CLP) regulation 1272/208/EC (see Table 2) and the Japanese GHS classification according to the National Institute of Technology and Evaluation (NITE) (see Table 3).

2.5. A detailed discussion related to each endpoint is presented in the following section.

Review of individual classifications

2.6. **Acute oral toxicity 6.1**

Current HSNO classification: 6.1C (O)

Applicant proposal: no change proposed

EPA evaluation: Mammalian toxicity studies with methyl bromide indicate that the substance is of moderate acute toxicity by the oral route (6.1C). This classification is consistent with the EU classification of methyl bromide. There are no additional data available and hence, there is no basis to re-evaluate this end point.

2.7. **Acute dermal toxicity 6.1**

Current HSNO classification: ND

Applicant proposal: no change proposed

EPA evaluation: The EPA agrees there is no basis to change the current classification for this endpoint. Since methyl bromide is a skin corrosive (8.2C), it is not scientifically justified to conduct a dermal toxicity study.

2.8. **Acute inhalation toxicity 6.1**

Current HSNO classification: 6.1B

Applicant proposal: 6.1C

EPA evaluation: the EPA agrees with the applicant's suggestion that there is sufficient valid information to re-evaluate to the 2010 6.1B classification. The current classification 6.1B is based on LC_{50} value of 405 ppm for which the study details, and methodology are in Japanese and difficult to interpret. A LC_{50} value of 780 ppm was calculated by Kato et al. (1986) from mortality at one week after exposure in rats. This classifies methyl bromide as 6.1(C) which is consistent with other regulators' classification of methyl bromide (EU and Japan).

2.9. **Acute toxicity (other routes) 6.1**

Current HSNO classification: ND

Applicant proposal: Not discussed

EPA evaluation: Although not discussed in the applicant's document, the EPA's review of the data indicates that methyl bromide should potentially be classified as respiratory irritant (HSNO 6.1E (inhalation route) based on depression in body temperature by >1.5 ºC in acute inhalation neurotoxicity studies in rats. This is in alignment with the EU's classification as STOT SE 3 (may cause respiratory irritation).

2.10. **Skin irritation 6.3 and corrosion 8.2**

Current HSNO classification: 8.2C

Applicant proposal: no change proposed

EPA evaluation: The EPA agrees with the applicant's conclusion that there is no basis to re-evaluate the current classification for skin corrosion.

2.11. **Eye irritation 6.4 and corrosion 8.3**

Current HSNO classification: 8.3A

Applicant proposal: no change proposed

EPA evaluation: The EPA agrees with the applicant's conclusion that there is no basis to re-evaluate the current classification for eye corrosion.

2.12. **Respiratory sensitisation 6.5A**

Current HSNO classification: ND

Applicant proposal: no change proposed

EPA evaluation: The EPA agrees with the applicant's conclusion that there is no basis to re-evaluate the current classification for respiratory sensitisation.

2.13. **Contact sensitisation 6.5B**

Current HSNO classification: ND

Applicant proposal: no change proposed

EPA evaluation: The EPA agrees with the applicant's conclusion that there is no basis to re-evaluate the current classification for contact sensitisation and also notes that since methyl bromide is a skin corrosive (8.2C), it is not scientifically justified to conduct a skin sensitisation study.

2.14. **Mutagenicity 6.6**

Current HSNO classification: 6.6B

Applicant proposal: no change proposed

EPA evaluation: The EPA agrees with the applicant's conclusion that there is no basis to re-evaluate the current classification for mutagenicity. This classification is aligned with the EU classification.

2.15. **Carcinogenicity 6.7**

Current HSNO classification: No

Applicant proposal: no change proposed

EPA evaluation: The EPA agrees with the applicant's conclusion that there is no basis to re-evaluate the current classification for carcinogenicity. Based on overall weight of evidence, methyl bromide is not considered a carcinogen. This is consistent with other regulators' classification.

