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Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade

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Item 5 (c) (vi) of the provisional agenda*

Technical work: review of notifications of final regulatory action: methyl bromide

Methyl bromide: notification from the Netherlands reviewed by the Chemical Review Committee and the rationale for its conclusion

Note by the Secretariat

As is mentioned in the note by the Secretariat on methyl bromide: notifications of final regulatory action (UNEP/FAO/RC/CRC.18/10), the annex to the present note sets out the notification of final regulatory action for methyl bromide in the pesticide category from the Netherlands reviewed by the Chemical Review Committee at its first meeting and the rationale for its conclusion. The present note, including its annex, has not been formally edited.

* UNEP/FAO/RC/CRC.18/1.

Annex

Methyl bromide: notification from the Netherlands reviewed by the Chemical Review Committee and the rationale for its conclusion

List of documents:

1. Notification of final regulatory action for methyl bromide in the pesticide category and supporting documentation submitted by the Netherlands and reviewed by the Chemical Review Committee at its first meeting.
2. Rationale adopted by the Chemical Review Committee at its first meeting for its conclusion on the notification of final regulatory action for methyl bromide in the pesticide category submitted by the Netherlands.

FORM FOR NOTIFICATION OF FINAL REGULATORY ACTION TO BAN OR SEVERELY RESTRICT A CHEMICAL

IMPORTANT: See instructions before filling in the form

COUNTRY: THE NETHERLANDS

PART I: PROPERTIES, IDENTIFICATION AND USES

1.	**IDENTITY OF CHEMICAL**	
1.1	**Common name**	Methylbromide; bromomethane
1.2	**Chemical name according to an internationally recognized nomenclature (e.g. IUPAC), where such nomenclature exists**	bromomethane; monobromomethane; methane,bromo
1.3	**Trade names and names of preparations**	Dowfume; Halon 1001; UN 1062; M-B-R 98; A13-01916; Bercema; Tri-Brom-Methyl-Bromide-Rodent-Fumigant; Brom-O-Sol; Caswell-No-555; CURAFUME; Detia Gas Ex-M; Dowfume MC-2; Dowfume MC-33 Dowfume MC-2 Soil Fumigant; EDCO; EMBAFUME; EPA-Pesticide-Chemical-Code-053201; M-B-C Fumigant; Brom-O-Gas; Brom-O-Gas Methyl Bromide Soil Fumigant; HALTOX; ISCOBROME; KAYAFUME; MB; MBC-Soil-Fumigant; MBC-33 Soil Fumigant; MBX; Dowfume MC-2R; Dowfume MC-2 Fumigant; MEBR; Metabrom; Meth-O-Gas; METHOGAS; Superior Methyl Bromide-2; Methyl-fume; PESTMASTER; Pestmaster Soil Fumigant; Drexel-Plant-Bed-Gas; ROTOX; TERABOL; Terr-O-Gas; ZYTOX(HSDB) Celfume; Dawson 100; Metafume; Profume; R 40B1; RCRA wast number U029; Terr-O-Cide; Terr-O-Gas 67; Terr-O-Gas 100 (RTECS); Brozone; Isobrome (Norman & Dollinger, 1977)
1.4	**Code numbers**	
1.4.1	**CAS number**	74-83-9
1.4.2	**Harmonized System customs code**	2903 3033
1.4.3	**Other numbers (specify the numbering system)**	EINECS No. 200-813-2

PLEASE RETURN THE COMPLETED FORM TO:

Interim Secretariat for the Rotterdam Convention
Plant Protection Service
Plant Production and Protection Division, FAO
Viale delle Terme di Caracalla
00100 Rome, Italy

Tel: (+39 06) 5705 3441
Fax: (+39 06) 5705 6347
E-mail: pic@fao.org

OR

Interim Secretariat for the Rotterdam Convention
UNEP Chemicals
11-13, Chemin des Anémones
CH – 1219 Châtelaine, Geneva, Switzerland

Tel: (+41 22) 917 8183
Fax: (+41 22) 797 3460
E-mail: pic@unep.ch

1.5	**Indication regarding previous notification on this chemical, if any**
1.5.1	θ This is a first time notification of final regulatory action on this chemical.
1.5.2	θ This is a modification of a previous notification of final regulatory action on this chemical. The sections modified are: _____ X This notification replaces all previously submitted notifications on this chemical.
	Date of issue of the previous notification: _____

1.6 **Information on hazard classification where the chemical is subject to classification requirements**	
International classification systems	**Hazard class**
EU	T (toxic); N (dangerous for the environment; R23/25, R36/37/38, R40, R48/20, R50/53, R59
IARC	1986, 1987: Group 3 (*not classifiable as to its carcinogenicity to humans*, based on limited evidence for the carcinogenicity to experimental animals; inadequate evidence for the carcinogenicity to humans)
US EPA	Classification D: inadequate human and animal data
Other classification systems	**Hazard class**

1.7	**Use or uses of the chemical**
1.7.1	X **Pesticide**
	Describe the uses of the chemical as a pesticide in your country: Methylbromide was used as a soil disinfectant (fungicide/nematicide). Only application still allowed concern space fumigation by means of gas evaporation and are only permitted in gasproof spaces under very strict regulations.
1.7.2	θ **Industrial**
	Describe the industrial uses of the chemical in your country: Not relevant

1.8 Properties

1.8.1 Description of physico-chemical properties of the chemical

Identity	colourless gas
Formula	C1 H3 Br1
Molecular weight	94.94
Solubility	16000-18500 mg/l at 20 °C (IPCS) 11640 mg/l at 25 °C (EPIWIN)
Vapour pressure	732 mm Hg at 25 °C (EPIWIN) 1420 mm Hg at 20 °C (IPCS, DOSE)
Henry's law constant	8.49 E-3 atm-cu m/mole (EPIWIN) 6.24 E-3 atm-cu m/mole (HSDB)
logKow	1.19 (exp. EPIWIN, IPCS)
logKoc	1.155 (EPIWIN)
Freezing point	- 93 °C (IPCS, DOSE) - 105.39 °C (EPIWIN)
Boiling point	3.56 °C (IPCS, DOSE) 26.06 °C (EPIWIN)
BCF	1.646 (EPIWIN)

1.8.2 Description of toxicological properties of the chemical

1. Acute toxicity

Oral:	LD50 rat 214 mg/kg bw (IARC)
Dermal	no data
Inhalation:	2-h LC50 mouse 1540 mg/m^3 (DOSE) 1-h LC50 mouse 4680 mg/m^3 (IARC) 30-min LC50 rat 11000 mg/m^3 (IARC) 4-h LC50 rat 3026 mg/m^3 (HSDB) 8-h LC50 rat 1160 mg/m^3 (IARC) 8-h NOEC rat 63 mg/m^3 (RIVM/CSR) 24-h LC50 rat 50 mg/m^3 (IARC)

- In rats a concentration of 51400 mg/m^3 is lethal in 6 minutes, whereas a concentration of 884 mg/m^3 produces death in 26 hours. At 432 mg/m^3 no rats died after 22 hours (RIVM/CSR).
- Signs of toxicity after a single 8-h exposure included decreases in body temperature, body weight and locomotor activity at 500 mg/m^3 and above; no effects were seen at 250 mg/m^3 (RIVM/CSR)
- Acute toxic effects of 1 hr inhalatory exposure of mice to methylbromide at 870 to 5930 mg/m^3 included kidney lesions at 3500 mg/m^3 and above, decreased lung and liver weight at 2200 and 2700 mg/m^3 and decreased motor co-ordination at 5770 mg/m^3 (HSDB).

Irritation/Sensitization: There are no reports on skin effects in animals (IPCS, 1995).

2. Short-term toxicity

Oral

- Cats fed fumigated peanuts containing methylbromide at 0.5 to 1.25 mg /day for 4 months showed no changes in motor responses (HSDB).
- Dogs fed methylbromide fumigated pelleted food in doses equal to 35, 75 and 150 mg/kg/day for 6 to 8 weeks were observed for 1 year and showed no or minimal evidence of toxicity at 35 and 75 mg/kg/day. At 150 mg/kg/day the animals showed lethargy, occasional salivation and diarrhea, but no changes in blood chemistry, haematology, urinalysis of histology (HSDB).
- Cattle fed pelleted food containing methylbromide at 170, 511, 1062, 2633 and 4650 mg/kg for 49 days showed uncoordinated movement and gait and recumbency (HSDB).

Inhalation

- In a subacute study with male rats exposed by inhalation to methylbromide at 582, 776, 1164, or 1552 mg/m^3 paralysis of extremities and ataxia were noted at 1164 and 1552 mg/m^3. Necrosis of the heart occurred at all concentrations (HSDB).
- Biochemical examination of male rats exposed continuously by inhalation to methylbromide at 4, 19.4 or 39 mg/m^3 during 3 weeks revealed changes in blood glucose, creatinine phosphokinase, Hb, glutathione, SGPT, SGOT, LDH, serum total protein at 19.4 and 39 mg/m^3 (HSDB). Neurological effects were seen only at 39 mg/m^3.
- Exposure of 10 weeks old male rat by inhalation to methylbromide at 776 or 1164 mg/m^3 , 4 h/day, 5 day/week for 3 weeks resulted in relatively prolonged dysfunction of the peripheral nerves and disturbance in spontaneous circadian rhythm activity at 1164 mg/m^3. No macroscopic or microscopic abnormalities were found in CNS or in peripheral nerves (HSDB).
- Rats and rabbits exposed by inhalation to methylbromide at 252 mg/m^3 for 5 hours/day, 5 days/week during 4 weeks showed significantly reduced eye blink responses and nerve conduction velocity in rabbits, but had no effects on rats (HSDB).
- In a standard subacute inhalation study with mice trembling, jumpiness and paralysis were observed at all tested concentrations. The effects were slight at 48 and 100 mg/m^3 but obvious at concentrations >=200 mg/m^3. These effects were not reflected in histopathological abnormalities (RIVM/CSR).
- In a subacute inhalation study in rats and methylbromide at 0, 70, 200 or 600 mg/m^3 administered for 6 h/day, 5 or 7 days/week during 4 weeks staggered gait was observed in all animals at 200 mg/m^3 and above and in 3/12 animals at 70 mg/m^3. In addition at 600 mg/m^3 mortality and morphological blood abnormalities were noted, serum enzyme levels were elevated and histopathological changes occurred in heart and lungs (RIVM/CSR).
- Male rats exposed by inhalation to methylbromide at 0, 350, 680, 970 or 1260 mg/m^3 for 6 h/day during 5 days showed diarrhea, haemoglubinuria and in some cases, gait disturbances at 970 and 1260 mg/m^3. Vacuolar degeneration of the zona fasciculata of the adrenal glands, cerebellar granule cell degeneration, and nasal olfactory sensory cell degeneration were seen at 680 mg/m^{3}nd above. Cerebral cortical degeneration and minor alterations in testicular histology were seen only at 1260 mg/m^3. At 970 and 1260 mg/m^3 hepatocellular degeneration was seen. No changes in kidney and epididymis (HSDB).

