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Dietary Exposure Assessment of Food Enzymes

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European Food Safety Authority

Overview

- History
- Food Enzyme Exposure Assessment Approach
- Input Parameters
- Intake Model Overview
- FEIM tool
- Developments

Statement on Exposure assessment of food enzymes (2016)

- General food law requires an independent scientific assessment of risk to human health prior to authorising the placing on the market of certain substances to be used in food.
- Regulation (EC) No 1331/2001 provides for a common assessment and authorisation procedure for food enzymes, including a risk assessment carried by EFSA.
- 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 EFSA.
- However, the originally recommended methodology for exposure assessment was deemed unsuitable and resulted in a change of approach.
- A scientific **statement** which had been subject to **public and stakeholder consultation**, was **published** on the EFSA website.
- The scientific statement is accompanied by an **Appendix B**, which is subject to periodic updates and which tracks progress made.
- It was agreed to develop process specific exposure tools ("FEIM") based on actual food consumption data

References: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2016.4581; https://www.efsa.europa.eu/en/applications/foodingredients/tools

Food Enzyme Risk Assessment scheme

Production organism
- Taxonomy & intrinsic safety concern
- Genetic modification & introduced elements

Manufacturing process
- Raw materials, fermentation/extraction, purification, concentration, etc.

Food enzyme specification
- Biochemical composition (TOS)
- Chemical reaction, pH and Temp, stability, etc.
- Purity
- Suitability of the tox batch

Toxicological tests
- *In vitro* bacterial reverse mutation test
- *In vitro* mammalian chromosomal aberration test
- Repeated dose 90-day oral toxicity study in rodents

Intended conditions of use
- Food processes harmonisation with EC doc
- Transfer and removal of FE-TOS in foods

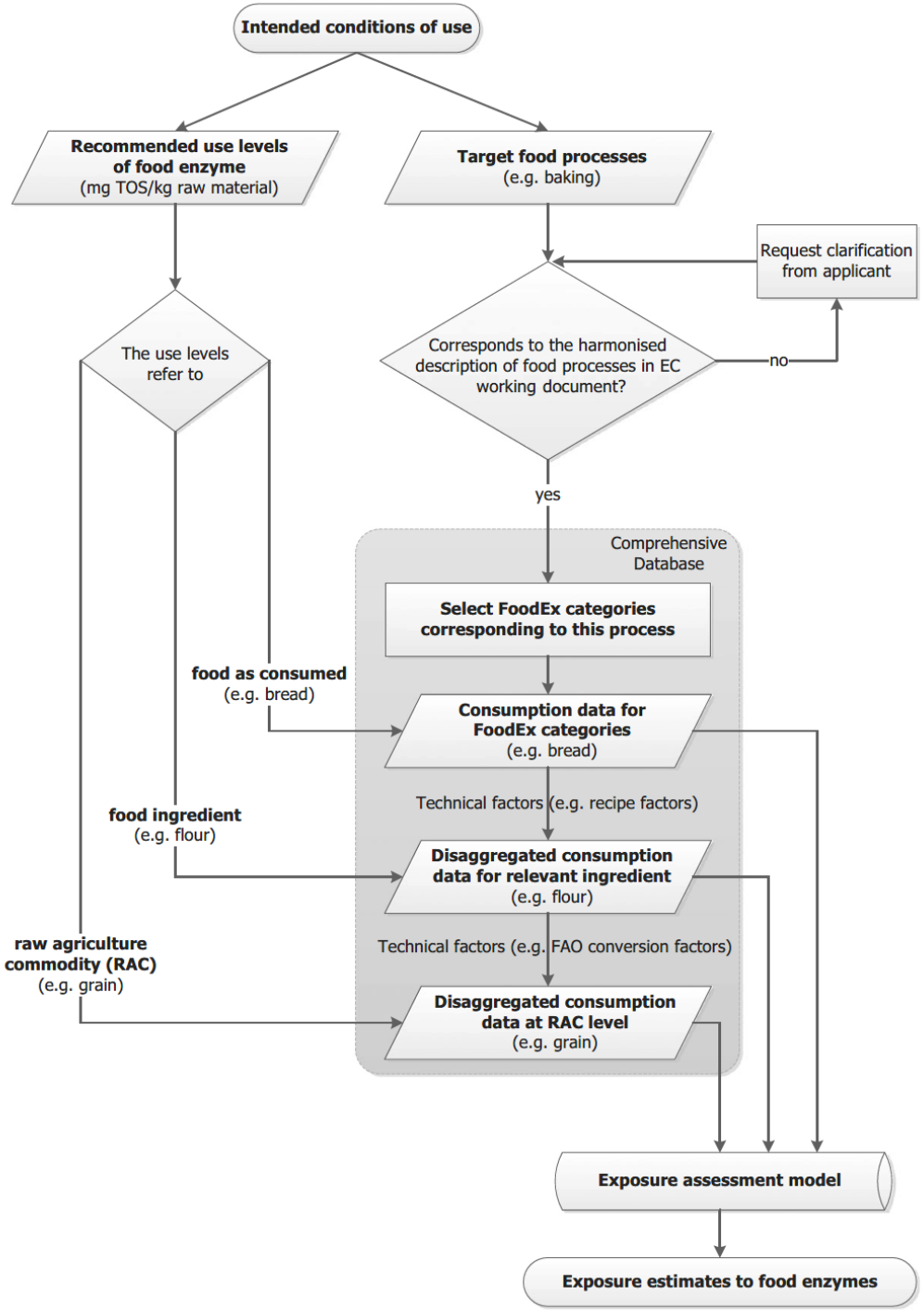
Dietary exposure
- Is calculation needed?
- If yes, use maximum use level for all dossiers

