Committee for Risk Assessment

RAC

Annex 4

Records

of the targeted public consultation following the submission of a study relating to the classification for respiratory sensitisation of

methyl methacrylate methyl 2-methylprop-2-enoate methyl 2-methylpropenoate

EC Number: 201-297-1
CAS Number: 80-62-6

CLH-O-0000006852-69-01/F

Adopted

18 March 2021

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ANNEX 4 – RECORDS OF THE TARGETED PUBLIC CONSULTATION ON METHYL METHACRYLATE METHYL 2-METHYLPROP-2-ENOATE METHYL 2-METHYLPROPENOATE

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

The proposal for the harmonised classification and labelling (CLH) of **methyl methacrylate methyl 2-methylprop-2-enoate methyl 2-methylpropenoate** (EC 201-297-1; CAS 80-62-6) was submitted by France and was subject to a consultation from 06/05/2019 to 05/07/2019.

The CLH opinion for this substance was originally scheduled for discussion by the Committee for Risk Assessment (RAC) at its March 2020 meeting and included information from a recently published study which is additional to that included in the CLH report to support its conclusions on classification for respiratory sensitisation. An ad hoc consultation was launched from 13/02/2020 to 27/02/2020 and the comments received are listed below.

ECHA accepts no responsibility or liability for the content of this table.

Substance name: methyl methacrylate methyl 2-methylprop-2-enoate methyl 2-methylpropenoate
EC number: 201-297-1
CAS number: 80-62-6
Dossier submitter: France

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Germany	<confidential>	Company-Downstream user	1
Comment received				
Als langjähriger Verarbeiter von MMA-basierten Dach-/ und Bodenbeschichtungen weisen wir darauf hin, dass in unserem Betrieb bisher keine Atemwegserkrankungen wie Asthma, durch den Umgang mit MMA-haltigen Produkten aufgetreten sind. Wir halten daher die Einstufung von MMA als atemwegssensibilisierend für nicht erforderlich.				
RAC's response				
First, RAC would like to remind that classification concerns the intrinsic properties of a substance and therefore the scope here is the hazard assessment of MMA, not its risk assessment. Furthermore, case reports on MMA-induced occupational asthma, for example in the European occupational diseases databases, concern particularly nail beauticians and dental and medical prosthesis technicians. It should be noted that particular exposure conditions, not applicable to all uses, may play a role. Therefore, lack of MMA-induced asthma cases in the particular use scenarios of specific companies or sectors does not demonstrate a lack of intrinsic respiratory sensitising potential by MMA. In addition, underdiagnosis and underreporting of MMA-induced asthma cases is conceivable, as the possibility of MMA-induced respiratory sensitisation is not well known among physicians.				

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Germany	Röhm GmbH	Company-Manufacturer	2
Comment received				
We highly appreciate the opportunity to comment on this publication at this stage of the CLH process. We recognize the efforts of the authors to investigate the phenotypic patterns of OA and the high level of accuracy for an OA diagnosis when done with the presented diagnostic				

tools. We therefore do not doubt the diagnosis of OA as such from a diagnostic perspective.
However, from a risk assessment perspective we have detected several serious deficiencies in this publication despite of additionally available data provided by the corresponding author of the publication in attachment #1 to our feedback:
- Lack of data available data to assign causality to specific substances or agents prohibiting an independent review according to ECHA
- Missing information on workplace and SIC exposure levels to MMA is impairing a valid uncertainty analysis for potential co-exposure and potentially irritating peak exposures
- Grouping approach inconsistent with ECHA RAAF guidance and inappropriate for substance specific CLH review
- Indifferent response patterns of methacrylates and other LMW agents
- Lack of rigor in the assignment of occupational asthma types to CLP specifications and to WHO definitions
- Inconsistencies in the used QSAR model for an "asthma hazard index"
- Further inconsistencies and deficiencies in in the methodological approach, thereby interfering with the WHO scheme for OA
Based on these deficiencies, we conclude that this publication is of insufficient quality for hazard assessment purposes.
We believe that some, but not all, limitations can be addressed with additional details on case-by-case level and on methodology so that we have contacted the corresponding authors already for responsible care reasons. We would like to outline at this point that we have also contacted ANSES as dossier submitting authority and owner of the RNV3P database before and after the public consultation period in 2019. Our requests on relevant details of the RNV3P cases - thereby following our obligations as registrants of MMA - were however rejected or not answered for the time being.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 2020-02-25_MMA_Targ_Cons_Feedback_Roehm_REACh_TF_complete.pdf

RAC's response

It is important to remember that classification proposals do not concern risk assessment. For the hazard assessment of MMA, in addition to the data included in the Suojalehto *et al.* (2019) publication and the additional data from the authors included in the attachment of the comment, RAC received further additional data from the authors. This data included information on six cases, where MMA could be determined, after a careful examination by experts, as the predominant exposure at the workplace. These six subjects also had positive responses to MMA in the SIC, widely considered to be the reference standard of diagnosis of sensitiser-induced occupational asthma. The SICs were designed to recreate an exposure comparable to that at the subjects' workplaces. Importantly, the concentration levels were kept well below irritant concentrations and relevant OELs (8 h OELs are 10–50 ppm across Europe). Furthermore, in the SICs in Suojalehto *et al.* (2019), also placebo exposures were conducted for the subjects. The aim of the placebo test is to expose a subject with a similarly irritant, non-sensitizing agent. If the patients' positive reactions would have been due to respiratory irritation, they should have had a positive reaction also in the placebo exposure. Moreover, it should be noted that also negative responses in the SIC are relatively common in asthmatics tested for MMA. Therefore, it is not plausible that MMA purely induces reactions in asthmatics due to its respiratory irritant properties.

