Draft Statement on Exposure Assessment of Food Enzymes

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Info Session on Applications – Food Enzymes – Technical meeting with stakeholders on refinement of exposure estimates

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RISK ASSESSMENT

- Hazard Identification
- Hazard Characterisation
- Exposure Assessment
- Risk Characterisation

EXPOSURE ASSESSMENT

- Complex task and has been subject to several specific opinions and guidelines (EFSA, WHO/FAO, EFCOSUM, FOSIE, EC etc.)
- Exposure assessment is an integral part of the work of the EFSA Scientific Committee and Panels
- Specifically addressed by EFSA Scientific Committee in 2005[1]
- EFSA Overview of procedures and recommendations in 2011[2]

1 EFSA (2005) Opinion of the Scientific Committee on a request from EFSA related to Exposure Assessments

2 EFSA (2011) Overview of the procedures currently used at EFSA for the assessment of dietary exposure to different chemical substances

1. **Principles of exposure assessment**
2. The Bugdet method
3. The CEF proposal for exposure assessment of food enzymes

EFSA EXPOSURE PRINCIPALS

- 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’
- When screening methods cannot rule out a safety concern, more refined methods should be applied.
- Cover a minimum of 95% of the whole population
- Covered population groups: infants, toddlers, children, adolescents, adults, elderly
- Brand loyal consumers

OUR MILESTONES ON EXPOSURE ASSESSMENT

Jun 2005 Scientific committee opinion on exposure assessment

JUL 2009 EFSA GD on submission of food enzyme dossier

DEC 2011 EFSA overview on the exposure assessment

OCT 2015 Publication of CEF Panel draft statement on exposure

3 FEB 2016 3rd EFSA Info session

FEB 2016 Public consultation

Summer 2016 Adoption of CEF Panel statement on exposure

EFSA GD ON FOOD ENZYMES DATA SUBMISSION - 2009

- *'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.'*

- In line with general guidance on the exposure assessment to food chemicals at the time

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THE BUDGET METHOD (ORIGINAL CONCEPT)

- Originally developed in 1960s/70s to derive "ceilings" (i.e. maximum permitted levels (MPLs)) for additives in food and beverages for which an ADI was set
- Lack of actual food consumption data
- In lieu intake data based on energy and liquid requirement of a 1-2 year old child