MoE

EFSA safety conclusion
Any toxicological concern to use the FE under the intended conditions of use?

Allergenicity
- The enzyme itself
- Compounds from the source organism
- Compounds from the manufacturing process

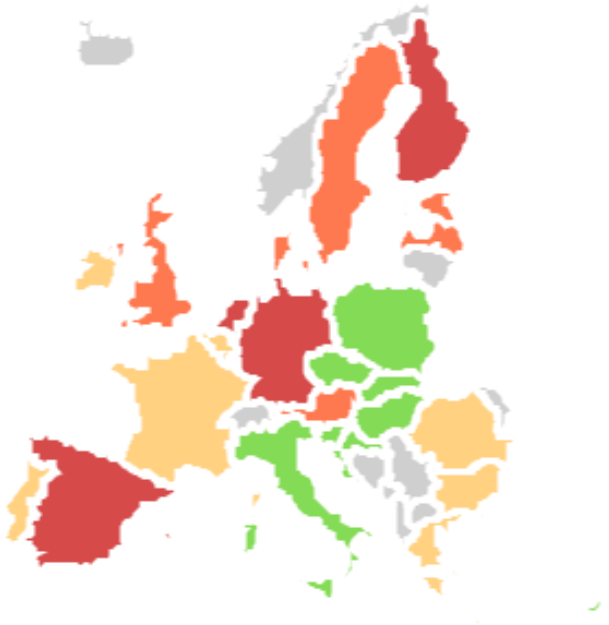
Food Enzyme Exposure Asssessment Approach



Input parameters

- Intended use/use level
- EFSA Comprehensive Consumption database
- EC working document - description of food processes in which food enzymes are intended to be used
- Process specific FoodEx food categories
- Technical factors

COMPREHENSIVE CONSUMPTION DATABASE



- Covering most European countries (n=25) and different age/population groups
- Data reliability increased by harmonised data collection methods in recent years
- EFSA uses the FoodEx food classification system to categorise foods and beverages included in the database

Population Group	Infants	Toddlers	Other children	Adolescents	Adults	Elderly	Very elderly	Lactating women	Pregnant women
Number of surveys (n=60)	11	18	29	27	35	23	19	2	2

