CHEMICAL SAFETY REPORT

Substance Name: magnesium sulfate

EC Number: 231-298-2

CAS Number: 7487-88-9

Registrant's Identity: Macco Organiques, s.r.o., Czech Republic

Table of Contents

Part A 1
1. SUMMARY OF RISK MANAGEMENT MEASURES 1
2. DECLARATION THAT RISK MANAGEMENT MEASURES ARE IMPLEMENTED 1
3. DECLARATION THAT RISK MANAGEMENT MEASURES ARE COMMUNICATED 1
Part B 2
1. IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES 2
1.1. Name and other identifiers of the substance 2
1.2. Composition of the substance 2
1.3. Physico-chemical properties 2
2. MANUFACTURE AND USES 5
2.1. Manufacture 5
2.2. Identified uses 5
2.3. Uses advised against 17
3. CLASSIFICATION AND LABELLING 17
3.1. Classification and labelling according to CLP / GHS 17
3.2. Classification and labelling according to DSD / DPD 19
3.2.1. Classification and labelling in Annex I of Directive 67/548/EEC 19
3.2.2. Self classification(s) 19
3.2.3. Other classification(s) 20
4. ENVIRONMENTAL FATE PROPERTIES 20
4.1. Degradation 20
4.1.1. Abiotic degradation 20
4.1.1.1. Hydrolysis 20
4.1.1.2. Phototransformation/photolysis 21
4.1.1.2.1. Phototransformation in air 21
4.1.1.2.2. Phototransformation in water 21
4.1.1.2.3. Phototransformation in soil 21
4.1.2. Biodegradation 21
4.1.2.1. Biodegradation in water 21
4.1.2.1.1. Estimated data 21
4.1.2.1.2. Screening tests 21
4.1.2.1.3. Simulation tests (water and sediments) 21
4.1.2.1.4. Summary and discussion of biodegradation in water and sediment 22
4.1.2.2. Biodegradation in soil 22
4.1.3. Summary and discussion of degradation 22
4.2. Environmental distribution 22
4.2.1. Adsorption/desorption 22
4.2.2. Volatilisation 23
4.2.3. Distribution modelling 23
4.2.4. Summary and discussion of environmental distribution 23
4.3. Bioaccumulation 23
4.3.1. Aquatic bioaccumulation 23
4.3.2. Terrestrial bioaccumulation 23
4.3.3. Summary and discussion of bioaccumulation 23
4.4. Secondary poisoning 24
5. HUMAN HEALTH HAZARD ASSESSMENT 25
5.1. Toxicokinetics (absorption, metabolism, distribution and elimination) 25
5.1.1. Non-human information 25
5.1.2. Human information 26
5.1.3. Summary and discussion of toxicokinetics 26
5.2. Acute toxicity 26
5.2.1. Non-human information 26
5.2.1.1. Acute toxicity: oral 26
5.2.1.2. Acute toxicity: inhalation 27
5.2.1.3. Acute toxicity: dermal 27
5.2.1.4. Acute toxicity: other routes 27

5.2.2. Human information 28
5.2.3. Summary and discussion of acute toxicity 28
5.3. Irritation 29
5.3.1. Skin 29
5.3.1.1. Non-human information 29
5.3.1.2. Human information 29
5.3.2. Eye 29
5.3.2.1. Non-human information 29
5.3.2.2. Human information 30
5.3.3. Respiratory tract 30
5.3.3.1. Non-human information 30
5.3.3.2. Human information 30
5.3.4. Summary and discussion of irritation 30
5.4. Corrosivity 31
5.4.1. Non-human information 31
5.4.2. Human information 31
5.4.3. Summary and discussion of corrosion 31
5.5. Sensitisation 31
5.5.1. Skin 31
5.5.1.1. Non-human information 31
5.5.1.2. Human information 32
5.5.2. Respiratory system 32
5.5.2.1. Non-human information 32
5.5.2.2. Human information 32
5.5.3. Summary and discussion of sensitisation 32
5.6. Repeated dose toxicity 32
5.6.1. Non-human information 32
5.6.1.1. Repeated dose toxicity: oral 32
5.6.1.2. Repeated dose toxicity: inhalation 34
5.6.1.3. Repeated dose toxicity: dermal 34
5.6.1.4. Repeated dose toxicity: other routes 34
5.6.2. Human information 34
5.6.3. Summary and discussion of repeated dose toxicity 35
5.7. Mutagenicity 36
5.7.1. Non-human information 36
5.7.1.1. In vitro data 36
5.7.1.2. In vivo data 37
5.7.2. Human information 37
5.7.3. Summary and discussion of mutagenicity 37
5.8. Carcinogenicity 38
5.8.1. Non-human information 38
5.8.1.1. Carcinogenicity: oral 38
5.8.1.2. Carcinogenicity: inhalation 39
5.8.1.3. Carcinogenicity: dermal 39
5.8.1.4. Carcinogenicity: other routes 39
5.8.2. Human information 39
5.8.3. Summary and discussion of carcinogenicity 39
5.9. Toxicity for reproduction 40
5.9.1. Effects on fertility 40
5.9.1.1. Non-human information 40
5.9.1.2. Human information 41
5.9.2. Developmental toxicity 41
5.9.2.1. Non-human information 41
5.9.2.2. Human information 42
5.9.3. Summary and discussion of reproductive toxicity 42
5.10. Other effects 43
5.10.1. Non-human information 43
5.10.1.1. Neurotoxicity 43
5.10.1.2. Immunotoxicity 43
5.10.1.3. Specific investigations: other studies 43

5.10.2. Human information ... 43
5.10.3. Summary and discussion of specific investigations ... 44
5.11. Derivation of DNEL(s) / DMEL(s) ... 44
5.11.1. Overview of typical dose descriptors for all endpoints ... 44
5.11.2. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptor for critical health effects ... 48
6. HUMAN HEALTH HAZARD ASSESSMENT OF PHYSICO-CHEMICAL PROPERTIES ... 57
6.1. Explosivity ... 57
6.2. Flammability ... 58
6.3. Oxidising potential ... 59
7. ENVIRONMENTAL HAZARD ASSESSMENT ... 60
7.1. Aquatic compartment (including sediment) ... 60
7.1.1. Toxicity test results ... 60
7.1.1.1. Fish ... 60
7.1.1.1.1. Short-term toxicity to fish ... 60
7.1.1.1.2. Long-term toxicity to fish ... 62
7.1.1.2. Aquatic invertebrates ... 62
7.1.1.2.1. Short-term toxicity to aquatic invertebrates ... 62
7.1.1.2.2. Long-term toxicity to aquatic invertebrates ... 63
7.1.1.3. Algae and aquatic plants ... 63
7.1.1.4. Sediment organisms ... 64
7.1.1.5. Other aquatic organisms ... 65
7.1.2. Calculation of Predicted No Effect Concentration (PNEC) ... 65
7.1.2.1. PNEC water ... 65
7.1.2.2. PNEC sediment ... 65
7.2. Terrestrial compartment ... 65
7.2.1. Toxicity test results ... 65
7.2.1.1. Toxicity to soil macro-organisms ... 66
7.2.1.2. Toxicity to terrestrial plants ... 66
7.2.1.3. Toxicity to soil micro-organisms ... 66
7.2.1.4. Toxicity to other terrestrial organisms ... 66
7.2.2. Calculation of Predicted No Effect Concentration (PNEC soil) ... 67
7.3. Atmospheric compartment ... 67
7.4. Microbiological activity in sewage treatment systems ... 67
7.4.1. Toxicity to aquatic micro-organisms ... 67
7.4.2. PNEC for sewage treatment plant ... 68
7.5. Non compartment specific effects relevant for the food chain (secondary poisoning) ... 68
7.5.1. Toxicity to birds ... 68
7.5.2. Toxicity to mammals ... 68
7.5.3. Calculation of PNECoral (secondary poisoning) ... 68
7.6. Conclusion on the environmental hazard assessment and on classification and labelling ... 69
8. PBT AND VPVB ASSESSMENT ... 70
9. EXPOSURE ASSESSMENT ... 70
10. RISK CHARACTERISATION ... 70
REFERENCES ... 71

List of Tables

Table 1. Substance identity ... 2
Table 2. Constituents ... 2
Table 3. Overview of physico-chemical properties ... 2
Table 4. Overview of quantities (in tonnes/year) ... 5
Table 5. Uses by workers in industrial settings ... 6
Table 6. Uses by professional workers ... 12
Table 7. Uses by consumers ... 15
Table 8. Classification according to Directive 67/548/EEC criteria ... 19
Table 9. Overview of experimental studies on absorption, metabolism, distribution and elimination ... 26
Table 10. Overview of experimental studies on acute toxicity after oral administration ... 26
Table 11. Overview of experimental studies on acute toxicity after dermal administration ... 27
Table 12. Overview of studies on acute toxicity (other routes) ... 28
Table 13. Overview of experimental studies on skin irritation ... 29
Table 14. Overview of experimental studies on eye irritation ... 29
Table 15. Overview of experimental studies on skin sensitisation ... 31
Table 16. Overview of experimental studies on repeated dose toxicity after oral administration ... 32
Table 17. Overview of experimental in vitro genotoxicity studies ... 36
Table 18. Overview of experimental studies on carcinogenicity after oral administration ... 38
Table 19. Overview of experimental studies on fertility ... 40
Table 20. Overview of experimental studies on developmental toxicity ... 41
Table 21. Available dose-descriptor(s) per endpoint for the submission substance as a result of its hazard assessment ... 45
Table 22. DN(M)ELs for workers ... 49
Table 23. DN(M)ELs for the general population ... 53
Table 24. Overview of information on explosivity ... 57
Table 25. Overview of information on flammability ... 58
Table 26. Overview of information on oxidising potential ... 59
Table 27. Overview of short-term effects on fish ... 61
Table 28. Overview of short-term effects on aquatic invertebrates ... 62
Table 29. Overview of effects on algae and aquatic plants ... 63
Table 30. PNEC water ... 65
Table 31. PNEC sediment ... 65
Table 32. PNEC soil ... 67
Table 33. Overview of effects on micro-organisms ... 67
Table 34. PNEC sewage treatment plant ... 68
Table 35. PNEC oral ... 68

Part A

1. SUMMARY OF RISK MANAGEMENT MEASURES

The substance is not classified as dangerous according to the criteria of the Dangerous Substances Directive (67/548/EEC) or the Classification, Labelling and Packaging of Substances and Mixtures (CLP Regulation; 1272/2008/EC). Specific Risk Management Measures are therefore not required. Nevertheless, the exposure of workers during and after normal operations should be minimised by the use of good industrial hygiene practice, the general measures necessary for safety and health protection of workers (article 6 of Directive 89/391/EC) and the reduce-to-a-minimum principle (article 6 of Chemical Agents Directive 98/24/EC).

2. DECLARATION THAT RISK MANAGEMENT MEASURES ARE IMPLEMENTED

The substance is not classified as dangerous, therefore specific RMMs are not required.

3. DECLARATION THAT RISK MANAGEMENT MEASURES ARE COMMUNICATED

The substance is not classified as dangerous, therefore specific RMMs are not required. Guidance on safe use is communicated to downstream users by means of product labels, MSDSs and by statutory controls on use and environmental release.

Part B

1. IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

1.1. Name and other identifiers of the substance

The substance **magnesium sulfate** is a mono constituent substance (origin: inorganic) having the following characteristics and physical–chemical properties (see the IUCLID dataset for further details).

The following public name is used: Magnesium sulphate.

Table 1. Substance identity

EC number:	231-298-2
EC name:	magnesium sulphate
CAS number (EC inventory):	7487-88-9
CAS name:	magnesium sulphate
IUPAC name:	magnesium sulphate
Molecular formula:	H2O4S.Mg
Molecular weight range:	

Structural formula:

1.2. Composition of the substance

Name: magnesium sulphate

Degree of purity: >= 60.0 — < 100.0 % (w/w)

Table 2. Constituents

Constituent	Typical concentration	Concentration range	Remarks
magnesium sulfate EC no.: 231-298-2	60 - 80.0 % (w/w)	>= 60.0 — < 100.0 % (w/w)	

1.3. Physico-chemical properties

Table 3. Overview of physico-chemical properties

Property	Results	Value used for CSA / Discussion
Physical state at 20°C and 1013 hPa	Magnesium sulphate monohydrate occurs in nature as the mineral kieserite. No data on appearance of the monohydrate in the	**Value used for CSA:** solid

Property	Results	Value used for CSA / Discussion
	handbook. Trihydrate: crystals; heptahydrate: white crystals or powder.	
Melting / freezing point	Based on several handbooks, the melting point of magnesium sulphate was established to be approximately 1124°C, with decomposition taking place.	**Value used for CSA:** 1124 °C at 1013 hPa
Relative density	Based on several handbooks, the relative density of magnesium sulphate was established to be 2.66.	**Value used for CSA:** 2.66 at 20°C
Water solubility	Based on several handbooks, the water solubility of magnesium sulphate was established to be 360 g/L at 20ºC.	**Value used for CSA:** 360 g/L at 20 °C
Flammability	Based on the molecular structure of the inorganic substance magnesium sulphate, it was concluded that this substance is not flammable when coming into contact with an ignition source, with water or with air.	**Value used for CSA:** non flammable
Explosive properties	Based on the chemical composition, magnesium sulphate appears to be not explosive.	**Value used for CSA:** non explosive
Oxidising properties	Based on the chemical composition, magnesium sulphate appears to have no oxidising properties.	**Value used for CSA:** Oxidising: no
Granulometry	Using the laser diffraction test (dry powder module), the MMAD of magnesium sulphate was determined to be 27.645 µm, while 36.47% by volume of sample was seen to be < 10.00 µm.	

Data waiving

Information requirement: Boiling point

Reason: other justification

Justification: In accordance with Column 2 of REACH Annex VII, the boiling point (required in section 7.3) does not need to be conducted as the substance decomposes before boiling and the melting point is above 300°C.

Information requirement: Vapour pressure

Reason: other justification

Justification: In accordance with column 2 of REACH Annex VII, the vapour pressure (required in section 7.5) does not need to be conducted as the melting point is above 300°C.

Information requirement: Surface tension

Reason: other justification

Justification: In accordance with column 2 of REACH Annex VII, surface tension (required in section 7.6) does not need to be conducted as no surface activity is expected. No surface activity is expected for an inorganic salt at the maximum test concentration of 1 g/L.

Information requirement: Partition coefficient n-octanol/water (log value)

Reason: other justification

Justification: In accordance with column 2 of REACH Annex VII, the partition coefficient n-octanol/water (required in section 7.8) does not need to be conducted as the substance is inorganic.

Information requirement: Flash point

Reason: other justification

Justification: In accordance with column 2 of REACH Annex VII, flash point (required in section 7.9) does not need to be conducted as the substance is inorganic.

