SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

ammonium thiocyanate

EC No 217-175-6

CAS No 1762-95-4

Evaluating Member State(s): Czech Republic

Dated: 01 August 2016

Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2015

Member State concluded the evaluation without any further need to ask more information from the registrants under Article 46(1) decision.

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

This document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating Member State, it does not preclude other Member States or the European Commission from initiating regulatory risk management measures which they deem appropriate.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

Contents

Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

Ammonium thiocyanate was originally selected for substance evaluation in order to clarify concerns about:

- suspected endocrine disruptor,
- suspected reproductive toxicity and (neuro)developmental toxicity,
- exposure assessment.

During the evaluation no further concerns to be clarified were identified.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Not applicable.

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the substance has led the evaluating Member State (eMSCA) to the following conclusions, as summarised in the table below.

Table 1

CONCLUSION OF SUBSTANCE EVALUATION Conclusions	Tick box
Need for follow-up regulatory action at EU level	
Harmonised Classification and Labelling	
Identification as SVHC (authorisation)	
Restrictions	
Other EU-wide measures	
No need for regulatory follow-up action at EU level	x

4. FOLLOW-UP AT EU LEVEL

4.1. Need for follow-up regulatory action at EU level

4.1.1. Harmonised Classification and Labelling

Not applicable.

4.1.2. Identification as a substance of very high concern, SVHC (first step towards authorisation)

Not applicable.

4.1.3. Restriction

Not applicable.

4.1.4. Other EU-wide regulatory risk management measures

Not applicable.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

5.1. No need for regulatory follow-up at EU level

Table 2

REASON FOR REMOVED CONCERN The concern could be removed because	Tick box
Clarification of hazard properties/exposure	x
Actions by the registrants to ensure safety, as reflected in the registration dossiers (e.g. change in supported uses, applied risk management measures, etc.)	

All available information (registration dossier, Chemical Safety Report (CSR) and literature data and review) was used to clarify the concerns. The available information is sufficient and reliable to conclude the substance evaluation. There is no need for new studies and information under SEv process.

The following conclusions were prepared to conclude the SEv process:

Endocrine disrupting effect

According to existing knowledge, thiocyanates do not impair the activity of the thyroid gland itself. Thiocyanates only reduce the entry of iodide ions into the thyroid gland via competitive anion inhibition. In this manner, the subsequent reaction chain is limited due to lack of iodine compounds. However, thiocyanates do not directly affect these reactions neither enter into them nor block them. The only cause is a limited intake of iodine. From the foregoing it can be concluded that the actual activity of the thyroid gland is not affected by thiocyanates, so from this point of view it is not an endocrine disrupting effect according to the definition of WHO. The eMSCA concludes that based on the available information the concern for endocrine disruption for human health is not substantiated.

Reproductive toxicity

It can be concluded that a relationship exists between lack of iodine in organism and developmental disorders of foetus. These developmental disorders are secondary effects of maternal toxicity (hypothyroidism). Lack of iodine can also be caused by thiocyanate treatment limiting intake of iodine into the body. Although the true iodine deficiency (caused by lack of iodine in the organism) may lead to permanent severe brain damage of the foetus, with thiocyanate treatment (with sufficient of iodine in the body) such severe developmental defects have not been proven. According to available data and pursuant to rules for classification of reproductive toxicity, the eMSCA concludes that the lack of iodine and the consequent developmental disorders caused by thiocyanate are not significant enough to warrant classification for reproductive toxicity.

Exposure and high RCR

Exposure scenarios were processed using CHESAR software. The structure of exposure scenarios including descriptors was taken from registration dossier and CSR for ammonium thiocyanate.

Estimated exposure to the substance seems to be under control. Based on the available data it appears that all the exposure values are below the derived DNEL(s) and all the RCRs (including those for combined exposures) are below 1. Therefore the eMSCA considers that the risks are controlled.

5.2. Other actions

Not applicable.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

Not applicable, see section 5.

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Ammonium thiocyanate was originally selected for substance evaluation in order to clarify concerns about:

- suspected endocrine disruptor,
- suspected reproductive toxicity and (neuro)developmental toxicity,
- exposure assessment.

During the evaluation no further concerns to be clarified were identified.

