Risk Management Option Analysis Conclusion Document

Substance Name: benzene-1,2,4-tricarboxylic acid 1,2-anhydride

EC Number: 209-008-0

CAS Number: 552-30-7

Authority: NL-CA

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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

TMA has a harmonized classification according to the entry in table 3.1 in Annex VI of CLP Regulation (Regulation (EC) 1272/2008):

Table: Harmonised classification

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)		
607-097-00-4		209-008-0	552-30-7	H317, H318, H334, H335	H317, H318, H334, H335	-	-

H317: Skin Sens. 1
H318: Eye Dam. 1
H334: Resp. Sens. 1
H335: STOT SE 3

Further, TMA is self classified for the following hazard classes notified among the aggregated self classifications in the C&L Inventory:

- H370 and H372 instead of H335
- H370: STOT SE 1
- H372: STOT RE 1
- H332: Acute Tox. 4

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)	X
Restriction under REACH	
Other EU-wide regulatory measures	
Need for action other than EU regulatory action	
No action needed at this time	

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

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

TMA is judged to meet the SVHC Roadmap 2020 criteria for potential SVHC identification:

Table: SVHC Roadmap 2020 criteria

	Yes	No
a) Art 57 criteria fulfilled?	X (57f)	
b) Registrations in accordance with Article 10?	X	
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	

TMA has similar properties to two other cyclic anhydrides that have gone through an Annex XV dossier SVHC (art. 57f) and were placed on the Candidate List after MSC decision. Basically, the same rationale could apply to trimellitic anhydride, as it appears that the underlying information on toxicity and uses is similar. However, a complete exposure assessment is missing in the registration dossier, which should be provided by the registrant. Even with the new information on exposure obtained from personal communication with the lead registrant, a sensible risk assessment cannot be performed covering all PROCs, downstream users and sites. There are almost 1000 notifiers for TMA.

Rationale for 57f criteria:
Severity: may result in occupational rhinoconjunctivitis and asthma, less frequent consequences are the severe diseases: pulmonary disease–anaemia syndrome, contact eczema, contact urticaria, allergic laryngitis, and allergic alveolitis.
Reversibility: sensitization and certain effects as a results of prolonged exposure are irreversible. Adaptive effects are reversible upon cessation of the exposure, but will emerge and worsen upon new contact.
Threshold: no threshold could be set.
Time to effect: for severe effects there appears to be some latency time and prolonged exposures are sometimes required. Effects are also observed after high acute exposure.
Total: indication of high priority for identifying the substance as an SVHC.

There is no consumer use of TMA. Although the local emission data in the registration dossier may indicate a concern for the general public, it is not very likely that there is an actual concern since TMA will be readily hydrolysed to its non-sensitizing hydrolysis product trimellitic acid. This is in line with the conclusion drawn by OECD in its report on TMA and trimellitic acid (OECD SIDS, 2002). Therefore, health effects are anticipated in the worker population only.

Emission data available from the registration dossier for the local area show air concentrations exceeding the risk levels set by the Dutch Health Council indicating concern that levels at the workplace are similar or higher. The additional data from the registrants (received after personal communication, claimed confidential) suggest otherwise, showing lower exposure estimates, and possibly also lower local concentrations at those workplaces for which information was provided. This additional information from the registrants indicate that the exposures are likely to be lower than the additional risk levels set by the Dutch Health Council. However, the registrants did not provide exposure estimates for all PROCs. On the other hand, the exposure estimates were provided for those PROCs likely to have the highest exposure. Based on

the provided information, the exposure related to these PROCs does not lead to an immediate concern, provided the described RMMs are in place. It should be noted that such RMMs are possibly not in place at sites run by DUs, and that some concern thus remains for worker exposure at DU. Other data in public literature do show higher exposures of workers to TMA than the exposure levels provided by the registrant for those PROCs for which highest worker exposure is expected but may be outdated. Based on the additional information, and a lack of respiratory sensitization cases in the last decade, according to a medical declaration by the manufacturer, it seems that risks for sensitization are low under the currently applied work conditions. Again, such strict working conditions may not apply to all sites where TMA is used.

Furthermore, with regard to the medical statement made by the registrants, a note of caution for the possible and likely underreporting of respiratory sensitization cases should be taken. Also, it may be possible that workers have been relocated before they developed symptoms of sensibilization, based on findings during medical examination (e.g. based on elevated IgE specific reactions as a criterion for relocation). This would mean that those subjects would not show symptoms, but also cannot work with TMA thereafter as they are still sensitized, and may have to change jobs.

The availability of possible alternatives of TMA has not been extensively investigated by the eMSCA. From the perspective of chemical reactivity, other (cyclic) anhydrides or other substances such as certain amines might be suggested as possible alternatives for the use of TMA in the production of polymers and esters, although it is unknown if these type of substances are technically and economically feasible in specific applications. These substances are generally under suspicion or are known skin or respiratory sensitizers. But they might be preferred over TMA when their potency is less than the potency of TMA. TMA is amongst the most potent cyclic anhydrides according to the copied table from the Health Council:

Table 12. Critical effects (sensitisation and work-related symptoms) in man with corresponding exposure levels of cyclic acid anhydrides.

