Regulatory Management Option Analysis Conclusion Document

Substance Name:

Group of isothiazolinones including:

- **2-methyl-2H-isothiazol-3-one (MIT),**
- **reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one (CMIT) and MIT CMIT/MIT (3:1),**
- **1,2-benzisothiazolin-3-one (BIT),**
- **2-n-octyl-4-isothiazolin-3-one (OIT),**
- **2-methyl-2H-isothiazol-3-one hydrochloride (MITH)**

EC Number:

CAS Number:

Authority: The Netherlands

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Foreword

The purpose of Risk Management Option analysis (RMOA) is to help authorities decide whether further regulatory risk management activities are required for a substance and to identify the most appropriate instrument to address a concern.

RMOA is a voluntary step, i.e., it is not part of the processes as defined in the legislation. For authorities, documenting the RMOA allows the sharing of information and promoting early discussion, which helps lead to a common understanding on the action pursued. A Member State or ECHA (at the request of the Commission) can carry out this case-by-case analysis in order to conclude whether a substance is a 'relevant substance of very high concern (SVHC)' in the sense of the SVHC Roadmap to 2020[1].

An RMOA can conclude that regulatory risk management at EU level is required for a substance (e.g. harmonised classification and labelling, Candidate List inclusion, restriction, other EU legislation) or that no regulatory action is required at EU level. Any subsequent regulatory processes under the REACH Regulation include consultation of interested parties and appropriate decision making involving Member State Competent Authorities and the European Commission as defined in REACH.

This Conclusion document provides the outcome of the RMOA carried out by the author authority. In this conclusion document, the authority considers how the available information collected on the substance can be used to conclude whether regulatory risk management activities are required for a substance and which is the most appropriate instrument to address a concern. With this Conclusion document the Commission, the competent authorities of the other Member States and stakeholders are informed of the considerations of the author authority. In case the author authority proposes in this conclusion document further regulatory risk management measures, this shall not be considered initiating those other measures or processes. Since this document only reflects the views of the author authority, it does not preclude Member States or the European Commission from considering or initiating regulatory risk management measures which they deem appropriate.

[1] For more information on the SVHC Roadmap: http://echa.europa.eu/addressing-chemicals-of-concern/substances-of-potential-concern/svhc-roadmap-to-2020-implementation

1. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

This RMOA is focused on occupational and consumer exposure to isothiazolinones. Isothiazolinones are used as preservatives in many industrial and consumer products, such as water based paints, glues, detergents and cleaning agents, household products, in cosmetic products and toys (e.g. toy slimes) and also as biocidal agents e.g. slimicides. Thus, isothiazolinones are widely used and the use of isothiazolinones is regulated by several legislations.

Harmonised classification as a skin sensitiser has been established for 2-methyl-2H-isothiazol-3-one (MIT), 1,2-benzisothiazol-3(2H)-one (BIT), 2-octyl-2H-isothiazol-3-one (OIT), and the reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one (CMIT) and MIT (CMIT/MIT (3:1)). For 2-methyl-2H-isothiazol-3-one hydrochloride (MITH) an intention for harmonised classification has been issued. For some other isothiazolinones, such as CMIT, no harmonised classification has been established yet.

Preservatives in cosmetics are regulated under the Cosmetics regulation (Regulation (EC) No 1223/2009); only preservatives listed on the authorisation list in Annex V are allowed in cosmetic products. In case of isothiozalinones, only MIT and CMIT/MIT (3:1) in rinse off cosmetics are included in this list, in concentrations of <0.0015%. BIT is not allowed as a preservative in cosmetics under Cosmetics regulation. However in the ECHA registration dossier[2] applications in cosmetic products are listed for BIT.

Currently, preservatives used in detergents should be listed, irrespective of their concentration (Regulation (EC) No 648/2004). Detergents are also in the scope of REACH and CLP and thus regulated under these directives.

The Toy Safety Directive sets concentration limits for several isothiazolinones in aqueous toys such as toy slimes (Directive 2009/48/EC).

Of note, revisions of the Detergents Regulation and the Toy Safety Directive is currently ongoing[3,4].

The isothiazolinones that are within the scope of this RMOA are also regulated under the Biocidal Products Regulation (BPR; Regulation (EU) No 528/2012). Although treated articles (e.g. paints and detergents) do not undergo a product authorisation, placing on the market of these products can be subject to specific conditions set at the active substance approval. BIT, MIT and OIT are currently under review for several applications under the BPR.

Please note:

France, Germany and Ireland are working on a group of 'skin sensitising substances in consumer mixtures[5]' preparing for a possible restriction. At this moment it is not yet clear if isothiazolinones are in the scope of this group.

