[Possibility for MSCA Logo]

Risk Management Option Analysis Conclusion Document

Substance Name: **Amylase, α-**
EC Number: **232-565-6**
CAS Number: **9000-90-2**

Authority: **United Kingdom**
Date: **March 2018**

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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

Amylase, α- (AA) is included in the Community Rolling Action Plan (CoRAP) and was evaluated by the UK REACH CA in 2015. The conclusion and evaluation report are available at: https://echa.europa.eu/documents/10162/a7e7c131-ab90-40e3-a754-577a60da5680 (accessed 21 March 2018).

AA is listed in the classification and labelling inventory, index no. 647-015-00-4. It has the following harmonised classification:

- Resp Sens 1; H334

There are several other pieces of EU legislation that include provisions which apply to AA (and other enzymes). Since the RMOA targets the uses for AA that were covered in the REACH substance evaluation, the RMOA focuses on legislation that is relevant to these uses (i.e. worker protection legislation, consumer protection legislation and relevant product specific legislation). Specific provisions for enzymes including AA are also included in legislation relating to animal feed additives, cosmetics, pharmaceuticals and food safety. These provisions usually apply to enzymes as a generic group rather than individual enzymes. Further information on these additional uses can be found in an old document prepared for the European Commission (EU, 2002)[2].

Worker protection:
Chemical Agents Directive (98/24/EC)[3]
Under this legislation AA is regarded as a hazardous chemical agent and is subject to the general provisions in this directive.

Consumer protection:
General Product Safety Directive (2001/95/EC)[4]
Mixtures containing AA that are available for use by the general public are in scope of this directive. In the future, the GPSD may be replaced with a new Regulation[5]. Products containing enzymes including AA are expected to fall within the scope of the proposed new Regulation.

Product specific legislation:
The Detergents Regulation (EC) No 648/2004[6]
In relation to enzymes including AA, the Regulation includes a requirement that all detergent products containing enzymes should list this as an ingredient on the label irrespective of the concentration present in the product (Article 11(3)). Typically detergent products will not list the specific enzymes or enzyme activities that are present in the formulation but may use words such as “contains enzymes”. Several of the uses

[2] EU (2002). Office for Official Publications of the European Communities. Collection of Information on Enzymes. Contract No B4-3040/2000/278245/MAR/E2. ISBN 92-894-4218-2. Available at: http://ec.europa.eu/environment/archives/dansub/pdfs/enzymerepcomplete.pdf (accessed 21 March 2018).

[3] Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC).

[4] Directive 2001/95/EC of the European Parliament and of the Council of 3 December 2001 on general product safety (Text with EEA relevance).

[5] http://eur-lex.europa.eu/procedure/EN/2013_49 (accessed 21 March 2018).

[6] Regulation (EC) No 648/2004 of the European Parliament and of the Council of 31 March 2004 on detergents (Text with EEA relevance).

identified in REACH registrations for AA cover products that fall within the scope of the Detergents Regulation.

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. Although the RMOA specifically examined options to address the concerns that were identified during the substance evaluation and focussed on the AA enzymes that are covered by EC number 232-565-6, the conclusions may be relevant for other enzymes.

Enzymes of the amylase class catalyse the hydrolysis of α-1-4 glucosidic linkages of polysaccharides such as starch, glycogen or their degradation products. AA attacks sub terminal and internal 1:4 links in the starch molecule to break the long chains into small fragments. AA enzymes are derived from a variety of organisms and represent a diverse group of substances whose molecular weights vary from 10000 to 140000 but which share the same enzymatic activity. Enzymes from different organisms express optimum enzymatic activity under different conditions and this determines the uses to which enzymes are put. Commercial AA enzymes are usually derived from either bacterial or fungal sources. AA derived from bacterial sources tends to be preferred for manufacture of detergents and textile processing.

AA is classified as a respiratory sensitiser. There is evidence for the induction of sensitisation (raised levels of substance specific IgE) in people working with this substance (Budnik *et al*, 2016). Also cases of occupational asthma linked to enzymes are reported to the Health and Occupation Reporting Network (THOR, a work related ill-health reporting scheme operating in the UK) at a rate of around 1-2 per year (not including cases in bakery workers). Since AA containing products are manufactured and used across the EU, it is reasonable to conclude that the THOR data will reflect the situation in other EU Member States (MS) suggesting an ongoing concern which warrants attention. It is preferable to take a consistent approach across all MS and hence Union-wide action is justified.

The evaluation performed by the UK in 2015 found that although the risk management advice provided in exposure scenarios appears to be suitable and adequate, this information is not necessarily being communicated in an effective manner to the workers using enzyme-containing products who may be several steps removed from the registrants in supply chains. The evaluation also identified a possible risk for consumers if hand dishwashing liquids containing AA (and other enzymes) are used for activities other than washing dishes (e.g. making bubble blowing liquids for children). The Risk Management Options Analysis (RMOA) process was therefore initiated to identify the most appropriate regulatory approach to:

i) ensure suitable good practice advice is developed and communicated to all workplace users of AA containing products; and,

ii) ensure that potential risks to consumers who may choose to buy hand dishwashing liquids containing AA are adequately managed taking into account all foreseeable uses.

For workers, none of the options for formal regulatory action that were discussed in the RMOA seemed able to provide the additional good practice communication that is needed. Industry-led initiatives do have the potential to achieve the identified aims. The RMOA therefore recommends that the following actions should be initiated:

- Enzyme suppliers and product formulators should continue to work together to develop a range of communication tools that will help end users of products containing AA (and other enzymes) understand the risks associated with these products and manage those risks appropriately.
- Based on the potential for exposure, it would be useful to prioritise guidance aimed at the textiles sector, use in rotary vacuum drum filtration processes, professional hard surface cleaning and cleaning medical devices.
- Over time it will be helpful to extend communications to all sectors where enzymes are used. When new applications are developed, alongside product development, it will be useful to develop a suite of safe use communication tools covering these new applications.