2.16. **Developmental/Reproductive toxicity 6.8**

Current HSNO classification: 6.8B

Applicant proposal: no change proposed

EPA evaluation: The EPA agrees with the applicant's conclusion that there is no basis to re-evaluate the current classification for developmental/reproductive effects. The EPA notes that this classification does not seem to be consistent across regions as methyl bromide is not classified for developmental/reproductive toxic effects in EU while evidence suggest that it is the case for Japan and potentially other regions.

2.17. **Developmental/Reproductive toxicity via lactation 6.8C**

Current HSNO classification: ND

Applicant proposal: no change proposed

EPA evaluation: The EPA agrees with the applicant's conclusion that there is no basis to re-evaluate the current classification for developmental/reproductive toxicity via lactation.

2.18. **Specific target organ toxicity – oral (6.9)**

Current HSNO classification: No

Applicant proposal: no change proposed

EPA evaluation: The EPA agrees with the applicant's conclusion that there is no basis to re-evaluate the current classification for specific target organ toxicity– oral.

2.19. **Specific target organ toxicity – dermal (6.9)**

Current HSNO classification: ND

Applicant proposal: no change proposed

EPA evaluation: The EPA agrees with the applicant's conclusion that there is no basis to re-evaluate the current classification for specific target organ toxicity single dose – dermal.

Specific target organ toxicity– inhalation (6.9)

Current HSNO classification: 6.9A (neurotoxicity)

Applicant proposal: no change proposed

EPA evaluation: The EPA agrees with the applicant's conclusion that there is no basis to re-evaluate the current classification for specific target organ toxicity repeated dose – inhalation. The classification is aligned with that of other regulators. The current HSNO classification does not allow clear differentiation between single dose and repeated dose exposure so that classification for 6.1E (inhalation route) might be warranted (see paragraph 2.9).

Conclusion

2.20. The human health hazard classifications of methyl bromide determined by the EPA are 6.1C (oral), 6.1C (inhalation), 6.1E (respiratory irritant), 8.2C, 8.3A, 6.6B, 6.8B and 6.9A (Table 2). The hazard classifications of methyl bromide were determined based on the available information in international regulatory reports [European Food Safety Authority (EFSA 2011), European Commission (EC 2006)] and classifications established overseas.

3. Environmental risk assessment

Introduction

3.1. The applicant's document: "*Consideration of environmental fate and ecotoxicity data available since NZ EPA reassessment of methyl bromide in 2009*" by Australian Environment Agency provides comments on the availability and potential relevance of new information that would change the conclusions of the original reassessment decision of methyl bromide in relation to its effects in the environment.

3.2. In this section, the EPA provides its conclusions related to the points made by Australian Environment Agency.

Review of effects to the environment

3.3. The Australian Environment Agency's (2018) report evaluates the following adverse environmental effects.

Dissipation

3.4. Under point 5.3.12 of the application document for the reassessment of methyl bromide, the following is mentioned:

"*Methanol is readily and rapidly degraded in a wide variety of environmental media and has low bioconcentration and low toxicity (World Health Organisation). Although methanol has the potential to leach into groundwater, significant contamination is unlikely given the rapid rate of biodegradation (Environmental Health & Safety). The ecotoxicity of the degradation products is less than the ecotoxicity of the parent compound methyl bromide*."

3.5. The applicant's report concludes there are no further studies or information available since the 2009 assessment and 2010 decision that would change this conclusion.

3.6. Under point 5.3.13 of the application document for the reassessment of methyl bromide, the following is mentioned:
"*Alternative pathways of degradation of methyl bromide in soil are a reaction with soil organic matter and microbial degradation. In organic-matter-rich soils degradation is more rapid than in organic-matter-poor soils*."

3.7. The applicant's report concludes there are no further studies or information available since the 2009 assessment and 2010 decision that would change this conclusion.

3.8. The EPA is not aware of any information that would change the conclusion of the 2009/2010 reassessment of methyl bromide in relation to these two points.