Information requirement: Flammability

Reason: study scientifically unjustified

Justification: In accordance with REACH Annex XI, testing may be omitted if testing does not appear scientifically necessary. Magnesium sulphate is inorganic and commonly known to be not flammable (stable salt). It does not contain groups that may react with oxygen, thus is not expected to propagate combustion along a test substance pile, and is therefore considered not flammable.

Information requirement: Flammability

Reason: study scientifically unjustified

Justification: The molecular structure of Magnesium sulphate does not contain groups that might lead to ignition in contact with water and/or to the evolution of a flammable gas. In accordance with REACH Annex XI, testing may be omitted if testing does not appear scientifically necessary.

Information requirement: Flammability

Reason: study scientifically unjustified

Justification: The molecular structure of Magnesium sulphate does not contain groups that might lead to ignition in contact with air. In accordance with REACH Annex XI, testing may be omitted if testing does not appear scientifically necessary.

Information requirement: Self-ignition temperature

Reason: study scientifically unjustified

Justification: Magnesium sulphate does not contain groups that may react with oxygen and therefore will not auto-ignite at temperatures between room temperature and ca. 1124°C (melting). In accordance with REACH Annex XI, testing may be omitted if testing does not appear scientifically necessary.

Information requirement: Stability in organic solvents and identity of relevant degradation products

Reason: other justification

Justification: In accordance with Column 2 of REACH Annex IX, stability in organic solvents and identity of relevant degradation products (required in section 7.15) does not need to be conducted as the substance is inorganic.

Information requirement: Dissociation constant

Reason: study scientifically unjustified

Justification: In accordance with section 1 of Annex XI of REACH, a dissociation constant study (required in section 7.16) is not considered necessary as the substance is inorganic, as such does not exist in water, only the ions exist in water, and thus does not have relevant functional groups. See also the Guidance on information requirements and chemical safety assessment, Chapter R.7a.

Information requirement: Viscosity

Reason: study technically not feasible

Justification: In accordance with REACH Annex XI, testing may be omitted if it is technically not possible to conduct the study. Test method is not applicable to solids. Viscosity is only relevant to liquids.

2. MANUFACTURE AND USES

Quantities

Table 4. Overview of quantities (in tonnes/year)

Year	Total tonnage	Own use	Used for article	Used as intermediate under strictly controlled conditions	Used for research purposes
2010	Manufactured: 190	0	0	0	0
2011	Manufactured: 385	0	0	0	0
2012	Manufactured: 452	0	0	0	0

2.1. Manufacture

Manufacturing process

This process is based on the direct reaction of sulphuric acid with natural magnesite according to the following equation:

$MgCO3 + H2SO4 \rightarrow MgSO4 + H2O + CO2$

This may occur as a deliberate direct process.The quality and strength of the solution produced will depend on the purity of the raw materials and the concentration of the acid used.
Purification steps (e.g. addition of MgO slurry) allow precipitating impurities like iron and other metals, which are then separated by filtration.
Liquor produced via this route may be used in the production of flakes, prills or crystals.

2.2. Identified uses

Table 5. Uses by workers in industrial settings

Confidential	IU number	Identified Use (IU) name	Substance supplied to that use	Use descriptors
		Fertilizer	in a mixture	**Process category (PROC):** PROC 3: Use in closed batch process (synthesis or formulation) PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact) PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 14: Production of preparations or articles by tabletting, compression, extrusion, pelletisation PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) **Market sector by type of chemical product:** PC 12: Fertilisers **Environmental release category (ERC):** ERC 2: Formulation of preparations **Sector of end use (SU):** SU 10: Formulation [mixing] of preparations and/or re-packaging (excluding alloys) **Subsequent service life relevant for that use?:** yes
		Intermediates	in a mixture	**Process category (PROC):** PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing)

Confidential	IU number	Identified Use (IU) name	Substance supplied to that use	Use descriptors
				Market sector by type of chemical product: PC 12: Fertilisers **Environmental release category (ERC):** ERC 1: Manufacture of substances **Sector of end use (SU):** SU 8: Manufacture of bulk, large scale chemicals (including petroleum products) **Subsequent service life relevant for that use?:** yes
		Other magnesium sulphate	as such (substance itself)	**Process category (PROC):** PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact) PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) **Market sector by type of chemical product:** PC 1: Adhesives, sealants PC 18: Ink and toners PC 21: Laboratory chemicals PC 23: Leather tanning, dye, finishing, impregnation and care products PC 26: Paper and board dye, finishing and impregnation products: including bleaches and other processing aids **Environmental release category (ERC):** ERC 2: Formulation of preparations **Sector of end use (SU):** SU 10: Formulation [mixing] of preparations and/or re-packaging (excluding alloys)

Confidential	IU number	Identified Use (IU) name	Substance supplied to that use	Use descriptors
				Subsequent service life relevant for that use?: yes
		Intermediates	as such (substance itself)	**Process category (PROC):** PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities **Market sector by type of chemical product:** PC 19: Intermediate **Environmental release category (ERC):** ERC 1: Manufacture of substances **Sector of end use (SU):** SU 8: Manufacture of bulk, large scale chemicals (including petroleum products) **Subsequent service life relevant for that use?:** yes
		Wide range of chemicals (end use)	as such (substance itself) in a mixture	**Process category (PROC):** PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) **Market sector by type of chemical product:** PC 21: Laboratory chemicals **Environmental release category (ERC):** ERC 1: Manufacture of substances **Sector of end use (SU):**

Confidential	IU number	Identified Use (IU) name	Substance supplied to that use	Use descriptors
				SU 9: Manufacture of fine chemicals **Subsequent service life relevant for that use?:** yes
		Laboratory chemicals	as such (substance itself)	**Process category (PROC):** PROC 15: Use as laboratory reagent **Environmental release category (ERC):** ERC 8a: Wide dispersive indoor use of processing aids in open systems **Sector of end use (SU):** SU 0: Other: Uses of substances as such or in preparations in industrial sites **Subsequent service life relevant for that use?:** yes
		Pharmaceuticals	in a mixture	**Process category (PROC):** PROC 3: Use in closed batch process (synthesis or formulation) PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) PROC 14: Production of preparations or articles by tabletting, compression, extrusion, pelletisation **Market sector by type of chemical product:** PC 29: Pharmaceuticals **Environmental release category (ERC):** ERC 2: Formulation of preparations **Sector of end use (SU):** SU 10: Formulation [mixing] of preparations and/or re-packaging (excluding alloys) **Subsequent service life relevant for that use?:** yes
		Ink and Toners	in a mixture	**Process category (PROC):** PROC 0: Other:

Confidential	IU number	Identified Use (IU) name	Substance supplied to that use	Use descriptors
				Environmental release category (ERC): ERC 5: Industrial use resulting in inclusion into or onto a matrix **Sector of end use (SU):** SU 0: Other: Uses of substances as such or in preparations at industrial sites **Subsequent service life relevant for that use?:** yes **Article category related to subsequent service life (AC):** AC 8: Paper articles
		Leather tanning, dye, finishing, impregnation and care products	in a mixture	**Process category (PROC):** PROC 7: Industrial spraying PROC 13: Treatment of articles by dipping and pouring **Environmental release category (ERC):** ERC 5: Industrial use resulting in inclusion into or onto a matrix **Sector of end use (SU):** SU 0: Other: C15 - Manufacture of leather and related products **Subsequent service life relevant for that use?:** yes **Article category related to subsequent service life (AC):** AC 6: Leather articles
		Textile dyes, finishing and impregnating products, including bleaches and other processing aids	in a mixture	**Process category (PROC):** PROC 7: Industrial spraying PROC 13: Treatment of articles by dipping and pouring **Environmental release category (ERC):** ERC 5: Industrial use resulting in inclusion into or onto a matrix

Confidential	IU number	Identified Use (IU) name	Substance supplied to that use	Use descriptors
				Sector of end use (SU): SU 0: Other: C13 - Manufacture of textiles **Subsequent service life relevant for that use?:** yes **Article category related to subsequent service life (AC):** AC 5: Fabrics, textiles and apparel
		Adhesives, sealants	in a mixture	**Process category (PROC):** PROC 10: Roller application or brushing PROC 14: Production of preparations or articles by tabletting, compression, extrusion, pelletisation **Environmental release category (ERC):** ERC 5: Industrial use resulting in inclusion into or onto a matrix **Subsequent service life relevant for that use?:** yes **Article category related to subsequent service life (AC):** AC 8: Paper articles
		Paper and board dye, finishing and impregnation products: including bleaches and other processing aids	in a mixture	**Process category (PROC):** PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 7: Industrial spraying PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact) PROC 13: Treatment of articles by dipping and pouring **Environmental release category (ERC):** ERC 5: Industrial use resulting in inclusion into or onto a matrix **Sector of end use (SU):** SU 6b: Manufacture of pulp, paper and paper products **Subsequent service life relevant for that use?:** yes

Table 6. Uses by professional workers

Confidential	IU number	Identified Use (IU) name	Substance supplied to that use	Use descriptors
		Fertilizers	in a mixture	**Process category (PROC):** PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 11: Non industrial spraying PROC 19: Hand-mixing with intimate contact and only PPE available. PROC 26: Handling of solid inorganic substances at ambient temperature **Market sector by type of chemical product:** PC 12: Fertilisers **Environmental release category (ERC):** ERC 8b: Wide dispersive indoor use of reactive substances in open systems ERC 8e: Wide dispersive outdoor use of reactive substances in open systems **Sector of end use (SU):** **Subsequent service life relevant for that use?:** yes
		Leather tanning, dye, finishing, impregnation and care products	in a mixture	**Process category (PROC):** PROC 10: Roller application or brushing PROC 11: Non industrial spraying PROC 19: Hand-mixing with intimate contact and only PPE available. **Environmental release category (ERC):** ERC 8b: Wide dispersive indoor use of reactive substances in open systems ERC 8e: Wide dispersive outdoor use of reactive substances in open systems **Sector of end use (SU):**

Confidential	IU number	Identified Use (IU) name	Substance supplied to that use	Use descriptors
				Subsequent service life relevant for that use?: yes **Article category related to subsequent service life (AC):**
		Adhesives and Sealants	in a mixture	**Process category (PROC):** PROC 10: Roller application or brushing **Environmental release category (ERC):** ERC 8c: Wide dispersive indoor use resulting in inclusion into or onto a matrix **Sector of end use (SU):** **Subsequent service life relevant for that use?:** yes **Article category related to subsequent service life (AC):**
		Adhesives and Sealants	in a mixture	**Process category (PROC):** PROC 10: Roller application or brushing **Environmental release category (ERC):** ERC 8c: Wide dispersive indoor use resulting in inclusion into or onto a matrix **Sector of end use (SU):** **Subsequent service life relevant for that use?:** yes **Article category related to subsequent service life (AC):**
		Pharmaceutical	as such (substance itself) in a mixture	**Environmental release category (ERC):** ERC 8b: Wide dispersive indoor use of reactive substances in open systems **Sector of end use (SU):** **Subsequent service life relevant for that use?:** yes
		Ink and Toner	in a mixture	**Process category (PROC):**

Confidential	IU number	Identified Use (IU) name	Substance supplied to that use	Use descriptors
				PROC 0: Other: **Environmental release category (ERC):** ERC 8c: Wide dispersive indoor use resulting in inclusion into or onto a matrix **Sector of end use (SU):** **Subsequent service life relevant for that use?:** yes **Article category related to subsequent service life (AC):**
		Laboratory chemicals	as such (substance itself) in a mixture	**Process category (PROC):** PROC 15: Use as laboratory reagent **Market sector by type of chemical product:** PC 21: Laboratory chemicals **Environmental release category (ERC):** ERC 8a: Wide dispersive indoor use of processing aids in open systems **Sector of end use (SU):** **Subsequent service life relevant for that use?:** yes
		Cosmetics, personal care products	in a mixture	**Market sector by type of chemical product:** PC 39: Cosmetics, personal care products **Environmental release category (ERC):** ERC 8b: Wide dispersive indoor use of reactive substances in open systems **Sector of end use (SU):** **Subsequent service life relevant for that use?:** yes

Table 7. Uses by consumers

Confidential	IU number	Identified Use (IU) name	Use descriptors
		Private households	**Chemical product category (PC):** PC 12: Fertilisers **Environmental release category (ERC):** ERC 8b: Wide dispersive indoor use of reactive substances in open systems ERC 8e: Wide dispersive outdoor use of reactive substances in open systems **Subsequent service life relevant for that use?:** yes
		Ink and Toner	**Chemical product category (PC):** PC 18: Ink and toners **Environmental release category (ERC):** ERC 8c: Wide dispersive indoor use resulting in inclusion into or onto a matrix **Subsequent service life relevant for that use?:** yes
		Adhesives and Sealants	**Chemical product category (PC):** PC 1: Adhesives, sealants **Environmental release category (ERC):** ERC 8c: Wide dispersive indoor use resulting in inclusion into or onto a matrix **Subsequent service life relevant for that use?:** yes
		Pharmaceuticals	**Chemical product category (PC):** PC 29: Pharmaceuticals **Environmental release category (ERC):** ERC 8b: Wide dispersive indoor use of reactive substances in open systems **Subsequent service life relevant for that use?:** yes
		Cosmetics, personal care	**Chemical product category (PC):** PC 39: Cosmetics, personal care products

Confidential	IU number	Identified Use (IU) name	Use descriptors
		products	**Environmental release category (ERC):** ERC 8b: Wide dispersive indoor use of reactive substances in open systems **Subsequent service life relevant for that use?:** yes

2.3. Uses advised against

None.

3. CLASSIFICATION AND LABELLING

3.1. Classification and labelling according to CLP / GHS

Name: magnesium sulphate

Implementation: EU

State/form of the substance: solid

Related composition: magnesium sulphate

Classification

The substance is classified as follows:

- for physical-chemical properties:

Explosives:	Reason for no classification: conclusive but not sufficient for classification
Flammable gases:	Reason for no classification: data lacking
Flammable aerosols:	Reason for no classification: data lacking
Oxidising gases:	Reason for no classification: data lacking
Gases under pressure:	Reason for no classification: data lacking
Flammable liquids:	Reason for no classification: data lacking
Flammable solids:	Reason for no classification: conclusive but not sufficient for classification
Self-reacting substances and mixtures:	Reason for no classification: conclusive but not sufficient for classification
Pyrophoric liquids:	Reason for no classification: data lacking
Pyrophoric solids:	Reason for no classification: conclusive but not sufficient for classification
Self-heating substances and mixtures:	Reason for no classification: conclusive but not sufficient for classification
Substances and mixtures which in contact with water emits flammable gases:	Reason for no classification: conclusive but not sufficient for classification

Oxidising liquids:	Reason for no classification: data lacking
Oxidising solids:	Reason for no classification: conclusive but not sufficient for classification
Organic peroxides:	Reason for no classification: data lacking
Corrosive to metals:	Reason for no classification: data lacking

- for health hazards:

Acute toxicity - oral:	Reason for no classification: conclusive but not sufficient for classification
Acute toxicity - dermal:	Reason for no classification: conclusive but not sufficient for classification
Acute toxicity - inhalation:	Reason for no classification: conclusive but not sufficient for classification
Skin corrosion/irritation:	Reason for no classification: conclusive but not sufficient for classification
Serious damage/eye irritation:	Reason for no classification: conclusive but not sufficient for classification
Respiration sensitization:	Reason for no classification: data lacking
Skin sensitation:	Reason for no classification: conclusive but not sufficient for classification
Aspiration hazard:	Reason for no classification: data lacking
Reproductive Toxicity:	Reason for no classification: conclusive but not sufficient for classification
Reproductive Toxicity: Effects on or via lactation:	Reason for no classification: data lacking
Germ cell mutagenicity:	Reason for no classification: conclusive but not sufficient for classification
Carcinogenicity:	Reason for no classification: conclusive but not sufficient for classification
Specific target organ toxicity - single:	Reason for no classification: conclusive but not sufficient for classification
Specific target organ toxicity - repeated:	Reason for no classification: conclusive but not sufficient for classification

- for environmental hazards:

Hazards to the aquatic environment:	Reason for no classification: conclusive but not sufficient for classification
Hazardous to the atmospheric environment:	Reason for no classification: conclusive but not sufficient for classification

Labelling

Signal word: No signal word

3.2. Classification and labelling according to DSD / DPD

3.2.1. Classification and labelling in Annex I of Directive 67/548/EEC

This substance is not classified in the Annex I of Directive 67/548/EEC as such, but it may be included in one of the group entries.