Acid anhydride	Exposure level ($\mu g/m^3$)	Critical effect	Reference
PA	1 500 –17 400	Sensitisation Asthma	(136)
TCPA	140-590	Sensitisation Work-related respiratory symptoms	(118)
TMA	10-40	Sensitisation Work-related respiratory symptoms	(13)
HHPA and MHHPA	10-50	Sensitisation	(195)
MTHPA	5-20	Sensitisation Rhinoconjunctivitis Asthma	(134, 202)

Consequently, from a risk assessment perspective there may be more preferable alternative cyclic anhydrides that are possibly less potent sensitizers than TMA based on the above table. However, those alternatives may be subject to concern as well in view of their intrinsic toxicological properties and there is no information on the technical, practical and economic feasibility of substitution. The eMSCA performed a brief literature search to obtain any readily available information on possible alternatives to TMA, but

did not attempt to obtain a complete overview of possible alternatives. Based on this work no information was found on other possible less toxic substitutes.

As indicated previously, TMA is used in relatively high tonnage levels by approximately 1000 users. These users at this moment gain from the economic benefits of TMA. In case of implementation of a risk management measure these users would be somehow affected. However, as no information is available on the availability of technical and economically feasible alternatives of TMA, it is at this moment difficult to estimate the potential socio-economic loss (or costs) of TMA in case of implementation of a risk management measure.
On the other hand, current use might cause health effects in workers that are deemed serious as the effects are indicated to be of 'equivalent level of concern'. Health effects will result in health care costs, potential loss in working time and intangible costs for patients (disease burden). The number of notifiers of TMA (1000) indicate a potentially substantial worker population that might be exposed to TMA. However, no actual information on the number of workers exposed is available, and there is no information on the actual TMA levels workers are exposed to. The (confidential) information that was provided by the lead registrant suggest that exposure levels are below the level of concern, however, it is unclear whether levels remain below that level for al (downstream) users. Fact that no recent cases of health effects are reported suggests that exposure levels are indeed limited, however, there could be under reporting of cases.

Overall it is at the moment difficult to estimate economic benefits of the use of TMA or to estimate the potential health effects of the use of TMA. A more elaborated socio-economic analysis would be required to be able to say more on the balance of costs and benefits of continued use or of implementation of a risk management measure that could be used as underpinning of a policy decision on TMA. However, such a more elaborated SEA is beyond the scope of this RMOA.

It cannot be assessed if the uses that pose a risk are minor or significant compared to other uses since detailed information is lacking for all sites of TMA use. RMMs are considered very strict during manufacture and formulation of polymers and esters, however, exposure was not quantified for all activities. Furthermore, a threshold cannot be established protecting both naïve and previously sensitized subjects. The Dutch Health Council did propose additional risk levels (not protecting previously sensitized subjects), but they cannot be compared to exposure levels for all activities since for some of the activities exposure data are missing. The data in open literature suggest that the risk levels were exceeded at least 10 fold. The number of cases needs to be investigated in open literature and in WHO CICADS, where some cases are described, but it is noted that the data are rather old (< 2000). The target population is potentially high due to high tonnage levels and its use in large polymer and ester producing industries (approximately 1000 notifiers). Further the registration dossier describes a number of PROCs that are known for their high exposure potential: i.e. PROC 5 (Mixing or blending in batch processes for formulation of preparations) – 7 (industrial spraying) – 8a (transfer of substances at non-dedicated facilities) – 10 (roller application or brushing) and PROC 11 (non-industrial spraying), however communication with the (lead) registrant(s) concluded that these PROCs, with the exception of PROC 5 are not in place anymore. The eMSCA evaluated the new information and considers that withdrawal of PROCs 7-10-11 are sufficiently justified by the additional information provided by the registrants, but PROC 8a (opening of big bags) should not be changed to PROC 8b as there are doubts whether manually opening of bags may be considered a dedicated procedure. The withdrawal of these PROCs should be made official by the registrants via an update of their registration dossier.

Identification and assessment of risk management options

- *List of potential RMOs and/or combination thereof;*

Prior to or in parallel any RMO considered below, a Compliance Check (CCH) should be performed to obtain quantitative exposure information and resolve other compliance check issues on environmental toxicity. Information most valuable for the present concern (worker health through handling TMA) would be the further insight in the exposure scenario's for TMA for all PROCs indicated in the registration dossier, and representative data for all use locations. However, past experience suggests it is difficult to obtain detailed information on exposure via the process of CCH. The information required would go beyond the basic data demands under REACH.

