Overview presentation

1. EU Agency Ecosystem
2. Roots of EFSA
3. Scientific advice: building blocks
4. Common framework: additives, enzymes, flavourings
5. Food additives:
   - new and
   - existing
6. Food enzymes: all new
   - GMO
   - exposure assessment
7. Flavourings: previously established process
8. Discussion and Conclusions
Overview, not presented today

- Sources of vitamins, minerals and other substances added for nutritional purposes
- Nutrient sources falling under novel food (Reg. 258/97)
- Other substances intentionally added (e.g. botanicals)
- Processing aids (no specific legislation),
- Food contact materials and
- Recycling of plastics and active and/or intelligent packagings
1. CEDEFOP – European Centre Development Vocational Training (Thessaloniki, GR)
2. ECDC – European Centre for Disease Prevention and Control (Stockholm, SE)
3. ECHA – European Chemicals Agency (Helsinki, FI)
4. EEA – European Environment Agency (Copenhagen, DK)
5. EIGE - European Institute for Gender Equality (Vilnius, LT)
6. EFSA – European Food Safety Authority (Parma, IT)
7. EMA – European Medicines Agency (London, UK)
EU ANSA Members

8. **EMCDDA** – European Monitoring Centre for Drugs and Drug Addiction (Lisbon, PT)

9. **ENISA** – European Network and Information Security Agency (Heraklion, GR)

10. **EU-OSHA** – EU Agency for Safety and Health at Work (Bilbao, ES)

11. **EUROFOUND** – European Foundation for the Improvement of Living and Working Conditions (Dublin, IE)

12. **FRA** – Fundamental Rights Agency (Vienna, AT)

13. **FRONTEX** – European Agency for the Management of Operational Cooperation at the External Borders (Warsaw, PL)
Re-casting of EU food safety system and policy

- Food scares (e.g. BSE, dioxins)
- Loss of consumer confidence
- Loss of confidence in EU food trade
- Damaged trust in public authorities
- Creation of national food agencies

EFSA as independent source of scientific advice and communication

Committed since 2002 to ensuring that Europe’s food is safe
The Focus: on **Food Safety**, but wide i.e.

- **Whole Food Chain**, and
- via plants, feed, animals and food
- **linked to the Environment**

also, but less, on Efficacy

The Challenge: become recognised as **Authority** in Europe and internationally

i.e. **gain trust**
Expertise:
Spread over 10 Scientific Panels

- Plant Health
- Plant Protection
- Genetically modified organisms
- Animal feed
- Animal health and welfare and their diseases
- Biological food chain hazards
- Food chain contaminants
- Food additives, flavourings and processing aids
- Dietary, nutritional and novel food
- Food packaging
How do you make a good scientific evaluation?

*It is like preparing a ‘good’ meal…*

- Mandate - *What dish does the customer request?*
- Information – *What are the ingredients to be used?*
- Quality expertise – *Who are good cooks?*
- Methods – *What is the ‘best’ recipe?*
- Output – *How do you serve it?*
• Regulatory dossier:
  ✓ defined in sectorial legislation
  ✓ EFSA consultation

• Types of information requirements for the sponsor to provide is part of the legislation, incl.
  ✓ areas of safety to be covered
  ✓ quality standards
  ✓ possible inclusion of published studies
Methods: Classical Risk Assessment Paradigm

- **Risk** = **Seriousness** × **Vulnerability** × **Scale**

- **Seriousness**: How *severely* affected?
  - Hazard Identification: nature of the effects
  - Hazard Characterisation: Dose-Response estimation

- **Vulnerability**: How *likely* to be affected?
  - Exposure Assessment,

- **Scale**: breakdown of exposure by age, gender, etc.

Food Safety Model: no Risk
Classical single hazard approach

Evaluation of one single chemical compound

Single hazard

Various potential risks

- Risk 1
- Risk 2
- Risk 3
Methods: Deliberately Introduced New Micro-organisms or Chemicals

• Hazard Identification and Characterisation:
  - GLP studies in lab animals, conducted by Sponsor
  - Extrapolation to man using Safety Factors

• Exposure Assessment:
  - Based on use assumptions, defined in the assessment
  - Reliable food (and feed) consumption data
• **Hazard Identification and Characterisation:**
  - Peer-reviewed experimental and observational studies from a variety of sources
  - With or without GLP studies from sponsor

• **Exposure:**
  - Based on existing ‘monitoring’ programmes
  - Reliable food (and feed) consumption (and composition) data
Methods: Import Risk Assessment  
Plant & Animal Health