The grouping approach used in the publication is of little importance, as read-across was not used for the classification. In addition, RAC does not consider that the indifferent response patterns of methancrylates and other low molecular weight agents detected in the study would either give support or be against the classification proposal, as the mechanism of asthma induced by acrylates or methacrylates is currently not known

(although the mechanism is considered as clearly immunological by experts). According to the CLP Regulation, demonstrating the mechanism is also not required in order to classify for respiratory sensitisation. The QSAR model used in the study was not given much emphasis in the RAC opinion. Finally, it should be noted that the study was not designed to be used for classification purposes, and that most of the general guidelines for methodologies are not applicable to such clinical case series. Nevertheless, the aforementioned additional information provided to RAC was evaluated by RAC as relevant for the hazard assessment of MMA.

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2020	Germany	<confidential>	Company-Downstream user	3
Comment received				
Als langjähriger Verarbeiter von MMA-basierten Dach-/ und Bodenbeschichtungen weisen wir darauf hin, dass in unserem Betrieb bisher keine Atemwegserkrankungen wie Asthma, durch den Umgang mit MMA-haltigen Produkten aufgetreten sind. Wir halten daher die Einstufung von MMA als atemwegssensibilisierend für nicht erforderlich.				
RAC's response				
Please see the response to comment number 1.				

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2020	Germany	<confidential>	Company-Downstream user	4
Comment received				
Als langjähriger Verarbeiter von MMA-basierten Dach-/ und Bodenbeschichtungen weisen wir darauf hin, dass in unserem Betrieb bisher keine Atemwegserkrankungen wie Asthma, durch den Umgang mit MMA-haltigen Produkten aufgetreten sind. Wir halten daher die Einstufung von MMA als atemwegssensibilisierend für nicht erforderlich.				
RAC's response				
Please see the response to comment number 1.				

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2020	Germany	Follmann-Chemie GmbH	Company-Manufacturer	5
Comment received				
Vielen Dank für die Möglichkeit den Einstufungsvorschlag zu kommentieren. Gemäß den vorliegenden Studien halten wir den Einstufungsvorschlag für MMA als atemwegssensibilisierend für nicht gerechtfertigt, da die angeführten Daten und Studien nicht ausreichend erscheinen. Dies wird auch aus den eingereichten Informationen des MMA-Konsortiums deutlich und durch den Kommentar der BAUA aus Deutschland, die die Datenlage ebenfalls als nicht ausreichend ansieht, gestärkt. Durch die angegliederten REACh Prozesse, die diese Einstufung nach sich ziehen könnte, wie z.B. SVHC-Einstufung, Beschränkungen, etc., halten wir den Vorschlag der Neueinstufung von MMA ohne weitere wissenschaftlich fundierte toxikologische Nachweise für stark risikobehaftet. Die angefügten Studien zeigen Auffälligkeiten bei einer speziellen Gruppe von Anwendern im zahnmedizinischen bzw. kosmetischen Sektor, in denen jeweils nur geringe Mengen MMA verarbeitet werden (zum Teil ohne Arbeitsschutzmaßnahmen). Weiterhin wurde nicht bewertet, ob andere Stoffe oder Lebensumstände der betroffenen Personen als Auslöser für Asthma gewertet werden müssen. Auffällig erscheint uns hierbei, dass es				

keine signifikant hohe Anzahl von Asthmaerkrankungsfällen aus der industriellen und gewerblichen Anwendung von MMA gibt, in denen das Material in sehr viel größeren Mengen zur Herstellung von Beschichtungen oder beim Verarbeiten von Beschichtungen im Bodenbereich und bei Straßenmarkierungsarbeiten, angewendet wird.
Die Auswirkungen durch die Einstufung von MMA als atemwegssensibilisierend wären für die verarbeitende Industrie einschneidend, da sich die Arbeitsschutzmaßnahmen (bisher Absaugung und Grenzwertüberwachung) massiv verschärfen würden. Sofern keine weiterführenden technischen Maßnahmen durchgeführt werden könnten, wäre ggf. sogar das langfristige Tragen von Atemschutzmasken notwendig. Dies würde zu einer erheblichen Einschränkung bei der Produktion und insbesondere bei der Verarbeitung führen.
Als Hersteller von MMA Beschichtungen, mit mehr als 20-jähriger Expertise, weisen wir darauf hin, dass bei uns keine Atemwegserkrankungen durch den Umgang mit MMA im Betrieb aufgetreten sind, was wir durch unsere arbeitsmedizinische Vorsorge sicherstellen können. Die derzeitige Sicherstellung der Einhaltung der bestehenden Grenzwerte durch lokale-/ und Hallenabsaugung sowie Belüftung bei der Verarbeitung von MMA sehen wir als ausreichende Schutzmaßnahme an, um die Mitarbeiter effektiv zu schützen.
Aufgrund der oben dargestellten Aspekte halten wir die Neueinstufung von MMA als atemwegssensibilisierend für nicht gerechtfertigt.