Ozone-depletion

3.9. Under point 5.3.4 of the application document for the reassessment of methyl bromide, the following is mentioned:
"*Methyl bromide is a powerful ozone-depleting substance. Concerns about the depletion of the ozone layer exist, because the ozone layer reduces the amount of harmful ultraviolet (UV) radiation that reaches the Earth. Any significant change to this layer can have consequences for human health and the environment and will have further impacts on agriculture. Effects for terrestrial ecosystems include possible damaging effects for plants and microbes, but these organisms also have protective and repair processes. Terrestrial ecosystem responses to increases in UV are primarily in interactions among species rather than in the performance of individual species. Effects on aquatic ecosystems include possible adverse effects on the growth, photosynthesis and reproduction of phytoplankton, thus affecting the food web*."

3.10. The applicant's report concludes there are no new environmental fate data for methyl bromide that would change this conclusion.

3.11. The EPA is not aware of any information that would change the conclusion of the 2009/2010 reassessment of methyl bromide in relation to this point. Methyl bromide's potential to harm the ozone layer is well documented and acknowledged globally (classified as such in EU and Japan for instance and listed in Annexes to the Montreal Protocol).

Ecotoxicity

3.12. Under point 5.3.6 of the application document for the reassessment of methyl bromide, the following is mentioned:
"*Valued terrestrial vertebrates and invertebrates are unlikely to be found in the surroundings of a treated building/container where methyl bromide will be vented. Furthermore, methyl bromide will quickly volatilise and dissipate in the atmosphere. Since the likelihood of exposure is so low, the direct risks to terrestrial vertebrates and invertebrates are considered to be negligible. Similarly, due to a lack of direct exposure to aquatic organisms or direct contamination of surface water the direct risks to aquatic organisms are considered to be negligible*."

3.13. The applicant's report concludes there are no further studies or information available since the 2009 assessment and 2010 decision that would change this conclusion. Reference is being made to a data gap identified in the EFSA conclusions (EFSA 2011) in relation to indirect exposure of soil, surface water and groundwater via leakage from containers to the atmosphere during fumigation and subsequent deposition. However, given the nature of the application of methyl bromide in New Zealand as Quarantine and Preshipment Uses (QPU), the EPA estimate that there is no new information that would alter the original reassessment conclusions.

3.14. Under point 5.3.3 of the application document for the reassessment of methyl bromide, the following is mentioned:
"*Methyl bromide used as a soil fumigant in the appropriate concentrations will, as intended, eradicate all organisms in the soil environment. However, this reassessment does not address the risks associated with soil fumigation but is restricted to the QPS use of methyl bromide*."

3.15. The applicant's report mentions that non-QPS uses are no longer supported in New Zealand and concludes that as there is no direct soil fumigation application, there is limited (no) value in considering any further ecotoxicity data related to soil organisms that have become available since the 2009 assessment due to negligible exposure to this environmental compartment

3.16. The EPA agrees with the applicant's statement on the matter, which also implies that the assigned classification of methyl bromide as 9.1A, 9.2A, 9.3B and 9.4A are likely to remain unchanged.

Conclusions of the ecological risk assessment

3.17. The conclusion of the applicant's report is that there are no further studies or information available since the 2009 assessment and 2010 decision that would change any conclusions relating to the environment.

3.18. The EPA agrees with that conclusion which is linked to the fact that under the proposed conditions of use, the likelihood of exposure of non-target organisms is low and the associated risks will be negligible with the controls in place.

4. Hazard classification of methyl bromide

4.1. The hazard classifications of methyl bromide are listed in Table 1 below.

Table 1: Applicant and EPA classifications of methyl bromide (human health and environmental)

