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ERC guidance on the first steps for registration of enzymes under REACH (REG (EC) No 1907/2006)

1. Purpose

Enzyme manufacturers and importers in the EU must register enzymes before annual tonnage exceeds 1 ton/year and if uses are within the scope of registration. Enzymes are not in the scope of REACH registration if they meet the criteria set in Article 5, for example, enzymes used as feed additives within the scope of Regulation (EC) No 1831/2003 or as processing aids for manufacture of food in accordance with the Food Improvement Agents Package (FIAP).

The first step towards registration is to submit an inquiry dossier so that the European Chemical Agency (ECHA) can assess if the enzyme was already registered or not[1]. In addition to ERC guidance documents, this document provides guidance in order to properly identify and document an enzyme for an inquiry dossier and accordingly for registration.

References used in this guidance are:

- ECHA's "**Guidance for identification and naming of substances under REACH and CLP** " Section 4.3.2.3 Enzymes and Section 5. Criteria for checking if substances are the same (May 2017 version 2.1)
- ERC's **guidance**

2. Enzyme identification and tonnage calculation

Tonnage calculation

Please see ERC's guidance on the following webpage
http://www.enzymes-reach.org/content/documents

Enzyme identification

An enzyme should be identified according to the **Enzyme Nomenclature** defined by the Nomenclature Committee of the International Union of Biochemistry (IUBMB) based on catalytic activities. Please see ECHA's "Guidance for identification and naming of substances under REACH

[1] According to ECHA new dated June 5, 2018, "If you have pre-registered or inquired about your phase-in substance before the deadline of June 1, 2018, you can register it directly (until further notice, you can still use the pre-registration number)".

and CLP" Section 4.3.2.3 Enzymes. Further guidance is also provided by ERC (see weblink under 'Tonnage calculation').

3. Inquiry dossier

Submission of an inquiry dossier is a prerequisite for registration (see foot note1). The most critical information is

- Identification of enzymes according to IUBMB (see the previous section) – IUCLID Section 1.1
- Documentation that the hazardous properties warrant the same IUBMB enzyme class. – IUCLID Section 1.2
- Determination of constituents – IUCLID Section 1.2 and 1.5

IUCLID Section 1.1 Identification

Identification of substance
An enzyme should be identified as described in the previous section. A new reference substance object may have to be created manually. Otherwise it is downloadable from the inventory provided by ECHA or in REACH-IT after CLP notification.

Reference substance
For sameness discussion with other (potential) co-registrants, it is advisable to document in "Description" that the production organism meets the criteria as mentioned in ERC's document on "Safety evaluation of technical enzyme products with regards to the REACH legislation".

Alpha-amylase is used as an example below.

> Alpha-amylase
> EC 232-565-6
> IUBMB 3.2.1.1
> CAS 9000-90-2
>
> Description: The enzyme is produced by organisms which meet the criteria for "Safe Strain Lineage Concept" in "Safety evaluation of technical enzyme products with regards to the REACH legislation" dated March 25, 2009, published by Enzyme REACH Consortium (http://www.enzymes-reach.org/).

IUCLID Section 1.2 Compositions

Description
In this section, the manufacturing processes and a source should be provided if a substance is UVCB (Chemical Substances of Unknown or Variable Composition, Complex Reaction Products and Biological Materials). An enzyme is a UVCB substance, however for enzymes it is not necessary to provide a source when the classification condition is met, according to the ECHA's Substance Identification description "*Enzyme concentrates with the same IUBMB number can be regarded as the same substance, despite using different production organism, provided that the hazardous properties do not differ significantly and warrant the same classification*". If a production strain(s) meets the criteria in ERC's document on "Safety evaluation of technical enzyme products with regards to the REACH legislation" then this classification condition is met. It is advisable to document this clearly in this section or as an attachment. A generic description of the production process should also be provided as an attachment.

Constituents
Constituents should be provided using groups such as active enzyme protein, other protein + peptides and amino acids, carbohydrates, lipids and inorganic salts based on the analysis in IUCLID Section 1.4. Please note that if a constituent is ≥ 10 % (w/w) or relevant for classification and labelling and/or PBT, it should be identified. For further information, please see ECHA's "Guidance for identification and naming of substances under REACH and CLP".

IUCLID Section 1.5 Analytical information

Methods and results of analysis
Analytical methods and results corresponding to IUCLID Section 1.2 must be provided. For active enzyme protein, an enzyme assay method measuring the activity as described in IUBMB enzyme nomenclature should be provided. Analytical methods and results for other grouped constituents should also be provided.

4. Registration

If ECHA concludes that the inquired enzyme is the same as the one which is already registered, they will provide the contact details of the Lead Registrant. If the Lead Registrant is a member of ERC, cost and data sharing polices used for that enzyme joint dossier are available at the ERC website.