• Define:
  - Pest(s)
  - Affected areas and pathways

• Assessment of probability of EU:
  - Entry
  - Establishment
  - Spread

• Assessment of potential consequences

• Uncertainty and sensitivity analysis

• Risk management options

Example of Plant Pest Import Risk Assessment

Regulation (EC) No 1331/2008 &
Implementing Reg. (EU) No 234/2011

- Establishing common authorisation procedure
- Roles of EFSA and the Commission
- Procedural arrangements: submission of dossier
- Timelines: 9-months, stop-the-clock
- Data requirements for each area
PROCEDURAL ASPECTS

Regulation (EC) 1331/2008

Dossier:
- New FA
- Extension of use
- Changes to specs/manufacturing

EFSA ANS Panel
- Request for additional info
- Technical hearings

Mandate + dossier

European Commission

Applicant
Definition:

Any substance not normally consumed as a food in itself and not normally used as a characteristic ingredient of food, whether or not it has nutritive value,

the intentional addition of which to food for a technological purpose in the manufacture, processing, preparation, treatment, packaging, transport or storage of such food

results, or may be reasonably expected to result, in it or its by-products becoming directly or indirectly a component of such foods
Regulation (EC) No 1333/2008 on food additives

- General and specific conditions of use
- Annex II: additives in food
- Annex III: additives in additives, enzymes, flavourings and nutrients

EFSA Scientific Opinion for Data Requirements, 2009

Regulation (EU) No 231/2012 laying down specifications on food additives:

- Definitions
- Purity criteria
MAIN SECTIONS OF THE DOSSIER

- Manufacturing, Specifications, Stability
- Testing strategy and rationale for studies
- Toxicological studies
  - toxicokinetics
  - subchronic and chronic
  - genotox and carcinogenicity
  - repro and developmental tox
- Proposed uses & Exposure assessment
- Current authorisations & evaluations
- Supplementary information
- ANNEXES
ANS PANEL STANDING WORKING GROUPS (SWG)

- **SWG on Applications** with expertise in
  - chemistry and food technology,
  - kinetics,
  - genotoxicity, general and reproductive toxicology,
  - exposure assessment and
  - risk assessment

- **SWG on Exposure Assessment** with expertise in exposure assessment
HAZARD CHARACTERISATION: TIERED APPROACH

Tier 1
- Absorption
- Genotoxicity in vitro
- Extended 90-day toxicity study

Tier 2
- ADME: single dose
- Genotoxicity in vivo
- Chronic toxicity
- Carcinogenicity
- EOGRTS
- Prenatal developmental toxicity

Tier 3
- ADME: repeated dose, volunteer studies
- Carcinogenicity: Mode of Action
- Reproductive and Developmental toxicity
- Specialised studies (immunotox, neurotox, endocrine act, mode of action)

Triggers for considering Tier 2
- Positive in vitro genotoxicity
- Systemic availability
- Toxicity in 90-day study

Triggers for considering Tier 3
- Chronic carcinogenicity
- Positive in vivo genotoxicity
- Bioaccumulation
- Repr and developmental
RISK CHARACTERISATION

The risk assessment scheme:

**HAZARD CHARACTERISATION**

**HAZARD IDENTIFICATION**

**RISK CHARACTERISATION**

**EXPOSURE ASSESSMENT**

Levels in food, dietary exposure, food consumption, relevant food groups, time trends

ADME, acute/sub-chronic/chronic toxicity, human data, genotox, reprotox, etc. Derivation of a health based guidance value (e.g. ADI, MOS)

Relate exposure to acceptable daily intake (ADI)
EXPOSURE ASSESSMENT: GENERAL METHODOLOGY

\[ \sum (\text{chemical concentration} \times \text{food consumption}) \]

\[ \text{body weight} \]

Chemical occurrence → Dietary Exposure Assessment → Food consumption
Regulation (EU) No 257/2010 re-evaluation programme