ENERGY REQUIREMENT WITH AGE

Hansen, 1979

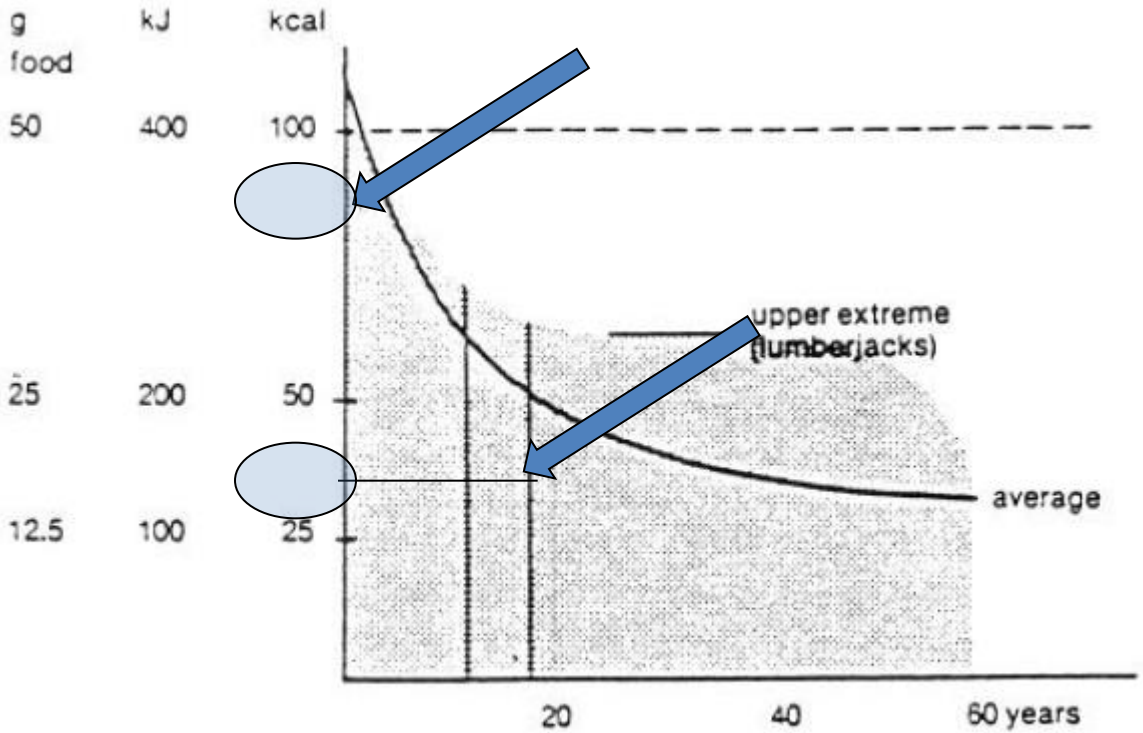


Figure 2. *Variation in energy intake with age expressed per kg of body weight per day.*

Source: Hansen SC (1979) **Conditions for use of food additives based on a budget for an acceptable daily intake.** *Journal of Food Protection* 42:429–432

LIQUID REQUIREMENT WITH AGE

Hansen, 1979

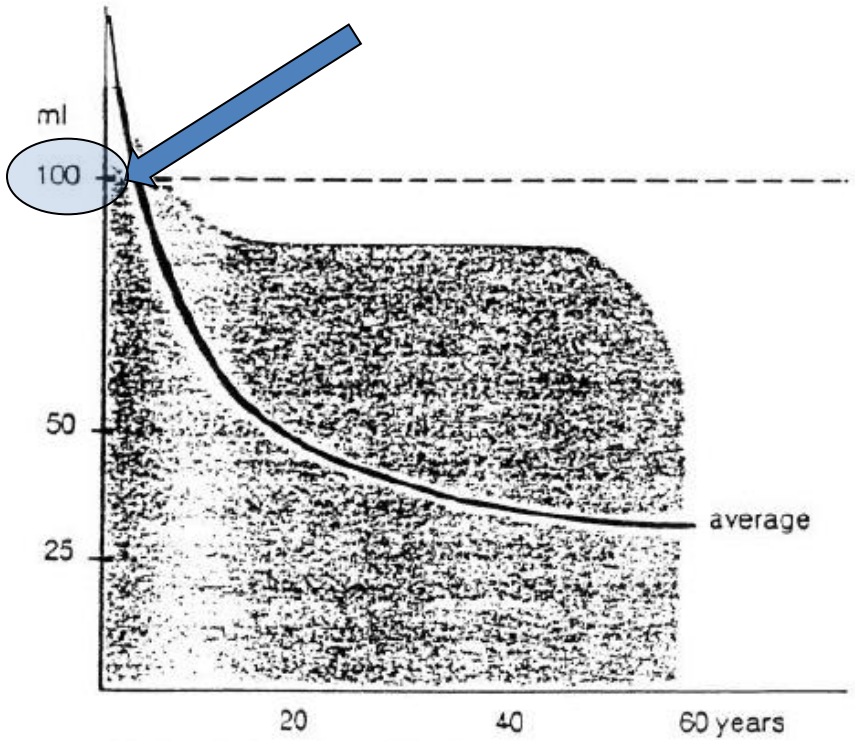


Figure 1. *Variation in liquid intake with age expressed per kg of body weight per day.*

Source: Hansen SC (1979) **Conditions for use of food additives based on a budget for an acceptable daily intake.** *Journal of Food Protection* 42:429–432

THE 3 BASIC ASSUMPTIONS BY HANSEN (1966, 1979 AND 1990)

- **Energy requirement: 100 kcal/kg bw/day**
  (corresponds to the need of a 1 year old child)

- **Liquid requirement: 100 ml/kg bw/day (excluding milk)**
  (corresponds to the need of a 2 year old child)

- **Energy density of food: 200 kcal/100 g food**
  (equal to 2 kcal/g food or 50 kcal/25 g based on FAO, 1964)

CALCULATION OF THE FOOD AMOUNT

Energy requirement

(1 year old child)