An example of "intended uses" from dossiers

From food process to food category - not an easy task

- In total 99 different descriptions

"Indicative food uses" and/or	"Process" description in dossiers
• Baking • Baking and other cereal based processes • Production of bakery products • Production of bakery products and other cereal based products (e.g. pasta, noodles, snacks) • Cereal based processes • Cereal processing • Production of beer • Production of beer and other cereal based processes • Beverage processes • Beverage processing • Beverage alcohol processes • Production of cereal based distilled alcoholic beverages • Production of cereal based distilled alcoholic beverages (cider production)	Solid • Baking processes and other cereal based processes ? Liquid • Brewing processes and other cereal based beverage processes • Processing for grain alcohol • Potable alcohol production • Beverage alcohol (distilling) processes

Harmonisation: "intended uses" for authorisation

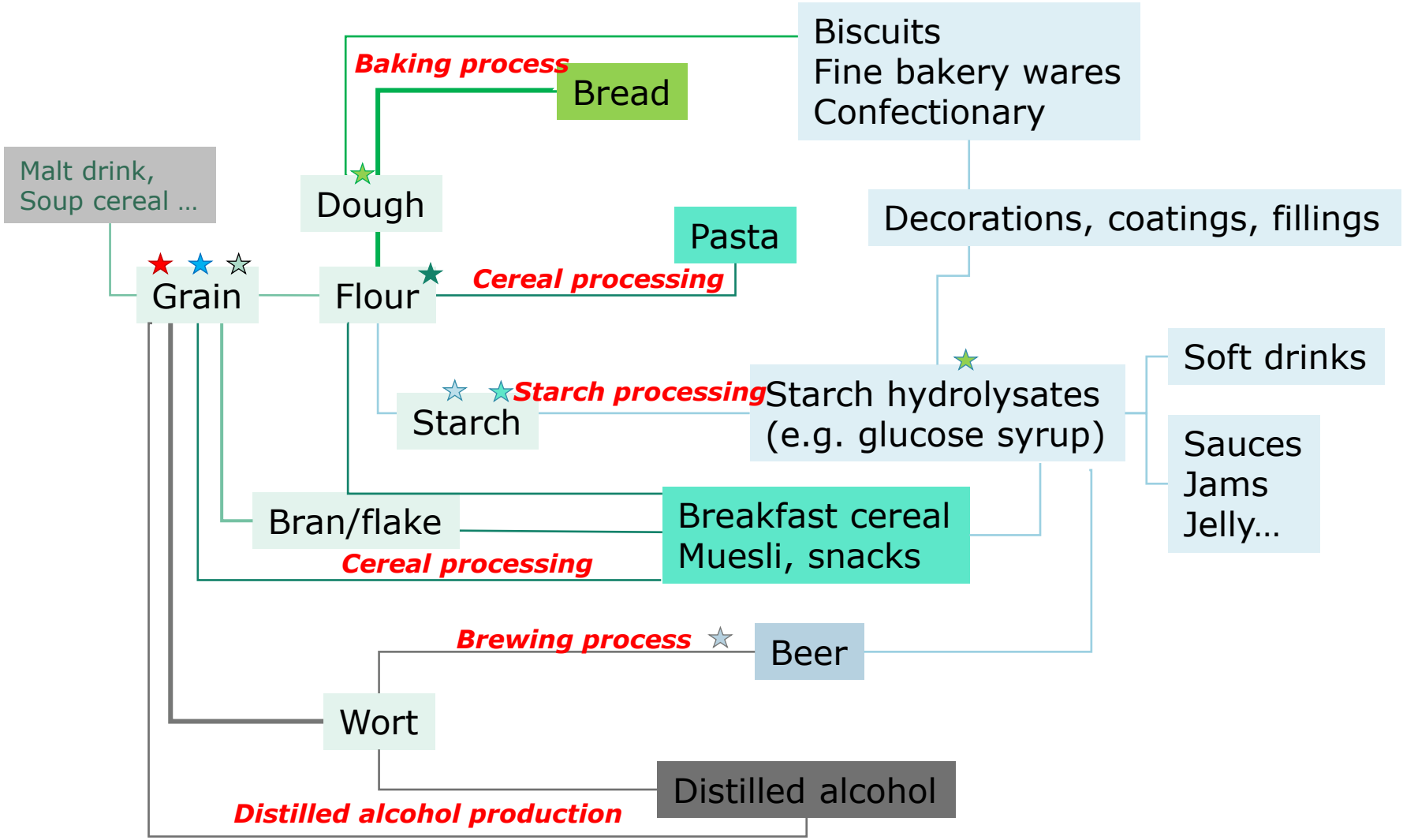
EC working document to harmonise description of food processes in which food enzymes are intended to be used