ECHA is preparing an ARN on isothiazolinones. The information in this RMOA can be used for this ARN.

[2] Source: https://echa.europa.eu/nl/registration-dossier/-/registered-dossier/22961/3/1/6
[3] Source: https://single-market-economy.ec.europa.eu/publications/com2023217-proposal-regulation-detergents-and-surfactants_en
[4] Source: https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/13164-Protecting-children-from-unsafe-toys-and-strengthening-the-Single-Market-revision-of-the-Toy-Safety-Directive_en
[5] skin sensitising substances in consumer mixtures ; https://ec.europa.eu/docsroom/documents/49734

2. CONCLUSION OF RMOA

It is concluded that additional regulatory management measures are needed.

Conclusions	**Tick box**
Need for follow-up regulatory action at EU level:	X
Harmonised classification and labelling	
Identification as SVHC (authorisation)	
Restriction under REACH	X
Other EU-wide regulatory measures	
Need for action other than EU regulatory action	
No action needed at this time	

It is concluded that the following risk management measures are considered most appropriate to address the concern for adverse health effects to workers and consumers caused by exposure to isothiazolinones:

- *A restriction under REACH. The following restriction options can be considered:*

  1) A combination of:

     a. Setting a limit for the concentration of isothiazolinones allowed in products in line with the minimum effective level of isothiazolinones. As the concentration of isothiazolinones needed for preservation differs per product group, different limits could be set for different product groups.

     b. Restricting the addition of more than one isothiazolinone in a mixture.

  2) Setting a concentration limit for the sum of all concentrations of isothiazolinones in a mixture taking into account relative potency factors of individual isothiazolinones. Please note that a pragmatic approach should be chosen in the absence of a scientific derivation of a concentration limit value.

The preference of the NL-CA would be option 2 due to practicability and feasibility.
A restriction is expected to result in a decreasing incidence of sensitisation among workers and consumers and prevention of regrettable substitutions.

3. NEED FOR FOLLOW-UP REGULATORY ACTION AT EU LEVEL

Table: SVHC Roadmap 2020 criteria

	Yes	No
a) Article 57 criteria fulfilled?[1]		X[2]
b) Registrations in accordance with Article 10?[2]	MIT, BIT, OIT, CMIT/MIT (3:1), MITH	No registration of other isothiazolinones
c) Registrations include uses within scope of authorisation?	X	
d) Known uses not already regulated by specific EU legislation that provides a pressure for substitution?	X	

[1]Article 57 could be fulfilled due to health hazard based on self-classification and epidemiological studies (Carc. 1A/1B, germ cell mut 1A/1B, reproductive toxicity 1A/1B, PBT, vPvB, ED according to CLP or equivalent level of concern).
[2]There is no precedent for fulfilling Article 57 based on skin sensitising properties.

Isothiazolinones are used in a wide variety of industrial, household and cosmetic products, so the possibility that consumers and workers come into contact with some substances in this group of skin sensitisers is high. These substances possess skin sensitising properties in varying potency. Exposure can lead to sensitisation of susceptible individuals, potentially resulting in allergic contact dermatitis following repeated exposure.

It is important to avoid regrettable substitutions of isothiazolinones. As currently no suitable alternatives are available as preservatives, it is not possible to completely ban the use of all isothiazolinones. However further regulation should lead to a decrease of sensitisation cases. For example, a high incidence of MIT sensitisation was previously described in Europe but is currently declining in most, but not all, European countries following regulatory measures[6]. As the use of other isothiazolinones, such as OIT and BIT is increasing[7,8], a group approach is recommended to limit exposure and the incidence of sensitization to these and other isothiazolinones.

3.1 Restriction under REACH

Restriction requires an unacceptable risk to human health or the environment arising from the manufacture, use or placing on the market of substances. Isothiazolinones are of concern mainly due to its skin sensitisation potency, wide-spread use, and exposure among consumers and workers. A restriction under REACH has been identified as the preferred regulatory option to reduce the sensitisation risk of workers and consumers. The following restriction options can be considered:

Elaboration on restriction option 1: a combination on setting a concentration limit for individual isothiazolinones in products for end-use with prohibiting adding more than one isothiazolinone to a single product for end-use:

- Setting a limit for the concentration of isothiazolinones allowed in products in line with the minimum effective level of isothiazolinones. As the concentration of

[6] Uter, W., et al. (2020). "The epidemic of methylisothiazolinone contact allergy in Europe: follow-up on changing exposures." Journal of the European Academy of Dermatology and Venereology 34(2): 333-339.
[7] Source: http://www.spin2000.net/spinmyphp/?pid=2634335
[8] Thomsen, A. V., et al. (2018). "Isothiazolinones are still widely used in paints purchased in five European countries: a follow-up study." Contact Dermatitis 78(4): 246-253.

isothiazolinones needed for preservation differs per product group, different limits could be set for different product groups.

