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Exposure assessment of food enzymes

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Abstract

In preparation of receiving dossiers on food enzymes, in 2009, the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids published guidance on data requirements and methodologies foreseen in the risk assessment of food enzymes. Based on experiences gained in assessing submitted dossiers, the Panel noted that the Budget method, an approach originally designed to assess food additives, was not appropriate for the purpose of assessing food enzymes. Consequently, the Panel undertook the task of developing an alternative assessment methodology. The Panel recommends the use of actual food consumption data for the assessment of dietary exposure to food enzymes. Consequently, individual data reported in the EFSA Comprehensive European Food Consumption Database will be used in the evaluation of food enzyme dossiers. It is envisaged that, during the evaluation of dossiers, a process-based tool, based on summary statistics reported in the EFSA Comprehensive European Food Consumption Database, will be developed. As each process will require information on several input parameters, it is foreseen that the tool will be rolled out process-by-process over a period of time in collaboration with stakeholders.

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1. Introduction

Regulation (EC) No 1331/2008¹ provides for a common assessment and authorisation procedure for food enzymes, including a risk assessment carried by the European Food Safety Authority (EFSA). The latter provision is in accordance with the framework for risk assessment in matters of food safety established by Regulation (EC) No 178/2002², which requires that the authorisation to place substances on the market must be preceded by an independent scientific assessment of the risks that they may pose to human health.

In 2009, the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF Panel) published a guidance document specifying the type of information that applicants should provide to enable EFSA to carry out the safety assessments of food enzymes (EFSA, 2009). However, difficulties encountered during the evaluation process led the Panel to the conclusion that more realistic scenarios than those originally recommended are required to estimate exposure to food enzymes. As a consequence, EFSA asked the CEF Panel to explain this change in approach in a scientific statement (see Section 1.1). The draft statement which was subject to public and stakeholder consultation (see Section 1.2) prior to adoption, was published at the EFSA website.³

This statement, having undergone the procedures of consultation, aims to provide an overview of the issues that necessitated a change in approach and to introduce the concept of the new approach and the technical considerations related to dietary exposure assessment with respect to food enzymes.

1.1. Background and Terms of Reference as provided by the requestor

The guidance on food enzymes stipulates that 'Potential human exposure to the food enzyme and to any other constituent or by-product of concern should be assessed considering all proposed uses. A conservative technique such as the 'Budget method' should be used ... assuming that they (i.e. foods and beverages) always contain the food enzyme at its proposed upper use level' (EFSA, 2009).

The CEF Panel had taken note of the difficulty in applying the Budget method to food enzymes as they are generally added during the processing of food and food ingredients. Based on the experiences gained in assessing the dossiers submitted, the CEF Panel considered the need to evaluate the exposure to enzymes through more realistic scenarios applying a tiered approach.

This consideration was found to be in line with the advice of EFSA to use 'a stepwise or tiered approach in which the initial steps rely on conservative screening methods to minimise estimation costs and focus resources on the most important issues for which there is a potential health concern' (EFSA, 2011a).

Terms of Reference

In accordance with Article 29(1) of Regulation (EC) No 178/2002, EFSA asked the CEF Panel to explain the principles of the refinement of exposure estimates for food enzymes in a scientific statement. This statement should be presented to stakeholders/applicants before adoption by the Panel.

1.2. Additional information

Stakeholder comments on the draft statement were collected from two events: an Info session and a public consultation.

Agenda and presentations of the Info session on 3 February 2016 are available online: <http://www.efsa.europa.eu/en/events/event/160203>

Comments received during the public consultation held on the EFSA website from 16 February to 31 March 2016 are summarised and discussed in a technical report 'Outcome of a public consultation on the CEF Panel's draft Statement on Exposure Assessment of Food Enzymes' (EFSA, 2016).

In addition, comments from an ad hoc meeting with the industry association AMFEP were taken into consideration (available online: <https://www.efsa.europa.eu/en/events/event/160818>).

¹ Regulation (EC) No 1331/2008 of the European Parliament and of the Council of 16 December 2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings. OJ L 354, 31.12.2008, p. 1–6.

² Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p. 1–24.

³ Available online: <https://www.efsa.europa.eu/sites/default/files/consultation/160216.pdf>

2. Dietary exposure assessment of food enzymes

2.1. Considerations specific to dietary exposure assessment of food enzymes

2.1.1. Purposes of the exposure assessment

The safety evaluation of food enzymes starts with a thorough characterisation of the production organism, the raw materials, the manufacturing process, chemical composition and the physicochemical properties of the food enzyme. The evaluation process aims to identify any potential hazardous compounds and to assess the risk to human health associated with the exposure to such hazards, aided by the use of toxicological tests. Substances of potential concern associated with the food enzyme could be the enzyme itself, natural constituents and/or contaminants of the production organism and/or the raw materials, and chemicals that are added initially and carried over during enzyme manufacturing process. The purpose of the exposure assessment is to provide a quantitative estimate of exposure to the food enzyme for humans with a view to aid characterisation of any risk associated with such an exposure.

2.1.2. Need for dietary exposure assessment

Food enzymes are used to enable or enhance specific chemical reactions during food production. They may be removed and/or inactivated during food processing. However, in the initial stages of dietary exposure assessment, it is generally assumed that the entire food enzyme is transferred into the food as consumed. Certain exceptions can be made; for example, processes, such as distillation, are not likely to lead to transfer of any non-volatile component into the distillate. Similarly, the production of highly purified sugar syrups via starch processing may be considered to result in negligible residues of the food enzyme in the final product, if any. The need for an exposure assessment will therefore be assessed on a case-by-case basis.

For applications concerning '*food enzymes, that are obtained from edible parts of plant or animals intended to be or reasonably expected to be ingested by humans*', Implementing Regulation (EU) No 562/2012⁴ stipulates that provision of toxicological data is not required under certain conditions. For these applications, a comparison is made between the exposure to the food enzyme resulting from its intended uses and the exposure to a comparable fraction of the source material resulting from the consumption of foods derived from this source. The outcome of this comparison is one of the criteria to justify that no toxicological data are required (EFSA, 2009).

For applications for which toxicological tests are required (EFSA, 2009), the risk is characterised through comparison of the estimated human exposure to a point of departure (POD) (e.g. no-observed-adverse-effect level or benchmark dose level) determined in subchronic oral toxicity studies performed on animals. A ratio, referred to as margin of exposure, between the POD and the estimated exposure is used by the CEF Panel in concluding on the safety of the food enzyme.

2.2. Exposure assessment methodology

2.2.1. Introduction

In accordance with recommendations⁵ of the Scientific Committee (EFSA, 2005), the Panel identified problems encountered in the exposure assessment of food enzymes and investigated possibilities for improvement and harmonisation of the process. As a consequence, the Panel considered it necessary to update the guidance provided in 2009.

Historically, due to the absence of appropriate food consumption data, the Budget method, originally developed for setting maximum use levels for food additives, was proposed as a screening tool in the assessment of food enzymes. However, based on the experiences gained in assessing dossiers submitted, the Panel noted that use of the Budget method for the purposes of assessing the

⁴ Commission Implementing Regulation (EU) No 562/2012 of 27 June 2012 amending Commission Regulation (EU) No 234/2011 with regard to specific data required for risk assessment of food enzymes. OJ L 168, 27.06.2012, p. 21–23.

⁵ 'EFSA should monitor problems encountered by the Panels and help to identify when there is a need for revising existing guidelines'.

dietary exposure to food enzymes was not appropriate and advocated an 'actual food consumption data-based assessment' methodology.

In particular, the following issues were considered in reaching this conclusion:

- Availability of more refined and accurate food consumption information at EFSA,⁶ which is representative for the European population.
- Harmonisation of exposure methodology used across EFSA Panels.
- Difficulty in identifying the proportion of solid foods and liquids potentially containing the food enzymes under investigation when these are mainly used as ingredients at industrial level.
- Application of technical conversion factors specific to each food production process.
- Necessity to consider the child population, and in particular toddlers, since they are often at the high end when calculating exposure, as recommended by EFSA (EFSA, 2011a).