3. Long-term toxicity

Oral

Because methyl bromide tends to volitize and exists mainly as a gas at room temperature, only a few (sub)chronic oral studies have been performed (ATSDR, 1992).

- In two oral gavage subchronic studies in rats irritation of the stomach was the chief effect. The 13-week study of Danse et al. (1984) reported a NOAEL of 0.4 mg/kg bw/day and a LOAEL of 2 mg/kg bw/day (ATSDR, 1992). Similar findings were reported by Boorman et al. (1986) and Hubbs and Harrington et al. (1986). In subsequent studies, these effects were shown to regress after termination of treatment (IPCS, 1995).
- Rats were fed diets fumigated with methylbromide (80, 200, or 500 mg total Br/kg food) for two years. A slight decrease in body weight was seen in males from week 60 onwards. A NOAEL of 200 mg/kg food could be established (IPCS, 1995).

Inhalation

- Mouse were exposed by inhalation to 0, 39, 128, and 389 mg/m^3 methylbromide 6 hours/day, 5 days/week during 2 years. Increased incidence of nonneoplastic lesions in brain, bone, heart and nose was seen at all doses. At 389 mg/m^3: high mortality, decrease in body weight and thymus weight, tremors, abnormal posture, and limb paralysis (NTP, 1992; cited in IPCS, 1995)
- Mouse were exposed to methylbromide at 0, 16, 62, or 250 mg/m^3 6 hours/day, 5 days/week for 2 years. Depression of body weight gain, changes in blood biochemistry (increase in CPK, inorganic P, and chloride and decrease in albumin) and atrophy of the granular layer of the cerebellum at 250 mg/m^3. The NOAEL was found to be 62 mg/m^3 (IPCS, 1995)
- In a chronic toxicity/carcinogenicity study, rats were exposed by inhalation to methylbromide at 0, 12, 116 or 349 mg/m^3, 6 hours/day, 5 days/week for 29 months. Increased incidences of degenerative and hyperplastic changes of the nasal olfactory epithelium were observed in all groups. Exposure to 349 mg/m^3 resulted in lesions in the heart and hyperkeratosis in the oesophagus and forestomach. See also 'carcinogenicity' (IPCS, 1995).

- Rats and guinea-pigs were exposed to 130-850 mg/m^3 methylbromide for 7.5-8 hours/day, 5 days/week during 6 months. All animals died after a few exposures to 850 mg/m^3; clinical signs of toxicity in rats at 420 mg/m^3 included poor general appearance, weight loss, pulmonary congestion and renal and hepatic lesions. No effects were observed at 130 and 250 mg/m^3 in rats and guinea-pigs (IARC). The NOAEL is 250 mg/m^3.
- Rats were exposed to methylbromide at 16, 78, or 389 mg/m^3, 6 hours/day, 5 days/week for 2 years. Inflammation of the nasal cavity was seen in males at all doses. At 78 mg/m^3 and above protein in urine decreased in males. At 389 mg/m^3 changes in haematology and blood biochemistry parameters and necrosis and repiratory metaplasia of the olfactory epithelium (IPCS, 1995).
- No effects on nerve conduction velocity, open field activity or co-ordination were seen in rats exposed to methylbromide at 214 mg/m^3, 6 hours/day, 5 days/week, 36 weeks over 12 months (IPCS, 1995).
- Rabbits were exposed by inhalation to 65-850 mg/m^3 methylbromide for 7.5-8 hours/day, 5 days/week during 6 months. Rabbits exposed to 130 and 250 mg/m^3 developed characteristic paralysis of the legs and died after several exposures; animals tolerated repeated exposures to 65 mg/m^3 (IARC). NOAEL is 65 mg/m^3.
- Rats and mice were exposed by inhalation to methylbromide for 12 or 13 weeks. Observed effects included mortality, growth retardation, crossing and curling of hindlimbs, increased testes weight and reduced sperm motility. For mice a LOEL and NOEL of 160 and 80 mg/m^3 were established, respectively. For rats the LOEL and NOEL were 240 and 120 mg/m^3, respectively (RIVM/CSR).
- Rats exposed by inhalation to methylbromide for 13 weeks showed increased WBC and decreases in plasma albumin, alkaline phosphatase, liver weight and small hepatocytes with eosinophilic cytoplasm at 170 mg/m^3; no effects were seen at 26 mg/m^3 (RIVM/CSR).
- Monkeys were exposed by inhalation to 130-420 mg/m^3 methylbromide for 7.5-8 hours/day, 5 days/week during 6 months. Exposure to 250 mg/m^3 led to hyperactivity, loss of equilibrium, inability to stand, convulsions and paralysis. No of such effects were observed at 130 mg/m^3 (IARC).
- Rabbits were exposed by inhalation to methylbromide at 105 and 252 mg/m^3; the animals received a total exposure duration of 900 hr over a period of 8 months. No signs of toxicity at 105 mg/m^3.
- At 252 mg/m^3 severe neuromuscular losses, impaired blink reflexes and decreased body weights were observed (HSDB).

Conclusion: Major clinical signs of toxicity after inhalation of methylbromide included neurological manifestations (twitching and paralysis), irritation of mucosal membranes, histopathological changes in brain, heart, liver and testis. The overall NOAEL for exposure by inhalation is 26 mg/m^3. According to FAO/WHO (1988), the level causing no effect in experimental animals was 12 mg bromide/kg bw/day (IPCS, 1995).

4. Reproductive toxicity, embryotoxicity and teratogenicity

Oral

- Oral exposure of female rats to methylbromide at 0, 3, 10, or 30 mg/kg bw/day during day 6-15 of gestation and female rabbits to 0, 1, 3, or 10 mg/kg bw/day during day 6-18 of gestation, resulted in maternal toxicity in the high-dose females of both species (decreased body weight and food consumption and erosive lesions in the stomach and surrounding organs) Foetuses remained unaffected (DOSE).
- Pregnant rats were administered methylbromide in peanut oil at 0, 0.5, 5, 25, or 50 mg/kg bw during day 5-20 of gestation. Signs of maternal toxicity were observed at 25 and 50 mg/kg bw (NOAEL is 5 mg/kg bw). Total resorption of embryos was seen at 50 mg/kg bw, probably due to the poor health of the pregnant animals. No effects on skeleton or internal organs at 25 mg/kg bw.

Inhalation

- In a sperm abnormality assay male mice were exposed by inhalation to methylbromide at 0, 78, or 272 mg/m^3, 7 hours/day, for 5 days. No sperm abnormalities were found (IPCS, 1995).
- Male rats exposed to methylbromide at 778 or 1167 mg/m^3, 4 hours/day, 5 days/week, for 6 weeks showed atrophy of seminal epithelium, incomplete spermatogenesis, and giant cells in seminal tubules at 778 and 1167 mg/m^3 (IPCS, 1995)

- Rats were exposed by inhalation to 0, 78 or 272 mg/m^3 methylbromide during pre- and/or gestational periods for 7 h/day, 5 days/week, for 21 and 19 days, respectively. Maternal body weights were reduced during gestation in the groups receiving pre- and gestational exposure to 272 mg/m^3. No toxic effects or anomalies were observed in fetuses (IARC).
- Rabbits were exposed by inhalation to methylbromide in concentrations of 0, 78 or 272 mg/m^3 for 7 h/day during gestation. Because of high maternal mortality in the high dose group exposure was stopped after 15 days. Fetuses of this dose group could not be examined. No maternal or fetal toxicity was observed at 78 mg/m^3 (IARC).
- Male rats (11-13 wk) were exposed by inhalation to methylbromide at 0 or 776 mg/m^3 for 6 h/day during 5 days; animals were sacrificed on day 1, 3, 5, and additional groups on day 6, 10, 17, 24, 38, 52, and 73. Plasma testosterone concentration and nonprotein sulfhydryl content of the liver and testis were reduced during exposure but returned to normal levels by day 8. Reproductive indices were not affected at any time point of examination (HSDB).
- Male rats and mice were exposed to methylbromide at 622 mg/m^3, 6 hours/day, 5 days/week for up to 6 weeks . Testicular degeneration with separation and sloughing of spermatocytes , late stage spermatids and intratubular giant cells and testicular atrophy with variable loss of all components of spermatogenic epithelium was seen in rats and less severe in mice (IPCS, 1995)
- Male mice exposed by inhalation to methylbromide at 39, 156, or 467 mg/m^3 for 13 weeks showed a decrease in body weight and an increase of epididymis and testis weight. A decrease in sperm density and an increase in the percentage abnormal sperm was also noted (IPCS, 1995)
- Male rats exposed by inhalation to methylbromide at 117, 233, or 467 mg/m^3 for 13 weeks showed a decrease in body weight and cauda epididymis weight, and an increase in testis weight. A decrease in sperm motility was also observed. (IPCS, 1995)
- In a multi-generation experiment rats were exposed by inhalation to methylbromide at 0, 12, 117, or 350 mg/m^3 6 hours/day, 5 days/week, for around 8 months. Body weight of males was depressed at pre-mating observation periods and at final sacrifice at 350 mg/m^3. No effects on body weight in the F1 generation. In the F2a litter a slight body weight depression was seen in gestating and lactating dams at 350 mg/m^3 and the female fertility index was marginally reduced at 117 and 350 mg/m^3. In the F1a generation survival of pups in late lactation was reduced at 350 mg/m^3. Body weight of pups were reduced at 117 and 350 mg/m^3 in the F1a, F2a and F2b generations. A decreased brain weight was seen in F0 males and in F1 males and females at 350 mg/m^3. Final body weights were reduced in F2b males at 350 mg/m^3 and F2b females at 117 and 350 mg/m^3. Analysis of F2b progeny organs revealed decreases in female brain , heart and kidney at 350 mg/m^3 and liver at 117 and 350 mg/m^3 (IPCS, 1995). The NOAEL is 12 mg/m^3.

Conclusion: No teratogenic effects have been observed in rats or rabbits. Embryotoxicity occurred in rats and rabbits only at doses that were also maternally toxic. In a rat multi-generation study a reduction in fertility index was observed in the second generation (IPCS, 1995).

5. Mutagenicity

In-vitro

- Positive results were found in *Salmonella typhimurium* TA100 in concentrations of 0.02-0.2% in desiccators without metabolic activation (IARC).
- Positive results were obtained in *Salmonella typhimurium* strain T100 in a liquid assay (10-100 mg/l) and in a plate assay (closed containers with 500-50000 mg/m^3) with metabolic activation (IARC).
- Methylbromide tested in a closed container at 500-5000 mg/m^3 was mutagenic to *S. typhimurium* TA1535 and TA100 (not to TA1537, TA1538 or TA98) and *Eschericha coli* WP2 *hcr* in the absence of metabolic activation (IARC).
- Methylbromide (aqueous solution 0.5-6 mM) induced mutations to streptomycine independence in *E.coli* (IARC).
- In a fluctuation test, methylbromide (950-19000 mg/m^3) induced mutations to streptomycin resistance in *Klebsiella pneumoniae* (IARC).
- Treatment of barley kernels with 1.4 mM methylbromide for 24 h in closed vessels induced a few chlorophyll mutations (IARC).
- In primary cultures of rat hepatocytes, treated in air-tight bottles, methylbromide did not induce unscheduled DNA synthesis (IARC).