The evaluation did not identify specific concerns relating to the operating conditions and risk management measures identified for manufacture and formulation of enzyme-containing products. Given that some workers in these industries are found with raised levels of enzyme specific IgE and a small percentage develop symptoms of occupational rhinitis and/or asthma, it is recommended that working practices are regularly reviewed to ensure that best practice is being applied consistently at all sites and that the working practices recommended in best practice guidance are still the most appropriate to minimise worker exposure. For example, it may be possible to design processes/ tasks differently to prevent release of enzymes at source. Where this is not possible, it may be useful to consider the use of RPE even for situations where the worker DMEL of 60 ng/m^3 is not likely to be exceeded, but there is a likelihood that workers could still inhale airborne enzyme.

For consumer use, new information obtained by the registrants during preparation of the RMOA suggests that under worst case conditions, if bubble blowing solutions are made with enzyme-containing hand dishwashing liquids, levels of enzyme in air could rise to levels seen at enzyme production facilities. In light of this finding, the registrants set an upper concentration limit in the exposure scenario and have proposed additional instructions for use that can be included on product labels for both consumer and professional use hand dishwashing liquids. The RMOA has identified provisions in Article 11(3) of the Detergents Regulation which may provide a legal mechanism to include this information on product labels for products sold to the general public. Registrants should ensure all formulators are aware of relevant instructions to be included on labels for enzyme-containing hand dishwashing liquids.

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	
Need for action other than EU regulatory action	✓
No action needed at this time	

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

The RMOA did not identify a need to initiate new regulatory actions at the EU or national level.

3.1 Harmonised classification and labelling

AA is currently listed in Annex VI of the CLP Regulation with a harmonised classification of Resp. Sens 1. This classification must appear on product labels where the substance is supplied as itself and in mixtures containing 1% or more of the substance. There is a further requirement for mixtures containing 0.1% AA or more to include the supplemental hazard statement EUH208 to alert those who know they are sensitised to this enzyme that it is present in the product. Warnings of respiratory sensitisation potential are not permitted for mixtures containing less than 0.1%.

While it is currently not possible to identify a clear threshold for induction or elicitation, the evidence suggests that these processes can occur at dose levels in the ng/m^3 range. This raises a concern that mixtures containing AA may present a risk for respiratory sensitisation at concentrations below the generic cut off value of 1% established in CLP for classification of mixtures as Resp. Sens. 1 and that it may be desirable for warnings to be provided for mixtures containing less than 0.1% AA. This could be achieved if the threshold for classifying mixtures containing AA was lowered.

Currently, no information is available that would enable specific concentration limits (SCLs) to be established for AA and it is questionable if sufficient information is available to consider allocation of AA into the Resp. Sens. 1A sub-category at this time. For this reason it is not expected that new regulatory action can be taken under the CLP Regulation.

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

Although respiratory sensitisers may be identified as SVHCs according to Art 57(f) this is not seen as an appropriate step for AA. Article 56(6)(b) disapplies the requirement to obtain authorisation for uses of substances listed on Annex XIV where these substances are present in mixtures below the concentration limits which result in those mixtures being classified as dangerous. In the case of a substance classified as Resp. Sens. 1, this threshold is 1%. Since most AA containing formulations currently supplied to downstream users typically contain a maximum of 0.5% aep, this removes most of the products for which additional safe use guidance is needed from the scope of this provision. Inclusion on Annex XIV would also bring pressure on companies to substitute use of AA with alternatives. This is not identified as a desirable regulatory outcome given the many environmental benefits of enzyme technologies when compared with currently available alternatives. For these reasons, identification as an SVHC with eventual prioritization to Annex XIV is not seen as a useful risk management option for AA.

3.3 Restriction under REACH

Providing users adhere to the conditions of use specified in REACH exposure scenarios, no uses have been identified that give rise to unacceptable risks. There is therefore no basis to initiate a restriction.

3.4 Other Union-wide regulatory measures

The RMOA considered the feasibility of setting an EU wide OEL. In view of the high resources that are likely to be required for such an action and the current lack of a method that can measure personal exposures at relevant concentrations (low ng/m^3 range) with sufficient accuracy for compliance monitoring and enforcement action, this option was not considered to be useful.

No other EU-wide regulatory measures were identified.

4. NEED FOR ACTION OTHER THAN EU REGULATORY ACTION

The RMOA concluded that industry-led initiatives have the potential to provide the additional good practice communication that is needed for workers (see section 2). In light of the modified conditions of use applied to exposure scenarios for hand-dishwashing liquids no new regulatory action appears necessary at this time. Registrants should ensure all formulators are aware of relevant instructions to be included on labels for enzyme-containing hand dishwashing liquids.

5. NO ACTION NEEDED AT THIS TIME

Not applicable

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS IF NECESSARY

No formal timetable for follow-up actions is proposed. However, in the future it may be desirable to review the availability of guidance and the extent to which downstream users are adopting best practices, also to check labelling instructions on consumer hand dishwashing products containing enzymes to ensure appropriate instructions are given. The time frame for such a review will depend on the priority that is given to the risk management of AA (and other enzymes) compared with other substances. One factor will be the extent to which cases of ill-health continue to be reported.

Follow-up action	Date for follow-up	Actor