7.2. Procedure

Ammonium thiocyanate was included in the Community Rolling Action Plan on 17 March 2015 and the competent authority of the Czech Republic was nominated as the evaluating Member State. A category approach for ammonium thiocyanate was provided by registrant. The justification of similarity of category members is robustly supported and the eMSCA considered it being sufficient for substance evaluation purpose. Applied category approach seems to be adequate for evaluation of ammonium thiocyanate health effects.

Relevant data available in the CSR and the registration dossier were evaluated. For further information new literature research was made concerning ammonium thiocyanate and sodium/potassium thiocyanates (category members).

Based on the gathered information, it was concluded that data are sufficient for the substance evaluation.

Assessment of endocrine disrupting effect and reproductive toxicity has been evaluated on the basis of information listed in CSR and collected through the literature search. According to this information the endocrine disrupting potential of thiocyanates was assessed.

The aggregated tonnage was estimated using CHESAR software. The structure of exposure scenarios including descriptors was taken from registration dossier and CSR for ammonium thiocyanate.

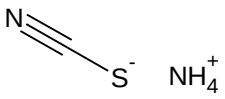
7.3. Identity of the substance

Table 3

SUBSTANCE IDENTITY	
Public name:	ammonium thiocyanate
EC number:	217-175-6
CAS number:	1762-95-4
Index number in Annex VI of the CLP Regulation:	615-004-00-3 (group entry)
Molecular formula:	HSCN · NH3
Molecular weight range:	76.12
Synonyms:	ammonium rhodanate ammonium rhodanide ammonium sulfocyanate ammonium sulfocyanide

Type of substance ☒ Mono-constituent ☐ Multi-constituent ☐ UVCB

Structural formula:



7.4. Physico-chemical properties

Table 4

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	solid
Vapour pressure	0.0152 Pa (20°C)
Water solubility	> 1000 g/L
Partition coefficient n-octanol/water (Log Kow)	n/a
Flammability	non flammable

Explosive properties	non explosive
Oxidising properties	non oxidising
Granulometry	n/a
Stability in organic solvents and identity of relevant degradation products	n/a
Dissociation constant	n/a

7.5. Manufacture and uses

7.5.1. Quantities

Table 5

AGGREGATED TONNAGE (PER YEAR)				
☐ 1 – 10 t	☐ 10 – 100 t	☐ 100 – 1000 t	☒ 1000- 10,000 t	☐ 10,000-50,000 t
☐ 50,000 – 100,000 t	☐ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☐ > 1000,000 t	☐ Confidential

7.5.2. Overview of uses

Table 6

USES	Use(s)
Formulation	ES2: Formulation and distribution of ammonium thiocyanate
Uses at industrial sites	ES3: Use in synthesis as a process chemical (not as a reactant) and as an intermediate (incl. transfers and laboratory activities) ES4: Use in spraying formulation ES5: Use in non-spraying formulations ES6: Building and construction (concrete)
Uses by professional workers	ES4: Use in spraying formulations ES5: Use in non-spraying formulations ES6: Building and construction (concrete) ES7: Laboratory settings (including material transfer and equipment cleaning)
Consumer Uses	Not used
Article service life	Not used

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

Table 7

HARMONISED CLASSIFICATION ACCORDING TO ANNEX VI OF CLP REGULATION (REGULATION (EC) 1272/2008)

Index No	International Chemical Identification	EC No	CAS No	Classification		Spec. Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement code(s)		
615-004-00-3	salts of thiocyanic acid, with the exception of those specified elsewhere in this Annex	-	-	Acute Tox. 4 Acute Tox. 4 Acute Tox. 4 Aquatic Chronic 3	H302 H312 H332 H412	-	A

Note A - Without prejudice to Article 17(2), the name of the substance must appear on the label in the form of one of the designations given in Part 3.
In Part 3, use is sometimes made of a general description such as '... compounds' or '... salts'. In this case, the supplier is required to state on the label the correct name, due account being taken of section 1.1.1.4.

7.6.2. Self-classification

- In the registration(s):

Acute Tox. 4; H302
Eye Dam. 1; H318

- The following hazard classes are in addition notified among the aggregated self-classifications in the C&L Inventory*:*

Eye Dam. 1; H318

7.7. Environmental fate properties

7.7.1. Degradation

Not relevant for this evaluation.

7.7.2. Environmental distribution

Not relevant for this evaluation.

7.7.3. Bioaccumulation

Not relevant for this evaluation.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

Not relevant for this evaluation.

7.8.2. Terrestrial compartment

Not relevant for this evaluation.