RAC's response

RAC would like to remind that the scope of the classification process is to consider the intrinsic hazard properties of the substance under the CLP Regulation. Risk assessment and risk management measures, as well as any measures under REACH, are out of the scope and should not have an influence on the classification process. Therefore, also the notion made that occupational safety measures are not used in some sectors using MMA (where a large portion of the reported asthma cases have been), is not relevant to hazard assessment.

It should be noted that particular exposure conditions, not applicable to all uses, may play a role in occupational asthma induced by MMA. Even if occupational asthma induced by MMA is mostly seen in a special group of users, such as in the dental or cosmetic sector, it indicates an intrinsic property to induce respiratory sensitisation, which must be considered relevant for classification.

Please also see to the response to comment number 1.

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2020	Germany	<confidential>	Company-Downstream user	6

Comment received

Als langjähriger Verarbeiter von MMA-basierten Dach-/ und Bodenbeschichtungen weisen wir darauf hin, dass in unserem Betrieb bisher keine Atemwegserkrankungen wie Asthma, durch den Umgang mit MMA-haltigen Produkten aufgetreten sind. Wir halten daher die Einstufung von MMA als atemwegssensibilisierend für nicht erforderlich.

RAC's response

Please see the response to comment number 1.

ANNEX 4 – RECORDS OF THE TARGETED PUBLIC CONSULTATION ON METHYL METHACRYLATE METHYL 2-METHYLPROP-2-ENOATE METHYL 2-METHYLPROPENOATE

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2020	Germany	Triflex GmbH & Co. KG	Company-Downstream user	7
Comment received				
Vielen Dank für die Möglichkeit den Einstufungsvorschlag zu kommentieren. Gemäß den vorliegenden Studien halten wir den Einstufungsvorschlag für MMA als atemwegssensibilisierend für nicht gerechtfertigt, da die angeführten Daten und Studien nicht ausreichend erscheinen. Dies wird auch aus den eingereichten Informationen des MMA-Konsortiums deutlich und durch den Kommentar der BAUA aus Deutschland, die die Datenlage ebenfalls als nicht ausreichend ansieht, gestärkt. Durch die angegliederten REACh Prozesse, die diese Einstufung nach sich ziehen könnte, wie z.B. SVHC-Einstufung, Beschränkungen, etc., halten wir den Vorschlag der Neueinstufung von MMA ohne weitere wissenschaftlich fundierte toxikologische Nachweise für stark risikobehaftet. Die angefügten Studien zeigen Auffälligkeiten bei einer speziellen Gruppe von Anwendern im zahnmedizinischen bzw. kosmetischen Sektor, in denen jeweils nur geringe Mengen MMA verarbeitet werden (zum Teil ohne Arbeitsschutzmaßnahmen). Weiterhin wurde nicht bewertet, ob andere Stoffe oder Lebensumstände der betroffenen Personen als Auslöser für Asthma gewertet werden müssen. Auffällig erscheint uns hierbei, dass es keine signifikant hohe Anzahl von Asthmaerkrankungsfällen aus der industriellen und gewerblichen Anwendung von MMA gibt, in denen das Material in sehr viel größeren Mengen zur Herstellung von Beschichtungen oder beim Verarbeiten von Beschichtungen im Bodenbereich und bei Straßenmarkierungsarbeiten, angewendet wird. Die Auswirkungen durch die Einstufung von MMA als atemwegssensibilisierend wären für die verarbeitende Industrie einschneidend, da sich die Arbeitsschutzmaßnahmen (bisher Absaugung und Grenzwertüberwachung) massiv verschärfen würden. Sofern keine weiterführenden technischen Maßnahmen durchgeführt werden könnten, wäre ggf. sogar das langfristige Tragen von Atemschutzmasken notwendig. Dies würde zu einer erheblichen Einschränkung bei der Produktion und insbesondere bei der Verarbeitung führen. Als Vertriebsgesellschaft mit entsprechender Anwendungstechnik blicken wir auf mehr als 20 Jahre Erfahrung bei der Verarbeitung von MMA Produkten zurück. Wir weisen darauf hin, dass bei uns bisher keine Atemwegserkrankungen durch den Umgang mit MMA-haltigen Produkten aufgetreten sind, was wir durch unsere arbeitsmedizinische Vorsorge sicherstellen können. Weiterhin ist uns durch unsere Kunden nicht bekannt das dort solche Erkrankungen aufgetreten sind. Aufgrund der oben dargestellten Aspekte halten wir die Neueinstufung von MMA als atemwegssensibilisierend für nicht gerechtfertigt.				
RAC's response				
Please see the response to comment number 5.				

