CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance aluminium sulfate[1]

European Food Safety Authority[2]

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SUMMARY

Aluminium sulfate is one of the 295 substances of the fourth stage of the review programme covered by Commission Regulation (EC) No 2229/2004,[3] as amended by Commission Regulation (EC) No 1095/2007.[4] In accordance with the Regulation, at the request of the Commission of the European Communities (hereafter referred to as 'the Commission'), the EFSA organised a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by Spain, being the designated rapporteur Member State (RMS). The peer review process was subsequently terminated following the applicant's decision, in accordance with Article 24e, to withdraw support for the inclusion of aluminium sulfate in Annex I to Council Directive 91/414/EEC.

Following the Commission Decision of 8 December 2008 (2008/941/EC)[5] concerning the non-inclusion of aluminium sulfate in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Chrysal International BV made a resubmission application for the inclusion of aluminium sulfate in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008.[6] The resubmission dossier included further data in response to the issues identified in the DAR.

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, the Netherlands, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report. The final version of the Additional Report was received by the EFSA on 9 March 2010.

In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA distributed the final version of the Additional Report to Member States and the applicant for comments on 18 March 2010. The EFSA collated and forwarded all comments received to the Commission on 22 April 2010.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission requested the EFSA to conduct a focused peer review in the areas of mammalian toxicology and environmental fate and behaviour and deliver its conclusions on aluminium sulfate.

[1] On request from the European Commission, Question No EFSA-Q-2010-00161, issued on 28 October 2010.
[2] Correspondence: praper@efsa.europa.eu
[3] OJ L 379, 24.12.2004, p.13
[4] OJ L 246, 21.9.2007, p. 19
[5] OJ L 335, 13.12.2008, p.91
[6] OJ L 15, 18.01.2008, p.5

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The conclusions laid down in this report were reached on the basis of the evaluation of the representative use of aluminium sulfate as a bactericide on cut flowers, as proposed by the applicant. Full details of the representative use can be found in Appendix A to this report.

For the physical-chemical properties section no critical areas of concern were identified. Data gaps were identified for batch analysis data, an Annex II data package for the active substance and a shelf-life study to demonstrate the stability of aluminium sulfate.

No areas of concern and no data gaps were identified in the mammalian toxicology section.

Based on the representative use on cut flowers, no residues are expected to occur in food of plant or animal origin and therefore a consumer risk assessment is not required.

No areas of concern were identified in the environmental fate and behaviour section.

The risk to non-target organisms was assessed as low for the representative use of aluminium sulfate.

KEY WORDS

aluminium sulfate, aluminium sulphate, peer review, risk assessment, pesticide, bactericide

TABLE OF CONTENTS

BACKGROUND

Legislative framework

Commission Regulation (EC) No 2229/2004,[7] as amended by Commission Regulation (EC) No 1095/2007,[8] lays down the detailed rules for the implementation of the fourth stage of the work programme referred to in Article 8(2) of Council Directive 91/414/EEC. This regulates for the European Food Safety Authority (EFSA) the procedure for organising, upon request of the Commission of the European Communities (hereafter referred to as 'the Commission'), a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by the designated rapporteur Member State.

Commission Regulation (EC) No 33/2008[9] lays down the detailed rules for the application of Council Directive 91/414/EEC for a regular and accelerated procedure for the assessment of active substances which were part of the programme of work referred to in Article 8(2) of Council Directive 91/414/EEC but which were not included in Annex I. This regulates for the EFSA the procedure for organising the consultation of Member States and the applicant(s) for comments on the Additional Report provided by the designated RMS, and upon request of the Commission the organisation of a peer review and/or delivery of its conclusions on the active substance.

Peer review conducted in accordance with Commission Regulation (EC) No 2229/2004

Aluminium sulfate is one of the 295 substances of the fourth stage of the review programme covered by Commission Regulation (EC) No 2229/2004, as amended by Commission Regulation (EC) No 1095/2007. In accordance with the Regulation, at the request of the Commission, the EFSA organised a peer review of the DAR provided by the designated rapporteur Member State, Spain, which was received by the EFSA on 29 January 2008 (Spain, 2007).

The peer review was initiated on 31 March 2008 by dispatching the DAR to Member States and the applicant Chrysal International BV for consultation and comments.