7.8.3. Microbiological activity in sewage treatment systems

Not relevant for this evaluation.

7.8.4. PNEC derivation and other hazard conclusions

Not relevant for this evaluation.

7.8.5. Conclusions for classification and labelling

Not relevant for this evaluation.

7.9. Human health hazard assessment

Registrant used the read-across method for data collection and evaluation. Ammonium thiocyanate is ionic substance. Due to the ionic nature of the ammonium thiocyanate, toxicological behaviour of this substance may be considered based on SCN^- ion, especially for systemic effects, as soluble thiocyanates are fully dissociated in solution.

The category approach for ammonium thiocyanate was provided by registrant. The justification of similarity of category members is robustly supported and the eMSCA considered it being sufficient for substance evaluation purpose. Applied category approach seems to be adequate for evaluation of ammonium thiocyanate health effects.

7.9.1. Toxicokinetics

Thiocyanates are a natural part of the environment; they are present in small quantities in the soil, water, plants and animals. Standard thiocyanate concentration reported[6] in human blood serum is 10 - 70 µmol/l (i.e. 0.6 – 4.0 mg/l) [6]. Smokers have thiocyanate concentration in blood serum higher[6]: 40 – cca 200 µmol/l (i.e. 2.3 – cca 11.6 mg/l).

Based on information from literature source, ammonium thiocyanate is slightly acutely toxic. Data differs according to animal species and the route of administration. The estimated lethal dose for humans is 15 to 30 g (ingestion of a single dose)[4].

Long-term toxicity studies, submitted in the registration dossier, revealed some adverse effects: squamous hyperplasia of the forestomach, hepatocellular hypertrophy of the liver, seminiferous epithelial degeneration of testes, lymphoid hyperplasia of the spleen, thymus atrophy or erythroid hyperplasia of the bone marrow. These effects were mainly observed at higher doses of thiocyanate and were not very significant.

Mutagenicity studies suggest that thiocyanates have no mutagenic effects. Sporadic hyperplastic lesions, reported mostly in long-term toxicity tests, can not be considered as carcinogenic effect of the evaluated substance.

Thiocyanates can be absorbed via oral or inhalation exposure. Dermal absorption may be taken into account, but it is not very likely as absorption through the skin is very slow. Absorption via inhalation exposure is likely to be rapid but ammonium thiocyanate dust is hygroscopic and the possibility of exposure to airborne dust is reduced. In the body the thiocyanate ion readily diffuses into all tissues[5] and finally is slowly excreted via urine and saliva.

7.9.2. Acute toxicity and Corrosion/Irritation

Not relevant for this evaluation.

7.9.3. Sensitisation

Not relevant for this evaluation.

7.9.4. Repeated dose toxicity

The sub-chronic (90-day) oral toxicity study of ammonium thiocyanate was performed on rats. The NOAEL = 20 mg/kg/day was identified, based on adverse effects in clinical biochemistry (decreased triglycerides and total cholesterol in serum) and histopathology (squamous hyperplasia of the forestomach, hepatocellular hypertrophy). Listed adverse effects were weak and seem to be a symptom of general toxicity.

The sub-acute (14-day) oral toxicity study of ammonium thiocyanate on rats was performed in particular as a range finding test for sub-cronic study above. The NOAEL = 100 mg/kg/day was derived, based on clinical hematology and biochemistry and organ weights (liver, thyroid).

Other reports related to long-term toxicity, available in registration dossier, are studies published in literature. In most cases these focus on influence of sodium or potassium thiocyanate on the thyroid gland. These studies are not followed according guideline and they are used as supporting information or weight of evidence. In one of these studies[14] effects of several antithyroid compounds (including KSCN) were inspected: thiocyanates induced clinical hypothyroidism if there was not supplemental iodine.

Adverse effects caused by prolonged intake of thiocyanate were reported in studies collected in registration dossier. The eMSCA concludes that these effects do not appear to be sufficiently strong for classification according to the Regulation (EC) No. 1272/2008.

7.9.5. Mutagenicity

Three *in-vitro* studies of mutagenicity of alkali metal thiocyanates were available in the registration dossier: The Bacterial Reverse Mutation Assay (ammonium thiocyanate), *In-vitro* Mammalian Chromosome Aberration Test (sodium thiocyanate) and *In-vitro* Mammalian Cell Gene Mutation Test (sodium thiocyanate). Results of all these tests are negative.