Date	Country	Organisation	Type of Organisation	Comment number
27.02.2020	United Kingdom	Lucite International	Company-Manufacturer	8
Comment received				
As members of both the Cefic Methacrylates Sector Group and the REACH Methacrylates Task Force we fully support the comments and documents submitted to this consultation by Röhm GmbH as lead registrant of Methy Methacrylate and would refer you to the detailed attachments supplied by Röhm GmbH.				

We believe that, whilst the publication aims to provide a review of the phenotypic patterns of Occupational Asthma (OA), it has some limitations for use in the CLH process and for regulatory purposes.

This conclusion is drawn from:
• the lack of data available to assign causality to a specific substance or for a review of the workplace environment to understand and assess the potential implications of co-exposure to other substances and peak exposure levels. This is also required in order to understand how the Specific Inhalation Challenge (SIC) was conducted.
• an inappropriate grouping of substances for regulatory purposes. The grouping of substances under the terminology 'acrylates' covering cyanoacrylates, methacrylates and plain acrylates is inconsistent with the ECHA RAAF guidance for regulatory purposes and is inappropriate for a specific substance review as it further clouds the ability to determine the causal agent.
• Inconsistencies in the assignment of asthma types to CLP specifications with no distinction between allergic OA and irritant induced OA
• Indifferent response patterns to methacrylates and other LMW agents

We are aware that the clinical diagnosis of asthma and the immune mechanisms involved are complex, but the assignment of causation to a specific chemical is not a precise science and more detailed information on the workplace exposure history of the cases than is presented in this paper or the original CLH proposal is required in order to assign causation. This was also an area of concern raised within the industry comments to the original CLH proposal.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Lucite Response to ECHA Consultation_Suojalehto_27022020.pdf

RAC's response

Please see the response to comment number 2.

Date	Country	Organisation	Type of Organisation	Comment number
27.02.2020	United States	Dow Europe GmbH	Company-Downstream user	9

Comment received

To whom it may concern,

Dow is writing to echo comments submitted by Röhm GmbH (Lead Registrant of MMA), the Methacrylate REACh Task Force and Cefic Methacrylate Sector Group (MSG). Dow believes the publication under comment is insufficient to provide useful information regarding respiratory sensitization potential of methyl methacrylate. As such, the publication adds no value to the CLH assessment.

Regards,
<confidential>
Global Product Sustainability Leader
Coatings and Monomers

RAC's response

Noted.

ANNEX 4 – RECORDS OF THE TARGETED PUBLIC CONSULTATION ON METHYL METHACRYLATE METHYL 2-METHYLPROP-2-ENOATE METHYL 2-METHYLPROPENOATE

Date	Country	Organisation	Type of Organisation	Comment number
27.02.2020	Germany	<confidential>	Company-Downstream user	10
Comment received				
Als langjähriger Verarbeiter von MMA-basierten Dach-/ und Bodenbeschichtungen weisen wir darauf hin, dass in unserem Betrieb bisher keine Atemwegserkrankungen wie Asthma, durch den Umgang mit MMA-haltigen Produkten aufgetreten sind. Wir halten daher die Einstufung von MMA als atemwegssensibilisierend für nicht erforderlich.				
RAC's response				
Please see the response to comment number 1.				

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Germany	<confidential>	Please select organisation type..	11
Comment received				
Als langjähriger Verarbeiter von MMA-basierten Dach-/ und Bodenbeschichtungen weisen wir darauf hin, dass in unserem Betrieb bisher keine Atemwegserkrankungen wie Asthma, durch den Umgang mit MMA-haltigen Produkten aufgetreten sind. Wir halten daher die Einstufung von MMA als atemwegssensibilisierend für nicht erforderlich.				
RAC's response				
Please see the response to comment number 1.				

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Germany	Evonik Resource Efficiency GmbH	Company-Importer	12
Comment received				
We highly appreciate the opportunity to comment on this publication at this stage of the CLH process. We recognize the efforts of the authors to investigate the phenotypic patterns of Occupational Asthma (OA) and the high level of accuracy for an OA diagnosis when done with the presented diagnostic tools. We therefore do not doubt the diagnosis of OA as such from a diagnostic perspective. However, we have detected several serious deficiencies in this publication from a regulatory perspective as follows. Lack of available data to assign causality to specific substances or agents prohibiting an independent review according to ECHA - Missing information on workplace and SIC exposure levels to MMA is impairing a valid uncertainty analysis for potential co-exposure and potentially irritating peak exposures - Grouping approach inconsistent with ECHA RAAF guidance and inappropriate for substance specific CLH review - Indifferent response patterns of methacrylates and other LMW agents - Lack of rigor in the assignment of occupational asthma types to CLP specifications and to WHO definitions - Inconsistencies in the used QSAR model for an "asthma hazard index" - Further inconsistencies and deficiencies in in the methodological approach, thereby interfering with the WHO scheme for OA				

Based on these deficiencies, we conclude that this publication is of insufficient quality for hazard assessment purposes. ECHA note – An attachment was submitted with the comment above. Refer to public attachment 2020-20-26_Comment on MMA_Evonik_public.pdf ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 2020-02-26_Evonik Resource Efficiency GmbH_Comment on MMA.pdf
RAC's response
Please see the response to comment number 2.