3.2.2. Self classification(s)

Chemical name: Magnesium sulphate

Table 8. Classification according to Directive 67/548/EEC criteria

Endpoints	Classification	Reason for no classification	Justification for (non) classification can be found in section
Explosiveness		conclusive but not sufficient for classification	6.1
Oxidising properties		conclusive but not sufficient for classification	6.3
Flammability		conclusive but not sufficient for classification	6.2
Thermal stability		data lacking	
Acute toxicity		conclusive but not sufficient for classification	5.2
Acute toxicity- irreversible damage after single exposure		conclusive but not sufficient for classification	5.2
Repeated dose toxicity		conclusive but not sufficient for classification	5.6
Irritation / Corrosion		conclusive but not sufficient for classification	5.3.4 and 5.4.3
Sensitisation		conclusive but not sufficient for classification	5.5.3

Endpoints	Classification	Reason for no classification	Justification for (non) classification can be found in section
Carcinogenicity		conclusive but not sufficient for classification	5.8.3
Mutagenicity - Genetic Toxicity		conclusive but not sufficient for classification	5.7.3
Toxicity to reproduction-fertility		conclusive but not sufficient for classification	5.9.3
Toxicity to reproduction-development		conclusive but not sufficient for classification	5.9.3
Toxicity to reproduction - breastfed babies		data lacking	5.9.3
Environment		conclusive but not sufficient for classification	7.6

3.2.3. Other classification(s)

None.

4. ENVIRONMENTAL FATE PROPERTIES

General discussion of environmental fate and pathways:

Magnesium sulphate does not hydrolyze nor is there evidence for photodegradation. In aqueous solution, magnesium sulphate is completely dissociated into the magnesium ion (Mg^{2+}) and the sulfate anion (SO_4^{2-}). Due to the inorganic nature of the substance standard biodegradation testing systems are not applicable. Based on the high water solubility and the ionic nature, magnesium sulphate is not expected to adsorb or bioaccumulate to a significant extent. Based on the physico-chemical properties of magnesium sulphate, water is expected to be the main target compartment. Based on the high water solubility, a low geoaccumulation potential and high mobility in soil is to be expected. However, due to ion-ion interactions it is to be expected that mobility in soil is significantly reduced. Magnesium sulphate will not volatilize from soil.

4.1. Degradation

4.1.1. Abiotic degradation

4.1.1.1. Hydrolysis

Data waiving

Reason: study scientifically unjustified

Justification: In accordance with REACH Annex XI, testing may be omitted if testing does not appear scientifically necessary. No hydrolysable group is present. In addition, the test method is not applicable as the substance will be completely dissociated into ions.

4.1.1.2. Phototransformation/photolysis

4.1.1.2.1. Phototransformation in air

Data waiving

Reason: study technically not feasible

Justification: Simple inorganic salts are not susceptible to photodegradation. In accordance with REACH Annex XI, testing may be omitted if it is technically not possible to conduct the study. Performance of the test is not relevant for a simple inorganic salt as magnesium sulphate.

4.1.1.2.2. Phototransformation in water

No data are available: not required.

4.1.1.2.3. Phototransformation in soil

No data are available: not required.

4.1.2. Biodegradation

4.1.2.1. Biodegradation in water

4.1.2.1.1. Estimated data

No data are available: not required and for inorganic substances not reliable to estimate.

4.1.2.1.2. Screening tests

Data waiving

Reason: study scientifically unjustified

Justification: In accordance with Column 2 of REACH Annex VII, Ready biodegradability (required in section 9.2.1.1) does not need to be conducted as the substance is inorganic.

4.1.2.1.3. Simulation tests (water and sediments)

Data waiving

Reason: other justification

Justification: In accordance with Column 2 of REACH Annex IX, biodegradation in water and sediment (required in section 9.2.1.2 and 4) does not need to be conducted if the substance is readily biodegradable. But as ready biodegradability testing does not need to be conducted as the substance is inorganic, the water and sediment simulation test is considered not necessary. In addition, according to the guidance on inforamtion requirements and chemical safety assessment, Chapter R7b, biodegradability testing is not required for an inorganic substance.

4.1.2.1.4. Summary and discussion of biodegradation in water and sediment

Discussion (screening testing)

As the substance is inorganic, no testing is required.

Discussion (simulation testing)

As the substance is inorganic, no testing is required.

4.1.2.2. Biodegradation in soil

Data waiving

Reason: other justification

Justification: In accordance with Column 2 of REACH Annex IX, biodegradability in soil (required in section 9.2.1.3) does not need to be conducted if the substance is readily biodegradable. But as ready biodegradability testing does not need to be conducted as the substance is inorganic, the soil simulation test is considered not necessary. In addition, according to the guidance on information requirements and chemical safety assessment, Chapter R7b, biodegradability testing is not required for an inorganic substance.

4.1.3. Summary and discussion of degradation

Abiotic degradation

In aqueous solution, magnesium sulphate is completely dissociated into the magnesium ion (Mg2+) and the sulfate anion (SO4 2-). Hydrolysis of magnesium sulfate does not occur.

Biotic degradation

Due to the inorganic nature of the substance standard testing systems are not applicable.

Sulfates can be retained in soil, both by incorporation into organic matter (e. g. as sulfate esters of humic acids) and adsorbed to soil particles such as hydrous iron and aluminum sesquioxides.

4.2. Environmental distribution

4.2.1. Adsorption/desorption

Data waiving

Reason: other justification

Justification: In accordance with Column 2 of REACH Annex VIII, the adsorption/desorption (required in section 9.3.1) does not need to be conducted as the substance has a low potential for adsorption. Simple inorganic salts with high aqueous solubility will exist in a dissociated form in an aqueous solution. Such a substance has a low potential for adsorption. In addition a screening study (OECD 121) could not be conducted as it is technically not feasible to perform and QSARs are not suitable for such substances.

4.2.2. Volatilisation

No data are available: not required. Volatilisation is unlikely.

4.2.3. Distribution modelling

No data are available: not required.

4.2.4. Summary and discussion of environmental distribution

Simple inorganic salts like magnesium sulphate, with high aqueous solubility will exist in a dissociated form in an aqueous solution. Such a substance has a low potential for adsorption. In addition, volatilization is also unlikely due to the properties of the substance.

4.3. Bioaccumulation

Simple inorganic salts with high aqueous solubility will exist in a dissociated form in an aqueous solution. Such a substance has a low potential for bioaccumulation.

4.3.1. Aquatic bioaccumulation

Data waiving

Reason: other justification

Justification: In accordance with Column 2 of REACH Annex IX, the bioaccumulation in aquatic species (required in section 9.3.2) does not need to be conducted as the substance has a low potential for bioaccumulation. Simple inorganic salts with high aqueous solubility will exist in a dissociated form in an aqueous solution. Such a substance has a low potential for bioaccumulation.

4.3.2. Terrestrial bioaccumulation

Data not available: not required. In addition, the substance has a low potential for bioaccumulation as it has a high aqueous solubility and will mainly exist in a dissociated form.

4.3.3. Summary and discussion of bioaccumulation

Aquatic bioaccumulation

Simple inorganic salts with high aqueous solubility will exist in a dissociated form in an aqueous solution. Such a substance has a low potential for bioaccumulation.

Terrestrial bioaccumulation

Simple inorganic salts with high aqueous solubility will exist in a dissociated form in an aqueous solution. Such a substance has a low potential for bioaccumulation.

4.4. Secondary poisoning

Based on the available information, there is no indication of a bioaccumulation potential and, hence, secondary poisoning is not considered relevant (see CSR chapter 7.5.3 "Calculation of PNECoral (secondary poisoning) ".

Justification for no PNEC oral derivation: Magnesium sulphate is highly soluble, and therefore it is assumed that the log Kow will be low. Furthermore, magnesium sulphate has a low bioaccumulation potential and therefore secondary poisoning is not considered a relevant route. Therefore, a PNEC oral has not been derived.

Interpretation of the available data with regard to the potential to bio-accumulate in the food chain:

As the substance has a low potential for bioaccumulation, secondary poisoning is not considered a relevant route of exposure.

5. HUMAN HEALTH HAZARD ASSESSMENT

The read across rationale for supporting substances is documented in a report (Read-across Approach for REACH registration of Sulphate substances) part of the IUCLID, section 0. The following substances are registered under REACH as part of the sulphate category:
1. Magnesium sulphate (CAS no. 7487-88-9, EC no. 231-298-2)
2. Potassium sulphate (CAS no. 7778-80-5, EC no. 231-915-5)

The following surrogates were used:

Surrogate	CAS no.	Comment
Calcium sulphate	7778-18-9 10101-41-4 (dihydrate)	OECD HPV sulphate category
Potassium magnesium sulphate	17855-14-0	OECD HPV sulphate category
Ammonium sulphate	7783-20-2	cation is ammonium and may be more toxic (OECD HPV ammonia category)
Sodium sulphate	7757-82-6 7727-73-3 (decahydrate)	

Substances in the sulphate category are all inorganic salts that contain a sulphate ion and are solid under ambient conditions. The vapour pressure of these salts is considered to be negligible. The sulphate salts are well soluble in water and dissociate into the sulphate ion and the corresponding cations in biological fluids and aquatic environments. The ions will enter the body electrolyte pool and are not expected to play a significant toxicological role. Inorganic salts are not expected to bioaccumulate.

Anion:
Sulphate is ubiquitous in aqueous environments. The European standard for drinking water is a maximum concentration of 250 mg/L.

Cation:
Most cations of this category (potassium and magnesium) are essential ions (called principle electrolytes and are present in the blood and various body fluids) playing an important role in sustaining health. Daily requirement of salts and minerals of an adult person depends very much on the cation, but can be found in several fruits, vegetables and animal products. The excess of salts taken as food additives are excreted in urine by the kidneys. The acceptable daily intake, as described by the Dutch Voedingscentrum, for calcium is 1-2.5 g/day, ca. 3.5 g potassium/day, maximum of 2.4 g sodium/day, 250-400 mg/day of magnesium.

The ammonium cation (NH_4^+) is not an essential ion, but a toxic waste product from animal metabolism that is re-used in protein synthesis via glutamate. Depending on the animal species, ammonium will be directly excreted to the environment or it will first be converted to urea, which is less toxic and can be stored more efficiently. In addition, ammonium is an important source of nitrogen for several plants.

The main assumption is that the cations are not expected to play a significant (eco)toxicological role at investigated doses and any (eco)toxicological effect seen will relate to the sulfate portion of the substances included in the category. Hence missing toxicological and ecotoxicological properties of one of the present substances, can be read across from another substance of the sulfate category.

5.1. Toxicokinetics (absorption, metabolism, distribution and elimination)

5.1.1. Non-human information

The results of experimental studies on absorption, metabolism, distribution and elimination are summarised in the following table:

Table 9. Overview of experimental studies on absorption, metabolism, distribution and elimination

Method	Results	Remarks	Reference
no guideline as it is an expert statement	50% oral, dermal and inhalation absorption	2 (reliable with restrictions) key study expert statement **Test material (Common name): magnesium sulphate**	Teunissen, M.S. (2010)

5.1.2. Human information

No data available.

5.1.3. Summary and discussion of toxicokinetics

In aqueous environments, such as the body the magnesium sulphate is completely dissociated into the magnesium (Mg2+) and the sulfate (SO4 2-) ions.

Absorption of sulphate depends on the amount ingested. 30 - 44% of sulfate was excreted in the 24-h urine after oral administration of magnesium or sodium sulfate (5.4 g sulfate) in volunteers. At high sulphate doses that exceed intestinal absorption, sulphate is excreted in feces. Intestinal sulphate may bind water into the lumen and cause diarrhoea in high doses. Sulphate is a normal constituent of human blood and does not accumulate in tissues. Sulphate levels are regulated by the kidney through a reabsorption mechanism. Sulphate is usually eliminated by renal excretion. It has also an important role in the detoxification of various endogenous and exogenous compounds, as it may combine with these to form soluble sulphate esters that are excreted in the urine (EPA, 2002).

Based on low MW, high water solubility, assumed low logPow high absorption is expected. However, the ion formation of the substance inmediately when in contact with a fluid decreases the absorption. The guidance has also been taken into consideration. Therefore, 50% absorption is taken for oral, dermal and inhalation exposure.

5.2. Acute toxicity

5.2.1. Non-human information

5.2.1.1. Acute toxicity: oral

The results of experimental studies are summarised in the following table:

Table 10. Overview of experimental studies on acute toxicity after oral administration

Method	Results	Remarks	Reference
rat (Sprague-Dawley) male/female oral: gavage OECD Guideline 425 (Acute Oral Toxicity: Up-and-Down Procedure)	LD50: > 2000 mg/kg bw (male/female)	2 (reliable with restrictions) key study experimental result	Product Safety Laboratories (2000)

Method	Results	Remarks	Reference
		read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): potassium magnesium sulphate (See endpoint summary for justification of read-across)**	

5.2.1.2. Acute toxicity: inhalation

Data waiving

Reason: other justification

Justification: In accordance with column 2 of REACH Annex VIII an acute inhalation toxicity study (as required in section 8.5.2) is not considered necessary, as for two routes of exposure, oral and dermal, acute toxicity studies are needed and available. In addition, the vapour pressure is assumed to be very low.

