EU Framework for the Scientific Assessment of Food Additives and Enzymes

Hubert Deluyker
Scientific Adviser to **EFSA** Director

past-Chair, **EU ANSA**


Assuralia
Huis der Verzekering
Maison de l'Assurance
European Society of Cardiology

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

EU Agencies – WORKING FOR YOU

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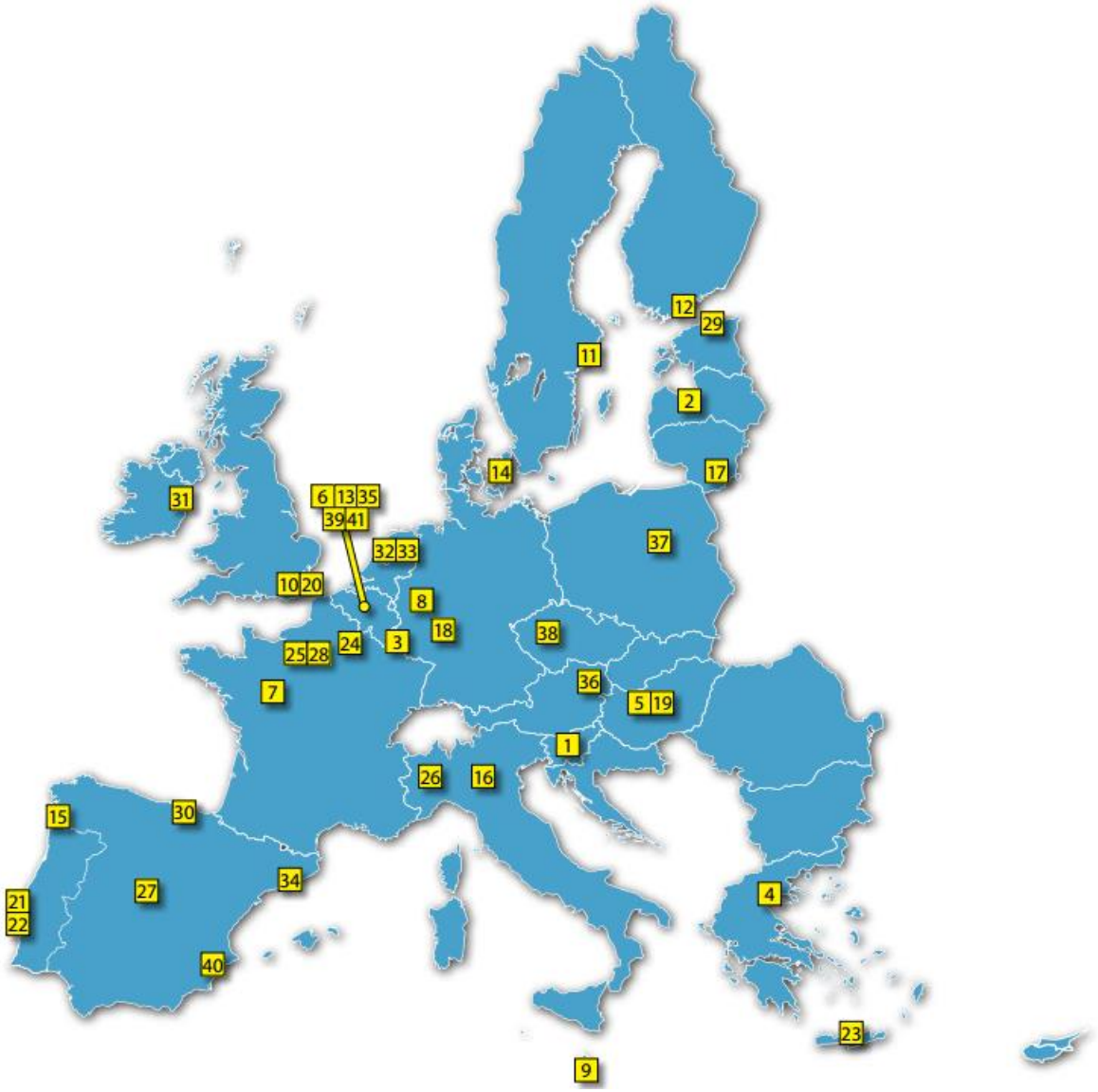
European Food Safety Authority



EU ANSA Members

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

As European veterinary experts met yesterday to discuss easing the ban on British beef, the Consumers' Association issued a report claiming the Government had failed to put consumers first in the BSE crisis. Have people been misled? Today, CHRIS ELLIOTT reports on how a Mid-Anglian scientist is attempting to put the crisis in perspective — by launching a crusade to banish misinformation about it.