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Germany	<confidential>	Company-Downstream user	13
Comment received				
Als langjähriger Verarbeiter von MMA-basierten Dach-/ und Bodenbeschichtungen weisen wir darauf hin, dass in unserem Betrieb bisher keine Atemwegserkrankungen wie Asthma, durch den Umgang mit MMA-haltigen Produkten aufgetreten sind. Wir halten daher die Einstufung von MMA als atemwegssensibilisierend für nicht erforderlich.				
RAC's response				
Please see the response to comment number 1.				

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Germany	Silikal GmbH	Company-Downstream user	14
Comment received				
Ad hoc comment on the publication Suojalehto et al. (2019) within the scope of the proposal for harmonised classification and labelling of Methyl Methacrylate (CAS# 80-62-6) ECHA note – An attachment was submitted with the comment above. Refer to public attachment 2020-02-26 - MMA-Feedback from company Silikal.pdf				
RAC's response				
Please see the response to comments number 1 and 2.				

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Germany	<confidential>	Company-Downstream user	15
Comment received				
Als langjähriger Verarbeiter von MMA-basierten Dach-/ und Bodenbeschichtungen weisen wir darauf hin, dass in unserem Betrieb bisher keine Atemwegserkrankungen wie Asthma, durch den Umgang mit MMA-haltigen Produkten aufgetreten sind. Wir halten daher die Einstufung von MMA als atemwegssensibilisierend für nicht erforderlich.				
RAC's response				
Please see the response to comment number 1.				

ANNEX 4 – RECORDS OF THE TARGETED PUBLIC CONSULTATION ON METHYL METHACRYLATE METHYL 2-METHYLPROP-2-ENOATE METHYL 2-METHYLPROPENOATE

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Germany	<confidential>	Company-Downstream user	16
Comment received				
Als langjähriger Verarbeiter von MMA-basierten Dach-/ und Bodenbeschichtungen weisen wir darauf hin, dass in unserem Betrieb bisher keine Atemwegserkrankungen wie Asthma, durch den Umgang mit MMA-haltigen Produkten aufgetreten sind. Wir halten daher die Einstufung von MMA als atemwegssensibilisierend für nicht erforderlich. Im Gegenteil: während bei EP-Produkten regelmäßig Allergien auftreten, sind die MMA-Materialien im Umgang noch sicherer: durch die verkürzte Reaktionszeit des Materials im Vergleich zu Alternativprodukten werden die austretenden Stoffe schneller gebunden, ein unkontrollierter Ausstoß in die Umwelt frühzeitig unterbunden.				
RAC's response				
Please see the response to comment number 1.				

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Belgium	3AComposites Polycasa	Company-Downstream user	17
Comment received				
3AComposites Polycasa is a member of the methacrylates sector group of the CEFIC organization and is a major downstream user of MMA. The following comments summarise 3AComposites Polycasa views on the proposed reclassification of MMA based on its participation in discussions with other members of the methacrylates sector group. We highly appreciate the opportunity to comment on this publication at this stage of the CLH process. We recognize the efforts of the authors to investigate the phenotypic patterns of OA and the high level of accuracy for an OA diagnosis when done with the presented diagnostic tools. We therefore do not doubt the diagnosis of OA as such from a diagnostic perspective. However, we have detected several serious deficiencies in this publication from a regulatory perspective: - Lack of available data to assign causality to specific substances or agents prohibiting an independent review according to ECHA - Missing information on workplace and SIC exposure levels to MMA is impairing a valid uncertainty analysis for potential co-exposure and potentially irritating peak exposures - Grouping approach inconsistent with ECHA RAAF guidance and inappropriate for substance specific CLH review - Indifferent response patterns of methacrylates and other LMW agents - Lack of rigor in the assignment of occupational asthma types to CLP specifications and to WHO definitions - Inconsistencies in the used QSAR model for an "asthma hazard index" - Further inconsistencies and deficiencies in in the methodological approach, thereby interfering with the WHO scheme for OA Based on these deficiencies, we conclude that this publication is of insufficient quality for hazard assessment purposes. We believe that some, but not all, limitations can be addressed with additional details on case-by-case level and on the methodology used therefore we have contacted the corresponding authors already for responsible care reasons. We would like to outline at this point that we have also contacted ANSES as dossier submitting authority and owner of the RNV3P database before and after the public consultation period in 2019. Our				

requests on relevant details of the RNV3P cases - thereby following our obligations as registrants of MMA - were however rejected or not answered for the time being. ECHA note – An attachment was submitted with the comment above. Refer to public attachment 200226_3AC_Polycasa_letter_to_ECHA_re_Proposed_MMA_Classification_as_Respiratory_Sensitiser_V1.pdf
RAC's response
Please see the response to comment number 2.