Based on the presently available information on TMA, the following pro's and con's are identified for the risk management options SVHC identification and authorization, Chemicals Agents Directive and Restriction:

RMO	Pro	Con
SVHC identification, Candidate list and authorization	Substance seems to have 57f properties. HHPA/MHHPA preceded and are very similar cases to TMA, and TMA cannot be used as alternative to those substances. There is no clear motivation why TMA should follow a different RMO. Once taken up in Annex XIV, RAC will establish risk levels, IND must proof safe use. This may be achieved within a relatively short period of time. Industry must evaluate the availability of substitutes. Authorization will force registrants to provide information about workplace safety at DU	Substance needs to be considered as SVHC first by MSC. It is not likely that this substance will be given high priority to move to the authorization list in view of the low number of uses and lack of recent cases.
Chemical Agents Directive	Worker safety issue. Experience in enforcement. Binding OEL could be derived, specific RMMs could be made obligatory New information from lead registrant suggests that risks can be controlled.	Current exposure limits OELs do not protect against respiratory sensitization. Unsure if something will happen on top of what has been implemented already without an additional regulatory incentive. Also uncertain within what timeframe a lower OEL would be proposed by SCOEL and implemented.
Restriction	Legislation can be tailor made. E.g. request certain operational conditions (BAT), monitoring programs, Deriving mandatory DMEL	Based on the available data, there seems to be no unacceptable risk for workers, consumers or the environment that has

		to be addressed at EU level. If restriction would have been considered, then it would be practically difficult to determine best available techniques (BAT) or issue permits. Subjects may still become sensitized. High costs preparing restriction dossier.

TMA is a known respiratory sensitizer, similar to HHPA and MHHPA for which it has been concluded that art 57f applies. Both substances are on the candidate list, but have not yet been prioritized for Annex XIV.

A similar route may be proposed for TMA as it has the same respiratory sensitizing properties and shows hazard potency in the same range. The uses of TMA (in polymer and ester production, but according to literature also in resins) are also quite similar to HHPA and MHHPA, which are mainly used in the production of epoxy resins and some polymers, and according to HHPA registration dossier contain a similar set of PROCs (though, new information by the (lead) registrant(s) did indicate that some of those PROCs are no longer applicable).

Case studies and case reports indicate that workers have been sensitized to TMA and have been diagnosed with e.g. rhinitis and allergic asthma amongst other (CICADS, 2009; Dutch Health Council, 2010; and references therein). Regarding the risks, a conclusion cannot be firmly drawn at this moment as still quantitative exposure information is missing for some of the PROCs and at specific sites. According to the medical officer, new cases have not been identified since the last decade, following stricter working conditions and monitoring programs. It is not completely clear what those new working conditions exactly are and whether workers have been relocated to avoid sensitisation related effects from occurring.

Conclusions on the most appropriate (combination of) risk management options

Based on the information provided by the (lead) registrant(s) it appears that the risks for respiratory sensitization can be controlled under very strict working conditions. However, such working conditions may not be in place at all sites where TMA is used and their use is not legally binding. Also remains uncertain how many unreported sensitization cases there are, and if challenged workers have been removed from their workplace in time before symptoms could develop. Moreover, to date the exposure information is not complete in the registration dossier nor does the newly provided information cover all activities. This leads the eMSCA to conclude that the available data is insufficient to substantiate if, or if not, TMA can be used safely under the current conditions.

The available information furthermore indicates that under the Worker legislation there is presently no incentive to lower the exposures to TMA as the OEL at this moment is 40 µg/m^3, which is not protective for respiratory sensitization and much higher than the risk

level of 1.8 µg/m^3 (1% additional risk) set by the Dutch Health Council. Lowering of the OEL by SCOEL could be considered but the timelines involved may be lengthy and does not build an incentive for substitution, which, in case of the respiratory sensitization properties and high potency, would be the most preferred risk management measure.

In the absence of a clear risk for workers, consumers or the environment, restriction under REACH is not an option.

The RMOA at this stage does not include cost-benefits analyses to further help discriminate in possible options. Therefore, costs to industry to substitute or comply with lower OELs or DNELs than the current OEL have not been assessed. It is anticipated that in the absence of recent worker cases and information on alternatives, benefits of continued use for industry would be substantial.

In the absence of a more preferable RMO, it is suggested to follow same route as HHPA and MHHPA, i.e. SVHC identification & Candidate list entry followed by Authorisation. The registrant would have to submit detailed exposure information when applying for authorization, thus making a CCH procedure to acquire exposure information redundant. Furthermore, the eMSCA expects that any more detailed information obtained via CCH, will not be able to remove the concern for worker health. The eMSCA therefore suggests not to await CCH but to proceed with the preparation of an Annex XV dossier for SVHC identification.

4. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS IF NECESSARY

Indication of a tentative plan is not a formal commitment by the authority. A commitment to prepare a REACH Annex XV dossier (SVHC, restrictions) and/or CLP Annex VI dossier should be made via the Registry of Intentions.

Follow-up action	Date for intention	Actor
Annex XV dossier for Authorization	2016	NL-CA