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Draft Statement on Exposure Assessment of Food Enzymes

EFSA Panel on Food Contact Material, Enzymes, Flavourings and Processing Aids (CEF)

Abstract

Following a request from EFSA, the Scientific Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF) was asked to explain the principles of the refinement of exposure estimates for food enzymes. Its guidance document on the submission of a dossier on food enzymes for safety evaluation suggests that the *'potential human exposure to the food enzyme and to any other constituent or by-product of concern should be assessed considering all proposed uses, and that a conservative technique such as the 'Budget method' should be used. The margin of exposure (MoE) between the estimated dietary exposure from use of the food enzyme and the no-observed-adverse-effect level (NOAEL) should be calculated'*. Since then, the CEF Panel has taken note of the difficulties in the application of the budget method to estimating exposure to food enzymes and proposes refined stepwise approach. © European Food Safety Authority, 2015

Keywords: food enzymes, exposure assessment, budget method, refinement

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49 **1. Introduction**

50 **1.1. Background and Terms of Reference as provided by EFSA**

51

52 The CEF guidance on food enzymes (CEF EFSA, 2009) which was adopted in 2009
53 stipulates that the *'Potential human exposure to the food enzyme and to any other*
54 *constituent or by-product of concern should be assessed considering all proposed uses. A*
55 *conservative technique such as the "budget method" should be used ... assuming that*
56 *they (i.e. foods and beverages) always contain the food enzyme at its proposed upper*
57 *use level.'*

58 The CEF Panel has taken note of the difficulty to apply the budget method to food
59 enzymes in general as they are added during processing of food and food ingredients.
60 Based on the experience acquired in the last months, the CEF Panel considered the need
61 to evaluate the exposure to enzymes through more realistic scenarios applying a tiered
62 approach.

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

67 In accordance with Article 29(1) of Regulation (EC) No 178/2002, the European Food
68 Safety Authority asks its scientific Panel on Food Contact Materials, Enzymes, Flavourings
69 and Processing Aids (CEF) to explain the principles of the refinement of exposure
70 estimates for food enzymes in a scientific statement. This statement shall be presented
71 to stakeholders/applicants before adoption by the CEF Panel.

72

73 **2. Data and Methodologies**

74

75 In 2009 CEF Panel adopted a guidance document on the submission of a dossier on food
76 enzymes for safety evaluation. This document aims to assist applicants in the preparation
77 and submission of applications and lays down the data requirements for the safety
78 evaluation of food enzymes (EFSA CEF Panel, 2009). The guidance suggests that the
79 *'potential human exposure to the food enzyme and to any other constituent or by-*
80 *product of concern should be assessed considering all proposed uses, and that a*
81 *conservative technique such as the 'budget method' should be used'* (Hansen, 1966,
82 1979; Douglass et al., 1997; European Commission, 1998; FAO/WHO, 2008).

83 It stipulates also that information on *'the type of foodstuffs in which the food enzyme is*
84 *intended to be used'* as well as *'the amount of food enzymes to be added to specific*
85 *foods (recommended use levels and maximum use levels)'* shall be provided in the
86 dossier. *"Furthermore, that information should be provided on the fate of the food*
87 *enzyme during the food processing."*

88 Finally the margin of exposure (MoE) should be calculated based on the estimated dietary
89 exposure from use of the food enzyme and the no-observed-adverse-effect level
90 (NOAEL).

91 Most of the applications submitted to EFSA to date contain an estimate of exposure
92 based on the budget method without further refinement. Maximum and/or normal use
93 levels are provided by applicants. However, in most cases detailed information on the
94 type of foodstuffs as consumed in which the food enzyme can be present is not provided.
95 Instead, food processes are described and non-exhaustive examples of food categories
96 are given, not allowing for the refinement of exposure.

97 **3. Assessment**

98

99 Food enzymes are typically not added to the final food rather they are added during
100 processing of food and food ingredients; therefore, assessing exposure to food enzymes
101 is complex and requires particular consideration.

102 In the application of the budget method, initially designed and used as a screening
103 method for food additives, several assumptions are made regarding:

104 a) food and beverage intake;

105 b) percentage of food and beverage that are processed; and

106 c) percentage of processed food and beverage containing the food additive.

107 The levels of consumption of foods and beverages considered are based on assumptions
108 regarding the physiological requirements for energy and liquids of a 2-year old child
109 (Hansen, 1979) - i.e. the daily consumption of 0.1 L/kg bw of liquid and the daily energy
110 intake of 100 kcal/kg bw from foods (equivalent to 0.05 kg/kg bw based on an estimated
111 energy density of 2 kcal/g food). These levels correspond to the daily consumption of 6
112 litres of non-milk beverages and 3 kg of food by a person with a body weight of 60 kg
113 (typical adult) and a daily consumption of 1.5 litres of non-milk beverages and 750
114 grams of food by a child with a body weight of 15 kg (typical 3-year old child)
115 (FAO/WHO, 2009). The Panel confirmed the conservativeness of these assumptions by
116 means of comparing the data with food consumption summary statistics from the EFSA
117 Comprehensive European Food Consumption Database¹.