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Germany	<confidential>	Company-Downstream user	18
Comment received				
Als langjähriger Verarbeiter von MMA-basierten Dach-/ und Bodenbeschichtungen weisen wir darauf hin, dass in unserem Betrieb bisher keine Atemwegserkrankungen wie Asthma, durch den Umgang mit MMA-haltigen Produkten aufgetreten sind. Wir halten daher die Einstufung von MMA als atemwegssensibilisierend für nicht erforderlich.				
RAC's response				
Please see the response to comment number 1.				

RESPIRATORY SENSITISATION

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Germany	Röhm GmbH	Company-Manufacturer	19
Comment received				
Based on the attached assessment we conclude that, at the current stage of knowledge on the presented cases, the publication does not have a significant impact on the complete data set of MMA. Thus, our position remains unchanged that we do not agree with the CLH proposal for the reasons presented in the comment from the public consultation phase in summer 2019 and, instead, we propose that the current Annex VI for MMA entry remains unchanged. If RAC believes that this publication represents a relevant line of evidence, we would appreciate any opportunity to follow up on the missing case details during this CLH process. ECHA note – An attachment was submitted with the comment above. Refer to public attachment 2020-02-25_MMA_Targ_Cons_Feedback_Roehm_REACh_TF_complete.pdf				
RAC's response				
Noted. Please also see the response to comment number 2.				

ANNEX 4 – RECORDS OF THE TARGETED PUBLIC CONSULTATION ON METHYL METHACRYLATE METHYL 2-METHYLPROP-2-ENOATE METHYL 2-METHYLPROPENOATE

Date	Country	Organisation	Type of Organisation	Comment number
27.02.2020	Belgium	European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC)	Industry or trade association	20

Comment received

Dear Madam, Dear Sir,

The European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) only became aware of the CLH proposal by the French MSCA after the public consultation period had closed so did not have the opportunity to comment on it.

ECETOC identifies concerns relating to what we believe to be an over simplification of what are generally considered as insufficiently understood and complex aspects of clinical diagnosis and underlying toxicology of respiratory asthma, combined with an inappropriate use of weight-of-evidence (WoE) to compensate for a low strength of evidence associated with considerable uncertainty. These concerns apply to both the Suojalehto et al. publication and the original CLH proposal by the French MSCA.

ECETOC is of the opinion that further details of the clinical cases and the clinical tests that have been performed is necessary for an informed discussion and decision on the Classification of this substance.

ECETOC will attend RAC 52.

Kind regards

ECHA note – An attachment was submitted with the comment above. Refer to public attachment ECETOC comments on Suojalehto paper 27Feb2020 FINAL CLEAN.pdf

RAC's response

As pointed out in the attachment with a detailed comment, the prevalence of asthma cases in the MMA exposed population is unknown. As a consequence, sub-chategorisation into Resp. Sens. 1A or 1B is not possible.

In addition, it should be noted that overall, it is possible that MMA-induced occupational asthma cases are underdiagnosed and underreported. As MMA is not classified as a respiratory sensitiser, physicians are likely to generally not suspect it as a causative agent behind (occupational) asthma cases. It is also possible that particular exposure conditions, not applicable to all uses, play a role. According to many comments received in the public consultation, occupational asthma cases have not been detected in the production or processing of coatings for floors and road markings, or in workers using MMA-based roof and floor coatings. RAC would like to point out that these uses or professions have not been prevalent in the reported MMA-related occupational asthma cases across the European occupational disease registers or scientific publications, either. Instead, the common professions seen are dental and medical prosthesis technicians and nail beauticians (using MMA for acrylic nails). In both of these occupationas, liquid-powder mixtures are used, in which the liquid is typically 100% MMA.

RAC acknowledges that the underlying mechanisms are currently insufficiently understood and are likely complex. However, demonstration of the mechanism is not a prerequisite

for classification of a substance as respiratory sensitiser according to the CLP regulation. Furthermore, clinical experts currenty view the mechanism as clearly immunological.

For the more general concerns raised in the attachment related to the SIC, please see the response to comment number 2. Concerning the underlying mechanisms of late asthmatic response (LAR), it is true they are not fully understood. However, the papers on animal models for asthma referred to in the comment (counter-arguing the currently widely-accepted presence of an underlying immunological mechanism) are rather hypotheses than evidence accepted by the scientific community. Moreover, a positive response in a well-conducted SIC is not based on solely the presence of LAR; also immunological parameters are assessed whenever possible. Furthermore, in the SICs in Suojalehto *et al.* (2019), also placebo exposures were conducted. If the patients' positive reactions would have been based on respiratory irritation, they should have had a positive reaction also in the placebo exposure. Finally, also negative responses in the SIC are relatively common in asthmatics tested for MMA. Therefore, it is not plausible that MMA purely induces reactions in asthmatics due to its respiratory irritant properties.