5.2.1.3. Acute toxicity: dermal

The results of experimental studies are summarised in the following table:

Table 11. Overview of experimental studies on acute toxicity after dermal administration

Method	Results	Remarks	Reference
rat (Crl:WI (Han)) male/female Coverage: occlusive OECD Guideline 402 (Acute Dermal Toxicity) EU Method B.3 (Acute Toxicity (Dermal)) EPA OPPTS 870.1200 (Acute Dermal Toxicity) Japanese Ministry of Agriculture, Forestry and Fisheries (JMAFF), 12 Nousan, Notification No 8147, November 2000; including the most recent partial revisions.	LD50: > 2000 mg/kg bw (male/female) based on: test mat.	1 (reliable without restriction) key study experimental result read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): potassium sulphate (See endpoint summary for justification of read-across)**	Dr. C.G.M. Beerens-Heijnen (2010a)

5.2.1.4. Acute toxicity: other routes

The results of studies on acute toxicity (other routes) are summarised in the following table:

Table 12. Overview of studies on acute toxicity (other routes)

Method	Results	Remarks	Reference
no data no data not mentioned		4 (not assignable) supporting study **Test material (EC name): magnesium sulphate**	Richard J. Lewis, Sr. (1994)
mouse intraperitoneal not mentioned	LD50: 1029 mg/kg bw	4 (not assignable) supporting study **Test material (EC name): magnesium sulphate**	RTECS 1998 (1998)
dog intraperitoneal not mentioned	LDLo: 1200 mg/kg bw	4 (not assignable) supporting study **Test material (EC name): magnesium sulphate**	Anonymous (1935)

5.2.2. Human information

No information available.

5.2.3. Summary and discussion of acute toxicity

No reliable acute toxicity studies are available for magnesium sulphate. However, several second source publications show a high acute oral toxicity for magnesium sulphate. This is confirmed by reliable acute oral toxicity study performed in rats according to OECD 425 with potassium magnesium sulphate (LD50 > 2000 mg/kg bw). For acute dermal toxicity a reliable OECD, EC and EPA guideline study with potassium sulphate is available, showing an LD50>2000 mg/kg bw. In addition, reliable OECD guideline studies with ammonium sulphate (Yamanaka et all., 1990) also show acute oral and dermal toxicity values (LD50) of > 2000 mg/kg bw. A reliable acute oral toxicity study with ammonium phosphate sulphate also showed an LC50>2000 mg/kg bw. Therefore, acute toxicity studies with two possible routes of exposure are available and thus no acute inhalation study is required. However, a study with ammonium sulphate is available showing an LC50 of > 1200 mg/m3 (highest attainable concentration).

The following information is taken into account for any hazard / risk assessment:

No reliable study with magnesium sulphate is present. With potassium sulphate a reliable acute dermal toxicity study in rats (according to OECD 402) has been performed showing an LD50 > 2000 mg/kg bw. Reliable acute oral toxicity studies with rats according to OECD 425, one with potassium magnesium sulphate and another one with ammonium phosphate sulphate have been performed, and both showed LD50s>2000 mg/kg bw.

Value used for CSA:

LD50 (oral): >2000 mg/kg bw

LD50 (dermal): >2000 mg/kg bw

Justification for classification or non classification

All data available show that magnesium sulphate does not have to be classified for acute toxicity according to Directive 67/548/EC and the CLP Directive.

5.3. Irritation

5.3.1. Skin

5.3.1.1. Non-human information

The results of experimental studies on skin irritation are summarised in the following table:

Table 13. Overview of experimental studies on skin irritation

Method	Results	Remarks	Reference
in vitro study EU method B.46 (In Vitro Skin Irritation: Reconstructed Human Epidermis Model Test) OECD Draft Proposal for a New Guideline: In Vitro Skin Irritation: Reconstructed Human Epidermis (RhE) Test Method	not irritating percentage viability: 105 (percentage of control) (Time point: 15 minutes)	1 (reliable without restriction) key study experimental result read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): potassium sulphate (See endpoint summary for justification of read-across)**	Drs. C.A.F. Buskens (2010)

Data waiving

Reason: study scientifically unjustified

Justification: According to section 1.4, Annex XI of REACH, an in vivo study is not scientifically necessary, as the in vitro study present in this dossier is accepted by ESAC in 2007 (at the 26th meeting at ECVAM) to be a reliable and stand alone test for skin irritation and thus a replacement of the in vivo study.

5.3.1.2. Human information

No information available.

5.3.2. Eye

5.3.2.1. Non-human information

The results of experimental studies on eye irritation are summarised in the following table:

Table 14. Overview of experimental studies on eye irritation

Method	Results	Remarks	Reference

Method	Results	Remarks	Reference
rabbit (New Zealand White) OECD Guideline 405 (Acute Eye Irritation / Corrosion) EU Method B.5 (Acute Toxicity: Eye Irritation / Corrosion) EPA OPPTS 870.2400 (Acute Eye Irritation) Japanese Ministry of Agriculture, Forestry and Fisheries (JMAFF), 12 Nousan, Notification No 8147, November 2000, including the most recent partial revisions.	not irritating Cornea score: 0 of max. 4 (mean) (Time point: 24, 48 and 72 hours) Iris score: 0 of max. 2 (mean) (Time point: 24, 48 and 72 hours) (fully reversible within: 24 hrs) Conjunctivae score: 1 of max. 3 (mean) (Time point: 24, 48 and 72 hours) (fully reversible within: 48 hours in one animal and within 14 days in the other two animals.) 0 of max. 3 (mean) (Time point: 24, 48 and 72 hours) (fully reversible within: 24 hours in one animal and 48 hours in the other two animals) Chemosis score: 0 of max. 4 (mean) (Time point: 24, 48 and 72 hours) (fully reversible within: 24 hours in two animals and 48 hours in the other animal)	1 (reliable without restriction) key study experimental result read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): potassium sulphate (See endpoint summary for justification of read-across)**	Dr. C.G.M. Beerens-Heijnen (2010b)

5.3.2.2. Human information

No information available.

5.3.3. Respiratory tract

5.3.3.1. Non-human information

No information available.

5.3.3.2. Human information

No information available.

5.3.4. Summary and discussion of irritation

For both the skin and eye irritation no studies for magnesium sulphate are available. In the category of inorganic sulphates, well performed study (reports) are present for a. o. potassium sulphate. For skin irritation an in vitro test with human skin according to EU guideline B46 and draft OECD guidelines with potassium sulphate the soluble grade (incl. 15% KHSO4) shows no irritation. This is considered to be the worst case form compared to the potassium sulphate solid form (and thus also the magnesium sulphate). An in vivo eye irritation study in rabbits performed according to OECD 405 shows that potassium sulphate (solid) is not irritating. Although some irritation was observed in the first 24 hours, this was in most animals reversible within 48 hours. Two animals showed some redness (score 1) up to 7 days after exposure, but reversible within 14 days. As

magnesium sulphate does not contain KHSO4, this study can be used for magensium sulphate. In addition skin and eye irritation studies with ammonium sulphate also show no irritation. Therefore, magnesium sulphate is considered to be not irritant to skin and eyes.

The following information is taken into account for any hazard / risk assessment:

No studies with magnesium sulphate are available. Based on reliable studies with potassium sulphate showing no to minimal irritation to the skin and eye, it is concluded that that magnesium sulphate is not irritating to skin and eye. Results with ammonium sulphate are in agreement with this.

Value used for CSA:

Skin irritation / corrosion: not irritating

Eye irritation: not irritating

Justification for classification or non classification

Based on the available data magnesium sulphate does not have to be classified for skin or eye irritation according to Directive 67/548/EC and to the CLP Directive.

5.4. Corrosivity

5.4.1. Non-human information

The substance is not considered to be corrosive. See chapter 5.3 for information on irritation.

5.4.2. Human information

No information available.

5.4.3. Summary and discussion of corrosion

The substance is not considered to be corrosive. See chapter 5.3 for information on irritation.

5.5. Sensitisation

5.5.1. Skin

5.5.1.1. Non-human information

The results of experimental studies on skin sensitisation are summarised in the following table:

Table 15. Overview of experimental studies on skin sensitisation

Method	Results	Remarks	Reference
mouse (CBA) female Local lymph node assay OECD Guideline 429 (Skin Sensitisation: Local Lymph Node Assay)	not sensitising Stimulation index: The SI values calculated for the substance concentrations 10, 25 and 50% were 0.8, 1.2 and 1.0 respectively. See table 4 and figure 1 of attached document 'Figures	1 (reliable without restriction) key study experimental	Dr. C.G.M. Beerens-Heijnen (2010c)

Method	Results	Remarks	Reference
EU Method B.42 (Skin Sensitisation: Local Lymph Node Assay) EPA OPPTS 870.2600 (Skin Sensitisation)	and tables'.	result **Test material (EC name): magnesium sulphate**	

5.5.1.2. Human information

No information available.

5.5.2. Respiratory system

5.5.2.1. Non-human information

No data available: not required.

5.5.2.2. Human information

No information available.

5.5.3. Summary and discussion of sensitisation

Skin sensitisation

In a skin sensitisation study (LLNA) with magnesium sulphate itself, according to OECD 429, EU B.42 and OPPTS 870.2600 it was shown that the substance is not sensitising. All auricular lymph nodes of the animals of the experimental and control groups were considered normal in size. No macroscopic abnormalities of the surrounding area were noted in any of the animals.

The following information is taken into account for any hazard / risk assessment:

In a LLNA study with magnesium sulpate it is clear that the substance does not show any sensitising properties.

Value used for CSA: not sensitising

Justification for classification or non classification

According to Directive 67/548/EC and the CLP Directive no classification of magnesium sulphate for sensitisation is required based on the reliable data present.

5.6. Repeated dose toxicity

5.6.1. Non-human information

5.6.1.1. Repeated dose toxicity: oral

The results of experimental studies are summarised in the following table:

Table 16. Overview of experimental studies on repeated dose toxicity after oral administration

Method	Results	Remarks	Reference
rat (Crj: CD(SD)) male/female combined repeated dose and reproduction / developmental screening (oral: gavage) 0, 50, 750, and 1,500 mg/kg/day (Doses were selected based on parameters assessed in a range-finding study at concentrations up to 1,000 mg/kg/day) (nominal in diet) Exposure: Animals in the study were divided between two subgroups (toxicity and reproductive subgroups). The exposure period for males and females in the toxicity subgroup was 28 days. The exposure period for reproductive subgroup males was at most 28 days. The exposure period for reproductive subgroup females was at most 53 days (14 days pre-mating, 14 days mating, and gestational and lactational periods up to lactation day 4). (7 days/week) OECD Guideline 422 (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test)	NOAEL: >= 1500 mg/kg bw/day (nominal) (male/female) based on: test mat. (General toxicity) NOAEL: >= 1500 mg/kg bw/day (nominal) (male/female) based on: test mat. (reproduction/developmental toxicity) LOAEL: > 1500 mg/kg bw/day (nominal) based on: test mat. (No adverse effects were seen on general toxicity endpoints. No adverse effects were seen on reproduction/developmental toxicity endpoints)	2 (reliable with restrictions) key study experimental result read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): potassium sulphate (See endpoint summary for justification of read-across)**	Product Safety Laboratories (2002a)
rat (Fischer 344) male/female chronic (oral: feed) 42, 256, 1527 mg/kg bw/day (males); 48, 284, 1490 mg/kg bw/d (females (actual ingested, 52-week chronic toxicity study) 0.1, 0.6, 3.0% in the diet (nominal in diet, 52-week chronic toxicity study) 564.1, 1288.2 mg/kg bw/d (males); 649.9, 1371.4 mg/kg bw/d (females) (actual ingested, 2-year carcinogenicity study) 1.5, 3 % in the diet (nominal in diet 2-year carcinogenicity study) Exposure: 52 and 104 weeks (continuously in the diet) equivalent or similar to OECD Guideline 453 (Combined Chronic Toxicity / Carcinogenicity Studies)	NOAEL: 256 mg/kg bw/day (actual dose received) (male) (0.6% in the diet) NOAEL: 284 mg/kg bw/day (actual dose received) (female) (0.6% in the diet)	1 (reliable without restriction) key study experimental result read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): ammonium sulphate (See endpoint summary for justification of read-across)**	Ota Y. et al. (2006)

Method	Results	Remarks	Reference
rat (Fischer 344/DuCrj) male/female subchronic (oral: feed) 220, 441, 886, 1792 mg/kg bw/d (males); 239, 484, 961, 1975 mg/kg bw/d (females) (actual ingested) 0.38, 0.75, 1.5, 3% in the diet (nominal in diet) Exposure: 13 weeks (continuously in the diet) no data	NOAEL: 886 mg/kg bw/day (actual dose received) (male) (1.5% in the diet; based on diarrhea observed in 3% males during the administration period.) NOAEL: 1975 mg/kg bw/day (actual dose received) (female) (3% in the diet; highest dose applied)	2 (reliable with restrictions) supporting study experimental result read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): ammonium sulphate (See endpoint summary for justification of read-across)**	Takagi H et al. (1999)

5.6.1.2. Repeated dose toxicity: inhalation

Data waiving

Information requirement (Test type):

Reason: other justification

Justification: According to column 2 of REACH Annex VIII and IX, the likely route of exposure shall be chosen for repeated dose toxicity studies. However, as already oral toxicity studies are present, and oral exposure is possible for the general population, no other repeated dose study with inhalation exposure seems to be necessary.

5.6.1.3. Repeated dose toxicity: dermal

Data waiving

Information requirement (Test type):

Reason: other justification

Justification: According to column 2 of REACH Annex VIII and Annex IX, the likely route of exposure shall be chosen for repeated dose toxicity studies. However, as already oral toxicity studies are present, and oral exposure is possible for the general population, no other repeated dose study with dermal exposure seems to be necessary.

5.6.1.4. Repeated dose toxicity: other routes

No information available.

5.6.2. Human information

No information available.

5.6.3. Summary and discussion of repeated dose toxicity

Discussion

Oral

No studies with magnesium sulphate are present. However, reliable repeated dose toxicity studies are present for other sulphate compounds from the sulphate category. A 28-day oral OECD 422 study has been performed in rats (5 rats/sex/dose) via gavage, containing 50, 750 or 1500 mg/kg bw/day potassium sulphate. There were no treatment-related deaths and no signs of overt clinical toxicity. There were no effects on body weight, food consumption, or food efficiency. Functional observational battery (FOB) and motor activity tests identified no treatment-related changes in behavior, function, or motor activity. Dams at 1,500 mg/kg/day experienced slightly lower food consumption and body weight than the controls during the gestation period only. Because of their moderate and transient nature, these observable effects were considered a LOEL rather than a LOAEL. No treatment-related histopathological changes were reported. Therefore, it was concluded that the NOAEL is 1500 mg/kg bw/day (or higher, highest dose tested).

In a 13-week study rats (10/sex/dose) were exposed to diet containing 0, 0.38, 0.75, 1.5 or 3 % ammonium sulfate (corresponding to 0, 222, 441, 886, 1792 mg/kg bw/day in males and to 0, 239, 484, 961, 1975 mg/kg bw/day in females). No substance-related changes were found in body weights, haematology and serum parameters, or in the histological examinations (brain, heart, lung, liver, kidney, adrenal gland, spleen, testes, thymus). The relative testes weight was significantly increased at all doses, but no histological effects were found, not considered to be treatment related. Male animals of the highest dose group exhibited diarrhea during the administration period. According to the authors the NOAEL (male) was 886 mg/kg bw/day and the NOAEL (female) was 1975 mg/kg bw/day.