- Treatment of L5178Y mouse lymphoma cells with 0.030-30 mg/l methylbromide in air-tight bottles resulted in a dose-related increase in 6-thioguanine- and bromodeoxyuridine-resistant mutants (IARC).
- Exposure of human lymphocyte cultures to 4.3% methylbromide for 100 sec. Increased frequency of sister chromatid exchanges from 10.0 to 16.8 per cell (IARC).

In-vivo

- In a sex-linked recessive lethal test with *Drosophila melanogaster* (strain Berlin K) exposed to methylbromide at 70-750 mg/m^3 for increasing periods, mutation frequencies were significantly increased at the highest nontoxic concentrations (IARC).
- After exposure of *D. melanogaster* larvae to methylbromide at 0-20 mg/l, incidences of wing twin spots and wing single spots were increased (IARC)
- Mice exposed to ^{14}C-methylbromide by inhalation or i.p. injection showed alkylation of guanine-N-7 in DNA of liver and spleen (IARC).
- In bone-marrow cells of rats exposed by inhalation for 6 hours/day, 5 days/week for 2 weeks, the incidence of polychromatic erythrocytes with micronuclei increased by ten fold in males and three fold in females at 1311 mg/m^3 (IARC).
- Increases in SCEs and micronuclei were observed in bone marrow cells of mice exposed by inhalation to methylbromide at 778 mg/m^3 6 hours/day, 5 days/week during 14 days. The increases were more pronounced in females (IPCS, 1995)
- No increases in SCEs and micronuclei were observed in bone marrow cells of mice exposed by inhalation to methylbromide at 467 mg/m^3 during 13 weeks.
- In bone-marrow cells and in peripheral blood cells of mice exposed by inhalation for 6 hours/day, 5 days/week for 2 weeks, the incidence of polychromatic erythrocytes with micronuclei in bone-marrow cells increased by ten fold in males at 776 mg/m^3 and by six fold in females at 600 mg/m^3 and those in peripheral blood cells increased by 32 fold in males at 776 mg/m^3 and by three fold in females at 600 mg/m^3 (IARC).

Conclusion:Methylbromide has been found to be mutagenic in several in-vitro and in-vivo test systems. It induces sex-linked recessive lethal mutations in Drosophila melanogaster and mutation in cultured mammalian cells. It does not induce unscheduled DNA synthesis or cell transformation in cultured mammalian cells. DNA methylation of the lever and spleen was observed in mice administered methylbromide by various routes. Micronuclei were induced in bone-marrow and peripheral blood cells of rats and mice (IPCS, 1995).

6. Carcinogenicity

- In a 13-weeks gavage study in rats and doses of 0, 0.4, 2, 10 or 50 mg/kg bw methylbromide in arachis oil, a dose-related increase in hyperplasia and hyperkeratosis of the forstomach epithelium was observed in both sexes. At 50 mg/kg bw papillomas of the forestomach were seen in 2/10 males and squamous-cell carcinomas (accompanied by marked hyperplasia, hyperkeratosis, inflammation andulceration) were noted in 7/10 males and 6/10 females. At 10 mg/kg bw hyperplasia was observed and at the lowest dose group (2 mg/kg bw) slight hyperplasia occurred. At 0.4 mg/kg bw no effects occurred (RICM/CSR, 1987).
- In rats exposed by inhalation to methylbromide at 0, 12, 120 or 360 mg/m^3 for 6 h/day, 5 days/week during 28 months, signs of toxicity at 360 mg/m^3 included mortality, decreased growth, increased incidence of haemothorax, and increased incidence of myocardial degeneration and thrombi in the heart. In addition the incidence of hyperkeratosis in the oesophagus and stomach was elevated a 120 mg/m^3. The incidence of degenerative and hyperplastic changes in the nasal cavity was dose-related increased at all dose levels. No increase in tumour incidence was noted. In this study 12 mg/m^3 was a marginal effect level (RIVM/CSR, 1987).
- Mice were exposed by inhalation to methylbromide at 0, 39, 128 or 390 mg/m^3 for 6 h/day, 5 days/week during 103 weeks. Mortality occurred at 390 mg/m^3 and surviving mice of this group showed signs of neurotoxicity (tremors, abnormal posture, tachypnea, and hind leg paralysis), neurobehaviour changes (less active and higher sensitivity in the startle response), nonneoplastic lesions in brain, heart, sternum and nose, degenerative changes in cerebellum and cerebrum, myocardial degeneration and cardiomyopathy, increased incidence of olfactory epithelial necrosis and metaplasia within the nasal cavity. No signs of carcinogenicity were found (NTP).

Conclusion:Long-term inhalation studies on rats and mice did not reveal any evidence of carcinogenicity. Lesions originally interpreted as carcinomas of the forestomach in rats following gavage administration, were shown in a subsequent study to regress after termination of treatment, and were considered not relevant for human risk assessment (IPCS, 1995).

7. Effects on human heath

- Inhalation of 1 mg/m^3 for 2 hours by a child: no toxic effects (DOSE)
- Lowest published lethal concentration after 2 hours inhalation of methylbromide is 232800 mg/m^3 for an adult human and 1000 mg/m^3 for a child (NTP). Lowest reported lethal concentration for several hours exposure is 6020 mg/m^3 (RIVM/CSR).
- Unintensional exposure of the skin of 6 persons to 40000 mg/m^3 for 40 min. led to redness and blistering (DOSE).
- Chronic methylbromide toxicity usually is limited to central nervous system, although mild elevation of serum hepatic aminotransferase levels has been reported in industrial workers (HSDB).
- A fumigator chronically exposed to methylbromide developed paresthesia of the extremities, dysesthesias and visual impairment secondary to optic atrophy (HSDB).
- Mild neurologic dysfunction (decreased finger sensitivity, reduced cognitive performance and behavioural abnormalities) was detected in soil fumigators (HSDB).
- Inhalation of mehtylbromide showed after 3-12 hours the following signs of toxicity:1) dizziness and headache, 2)anorexia, nausea, vomiting and abdominal pain, 3) lassitude, profound weakness, slurring of speech and staggering gait, 4) transient blurring of vision, diplopia, strabismus and temporary blindness, 5) mental confusion, mania, tremors and epileptic convulsions; 6) rapid respiration associated with signs of severe pulmonary edema, cyanosis, pallor and collaps; 7) coma, areflexia and death from respiratory or circulatory collapse (HSDB).
- A case of brief skin exposure to quickly decontaminated methylbromide spray, did not produce burn, but resulted in severe, delayed neuromuscular disturbances (twitching, fits, convulsions) and permanent brain damage (cerebellum and pyranedal tract) (HSDB).

Conclusion: the major health concern is from acute exposure. Delayed onset of symptoms may accur. Fatal poisoning has resulted from exposures to relatively high concentrations (from 33000 mg/m^3 or 8600 ppm onwards)of methylbromide vapours. Non-fatal poisoning has resulted from exposure to concentrations as low as 390-1950 mg/m^3. Organs affected by exposure include the nervous system, lung, nasal mucosa, kidney, eye, and skin. There are no epidemiological data on reproductive toxicity and carcinogenicity in humans. There are no data on any human health effects of methylbromide residues in food or drinking-water (IPCS, 1995).

Guideline values:
In 1966, the FAO/WHO established and acceptable daily intake (ADI) of 1 mg/kg bw as bromide ion. In 1988 this ADI was confirmed (FAO/WHO, 1988; cited in IPCS, 1995).

Estimated concentration of no concern of polluting agents in drinking water and air for humans:
the ECNC is derived from the NOAEL of 12 mg/m^3 in the 128-d reproduction study and corrected for continuous exposure to 2.1 mg/m^3. By applying an UF of 100 an ECNC of 20 µg/m^3 is established for air. The ECNC for drinking-water (assuming a human body weight of 70 kg, a drinking water volume of 2 liters per day, and an allocation of 10 percent) is 3.5 mg/l. (Rademaker & Linders, 1996).

On the basis of the subchronic NOAEL of 0.4 mg/kg bw in rats, the ATSDR established an intermediate duration MRL of 0.003 by adjusting the NOAEL for intermittent exposure and using an uncertainty factor of 100 (ATSDR).

In 1987, RIVM derived a guideline of 0.7 mg/m^3 for short-term exposures on the basis of a marginal effect level of 70 mg/m^3 from a subchronic study in rats and using an uncertainty factor of 100.
A guideline of 0.1 mg/m^3 was derived for long-term exposures, based on a marginal effect level of 12 mg/m^3 from a chronic rat study using an uncertainty factor of 100 (RIVM/CSR, 1987).

1.8.3 Description of ecotoxicological properties of the chemical

AQUATIC ORGANISMS

Algae:	48-h EC50 for 2 species 3.2-5.0 mg/l (RIVM/CSR)
Crustacea:	48-h EC50 *Daphnia magna* 1.7 mg/l (RIVM/CSR)
	12-d NOEC (mort., reprod.) *Daphnia magna* 0.06 mg/l (RIVM/CSR)
Fish:	96-h LC50 *Menidia beryllina* 4.68 mg/l (BUA)-11 mg/l (DOSE)
	96-h LC50 *Lepomis macrochirus* 4.18 mg/l (BUA)- 12 mg/l (DOSE)
	48-h LC50 *Poecilia reticulata* 1.2 mg/l (BUA)
	96-h LC50 *P. reticulata* and *O.latipes* 0.8 mg/l (RIVM/CSR)
	96-h NOEC (mortality) *Poecilia reticulata* 0.56 mg/l (IPCS)
	96-h NOEC (mortality) *Oryzias latipes* 1.0 mg/l (IPCS)
	1-month NOEC (mortality) *P. reticulata* 0.06 mg/l (RIVM/CSR)
	1-month NOEC (mortality *O. latipes* 0.40 mg/l (RIVM/CSR)
	3- month NOEC (mortality) *P. reticulata* and *O.latipes* 0.32 mg/l (IPCS)

The potential impact of the main degradation product of methylbromide, inorganic bromide, was also evaluated:

Algae:	24-96 h EC50 (growth) *Scenedesmus pannonicus* 5800-10000 mg Br^-/l
	24-96 h NOEC (growth) *Scenedesmus pannonicus* 2500 mg Br^-/l
Crustacea:	48-h EC50 *Daphnia magna* 5800 mg Br^-/l
	48- h NOEC *Daphnia magna* 4300 mg Br^-/l
Fish	96-h LC50-values ranges from 16000 to 24000 mg Br^-/l
	96-h NOEC (mortality) 7800 mg Br^-/l
	96-h NOEC (abn. behaviour) ranges from 25 to 250 mg Br^-/l

The NOEC-values from medium-term toxicity tests using sodium bromide and 11 different freshwater species ranges from 10 mg/l for effect on reproduction of *Daphnia magna* and *Lymnea stagnalis* to 10000 mg/l for the effect on hatching growth in *Oryzias latipes* (IPCS)