Two other studies related to *in-vivo* mutagenicity of alkali metal thiocyanates have been found in literature noted in registration dossier. These tests were not performed according to EU or OECD standards but their results indicate negative genotoxicity of thiocyanates.

No positive result was observed in mutagenicity tests of alkali metal thiocyanates. The eMSCA concludes that based on the available information there is no concern for mutagenicity.

7.9.6. Carcinogenicity

There is a study in open literature that deals with carcinogenicity of sodium thiocyanate[2]. In this study Fisher 344 mice were treated for 2 years with sodium thiocyanate and/or sodium nitrite in drinking water. During the test no significant difference was found between the groups, treated or untreated, in survival, or in the incidence of any tumor that could be related to the treatment. The results indicate that sodium thiocyanate is without carcinogenic activity in rats, alone or combined with sodium nitrite.

Available mutagenicity tests showed no mutagenic properties of alkali metal thiocyanates. Sporadic hyperplastic lesions, found mostly in long-term toxicity tests, cannot be considered as carcinogenic effect of the evaluated substance.

On the basis of available information, the eMSCA concludes that based on the available information there is no indication that ammonium thiocyanate is a carcinogen.

7.9.7. Toxicity to reproduction (effects on fertility and developmental toxicity)

Effects on fertility

No reproductive toxicity study according to OECD or EU standards is available.

Two-generation study[3], that is reported in registration dossier, is primarily focused on the transport of some specific nutrients. Regardless of the fact that this study was not performed according to OECD or EU standards, it provides some useful information on reproductive toxicity. At constant dose level 25 mg/kg/day of potassium thiocyanate, variations in clinical chemistry were reported but no effect on the body weights or brain weights of the pups (F2) was observed.

Fertility effects assessment is based also on findings observed during the sub-chronic repeated dose toxicity test (90-day) with ammonium thiocyanate: slight seminiferous epithelial degeneration in two male rats at dose 500 mg/kg/day. This effect is very weak, in a few animals only and at the highest dose level only, so that toxicological relevance of this finding is doubtful.

No other significant effects on fertility are reported in other studies focused on the effects of thiocyanates on human or animal health collected in the registration dossier (especially repeated-dose toxicity studies). It should be noted however that in most of those studies it is not specified whether reproduction parameters were examined.

Based on the available information the eMSCA has not identified a concern for fertility.

Developmental toxicity

In a number of articles in literature, the relationship between thiocyanate treatment and thyroid gland function is investigated. It has long been known that thiocyanates affect the thyroid gland. Thyroid hormones are important factor for brain cell differentiation during intrauterine development and in period after birth[9]. In addition, thyroid hormones treatment increases the level of basal metabolic rate and oxygen consumption of most tissues, affects metabolism of nutrients, etc. Therefore, the action of thyroid hormones is important for the development of the unborn child and in the first period after birth.

The thyroid gland has a unique position in the endocrine system as essential part of its hormones contain iodine. Therefore, thyroid function depends on the iodine intake from the external environment. The whole iodine treatment takes place in the follicular cells of the thyroid gland.

Iodine is normally present in the blood plasma in very low concentrations. Thyroid cells concentrate iodine by a specific enzyme known as sodium-iodide symporter (NIS). Next step is the conversion of iodide to organic bound iodine which is part of the specific thyroid hormones[13]. When iodine deficiency, there is a lack of iodine-containing hormones which in severe cases can manifest developmental disorders.

Foetus in the mother's body is partially supplied from the mother's bloodstream through the placenta. From about 12 to 14 week of intrauterine development the foetal thyroid gland begins to produce its own hormones. In case of serious iodine deficiency production of these hormones in the thyroid gland both the mother and the foetus is limited. Consequently, there are disturbances in foetal development of various degree according to the severity of iodine deficiency.

The association between hypothyroidism and disorders of foetal development has been known for several decades. Chronic and severe iodine deficiency can cause impaired development of the brain called "endemic cretinism"[9]. However, so serious effect of the thiocyanate (with sufficient intake of iodine) has not been proved, not even for smoking mothers- who have permanently elevated levels of thiocyanate in the blood serum[10].