The peer review process was subsequently terminated following the applicant's decision, in accordance with Article 24e, to withdraw support for the inclusion of aluminium sulfate in Annex I to Council Directive 91/414/EEC.

Peer review conducted in accordance with Commission Regulation (EC) No 33/2008

Following the Commission Decision of 8 December 2008 (2008/941/EC)[10] concerning the non-inclusion of aluminium sulfate in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Chrysal International BV made a resubmission application for the inclusion of aluminium sulfate in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008. The resubmission dossier included further data in response to the issues identified in the DAR, as follows: the available toxicological database was insufficient to perform an adequate risk assessment and in the absence of an adequate AOEL an exposure risk assessment could not be done.

In accordance with Article 18, the Netherlands, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report (Netherlands, 2009). The final version of the Additional Report was received by the EFSA on 9 March 2010.

In accordance with Article 19, the EFSA distributed the final version of the Additional Report to Member States and the applicant for comments on 18 March 2010. In addition, the EFSA conducted a

[7] OJ L 379, 24.12.2004, p.13
[8] OJ L 246, 21.9.2007, p.19
[9] OJ L 15, 18.01.2008, p.5
[10] OJ L 335, 13.12.2008, p.91

public consultation on the Additional Report and the DAR. The EFSA collated and forwarded all comments received to the Commission on 22 April 2010. At the same time, the collated comments were forwarded to the RMS for compilation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response were evaluated by the RMS in column 3.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission decided to further consult the EFSA. By written request, received by the EFSA on 6 May 2010, the Commission requested the EFSA to arrange a consultation with Member State experts as appropriate and deliver its conclusions on aluminium sulfate within 6 months of the date of receipt of the request, subject to an extension of a maximum of 90 days where further information were required to be submitted by the applicant in accordance with Article 20(2).

The scope of the peer review and the necessity for additional information, not concerning new studies, to be submitted by the applicant in accordance with Article 20(2), was considered in a telephone conference between the EFSA, the RMS, and the Commission on 6 May 2010; the applicant was also invited to give its view on the need for additional information. On the basis of the comments received, the applicant's response to the comments, and the RMS' subsequent evaluation thereof, it was concluded that the EFSA should organise a consultation with Member State experts in the areas of mammalian toxicology and environmental fate and behaviour and that further information should not be requested from the applicant.

The outcome of the telephone conference, together with EFSA's further consideration of the comments is reflected in the conclusions set out in column 4 of the Reporting Table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, including those issues to be considered in consultation with Member State experts, were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table, together with the outcome of the expert discussions where these took place, were reported in the final column of the Evaluation Table.

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in October 2010.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative use as a bactericide on cut flowers, as proposed by the applicant. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the Peer Review Report (EFSA, 2010), which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The Peer Review Report comprises the following documents:

- the comments received,
- the Reporting Table (28 April 2010),
- the Evaluation Table (22 October 2010),
- the reports of the scientific consultation with Member State experts (where relevant).

Given the importance of the DAR and the Additional Report including its addendum (compiled version of September 2010 containing all individually submitted addenda; Netherlands, 2010) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Aluminium sulfate is the chemical name for the compound considered. There is no ISO common name.

The representative formulated product for the evaluation was 'Chrysal RVB' a soluble concentrate formulation (SL) containing 18.4 % w/w aluminium sulfate.

The representative use is as a cut flower treatment as a bactericide. Full details of the GAP can be found in the list of end points in Appendix A.

CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The minimum purity of the active substance is not currently available as there is a data gap for batch data to support the specification. As this is the case the possibility of relevant impurities cannot be concluded on.

The main data regarding the identity of aluminium sulfate are given in Appendix A. A data gap was identified for an Annex II physical-chemical properties package as the current data set is based on secondary literature which is not acceptable. As an alternative to data, reasoned cases can be considered to waive these requirements. For the plant protection product it should be noted that no low-temperature stability data were provided but this can be covered by appropriate labelling. A data gap was identified for a shelf-life study to demonstrate that aluminium sulfate is stable on storage or a reasoned case to waive this requirement.

In viw of the use of this product, as a cut flower treatment, methods of analysis for monitoring are not required.

2. Mammalian toxicity

The toxicological assessment of aluminium sulfate is essentially based on studies reported in the public literature that were partly carried out with other aluminium salts and are not guideline or GLP compliant studies.