TERRESTRIAL ORGANISMS

Birds:	hens fed on diets fumigated with methylbromide showed delayed sexual maturity, adversely affected egg flavour and taste of meat (IPCS)
Bees:	non-toxic to bees (DOSE)
Earthworms:	very toxic to earthworms (concentration not given) (IPCS)
Insecta:	24-h LC50 Coleoptera 4.51 mg/l (DOSE)
	LD50-values for 32 different insecta ranges from 9 to 32000 mg/m^3 (IPCS)
Gastropods:	doses of 128000-240000 mg/m^3 are lethal for slugs, snails and limpets (IPCS)
Macrophyta:	extremely phytotoxic (HSDB)
Soil microorganisms:	24-h LD50 *Phialophora cinerescens*
	Verticilium alboartum
	Fusarium oxysporium 6 mg/l (BUA)

- Methylbromide applied under plastic to soil organisms at concentrations of 300 000 mg/m^3 killed all insects; some nematodes and mites survived in small numbers (HSDB)
- Methylbromide did not cause any permanent changes in soil enzyme activity or affect the mycorrhizal root development of pine seedlings (IPCS)
- Methylbromide applied at 22000 mg/m^2 showed no long-term effects on aerobic soil bacteria and actinomycetes (IPCS)

ENVIRONMENTAL FATE

Methyl bromide released to soil is expected to be primarily lost by volatilization. Methyl bromide may also leach due to its weak adsorption to soil. Hydrolysis of methyl bromide to methanol and bromide ions and biodegradation may also occur in soil. Release of methyl bromide to water is expected to result primarily in volatilization. Hydrolysis to methanol and bromide ions will occur with a half-life of 20-26.7 days. Bioconcentration is not expected to be significant (HSDB)

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PART II: FINAL REGULATORY ACTION

2.	FINAL REGULATORY ACTION			
2.1	**The chemical is:**	θ **banned**	**OR**	**X severely restricted**
2.2	**Information specific to the final regulatory action**			
2.2.1	**Summary of the final regulatory action** In 1981, the use of methyl bromide as a soil disinfectant was prohibited. Based on Article16a of the Dutch Pesticide Law of 1962, an exemption could, however, be granted based on individual requests. In the following period of time, the policies of the Government aimed at a further decrease in the use of methyl bromide. In 1992 methyl bromide was completely banned for use as a soil disinfectant. In 1996, two space fumigation products on the basis of methyl bromide were extended until 1 December 2001.			
2.2.2	**Reference to the regulatory document** Decree of Ministry of Agriculture and Fisheries, Ministerial Order of 31 December1980/5 January 1981; CTB (1996). Verslag C-48, d.d. 5 juni 1996 te Wageningen (in Dutch).			
2.2.3	**Date of entry into force of the final regulatory action** 1992			

2.3	**Was the final regulatory action based on a risk or hazard evaluation?**	**X Yes**	**θ No**
	If yes, give information on such evaluation The final regulatory action to prohibit methyl bromide as a soil disinfectant was based on an evaluation of risks regarding storage/transport and use of methyl bromide, the emission of methyl bromide to air and the leaching potential of methyl bromide and bromide.		
	Reference to the relevant documentation RIVM (1987). Rapport van de commissie inzake het gebruik van methyl bromide voor grondontsmetting in landbouw. Doorn, A.M. et al. (authors) (in Dutch).		

2.4	Reasons for the final regulatory action	
2.4.1	**Is the reason for the final regulatory action relevant to the human health?**	X Yes No
	If yes, give summary of the known hazards and risks presented by the chemical to human health, including the health of consumers and workers	
	By the end of 1980 the occurrence of methyl bromide in a number of private drinking water pipes, in combination with new toxicological data (a number of positive mutagenicity tests) caused the start of regulatory actions. In addition, there was concern about safety aspects related to storage, transport and use of methyl bromide (possibility of emission to air) and the leaching potential (leaching to surface water or groundwater). In the Netherlands groundwater can be used for drinking water and therefore groundwater must remain free from pesticides (precaution principle). In later years, the effect on the ozone layer became also a subject of concern. Methyl bromide and bromide (active bromine species) are thought to be partly responsible for the destruction of the ozone layer. Methyl bromide is included in the Protocol of Montreal. At present, the use of methyl bromide is restricted to space fumigation in gasproof rooms and its use has been optimised so that risks for workers have been minimised. Strict regularisation caused a reduction in emissions to air and groundwater or surface water, so the potential risks to the general population are minimised. At the moment there is no Dutch policy to further reduce the use of methyl bromide. Future international policy (for example to further reduce the ozone depletion) will be of influence.	
	Reference to the relevant documentation	
	RIVM (1987). Rapport van de commissie inzake het gebruik van methyl bromide voor grondontsmetting in landbouw. Doorn, A.M. et al. (authors) (in Dutch).	
	Expected effect of the final regulatory action	
	Prevention of contamination of drinking water derived from groundwater. Minimising risks for workers and general population.	

2.4.2	**Is the reason for the final regulatory action relevant to the environment?**	X Yes	θ No
	If yes, give summary of the known hazards and risks to the environment		
	In 1981, the use of methyl bromide as a soil disinfectant was prohibited. This application was used in greenhouses. The emission fraction from greenhouses to the surrounding surface waters was estimated at 0.1% (fraction 0.001) of the applied dose in kg/m^3. Based on this emission value the toxicity to aquatic organisms could not be ignored. In the Netherlands the use of methyl bromide as a soil disinfectant is prohibited, because of the high toxicity to aquatic organisms and the effect on the ozone layer.		
	Reference to the relevant documentation		
	RIVM/CSR (1992). Methyl bromide (definitieve versie). Adviesrapport 91/670104/011. National Institute of Public Health and the Environment. 14-07-1992 (in Dutch). IPCS (1995) Environmental Health Criteria 166 Methyl Bromide. World Health Organization, Geneva, 1995.		
	Expected effect of the final regulatory action		
	Reduction of the risk for the aquatic environment.		

2.5	Category or categories where the final regulatory action has been taken	
2.5.1	**Final regulatory action has been taken for the chemical category**	θ **Industrial**
	Use or uses prohibited by the final regulatory action	
	Not relevant.	
	Use or uses that remain allowed	

2.5.2	**Final regulatory action has been taken for the chemical category**	X **Pesticide**
	Formulation(s) and use or uses prohibited by the final regulatory action	
	All applications except those mentioned below.	
	Formulation(s) and use or uses that remain allowed	
	The following two applications on the basis of methyl bromide were extended until 1.12.2001: - 'Methylbromide 100 voor ruimte ontsmetting' - 'Holland fumigation methylbromide' These applications concern space fumigation by means of gas evaporation and are only permitted in gasproof spaces under very strict regulations.	

2.5.3 Estimated quantity of the chemical produced, imported, exported and used, where available.		
	Quantity per year (MT)	**Year**
Produced		
Imported		
Exported		
Used		

2.6	Indication, to the extent possible, of the likely relevance of the final regulatory action to other states and regions

2.7	Other relevant information that may cover:
2.7.1	Assessment of socio-economic effects of the final regulatory action

2.7.2	Information on alternatives and their relative risks
2.7.3	Relevant additional information

PART III : GOVERNMENT AUTHORITIES

Ministry/Department and authority responsible for issuing/enforcing the final regulatory action	
Institution	Ministry of Housing, Spatial Planning and the Environment Ministry of Agriculture
Address	P.O. Box 30945 2500 GX The Hague The Netherlands
Telephone	+31 70 339 3939
Telefax	+31 70 339 1297
E-mail address	
Designated National Authority	
Institution	Ministry of Housing, Spatial Planning and the Environment
Address	P.O. Box 30945 2500 GX The Hague The Netherlands
Name of person in charge	drs. K.A. Gijsbertsen
Position of person in charge	Designated national authority
Telephone	+31 70 339 4744
Telefax	+31 70 339 1297
E-mail address	karel.gijsbertsen@minvrom.nl

Date, signature of DNA and official seal: The Hague, 18 December 2001

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UNEP/FAO/RC/CRC.1/18/Add.2

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Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade
Chemical Review Committee
First meeting
Geneva, 11–18 February 2005
Item 7 (e) of the provisional agenda*

Inclusion of chemicals in Annex III of the Rotterdam Convention: review of notifications of final regulatory actions to ban or severely restrict a chemical: methyl bromide

Methyl bromide: supporting documentation from Netherlands

Note by the secretariat

The secretariat has the honour to provide, in the annex to the present note, the supporting document supplied by the Netherlands in support of its final regulatory action on methyl bromide.

* UNEP/FAO/RC/CRC.1/1.

K0580091 190105

Annex

I – Focussed summary

II – slightly amended notification submitted 20 January 2005, containing electronic links to relevant documentation.

I – Focussed summary:

FOCUSSED SUMMARY – METHYL BROMIDE

I. INTRODUCTION

(a) The registration of methyl bromide was severely restricted on the market in the Netherlands. This decision was based on an evaluation of the environmental properties of methyl bromide, both with respect to its ecotoxicity and its negative influence on the stratospheric ozone layer. The first decision to regulate the use of methyl bromide in the Netherlands was taken in 1981 and since then re-established in several decisions. In 1992 a complete ban of the substance used as a soil fumigant was issued. Only space fumigations with methyl bromide in glass houses are still registered in the Netherlands.

(b) The decisions aim at a complete reduction of the risk of methyl bromide emission to air due to the full field application of the substance as a soil fumigant. It was estimated that the substance was able to leach to groundwater and surface water. Both water types are used as sources for the abstraction of water intended for drinking water. At the moment there is no policy to further reduce the use of methyl bromide as the precautions are considered sufficient to guarantee safe use. Strict regulation caused a reduction of emissions to air and groundwater and surface water. Thus, the potential risks to the general population are minimised.

(c) Registered plant protection products will receive a registration period of maximally 10 (ten) years in the Netherlands. Depending on whether or not there are problems with the application during this period a re-evaluation is possible on any moment. The re-evaluation takes place after the preparation of a summary and decision making document by the registration authorities. The re-evaluation is based on all relevant and available information sent to the authorities by the registrant. The registrant is informed on the decision taken and may appeal against the decision.

(d) The registration decision has been adapted in the Netherlands 11 times since the first decision in 1992. The decision focussed on the use of methyl bromide as a soil fumigant. Lastly, an amendment took place on 24 December 2004.

II. RISK EVALUATION

(a) The risk evaluation of the Netherlands focussed on the behaviour and effects of methyl bromide in air, groundwater and surface water. It took into account all relevant data on the substance concerning the physico-chemical data, among others the ozone depletion potential, data on the leaching potential, i.e. sorption and soil degradation, and data on the ecotoxicological effects of methyl bromide, e.g. the toxicity to fish.

(b) 1. ATSDR (1992). Toxicological profile for Bromomethane. U.S. Department of Health & Human Services, Public Health Service. Agency for Toxic Substances and Disease Registry, September 1992.

2. IARC (1987). World Health Organization, IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1-42. Supplement 7. Lyon, France, 1987.
3. IPCS (1995) Environmental Health Criteria 166 Methyl Bromide. World Health Organization, Geneva, 1995.
4. RIVM/CSR (1987). Evaluation of methyl bromide (confidential). 9 January 1987.
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6. WHO (World Health Organisation)/FAO. 1966 Evaluations of Some Pesticides in Food. Rome: FAO, p112.