The Panel had previously contemplated the use of the Budget method without the inclusion of factors accounting for the processing of food and the proportion of processed food containing a food enzyme. However, the application of such default factors had not been validated and was deemed unsuitable for the assessment of food enzymes, which are typically added during the manufacturing process. In addition, the Panel noted, that although the Budget method could be considered sufficiently conservative to cover the adult population, it did not present a conservative screening method for the highly exposed population group (i.e. toddlers), even when used without the above mentioned factors.

As an alternative, a screening tool based on actual food consumption data could have been derived. However, a large proportion of applications may require further refinement in the exposure assessment. Therefore, the development of such a screening tool was deemed not practical. Furthermore, in many cases, assessments of the same type of food enzyme derived from the same species of microorganism may only differ in the use levels required to obtain the intended effect and/or differ in the POD identified in the toxicological studies conducted. Therefore, for reasons of transparency, a uniform approach applicable to all dossiers was deemed most appropriate.

Given the quality of food consumption information available in the EFSA Comprehensive European Food Consumption Database (Comprehensive Database),⁷ and its representativeness of the European population, the Panel decided to derive exposure estimates for each application, as appropriate, using actual food consumption data from national dietary surveys available within EFSA. The use of the Comprehensive Database also facilitates a stepwise refinement of exposure estimates, if required.

Given the complexity associated with assessing exposure to food enzymes, the Panel decided to develop a methodology that aims to take account of the nature of use of food enzymes and their fate during food processing.

2.2.2. Food enzyme concentration data

The recommended typical or maximum food enzyme use levels are used to calculate the food enzyme concentration data, expressed as total organic solids (TOS)/kg raw material. The recommended use levels may refer to a raw agricultural commodity (e.g. grain), to a food ingredient (e.g. flour) or to a food as consumed (e.g. bread).

To aid the Panel in refining exposure estimates, stakeholders might be invited to provide more specific data, e.g. food category specific use levels.

2.2.3. Food consumption data

Since 2010, the Comprehensive Database has been populated with national data on food consumption at a detailed level. Competent authorities in the European countries provide EFSA with data on the level of food consumption by the individual consumer from the most recent national dietary surveys in their country (EFSA, 2011b). Currently, food consumption data covering infants, toddlers, children, adolescents, adults and the elderly are available from different dietary surveys carried out in the majority of European Union (EU) Member States. The Comprehensive Database represents the best available source of food consumption data across Europe at present.

⁶ <http://www.efsa.europa.eu/en/data/food-consumption-data>

⁷ <http://www.efsa.europa.eu/en/food-consumption/comprehensive-database>

2.2.4. Harmonisation of food enzyme concentration and food consumption data

For the purpose of estimating dietary exposure to food enzymes, food consumption data and food enzyme concentration data need to be expressed on the same basis, irrespective of the level of refinement required. Typically, food enzyme usage data is expressed on a raw material basis, whereas food consumption data typically refers to food as consumed. Consequently, tools allowing the interconversion of these data sets are needed to facilitate the assessment.

The use of the Comprehensive Database for the exposure assessment of food enzymes therefore may require disaggregation of foods and beverages into their ingredients and potentially also conversion back to the raw agricultural commodity, as appropriate. Alternatively, food enzyme use levels based on the raw material may be converted into use levels based on the relevant ingredient or food as consumed.

2.2.4.1. Recipe and technical conversion factors

Recipes or composite dishes can be disaggregated into single ingredients using available recipe databases/books or can be extrapolated from the list of ingredients available on food labels. For example, standard recipes can be used to estimate the amount of flour in bread.

Conversion of raw agriculture commodities to ingredients or food as consumed or vice versa is facilitated via the application of technical conversion factors. Some standard conversion factors are available, such as the Food and Agriculture Organization of the United Nations (FAO) technical conversion factors,⁸ and will be routinely used in the assessment to ensure transparency and consistency in all assessments. For example, an FAO technical factor is used to convert the amount of flour in bread back to the amount of grain, or vice versa.