Public just want truth about BSE says expert

EFSA as independent source of scientific advice and communication

EFSA Mandate

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

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Plant Health

Plant Protection

Genetically modified organisms

Biological food chain hazards

Animal health and welfare and their diseases

Animal feed

Food chain contaminants

Food additives Flavourings and Procesing 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?*

DATA: INFORMATION SUBMISSION TO EFSA

- **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** x **Vulnerability** x **Scale**

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

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

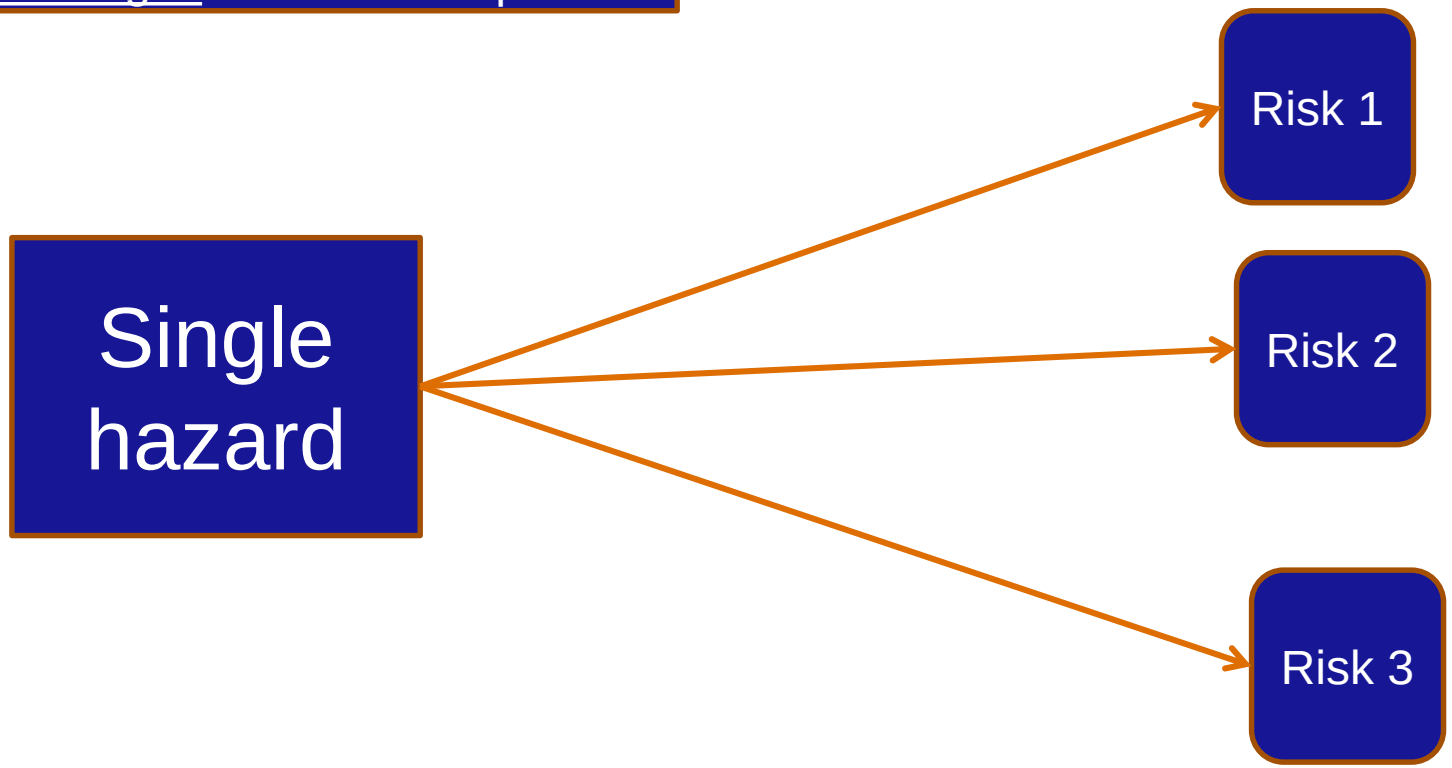
- **Scale:** breakdown of exposure by age, gender, etc.

Food Safety Model: no Risk

Classical single hazard approach

Evaluation of
one single chemical compound

Various potential risks



Methods: Deliberately Introduced *New* Micro-organisms or Chemicals

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- **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