(c) No specific toxicological or ecotoxicological studies were carried out in the Netherlands. The references mentioned under point (b) 4. and 5. refer to national summaries and evaluations of all at that moment available data.

(d) The ozone depletion factor of methyl bromide was c. 0.6 related to the substance CFCl3. The estimated concentration in groundwater amounted to c. 100 µg/L based on a soil degradation half-life time of c. 15 days and a sorption constant of c. 2.5 L/kg. The measured concentrations in surface water amounted c. 9 mg/l which resulted in the expectation of very high risk for fish.

III. RISK REDUCTION AND RELEVANCE TO OTHER STATES

(a) The use of methyl bromide in Dutch agriculture reduced dramatically because of the decision to ban the substance from the use as a soil fumigant. The normal dose rate of the substance for this application is 400 kg/ha. As the information is considered highly confidential by the industry an estimation of current use in the Netherlands is not possible.

(b) As a result of the regulations the use of methyl bromide in the Netherlands was severely reduced and consequently emissions to air and ground- and/or surfacewater were minimised. Therefore, no risks are to be expected any more to groundwater or aquatic organisms, notably fish in surface water in the Netherlands. Current use in surrounding countries is severely restricted as well.

(c) Current use in the Netherlands is restricted only to application as a space fumigant in gas proof rooms. Therefore, if the substance is applied using GLP there are considered to be no substantial risks to humans or the environment.

Interim Secretariat for the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade

UNEP

FORM FOR NOTIFICATION OF FINAL REGULATORY ACTION TO BAN OR SEVERELY RESTRICT A CHEMICAL

IMPORTANT: See instructions before filling in the form

COUNTRY: THE NETHERLANDS

PART I: PROPERTIES, IDENTIFICATION AND USES

1.	**IDENTITY OF CHEMICAL**	
1.1	**Common name**	Methyl bromide
1.2	**Chemical name according to an internationally recognized nomenclature (e.g. IUPAC), where such nomenclature exists**	methyl bromide, bromomethane (CAS), monobromomethane
1.3	**Trade names and names of preparations**	Methyl bromide 100 Dowfume; Halon 1001; UN 1062; M-B-R 98; A13-01916; Bercema; Tri-Brom-Methyl-Bromide-Rodent-Fumigant; Brom-O-Sol; Caswell-No-555; CURAFUME; Detia Gas Ex-M; Dowfume MC-2; Dowfume MC-33 Dowfume MC-2 Soil Fumigant; EDCO; EMBAFUME; EPA-Pesticide-Chemical-Code-053201; M-B-C Fumigant; Brom-O-Gas; Brom-O-Gas Methyl Bromide Soil Fumigant; HALTOX; ISCOBROME; KAYAFUME; MB; MBC-Soil-Fumigant; MBC-33 Soil Fumigant; MBX; Dowfume MC-2R; Dowfume MC-2 Fumigant; MEBR; Metabrom; Meth-O-Gas; METHOGAS; Superior Methyl Bromide-2; Methyl-fume; PESTMASTER; Pestmaster Soil Fumigant; Drexel-Plant-Bed-Gas; ROTOX; TERABOL; Terr-O-Gas; ZYTOX(HSDB) Celfume; Dawson 100; Metafume; Profume; R 40B1; RCRA wast number U029; Terr-O-Cide; Terr-O-Gas 67; Terr-O-Gas 100 (RTECS); Brozone; Isobrome (Norman & Dollinger, 1977)
1.4	**Code numbers**	
1.4.1	**CAS number**	74-83-9
1.4.2	**Harmonized System customs code**	2903 3033
1.4.3	**Other numbers (specify the numbering system)**	602-002-00-2 (EEC), 200-813-2 (EINECS)

1.5	Indication regarding previous notification on this chemical, if any
1.5.1	4 This is a first time notification of final regulatory action on this chemical.
1.5.2	4 This is a modification of a previous notification of final regulatory action on this chemical. The sections modified are: _____ X This notification replaces all previously submitted notifications on this chemical.
	Date of issue of the previous notification: 2002 (see PIC Circular XV, June 2002)

1.6 Information on hazard classification where the chemical is subject to classification requirements

International classification systems	Hazard class
WHO	T (toxic); N (dangerous for the environment; R23/25, R36/37/38, R40, R48/20, R50/53, R59
EPA	Classification D: inadequate human and animal data
EU (Annex I)	
IARC	Not classifiable (group 3, *as to its carcinogenicity to humans*, based on limited evidence for the carcinogenicity to experimental animals; inadequate evidence for the carcinogenicity to humans)

Other classification systems	Hazard class

1.7	Use or uses of the chemical
1.7.1	X **Pesticide**
	Describe the uses of the chemical as a pesticide in your country:
	Methyl bromide was used as a soil disinfectant (fungicide/nematicide). Only application still allowed concern space fumigation by means of gas evaporation and are only permitted in gas proof spaces under very strict regulations.
1.7.2	4 **Industrial**
	Describe the industrial uses of the chemical in your country:
	Not relevant.

1.8	Properties

1.8.1 Description of physico-chemical properties of the chemical

Identity	**colourless gas**
Formula	CH3Br
Chemical name	methyl bromide, bromomethane
Chemical type	
CAS number	74-83-9
Molecular weight	94.94
Solubility	16 - 18.5 g/L (c. 20 °C) in water freely soluble in alcohol, chloroform, ether, carbondisulfide, and benzene
log Kow	1.19
Vapour pressure	1893 kPa at 20 °C
Melting point	
Freezing point	- 93 °C (IPCS, DOSE)
Boiling point	3.56 °C at 1013 hPa
Dissociation constant	
Henry's law constant	0.533 kPa m^3 mol^{-1} (calculated using atmospheric pressure)
Conversion factor	1 ppm = 3.95 mg m^{-3} at 20 °C

1.8.2 Description of toxicological properties of the chemical

1.Acute toxicity to laboratory animals

Oral:	LD50 rat 214 mg/kg bw (IARC)
Dermal	no data
Inhalation:	2-h LC50 mouse 1540 mg/m^3 (DOSE) 1-h LC50 mouse 4680 mg/m^3 (IARC) 30-min LC50 rat 11000 mg/m^3 (IARC) 4-h LC50 rat 3026 mg/m^3 (HSDB) 8-h LC50 rat 1160 mg/m^3 (IARC) 8-h NOEC rat 63 mg/m^3 (RIVM/CSR) 24-h LC50 rat 50 mg/m^3 (IARC)

- In rats a concentration of 51400 mg/m^3 is lethal in 6 minutes, whereas a concentration of 884 mg/m^3 produces death in 26 hours. At 432 mg/m^3 no rats died after 22 hours (RIVM/CSR).
- Signs of toxicity after a single 8-h exposure included decreases in body temperature, body weight and locomotor activity at 500 mg/m^3 and above; no effects were seen at 250 mg/m^3 (RIVM/CSR)
- Acute toxic effects of 1 hr inhalatory exposure of mice to methyl bromide at 870 to 5930 mg/m^3 included kidney lesions at 3500 mg/m^3 and above, decreased lung and liver weight at 2200 and 2700 mg/m^3 and decreased motor co-ordination at 5770 mg/m^3 (HSDB).

Irritation/Sensitization: There are no reports on skin effects in animals (IPCS, 1995).

2. Short-term toxicity

Oral

- Cats fed fumigated peanuts containing methyl bromide at 0.5 to 1.25 mg /day for 4 months showed no changes in motor responses (HSDB).

- Dogs fed methyl bromide fumigated pelleted food in doses equal to 35, 75 and 150 mg/kg/day for 6 to 8 weeks were observed for 1 year and showed no or minimal evidence of toxicity at 35 and 75 mg/kg/day. At 150 mg/kg/day the animals showed lethargy, occasional salivation and diarrhea, but no changes in blood chemistry, haematology, urinalysis of histology (HSDB).
- Cattle fed pelleted food containing methyl bromide at 170, 511, 1062, 2633 and 4650 mg/kg for 49 days showed uncoordinated movement and gait and recumbency (HSDB).

Inhalation

- In a subacute study with male rats exposed by inhalation to methyl bromide at 582, 776, 1164, or 1552 mg/m^3 paralysis of extremities and ataxia were noted at 1164 and 1552 mg/m^3. Necrosis of the heart occurred at all concentrations (HSDB).
- Biochemical examination of male rats exposed continuously by inhalation to methyl bromide at 4, 19.4 or 39 mg/m^3 during 3 weeks revealed changes in blood glucose, creatinine phosphokinase, Hb, glutathione, SGPT, SGOT, LDH, serum total protein at 19.4 and 39 mg/m^3 (HSDB). Neurological effects were seen only at 39 mg/m^3.
- Exposure of 10 weeks old male rat by inhalation to methyl bromide at 776 or 1164 mg/m^3 , 4 h/day, 5 day/week for 3 weeks resulted in relatively prolonged dysfunction of the peripheral nerves and disturbance in spontaneous circadian rhythm activity at 1164 mg/m^3. No macroscopic or microscopic abnormalities were found in CNS or in peripheral nerves (HSDB).
- Rats and rabbits exposed by inhalation to methyl bromide at 252 mg/m^3 for 5 hours/day, 5 days/week during 4 weeks showed significantly reduced eye blink responses and nerve conduction velocity in rabbits, but had no effects on rats (HSDB).
- In a standard subacute inhalation study with mice trembling, jumpiness and paralysis were observed at all tested concentrations. The effects were slight at 48 and 100 mg/m^3 but obvious at concentrations >=200 mg/m^3. These effects were not reflected in histopathological abnormalities (RIVM/CSR).
- In a subacute inhalation study in rats and methyl bromide at 0, 70, 200 or 600 mg/m^3 administered for 6 h/day, 5 or 7 days/week during 4 weeks staggered gait was observed in all animals at 200 mg/m^3 and above and in 3/12 animals at 70 mg/m^3. In addition at 600 mg/m^3 mortality and morphological blood abnormalities were noted, serum enzyme levels were elevated and histopathological changes occurred in heart and lungs (RIVM/CSR).
- Male rats exposed by inhalation to methyl bromide at 0, 350, 680, 970 or 1260 mg/m^3 for 6 h/day during 5 days showed diarrhea, haemoglubinuria and in some cases, gait disturbances at 970 and 1260 mg/m^3. Vacuolar degeneration of the zona fasciculata of the adrenal glands, cerebellar granule cell degeneration, and nasal olfactory sensory cell degeneration were seen at 680 mg/m^{3}nd above. Cerebral cortical degeneration and minor alterations in testicular histology were seen only at 1260 mg/m^3. At 970 and 1260 mg/m^3 hepatocellular degeneration was seen. No changes in kidney and epididymis (HSDB).

3. Long-term toxicity

Oral

Because methyl bromide tends to volatilise and exists mainly as a gas at room temperature, only a few (sub)chronic oral studies have been performed (ATSDR, 1992).