Hazard Class/Subclass	Hazard Classification			Remarks
	Current (HSR001635)	Applicant's	EPA Staff Proposed	
Subclass 6.1 Acute toxicity (oral)	6.1C	6.1C	6.1C	a) LD_{50}: 86 mg/kg bw (females); 120-160 mg/kg bw (males) b) LD_{50}: 104 mg/kg bw for liquid Methyl Bromide and 133 mg/kg bw for microencapsulated Methyl Bromide
Subclass 6.1Acute toxicity (dermal)	ND	ND	NA	Classification not required as methyl bromide is skin corrosive.
Subclass 6.1 Acute toxicity (inhalation)	6.1B	6.1C	6.1C	LC_{50} value of 780 ppm
Subclass 6.1 Respiratory Irritant	-	-	6.1E	Depression in body temperature by >1.5 ºC
Subclass 6.1 Aspiration hazard	-	-	-	
Subclass 6.3/8.2 Skin irritancy/corrosion	8.2C	8.2C	8.2C	Severe, second degree burns with large blisters that do not completely penetrate the dermis in workers. Animal studies scientifically not necessary
Subclass 6.4/8.3 Eye irritancy/corrosion	8.3A	8.3A	8.3A	Scientific/occupational literature support the current 8.3A,
Subclass 6.5A Respiratory sensitisation	ND	No	ND	

Hazard Classification				
Hazard Class/Subclass	**Current (HSR001635)**	**Applicant's**	**EPA Staff Proposed**	**Remarks**
Subclass 6.5B Contact sensitisation	ND	ND	No	Classification not required as methyl bromide is skin corrosive. Therefore, due to animal welfare it is not scientifically justified to conduct skin sensitization study.
Subclass 6.6 Mutagenicity	6.6B	6.6B	6.6B	
Subclass 6.7 Carcinogenicity	No	No	No	
Subclass 6.8 Reproductive/ developmental toxicity	6.8B	6.8B	6.8B	
Subclass 6.8 Reproductive/ developmental toxicity (*via* lactation)	ND	ND	ND	
Subclass 6.9 Target organ systemic toxicity (oral)	No	No	No	
Subclass 6.9 Target organ systemic toxicity (dermal)	ND	ND	No	
Subclass 6.9 Target organ systemic toxicity (inhalation)	6.9A	6.9A	6.9A	
Subclass 9.1 Aquatic ecotoxicity	9.1A		9.1A	No change. No basis to re-evaluate. No new data are available.
Subclass 9.2 Soil ecotoxicity	9.2A		9.2A	No change. No basis to re-evaluate. No new data are available.
Subclass 9.3 Terrestrial vertebrate ecotoxicity	9.3B		9.3B	No change. No basis to re-evaluate. No new data are available.

Hazard Classification				
Hazard Class/Subclass	**Current (HSR001635)**	**Applicant's**	**EPA Staff Proposed**	**Remarks**
Subclass 9.4 Terrestrial invertebrate ecotoxicity	9.4A		9.4A	No change. No basis to re-evaluate. No new data are available.

NA: Not Applicable. For instance testing for a specific endpoint may be omitted if it is technically not possible to conduct the study as a consequence of the properties of the substance: eg very volatile, highly reactive or unstable substances cannot be used, mixing of the substance with water may cause danger of fire or explosion or the radio-labelling of the substance required in certain studies may not be possible.

ND: No Data or poor quality data [according to Klimisch criteria (Klimisch, Andreae et al. 1997)]. There is a lack of data for one or more components.

No: Not classified based on actual relevant data available for the substance or all of its components. The data are conclusive and indicate the threshold for classification is not triggered.

Conclusion

4.2. No new or additional data were available since the 2009 reassessment of methyl bromide, hence there is no basis to re-evaluate the current health hazard classifications [6.1C (O), 6.1B (I), 6.1E (resp. irrit) 8.2C, 8.3A, 6.6B, 6.8B, 6.9A]. However, the EPA has proposed respiratory irritation classification (6.1E) based on depression in body temperature by >1.5 ºC in acute inhalation neurotoxicity studies in rats.

4.3. In regard to ecotoxicity, there is no basis to re-evaluate the current hazard classifications (9.1A, 9.2A, 9.3B and 9.4A) as no new data are available since the 2009 reassessment and 2010 decision.

Appendix A: References

EC (2006). Draft Assessment Report - Initial risk assessment provided by the rapporteur Member State The United Kingdom for the existing active substance methyl bromide.

EFSA (2011). "Conclusion on the peer review of the pesticide risk assessment of the active substance methyl bromide." EFSA Journal **9**(1): 1893.