When given orally, less than 1 % of aluminium from aluminium sulfate is absorbed. The sulfate ion is absorbed to a much higher extent. It is not acutely toxic by the oral or dermal routes. In rats the oral LD_{50} is higher than 5000 mg/kg bw, and the dermal LD_{50} is higher than 2000 mg/kg bw. It is not irritating to skin but is a severe eye irritant (classification as R41 "Risk of serious damage to eyes" is proposed). Aluminium sulfate did not cause skin sensitisation in a local lymph node assay. It is irritating to the respiratory system (classification as R37 "Irritating to the respiratory system" is proposed). In short-term toxicity tests with rats, liver, kidney and brain were the target organs of toxicity. The relevant short-term LOAEL of 212 mg/kg bw/day was derived from a 21-day study in rats. Clastogenicity has been reported from both *in vitro* and *in vivo* genotoxicity tests. These results, however, were not considered relevant for the risk assessment since they were of limited validity. Overall, aluminium sulfate is considered not to be genotoxic. No long-term NOAEL has been derived since no suitable studies on long-term effects have been provided, however, there are no indications of a carcinogenic potential of aluminium sulfate in humans. No specific reproduction or developmental studies have been submitted. In the generic literature there is no indication that aluminium is associated with developmental or reproductive effects. Reports from the public literature show that aluminium compounds may cause cognitive impairments, histological changes in the brain and altered brain function in rodents.

Based on the intended use of the substance (treatment of cut flowers) neither an acceptable daily intake (ADI) nor an acute reference dose (ARfD) were derived. Instead of an acceptable operator exposure level (AOEL), a reference value of 0.002 mg/kg bw/day for aluminium has been allocated

based on a Tolerable Weekly Intake (TWI) for aluminium of 1 mg/kg bw/week reported for dietary exposure estimation to aluminium (EFSA, 2008) and corrected for an oral absorption rate of 1 %.

Based on the representative use it as assumed that operators and workers are the same person and that bystander exposure is irrelevant. Based on the UK and the German model in combination with a field study, calculated exposures without personal protective equipment (PPE) amounted to 10 – 17 % and to 19 – 23 % of the reference value of 0.002 mg/kg bw/day for poorly and strongly mechanised application respectively. When PPE (gloves) is used, these figures amount to 0.2 and 2 % respectively of the set reference value.

3. Residues

Conventional metabolism and residue data were not considered necessary to support the representative use of aluminium sulfate as a bactericide in water of cut flowers. No residues are expected to occur in food of plant and animal origin and therefore a consumer risk assessment is not required.

4. Environmental fate and behaviour

A description of the environmental fate and behaviour of aluminium in its different forms in environmental compartments, based on a literature review, was provided by the applicant and summarised in the DAR. The fate and behaviour of sulfate ions was not assessed in the available documentation.

No aerobic or anaerobic degradation data were available for aluminium sulfate, neither was photolysis in soil studied. These data were considered not necessary, taking into consideration that aluminium is a chemical element and its atoms do not degrade in the environment. Additionally, the formulated product is intended for exclusive use in enclosed spaces as a cut-flower post-harvest treatment and therefore soil exposure to aluminium sulfate is not expected. After use, aluminium sulfate is released in the domestic sewage with the cut-flower water. The spreading of sludge, used as a soil amendment and containing aluminium sulfate, is the primary pathway by which the ion of aluminium present in aluminium sulfate may enter the terrestrial environment. The use of sewage sludge in agriculture is regulated in Member States via the Council Directive 86/278/EEC.[11] Therefore, Member State experts agreed in the PRAPeR 82 meeting that a soil exposure assessment for aluminium sulfate is not required to support Annex I inclusion at the EU level from the representative use that has been assessed.

The predicted environmental concentrations (PECs) in waste water treatment plant effluents, surface water and sediment of primarily the ion of aluminium related to the use of aluminium sulfate were estimated with the EUSES 2.03 model,[12] which is designed for regulatory assessments for biocides and other general chemicals. Because of some uncertainties in the input parameters used in the modelling, the Member State experts agreed that the alternative simple box approach used to determine the aluminium ion quantity released to surface water related to the use of 'Chrysal RVB' should be used for risk assessment. This simplistic calculation resulted in a lower PEC in comparison with the value estimated with the EUSES model, and as a result it was concluded that no further action is required in reference to the aquatic exposure assessment.