- Re-evaluation of all food additives that were permitted before 20.01.2009
- Deadlines and priorities
- Procedure (call for data)
## Priorities and deadlines

as in Annex II of Reg (EU) No 257/2010

<table>
<thead>
<tr>
<th>Approved Food Colours (prioritized by batches)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First batch</strong></td>
<td><strong>Apr 2010</strong></td>
</tr>
<tr>
<td><strong>Second batch</strong></td>
<td><strong>Dec 2010</strong></td>
</tr>
<tr>
<td><strong>Third batch</strong></td>
<td><strong>Dec 2015</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Approved food additives other than colours and sweeteners</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preservatives and antioxidants</strong></td>
<td><strong>Dec 2015</strong></td>
</tr>
<tr>
<td><strong>Emulsifiers, stabilisers, gelling agent</strong></td>
<td><strong>Dec 2016</strong></td>
</tr>
<tr>
<td><strong>Remaining FA other than colours and sweeteners</strong></td>
<td><strong>Dec 2018</strong></td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Approved sweeteners</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>All sweeteners</strong></td>
<td><strong>Dec 2020</strong></td>
</tr>
</tbody>
</table>

*Exception of aspartame (E951) re-evaluated on December 2013
ANS PANEL WORKLOAD

By 2020 all the additives should be (re-)evaluated

Period: 2013-2015

<table>
<thead>
<tr>
<th>Type of Evaluation</th>
<th>2015</th>
<th>2013-2014</th>
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</thead>
<tbody>
<tr>
<td>Food Additives Re-evaluation</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>Food Additives New evaluation</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Food additives Extension of use</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Food additives Changes to specs, manufacturing</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Nutrient Sources</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Other Panel’s assessment</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Other EFSA assessments</td>
<td>3</td>
<td>7</td>
</tr>
</tbody>
</table>

In 2016 a total of approximately 40 opinions should be adopted
RE-EVALUATION: PROCEDURAL ASPECTS

Interested parties

Calls for data:
- Biological and toxicological
- Exposure

EFSA ANS Panel

Previous evaluations: SCF, JECFA

European Commission

Single mandate covering ~ 300 food additives

Industry Associations

Researchers

Member States
Challenges re-evaluation programme

• No dossiers
  ➢ Highly variable response to EFSA’s public call for data
  ➢ Scientific information and data available highly variable in terms of quality and quantity

• Consequence: potential data gaps for many food additives

• ANS Panel: *Statement on conceptual framework for risk assessment of certain food additives re-evaluated under Comm. Regulation (EU) No 257/2010*
Food additives are grouped according to the main functional class

Organization of ANS Panel WGs:

- SWG on applications
- SWG on food colours
- SWG on gums and other subst. from natural sources
- SWG on substances other than gums and colours
- SWG on starches, celluloses and pectines
- SWG on nitrates and nitrites
- SWG on exposure
STEPS OF THE RE-EVALUATION PROGRAMME

Re-evaluation process workflow

1. Preparation of pre-evaluation of document
2. Public call for data
3. Revision within Working Group
4. Additional call for data (if needed)
5. Preparation of draft opinion
6. Revision of opinion at ANS Panel
7. Adoption of the opinion (and publication)

1.5 - 2 years
• The *regulatory maximum level exposure assessment* (based on the maximum permitted level, **MPL**)

• The *refined exposure assessment scenario* is based on information on **reported use levels** by industry and **analytical results** submitted to EFSA by Member States:
  
  ➢ the **brand-loyal consumer** scenario: assumes that a consumer is **exposed long-term at the maximum reported use levels for one food category**

  ➢ The **non-brand-loyal consumer** scenario: assumes that the population is exposed long-term at the **mean reported use levels** in all foods
DEFINITIONS (REG (EC) NO 1332/2008)

• ‘Food Enzyme’ means a product obtained from plants, animals or micro-organisms or products thereof: containing one or more enzymes capable of catalysing a specific biochemical reaction
  ➢ NOT only the catalytic active protein which is e.g. scientifically meant by the term enzyme
  ➢ BUT also by-products of the source material, manufacturing process

• ‘Food Enzyme preparation’ means a formulation consisting of one or more food enzymes in which substances such as food additives and/or other food ingredients are incorporated to facilitate their storage, sale, standardisation, dilution or dissolution.
• Reg. (EC) No 1332/2008 on food enzymes
• Implementing Reg. (EU) No 234/2011 (Data Req.!!)
• Reg. (EU) No 562/2012 with specifications on food enzymes: specific data requirements
• 2009 EFSA-CEF Guidance for dossier
• 2011 EFSA-GMO Guidance for GMOs
• 2011.7.8 Explanatory note (v1) on Dossier Submission
  ➢ 2014.4.7 Explanatory note (v2)
  ✓ 2014.5.14 1st Scientific Opinion
  ✓ 2014.7.25 2nd-4th Scientific Opinions
  ➢ 2014.11.14 Explanatory note (v3)
  ✓ 2015.2.18 5th Scientific Opinion
• 2015.3.11 Legal deadline for receipt applications
• 2016 Draft CEF Panel Statement on dietary exposure
  ➢ 2016.2.3 EFSA Info session
  ➢ 2016.2.16-3.31 Public consultation
  ➢ Revision, work on-going
• 2016 Draft EC document on food processes
MAIN SECTIONS DOSSIER AND SCIENTIFIC OPINION

