Independent Authority for Public Revenue
Directorate General
General Chemical State Laboratory
Directorate of Energy, Industrial & Chemical Products

Risk Management Option Analysis Conclusion Document

Substance Name: (-)-pin-2(10)-ene

EC Number: 242-060-2

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Authority: EL

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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

Not applicable.

2. CONCLUSION OF RMOA

This conclusion is based on the REACH and CLP data as well as other available relevant information taking into account the SVHC Roadmap to 2020, where appropriate.

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

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

Since there had been information missing in the registration dossiers for the evaluation of the risks associated with the substance, a substance evaluation process was the first step in the risk management measures analysis. The SEv process led to the update of the registration dossier by the registrants in order to fill the data gaps identified, namely the high RCRs for certain exposure scenarios, the assessment of the consumers exposure, the evaluation of the environmental hazards of the substance and finally the evaluation of the respiratory sensitization hazard of the substance by including in the dossier the literature and data that were missing.

3.1 Harmonised classification and labelling

(-)-Pin-2(10)-ene does not have a harmonised C & L, but is self-classified as a skin sensitizer 1B and could potentially be a respiratory sensitizer. The data set on respiratory sensitisation provided by the registrants in the updated registration dossier, as a deliverable of the SEv process, is satisfactory, but the evaluation of the data and the application of the CLP criteria could be done differently.

It is important to note that according to the Reg. 1272/2008/EC classification criteria, there are no formally recognised and validated animal tests for respiratory sensitisation. Data from human observations indicating respiratory sensitisation (specific respiratory hypersensitivity and/or asthma, other hypersensitivity reactions such as rhinitis/conjunctivitis and alveolitis) in exposed populations can be used for classification purposes. Relevant information with respect to respiratory sensitisation may be available from case reports, epidemiological studies, medical surveillance, reporting schemes.

However, data from some animal studies may be indicative of the potential of a substance to cause respiratory sensitisation in humans (CLP Annex I, 3.4.2.1.3) and may provide supportive evidence in case human evidence is available. Respiratory sensitisation is considered a condition with the clinical character of an allergic reaction. However, immunological mechanisms do not have to be demonstrated.

There seems to be evidence for potential human respiratory sensitization by beta-pinene. Available studies are either using (-)-pin-2(10)-ene, as the test material or pinene isomers (e.g. alpha-pinene), racemic mixture thereof or structurally related substances, such as delta-carene. Indicatively, plywood mill workers in New Zealand exposed to pinene, among others, appear to have an increased risk of developing work-related respiratory symptoms, with asthma symptoms being more common than in the general population and associated with duration of employment and were reported to lessen or disappear during holidays (Fransman et al., 2003). Results from lung function tests in Swedish workers indicate chronic rather than acute reactions in the airways (Eriksson et al., 1997). In Finnish sawmill workers, work-related respiratory symptoms appeared to correlate with monoterpene exposure during processing of pine and with wood dust exposure during processing of spruce (Rosenberg et al., 2002). Recently, it has been suggested that human lung function may be negatively associated with the presence of alpha-pinene indoors in the Canadian population (Cakmak et al., 2014). Moreover, animal studies in BALB/c mice suggest that (+/-)-alpha-pinene/ozone reaction products may have moderate-lasting adverse effects on both the upper airways and pulmonary regions, important in the context of the etiology or exacerbation of lower airway symptoms in office workers, or of occupational asthma in workers involved in industrial cleaning operations (Rohr et al., 2002; Nielsen et al., 2005)., Results from in vitro studies suggest synergistic antitumor activity of paclitaxel applied together with alpha- or beta-pinene in tumor lung cells (Zhang et al., 2015). The effects of alpha- and beta-pinene were also studied on rat trachea in vitro and it was found that in tracheal rings they both potentiated the contractions induced by acetylcholine (ACh) (Lima et al., 2010).

The registrants in the updated dossier included enough new studies and claimed that occupational studies report respiratory parameters of workers, who were co-exposed to monoterpenes, but also to wood dust and potentially many other irritant substances, which is true. The toxicological effect of the other cofactors was not taken into account in those studies. The registrants reasoned that changes in the respiratory parameters showed chronic rather than acute reaction in the airways, which would probably be due to wood dust exposure rather than terpenes exposure (Eriksson, 1997). These results were confirmed, according to the registrants, by studies in human volunteers exposed for 2h to alpha-pinene, where no significant changes in respiratory parameters could be identified (Falk, 1990). Also, exposure of healthy volunteers to Oriented Strand Boards emissions did not elicit sensory irritations or pulmonary effects. More particularly, 2 h exposures to mixed emissions with terpenes concentrations up to 4.6 mg/m3 (including up to 0.7 mg/m3 beta-pinene) did not induce acute respiratory health effects in humans (Gminski, 2010). Based on the above, the registrants and concluded that classification for any inhalation hazard (respiratory tract irritation or respiratory sensitisation) is not warranted.

It has been made evident that evaluation of human data for (-)-pin-2(10)-ene, which can be ambiguous and lead to different conclusions, along with supporting animal data, has to be assessed through a regulatory process of an Annex VI CLH dossier after the conclusion of the SEv process. In this CLH dossier development process, the issue of substance identity of the test material which causes the respiratory sensitisation effects (i.e. (-)-pin-2(10)-ene, pinene isomers (e.g. alpha-pinene), racemic mixture thereof or structurally related substances, such as delta-carene) would also be clarified.

The Registrants could possibly act as CLH dossier submitter. It is not mandatory for a MSCA to submit the CLH dossier since (-)-pin-2(10)-ene, as it is not a biocidal active substance (art. 36 and 37 Reg. 1272/2008/EC). If there is no registry of intention by the end of 2016, then MSCAs should review the situation and decide accordingly

(-)-Pin-2(10)-ene is registered for uses within the scope of authorisation (i.e., formulation

of substances and mixtures). The substance meets the relevant criteria in the Roadmap (Chapter 4), and therefore initiation of the authorisation by including the substance in the Candidate List should also be considered. Alternatively, a restriction process based on specific uses could be a viable solution for addressing and adequately controlling the risk on an EU wide basis. This assumes that the CLH process does substantiate the sensitizing risks of (-)-pin-2(10)-ene. In conclusion we propose the following approach, after the conclusion of the SEv process:

- ✓ Preparation of a CLH dossier
- ✓ Preparation of a restriction dossier/suggestion for an OEL to SCOEL

Depending on the outcome of 1 and 2 inclusion of (-)-pin-2(10)-ene in the candidate list and/or restriction on specific uses, especially the ones that consumers are exposed to, could be initiated.