Methods: Micro-organism or Chemical *Potentially Already Present*

- **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

http://www.efsa.europa.eu/en/efsajournal/pub/3128.htm

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

Applicant

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

European Commission

Mandate + dossier

EFSA
ANS Panel

- **Request for additional info**
- **Technical hearings**

FOOD ADDITIVES - ANS PANEL

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

FOOD ADDITIVES - NEW

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

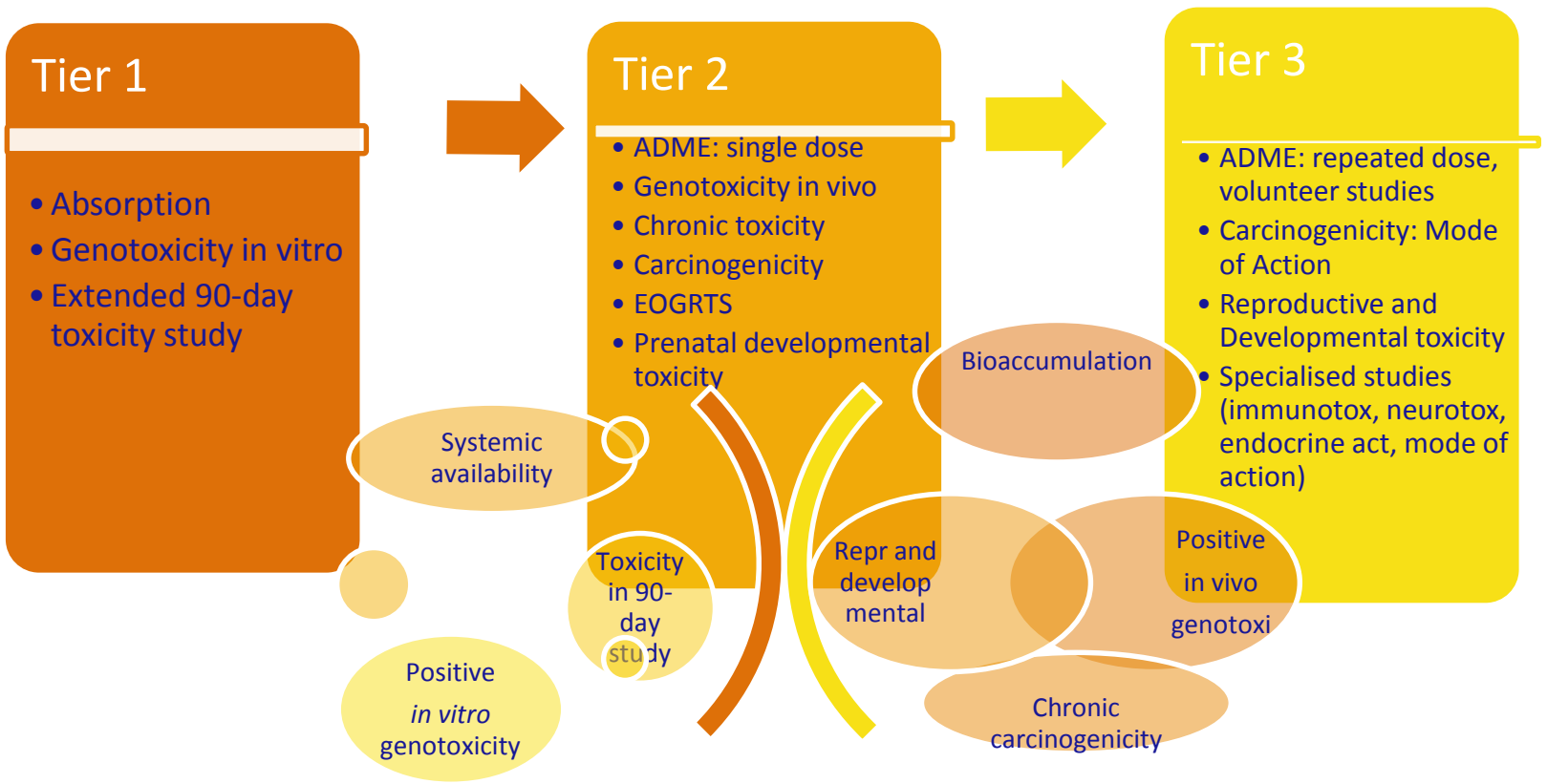
MAIN SECTIONS OF THE DOSSIER AND OF SCIENTIFIC OPINION

ANS PANEL STANDING WORKING GROUPS (SWG)