- In two oral gavage subchronic studies in rats irritation of the stomach was the chief effect. The 13-week study of Danse et al. (1984) reported a NOAEL of 0.4 mg/kg bw/day and a LOAEL of 2 mg/kg bw/day (ATSDR, 1992). Similar findings were reported by Boorman et al. (1986) and Hubbs and Harrington et al. (1986). In subsequent studies, these effects were shown to regress after termination of treatment (IPCS, 1995).
- Rats were fed diets fumigated with methyl bromide (80, 200, or 500 mg total Br/kg food) for two years. A slight decrease in body weight was seen in males from week 60 onwards. A NOAEL of 200 mg/kg food could be established (IPCS, 1995).

Inhalation

- Mouse were exposed by inhalation to 0, 39, 128, and 389 mg/m^3 methyl bromide 6 hours/day, 5

days/week during 2 years. Increased incidence of non-neoplastic lesions in brain, bone, heart and nose was seen at all doses. At 389 mg/m^3: high mortality, decrease in body weight and thymus weight, tremors, abnormal posture, and limb paralysis (NTP, 1992; cited in IPCS, 1995)

- Mouse were exposed to methyl bromide at 0, 16, 62, or 250 mg/m^3 6 hours/day, 5 days/week for 2 years. Depression of body weight gain, changes in blood biochemistry (increase in CPK, inorganic P, and chloride and decrease in albumin) and atrophy of the granular layer of the cerebellum at 250 mg/m^3. The NOAEL was found to be 62 mg/m^3 (IPCS, 1995)

In a chronic toxicity/carcinogenicity study, rats were exposed by inhalation to methyl bromide at 0, 12, 116 or 349 mg/m^3, 6 hours/day, 5 days/week for 29 months. Increased incidences of degenerative and hyperplastic changes of the nasal olfactory epithelium were observed in all groups. Exposure to 349 mg/m^3 resulted in lesions in the heart and hyperkeratosis in the oesophagus and fore stomach. See also 'carcinogenicity' (IPCS, 1995).

- Rats and guinea-pigs were exposed to 130-850 mg/m^3 methyl bromide for 7.5-8 hours/day, 5 days/week during 6 months. All animals died after a few exposures to 850 mg/m^3; clinical signs of toxicity in rats at 420 mg/m^3 included poor general appearance, weight loss, pulmonary congestion and renal and hepatic lesions. No effects were observed at 130 and 250 mg/m^3 in rats and guinea-pigs (IARC). The NOAEL is 250 mg/m^3.
- Rats were exposed to methyl bromide at 16, 78, or 389 mg/m^3, 6 hours/day, 5 days/week for 2 years. Inflammation of the nasal cavity was seen in males at all doses. At 78 mg/m^3 and above protein in urine decreased in males. At 389 mg/m^3 changes in haematology and blood biochemistry parameters and necrosis and repiratory metaplasia of the olfactory epithelium (IPCS, 1995).
- No effects on nerve conduction velocity, open field activity or co-ordination were seen in rats exposed to methyl bromide at 214 mg/m^3, 6 hours/day, 5 days/week, 36 weeks over 12 months (IPCS, 1995).
- Rabbits were exposed by inhalation to 65-850 mg/m^3 methyl bromide for 7.5-8 hours/day, 5 days/week during 6 months. Rabbits exposed to 130 and 250 mg/m^3 developed characteristic paralysis of the legs and died after several exposures; animals tolerated repeated exposures to 65 mg/m^3 (IARC). NOAEL is 65 mg/m^3.
- Rats and mice were exposed by inhalation to methyl bromide for 12 or 13 weeks. Observed effects included mortality, growth retardation, crossing and curling of hindlimbs, increased testes weight and reduced sperm motility. For mice a LOEL and NOEL of 160 and 80 mg/m^3 were established, respectively. For rats the LOEL and NOEL were 240 and 120 mg/m^3, respectively (RIVM/CSR).
- Rats exposed by inhalation to methyl bromide for 13 weeks showed increased WBC and decreases in plasma albumin, alkaline phosphatase, liver weight and small hepatocytes with eosinophilic cytoplasm at 170 mg/m^3; no effects were seen at 26 mg/m^3 (RIVM/CSR).
- Monkeys were exposed by inhalation to 130-420 mg/m^3 methyl bromide for 7.5-8 hours/day, 5 days/week during 6 months. Exposure to 250 mg/m^3 led to hyperactivity, loss of equilibrium, inability to stand, convulsions and paralysis. No of such effects were observed at 130 mg/m^3 (IARC).
- Rabbits were exposed by inhalation to methyl bromide at 105 and 252 mg/m^3; the animals received a total exposure duration of 900 hr over a period of 8 months. No signs of toxicity at 105 mg/m^3.
- At 252 mg/m^3 severe neuromuscular losses, impaired blink reflexes and decreased body weights were observed (HSDB).

Conclusion: Major clinical signs of toxicity after inhalation of methyl bromide included neurological manifestations (twitching and paralysis), irritation of mucosal membranes, histopathological changes in brain, heart, liver and testis. The overall NOAEL for exposure by inhalation is 26 mg/m^3. According to FAO/WHO (1988), the level causing no effect in experimental animals was 12 mg bromide/kg bw/day (IPCS, 1995).

4. Reproductive toxicity, embryotoxicity and teratogenicity

Oral

- Oral exposure of female rats to methyl bromide at 0, 3, 10, or 30 mg/kg bw/day during day 6-15 of

gestation and female rabbits to 0, 1, 3, or 10 mg/kg bw/day during day 6-18 of gestation, resulted in maternal toxicity in the high-dose females of both species (decreased body weight and food consumption and erosive lesions in the stomach and surrounding organs) Foetuses remained unaffected (DOSE).

- Pregnant rats were administered methyl bromide in peanut oil at 0, 0.5, 5, 25, or 50 mg/kg bw during day 5-20 of gestation. Signs of maternal toxicity were observed at 25 and 50 mg/kg bw (NOAEL is 5 mg/kg bw). Total resorption of embryos was seen at 50 mg/kg bw, probably due to the poor health of the pregnant animals. No effects on skeleton or internal organs at 25 mg/kg bw.

Inhalation

- In a sperm abnormality assay male mice were exposed by inhalation to methyl bromide at 0, 78, or 272 mg/m^3, 7 hours/day, for 5 days. No sperm abnormalities were found (IPCS, 1995).
- Male rats exposed to methyl bromide at 778 or 1167 mg/m^3, 4 hours/day, 5 days/week, for 6 weeks showed atrophy of seminal epithelium, incomplete spermatogenesis, and giant cells in seminal tubules at 778 and 1167 mg/m^3 (IPCS, 1995)
- Rats were exposed by inhalation to 0, 78 or 272 mg/m^3 methyl bromide during pre- and/or gestational periods for 7 h/day, 5 days/week, for 21 and 19 days, respectively. Maternal body weights were reduced during gestation in the groups receiving pre- and gestational exposure to 272 mg/m^3. No toxic effects or anomalies were observed in fetuses (IARC).
- Rabbits were exposed by inhalation to methyl bromide in concentrations of 0, 78 or 272 mg/m^3 for 7 h/day during gestation. Because of high maternal mortality in the high dose group exposure was stopped after 15 days. Fetuses of this dose group could not be examined. No maternal or fetal toxicity was observed at 78 mg/m^3 (IARC).
- Male rats (11-13 wk) were exposed by inhalation to methyl bromide at 0 or 776 mg/m^3 for 6 h/day during 5 days; animals were sacrificed on day 1, 3, 5, and additional groups on day 6, 10, 17, 24, 38, 52, and 73. Plasma testosterone concentration and non-protein sulfhydryl content of the liver and testis were reduced during exposure but returned to normal levels by day 8. Reproductive indices were not affected at any time point of examination (HSDB).
- Male rats and mice were exposed to methyl bromide at 622 mg/m^3, 6 hours/day, 5 days/week for up to 6 weeks . Testicular degeneration with separation and sloughing of spermatocytes , late stage spermatids and intratubular giant cells and testicular atrophy with variable loss of all components of spermatogenic epithelium was seen in rats and less severe in mice (IPCS, 1995)
- Male mice exposed by inhalation to methyl bromide at 39, 156, or 467 mg/m^3 for 13 weeks showed a decrease in body weight and an increase of epididymis and testis weight. A decrease in sperm density and an increase in the percentage abnormal sperm was also noted (IPCS, 1995)
- Male rats exposed by inhalation to methyl bromide at 117, 233, or 467 mg/m^3 for 13 weeks showed a decrease in body weight and cauda epididymis weight, and an increase in testis weight. A decrease in sperm motility was also observed. (IPCS, 1995)
- In a multi-generation experiment rats were exposed by inhalation to methyl bromide at 0, 12, 117, or 350 mg/m^3 6 hours/day, 5 days/week, for around 8 months. Body weight of males was depressed at pre-mating observation periods and at final sacrifice at 350 mg/m^3. No effects on body weight in the F1 generation. In the F2a litter a slight body weight depression was seen in gestating and lactating dams at 350 mg/m^3 and the female fertility index was marginally reduced at 117 and 350 mg/m^3. In the F1a generation survival of pups in late lactation was reduced at 350 mg/m^3. Body weight of pups were reduced at 117 and 350 mg/m^3 in the F1a, F2a and F2b generations. A decreased brain weight was seen in F0 males and in F1 males and females at 350 mg/m^3. Final body weights were reduced in F2b males at 350 mg/m^3 and F2b females at 117 and 350 mg/m^3. Analysis of F2b progeny organs revealed decreases in female brain , heart and kidney at 350 mg/m^3 and liver at 117 and 350 mg/m^3 (IPCS, 1995). The NOAEL is 12 mg/m^3.

Conclusion: No teratogenic effects have been observed in rats or rabbits. Embryotoxicity occurred in rats and rabbits only at doses that were also maternally toxic. In a rat multi-generation study a reduction in fertility index was observed in the second generation (IPCS, 1995).

5. Mutagenicity

In-vitro

- Positive results were found in *Salmonella typhimurium* TA100 in concentrations of 0.02-0.2% in desiccators without metabolic activation (IARC).
- Positive results were obtained in *Salmonella typhimurium* strain T100 in a liquid assay (10-100 mg/l) and in a plate assay (closed containers with 500-50000 mg/m^3) with metabolic activation (IARC).
- Methyl bromide tested in a closed container at 500-5000 mg/m^3 was mutagenic to *S. typhimurium* TA1535 and TA100 (not to TA1537, TA1538 or TA98) and *Eschericha coli* WP2 *hcr* in the absence of metabolic activation (IARC).
- Methyl bromide (aqueous solution 0.5-6 mM) induced mutations to streptomycine independence in *E.coli* (IARC).
- In a fluctuation test, methyl bromide (950-19000 mg/m^3) induced mutations to streptomycin resistance in *Klebsiella pneumoniae* (IARC).
- Treatment of barley kernels with 1.4 mM methyl bromide for 24 h in closed vessels induced a few chlorophyll mutations (IARC).
- In primary cultures of rat hepatocytes, treated in air-tight bottles, methyl bromide did not induce unscheduled DNA synthesis (IARC).
- Treatment of L5178Y mouse lymphoma cells with 0.030-30 mg/l methyl bromide in air-tight bottles resulted in a dose-related increase in 6-thioguanine- and bromodeoxyuridine-resistant mutants (IARC).
- Exposure of human lymphocyte cultures to 4.3% methyl bromide for 100 sec. Increased frequency of sister chromatid exchanges from 10.0 to 16.8 per cell (IARC).