In relation to the groundwater exposure assessment, the Member State experts were of the opinion that as the only exposure pathway to this environmental compartment for aluminium sulfate for the representative use is through the application of sewage sludge on agricultural soils, calculation of PEC_{gw} was not necessary.

[11] Council Directive of 12 June 1986 on the protection of the environment, and in particular of the soil, when sewage sludge is used in agriculture (86/278/EEC) OJ L 181, 4.7.1986, p.6.
[12] European Commission, 2004. European Union System for the Evaluation of Substances.

'Chrysal RVB' raises no risk of release to air because aluminium compounds do not volatilize from water or moist soil surfaces.

5. Ecotoxicology

The ecotoxicology assessment of aluminium sulfate provided in the DAR was based upon a review of selected available literature and was not supported by any experimental studies.

'Chrysal RVB' (T534; 18.4 % w/w aluminium sulfate) is intended for exclusive use in enclosed spaces as a cut-flower post-harvest treatment. Therefore, exposure of birds or mammals, and thus acute, short-term dietary and chronic risks for birds or mammals were considered to be negligible or unlikely to occur. However, birds and mammals could be exposed to aluminium ion by consumption of surface water with residues of aluminium ion (acute) and consumption of fish containing residues of aluminium ion (long-term). Exposure via contaminated soil was not considered (see section 4). Although no reliable toxicity data were available for birds, there was enough evidence (e.g. drinking water limits for human consumption) to indicate that the risk to birds and mammals could be assessed as low.

Although no reliable toxicity data were available for aquatic organisms negligible acute risk to aquatic organisms should be expected in receiving waters with pH > 5.5 or < 8, based on comparison of expected exposure with existing limit values for aluminium in waste water plant effluents and drinking water limits. No long-term risk to aquatic organisms or bioaccumulation was expected.

The risk to bees and non-target arthropods was not assessed due to the indoor use. For the same reasons the risk of releases to the soil environment was considered to be severely limited, and certainly not exceeding background or naturally occurring releases. The risk from spreading aluminium sulfate contaminated sludge was not assessed (see section 4). Overall the risk to soil-living organisms and non-target plants was assessed as negligible. Moreover, a negligible risk to biological methods of sewage treatment micro-organisms was expected from 'Chrysal RVB' when applied according to the recommended indoor use.

6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments

6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Aluminium ion	No data, not required.	The risk to soil-dwelling organisms was assessed as low.

6.2. Ground water

Compound (name and/or code)	Mobility in soil	>0.1 µg/L 1m depth for the representative use (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
Aluminium ion	No data, not required.	No data, not required.	Yes	Yes	The risk to aquatic organisms in surface water was assessed as low.

6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Aluminium ion	Open literature data indicated that aluminium was very toxic to aquatic organisms. The risk to aquatic organisms was assessed as low.

6.4. Air

Compound (name and/or code)	Toxicology
Aluminium ion	LC_{50} values have not been reported. Based on a weight of evidence approach classification for acute inhalation toxicity is not necessary.

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- For each source (manufacturing site) a specification with supporting batch data and validated methods of analysis (relevant for the representative use evaluated; submission date proposed by the applicant: unknown; see section 1).;
- Physical-chemical properties Annex II data package or reasoned cases to waive these requirements (relevant for the representative use evaluated; submission date proposed by the applicant: unknown; see section 1).
- Shelf-life study to demonstrate the stability of aluminium sulfate or a reasoned case to waive this requirement (relevant for the representative use evaluated; submission date proposed by the applicant: unknown; see section 1).

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

- Appropriate labelling for cold temperature protection (e.g. protect from frost) should be considered.

ISSUES THAT COULD NOT BE FINALISED

- None.

CRITICAL AREAS OF CONCERN

- None.