118 As previously mentioned under points b) and c), the budget method makes assumptions
119 with regard to the percentage of foods/beverages that are processed and the percentage
120 of the latter containing a given food additive. A number of standard factors (typically
121 12.5%, 25% and 50%) have been applied in the assessment of additives, the choice of
122 which is based on the type and importance of the food group(s) in which the additive is
123 permitted, in relation to overall food/beverage intake. The assumptions underlying the
124 budget method and their suitability to assess food additive intake have previously been
125 examined (Douglas et al, 1997; ILSI, 1997), however, this has not been done in the case
126 of food enzymes. Therefore, the appropriateness of using such standard factors in the
127 exposure assessment to food enzymes requires further consideration, in particular since
128 application of the budget method and associated factors can lead to a considerable
129 overestimation of exposure (Douglas et al, 1997). In such cases a refinement of
130 exposure as recommended in the EFSA report (EFSA, 2011) is deemed necessary.

¹ <http://www.efsa.europa.eu/en/datexfoodcdb/datexfooddb>

131 As a consequence the CEF Panel agreed to adopt a tiered approach (as outlined in Annex
132 A) for the assessment of exposure to food enzymes.

133 **Tier 1:** As a first initial screening step, the budget method will be used for all enzymes
134 under evaluation without the use of above described standard factors. If the MoE derived
135 from this exposure estimate is sufficiently high (s. Annex A), no further assessment is
136 required.

137 For those cases where the calculated MoE according to Tier 1 is insufficient (s. below),
138 the exposure assessment will be refined through one of two possible alternative
139 evaluation steps (s. Annex A), as follows:

140 **Tier 2a:** For those cases where information on the occurrence of the enzyme in
141 food/beverages as consumed is available and allows for a calculation of the exposure
142 using specific food categories in the EFSA Comprehensive European Food Consumption
143 Database, the latter will be used. The so derived exposure estimates will be based on
144 individual food consumption reported for the European populations.

145 **Tier 2b:** For all other cases, the budget method will be used with factors specific to the
146 respective enzyme. Such factors will be derived using all available information (e.g. the
147 use of the enzyme during food processing, the proportion of processed food and the
148 presence of the food enzyme therein).

149

150 The use levels provided by the applicants often are expressed as food enzyme on a per
151 substrate basis (e.g. enzyme activity per amount of dry matter starch) or for a raw
152 material (e.g. enzyme activity per amount of grain used in beer production). In both
153 cases, the provided use level of the enzyme does not refer to the food/food ingredient as
154 consumed. Therefore the amount of substrate or raw material in relation to the amount
155 of food as consumed has to be taken into account in the exposure calculation
156 independent of any tier applied in form of a conversion factor.

157 As each safety assessment is performed on a case-by-case basis requiring expert
158 judgement of the entire toxicological database and information related to the intrinsic
159 properties of specific food enzyme, no generally acceptable value can be established for
160 MoE. As a first indication, a MoE of 300 (Factor 10 for inter-species difference, factor 10
161 for intra-species difference and factor 3 for the extrapolation from short-term studies to
162 chronic studies, EFSA Scientific Committee, 2012) may be regarded as sufficient provided
163 the data are complete and the quality of the data is acceptable.

164 **References**

165

166 Douglass JS, Barraj LM, Tennant DR and Long WR, 1997, Evaluation of the budget method for
167 screening food additive intakes. *Food Addit Contam*, 14, 791–802.

168 EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids, 2009, Guidance of
169 the Scientific Panel of Food Contact Material, Enzymes, Flavourings and Processing Aids (CEF) on
170 the Submission of a Dossier on Food Enzymes for Safety Evaluation, *The EFSA Journal*, 1305, 1-26,
171 doi: 10.2903/j.efsa.2009.1305

172 EFSA Scientific Committee, 2012, Guidance on selected default values to be used by the EFSA
173 Scientific Committee, Scientific Panels and Units in the absence of actual measured data. *EFSA*
174 *Journal*, 10(3), 2579, 32 pp. doi:10.2903/j.efsa.2012.2579.

175 European Food Safety Authority, 2011, Overview of the procedures currently used at EFSA for the
176 assessment of dietary exposure to different chemical substances *EFSA Journal*, 9(12), 2490, 33 pp.
177 doi:10.2903/j.efsa.2011.2490.

178 European Commission, 1998, Report on methodologies for the monitoring of food additive intake
179 across the European Union. Report of a working group on scientific cooperation on questions
180 relating to food. Task 4.2. Luxembourg, Office of Publications of the European Communities
181 (SCOOP/INT/REPORT/2).

182 FAO/WHO, 2009, Principles and Methods for the Risk Assessment of Chemicals in Food. Chapter 6:
183 Dietary exposure assessment of chemicals in food. *Environmental Health Criteria* 240, 6-2, 6-92.

184 Hansen SC, 1966, Acceptable daily intake of food additives and ceiling on levels of use. *Food and*
185 *Cosmetics Toxicology*, 4, 427-432.

186 Hansen SC, 1979, Conditions for use of food additives based on a budget method for an acceptable
187 daily intake. *J Food Prot*, 42, 429–434.

188 **Abbreviations**

CEF	Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
EFSA	European Food Safety Authority
NOAEL	No-observed-adverse-effect level
MoE	Margin of Exposure

Annex A – Flowchart of the tiered approach for the exposure assessment of food enzymes