In-vivo

- In a sex-linked recessive lethal test with *Drosophila melanogaster* (strain Berlin K) exposed to methyl bromide at 70-750 mg/m^3 for increasing periods, mutation frequencies were significantly increased at the highest non-toxic concentrations (IARC).
- After exposure of *D. melanogaster* larvae to methyl bromide at 0-20 mg/l, incidences of wing twin spots and wing single spots were increased (IARC)
- Mice exposed to ^{14}C-methylbromide by inhalation or i.p. injection showed alkylation of guanine-N-7 in DNA of liver and spleen (IARC).
- In bone-marrow cells of rats exposed by inhalation for 6 hours/day, 5 days/week for 2 weeks, the incidence of polychromatic erythrocytes with micronuclei increased by ten fold in males and three fold in females at 1311 mg/m^3 (IARC).
- Increases in SCEs and micronuclei were observed in bone marrow cells of mice exposed by inhalation to methyl bromide at 778 mg/m^3 6 hours/day, 5 days/week during 14 days. The increases were more pronounced in females (IPCS, 1995)
- No increases in SCEs and micronuclei were observed in bone marrow cells of mice exposed by inhalation to methyl bromide at 467 mg/m^3 during 13 weeks.
- In bone-marrow cells and in peripheral blood cells of mice exposed by inhalation for 6 hours/day, 5 days/week for 2 weeks, the incidence of polychromatic erythrocytes with micronuclei in bone-marrow cells increased by ten fold in males at 776 mg/m^3 and by six fold in females at 600 mg/m^3 and those in peripheral blood cells increased by 32 fold in males at 776 mg/m^3 and by three fold in females at 600 mg/m^3 (IARC).

Conclusion: Methyl bromide has been found to be mutagenic in several in-vitro and in-vivo test systems. It induces sex-linked recessive lethal mutations in Drosophila melanogaster and mutation in cultured mammalian cells. It does not induce unscheduled DNA synthesis or cell transformation in cultured mammalian cells. DNA methylation of the lever and spleen was observed in mice administered methyl bromide by various routes. Micronuclei were induced in bone-marrow and peripheral blood cells of rats and mice (IPCS, 1995).

6. Carcinogenicity

- In a 13-weeks gavage study in rats and doses of 0, 0.4, 2, 10 or 50 mg/kg bw methyl bromide in arachis oil, a dose-related increase in hyperplasia and hyperkeratosis of the fore stomach

epithelium was observed in both sexes. At 50 mg/kg bw papillomas of the fore stomach were seen in 2/10 males and squamous-cell carcinomas (accompanied by marked hyperplasia, hyperkeratosis, inflammation andulceration) were noted in 7/10 males and 6/10 females. At 10 mg/kg bw hyperplasia was observed and at the lowest dose group (2 mg/kg bw) slight hyperplasia occurred. At 0.4 mg/kg bw no effects occurred (RICM/CSR, 1987).

- In rats exposed by inhalation to methyl bromide at 0, 12, 120 or 360 mg/m^3 for 6 h/day, 5 days/week during 28 months, signs of toxicity at 360 mg/m^3 included mortality, decreased growth, increased incidence of haemothorax, and increased incidence of myocardial degeneration and thrombi in the heart. In addition the incidence of hyperkeratosis in the oesophagus and stomach was elevated a 120 mg/m^3. The incidence of degenerative and hyperplastic changes in the nasal cavity was dose-related increased at all dose levels. No increase in tumour incidence was noted. In this study 12 mg/m^3 was a marginal effect level (RIVM/CSR, 1987).
- Mice were exposed by inhalation to methyl bromide at 0, 39, 128 or 390 mg/m^3 for 6 h/day, 5 days/week during 103 weeks. Mortality occurred at 390 mg/m^3 and surviving mice of this group showed signs of neurotoxicity (tremors, abnormal posture, tachypnea, and hind leg paralysis), neurobehaviour changes (less active and higher sensitivity in the startle response), non-neoplastic lesions in brain, heart, sternum and nose, degenerative changes in cerebellum and cerebrum, myocardial degeneration and cardiomyopathy, increased incidence of olfactory epithelial necrosis and metaplasia within the nasal cavity. No signs of carcinogenicity were found (NTP).

Conclusion: Long-term inhalation studies on rats and mice did not reveal any evidence of carcinogenicity. Lesions originally interpreted as carcinomas of the fore stomach in rats following gavage administration, were shown in a subsequent study to regress after termination of treatment, and were considered not relevant for human risk assessment (IPCS, 1995).

7. Effects on human heath

- Inhalation of 1 mg/m^3 for 2 hours by a child: no toxic effects (DOSE)
- Lowest published lethal concentration after 2 hours inhalation of methyl bromide is 232800 mg/m^3 for an adult human and 1000 mg/m^3 for a child (NTP). Lowest reported lethal concentration for several hours exposure is 6020 mg/m^3 (RIVM/CSR).
- Unintentional exposure of the skin of 6 persons to 40000 mg/m^3 for 40 min. led to redness and blistering (DOSE).
- Chronic methyl bromide toxicity usually is limited to central nervous system, although mild elevation of serum hepatic aminotransferase levels has been reported in industrial workers (HSDB).
- A fumigator chronically exposed to methyl bromide developed paresthesia of the extremities, dysesthesias and visual impairment secondary to optic atrophy (HSDB).
- Mild neurologic dysfunction (decreased finger sensitivity, reduced cognitive performance and behavioural abnormalities) was detected in soil fumigators (HSDB).
- Inhalation of methyl bromide showed after 3-12 hours the following signs of toxicity:1) dizziness and headache, 2)anorexia, nausea, vomiting and abdominal pain, 3) lassitude, profound weakness, slurring of speech and staggering gait, 4) transient blurring of vision, diplopia, strabismus and temporary blindness, 5) mental confusion, mania, tremors and epileptic convulsions; 6) rapid respiration associated with signs of severe pulmonary edema, cyanosis, pallor and collaps; 7) coma, areflexia and death from respiratory or circulatory collapse (HSDB).
- A case of brief skin exposure to quickly decontaminated methyl bromide spray, did not produce burn, but resulted in severe, delayed neuromuscular disturbances (twitching, fits, convulsions) and permanent brain damage (cerebellum and pyranedal tract) (HSDB).

Conclusion: the major health concern is from acute exposure. Delayed onset of symptoms may accur. Fatal poisoning has resulted from exposures to relatively high concentrations (from 33000 mg/m^3 or 8600 ppm onwards)of methyl bromide vapours. Non-fatal poisoning has resulted from exposure to concentrations as low as 390-1950 mg/m^3. Organs affected by exposure include the nervous system, lung, nasal mucosa, kidney, eye, and skin. There are no epidemiological data on reproductive toxicity and carcinogenicity in humans. There are no data on any human health effects of methyl bromide

residues in food or drinking-water (IPCS, 1995).

Guideline values:
In 1966, the FAO/WHO established and acceptable daily intake (ADI) of 1 mg/kg bw as bromide ion. In 1988 this ADI was confirmed (FAO/WHO, 1988; cited in IPCS, 1995).

Estimated concentration of no concern of polluting agents in drinking water and air for humans: the ECNC is derived from the NOAEL of 12 mg/m^3 in the 128-d reproduction study and corrected for continuous exposure to 2.1 mg/m^3. By applying an UF of 100 an ECNC of 20 µg/m^3 is established for air. The ECNC for drinking-water (assuming a human body weight of 70 kg, a drinking water volume of 2 liters per day, and an allocation of 10 percent) is 3.5 mg/l. (Rademaker & Linders, 1996).

On the basis of the subchronic NOAEL of 0.4 mg/kg bw in rats, the ATSDR established an intermediate duration MRL of 0.003 by adjusting the NOAEL for intermittent exposure and using an uncertainty factor of 100 (ATSDR).

In 1987, RIVM derived a guideline of 0.7 mg/m^3 for short-term exposures on the basis of a marginal effect level of 70 mg/m^3 from a subchronic study in rats and using an uncertainty factor of 100. A guideline of 0.1 mg/m^3 was derived for long-term exposures, based on a marginal effect level of 12 mg/m^3 from a chronic rat study using an uncertainty factor of 100 (RIVM/CSR, 1987).

1.8.3 Description of ecotoxicological properties of the chemical

AQUATIC ORGANISMS

Fish	*Poecilia reticulata* 96h-LC50 = 16 g Br^-/L	(1)*
	Poecilia reticulata 96h-NOEC = 0.025 g Br^-/L	(1)*
	Oryzias latipes 96h-LC50 = 24 g Br^-/L	(1)*
	Oryzias latipes 96h-NOEC = 0.025 g Br^-/L	(1)*
	Cyprinus carpio 4h-LC50 = 17 mg/L	(3)
	Lepomis macrochirus 96h-LC50 = 11 mg$^-$/L	(3)
	Poecilia reticulata 1m-NOEC = 0.06 mg/L	(3)
	Oryzias latipes 1m-NOEC = 0.4 mg/L	(3)
	Oryzias latipes 3m-NOEC = 0.23 mg/L	(3)
	* refers to sodium bromide	
Crustacea	*Daphnia magna* 48h-LC50 = 11 g Br^-/L	(1)*
	Daphnia magna 48h-NOEC = 4.3 g Br^-/L	(1)*
	Daphnia magna 48h-LC50 = 2.2 mg/L	(3)
	Daphnia magna 12d-NOEC = 0.06 mg/L	(3)
	* refers to sodium bromide	
Algae	*Scenedesmus pannonicus* 96h-NOEC = 2.5 g Br^-/L	(1)*
	Chlorella pyrenoidosa 48h-EC50 = 5 mg/L	(3)
	Scenedesmus quadricauda 48h-EC50 = 3.2 mg/L	(3)
	* refers to sodium bromide	
Molluscs	*Lymnaea stagnalis* 40d-NOEC = 10 mg/L	(1)
Aquatic insects	*Culex pipiens* 25d-NOEC = 100 mg/L	(1)

TERRESTRIAL ORGANISMS

Birds	Chicken 24h-NOEC = 32 g/m^3	(1)
Bees	Non-toxic to bees	

Earthworms	very toxic to earthworms (concentration not given) (IPCS)
Insecta:	24-h LC50 Coleoptera 4.51 mg/l (DOSE) LD50-values for 32 different insecta ranges from 9 to 32000 mg/m^3 (IPCS)
Gastropods:	doses of 128000-240000 mg/m^3 are lethal for slugs, snails and limpets (IPCS)
Macrophyta:	extremely phytotoxic (HSDB)
Soil microorganisms:	24-h LD50 *Phialophora cinerescens* *Verticilium alboartum* *Fusarium oxysporium* 6 mg/l (BUA)