REFERENCES

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APPENDICES

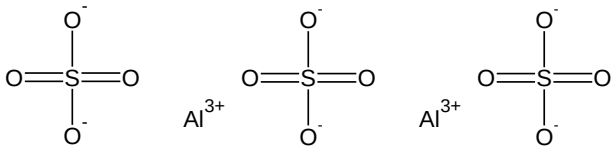
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Aluminium sulfate (No ISO common name)
Function (*e.g.* fungicide)	Bactericide

Rapporteur Member State	Spain
Co-rapporteur Member State	

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	Aluminium sulfate
Chemical name (CA) ‡	Aluminium sulfate
CIPAC No ‡	not available
CAS No ‡	10043-01-3
EC No (EINECS or ELINCS) ‡	EINECS: 233-135-0
FAO Specification (including year of publication) ‡	No FAO specification
Minimum purity of the active substance as manufactured ‡	Open
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Open
Molecular formula ‡	$Al_2(SO_4)_3$
Molecular mass ‡	342.14 g/mol (anhydrous) 594.34 g/mol (with 14 H_2O)
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Open for an Annex II data package.

Melting point (state purity) ‡	
Boiling point (state purity) ‡	
Temperature of decomposition (state purity)	
Appearance (state purity) ‡	
Vapour pressure (state temperature, state purity) ‡	
Henry's law constant ‡	
Solubility in water (state temperature, state purity and pH) ‡	
Solubility in organic solvents ‡ (state temperature, state purity)	
Surface tension ‡ (state concentration and temperature, state purity)	
Partition co-efficient ‡ (state temperature, pH and purity)	
Dissociation constant (state purity) ‡	
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	
Flammability ‡ (state purity)	
Explosive properties ‡ (state purity)	
Oxidising properties ‡ (state purity)	

Summary of representative uses evaluated (*Aluminium Sulfate*)*

Crop and/ or situation	Member State or Country	Product name	FG or I	Pests or Group of pests controlled	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days)	Remarks
(a)			(b)	(c)	Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	kg as/hL min – max (l)	water L/ha min – max	kg as/ha min – max (l)	(m)	
Cut flowers		Chrysal RVB	I	Bactericide	SL	18.4 % w/w Aluminium sulfate	Cut stems are placed in the solution for at least 4 hours to allow the activity of the product.	During the post-harvest chain of cut flowers, from the grower to the consumer	1	n.a	4.45* 10^{-2}	n.a	n.a	n. a.	

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).
(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated
(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha
(m) PHI - minimum pre-harvest interval

Methods of Analysis

Analytical methods for the active substance (OECD data point IIA 4.2)

Technical as (analytical technique)	Complexometric titration with EDTA
Impurities in technical as (analytical technique)	AAS, ICP-MS
Plant protection product (analytical technique)	Complexometric titration with EDTA

Analytical methods for residues (OECD data points IIA, 4.3 to IIA 4.8)

Residue definitions for monitoring purposes

Food of plant origin		Not required.
Food of animal origin		Not required.
Soil		Not required.
Water	surface	Not required.
	drinking/ground	Not required.
Air		Not required.

Monitoring/Enforcement methods

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Not required.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not required.
Soil (principle of method and LOQ)	Not required.
Water (principle of method and LOQ)	Not required.
Air (principle of method and LOQ)	Not required.
Body fluids and tissues (principle of method and LOQ)	Not required aluminium sulfate is not regarded as toxic or very toxic.

Mammalian Toxicology

Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1) [(1)]

Rate and extent of oral absorption ‡	Less than 1 % (for aluminium) with different aluminium chemical species. For the risk assessment a value of 1 % was used.
Distribution ‡	In blood, aluminium is present in plasma bound to transferrin (89 % of aluminium in plasma).
Potential for accumulation ‡	Aluminium shows slight potential for accumulation in the brain, bone, muscle and kidney (orally exposed animals).
Rate and extent of excretion ‡	Most of aluminium ingested is unabsorbed and excreted in the faeces (76 – 98 % of oral dose). Absorbed aluminium is eliminated via the urine.
Metabolism in animals ‡	No metabolism occur
Toxicologically relevant compounds ‡ (animals and plants)	aluminium sulfate
Toxicologically relevant compounds ‡ (environment)	aluminium sulfate

[(1)] Data from different aluminium chemical species (not aluminium sulfate)

Acute toxicity (Annex IIA, point 5.2) [(2)]

Rat LD_{50} oral ‡	LD_{50} > 5000 mg/kg bw	
Rat LD_{50} dermal ‡	Based on the data from the representative formulation (Chrysal RVB), an LD_{50} > 2000 mg/kg bw can be assumed.	
Rat LC_{50} inhalation ‡	No classification, based on weight of evidence (no study provided)	
Skin irritation ‡	Not irritating	
Eye irritation ‡	Severely irritating	**R41**
Skin sensitization ‡	Non sensitiser (LLNA)	
Respiratory system irritation	Irritating to respiratory system	**R37**