To aid the Panel in deriving factors currently not covered by the FAO data set, stakeholders will be invited to contribute to this task.

2.2.5. Exposure assessment model

Typically, unless the need for acute exposure assessment is indicated, chronic exposure to food enzymes will be calculated, based on individual consumption data reported in the Comprehensive Database (see Annex A).

The methodology employed aims to take account of the nature of use of food enzymes and their fate during food processing. Consequently, each application will require assessment of each individual food process for which the food enzyme is intended to be used.⁹

FoodEx categories and/or specific foods relevant to each food process under consideration will be selected from the Comprehensive Database.

To facilitate matching of the reported use levels with foods identified in the Comprehensive Database, the selected foods will be converted into the corresponding ingredient/raw agriculture commodity or, alternatively, the reported use levels will be expressed on a food as consumed basis, via the application of conversion factors. The approach to follow will be decided on a case-by-case basis.

The identified FoodEx categories will be assumed to contain the food enzyme-TOS at the corresponding recommended use level, and exposure will be calculated by multiplying the intake of each individual eating occasion of the relevant food by the matching food enzyme-TOS.

Exposure to each identified FoodEx category will subsequently be summarised for each survey participant in the database, to derive a total exposure for each person per day. Finally, these exposure estimates will be added up to derive a total exposure over the survey period per survey participant, and will then be averaged over the number of survey days and normalised for individual body weight (bw), resulting in an average daily exposure per kg bw for the survey period. This process will be followed for all survey participants in the database, resulting in distributions of individual average daily exposure for each survey and population group. Based on these distributions, the mean and 95th percentile average exposures are reported. High-level exposure/intake will be calculated for only those population groups where the sample size is sufficiently large to allow calculation of the 95th percentile (EFSA, 2011b).

⁸ <http://www.fao.org/economic/the-statistics-division-ess/methodology/methodology-systems/technical-conversion-factors-for-agricultural-commodities/en/>

⁹ A EC working document describing the food processes in which food enzymes are intended to be used - not yet published at the adoption of this statement.

In accordance with the currently applicable guidance provided in the EFSA opinion related to uncertainties in dietary exposure assessment (EFSA, 2007), sources of uncertainties will be identified and evaluated with regard to their impact on the overall exposure calculation.

2.3. Reporting exposure estimates

Exposure estimates to food enzymes will be reported for six population groups (infants, toddlers, children, adolescents, adults and the elderly). For both mean and 95th percentile intake, the range of minimum–maximum value observed across the selected surveys will be reported. This mirrors the level of reporting provided by both the EFSA Panel on Food Additives and Nutrient Sources added to Food and the EFSA Panel on Contaminants in the Food Chain, and fulfils the long-term objective of EFSA, aiming as much as possible to harmonise exposure assessment across the different (classes of) substances through the development of standardised methodologies and also to further harmonise the way exposure is estimated in EFSA by the different Panels (EFSA, 2011a).

2.4. Way forward

As discussed in Section 2.2.1, each application will require assessment of each individual food process in which the food enzyme is intended to be used.

Assessment of different food processes will require the application of the corresponding process and technical conversion factors, which are to be derived in collaboration with stakeholders, where required.

The Panel will apply the procedure described in Section 2.2.5 to calculate exposure using individual data reported in the Comprehensive Database.

In addition, a publicly available process-based tool will be developed. It is likely to be based on summary statistics, similar to the Food Additive Intake Model (FAIM) template used for food additives. As each food process will require specific information on several input parameters, input from industrial associations and/or applicants for more technical data and factors will be sought as appropriate. It is foreseen that the tool will be rolled out process-by-process over a period of time.