Regardless of practically the same cause, differences were found between lack of dietary iodine (iodine deficient diet) and iodine deficiency induced by thiocyanate. This is corroborated by experiment[8], in which several groups of rats were fed by a low iodine diet or control diet with addition of potassium thiocyanate (with sufficiency of iodine). Treatment was discontinued or applied to particular groups in different periods (pregnancy, lactation). The study demonstrated that effect of thiocyanates has not a more significant negative effect on development of pups in comparison with the effect of a low-iodine diet.

Two-generation study[3], that is reported in registration dossier, is primarily focused on transport of some specific nutrients. Despite the fact that this study was not performed according to OECD or EU standards, it provides some useful information on reproductive toxicity. At constant dose level 25 mg/animal/day of potassium thiocyanate, variations in clinical chemistry were reported but no effect on the body weights or brain weights of the pups (F2) was observed.

Reducing the rate of brain microtubule formation reported in the literature[11] may be the intrinsic mechanism of action (or part of this mechanism) of iodine deficiency in organism. Lasting alterations in brain development were observed only during long exposure low-iodine diet while it has not been demonstrated whether it is possible to induce such iodine deficiency via thiocyanate treatment. On the other hand, it has been documented that with sufficient intake of iodine (regardless of the presence of thiocyanate) damage is not nearly as severe[12]. Iodine transport seems to be only partially affected despite high thiocyanate levels, suggesting that thiocyanate-insensitive iodide transporters, alternative to NIS hormone, are active or that NIS hormone is autoregulated to keep iodide transport unaltered[10].

Based on these findings, it can be concluded that a relationship exists between lack of iodine in organism and developmental disorders of foetus. From the above considerations it can be concluded that these developmental disorders are secondary effects of maternal toxicity (hypothyroidism). Lack of iodine can also be caused by thiocyanate treatment limiting intake of iodine into the body. At this point it should be emphasized that although the true iodine deficiency (caused by lack of iodine in the organism) may lead to permanent severe brain damage of the foetus, with thiocyanate treatment (with sufficient of iodine in the body) such severe developmental defects has not been proven. Pursuant to rules for classification of reproductive toxicity in the Regulation (EC) No. 1272/2008 (CLP) and based on the available information, the eMSCA concludes that lack of iodine and the consequent developmental disorders caused by thiocyanate are not significant enough (moreover they are associated with maternal toxicity) to warrant classification for reproductive toxicity with effects on development.

7.9.8. Hazard assessment of physico-chemical properties

Not relevant for this evaluation.

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

Not relevant for this evaluation.

7.9.10. Conclusions of the human health hazard assessment and related classification and labelling

Not relevant for this evaluation.

7.10. Assessment of endocrine disrupting (ED) properties

7.10.1. Endocrine disruption – Environment

Not relevant for this evaluation.

7.10.2. Endocrine disruption - Human health

Assessment of endocrine effect was carried out according to definition of WHO[(1)]:

An endocrine disruptor is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations.

The eMSCA considers that ammonium thiocyanate does not meet the initial part of the definition of WHO[(1)] as the term "exogenous" means external, unnatural to an (human) organism. In fact, thiocyanates are usual part of the environment including human/animal bodies.

Thiocyanates are potent inhibitor of iodide transport and they are a competitive substrate for the thyroid peroxidase. Blockage of the iodide trapping mechanism has a negative effect on the thyroid gland, similar to iodine deficiency. The blood levels of iodine-based hormones T_4 (thyroxine) and T_3 (tri-iodothyronine) are decreased, resulting a in a compensatory increase in the secretion of TSH by the pituitary gland. The hypertrophy and hyperplasia of follicular cells following sustained exposure results in an increased thyroid weight and the development of goiter[(7)].

Besides thiocyanates, the effect of thyroid disrupting compounds on the sodium-iodide symporter receptor protein has been illustrated with several environmental chemicals, including, perchlorate, bromate, and nitrate. Each of these compounds compete with iodine for binding to the sodium-iodide symporter transport protein inhibiting the uptake of iodine into the follicular thyroid cell. The putative effect of this inhibition is a decreased synthesis of thyroid hormones T_4 and T_3.

The whole iodine treatment takes place in the follicular cells of the thyroid gland. Follicular thyroid cells active isolate inorganic salts of iodine from the blood by means of sodium-iodide symporter (NIS) - transmembrane glycoprotein which transports iodide anions into the cell. Inside the cell, iodide is covalently bind to tyrosine using an enzyme thyroid peroxidase (TPO). Monoiodotyrosine and/or diiodotyrosine subsequently condense to thyroid hormones T_3 or T_4. These hormones in an inactive form are accumulated in the follicles of the thyroid gland. Only after signaling which is mediated by thyrotropin (thyroid stimulating hormone (TSH), synthesized in the anterior pituitary gland), they are activated and in an active form are released into the blood.