100 kcal/kg bw/day

+

Energy density of food

2 kcal/g food

→

100 kcal/kg bw/day

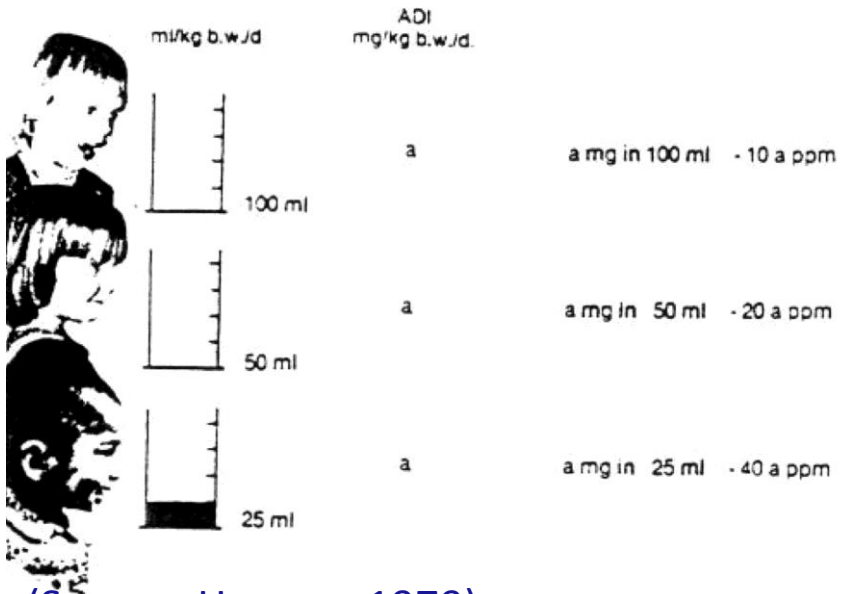
equal to

50 g/kg bw/day

CALCULATION OF MPLs

- MPLs calculated based on these assumptions
  - Intake of 50g solid food/kg bw
  - Intake of 100ml liquids (excl. milk)

- MPLs doubled and sometimes re-doubled based on restrictions of use of specific additive in certain food categories



(Source: Hansen, 1979)

THE BUDGET METHOD AS SCREENING TOOL (1)

- Concept reversed and used as screening tool for exposure assessment to food additives

- Following same but now reversed concept (of doubling MPLs depending on additive use), food intake halved and sometimes re-halved depending on permitted use of specific additive
  - Presence and proportion factors
  - 50g-25g-12.5g of food intake
  - 100ml-50ml-25ml liquid intake

THE BUDGET METHOD AS SCREENING TOOL (2)

- Evolved into standard assumption: half of food consumed is processed and half of processed food contains additive:

50% X 50% = 25%

- Based on proposed/permitted use and use levels of additives, which have a function (and MPL) in the final food as consumed

USE OF BUDGET METHOD FOR FOOD ENZYMES (1)

- Assumption on energy and liquid requirement (consumption) independent from the Food Enzyme under evaluation
- Assumptions on presence in food (occurrence) and proportion of food containing the Food Enzyme, specific to the Food Enzyme under evaluation.
- Classic budget method presence and proportion factors are based on permitted/proposed use and use levels of food additives having a technological function in the final food
- Food enzymes are not the same as food additives

USE OF BUDGET METHOD FOR FOOD ENZYMES (2)

- Proposed use levels for food enzymes often refer to the specific process in which they are used
- Usage data often expressed on a per unit substrate basis (e.g. per gram starch) or raw material (e.g. kg potatoes)
- Information on the presence of enzyme in final food;
  - Requires extrapolation from substrate / raw material to final food as consumed
  - Requires knowledge of the proportion of the ingredient/raw material, produced by the proposed process, into the final food as consumed

USE OF BUDGET METHOD FOR ENZYMES (3)

- Consequently, "presence and proportion factors" for enzymes are influenced by several different parameters
  - Food process in which they are used
  - Target substrate on which enzyme imparts function
  - Food categories covered by food process
  - Survival of food enzyme preparation constituents in the final food
  - Amount of final food consumed