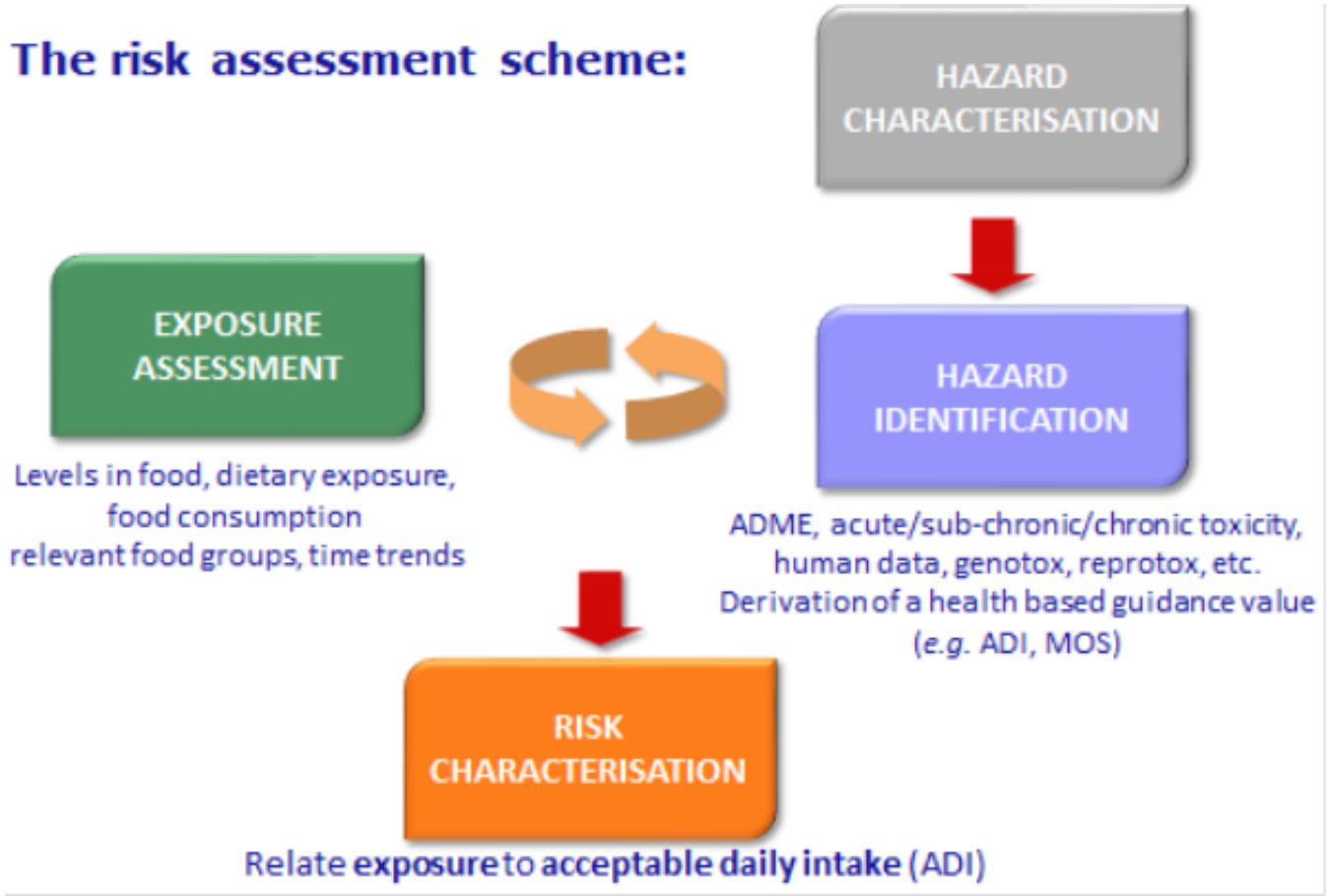
- **SWG on Applications** with expertise in
  - chemistry and food technology,
  - kinetics,
  - genotoxicity, general and reproductive toxicology,
  - exposure assessment and
  - risk assessment

- **SWG on Exposure Assessment** with expertise in exposure assessment

HAZARD CHARACTERISATION: TIERED APPROACH



RISK CHRACTERISATION



EXPOSURE ASSESSMENT: GENERAL METHODOLOGY

$$\frac{\sum(\text{chemical concentration} \times \text{food consumption})}{\text{body weight}}$$

Chemical occurrence → Dietary Exposure Assessment ← Food consumption

FOOD ADDITIVES – RE-EVALUATION

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)