A chronic oral toxicity and carcinogenicity study was conducted in rats, similar to the requirements of OECD TG 453. In the subchronic part of the study, groups of 10 rats/sex were fed a diet containing the test substance (purity not given) at concentrations of 0, 0.1, 0.6, or 3% for 1 year. These concentrations corresponded to average daily intakes of 0, 42, 256, and 1527 mg/kg bw/d for males and 0, 48, 248, and 1490 mg/kg bw/d for females, respectively. For investigation of the carcinogenic potential, groups of 50 rats/sex were fed a diet containing the test substance (purity not given) at concentrations of 0, 1.5, or 3% for 2 years. These concentrations corresponded to average daily intakes of 0, 465.1, and 1288.2 mg/kg bw/d for males and 0, 649.9, and 1371.4 mg/kg bw/d for females respectively. Absolute and relative kidney weights were increased at the high dose level for both sexes. Absolute spleen weights were decreased and relative liver weights were increased in high dose males. No macroscopic changes were recorded by gross pathology, except for massive nodular or focal lesions suggesting neoplastic changes. At histopathological examination, non-neoplastic and neoplastic lesions were noted in the control and treatment groups, with no significant inter-group difference in their incidences or severity. The authors concluded that the no observed adverse effect level of ammonium sulfate was the 0.6% diet, which is equivalent to 256 and 284 mg/kg bw/d in males and females, respectively, and the compound is noncarcinogenic under the conditions of the study. There was no evidence of a long-term carcinogenic activity of the test substance.

Dermal

No dermal studies are present.

Inhalation

No inhalation studies are present.

The following information is taken into account for any hazard / risk assessment:

No reliable studies with magnesium sulphate are available. A subacute oral toxicity study in rats with potassium sulphate shows no toxicity up to the highest dose tested (1500 mg/kg bw/day). In a chronic study with ammonium sulphate absolute and relative kidney weights were increased at the high dose level for both sexes, absolute spleen weights were decreased and relative liver weights were increased in high dose males.

Based on these reliable studies with potassium sulphate and ammonium sulphate for oral repeated dose toxicity, the rat oral NOAEL for the sulphate category is 1500 mg/kg bw/day for subacute toxicity. For chronic toxicity

the NOAEL for the sulphate category is 256 mg/kg bw/day.

Value used for CSA (route: oral):

NOAEL: 256 mg/kg bw/day (chronic; rat)

Justification for classification or non classification

The high NOAELs found in the subacute oral toxicity study with potassium sulphate in rats and in a chronic oral toxicity study with ammonium sulphate, indicate that no classification is required for magnesium sulphate according to Directive 67/548/EC and the CLP directive.

5.7. Mutagenicity

5.7.1. Non-human information

5.7.1.1. In vitro data

The results of experimental studies are summarised in the following table:

Table 17. Overview of experimental in vitro genotoxicity studies

Method	Results	Remarks	Reference
bacterial reverse mutation assay (e.g. Ames test) (gene mutation) S. typhimurium TA 1535, TA 1537, TA 98 and TA 100 (met. act.: with and without) E. coli WP2 uvr A (met. act.: with and without) Doses: 75, 200, 600, 1,800, and 5,000 µg/plate OECD Guideline 471 (Bacterial Reverse Mutation Assay)	Evaluation of results: negative Test results: negative for S. typhimurium TA 1535, TA 1537, TA 98 and TA 100(all strains/cell types tested); met. act.: with and without; cytotoxicity: no, but tested up to limit concentrations negative for E. coli WP2 uvr A(all strains/cell types tested); met. act.: with and without; cytotoxicity: no, but tested up to limit concentrations	1 (reliable without restriction) key study experimental result read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): potassium sulphate (See endpoint summary for justification of read-across)**	Wagner, V.O. and Klug, M.L. (2001)
mammalian cell gene mutation assay (gene mutation) mouse lymphoma L5178Y cells (met. act.: with and without) Doses: Dose range finding test: Without and with S9-mix, 3 hours treatment: 3, 10, 33, 100 and 333 µg/mL Without S9-mix, 24 hours treatment: 3, 10, 33, 100 and 333 µg/ml and 0.003, 0.01, 0.03, 0.1, 0.3, 1 and 3 µg/mL Experiment 1: Without S9-mix, 3 hours	Evaluation of results: negative Test results: negative for mouse lymphoma L5178Y cells(strain/cell type: L5178Y/TK+/-3.7.2C); met. act.: with and without; cytotoxicity: no (but cytotoxicity found in screening study.)	1 (reliable without restriction) key study experimental result **Test material (EC name): magnesium sulphate**	C.M. Verspeek-Rip (2010)

Method	Results	Remarks	Reference
treatment: 0.003, 0.03, 0.1, 0.25, 0.5, 1, 1.4 and 2 µg/mL With S9-mix, 3 hours treatment: 0.01, 0.03, 0.1, 0.3, 1, 3, 10 and 12 µg/mL Experiment 2 Without S9-mix, 24 hours treatment: 0.01, 0.03, 0.1, 0.25, 0.5, 1, 1.4 and 1.8 µg/mL With S9-mix, 3 hours treatment: 0.01, 0.1, 1, 10, 12, 14, 16 and 17 µg/mL OECD Guideline 476 (In vitro Mammalian Cell Gene Mutation Test) EU Method B.17 (Mutagenicity - In Vitro Mammalian Cell Gene Mutation Test)			
in vitro mammalian chromosome aberration test (chromosome aberration) Chinese hamster Ovary (CHO) (met. act.: with and without) Doses: 217.5, 435, 870, and 1,740 µg/mL OECD Guideline 473 (In vitro Mammalian Chromosome Aberration Test)	Evaluation of results: negative Test results: negative for Chinese hamster Ovary (CHO)(all strains/cell types tested); met. act.: with and without; cytotoxicity: no	1 (reliable without restriction) key study experimental result read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): potassium sulphate (See endpoint summary for justification of read-across)**	Gudi, R and Brown, C. (2001)

5.7.1.2. In vivo data

No information available.

5.7.2. Human information

No information available.

5.7.3. Summary and discussion of mutagenicity

Discussion

No Ames or chromosome aberration study with magensium sulphate is present.

However, an in vitro Ames test performed according to OECD test guideline 471 with potassium sulphate showed no mutagenicity with or without metabolic activation in 4 strains of Salmonella typhimurium (TA98, TA100, TA1535 and TA1537) and in E. coli bacteria (WP2 uvr A). The substance was tested up to the maximum concentration. In a second in vitro study according to OECD test guideline 473, CHO cells were exposed to 217.5, 435, 870, and 1,740 µg/mL with and without metabolic activation. No chromosome abberrations were found.

An in vitro TK assay in L5178Y mouse lymphoma cells with magnesium sulphate performed according to OECD 476 was present, showing no genotoxicity. Cells were exposed to a maximum of 2 µg/mL without metabolic activation and to a maximum of 17 µg/mL with metabolic activation and treated for 3 or 24 hours. Test concentrations were based upon cytotoxicity found in the screening study at

at dose levels of 1 or 3 µg/mL in the absence of metabolic activation for 24 or 3 hours treatment, respectively and at dose levels of 33 µg/mL in the presence of metabolic actvation.

In addition, ammonium sulphate also showed no mutagenicity in several in vitro tests, such as the Ames test and a chromosome aberration study.

The following information is taken into account for any hazard / risk assessment:

Only in vitro studies are present for sulphate salts. Potassium and ammonium sulphate were not mutagenic in Ames and chromosome aberration studies. Magensium sulphate itself was negative in a TK assay in mouse lymphoma cells.

Value used for CSA: Genetic toxicity: negative

Justification for classification or non classification

The available data indicate that no classification is required with regard to mutagenicity for magnesium sulphate according to Directive 67/548/EC and the CLP directive.

5.8. Carcinogenicity

5.8.1. Non-human information

5.8.1.1. Carcinogenicity: oral

The results of experimental studies are summarised in the following table:

Table 18. Overview of experimental studies on carcinogenicity after oral administration

Method	Results	Remarks	Reference
rat (Fischer 344) male/female oral: feed 42, 256, 1527 mg/kg bw/day (males); 48, 284, 1490 mg/kg bw/d (females) (actual ingested (52-week chronic toxicity study)) 0.1, 0.6, 3.0% in the diet (nominal in diet (52-week chronic toxicity study)) 564.1, 1288.2 mg/kg bw/d (males); 649.9, 1371.4 mg/kg bw/d (females) (actual ingested (2-year carcinogenicity study))	NOAEL (toxicity): 256 mg/kg bw/day (male) (estimated from the chronic toxicity study) NOAEL (toxicity): 284 mg/kg bw/day (female) (estimated from the chronic toxicity study)	1 (reliable without restriction) key study experimental result read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): ammonium sulphate (See endpoint summary for justification of**	Ota Y. et al. (2006)

Method	Results	Remarks	Reference
1.5, 3 % in the diet (nominal in diet (2-year carcinogenicity study)) Exposure: 52 and 104 weeks (continuously in the diet) equivalent or similar to OECD Guideline 453 (Combined Chronic Toxicity / Carcinogenicity Studies)		**read-across)**	

5.8.1.2. Carcinogenicity: inhalation

No information available.

5.8.1.3. Carcinogenicity: dermal

No information available.

5.8.1.4. Carcinogenicity: other routes

No information available.

5.8.2. Human information

No information available.

5.8.3. Summary and discussion of carcinogenicity

Data waiving

Reason: other justification

Justification: In accordance with column 2 of REACH Annex X, no carcinogenicity study (required in section 8.9.1) needs to be proposed as magnesium sulphate is not genotoxic.

Discussion

No study is available with magnesium sulphate neither required as the substance is not genotoxic. However, a chronic oral toxicity and carcinogenicity study was conducted in rats, similar to the requirements of OECD Testguideline 453 with ammonium sulphate. For investigation of the carcinogenic potential, groups of 50 rats/sex were fed a diet containing the test substance at concentrations of 0, 1.5, or 3% for 2 years. These concentrations corresponded to average daily intakes of 0, 564.1, and 1288.2 mg/kg bw/d for males and 0, 4649.9, and 1371.4 mg/kg bw/d for females respectively.

Absolute and relative kidney weights were increased at the high dose level for both sexes. Absolute spleen weights were decreased and relative liver weights were increased in high dose males. No macroscopic changes were recorded by gross pathology, except for massive nodular or focal lesions suggesting neoplastic changes. At histopathological examination, non-neoplastic and neoplastic lesions were noted in the control and treatment groups, with no significant inter-group difference in their incidences or severity.

The authors concluded that the no observed adverse effect level of ammonium sulfate was the 0.6% diet, which

is equivalent to 256 and 284 mg/kg bw/d in males and females, respectively, and the compound is noncarcinogenic under the conditions of the study. There was no evidence of a long-term carcinogenic activity of the test substance.

The following information is taken into account for any hazard / risk assessment:

Although no carcinogenicity study seems to be required for magnesium sulphate as the substance is not genotoxic, a reliable chronic/carcinogenicity study is available for ammonium sulphate. No evidence of a carcinogenic potential was observed in this study with rats following closely the requirements of OECD testguideline 453.

Value used for CSA (route: oral):

NOAEL: 284 mg/kg bw/day

Justification for classification or non classification

Magnesium sulphate does not have to be classified for carcinogenicity according to the Directive 67/548/EC or CLP Directive.

5.9. Toxicity for reproduction

5.9.1. Effects on fertility

5.9.1.1. Non-human information

The results of experimental studies are summarised in the following table:

Table 19. Overview of experimental studies on fertility

Method	Results	Remarks	Reference
rat (Wistar) male/female Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening oral: gavage 0, 50, 750, and 1,500 mg/kg/day Exposure: 28 days (daily) OECD Guideline 422 (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test)	NOAEL (reproduction/developmental toxicity) : >= 1500 mg/kg bw/day (nominal) (male/female) based on: test mat. (highest dose tested: no effects)	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): potassium sulphate (See endpoint summary for justification of read-across)**	Product Safety Laboratories (2002b)
mouse (ICR) male/female one-generation study oral: drinking water 625, 1250, 2500 or 5000 mg sulfate/l in drinking water (nominal in water) Exposure: Exposure period: from one week prior to breeding until study end (day 21 of second parity)	NOAEL (P): 5000 mg/L drinking water (female)	2 (reliable with restrictions) supporting study read-across from supporting substance (structural analogue or surrogate) **Test material (CAS number): 7727-73-3**	Andres CJ and Cline TR (1989)

Method	Results	Remarks	Reference
Premating exposure period (males): no treatment (tap water ad lib) Premating exposure period (females): 1 week (continuously in the drinking water) equivalent or similar to OECD Guideline 415 (One-Generation Reproduction Toxicity Study)		**(See endpoint summary for justification of read-across)**	

Data waiving

Reason: other justification

Justification: In accordance with column 2 of Annex IX and X no further studies are considered necessary. Magnesium sulphate dissociates into Mg+ and sulfate ions. Sulphate is a normal body and nutritional component and is regulated within the body. Mg+ is also a necessary element of which the ADI is 400 mg/day. Together with the available data showing no effects, an additional study is not considered necessary.

5.9.1.2. Human information

No information available.

5.9.2. Developmental toxicity

5.9.2.1. Non-human information

The results of experimental studies are summarised in the following table:

Table 20. Overview of experimental studies on developmental toxicity

Method	Results	Remarks	Reference
rat (Wistar) oral: gavage 0, 50, 750, 1500 mg/kg bw/day (nominal conc. (Control animals: Received the vehicle (distilled water) only at the same volume as the test groups.)) Exposure: Animals in the study were divided between two subgroups (toxicity and reproductive subgroups). The exposure period for males and females in the toxicity subgroup was 28days. The exposure period for the reproductive subgroup males was at most 28 days. The exposure period for reproductive subgroup females was at most 53 days (14 days mating and gestatioale	NOAEL (developemental/reproduction tox.): >= 1500 mg/kg bw/day (nominal) based on: test mat. (highest dose tested, no effects)	1 (reliable without restriction) key study read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): potassium sulphate (See endpoint summary for justification of read-across)**	Product Safety Laboratories (2002c)

Method	Results	Remarks	Reference
and lactational periods up to lactation day 4) (daily) OECD 422 and OPPTS 870.3650			

Data waiving

Reason: other justification

Justification: In accordance with column 2 of Annex IX and X no further studies are considered necessary. Magnesium sulphate dissociates into Mg+ and sulfate ions. Sulphate is a normal body and nutritional component and is regulated within the body. Mg+ is also a necessary element of which the ADI is 400 mg/day. Together with the available data showing no effects, an additional study is not considered necessary.

5.9.2.2. Human information

No information available.