This (simplified) mechanism takes place regardless of the presence of thiocyanates or their concentration with the exception of iodine intake.

According to information above, thiocyanates do not impair the activities of the thyroid gland itself. Thiocyanates only reduce the entry of iodide ions into the thyroid gland via competitive anion inhibition. In this manner, the subsequent reaction chain is limited due to lack of iodine compounds (including lack of hormones T_3 and T_4). However, thiocyanates do not directly affect these reactions neither enter into them nor block them. The only consequence is a limited intake of iodine. From the foregoing it can be concluded that the actual activity of the thyroid gland is not affected by thiocyanates, so from this point of view it is not an endocrine disrupting effect according to the definition of WHO[(1)]. The eMSCA concludes that based on the available information, the concern for endocrine disruption is not confirmed.

7.10.3. Conclusion on endocrine disrupting properties (combined/separate)

Endocrine activity of ammonium thiocyanate in relation to the environment is not part of concerns for this evaluation.

Assessment of the effects of ammonium thiocyanate on the human endocrine system was carried out with special attention to activity on thyroid gland. According to collected information, thiocyanates do not impair the activities of the thyroid gland itself. Thiocyanates only reduce the entry of iodide ions into the thyroid gland via competitive anion inhibition. In this manner, the subsequent reaction chain is limited due to lack of iodine compounds. However, thiocyanates do not directly affect these reactions neither enter into them nor block them. The only cause is a limited intake of iodine. From the foregoing it can be concluded that the actual activity of the thyroid gland is not affected by thiocyanates, so from this point of view it is not an endocrine disrupting effect according to the definition of WHO. Based on the available information may be concluded that the concern for endocrine disruption for human health is not substantiated.

7.11. PBT and vPvB assessment

Not relevant for this evaluation.

7.12. Exposure assessment

7.12.1. Human health

7.12.1.1. Worker

The eMSCA has carried out an exposure assessment based on the information provided in the registration dossier and agrees with the Registrants' assessment and concludes that there is no concern for occupational exposure. More detailed information are stated in Part C – Confidential Annex.

7.12.1.2. Consumer

Exposure of consumers is not expected.

7.12.2. Environment

Not relevant for this evaluation.

7.12.3. Combined exposure assessment

Not relevant for this evaluation.

7.13. Risk characterisation

Some potential risks for human health, arising from the use of ammonium thiocyanate, have been identified: This substance was classified as Acute Toxic (category 4) and Eye Damage (category 1). During long-term administration of ammonium thiocyanate adverse effects were observed as well although their influence was not very strong.

Dermal exposure is conceivable but the experimental assay demonstrated a low degree of penetration of thiocyanate through a skin. Inhalation exposure is probable and rapid but

formation of an inhalable fraction (dust) is limited as solid ammonium thiocyanate is hygroscopic and spraying applications are characterized as big droplets/not nebulizing (i.e. low/medium dustiness).

The structure of exposure scenarios including descriptors was taken from registration dossier and CSR for ammonium thiocyanate. Required RMM are noted for each scenario (Part C – Confidential Annex). Under circumstances which are specified in these scenarios all risks resulting from the use of ammonium thiocyanate are under control (relevant RCRs are below 1), therefore the eMSCA concludes that there is no concern for occupational exposure.

Environmental exposure is not relevant for this evaluation.

7.14. References

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7.15. Abbreviations

CAS	Chemical Abstract Services
CoRAP	Community Rolling Action Plan
CSR	chemical safety report
DNEL	derived no effect level
ECHA	European Chemicals Agency
ES	exposure scenario
NIS	sodium-iodide symporter
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
PBT/vPvB	persistent, bioaccumulative and toxic / very persistent and very bioaccumulative substances
(Q)SAR	quantitative structure-activity relationship
RCR	risk characterization ratio
RMM	risk management measuring
T_3	triiodothyronine (thyroid hormone)
T_4	thyroxine (thyroid hormone)
TPO	thyroid peroxidase
TSH	thyroid stimulating hormone
WHO	World Health Organization

Part C – Confidential Annex has been removed for this public document.