Food additives re-evaluation programme

Priorities and deadlines

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

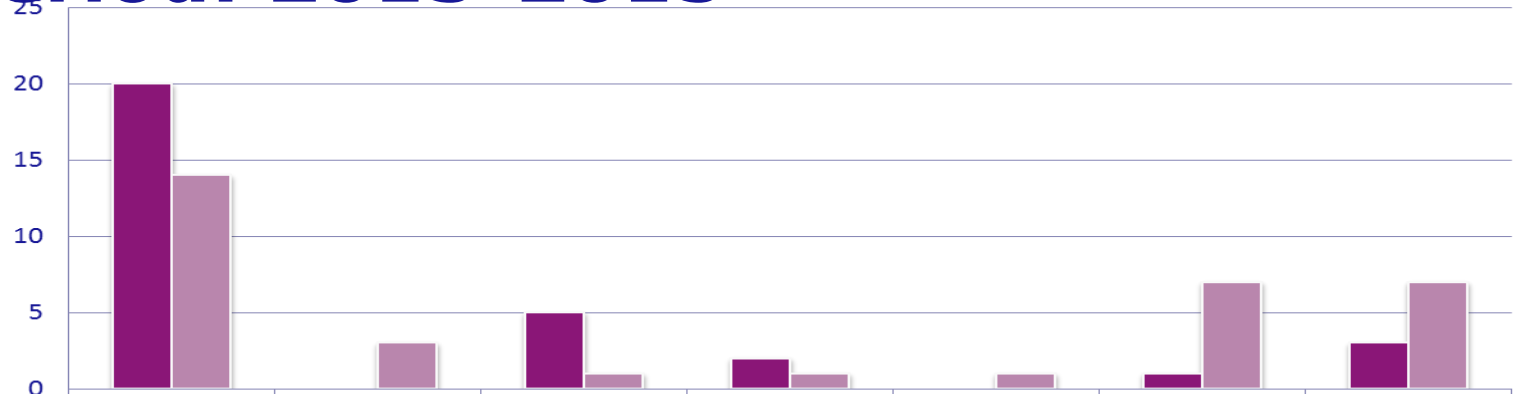
Approved Food Colours (prioritized by batches)	
First batch	*Apr 2010*
Second batch	*Dec 2010*
Third batch	*Dec 2015*
Approved food additives other than colours and sweeteners	
Preservatives and antioxidants	*Dec 2015*
Emulsifiers, stabilisers, gelling agent	*Dec 2016*
Remaining FA other than colours and sweeteners	*Dec 2018*
Approved sweeteners	
*All sweeteners**	*Dec 2020*