1. Baking processes
2. Brewing processes
3. Cereal-based processes
4. Coffee processing
5. Confectionery processing
6. Dairy processing
7. Distilled alcohol production
8. Egg processing
9. Fats and oils processing
10. Flavouring production
11. Fruit and vegetable processing
12. Grain treatment and starch processing
13. Protein processing
14. Savoury snacks processing
15. Sugar processing
16. Tea processing as well as Herbal and fruit infusions processing
17. Wine production
18. Yeast processing

A very useful document!

Does it cover all uses described in received dossiers?

An Example of Food Enzymes - Food Processes – Food Categories



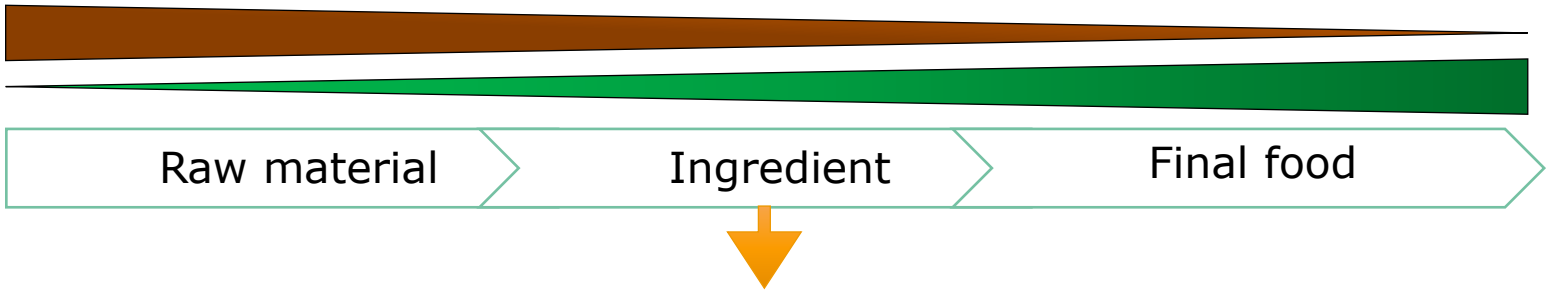
Simplified scheme

stars indicating food enzymes

Food enzyme exposure assessment – technical factors

Enzyme use level
[Applicant's dossier]

Food consumption data
[EFSA Comprehensive Database]



- Data conversion (recipes, ingredient fractions, technical factors (e.g. concentration, dilution, yield), conversion from processed to raw, etc.)
- Various sources (e.g. FAO, RPC, open sources) – subject to feedback mechanism via open call

TOS per final food x consumption of final food

TOS per ingredient x consumption of ingredient

TOS per raw material x consumption of raw material

Simplified concept

An Example of Dietary Exposure Estimation

Food enzyme for baking processes

FoodEx code	FoodEx category	FAO conversion factor from FoodEx food group to raw material[(a)]	Recipe fraction	mg TOS/kg flour
A.01.04	Bread and rolls (unspecified)	1	0.7	20
A.01.04.001	Wheat bread and rolls	1	0.7	20
A.01.04.005.007	Pita bread	1	0.7	20
A.01.07.001.004	Cheese cream cake	1	0.24	20
A.01.07.001.016	Croquembouche	1	0.25	20
A.01.07.001.019	Flan	1	0.5	20
A.01.07.001.020	Fruit cake	1	0.6	20
A.01.07.001.029	Profiterole	1	0.15	20
A.01.07.001.048	Baklava	1	0.15	20
A.01.07.002	Biscuits (cookies)	1	0.9	20

PROCESS SPECIFIC FOOD CATEGORIES

- Process specific Foodex food categories are selected from the Comprehensive Database
- Selection is influenced by:
  - Material to which FE is added
  - Specific process
  - Information provided by applicant
  - Ingredient search on Mintel Database
  - RPC (raw product commodity) database search
  - Other open sources
- Subject to feedback mechanism via open call for stakeholders prior to finalisation of individual process evaluation and process specific tool