⇨ Specific to each individual Food Enzyme

1. Principles of exposure assessment
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PROPOSED TIERED APPROACH

- Use of crude assumptions on food consumption in Budget Method as Tier 1 without the use of "presence and proportion factors", i.e.:

Budget Method Assumptions		**Enzyme concentration**		**Estimated exposure**
Solid food intake 50 g/kg bw	x	max TOS/kg solid food	=	Exposure estimate from solid food
Liquid intake 100 ml/kg bw	x	max TOS/L liquid	=	Exposure estimate from liquids
Combined exposure from intake of solid food and liquids				Total exposure estimate

RULE ON REFINEMENT (EFSA, 2011)

When screening methods cannot rule out a safety concern, more refined methods should be applied

REQUIREMENT OF REFINEMENT STEPS

- Based on the Margin of Exposure (MOE) and associated risk characterisation

MOE = NOAEL/total combined exposure

- MOE not of concern: assessment complete
- MOE of concern: refinement required

REFINEMENT METHODOLOGY

- Based on EFSA recommendation real food consumption data should be used in Tier 2
- Available sources for European food consumption data:
  - Data from 27 surveys from 14 MS (2011-2014)
  - Comprehensive Database summary statistics[1]
  - FAIM Template[2]
  - Full Comprehensive Database based on individual food consumption

1 http://www.efsa.europa.eu/en/food-consumption/comprehensive-database
2 http://www.efsa.europa.eu/en/applications/foodingredients/regulationsandguidance

PROPOSED TIER 2A

- Combination of actual food consumption data with proposed use levels of Food Enzymes

- Requires compatibility of input data (possible at different levels)

Exposure = consumption x concentration

  - Consumption data provided based on a 4-level food categorisation system using FoodEx1 classification system
  - Concentration data has to be matched to food data available in the database
  - Matching is possible at different levels of detail, and executed as required

PROPOSED TIER 2A

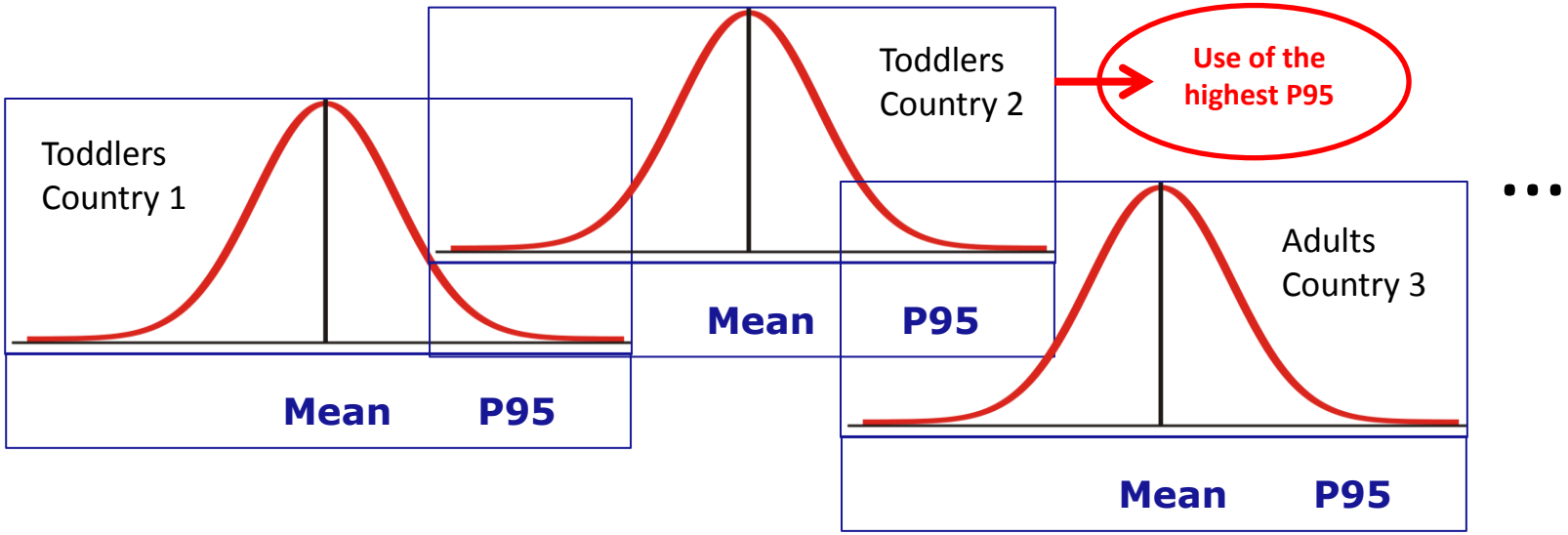
- If Food Enzyme concentration data can be matched to food group(s), exposure distributions can be calculated for each survey and each individual in the comprehensive database
- Average and above average exposure (e.g. P95) values are typically calculated
- Evaluation based on highest P95 across all surveys = 95% of the European population is protected
- When using summary statistics, P95 cannot be calculated, but only approximated