- Specifications and properties
- Source materials: animal, plant, basidiomy, micro-org.
- Manufacturing process, incl. purification
- Reaction and fate in foods
- Toxicological studies
  - Subchronic toxicity
  - Genotoxicity: two in vitro tests
  - Rationale for exceptions:
    - history of safe use,
    - QPS micro-organism,
    - Micro-organism already tested
  - Allergenicity: sequence homologies and/or structural similarities with known allergens (GMO, 2011)
- Needs and use conditions (proposed dosage)
- Dietary exposure
- Current authorisations and evaluations
<table>
<thead>
<tr>
<th>Total FE applications</th>
<th>Genetically Modified Microorganisms (GMM) source</th>
<th>Non-GMM source</th>
<th>Animal/plant source</th>
</tr>
</thead>
<tbody>
<tr>
<td>303=264 microbial source 38 non-microbial source</td>
<td>127 (42%)</td>
<td>137</td>
<td>38</td>
</tr>
</tbody>
</table>

Data requirements: GMM SOURCES

- Characteristic of the parental and the recipient organisms
- Characteristic of the donor organisms of vector(s), gene(s) and other sequences used in the genetic modification process
- Description of the genetic modification process
  - Safety aspects of the genetic modification
  - Safety for the environment
• **SWG on Enzymes** with expertise in
  - food technology, chemistry and biotechnology,
  - general & sub-chronic toxicity and genotoxicity,
  - exposure assessment and
  - genetically modified organisms

**HAZARD CHARACTERISATION**

• In principle also a tiered approach
An example of Food Enzymes - Food Processes – Food Categories

Simplified scheme showing main steps only

- **Grain**
  - Malt drink, Soup cereal ...
  - **Flour**
    - **Baking process**
      - Bread
    - **Cereal process**
      - Starch
      - Starch process
      - Starch hydrolysates (e.g. glucose syrup)
      - Breakfast cereal
      - Muesli, snacks
  - **Bran/flake**
    - Cereal process
  - Wort
    - Brewing process
    - Distilled alcohol
  - **Wort**
    - **Brewing process**
      - Beer
    - **Cereal-based distilled alcohol**
  - **Beer**
  - **Sausages**
    - Jams
    - Jelly...
  - **Soft drinks**
  - **Biscuits**
    - Fine bakery wares
    - Confectionary
  - **Decorations, coatings, fillings**

☆ = addition of food enzyme
CHALLENGES FOR EXPOSURE ASSESSMENT

• ‘Budget method’ = overall conservative
  
  ➢ food intake estimates; conservative for adults but not for toddlers
  ➢ standard factors for additive use in processed foods

• Enzymes not linked to a food, but rather to a process

• Exposure Assessment Refinement
  
  ➢ Tier 1. Initial step – Budget method
  ➢ Tier 2a. Data on enzyme occurrence in food
  ➢ Tier 2b. Refined budget method based on:
    ✓ data from use in processing and
    ✓ proportion of these ingredients in the food consumed
COMBINATION OF RAW MATERIAL VALUES WITH FOOD CONSUMPTION DATA

- Cellulase
- β-glucanase
- Xylanase
- α&β-amylase
- Amyloglucosidase

**Barley**

Mashing, etc

FEs are denatured during the mashing step when temp is above 80°C

**Wort**

β-glucanase

α&β-amylase

Storage tank

Filtration, pasteurisation

Distilled alcohol production

Filtration removes impurity (protein precipitates, depending on pore sizes even salts) from final products

**Distillation**

Further inactivation of FEs when the temp is close to 100°C

**Brewing process**

Filtration

β-glucanase

α-acetolactate decarboxylase

Boil

Fermentation

Storage tank

Source of concentration data
- Raw material

Source of consumption data
- Foods as consumed
What makes people ill?

Evaluation of various ‘risk factors’

- Chemicals
- Micro-organisms
- Processing methods

Emerging risk

Increased disease incidence
QUESTIONS?