[(2)] The studies have been performed with ALUM 17 (which is $Al_2(SO_4)_3$ 14 H_2O or alternatively as 17 % Al_2O_3. which is the notified active substance

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver, kidney and brain in rats. Multifocal degeneration of the liver, swelling and degeneration of cortical and distal renal tubules, degeneration of nerve cells[(3)]	
Relevant oral NOAEL ‡	21-day, rat: LOAEL: 212 mg $Al_2(SO_4)_3$ /kg bw/day.[(3)]	
Relevant dermal NOAEL ‡	No data, not required	

Relevant inhalation NOAEL ‡	No data, not required	

(3) These findings should be considered only as an approximation since the data presented in the reports were of limited validity and adequacy.

Genotoxicity ‡ (Annex IIA, point 5.4)

Overall, unlikely to be genotoxic. However, clastogenicity observed in *in vitro* and *in vivo* tests with limited validity.	

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	No specific studies provided. There are no indications for a carcinogenic potential of aluminium (ATSDR 2008, EFSA 2008)	
Relevant NOAEL ‡	No data, not required	
Carcinogenicity ‡	Increase of undefined tumours in old rodent studies, not in a more recent study. No evidence for carcinogenicity in humans.	

Reproductive toxicity (Annex IIA, point 5.6)

Multigeneration study

Reproduction target / critical effect ‡	No specific studies provided. Aluminium is not associated with reproductive effects (ATSDR 2008).	
Relevant parental NOAEL ‡	No data, not required	
Relevant reproductive NOAEL ‡	No data, not required	
Relevant offspring NOAEL ‡	No data, not required	

Developmental toxicity

Developmental target / critical effect ‡	No specific studies provided. Aluminium is not associated with developmental effects (ATSDR 2008).	
Relevant maternal NOAEL ‡	No data, not required	
Relevant developmental NOAEL ‡	No data, not required	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data, not required	
Repeated neurotoxicity ‡	Cognitive impairments Histopathological changes in the brain. Significant alterations in motor function, sensory function, and cognitive function have been detected following exposure of	

	adult or weanling rats and mice or following gestation and/or lactation exposure of rats and mice.	
Delayed neurotoxicity ‡	Not relevant for this type of chemical.	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No study provided
Studies performed on metabolites or impurities ‡	Not relevant

Medical data ‡ (Annex IIA, point 5.9) [4]

	Occupational exposure studies in aluminium reduction plants suggest that the lungs and nervous system may be the most sensitive targets of toxicity following inhalation exposure.

[4] Data from different aluminium chemical species (not aluminium sulfate)

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	Not relevant		
Tolerable systemic exposure[5]‡	0.002 mg Al/kg bw/day, equivalent to 0.14 mg Al/day for a 70 kg person	Risk assessment based on the Tolerable Weekly Intake (TWI) proposed by EFSA (2008).	
ARfD ‡	Not relevant		

[5] In this case not an AOEL, but a daily TWI has been derived. Based on the TWI, the weekly exposure has been calculated back to a daily exposure resulting in a reference value corresponding to an AOEL.

Dermal absorption ‡ (Annex IIIA, point 7.3)

Chrysal RVB (T534)	1 % based on oral absorption

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Pre treatment of cut flowers. Without PPE: 10 – 23 % of the tolerable systemic exposure (UK- and DE-model in combination with field study) With PPE (gloves): 0.2 – 2 % of the tolerable systemic exposure (UK and German models in combination with field study)

Workers	See operator. It is assumed that operator and workers are the same person.
Bystanders	Not relevant.

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

	RMS/peer review proposal
Aluminium sulfate	**Xi** "Irritant" **R41** "Risk of serious damage to eyes." **R37** "Irritating to respiratory system"

Residue Data

Not applicable. Not considered relevant for Annex I inclusion due to the representative uses as plant protection product applied in water of cut-flowers. Therefore, no residues are expected to occur in food or in feed.