5.9.3. Summary and discussion of reproductive toxicity

Discussion

Effects on fertility

No studies with magnesium sulphate are present. An OECD 422 study with rats shows no effects at all up to doses of 1500 mg/kg bw/day of potassium sulphate. No effects were found on reproduction parameters, neither embryotoxic or developmental effects were seen. No further studies with potassium sulphate were present.

In a 90-day toxicity study with ammonium sulfate no histological changes of testes were observed up to 1792 mg/kg bw/day. The ovaries were not examined.

In a one-generation study according to OECD 415 in female mice, sodium sulphate was given in drinking water at levels up to 5000 mg/L (ca. 1790 -6560 mg/kg bw/day), beginning one week prior to breeding and up to 14 days during lactation. No differences were found in litter size, litter weaning weights or gestational or lactational weight gain of the dams among sulphate treatements. No toxicity to the dams was found. Litters were not examined histopathologically and fertility indices were not measured. Only females were treated.

No further studies are considered necessary. Magnesium sulphate dissociates into Mg2+ and sulphate ions. Sulphate is a normal body and nutritional component and is regulated within the body. Mg2+ is also a necessary element of which the ADI is 400 mg/day. Together with the available data showing no effects, an additional 2 -generation reproduction is not considered necessary.

The following information is taken into account for any hazard / risk assessment:

No reliable study on magnesium sulphate is available. In a reliable OECD screening study in rats with potassium sulphate no effects were found up to the highest dose tested (1500 mg/kg bw/d). No further studies with potassium sulphate itself were present. However, in repeated dose studies with ammonium sulphate no effects on reproduction organs were found and in addition in a limited one-generation study where only females were treated with sodium sulphate no effects were found. In addition magnesium sulphate dissociates into Mg+ and sulfate ions, which are nutritional components regulated by the body. The overall conclusion for magnesium sulphate is that the substance may present a hazard to fertility but only at parentally toxic doses.

Value used for CSA (route: oral): NOAEL: ≥1500 mg/kg bw/day

Developmental toxicity

No studies with magnesium sulphate are present. An OECD 422 study with rats shows no effects at all up to doses of 1500 mg/kg bw/day of potassium sulphate. No effects were found on reproduction parameters, neither embryotoxic or developmental effects were seen. No further studies with potassium sulphate were present. With other sulphate compounds also no studies are available relating to developmental toxicity. However, in repeated dose studies with ammonium sulphate no effects on reproduction organs were found and in addition in a limited one-generation study where only females were treated with sodium sulphate no effects were found.

No further studies are considered necessary. Magnesium sulphate dissociates into Mg2+ and sulphate ions. Sulphate is a normal body and nutritional component and is regulated within the body. Mg2+ is also a necessary element of which the ADI is 400 mg/day. Together with the available data showing no effects, a developmental toxicity study is not considered necessary.

The following information is taken into account for any hazard / risk assessment:

No reliable study on magnesium sulphate is available.

In a reliable OECD screening study in rats with potassium sulphate no effects were found up to the highest dose tested (1500 mg/kg bw/d). No further studies with potassium sulphate itself were present. However, in repeated dose studies with ammonium sulphate no effects on reproduction organs were found and in addition in a limited one-generation study where only females were treated with sodium sulphate no effects were found. In addition, magnesium sulphate dissociates into Mg+ and sulphate ions which are nutritional components regulated by the body. The overall conclusion for magnesium sulphate is that there is no evidence that the substance may present a risk for developmental toxicity.

Value used for CSA (route: oral): NOAEL: ≥1500 mg/kg bw/day

Justification for classification or non classification

The results of the OECD screening study (a very high NOAEL) and data with other sulphate compounds do indicate that no classification is required for magnesium sulphate according to Directive 67/548/EC and the CLP directive for reproduction toxicity.

5.10. Other effects

5.10.1. Non-human information

5.10.1.1. Neurotoxicity

No information available.

5.10.1.2. Immunotoxicity

No information available.

5.10.1.3. Specific investigations: other studies

No information available.

5.10.2. Human information

No information available.

5.10.3. Summary and discussion of specific investigations

No information available.

5.11. Derivation of DNEL(s) / DMEL(s)

5.11.1. Overview of typical dose descriptors for all endpoints

Table 21. Available dose-descriptor(s) per endpoint for the submission substance as a result of its hazard assessment

Endpoint		Dose descriptor	Qualitative assessment	Remarks on study
Acute toxicity	oral	LD50: >2000 mg/kg bw		No reliable study with magnesium sulphate is present. With potassium sulphate a reliable acute dermal toxicity study in rats (according to OECD 402) has been performed showing an LD50 > 2000 mg/kg bw. Reliable acute oral toxicity studies with rats according to OECD 425, one with potassium magnesium sulphate and another one with ammonium phosphate sulphate have been performed, and both showed LD50s>2000 mg/kg bw.
Acute toxicity	dermal	LD50: >2000 mg/kg bw		
Acute toxicity	inhalation			
Irritation / Corrosivity	skin		not irritating	No studies with magnesium sulphate are available. Based on reliable studies with potassium sulphate showing no to minimal irritation to the skin and eye, it is concluded that that magnesium sulphate is not irritating to skin and eye. Results with ammonium sulphate are in agreement with this.
Irritation / Corrosivity	eye		not irritating	
Irritation / Corrosivity	respiratory tract			
Sensitisation	skin		not sensitising	In a LLNA study with magnesium sulpate it is clear that the substance does not show any sensitising properties.
Repeated dose toxicity: sub-acute / sub-chronic / chronic	oral	NOAEL: 256 mg/kg bw/day (chronic; rat)		No reliable studies with magnesium sulphate are available. A subacute oral toxicity study in rats with potassium sulphate shows no toxicity up to the highest dose tested (1500 mg/kg bw/day). In a chronic study with ammonium sulphate absolute and relative kidney weights were increased at the high dose level for both sexes, absolute spleen weights were decreased and relative liver weights were increased in high dose males. Based on these reliable studies with potassium sulphate and ammonium sulphate for oral repeated dose toxicity, the rat oral NOAEL for the sulphate category is 1500 mg/kg bw/day for subacute toxicity. For chronic toxicity the NOAEL for the sulphate category is 256 mg/kg bw/day.
Repeated dose toxicity: sub-acute / sub-chronic / chronic	dermal			
Repeated dose toxicity: sub-acute / sub-chronic / chronic	inhalation			

Endpoint		Dose descriptor	Qualitative assessment	Remarks on study
Mutagenicity	in vitro / in vivo		Genetic toxicity: negative	Only in vitro studies are present for sulphate salts. Potassium and ammonium sulphate were not mutagenic in Ames and chromosome aberration studies. Magensium sulphate itself was negative in a TK assay in mouse lymphoma cells.
Carcinogenicity	oral	NOAEL: 284 mg/kg bw/day		Although no carcinogenicity study seems to be required for magnesium sulphate as the substance is not genotoxic, a reliable chronic/carcinogenicity study is available for ammonium sulphate. No evidence of a carcinogenic potential was observed in this study with rats following closely the requirements of OECD testguideline 453.
Carcinogenicity	dermal			
Carcinogenicity	inhalation			
Reproductive toxicity: fertility impairment	oral	NOAEL: ≥1500 mg/kg bw/day		No reliable study on magnesium sulphate is available. In a reliable OECD screening study in rats with potassium sulphate no effects were found up to the highest dose tested (1500 mg/kg bw/d). No further studies with potassium sulphate itself were present. However, in repeated dose studies with ammonium sulphate no effects on reproduction organs were found and in addition in a limited one-generation study where only females were treated with sodium sulphate no effects were found. In addition magnesium sulphate dissociates into Mg+ and sulfate ions, which are nutritional components regulated by the body. The overall conclusion for magnesium sulphate is that the substance may present a hazard to fertility but only at parentally toxic doses.
Reproductive toxicity: fertility impairment	dermal			
Reproductive toxicity: fertility impairment	inhalation			
Reproductive toxicity: developmental toxicity	oral	NOAEL: ≥1500 mg/kg bw/day		No reliable study on magnesium sulphate is available. In a reliable OECD screening study in rats with potassium sulphate no effects were found up to the highest dose tested (1500 mg/kg bw/d). No further studies with potassium sulphate itself were present. However, in repeated dose studies with ammonium sulphate no effects on reproduction organs were found and in addition in a limited one-generation study where only females were treated with sodium sulphate no effects were found. In addition, magnesium sulphate dissociates into Mg+ and sulphate ions which are nutritional components regulated
Reproductive toxicity: developmental toxicity	dermal			
Reproductive	inhalation			

Endpoint		Dose descriptor	Qualitative assessment	Remarks on study
toxicity: developmental toxicity				by the body. The overall conclusion for magnesium sulphate is that there is no evidence that the substance may present a risk for developmental toxicity.

5.11.2. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptor for critical health effects

Table 22. DN(M)ELs for workers

Exposure pattern	Route	Descriptor	DNEL / DMEL	(Corrected) Dose descriptor *)	Most sensitive endpoint	Justification
Acute - systemic effects	Dermal					As an acute toxicity hazard leading to Classification and Labelling of the substance has not been identified, the long-term DNEL is considered sufficient to ensure that effects from acute exposure to the substance do not occur (in accordance with ECHA Guidance on information requirements and chemical safety assessment: Chapter R.8: Characterisation of dose [concentration]-response for human health, May 2008 and Part B: Hazard Assessment, Draft new chapter B.8 Scope of Exposure Assessment, March 2010).
Acute - systemic effects	Inhalation					As an acute toxicity hazard leading to Classification and Labelling of the substance has not been identified, the long-term DNEL is considered sufficient to ensure that effects from acute exposure to the substance do not occur (in accordance with ECHA Guidance on information requirements and chemical safety assessment: Chapter R.8: Characterisation of dose [concentration]-response for human health, May 2008 and Part B: Hazard Assessment, Draft new chapter B.8 Scope of Exposure Assessment, March 2010).
Acute - local effects	Dermal					Since no local effects were noted after dermal and inhalatory exposure, local DNELs were not derived.
Acute - local effects	Inhalation					Since no local effects were noted after dermal and inhalatory exposure, local DNELs were not derived.
Long-term - systemic effects	Dermal	DNEL (Derived No Effect Level)	21.3 mg/kg bw/day	NOAEL: 255.6 mg/kg bw/day (based on AF of	repeated dose toxicity	See discussion.

Exposure pattern	Route	Descriptor	DNEL / DMEL	(Corrected) Dose descriptor *)	Most sensitive endpoint	Justification
				12)		
Long-term - systemic effects	Inhalation	DNEL (Derived No Effect Level)	37.6 mg/m³	NOAEC: 451.2 mg/m³ (based on AF of 12)	repeated dose toxicity	See discussion.
Long-term - local effects	Dermal					Since no local effects were noted after dermal and inhalatory exposure, local DNELs were not derived.
Long-term - local effects	Inhalation					Since no local effects were noted after dermal and inhalatory exposure, local DNELs were not derived.

**) The (corrected) dose descriptor starting points have been automatically calculated by multiplying the values of the fields "D(N)MEL" and "Assessment factor" provided in the Endpoint summary of IUCLID section 7. Toxicological information. It reflects the value after any corrections, e.g. route-to-route extrapolation. See column "Justification" for the rationale behind such modifications and the use of assessment factors.*

Discussion

Starting point: NOAEL 256 mg/kg bw/day from a chronic oral study in rats.

Route-to-route extrapolation

For the derivation of the DNELs:

Long-term – dermal, systemic effects

Long-term – inhalation, systemic effects

Route-to-route extrapolation has been performed. In absence of relevant data, only differences between the different routes as determined by the assumed percentages of absorption into the systemic circulation could be accounted for (see toxicokinetic assessment).

Absorption oral (rat) = Absorption oral (human) = 50%

Absorption dermal (human) = 50%

Absorption inhalation (human) = 50%

The DNELs for human exposure are derived according to the ECETOC guidance (final draft).

Dermal DNEL

Route-to-route extrapolation:

Dermal NOAEL = oral NOAEL * ABSoral-rat/ABSderm-human = 256 * 50/50 = 256 mg/kg bw

Safety factors:

- Interspecies extrapolation: 4
- Intraspecies extrapolation: 3
- Exposure duration: 1 (assuming chronic worker exposure)
- Dose response: 1
- Quality of the data base: 1

Total safety factor: 12

Based on the above, the long-term DNEL for systemic effects after dermal worker exposure is set at 21.3 mg/kg bw/day.

Inhalation DNEL

Route-to-route extrapolation:

Inhalation NOAEL = oral NOAEL * ABSoral-rat/ABSinh-human = 256 * 50/50 = 256 mg/kg bw

Corrected inhalatory NOAEC = 256 * 1/0.38 * 6.7 m^3/10 m^3= 451 mg/m3

Safety factors:

- Interspecies extrapolation: 4

- Intraspecies extrapolation: 3
- Exposure duration: 1 (assuming chronic worker exposure)
- Dose response: 1
- Quality of the data base: 1

Total safety factor: 12

Based on the above, the long-term DNEL for systemic effects after inhalation exposure of the worker, is set at 37.6 mg/m^3.

Table 23. DN(M)ELs for the general population

Exposure pattern	Route	Descriptor	DNEL / DMEL	(Corrected) Dose descriptor *)	Most sensitive endpoint	Justification
Acute - systemic effects	Dermal					As an acute toxicity hazard leading to Classification and Labelling of the substance has not been identified, the long-term DNEL is considered sufficient to ensure that effects from acute exposure to the substance do not occur (in accordance with ECHA Guidance on information requirements and chemical safety assessment: Chapter R.8: Characterisation of dose [concentration]-response for human health, May 2008 and Part B: Hazard Assessment, Draft new chapter B.8 Scope of Exposure Assessment, March 2010).
Acute - systemic effects	Inhalation					As an acute toxicity hazard leading to Classification and Labelling of the substance has not been identified, the long-term DNEL is considered sufficient to ensure that effects from acute exposure to the substance do not occur (in accordance with ECHA Guidance on information requirements and chemical safety assessment: Chapter R.8: Characterisation of dose [concentration]-response for human health, May 2008 and Part B: Hazard Assessment, Draft new chapter B.8 Scope of Exposure Assessment, March 2010).
Acute - systemic effects	Oral					As an acute toxicity hazard leading to Classification and Labelling of the substance has not been identified, the long-term DNEL is considered sufficient to ensure that effects from acute exposure to the substance do not occur (in accordance with ECHA Guidance on information requirements and chemical safety assessment: Chapter R.8: Characterisation of dose [concentration]-response for human health, May 2008 and Part B: Hazard Assessment, Draft new chapter B.8 Scope of Exposure Assessment, March 2010).
Acute - local	Dermal					Since no local effects were noted after dermal and

Exposure pattern	Route	Descriptor	DNEL / DMEL	(Corrected) Dose descriptor *)	Most sensitive endpoint	Justification
effects						inhalatory exposure, local DNELs were not derived.
Acute - local effects	Inhalation					Since no local effects were noted after dermal and inhalatory exposure, local DNELs were not derived.
Long-term - systemic effects	Dermal	DNEL (Derived No Effect Level)	12.8 mg/kg bw/day	NOAEL: 256.0 mg/kg bw/day (based on AF of 20)	repeated dose toxicity	See discussion.
Long-term - systemic effects	Inhalation	DNEL (Derived No Effect Level)	11.1 mg/m³	NOAEC: 222.0 mg/m³ (based on AF of 20)	repeated dose toxicity	See discussion.
Long-term - systemic effects	Oral	DNEL (Derived No Effect Level)	12.8 mg/kg bw/day	NOAEL: 256.0 mg/kg bw/day (based on AF of 20)	repeated dose toxicity	See discussion.
Long-term - local effects	Dermal					Since no local effects were noted after dermal and inhalatory exposure, local DNELs were not derived.
Long-term - local effects	Inhalation					Since no local effects were noted after dermal and inhalatory exposure, local DNELs were not derived.