RAC agrees that the original classification proposal had some shortcomings, and the detailed comments received also in the original public consultation were taken into account. Subsequently, additional key elements were identified and evaluated by RAC in order to form the RAC opinion.

Date	Country	Organisation	Type of Organisation	Comment number
27.02.2020	United Kingdom	Lucite International	Company-Manufacturer	21
Comment received				
We believe that the publication does not provide additional information to support the classification of methyl methacrylate as a respiratory sensitiser. Our opinion remains that the weight of evidence supports that the current Annex VI entry remains unchanged and we continue to fully support the original comprehensive comments submitted by Evonik Röhm GmbH as Lead Registrant on behalf of the Methacrylates REACH Task Force https://echa.europa.eu/harmonised-classification-and-labelling-targeted-consultations/-/substance-rev/25111/term ECHA note – An attachment was submitted with the comment above. Refer to public attachment Lucite Response to ECHA Consultation_Suojalehto_27022020.pdf				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
27.02.2020	Finland		MemberState	22
Comment received				
FI CA supports the proposal of Resp. Sens. 1 without sub-categorization. As methyl methacrylate is a respiratory irritant (harmonised classification Skin Irrit. 2), distinguishing the mechanism that leads to asthma can be difficult. However, the recent publication by Suojalehto et al. (2019) provides evidence for methyl methacrylate-induced asthma with a latency period between exposure and reaction, triggering an immune response.				
RAC's response				
Noted.				

ANNEX 4 – RECORDS OF THE TARGETED PUBLIC CONSULTATION ON METHYL METHACRYLATE METHYL 2-METHYLPROP-2-ENOATE METHYL 2-METHYLPROPENOATE

Date	Country	Organisation	Type of Organisation	Comment number
27.02.2020	Germany	<confidential>	Company-Manufacturer	23
Comment received				
AD hoc comment on the publication Suojalehto et al. (2019) within the scope of the proposal for harmonised classification and labelling of Methyl Methacrylate (CAS 80-62-6) ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 200227_Comment on MMA consultation_Westwood.pdf				
RAC's response				
Please see the response to comments number 1 and 2.				

Date	Country	Organisation	Type of Organisation	Comment number
21.02.2020	Sweden		MemberState	24
Comment received				
The publication (Suojalehto et al., 2019) highlights the role of reactive acrylates, including methyl methacrylate methyl 2-methylprop-2-enoate methyl 2-methylpropenoate (MMA), in the development of occupational asthma. As such, the Swedish CA considers that the information supports the DS proposal for harmonized classification of MMA as Resp. Sens. 1, H334.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Germany	Deutsche Bauchemie	Industry or trade association	25
Comment received				
Deutsche Bauchemie, the German Association of the manufacturers of construction chemical products would like to take this opportunity to provide the following comments. Our member companies are formulators of methyl methacrylate (MMA) containing mixtures for the end use in the construction sector by professional users. The relevant formulators and manufacturers of MMA are working together in our dedicated WG for more than 20 years and are focussing on topics such as occupational safety and health. In this context, we are in a close cooperation with the German accident insurance institutions for the Construction Industry (Berufsgenossenschaft der Bauwirtschaft). Against the background of the CLH proposal, we have asked the formulators of MMA-based mixtures and the end-users of these products in the construction sector whether there were any problems with respiratory sensitisation (asthma cases) during formulation and end-use. We have received consistent feedback that no asthma cases are known in the construction sector in connection with MMA. This was confirmed by the German accident insurance institution for the Construction Industry (BG Bau Berufsgenossenschaft der Bauwirtschaft). As well the German BG Bau is not aware of any asthma cases in connection with the use of MMA-containing products. An evaluation by the German accident insurance institution for the Construction Industry has shown that no occupational respiratory diseases caused by methyl methacrylate occurred in the period from 2008 to 2019 in the construction sector. Furthermore, we support the comments of the lead registrant from MMA with regard to				

the weaknesses of the study from Suojalehto et al. We share the opinion that the study is not an appropriate basis for the classification as respiratory sensitizer.

A classification of MMA as a respiratory sensitizer would lead to additional significantly tightened occupational safety measures. Since there are no asthma cases in the construction sector, these additional occupational safety measures would not be appropriate and would unnecessarily complicate the work on the construction sites. Instead, it makes more sense to continue the ongoing activities to optimize exhaust ventilation at the workplace and to monitor the occupational exposure level (OEL) for MMA.

Because of the facts mentioned, we are of the opinion that it is not appropriate to classify MMA as respiratory sensitizer.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment MMA_CLH_targeted_consultation_DBC_2020-02-26.pdf

RAC's response

Please see the response to comments number 1, 2 and 5.