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

ANS PANEL WORKLOAD

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

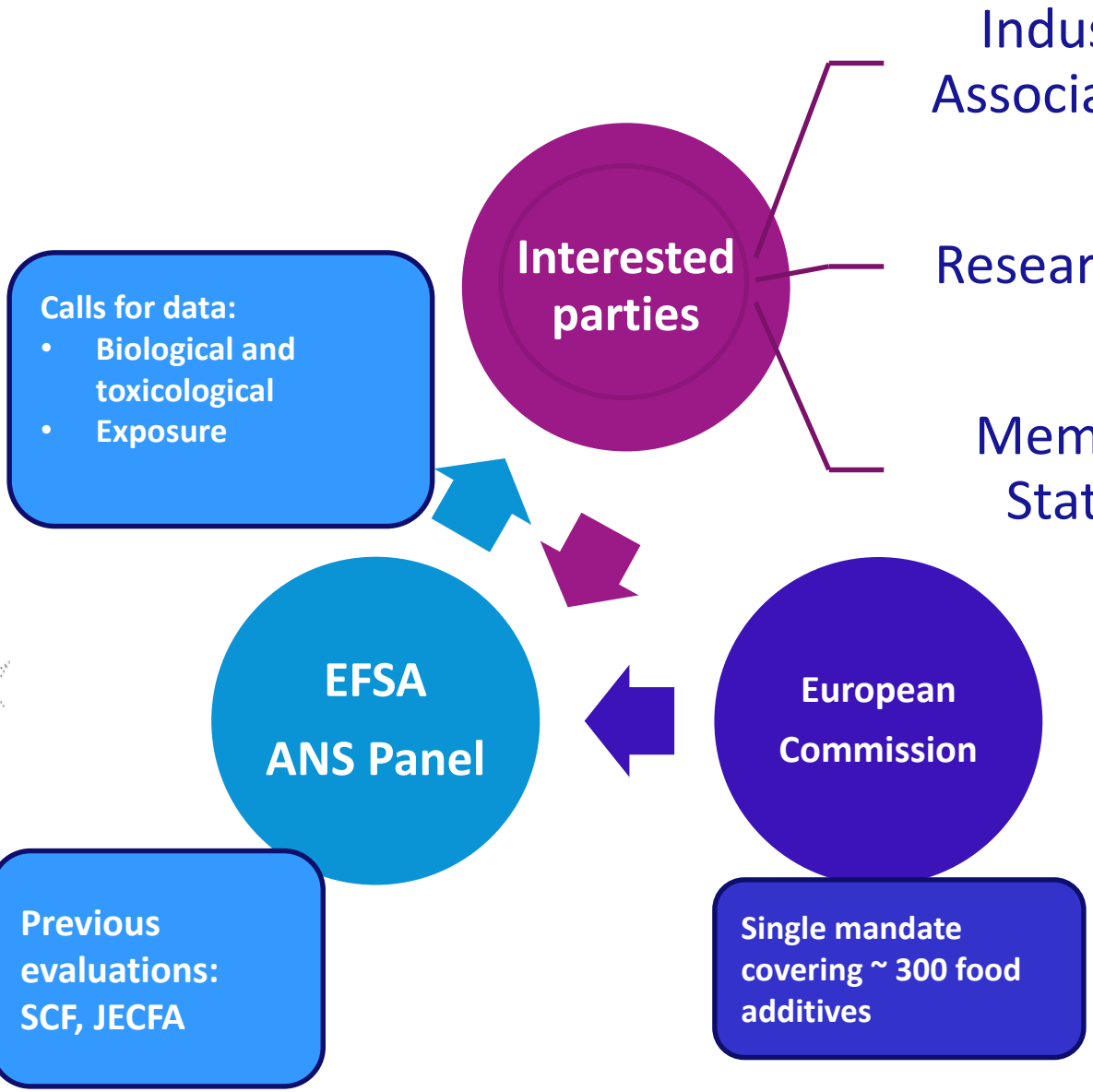
Period: 2013-2015



	Food Additives Re-evaluation	Food Additives New evaluation	Food additives Extension of use	Food additives Changes to specs, manufacturing	Nutrient Sources	Other Panel's assessment	Other EFSA assessments
2015	20	0	5	2	0	1	3
2013-2014	14	3	1	1	1	7	7

In 2016 a total of approximately 40 opinions should be adopted

RE-EVALUATION: PROCEDURAL ASPECTS



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 re-evaluation programme

- 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

1.5 - 2 years

EXPOSURE/DIETARY INTAKE: DIFFERENT SCENARIOS

- 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

FOOD ENZYMES – CEF PANEL: ALL

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.cal reaction;

FOOD ENZYMES – CEF PANEL: ALL

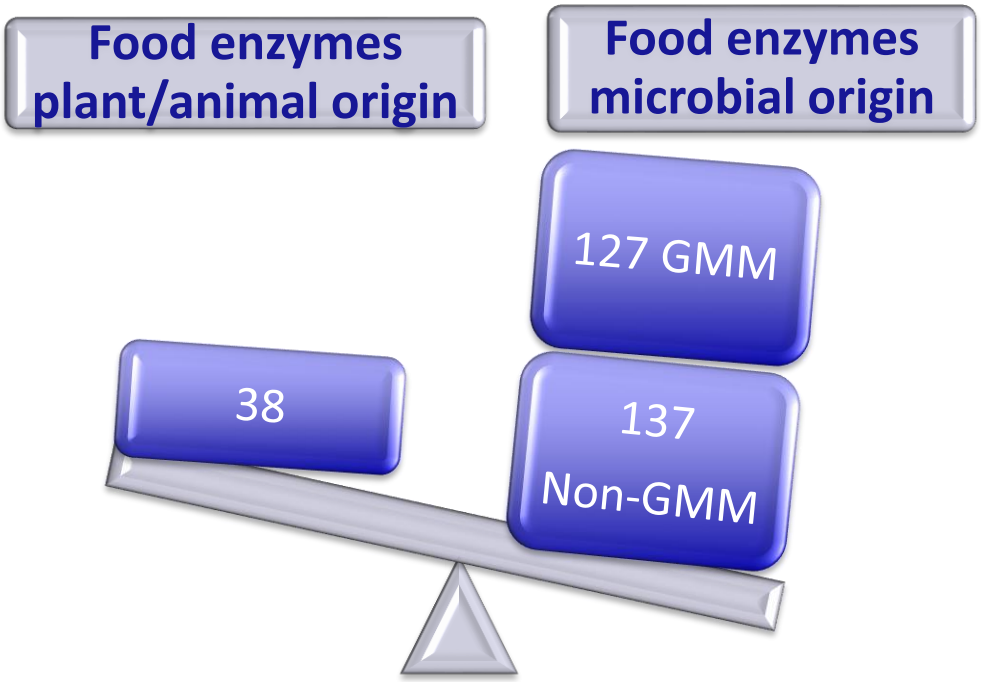
- **Reg. (EC) No 1332/2008 on food enzymes**
- ***Implementing Reg. (EU) No 234/2011 (Data Req.!)***
- **Reg. (EU) No 562/2012 with specifications on food enzymes: specific data requirements**
- **2009 EFSA-CEF Guidance for dossier**
- **2011 EFSA-GMO Guidance for GMOs**
- **2011.7.8 Explanatory note (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 5t 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**