**) The (corrected) dose descriptor starting points have been automatically calculated by multiplying the values of the fields "D(N)MEL" and "Assessment factor" provided in the Endpoint summary of IUCLID section 7. Toxicological information. It reflects the value after any corrections, e.g. route-to-route extrapolation. See column "Justification" for the rationale behind such modifications and the use of assessment factors.*

Discussion

Starting point: NOAEL 256 mg/kg bw/day from a chronic oral study in rats.

Route-to-route extrapolation

For the derivation of the DNELs:

Long-term – dermal, systemic effects

Long-term – inhalation, systemic effects

Route-to-route extrapolation has been performed. In absence of relevant data, only differences between the different routes as determined by the assumed percentages of absorption into the systemic circulation could be accounted for (see toxicokinetic assessment).

Absorption oral (rat) = Absorption oral (human) = 50%

Absorption dermal (human) = 50%

Absorption inhalation (human) = 50%

The DNELs for human exposure are derived according to the ECETOC guidance (final draft).

Oral DNEL
Safety factors:

- Interspecies extrapolation: 4
- Intraspecies extrapolation: 5
- Exposure duration: 1 (assuming chronic exposure of the general population)
- Dose response: 1
- Quality of the data base: 1

Total safety factor: 20

Based on the above, the long-term DNEL for systemic effects after oral exposure of the general population, is set at 12.8 mg/kg bw/d.

Dermal DNEL

Route-to-route extrapolation:

Dermal NOAEL = oral NOAEL * ABSoral-rat/ABSderm-human = 256 * 50/50 = 256 mg/kg bw

Safety factors:

- Interspecies extrapolation: 4
- Intraspecies extrapolation: 5
- Exposure duration: 1 (assuming chronic exposure of the general population)
- Dose response: 1
- Quality of the data base: 1

Total safety factor: 20

Based on the above, the long-term DNEL for systemic effects after dermal exposure of the general population is set at 12.8 mg/kg bw/day.

Inhalation DNEL

Route-to-route extrapolation:

Inhalation NOAEL = oral NOAEL * ABSoral-rat/ABSinh-human = 256 * 50/50 = 256 mg/kg bw

Corrected inhalatory NOAEC = 256 * 1/1.15 = 223 mg/m3

Safety factors:

- Interspecies extrapolation: 4
- Intraspecies extrapolation: 5
- Exposure duration: 1 (assuming chronic exposure of the general population)
- Dose response: 1
- Quality of the data base: 1

Total safety factor: 20

Based on the above, the long-term DNEL for systemic effects after inhalation exposure of the general population is set at 11.1 mg/m^3.

6. HUMAN HEALTH HAZARD ASSESSMENT OF PHYSICO-CHEMICAL PROPERTIES

6.1. Explosivity

The available information on explosivity is summarised in the following table:

Table 24. Overview of information on explosivity

Method	Results	Remarks	Reference
EU Method A.14 (Explosive properties) United Nations (UN), UN no. ST/SG/AC.10/11/Rev. 4: Recommendations on the Transport of Dangerous Goods, Part I: Classification Procedures, Test Methods and Criteria Relating to Explosives of Class 1, Section 13: "Test Series 3", 2003. United Nations (UN), UN no. ST/SG/AC.10/11/Rev. 4: Recommendations on the Transport of Dangerous Goods, Appendix 6: "Screening Procedures", 2003.	Evaluation of results: non explosive Study results: Remarks: A test substance is considered explosive when it can react to produce very rapid increases in temperature or pressure. The test substance does not contain chemical groups which are associated with explosive properties.	1 (reliable without restriction) key study statement **Test material (EC name): magnesium sulphate**	Ir. M.J.C. Brekelmans (2010)
no data	Study results: Explosive (not specified): no	4 (not assignable) supporting study **Test material (EC name): magnesium sulphate**	Mallinckrodt Baker Inc. (2005)

The following information is taken into account for any hazard / risk assessment:

Based on the chemical composition, magnesium sulphate appears to be not explosive.

Classification according to GHS

Name: magnesium sulfate

Related composition: magnesium sulphate

State/form of the substance: solid

Reason for no classification: conclusive but not sufficient for classification

Classification according to DSD / DPD

Classification status: 67/548/EEC self classification (Magnesium sulphate)

Reason for no classification: conclusive but not sufficient for classification

Justification for classification or non-classification:

Magnesium sulphate appears to be not explosive. Therefore, the substance does not need to be classified for explosive properties according to Directive 67/548/EC and the CLP Directive.

6.2. Flammability

The available information on flammability is summarised in the following table:

Table 25. Overview of information on flammability

Method	Results	Remarks	Reference
Method followed is unknown, data taken from SDS.	Evaluation of results: non flammable	4 (not assignable) supporting study SDS **Test material (EC name): magnesium sulphate**	Mallinckrodt Baker, Inc (2005)

Data waiving: see CSR section 1.3 Physico-chemical properties.

The following information is taken into account for any hazard / risk assessment:

Based on the molecular structure of the inorganic substance magnesium sulphate, it was concluded that this substance is not flammable when coming into contact with an ignition source, with water or with air.

Classification according to GHS

Name: magnesium sulfate

Related composition: magnesium sulphate

State/form of the substance: solid

Reason for no classification (Flammable gases): data lacking

Reason for no classification (Flammable aerosols): data lacking

Reason for no classification (Flammable liquids): data lacking

Reason for no classification (Flammable solids): conclusive but not sufficient for classification

Classification according to DSD / DPD

Classification status: 67/548/EEC self classification (Magnesium sulphate)

Reason for no classification: conclusive but not sufficient for classification

Justification for classification or non-classification:

Based on the molecular structure of the inorganic substance magnesium sulphate, it was concluded that the substance is not flammable when coming into contact with an ignition source, with water or with air. Therefore, the substance does not need to be classified for flammability according to the Directive 67/548/EC and the CLP directive.

6.3. Oxidising potential

The available information on the oxidising potential is summarised in the following table:

Table 26. Overview of information on oxidising potential

Method	Results	Remarks	Reference
EU Method A.17 (Oxidising Properties (Solids)) United Nations (UN), UN no. ST/SG/AC.10/11/Rev. 4: Recommendations on the Transport of Dangerous Goods, Part III: Classification Procedures, Test Methods and Criteria Relating to Explosives: "Test for Oxidizing Solids", 2003. United Nations (UN), UN no. ST/SG/AC.10/11/Rev. 4: Recommendations on the Transport of Dangerous Goods, Appendix 6: "Screening Procedures", 2003.	Evaluation of results: no oxidising properties Remarks: A test substance is considered an oxidizing substance when the burning time of a mixture of the substance and cellulose in a 4:1 or 1:1 sample-to-cellulose ratio (by mass) is less than or equal to the mean burning time of a 3:7 reference mixture (by mass) of potassium bromate and cellulose. The test substance does not contain groups that act as an oxidizing agent. The oxygen atoms are part of a sulphate group which has no oxidizing properties.	1 (reliable without restriction) key study statement **Test material (EC name): magnesium sulphate**	Ir. M.J.C. Brekelmans (2010)

The following information is taken into account for any hazard / risk assessment:

Based on the chemical composition, magnesium sulphate appears to have no oxidising properties.

Classification according to GHS

Name: magnesium sulfate

Related composition: magnesium sulphate

State/form of the substance: solid

Reason for no classification (Oxidising gases): data lacking

Reason for no classification (Oxidising liquids): data lacking

Reason for no classification (Oxidising solids): conclusive but not sufficient for classification

Classification according to DSD / DPD

Classification status: 67/548/EEC self classification (Magnesium sulphate)

Reason for no classification: conclusive but not sufficient for classification

Justification for classification or non-classification:

Magnesium sulphate appears to have no oxidising properties. Therefore, the substance does not need to be classified for oxidising properties according to Directive 67/548/EC and the CLP Directive.

7. ENVIRONMENTAL HAZARD ASSESSMENT

The read across rationale for supporting substances is documented in a report (Read-across Approach for REACH registration of Sulphate substances) part of the IUCLID, section 0. The following substances are registered under REACH as part of the sulphate category:
1. Magnesium sulphate (CAS no. 7487-88-9, EC no. 231-298-2)
2. Potassium sulphate (CAS no. 7778-80-5, EC no. 231-915-5)

The following surrogates were used:

Surrogate	CAS no.	Comment
Calcium sulphate	7778-18-9 10101-41-4 (dihydrate)	OECD HPV sulphate category
Potassium magnesium sulphate	17855-14-0	OECD HPV sulphate category
Ammonium sulphate	7783-20-2	cation is ammonium and may be more toxic (OECD HPV ammonia category)
Sodium sulphate	7757-82-6 7727-73-3 (decahydrate)	

Substances in the sulphate category are all inorganic salts that contain a sulphate ion and are solid under ambient conditions. The vapour pressure of these salts is considered to be negligible. The sulphate salts are well soluble in water and dissociate into the sulphate ion and the corresponding cations in biological fluids and aquatic environments. The ions will enter the body electrolyte pool and are not expected to play a significant toxicological role. Inorganic salts are not expected to bioaccumulate.

Anion:
Sulphate is ubiquitous in aqueous environments. The European standard for drinking water is a maximum concentration of 250 mg/L.

Cation:
Most cations of this category (potassium and magnesium) are essential ions (called principle electrolytes and are present in the blood and various body fluids) playing an important role in sustaining health. Daily requirement of salts and minerals of an adult person depends very much on the cation, but can be found in several fruits, vegetables and animal products. The excess of salts taken as food additives are excreted in urine by the kidneys. The acceptable daily intake, as described by the Dutch Voedingscentrum, for calcium is 1-2.5 g/day, ca. 3.5 g potassium/day, maximum of 2.4 g sodium/day, 250-400 mg/day of magnesium.

The ammonium cation (NH_4^+) is not an essential ion, but a toxic waste product from animal metabolism that is re-used in protein synthesis via glutamate. Depending on the animal species, ammonium will be directly excreted to the environment or it will first be converted to urea, which is less toxic and can be stored more efficiently. In addition, ammonium is an important source of nitrogen for several plants.

The main assumption is that the cations are not expected to play a significant (eco)toxicological role at investigated doses and any (eco)toxicological effect seen will relate to the sulfate portion of the substances included in the category. Hence missing toxicological and ecotoxicological properties of one of the present substances, can be read across from another substance of the sulfate category.

7.1. Aquatic compartment (including sediment)

7.1.1. Toxicity test results

7.1.1.1. Fish

7.1.1.1.1. Short-term toxicity to fish

The results are summarised in the following table:

Table 27. Overview of short-term effects on fish

Method	Results	Remarks	Reference
Pimephales promelas freshwater static USEPA. 1991. EPA/600/4-90/027 USEPA. 1991. EPA/600/6-91/003	LC50 (96 h): 680 mg/L test mat.	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): potassium sulphate (See endpoint summary for justification of read-across)**	Mount, D.R., Gulley, D.D., Hockett, R., Garrison, T.D., and Evans, J.M (1997)
Oncorhynchus mykiss freshwater static OECD Guideline 203 (Fish, Acute Toxicity Test)	LC50 (96 h): > 63.6 mg/L test mat.	2 (reliable with restrictions) supporting study read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): potassium magnesium sulphate (See endpoint summary for justification of read-across)**	Madsen, T.J. and Bussard, J.B. (2000)
Lepomis macrochirus freshwater static	LC50 (24 h): 19000 mg/L	4 (not assignable) supporting study **Test material (EC name): magnesium sulphate**	Dowden, B.F., Bennett, H.J., (1965)
Gambusia affinis static	LC50 (24 h): 15500 mg/L LC50 (48 h): 15000 mg/L LC50 (96 h): 15000 mg/L	4 (not assignable) supporting study experimental result **Test material (EC name): magnesium sulphate**	Wallen, I.E., Greer, W.C., Lasater, R. (1957)
Leuciscus idus melanotus static German standard methods for the analysis of water, waste water and sludge; bio assays (group L); determination of the effect of	LC50 (48 h): 14000 mg/L	4 (not assignable) supporting study experimental result **Test material (EC name): magnesium**	INNOLAB GmbH & Co. KG, (1994a)

Method	Results	Remarks	Reference
substances in water to fish - fish test (L 15)		**sulphate**	

Discussion

No reliable data on magnesium sulphate itself are present. Several supporting studies show LC50s from 24 -96 hr of > 10000 mg/L. A key study on potassium sulphate and potassium magnesium sulphate is available. As for the potassium magnesium sulphate no effect has been found at the highest dose tested (63.3 mg/L) and the sulphate contains a double salt, the study with potassium sulphate is a key study. The static study was performed according to EPA test guidelines with fathead minnow fish and a 96hr LC50 of 680 mg/L was determined. Although fish were fed once during the study it is not expected that this will affect the result. Analytical monitoring was performed.

The following information is taken into account for acute fish toxicity for the derivation of PNEC:

No reliable data on acute toxicity to fish are available for magnesium sulphate. Based on a reliable study on potassium sulphate the LC50 for freshwater fish for the sulfate category is 680 mg/L.

Value used for CSA:

LC50 for freshwater fish: 680 mg/L

7.1.1.1.2. Long-term toxicity to fish

Data waiving

Reason: other justification

Justification: In accordance with column 2 of REACH Annex IX, no long term toxicity testing is proposed (required in section 9.1.6) as the chemical safety assessment does not indicate a need to further investigate the effects on fish. All data available on magnesium sulphate itself and on the other sulphates show a very low toxicity of magnesium sulphate. In addtion, the substance does have a very high water solubility and its chemical properties do not indicate bioaccumulation. Therefore, the study is not considered necessary.