Appendix B: EU classification of methyl bromide according to GHS

Table 2: CLP EU classification of methyl bromide

Classification			Labelling	
Hazard Class and Category Code(s)	Hazard Statement Code(s)	Hazard Statement Code(s)	Supplementary Hazard Statement Code(s)	Pictograms, Signal Word Code(s)
Press. Gas				GHS09 GHS08 GHS04 GHS06 Dgr
Acute Tox. 3 *	H301	H301		
Skin Irrit. 2	H315	H315		
Eye Irrit. 2	H319	H319		
Acute Tox. 3 *	H331	H331		
STOT SE 3	H335	H335		
Muta. 2	H341	H341		
STOT RE 2 *	H373	H373		
Aquatic Acute 1	H400	H400		
Ozone 1	H420	H420		

Appendix C: Japan classification of methyl bromide according to GHS

Table 3: Japan NITE classification of methyl bromide

Hazard class	Classification	Signal word	Hazard statement	Precautionary statement	Rationale for the classification
Acute toxicity （Oral）	Category 3	Danger	H301: Toxic if swallowed	P301+P310: IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician. P264: Wash ... thoroughly after handling. P270: Do not eat, drink or smoke when using this product. P321: Specific treatment （see ... on this label）. P330: Rinse mouth. P405: Store locked up. P501: Dispose of contents/container to ...	Based on a LD50 value of 104,214 mg/kg for rats (SIDS (2002), Initial Risk Assessment Report (NITE, CERI, NEDO) No. 126 (2008)), the substance was classified into Category 3.
Acute toxicity （Dermal）	Classification not possible		-	-	-
Acute toxicity （Inhalation: Gases）	Category 3	Danger	H331: Toxic if inhaled	P304+P340: IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing. P403+P233: Store in a well-ventilated place. Keep container tightly closed. P261: Avoid breathing dust/fume/gas/mist/vapours/spray. P271: Use only outdoors or in a well-ventilated area. P311: Call a POISON CENTER or doctor/physician. P321: Specific treatment （see ... on this label）. P405: Store locked up. P501: Dispose of contents/container to ...	Based on a LC_{50} value of 781 ppm in a rat inhalation exposure test (gas) (EHC 166 (1995)), the substance was classified into Category 3.

Hazard class	Classification	Signal word	Hazard statement	Precautionary statement	Rationale for the classification
Acute toxicity （Inhalation: Vapours）	Not applicable	-	-	-	Gas (GHS definition)
Acute toxicity （Inhalation: Dusts and mists ）	Not applicable	-	-	-	Gas (GHS definition)
Skin corrosion/irritation	Category 2	Warning	H315: Causes skin irritation	P302+P352: IF ON SKIN: Wash with plenty of soap and water. P332+P313: If skin irritation occurs: Get medical advice/attention. P264: Wash ... thoroughly after handling. P280: Wear protective gloves/protective clothing/eye protection/face protection. P321: Specific treatment （see ... on this label）. P362: Take off contaminated clothing and wash before reuse.	Since there are a number of case reports describing skin irritation (ACGIH (7th, 2001), ATSDR (1992), SIDS (2002)), the substance was classified into Category 2. In a test where the substance (liquid) was applied to the back of rabbits, very slight erythema was observed in 1/6 animals within 24-hour, which disappeared within 48-hour (Test Data for Supporting Registration of Pesticides (1979)). Application of the substance to the back of rats led to the impairments to the epidermal cells and consequently necrosis (HSDB (2002)). In EU classification, the substance is classified into Xi; R38.
Serious eye damage/eye irritation	Category 2B	Warning	H320: Causes eye irritation	P305+P351+P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P337+P313: If eye irritation persists: Get medical advice/attention. P264: Wash ... thoroughly after handling.	In a rabbit test (exposure of gas), observed positive reactions in iris and cornea disappeared within 5 days (Initial Risk Assessment Report (NITE, CERI, NEDO) No. 126 (2008), SIDS (2002)). Based on the report, the substance was classified into