PROPOSED TIER 2A

Total intake of survey period / Number of days in survey period = Average daily intake		X food enzyme concentration
Total intake of survey period / Number of days in survey period = Average daily intake		X food enzyme concentration
Total intake of survey period / Number of days in survey period = Average daily intake		X food enzyme concentration
Total intake of survey period / Number of days in survey period = Average daily intake		X food enzyme concentration

For each individual in the entire database and for each matched foodgroup or food category as required

EXPOSURE DISTRIBUTION



For each survey and population group in the Comprehensive Database

PROPOSED TIER 2A

- Level of matching to food group determined
  - Level of matching driven by level of refinement required
  - Based on format of Food Enzyme concentration data (substrate or food based)
  - Based on information on the type of final food in which Food Enzyme component is expected to be present
  - Based on suitable recipe data, e.g.
    - Varying flour content in bread, bakery ware, noodles, etc.
    - Sugar syrup content in sweets, soft drinks, etc.

REFINEMENT OF EXPOSURE ASSESSMENT UNDER TIER 2

Level 1		Level 2		Level 3	
Consumption	Concentration	Consumption	Concentration	Consumption	Concentration
Cereals and Cereal Based Products	x highest concentration	Bread and rolls	x relevant concentration	Bread	x relevant concentration
				Rolls	x relevant concentration
		Breakfast cereals	x relevant concentration	Muesli	x relevant concentration
				Extruded cereals	x relevant concentration
		Fine bakery wares	x relevant concentration	Cakes	x relevant concentration
				Biscuits	x relevant concentration
		Pasta	x relevant concentration	Noodles	x relevant concentration
				Pasta	x relevant concentration

Concentration in unit TOS per final food
Example only, list not exhaustive

PROPOSED TIER 2B

- When input data are not compatible

Exposure = consumption x concentration

- Absence of information to facilitate matching food consumption data with food enzyme concentration data

- Different approach from Tier 2A proposed

PROPOSED TIER 2B

- Use of a Budget Method type approach
- Incorporation of factors to better estimate proportion of food that potentially contains the Food Enzyme
  - Use of Comprehensive Database to approximate proportion of processed foods
  - Use of technical/scientific literature
  - Information provided by food industry

TIER 1

Budget method[1,2]

MoE sufficient[4]

No safety concern under proposed conditions of use and use levels

MoE not sufficient[4]

TIER 2

Info on occurrence in food/beverages available

yes

2a

EFSA Comprehensive Food Consumption Database[2]

no

2b

Budget method with specific factors[2,3]

MoE sufficient[4]

No safety concern under proposed conditions of use and use levels

MoE not sufficient[4]

Safety cannot be established at the proposed use and use levels

1) In tier 1: without the factors mentioned in section 3b) and 3c).
2) In tier 1 and 2: including conversion factors as appropriate.
3) Specific factors see in Section 3.
4) A generally accepted value for the Margin of Exposure (MoE) cannot be established as each safety assessment is performed on a case-by-case basis requiring expert judgement of the entire toxicological database and information related to the intrinsic properties of a specific food enzyme, no generally acceptable value can be established for MoE. As a first indication, a MoE of 300 (factor 10 for inter-species difference, factor 10 for intra-species difference and factor 3 for the extrapolation from short-term studies to chronic studies, EFSA Scientific Committee, 2012) may be regarded as sufficient provided the data are complete and the quality of the data is acceptable.

MoE – Margin of Exposure

Thank you !