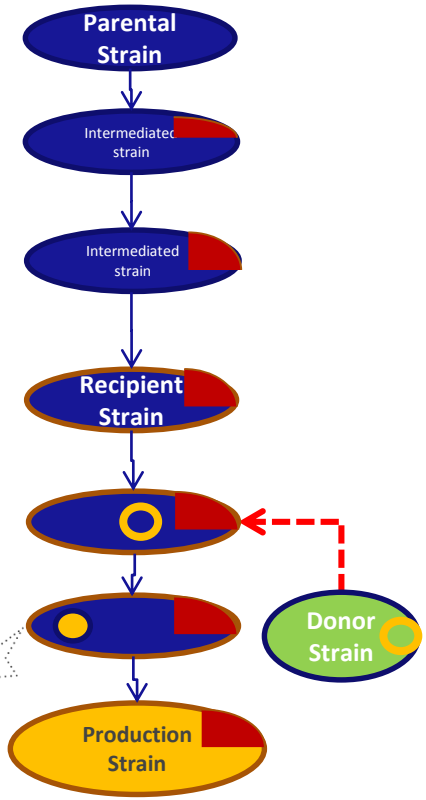
FOOD ENZYME DOSSIERS – APPLICATIONS FOR RA EVALUATION

Total FE applications	Genetically Modified Microorganisms (GMM) source	Non-GMM source	Animal/plant source
303= 264 microbial source 38 non-microbial source	127 (42%)	137	38



http://registerofquestions.efsa.europa.eu/roqFrontend/questionsListLoader?panel=ALL

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

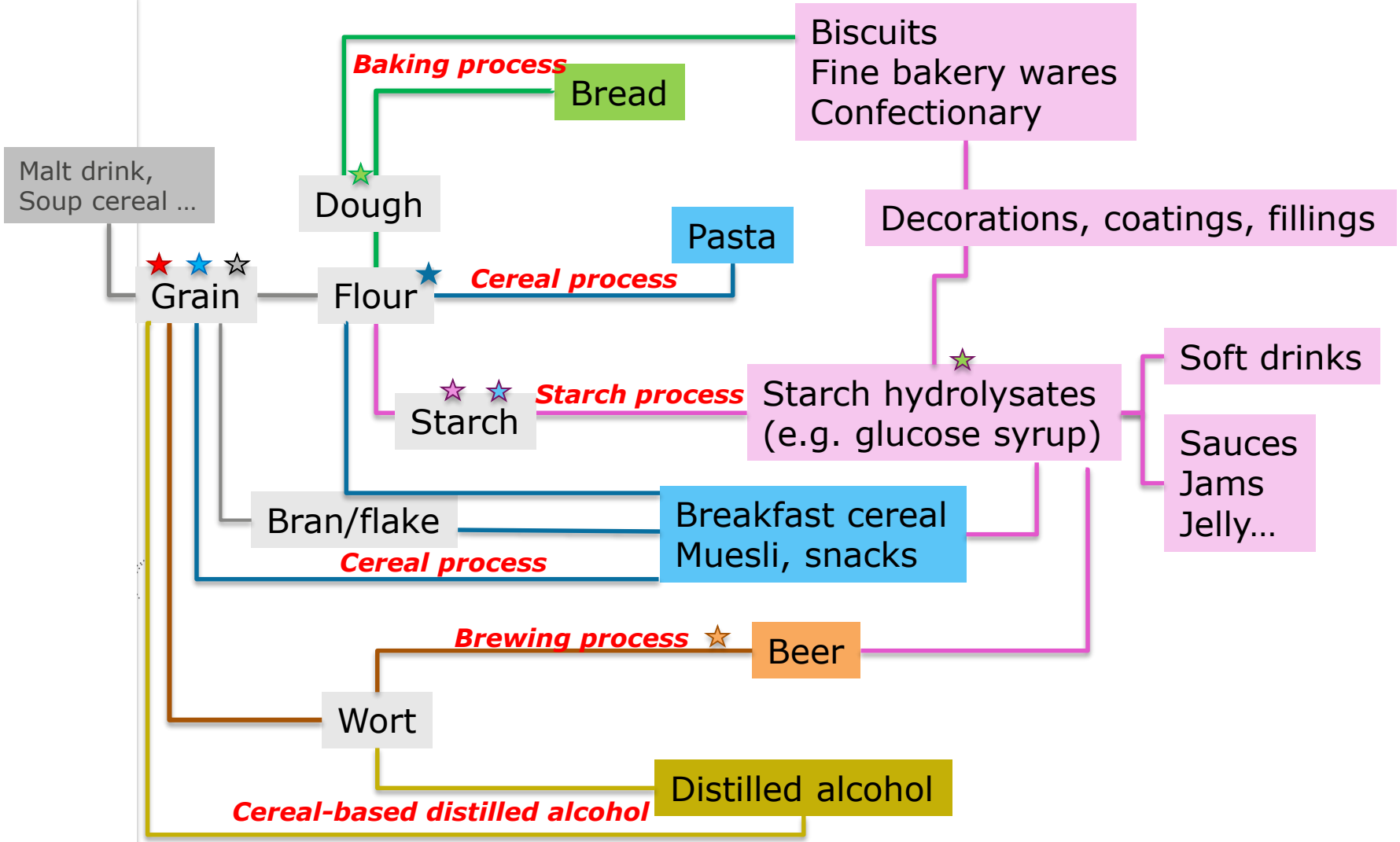
CEF PANEL'S STANDING WORKING GROUP (SWG)