Fate and behaviour in the environment

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

No data provided, not required

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡

No data provided, not required

Soil photolysis ‡

No data provided, not required

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

No data provided, not required

Soil adsorption/desorption (Annex IIA, point 7.1.2)

No data provided, not required

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

No data provided, not required

PEC (soil) (Annex IIIA, point 9.1.3)

Method of calculation	Not required as soil exposure is regulated by directive 86/278 in relation to the use of sludge from sewage treatment plants on agricultural land.
Application rate	-
Main route of entry	-
PEC_{soil}	Not required

Route and rate of degradation in water (Annex IIA, point 7.2.1)

No data provided, not required

PEC (surface water) (Annex IIIA, point 9.2.3)

Method of calculation	worst case direct exposure calculation
Main route of entry	Indirect release of waste water
PEC_{SW}	NON EUSES calculation. Based on $1.851*10^{10}$ cut flower stems in Europe and 50 stems/L in bucket→ $3.7*10^{8}$ litre water / year Dose rate 2 ml product/L → 7.4 *105 L product /year 50% market share → 370,000 L 'Chrysal RVB' / year 1 L 'Chrysal RVB' contains 35 gram Al (15.77 %) 370,000 litre 'Chrysal RVB' is corresponding with 12,950 kg = 13 ton aluminium / year NL represents 88% of the European market and is considered worst case scenario. 88% of 13 ton = 11.5 ton aluminium used by 8 auctions (or Dutch clocks). 58% of the sold flowers is transported dry. This means 58% of 'Chrysal RVB' is released by these auctions (42 % released at many different sites mainly out of the country). 58% of 11.5 ton = 6.7 ton aluminium / year in Holland turns up at 8 different WWTP. Simple calculation of the daily dose of aluminium load from 'Chrysal RVB' at the WWTP (based on 365 days of use a year with 100 % release in the sewage and a equally spread towards 8 WWTP) is: 6700 Kg aluminium / 365 = 18.4 kg aluminium a day which is approximately 2.3 kg total aluminium per WWTP / day. Total aluminium load versus dissolved aluminium vary from 20-4800. for the ratio total/dissolved Al a factor of 1000 was used. i.e. influent concentration 2.3 kg total Al per WWTP / day → effluent concentration 2.3 gram solved Al per WWTP / day. Capacity of a WWTP of 900 m3 / day (100,000 i.e.) dilution of concentration solved Al: 2300 mg / 900,000L = 2.5 µg / L. Release to large surface water with a dilution factor 10 → 0.25 µg/L

PEC (sediment)

Method of calculation	Not relevant under environmental conditions.

Main route of entry	-
$PEC_{sediment}$	Not required

PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation	Not required as soil exposure via sewage sludge is regulated by directive 98/278
Main route of entry	-
$PEC_{groundwater}$	Not required

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

	No data provided, not required

PEC (air)

Maximum concentration	According to the worst-case scenario and a very low vapour pressure (value by default for inorganic elements: 1*10-20 Pa at 25°C), the local PEC in air for Aluminium related to the use of 'Chrysal RVB' is estimated to be negligible

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology) or for which an environmental exposure assessment is triggered.	All compartments: Aluminium ion.

Monitoring data, if available (Annex IIA, point 7.4)

Soils	No reliable pertinent data identified
Sediment	No reliable pertinent data identified by the RMS.
Surface water (indicate location and type of study)	a) Lake Gardsjon (SE) [Al] 300-2500 µg/L[1] b) Swedish lakes [Al] 10-243 µg/L[1] c) Scotland [Al] 25-400 µg/L[1] d) Llyn Brianne catchment, Wales (UK) [Al] 120-430 µg/L[1] e) Cumbria (UK) [Al] 20-940 µg/L[1] f) Vosges mountain streams (FR) [Al] 64-351 µg/L[1] g) Boglakes (BE) [Al] <20-3770 µg/L[1] h) River Rhine (NL) [Al] 190-270 µg/L[2] i) Western Netherlands [Al] 120-1200 µg/L[2] (including suspended solid)
Ground water (indicate location and type of study)	Aluminium levels in groundwater wells at neutral pH generally fall below 0.1 mg/L (100 ppb). In areas receiving acid precipitation, Aluminium levels in groundwater may be more than 10 times the levels found in areas with neutral pH levels in the water.
Air (indicate location and type of study)	Background levels of Aluminium in the atmosphere generally range from 0.005 to 0.18 ng/m^3 In industrialized areas, the concentrations of Aluminium in air are > 1000 ng/m^3

[1] Environmental Health Criteria 194, WHO 1997: ISBN 92 4 157194 2
[2] van Dalen J P, 1993. Aluminium: een gevaar voor het aquatische mileu? Working document of Rijksinstituut voor Integraal Zoetwaterbeheer, 93.164X. 26 pp.