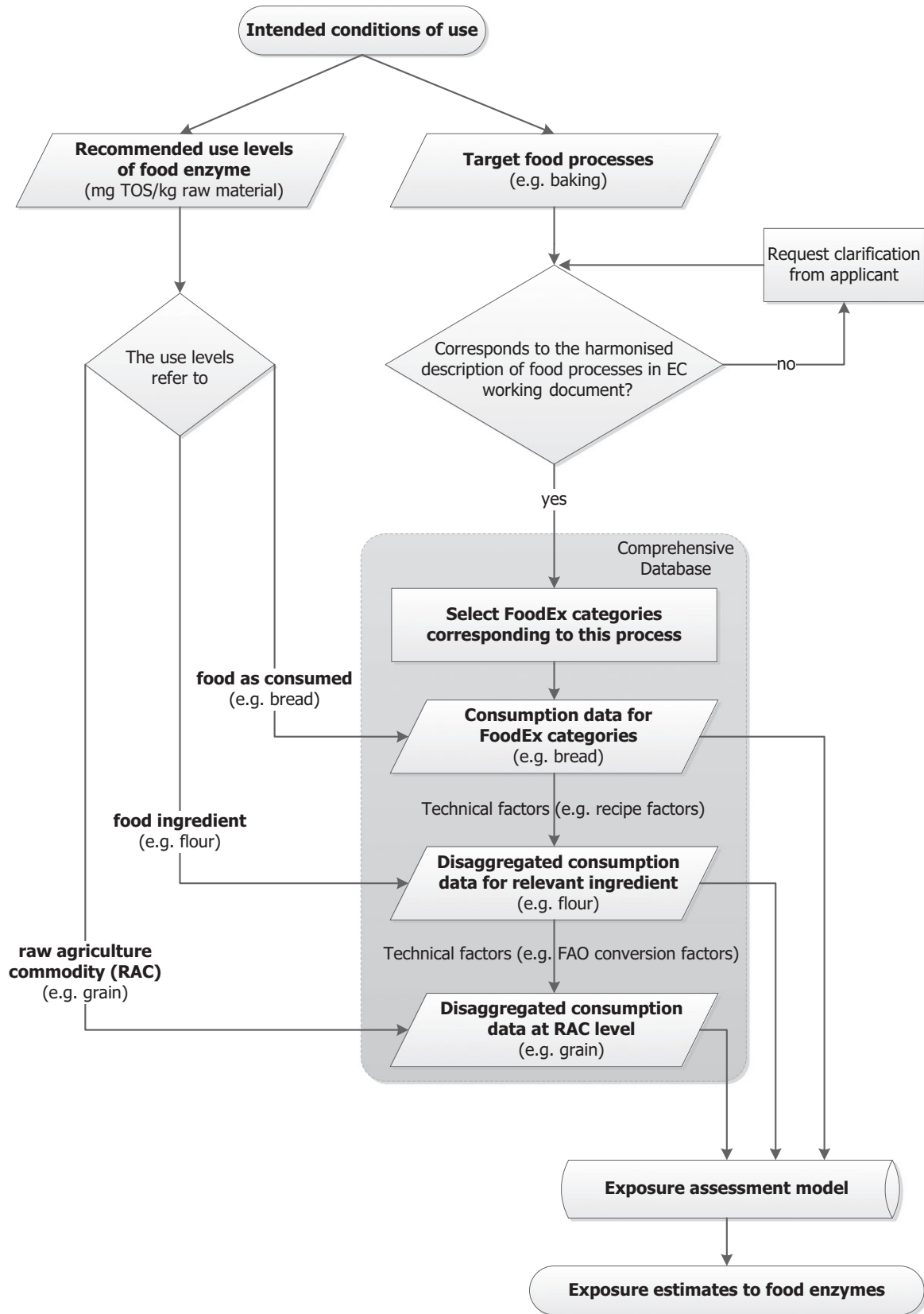
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Abbreviations

AMFEP	Association of Manufacturers and Formulators of Enzyme Products
bw	body weight
CEF	EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
FAIM	Food Additive Intake Model
FAO	Food and Agriculture Organization
POD	point of departure
TOS	total organic solids

Annex A – Flowchart of the exposure assessment methodology for food enzymes based on the EFSA Comprehensive European Food Consumption Database (Comprehensive Database)



Simplified scheme for showing main steps only