INFORMATION REQUIRED FROM STAKEHOLDERS

STAKEHOLDER ENGAGEMENT

STAKEHOLDER	METHOD	TOPICS
STAKEHOLDERS GENERAL	OPEN WEB CALL (EFSA WEBPAGE)	• Process specific FoodEx food categories • Inclusion and/or exclusion of categories • FoodEx category-specific technical factors • Technical factors
	WORKSHOPS	• All topics
INDIVIDUAL APPLICANTS	DIRECT	• Clarification on intended use • Clarification on raw material • Clarification on use level • Transfer of food enzyme residue in food
AMFEP	DIRECT	• Absence of transfer of FE into food (<LOD)

Exposure model

Exposure = consumption x concentration

Chronic (average) exposure calculated for each individual person

- Each individual survey
- Provides a distributional population exposure for each survey
- Statistical parameters summarised as as range (minimum – maximum) for each population class over all surveys
  - Mean intake
  - 95th percentile intake
- Evaluation based on highest P95 across all surveys = 95% of the European population is protected

Exposure model

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

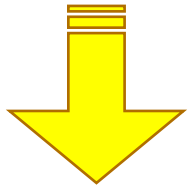
X food enzyme concentration

Total intake of survey period / Number of days in survey period = Average daily intake

X food enzyme concentration

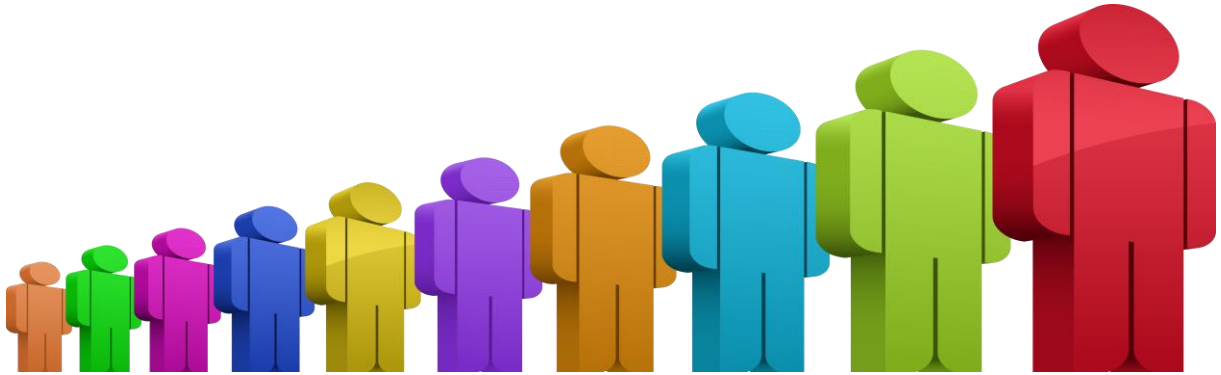
Total intake of survey period / Number of days in survey period = Average daily intake