- In line with the Cosmetics regulation, the use of isothiazolinones within the scope of the REACH regulation should be restricted to concentrations not exceeding the specific harmonised classification concentration limits for skin sensitisation. This limits the concentrations of individual isothiazolinones.
- However these concentration limits do not necessarily represent safe levels (for several sensitising substances no safe threshold level exists). Setting a concentration limit based on the limit where the isothiazolinones are still effective or based on what is available on the market could be another approach. The concentration of isothiazolinones needed for preservation differs per product group. Therefore different limits could be set for different product groups.
- However, this does not protect against exposure to different sources of isothiazolinones in a single mixture: it is possible that when more than one isothiazolinone is present in a mixture, that the specific concentration limits of each isothiazolinone individually are not exceeded but the total concentration is still too high. Therefore a restriction should also be established on adding more than one isothiazolinone to a single mixture.

Elaboration on restriction option 2: setting a limit for the total allowed concentration of isothiazolinones in a product for end-use. Isothiazolinones with a similar mode of action or cross sensitivity can be considered for this option. However data on cross-reactivity are scarce. Please note that the total concentration of preservatives needs to be at a level where preservation is effective.

The preference of the NL-CA would be option 2 due to practicability and feasibility.

The following restriction options were deemed less feasible, due to a lack of suitable alternative preservation agents:

- A total ban on the manufacture and use of isothiazolinones would prevent all (potential) health risk;
- A ban of high-risk uses.

3.2 BPR

For treated articles and biocidal products used in treated articles the following (combination of) regulatory management options are possible under the BPR:

- Setting concentration limits for individual isothiazolinones in treated articles (e.g. paints and detergents), corresponding to concentrations that do not trigger classification as a skin sensitiser under CLP (as already regulated for e.g. CMIT/MIT (3:1)).

This is a suitable option for preventing high concentrations of individual isothiazolinones. However, this option does not prevent adding other biocidal products containing isothiazolinones to the same treated article. This can result in a high total concentration of isothiazolinones treated articles.

- Setting a concentration limit for the sum of all concentrations of isothiazolinones in a treated article taking into account relative potency factors of individual isothiazolinones.
- Prohibiting the addition of more than one isothiazolinone to a biocidal product, combined with prohibiting the addition of more than one biocidal product containing isothiazolinones to treated articles and a concentration limit of individual

isothiazolinones in treated articles corresponding to concentrations that do not trigger classification as a skin sensitiser under CLP.

However, concentration limits for treated articles only apply to treated articles that are produced within the EU. When treated articles are produced outside the EU and imported in the EU, these concentration limits do not apply. Also the BPR only covers uses as biocidal products. Therefore, a restriction under REACH is deemed the preferred regulatory option.

3.3 Harmonised classification and labelling

Harmonised classification as skin sensitisers has been established for MIT, reaction mass of MIT/CMIT (3:1), BIT and OIT. For MITH an intention for harmonised classification has been issued. For some isothiazolinones, such as CMIT, no harmonised classification has been established yet. Classification of the whole group of isothiazolinones will avoid regrettable substitution. However, the isothiazolinones that are most commonly used already have a harmonised classification. For the isothiazolinones that are less commonly used, less information is available to derive a harmonised classification. Read-across might be sufficient for deriving a harmonised classification for some isothiozolinones without classifications, however, determining specific concentration limits solely using read-across is not feasible.

Currently, classification of a mixture only applies when concentrations of individual isothiazolinones exceed the specific concentration limits set under CLP. The sum of the concentrations of all isothiazolinones is currently not considered for classification. Applying additivity for classification of a mixture for skin sensitisation could therefore be an option. However, additivity is generally not applied for skin sensitisation. Additionally, additivity is usually based on the total mass of a substance or, more specifically, the mass % of the part of the molecule that is responsible for the health effect. Since the chemical structure of several isothiazolinones can be very different it is questionable if additivity can be applied to this group.

4. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS IF NECESSARY

An indication of a tentative plan is provided below.

Follow-up action	Date for follow-up	Actor
Restriction options: 1) A combination of: - Setting a limit for the concentration of isothiazolinones allowed in products in line with the minimum effective level of isothiazolinones. As the concentration of isothiazolinones needed for preservation differs per product group, different limits could be set for different product groups. - Restricting the addition of more than one isothiazolinone in a mixture. 2) Setting a concentration limit for the sum of all concentrations of isothiazolinones in a mixture taking into account relative potency factors of individual isothiazolinone.		