Hazard class	Classification	Signal word	Hazard statement	Precautionary statement	Rationale for the classification
					Category 2B. As relevant information, the substance is classified as Xi; R36/37/38 in EU classification.
Respiratory sensitization	Classification not possible	-	-	-	No data available.
Skin sensitization	Classification	-	-	-	No data available.
Germ cell mutagenicity	Category 2	Warning	H341: Suspected of causing genetic defects	P308+P313: IF exposed or concerned: Get medical advice/attention. P201: Obtain special instructions before use. P202: Do not handle until all safety precautions have been read and understood. P281: Use personal protective equipment as required. P405: Store locked up. P501: Dispose of contents/container to ...	Based on positive results in micronucleus test by inhalation exposure to mice and rats for 2 weeks (SIDS (2002)) and mouse micronucleus test (ACGIH (2001)), the substance was classified into Category 2. As relevant information, there are reports of positive results from in vivo DNA damage test (SIDS (2002)). From in vitro mutagenicity tests, there are reports of positive reverse mutation test and chromosomal aberration test (Initial Risk Assessment Report (NITE, CERI, NEDO) No. 126 (2008)).
Carcinogenicity	Not classified	-	-	-	Based on the classifications of "A4" in ACGIH (ACGIH (2001)), "Group 3" in IARC (IARC (1999)) and "D" in EPA (EPA (1990)), the substance was classified as "Not classified". In 2-year inhalation (systemic exposure) tests in rats and mice, increased incidences of tumors were not observed in both sexes of either species, and there were no evidences of carcinogenicity of methyl bromide in

Hazard class	Classification	Signal word	Hazard statement	Precautionary statement	Rationale for the classification
					F344/DuCrj (Fischer) rats or Crj:BDF1 mice (Results from Carcinogenicity tests (Ministry of Health, Labour and Welfare) (1989)).
Reproductive toxicity	Category 2	Warning	H361: Suspected of damaging fertility or the unborn child	P308+P313: IF exposed or concerned: Get medical advice/attention. P201: Obtain special instructions before use. P202: Do not handle until all safety precautions have been read and understood. P281: Use personal protective equipment as required. P405: Store locked up. P501: Dispose of contents/container to ...	In developmental toxicity tests in rabbits, increased incidence of anomalies (fused sternebrae, missing gallbladder or missing some lobe of lung) was observed in fetuses at dose levels in which maternal general toxicity was observed (SIDS (2002), IRIS (2002), Initial Risk Assessment Report (NITE, CERI, NEDO) No. 126 (2008)). Based on the data, the substance was classified into Category 2.
Specific target organ toxicity - Single exposure	Category 1 (nervous system, respiratory system, liver, kidney, digestive system)	Danger	H370: Causes damage to organs (nervous system, respiratory system, liver, kidney, digestive system)	P307+P311: IF exposed: Call a POISON CENTER or doctor/physician. P260: Do not breathe dust/fume/gas/mist/vapours/spray. P264: Wash ... thoroughly after handling. P270: Do not eat, drink or smoke when using this product. P321: Specific treatment （see ... on this label）. P405: Store locked up. P501: Dispose of contents/container to ...	In human exposure cases, confusion, convulsion, coma, reduced vision, nausea, vomiting, renal failure, gastrointestinal disorder and hepatotoxic symptoms are reported (Initial Risk Assessment Report (NITE, CERI, NEDO) No. 126 (2008)). Based on this information, the substance was classified into Category 1 (nervous system, kidney, alimentary system, liver). In animals, dyspnea, ataxia, changes in the stomach (distention, redness, adhesions, ulceration) (SIDS (access on 6, 2009) and hepatic necrosis were observed following oral exposure in rats and mice (EHC No. 166 (1995)). In addition, decreased locomotor activity, decreased respiratory rate and pneumonia-