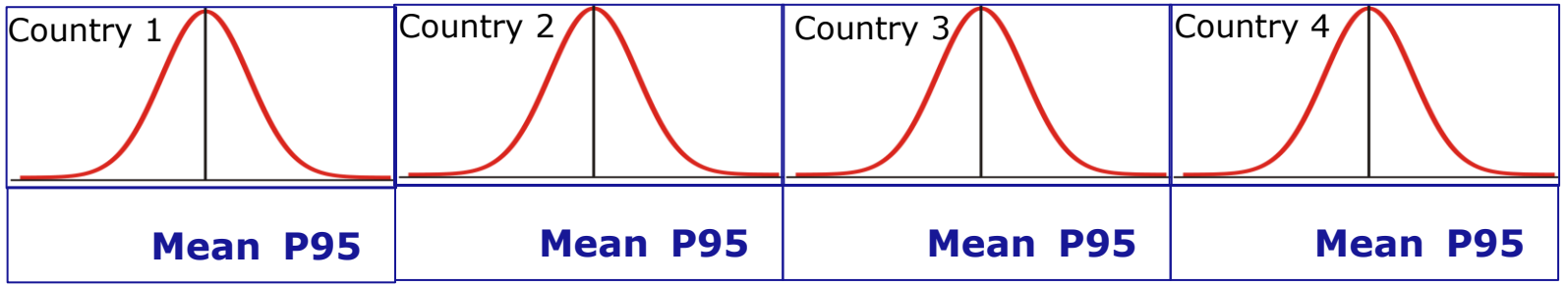
X food enzyme concentration



For each individual in the entire database

Exposure distribution





EXAMPLE TODDLERS (exposure in mg/kg bw/d)		
	Mean	P95
Country 1	0.5	4.0
Country 2	1.0	3.5
Country 3	2.0	3.0
Country 4	2.5	7.0

Mean	0.5 - 2.5
P95	3.0 **- 7.0**

An Example of Reporting Dietary Exposure Estimates

Table: Summary of estimated dietary exposure to the food enzyme–TOS in six population groups

	Estimated exposure (mg/kg body weight per day)					
Population group	**Infants**	**Toddlers**	**Children**	**Adolescents**	**Adults**	**The elderly**
Age range	3–11 months	12–35 months	3–9 years	10–17 years	18–64 years	≥65 years
Min–max mean (number of surveys)	0.001–0.003 (10)	0.003–0.006 (14)	0.003–0.006 (19)	0.002–0.004 (18)	0.001–0.002 (19)	0.001–0.002 (18)
Min–max 95th percentile (number of surveys)	0.002–0.012 (8)	0.006–0.010 (12)	0.005–0.011 (19)	0.003–0.008 (17)	0.002–0.005 (19)	0.002–0.004 (18)

The highest value is used to calculate the MoE, which in the opinion is reported as "*MoE of **at least** xxx*".

Developments - Overview

- Several processes finalised and details published in *Annex B* *(https://efsa.onlinelibrary.wiley.com/action/downloadSupplement?doi=10.2903%2Fj.efsa.2016.4581&file=efs24581-sup-0001-Annex_B.pdf)*
  - For some processes, calculation is not needed.
  - For others, FoodEx categories and technical factors are published.

- Single process intake calculators – open access
  - *FEIM – baking* *(https://zenodo.org/record/1297333#.XPZ30WxYZaQ)*
  - *FEIM – brewing* *(https://zenodo.org/record/1299219#.XPZ30mxYZaQ)*
  - *FEIM – cereal based processing* *(expected upload in Autumn 2019)*

Developments

Call-for-data has been completed, dossier assessment on-going

Intended food processes	Call-for-data	Nr of dossiers	Adopted opinions	Calculator
Baking processes	completed	71	42*	
Brewing processes				
Distilled alcohol production				n/a
Starch processing for glucose syrup production				n/a
Cereal-based processes		15	3	( )
Savoury snacks processing			0	( )
Grain treatment for flour/starch/gluten/fibre production			0	( )
Fats and oils processing for degumming		18	1	n/a
Fats and oils processing for interesterification			0	n/a
Sugar production and processing			0	n/a
Protein components for infant and follow-on formulae		6	0	( )

*corresponding to 45 question numbers

Developments

Call-for-data on-going or under preparation, dossier assessment is starting

Intended food processes	Call-for-data	Nr of dossiers	Calculator
Coffee processing for demucilage*	2019	10	(n/a) - tbc
Coffee processing*	2019		( )
Wine production*	2019	32	( )
Fruit and vegetable processing	2019		( )
Milk processing	2019	39	tbd
Dairy processing	2019		tbd

*Deadline: 18.09.2019
https://www.efsa.europa.eu/en/consultations/call/190617

Developments

Call-for-data still to be prepared, dossier assessment not yet started.

Intended food processes	Call-for-data	Nr of dossiers	Calculator
Tea processing as well as herbal and fruit infusion processing	2020	7	tbd
Egg processing	2020	17	tbd
Protein processing	2020	ca.80	tbd
Flavouring production	2020		tbd
Yeast processing	2020		tbd
Processes not covered in the EC working document	2020		