- **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

☆ = addition of food enzyme

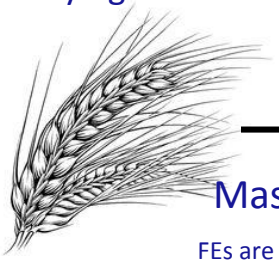
CHALLENGES FOR EXPOSURE ASSESSMENT

- '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

Brewing process

cellulase
β-glucanse
xylanase
α&β-amylase
amyloglucosidase



Barley

Mashing, etc

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

β-glucanse
α&β-amylase

Wort

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

boil

Storage tank

α-acetolactate decarboxylase

Filtration, pasteurisation

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

fermentation

Filtration

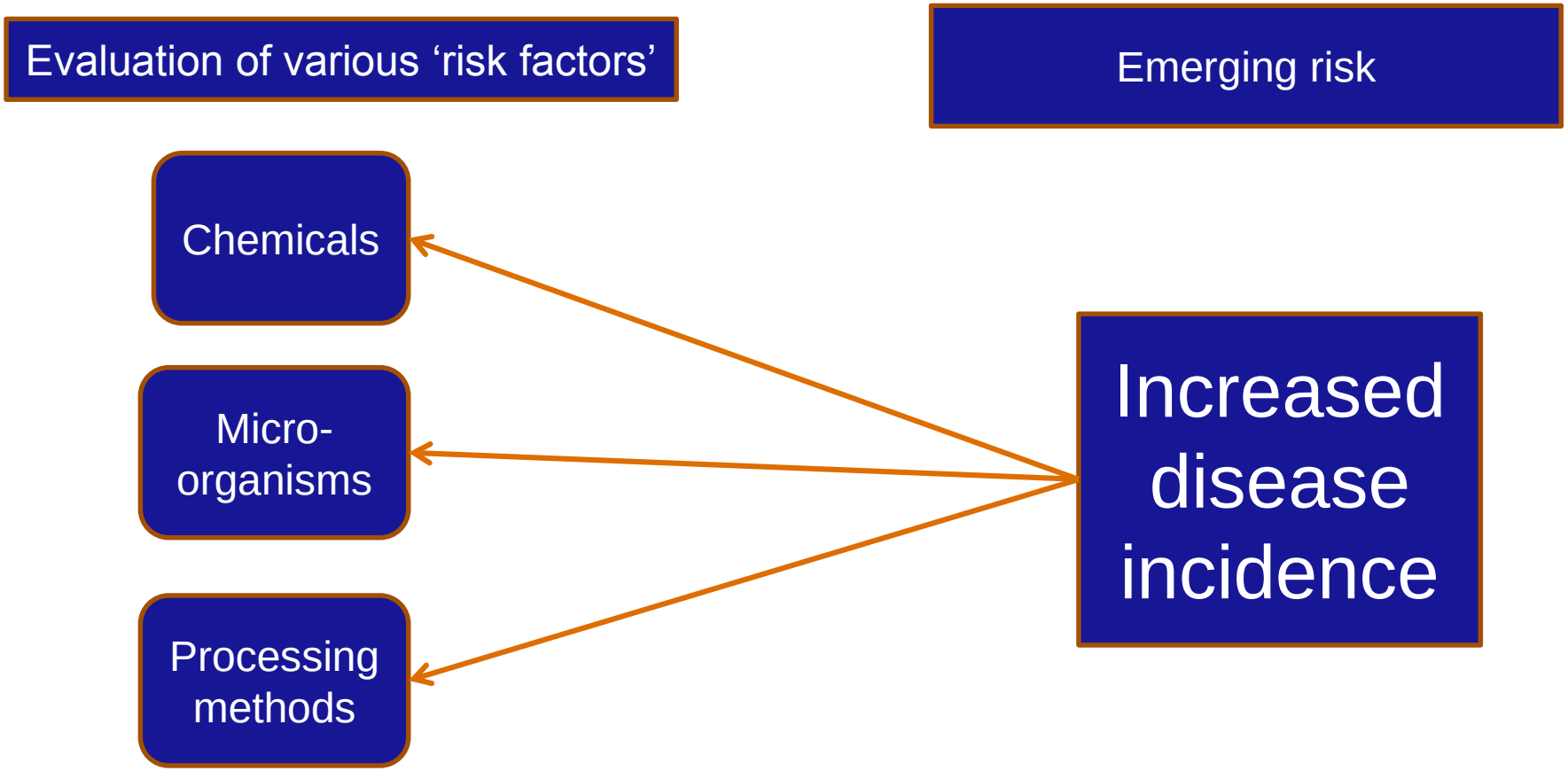
distillation

Distilled alcohol production

Source of concentration data
- Raw material

Source of consumption data
- Foods as consumed

What makes people ill?



QUESTIONS?