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Germany	Evonik Resource Efficiency GmbH	Company-Importer	26

Comment received

We conclude that, at the current stage of knowledge on the presented cases, the publication does not have a significant impact on the complete data set of MMA. Thus, our position remains unchanged that we do not agree with the CLH proposal for the reasons presented in the comment from the public consultation phase in summer 2019 and, instead, we propose that the current Annex VI for MMA entry remains unchanged.
If RAC believes that this publication represents a relevant line of evidence, we would appreciate any opportunity to follow up on the missing case details during this CLH process.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 2020-20-26_Comment on MMA_Evonik_public.pdf
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 2020-02-26_Evonik Resource Efficiency GmbH_Comment on MMA.pdf

RAC's response

Noted.

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Germany	Silikal GmbH	Company-Downstream user	27

Comment received

We have been made aware of the targeted consultation on the paper of Suojalehto et al. (2019) as part of the CLH process initiated by the French MSCA to classify Methyl Methacrylate (MMA) (CAS 80-62-6) as a Respiratory Sensitizer (H334) within the EU. While we do not have an in depth scientific knowledge of asthma and respiratory sensitization within our company we are aware not only that the clinical diagnosis of asthma and the immune mechanisms involved therein are complex and not fully understood, but the assignment of causation to specific chemical is not a precise science.

We do not know of cases of respiratory sensitization from our customers using MMA-based liquid plastics (flooring, mortar, waterproofing and road marking). According to our knowledge also the German employers' liability insurance association BG BAU is not aware of any case of MMA being a respiratory sensitizer.
In the opinion of our company experts the French MSCA proposal does not adequately recognise the uncertainty surrounding the use of clinical data in CLH decision making and specifically with respect to the current proposal concerning MMA.
We have seen and support the response comments of the REACh Task Force to the French MSCA to classify Methyl Methacrylate (MMA) (https://echa.europa.eu/de/registry-of-clh-intentions-until-outcome/-/dislist/details/0b0236e1815f6e18) which raised serious concerns as to the technical content and hope that more scientific input is sought before a decision is made.
As highlighted by the recently identified Suojalehto paper, we are particularly concerned that there is insufficient justification for the use of data on other acrylates, methacrylates and cyanoacrylates both in the original CLH proposal and more transparently in this paper. On this basis we are unsure how this paper provides any further evidence beyond that already identified. We therefore support the deprecatory position of the REACH Task Force on this paper on its use for risk assessment purposes.
We hope that the impending review by the Risk Assessment committee will consider these concerns seriously before making a decision on the classification of MMA since labelling it as a respiratory sensitizer will have a profound and damaging effect on an important sector of industry.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 2020-02-26 - MMA-Feedback from company Silikal.pdf

RAC's response

Noted. Please see the responses to earlier comments.

Date	Country	Organisation	Type of Organisation	Comment number
26.02.2020	Belgium	3AComposites Polycasa	Company-Downstream user	28

Comment received

We conclude that, at the current stage of knowledge on the presented cases, the publication does not have a significant impact on the complete data set of MMA. Thus, our position remains unchanged that we do not agree with the CLH proposal for the reasons presented in the comment from the public consultation phase in summer 2019 and, instead, we propose that the current Annex VI for MMA entry remains unchanged.
If RAC believes that this publication represents a relevant line of evidence, we would appreciate any opportunity to follow up on the missing case details during this CLH process.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 200226_3AC_Polycasa_letter_to_ECHA_re_Proposed_MMA_Classification_as_Respiratory_Sensitiser_V1.pdf

RAC's response

Noted.

ANNEX 4 – RECORDS OF THE TARGETED PUBLIC CONSULTATION ON METHYL METHACRYLATE METHYL 2-METHYLPROP-2-ENOATE METHYL 2-METHYLPROPENOATE

PUBLIC ATTACHMENTS
1. ECETOC comments on Suojalehto paper 27Feb2020 FINAL CLEAN.pdf [Please refer to comment No. 20]
2. Lucite Response to ECHA Consultation_Suojalehto_27022020.pdf [Please refer to comment No. 8, 21]
3. MMA_CLH_targeted_consultation_DBC_2020-02-26.pdf [Please refer to comment No. 25]
4. 2020-20-26_Comment on MMA_Evonik_public.pdf [Please refer to comment No. 12, 26]
5. 2020-02-26 - MMA-Feedback from company Silikal.pdf [Please refer to comment No. 14, 27]
6. 200226_3AC_Polycasa_letter_to_ECHA_re_Proposed_MMA_Classification_as_Respiratory_Sensitiser_V1.pdf [Please refer to comment No. 17, 28]
7. 2020-02-25_MMA_Targ_Cons_Feedback_Roehm_REACh_TF_complete.pdf [Please refer to comment No. 2, 19]

CONFIDENTIAL ATTACHMENTS
1. 200227_Comment on MMA consultation_Westwood.pdf [Please refer to comment No. 23]
2. 2020-02-26_Evonik Resource Efficiency GmbH_Comment on MMA.pdf [Please refer to comment No. 12, 26]