7.1.1.2. Aquatic invertebrates

7.1.1.2.1. Short-term toxicity to aquatic invertebrates

The results are summarised in the following table:

Table 28. Overview of short-term effects on aquatic invertebrates

Method	Results	Remarks	Reference
Daphnia magna freshwater static USEPA. 1991. EPA/600/4-90/027 USEPA. 1991. EPA/600/6-91/003	LC50 (48 h): 720 mg/L	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): potassium**	Mount, D.R., Gulley, D.D., Hockett, R., Garrison, T.D., and Evans, J.M. (1997)

Method	Results	Remarks	Reference
		sulphate (See endpoint summary for justification of read-across)	
Daphnia magna German standard methods for the analysis of water, waste water and sludge; bioassays (group L); determination of the effect of substances in water on microcrustacean (daphnia-shorttime-test) (L 11)	EC50 (24 h): 1700 mg/L	4 (not assignable) supporting study experimental result **Test material (EC name): magnesium sulphate**	INNOLAB GmbH & Co. KG, (1994b)

Discussion

No reliable data on magnesium sulphate itself are present. A supporting study shows LC50s of 24 hr of > 1000 mg/L. A key study on potassium sulphate is available. The static study was performed according to EPA test guidelines with daphnia magna exposed to 500, 1000, 1250, 1500, 2000, 2500, 5000, and 10000 mg/L (nominal concentrations) and a 48hr LC50 of 720 mg/L was determined. Analytical monitoring was performed.

The following information is taken into account for short-term toxicity to aquatic invertebrates for the derivation of PNEC:

No reliable study on magnesium sulphate is present. Based on a reliable 48-hours study with daphnia magna performed on potassium sulphate the LC50 is determined to be 720 mg/l.

Value used for CSA:

EC50/LC50 for freshwater invertebrates: 720 mg/L

7.1.1.2.2. Long-term toxicity to aquatic invertebrates

Data waiving

Reason: other justification

Justification: In accordance with column 2 of REACH Annex IX, no long term toxicity testing is proposed (required in section section 9.1.5) as the chemical safety assessment does not indicate a need to further investigate the effects on aquatic invertebrates. All data available on magnesium sulphate itself and on the other sulphates show a very low toxicity of magnesium sulphate. In addtion, the substance does have a very high water solubility and its chemical properties do not indicate bioaccumulation.

7.1.1.3. Algae and aquatic plants

The results are summarised in the following table:

Table 29. Overview of effects on algae and aquatic plants

Method	Results	Remarks	Reference
Chlorella vulgaris (algae) freshwater	EC50 (18 d): 2700 mg/L test mat. (nominal) based	2 (reliable with restrictions)	Tam NFY and Wong YS (1996)

Method	Results	Remarks	Reference
static other: 18 day batch test	on: cell number	key study read-across from supporting substance (structural analogue or surrogate) **Test material (EC name): ammonium sulphate (See endpoint summary for justification of read-across)**	OECD (2007)
Scenedesmus subspicatus (new name: Desmodesmus subspicatus) (algae) ISO 8692; German version EN 28692: 1993	EC50 (72 h): 2700 mg/L based on: biomass EC10 (72 h): 260 mg/L based on: biomass	4 (not assignable) supporting study experimental result **Test material (EC name): magnesium sulphate**	INNOLAB GmbH & Co. KG, (1994c)

Discussion

Effects on algae / cyanobacteria

No reliable algae study with magnesium sulphate is present. However, a supporting study showed an EC50 >100 mg/L. In addition, several limited documented studies showing high EC50 values for potassium sulphate are present. Also limited documented studies with magnesium sulphate are present, also showing a high EC50. However, in the sulfate category a reliable study with ammonium sulphate is present. This static 18-day test with Chlorella vulgaris showed an 18-d EC50 of 2700 mg/L based on cell number. As no extrapolation was possible to an EC10, the NOEC is considered to be at least 100 mg/L.

The following information is taken into account for effects on algae / cyanobacteria for the derivation of PNEC:

No reliable study is present for magnesium sulphate. Based on a reliable study with ammonium sulphate and the results being confirmed by studies with potassium and magnesium sulphate, the EC50 for freshwater algae is determined to be 2700 mg/L and the NOEC is ≥ 100 mg/L.

Value used for CSA:

EC50/LC50 for freshwater algae: 2700 mg/L

EC10/LC10 or NOEC for freshwater algae: ≥100 mg/L

7.1.1.4. Sediment organisms

Data waiving

Reason: other justification

Justification: In accordance with column 2 of REACH Annex X, no long term toxicity testing is proposed (required in section 9.5.1) as the chemical safety assessment does not indicate a need to further investigate the effects on sediment organisms. In addition, in accordance with section 1 of Annex XI of REACH, studies to sediment organisms do not seem to be necessary. All data available on magnesium sulphate itself and on the

other sulphates show a very low toxicity of magnesium sulphate. In addtion, the substance does have a very high water solubility and its chemical properties do not indicate bioaccumulation and/or adsorption to soil or sediment. Therefore, the study is not considered necessary.

7.1.1.5. Other aquatic organisms

No information available.

7.1.2. Calculation of Predicted No Effect Concentration (PNEC)

7.1.2.1. PNEC water

Table 30. PNEC water

PNEC	Assessment factor	Remarks/Justification
PNEC aqua (freshwater): 0.68 mg/L	1000	Extrapolation method: assessment factor See discussion.
PNEC aqua (marine water): 0.068 mg/L	10000	Extrapolation method: assessment factor See discussion.
PNEC aqua (intermittent releases): 6.8 mg/L	100	Extrapolation method: assessment factor See discussion.

7.1.2.2. PNEC sediment

Table 31. PNEC sediment

PNEC	Assessment factor	Remarks/Justification
No or insufficient data available at present		In the absence of any ecotoxicological data for sediment-dwelling organisms and for soil organisms, the PNEC sediment (freshwater), PNEC sediment (marine water) and PNEC soil might have been calculated using the equilibrium partitioning method (EPM) in EUSES, by using the PNEC aqua and the log Kow. The log Kow is not determined due to magnesium sulphate being an inorganic substance. For inorganic substances the equilibrium method can not be used, therefore no PNEC has been calculated. In addition, the aquatic compartment is the target compartment of magnesium sulphate considering its physico-chemical properties and inorganic nature.

7.2. Terrestrial compartment

7.2.1. Toxicity test results

7.2.1.1. Toxicity to soil macro-organisms

Data waiving

Information requirement: Toxicity to soil macro-organisms except arthropods

Reason: study scientifically unjustified

Justification: In accordance with section 1 of Annex XI of REACH, studies to soil organisms (required in section 9.4.1 and 9.4.4) does not seem to be necessary. All data available on magnesium sulphate itself and on the other sulphates show a very low toxicity of magnesium sulphate. In addtion, the substance does have a very high water solubility and its chemical properties do not indicate bioaccumulation and/or adsorption to soil. Therefore, the study is not considered necessary.

Information requirement: Toxicity to terrestrial arthropods

Reason: study scientifically unjustified

Justification: In accordance with section 1 of Annex XI of REACH, studies to soil organisms (required in section 9.4.1 and 9.4.4) does not seem to be necessary. All data available on magnesium sulphate itself and on the other sulphates show a very low toxicity of magnesium sulphate. In addtion, the substance does have a very high water solubility and its chemical properties do not indicate bioaccumulation and/or adsorption to soil. Therefore, the study is not considered necessary.

7.2.1.2. Toxicity to terrestrial plants

Data waiving

Reason: study scientifically unjustified

Justification: In accordance with section 1 of Annex XI of REACH, studies to soil organisms (required in section 9.4.3 and 9.4.6) does not seem to be necessary. All data available on magnesium sulphate itself and on the other sulphates show a very low toxicity of magnesium sulphate. In addition, the substance does have a very high water solubility and its chemical properties do not indicate bioaccumulation and/or adsorption to soil. Therefore, the study is not considered necessary.

7.2.1.3. Toxicity to soil micro-organisms

Data waiving

Reason: study scientifically unjustified

Justification: In accordance with section 1 of Annex XI of REACH, studies to soil organisms (required in section 9.4.2) does not seem to be necessary. All data available on magnesium sulphate itself and on the other sulphates show a very low toxicity of magnesium sulphate. In addtion, the substance does have a very high water solubility and its chemical properties do not indicate bioaccumulation and/or adsorption to soil. Therefore, the study is not considered necessary.

7.2.1.4. Toxicity to other terrestrial organisms

No information available.

7.2.2. Calculation of Predicted No Effect Concentration (PNEC soil)

Table 32. PNEC soil

PNEC	Assessment factor	Remarks/Justification
No or insufficient data available at present		In the absence of any ecotoxicological data for sediment-dwelling organisms and for soil organisms, the PNEC sediment (freshwater), PNEC sediment (marine water) and PNEC soil might have been calculated using the equilibrium partitioning method (EPM) in EUSES, by using the PNEC aqua and the log Kow. The log Kow is not determined due to magnesium sulphate being an inorganic substance. For inorganic substances the equilibrium method can not be used, therefore no PNEC has been calculated. In addition, the aquatic compartment is the target compartment of magnesium sulphate considering its physico-chemical properties and inorganic nature.

7.3. Atmospheric compartment

No information available.

7.4. Microbiological activity in sewage treatment systems

7.4.1. Toxicity to aquatic micro-organisms

The results are summarised in the following table:

Table 33. Overview of effects on micro-organisms

Method	Results	Remarks	Reference
Photobacterium phosphoreum German standard methods for the examination of water, waste water and sludge; bio-assays (group L); determination of the inhibitory effect of waste water on the light emission of Photobacterium phosphoreum (L 34)	EC50 (30 min): 84 g/L	4 (not assignable) supporting study experimental result **Test material (EC name): magnesium sulphate**	INNOLAB GmbH & Co. KG, (1994c)

Data waiving

Reason: study scientifically unjustified

Justification: In accordance with section 1 of Annex XI of REACH, a toxicity study to microorganisms (required in section 9.1.4) does not seem to be necessary. In view of the use of the substances (fertilizer) and the available data on the other trophic levels (fish, invertebrates and algae) with the different inorganic sulphates, no toxicity is expected from magnesium sulphate. In addition, sulphates are known to be important for some microorganisms, e. g. some anaerobic microorganisms use sulphates as electron acceptors. Therefore, it is concluded that the EC50 >100 mg/L for the inorganic sulphates and thus no study need to be conducted.

Discussion

In view of the use of the substances (fertilizer) and the available data on other trophic levels with the inorganic sulphates, we do not expect any of the sulfate substances to be toxic to activated sludge. In addition, sulfates are known to be important for some microorganisms - some anaerobic microorganisms use sulfates as electron acceptors. Therefore we conclude that the EC50 is above 100 mg/l for all inorganic sulphates.

Value used for CSA:

EC50/LC50 for aquatic micro-organisms: >100 mg/L

EC10/LC10 or NOEC for aquatic micro-organisms: 100 mg/L

7.4.2. PNEC for sewage treatment plant

Table 34. PNEC sewage treatment plant

Value	Assessment factor	Remarks/Justification
PNEC STP: 10 mg/L	10	Extrapolation method: assessment factor See discussion.

7.5. Non compartment specific effects relevant for the food chain (secondary poisoning)

7.5.1. Toxicity to birds

Data waiving

Information requirement: Toxicity to birds

Reason: other justification

Justification: In accordance with Column 2 of Annex X of REACH, a study with birds (required in section 9.6.1) does not seem to be necessary due to the data available for magnesium sulphate and for the other sulphates.

7.5.2. Toxicity to mammals

No additional data available as already present in chapter 5.

7.5.3. Calculation of PNECoral (secondary poisoning)

Table 35. PNEC oral

PNEC	Assessment factor	Remarks/Justification

PNEC	Assessment factor	Remarks/Justification
No potential for bioaccumulation		Magnesium sulphate is highly soluble, and therefore it is assumed that the log Kow will be low. Furthermore, magnesium sulphate has a low bioaccumulation potential and therefore secondary poisoning is not considered a relevant route. Therefore, a PNEC oral has not been derived.

7.6. Conclusion on the environmental hazard assessment and on classification and labelling

Environmental classification justification

Based on all the information available, both on magnesium sulphate itself as well as on other inorganic sulphates, the substance does not need to be classified according to Directive 67/548/EC and the CLP Directive for the environment. For inorganic substances no PBT or vPvB assessment is considered necessary (see Annex XIII of REACH).

General discussion

PNEC aqua (freshwater)

For the 3 trophic levels (fish, invertebrates (Daphnia) and algae), several studies on the short-term toxicity are available. Therefore the lowest L(E) C50 observed from all conducted studies, a 96h-LC50 of 680 mg/L for *Pimephales promelas* is used for the derivation of the PNEC. An AF of 1000 is used in accordance with the "Guidance on information requirements and chemical safety assessment, Chapter R.10".

PNEC aqua (freshwater): 0.68 mg/L

PNEC aqua (marine water)

For the 3 trophic levels (fish, invertebrates (Daphnia) and algae), several studies on the short-term toxicity are available. No studies with species in marine water are available, therefore the lowest L(E) C50 observed from all fresh water conducted studies, a 96h-LC50 of 680 mg/L for *Pimephales promelas* is used for the derivation of the PNEC. An AF of 10000 is then used in accordance with the "Guidance on information requirements and chemical safety assessment, Chapter R.10".

PNEC aqua (marine water): 0.068 mg/L

PNEC (intermittent releases)

For the 3 trophic levels (fish, invertebrates (Daphnia) and algae), several studies on the short-term toxicity are available. Therefore the lowest L(E) C50 observed from all conducted studies, a 96h-LC50 of 680 mg/L for *Pimephales promelas* is used for the derivation of the PNEC. An AF of 100 is used in accordance with the "Guidance on information requirements and chemical safety assessment, Chapter R.10".

PNEC (intermittent releases): 6.8 mg/L

The substance is inorganic, therefore no ready biodegradability test is available. In addition, no study on toxicity to micro-organisms is available. However, In view of the use of the sulphate substances (fertilizer) and the available data on the other trophic levels (fish, invertebrates and algae) with the different inorganic sulphates, no toxicity is expected from magnesium sulphate. In addition, sulphates are known to be important for some microorganisms, e. g. some anaerobic microorganisms use sulphates as electron acceptors. Therefore, it is concluded that the EC50 >100 mg/L and NOEC is 100 mg/L for inorganic sulphates and thus no study need to be conducted. An AF of 10 is used in accordance with the "Guidance on information requirements and chemical safety assessment, Chapter R.10".

PNEC STP: 10 mg/L

8. PBT AND VPVB ASSESSMENT

According to Annex XIII of Regulation (EC) No 1907/2006, no PBT and vPvB assessment has been conducted since magnesium sulphate is inorganic.

9. EXPOSURE ASSESSMENT

The substance is not classified as dangerous according to the criteria of the Dangerous Substances Directive (67/548/EEC) or the Classification, Labelling and Packaging of Substances and Mixtures (CLP Regulation; 1272/2008/EC) and therefore according to Article 14(4) of the REACH regulation an exposure assessment is not required.

10. RISK CHARACTERISATION

The substance is not classified as dangerous according to the criteria of the Dangerous Substances Directive (67/548/EEC) or the Classification, Labelling and Packaging of Substances and Mixtures (CLP Regulation; 1272/2008/EC) and therefore according to Article 14(4) of the REACH regulation a risk characterization is not required.

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