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

No classification is proposed.

Ecotoxicology

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Effects on birds	No data submitted. Not required
Effects on mammals	Rat LD50 oral: LD_{50} > 5000 mg/kg bw (The study has been performed with ALUM 17 (which is $Al_2(SO_4)_3 \cdot 14\ H_2O$ or alternatively as 17% Al_2O_3. This is the actual active substance, see also Vol. 4.)

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

No data submitted. Not required.

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale (Test type)	End point	Toxicity (mg/L)
Laboratory tests ‡				
Fish				
Jordanella floridae	Unknown	96 hr (static)	Mortality, LC_{50}	0.095*, [5]
Salvelinus fontinalis	Unknown	60 d	NOEC	0.029*, [5]
Aquatic invertebrate				
Ctenodrilus serratus	Aluminium chloride	96 h (static)	Mortality, EC_{50}	0.480[4, 5]
Lymnaea stagnalis	Aluminium nitrate	50 d (semistatic)	NOEC	0.1001, 5
Algae				
Chlorella pyrenoidosa	Aluminium	4 d (static)	IC_{50}	0.008[2, 5]
Aquatic plants				
Myriophyllum spicatum	Aluminium	32 d	EC_{50}	2.5[3, 5]

[1] expressed as Total Aluminium, [2] expressed as labile Aluminium, [3] expressed as Al3+, [4] Expressed as test substance, * Unknown

[5] The results of these studies are considered as supplemental because the quality of data cannot be verified on the basis of available information. However, they are considered acceptable for use in the first tier worst case risk assessment.

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2).

Group	Tox. Value (as µg/L)	PECswi* (µg/L)	Annex VI trigger	TER
FISH				
Acute (*Jordanella floridae*)	95	27	100	**3.56**
Chronic (*Salvelinus fontinalis*)	29	27	10	**1.09**
INVERTEBRATES				
Acute (*Ctenodrilus serratus*)	480	27	100	17.98
Chronic (*Lymnaea stagnalis*)	100	27	10	**3.75**
ALGA				
Chlorella pyrenoidosa	8	0.27**	10	30
AQUATIC PLANTS				
Myriophyllum spicatum	2500	0.27**	10	9363

*Effluent concentrations estimated by EUSES 2.03 for worst-case release point (Rijnsburg) according to worst-case scenario, from original DAR.
**expressed as "dissolved Aluminium" (estimation based on a reduction factor of 100 between total Aluminium concentration and dissolved Aluminium concentration). To be used in comparison only with endpoints known to be expressed as dissolved aluminium.

TER calculations are not ecologically relevant (see explanation below).

'Chrysal RVB' (T534) is intended for use in enclosed spaces as cut-flower post-harvest treatment at the dose rate of 2 mL/L of water. After treatment, residues of solutions could be discharged to the drains. Surface water could be contaminated by the product *via* discharge of residues by water treatment plants. No significant risk to aquatic organisms is expected from the use of 'Chrysal RVB' according to intended uses in receiving waters with pH > 5.5 and < 8. Therefore no further data is required.

Bioconcentration

No data submitted. Not required

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

No data submitted. Not required.

Hazard quotients for honey bees (Annex IIIA, point 10.4)

No data submitted. Not required.

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

No data submitted. Not required.

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Earthworms	
	No data submitted. Not required.
Other soil macro-organisms	
	No data submitted. Not required.

Toxicity/exposure ratios for soil organisms

Earthworms	
	No data submitted. Not required.
Other soil macro-organisms	
	No data submitted. Not required.

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

No data submitted. Not required.

Effects on biological methods for sewage treatment (Annex IIA 8.7)

No data submitted. Not required.

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Aluminium ion

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Aluminium sulfate	N, R50/R53
	RMS/peer review proposal
Chrysal RVB	N, R50/R53

ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstract Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GC	gas chromatography

GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LLNA	Local lymph node assay
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level

OM	organic matter content
Pa	Pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
TWI	tolerable weekly intake
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year