- Methyl bromide applied under plastic to soil organisms at concentrations of 300 000 mg/m^3 killed all insects; some nematodes and mites survived in small numbers (HSDB)
- Methyl bromide did not cause any permanent changes in soil enzyme activity or affect the mycorrhizal root development of pine seedlings (IPCS)
- Methyl bromide applied at 22000 mg/m^2 showed no long-term effects on aerobic soil bacteria and actinomycetes (IPCS)

ENVIRONMENTAL FATE

Methyl bromide released to soil is expected to be primarily lost by volatilization. Methyl bromide may also leach due to its weak adsorption to soil. Hydrolysis of methyl bromide to methanol and bromide ions and biodegradation may also occur in soil. Release of methyl bromide to water is expected to result primarily in volatilization. Hydrolysis to methanol and bromide ions will occur with a half-life of 20-26.7 days. Bioconcentration is not expected to be significant (HSDB)

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PART II: FINAL REGULATORY ACTION

2.	**FINAL REGULATORY ACTION**	
2.1	**The chemical is:**	**4 banned** **OR** **X severely restricted**
2.2	**Information specific to the final regulatory action**	
2.2.1	**Summary of the final regulatory action**	In 1981, the use of methyl bromide as a soil disinfectant was prohibited. Based on Article 16a of the Dutch Pesticide Law of 1962, an exemption could, however, be granted based on individual requests. in the following period of time, the policies of the Government aimed at a further decrease in the use of methyl bromide. In 1992 methyl bromide was completely banned for use as a soil disinfectant. In 1996, two space fumigation products on the basis of methyl bromide were extended until 1 December 2001.
2.2.2	**Reference to the regulatory document**	http://www.ctb.agro.nl/ctb_files/06476_01.html up to and including http://www.ctb.agro.nl/ctb_files/06476_11.HTML Decree of Ministry of Agriculture and Fisheries, Ministerial Order of 31 December1980/5 January 1981; CTB (1996). Verslag C-48, d.d. 5 juni 1996 te Wageningen (in Dutch).
2.2.3	**Date of entry into force of the final regulatory action**	1992, last amended 24th December 2004.

2.3	Was the final regulatory action based on a risk or hazard evaluation?	X Yes 4 No
	If yes, give information on such evaluation The final regulatory action to prohibit methyl bromide as a soil disinfectant was based on an evaluation of risks regarding storage/transport and use of methyl bromide, the emission of methyl bromide to air and the leaching potential of methyl bromide and bromide.	
	Reference to the relevant documentation http://www.ctb.agro.nl/ctb_files/06476_01.html up to and including http://www.ctb.agro.nl/ctb_files/06476_11.HTML RIVM (1987). Rapport van de commissie inzake het gebruik van methyl bromide voor grondontsmetting in landbouw. Doorn, A.M. et al. (authors) (in Dutch).	

2.4	Reasons for the final regulatory action	
2.4.1	Is the reason for the final regulatory action relevant to the human health?	X Yes 4 No
	If yes, give summary of the known hazards and risks presented by the chemical to human health, including the health of consumers and workers By the end of 1980 the occurrence of methyl bromide in a number of private drinking water pipes, in combination with new toxicological data (a number of positive mutagenicity tests) caused the start of regulatory actions. In addition, there was a concern about safety aspects related to storage, transport and use of methyl bromide (possibility of emission to air) and the leaching potential (leaching to surface water or groundwater). In the Netherlands groundwater can be used for drinking water and therefore groundwater must remain free from pesticides (precaution principle). In later years, the effect on the ozone layer became also subject of concern. Methyl bromide and bromide (active bromine species) are thought to be partly responsible for the destruction of the ozone layer. Methyl bromide is included in the Protocol of Montreal. At present, the use of methyl bromide is restricted to space fumigation in gas proof rooms and its use has been optimised so that risks for workers have been minimised. Strict regularisation caused a reduction in emissions to air and groundwater or surface water, so that the potential risks to the general population are minimised. At the moment there is no Dutch policy to further reduce the use of methyl bromide. Future international policy (for example to further reduce the ozone depletion) will be of influence.	
	Reference to the relevant documentation http://www.ctb.agro.nl/ctb_files/06476_01.html up to and including http://www.ctb.agro.nl/ctb_files/06476_11.HTML RIVM (1987). Rapport van de commissie inzake het gebruik van methyl bromide voor grondontsmetting in landbouw. Doorn, A.M. et al. (authors) (in Dutch).	

	Expected effect of the final regulatory action	
	Prevention of contamination of drinking water derived from groundwater. Minimising risks for workers and general population.	

2.4.2	**Is the reason for the final regulatory action relevant to the environment?**	X Yes 4 No
	If yes, give summary of the known hazards and risks to the environment	
	In 1981, the use of methyl bromide as a soil disinfectant was prohibited. This application was used in greenhouses. The emission fraction from greenhouses to the surrounding surface waters was estimated at 0.1% (fraction 0.001) of the applied dose in kg/m3. Based on this emission value the toxicity to aquatic organisms could not be ignored. In the Netherlands the use of methyl bromide as a soil disinfectant is prohibited, because of the high toxicity to aquatic organisms and the effect on the ozone layer.	
	Reference to the relevant documentation	
	http://www.ctb.agro.nl/ctb_files/06476_01.html up to and including http://www.ctb.agro.nl/ctb_files/06476_11.HTML RIVM/CSR (1992). Methyl bromide (definitieve versie). Adviesrapport 91/670104/011. National Institute of Public Health and the Environment. 14-07-1992 (in Dutch). IPCS (1995) Environmental Health Criteria 166 Methyl Bromide. World Health Organization, Geneva, 1995.	
	Expected effect of the final regulatory action	
	Reduction of risk for the aquatic environment.	

2.5	**Category or categories where the final regulatory action has been taken**	
2.5.1	**Final regulatory action has been taken for the chemical category**	4 **Industrial**
	Use or uses prohibited by the final regulatory action	
	Not relevant	
	Use or uses that remain allowed	

2.5.2	**Final regulatory action has been taken for the chemical category**	X **Pesticide**
	Formulation(s) and use or uses prohibited by the final regulatory action	
	All applications except those mentioned below.	

	Formulation(s) and use or uses that remain allowed
	The following two applications on the basis of methyl bromide were extended until 1. 12. 2001: - "Methyl bromide 100 voor ruimte ontsmetting" and - "Holland fumigation methyl bromide". These applications concern space fumigation by means of gas evaporation and are only permitted in gas proof spaces under very strict regulations.

2.5.3 Estimated quantity of the chemical produced, imported, exported and used, where available.		
	Quantity per year (MT)	**Year**
Produced		
Imported		
Exported		
Used		

2.6 Indication, to the extent possible, of the likely relevance of the final regulatory action to other states and regions	

2.7	Other relevant information that may cover:
2.7.1	Assessment of socio-economic effects of the final regulatory action

2.7.2	Information on alternatives and their relative risks
2.7.3	Relevant additional information

PART III : GOVERNMENT AUTHORITIES

Ministry/Department and authority responsible for issuing/enforcing the final regulatory action	
Institution	Ministry of Housing, Spatial Planning and the Environment Ministry of Agriculture
Address	P.O. Box 30945 2500 GX The Hague The Netherlands
Telephone	+31 70 339 3939
Telefax	+31 70 339 1297
E-mail address	
Designated National Authority	
Institution	Ministry of Housing, Spatial Planning and the Environment
Address	P.O. Box 30945 2500 GX The Hague The Netherlands
Name of person in charge	W.J. Kemmeren, M.Sc. (IPC 645)
Position of person in charge	Designated national authority
Telephone	+31 70 339 2407
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Date, signature of DNA and official seal: The Hague, 26 January 2005

Annex V

Rationales for conclusions by the Committee that notifications had met the criteria of the Annex II of the Rotterdam Convention

A. Notification for methyl bromide (CAS No. 74-83-9) from the Netherlands

1. In reviewing the notification of final regulatory action by the Netherlands to severely restrict methyl bromide**,** together with the supporting documentary information provided by the Party, the Committee was able to confirm that the action had been taken in order to protect human health and the environment. The major health concern is from acute exposure. Delayed onset of symptoms may occur. Fatal poisoning has resulted from exposures to relatively high concentration (from 33,000 mg/m^3 or 8,600 ppm onwards) of methyl bromide vapours. Non-fatal poisoning has resulted from exposure to concentrations as low as 390–1,950 mg/m^3. Organs affected by exposure include the nervous system, lung, nasal mucosa, kidney, eye and skin. Methyl bromide is an ozone-depleting substance and also has high toxicity for aquatic organisms. In addition, it was shown that it had potential following uses as a soil disinfectant to pollute surface water and to leach to groundwater.

2. The Committee established that the final regulatory action had been taken on the basis of risk evaluation and that the evaluation had been based on a review of scientific data. The available documentation demonstrated that the data had been generated in accordance with scientifically recognized methods, and that the data reviews had been performed and documented in accordance with generally recognized scientific principles and procedures. It also showed that the final regulatory action had been based on chemical-specific risk evaluations taking into account the conditions of exposure within the Netherlands.

3. The risk evaluation of the Netherlands focused on the behaviour and effects of methyl bromide in air, groundwater and surface water. It took into account data on the ozone-depleting potential, data on the leaching potential and data on the ecotoxicological effects of methyl bromide, e.g., the toxicity for fish. The ozone-depletion factor of methyl bromide was approximately 0.6, related to the substance CFC13. The estimated concentration in groundwater amounted to approximately 100 µg/L, based on a soil degradation half-life time of about 15 days and a sorption constant of about 2.5 L/kg. The measured concentrations in surface water amounted to approximately 9 mg/L, which resulted in the expectation of a very high risk for fish. The Committee agreed that the evaluation of the risks to aquatic organisms met the requirements of the criterion linked to the prevailing conditions of use in the Netherlands. With regard, however, to the effects of ozone depletion as a global concern, the Committee noted that the relevance of prevailing conditions for risk evaluation needed further discussion and guidance from the Conference of the Parties.

4. The Committee concluded that the final regulatory action provided a sufficiently broad basis to merit including methyl bromide in Annex III of the Rotterdam Convention in the pesticide category. It noted that the action had led to a decrease in the quantities of the chemicals used in the notifying Party. Previous uses as a soil disinfectant had been banned since 1992, and only the uses as space fumigant in gas proof rooms were still registered. The use of methyl bromide in Dutch agriculture had been reduced dramatically because of the decision to ban the substance from the use as a soil fumigant. As a result, emissions to air and to ground and surface water had been minimized. Hence, the risk for human health or environment in the notifying Party had been significantly reduced.

5. The Committee also took into account that the considerations underlying the final regulatory action were not of limited applicability since use of methyl bromide poses human health risks, environmental risks and global effects (methyl bromide is included in the Montreal Protocol). On the basis of information provided to the members at the first session of the Chemical Review Committee

and other available information, the Committee concluded also that there was evidence of ongoing international trade in methyl bromide.

6. The Committee noted that the final regulatory action was not based on concerns about intentional misuse of methyl bromide.

7. At its first session, the Committee concluded that the notification of final regulatory action by the Netherlands met the information requirements of Annex I and the criteria set out in Annex II to the Convention.
