Methacrylates sector group statement concerning the classification of MMA as a respiratory sensitizer

Updated March 2023

RAC opinion to classify MMA as a respiratory sensitiser

On 18 March 2021, the ECHA Committee for Risk Assessment (RAC) adopted a recommendation to classify Methyl methacrylate[1] (MMA, CAS No. 80-62-6, EC No. 201-297-1) as a respiratory sensitizer category 1 with the hazard statement H334 (i.e. may cause allergy or asthma symptoms or breathing difficulties if inhaled). The original proposal was made by the French national competent authority ANSES on 26 February 2019. The dossier had been returned to the RAC in March 2021 to reexamine their previous opinion of October 2020 in light of new information presented by industry.

The evidence used by RAC comprised reports of 6 positive Specific Inhalation Challenge (SIC) tests with MMA supported by occupational asthma claimed to be caused by MMA within National Surveillance databases that the RAC considers indicative of the involvement of immunological mechanisms.

Official Procedure

A RAC opinion does not result in any immediate changes to the harmonized classification of a substance according to the CLH process. The opinion has to be endorsed by the Competent Authorities for REACH and CLP (CARACAL) and accepted by the European Commission before inclusion in an Adaptation of Technical Progress (ATP) to CLP. This process is ongoing but is unlikely to result in implementation in law before the end of 2024 at the earliest.

Industry's Response to RAC's conclusions

The Methacrylates Sector Group (MSG), a sector group of Cefic, is committed to ensuring the health and safety of workers and protecting them from harmful levels of exposure to MMA at the workplace. We found that the current evidence presented in RAC opinions not sufficient to demonstrate that MMA causes asthma and should therefore result in classification as respiratory sensitizer category 1. MSG believes that further dialogue and sharing of information is necessary to ensure the most accurate and comprehensive assessment of the potential hazards associated with MMA.

MSG therefore called on the RAC to reconsider their opinion and also exchanged relevant supporting information with the European Chemicals Agency (ECHA) and EU Commission.

Prior to and during the RAC reviews in October 2020 and March 2021, the Methacrylates REACH Task Force (MRTF) and MSG provided data in written comments that supported the view that MMA is a classified

[1] Methacrylates - Petrochemicals Europe (petrochemistry.eu)

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irritant chemical that exacerbates but does not cause occupational asthma. This data is summarized as follows:

The RAC opinion primarily relied upon 6 positive Specific Inhalation Challenge (SIC) tests conducted with mixtures claimed to be containing predominately (>90%) MMA. Subsequent further investigation by the MSG has uncovered information to suggest that in at least 4 of the 6 cases the individuals were not exposed to predominantly MMA during the SIC test, as claimed. Furthermore, in the remaining 2 cases they were likely exposed to mixtures and there is no information available to conclude that MMA was predominantly present in these mixtures. As a result, the basis of the positive outcome of these studies cannot conclusively be attributed to MMA with the necessary scientific confidence.

The RAC interpreted the observation of Late Asthmatic Responses observed in some of these cases as proof of MMA acting through an immunological mechanism rather than through other mechanisms, such as irritation. In this regard, the available clinical science in published peer reviewed literature does not support this interpretation.

It was also considered by RAC that irritation, the alternative mechanism to sensitisation, could not have occurred during these 6 positive SIC tests on the basis that low average levels of exposure were measured during comparable (negative) SIC tests with other products containing MMA. However, peak concentrations are widely recognized as being responsible for causing irritation. Therefore since only average levels were measured and not peak levels, this analogous evidence is not conclusive that irritation could not have occurred and caused the observed symptoms.

Further evidence that high peak exposures capable of causing irritation were likely to have occurred during these 6 SIC tests was provided by MRTF and MSG in the form of reliable exposure measurements from the German dental industry. These data demonstrated that despite low average exposure levels, significant peak exposures occur in workplace situations that were being simulated in the SIC tests. This evidence was disregarded without justification.

Regarding the supporting clinical cases from National Surveillance databases referenced in the RAC opinion, RAC acknowledged the low reliability of this evidence, recognizing that it is difficult to determine the exact cause of the asthma since only limited and insufficient clinical data is available from these databases upon which to make this determination. Additional factors such as co-exposure to other chemicals in the workplace cannot reliably be excluded as the cause of the development of asthma, or provocation of responses in hyperreactive individuals. These chemicals that are often also used in the workplaces include irritant chemicals, dusts and in some cases substances already classified as respiratory sensitizers.

In line with a recent recommendation by Meek et al. (2023)[2], MSG is of the view that RAC should complete a formal weight of evidence assessment consistent with CLP criteria for classification as a Respiratory Sensitiser. Such an assessment has been conducted and published in peer reviewed scientific literature[3] concluding that the available evidence for MMA does not support classification as respiratory sensitizer cat

[2] Meek, Bridges, Fasey, *et al.; Arch Toxicol* (2023). https://doi.org/10.1007/s00204-023-03448-w

[3] Pemberton & Kimber; Crit Rev Toxicol. 2022 Feb;52(2):139-166. https://pubmed.ncbi.nlm.nih.gov/35607993/

1. This evaluation is consistent with the absence of asthma in major industries, such as cast acrylic sheet manufacture, where workers are exposed to even higher levels of MMA than those in the industries in which occupational asthma due to MMA is claimed, i.e., dental care and artificial nails.

MSG is committed to continuing cooperation with all relevant stakeholders to achieve a comprehensive and transparent scientific (re)assessment of the evidence with regard to respiratory sensitization. To further progress this endeavor, MRTF has recently funded two additional initiatives by renowned experts which highlight critical issues with the evidence upon which the classification proposal? was taken which stresses the importance of a proper weight-of-evidence assessment for MMA. We are willing to engage in further dialogue with ECHA and other stakeholders to address any concerns related to the hazard assessment of MMA.

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