Hazard class	Classification	Signal word	Hazard statement	Precautionary statement	Rationale for the classification
					like changes were observed at dose levels within the guidance value range for Category 1 (2500 ppmV/4h or less) following inhalation exposure in rats and mice (Test Data for Supporting Registration of Pesticides (1980)). Based on the data, the substance was classified into Category 1 (respiratory system). Although there is a report of congestion in the kidney and adrenal gland (Test Data for Supporting Registration of Pesticides (1980)), the details are unknown.
Specific target organ toxicity - Repeated exposure	Specific target organ toxicity - Repeated exposure	Danger	H372: Cause damage to organs through prolonged or repeated exposure (nervous system, heart, blood)	P260: Do not breathe dust/fume/gas/mist/vapours/spray. P264: Wash ... thoroughly after handling. P270: Do not eat, drink or smoke when using this product. P314: Get medical advice/attention if you feel unwell. P501: Dispose of contents/container to ...	Since effects on the cranial nerves are reported in humans (Initial Risk Assessment Report (NITE, CERI, NEDO) No. 126 (2008)), the substance was classified into Category 1 (nervous system). In a 13-week inhalation test in rats decreases in hematocrit, hemoglobin and erythrocyte count were observed at 87 ppm, which falls within the guidance value range for Category 2 (50 - 250 ppmV) (Initial Risk Assessment Report (NITE, CERI, NEDO) No. 126 (2008), NTP TR385 (1992)). In addition, in a 13-week oral dose test in rats, anemia was observed at 36 mg/kg/day, which falls within the guidance value range for Category 1 (less than 50 mg/kg/day) (IRIS (2002)). Based on the data, the substance was classified into Category 1 (blood). In a 3-week inhalation exposure test in rats (Initial Risk Assessment

Hazard class	Classification	Signal word	Hazard statement	Precautionary statement	Rationale for the classification
					Report (NITE, CERI, NEDO) No. 126 (2008)), degeneration of myocardium, degeneration and necrosis in the testis, lethargy, tremor and paralysis of limbs were observed at 26.7 ppm and higher levels, which falls within the guidance value range for Category 1 (less than 50 ppm). Additionally, necrosis and fibrillization of myocardium are reported at 33.3 ppm and higher levels in another 3-week inhalation exposure test in rats (Initial Risk Assessment Report (NITE, CERI, NEDO) No. 126 (2008)). Based on the data, the substance was classified into Category 1 (heart). In 13 - 25 week oral dose tests (Initial Risk Assessment Report (NITE, CERI, NEDO) No. 126 (2008)), chronic inflammation and fibrillization in the stomach were observed at 36 - 50 mg/kg/day, which fall within the guidance value range for Category 1 (less than 50 ppm), and lymphocytic infiltration in the glandular stomach and chronic inflammation in the esophagus were observed at 50 mg/kg/day. These data were not used for classification, since the effects were attributed to irritation of the substance. Findings of degeneration and necrosis in the testis noted in a 3-week inhalation exposure test in rats correspond to Category 2 of reproductive toxicity, and were not used for this classification.

Hazard class	Classification	Signal word	Hazard statement	Precautionary statement	Rationale for the classification
Aspiration hazard	Not applicable	-	-	-	Gas (GHS definition)
Hazardous to the aquatic environment （Acute）	Category 1	Warning	H400: Very toxic to aquatic life	P273: Avoid release to the environment. P391: Collect spillage. P501: Dispose of contents/container to ...	Classified into Category 1 from its 96h-LC50 = 0.7 mg/L for fish (Oryzias latipes) (Hazard Assessment Report (CERI, NITE), 2008).
Hazardous to the aquatic environment （Long-term）	Category 1	Warning	H410: Very toxic to aquatic life with long lasting effects	P273: Avoid release to the environment. P391: Collect spillage. P501: Dispose of contents/container to ...	Classified into Category 1 since its acute toxicity is Category 1 and it is not rapidly degradable (BOD degradation rate: 15, 17% (Biodegradation and Bioconcentration of Existing Chemical Substances under the Chemical Substances Control Law, 1991)).
Hazardous to the ozone layer	Category 1	Warning	H420: Harms public health and the environment by destroying zone in the upper atmosphere	P502: Refer to manufacturer/supplier for information on recovery/recycling.	This substance is listed in Annexes to the Montreal Protocol.