SWACCs
5 December 2023

# HOW EFSA IS USING SCIENTIFIC INFORMATION IN ITS WORK

George Kass
Lead Expert

EUROPEAN FOOD SAFETY AUTHORITY

*Disclaimer: The views, thoughts and opinions presented are not necessarily those of EFSA*

1. Food safety in the EU
2. Data requirements for regulatory risk assessment in food safety
    - General considerations
    - Legislative perspective
    - Integration of data: qualitative and quantitative aspects
3. Hazard data sources
    - Traditional sources
    - 3R opportunities
    - 3R challenges
4. Where do we go from here?

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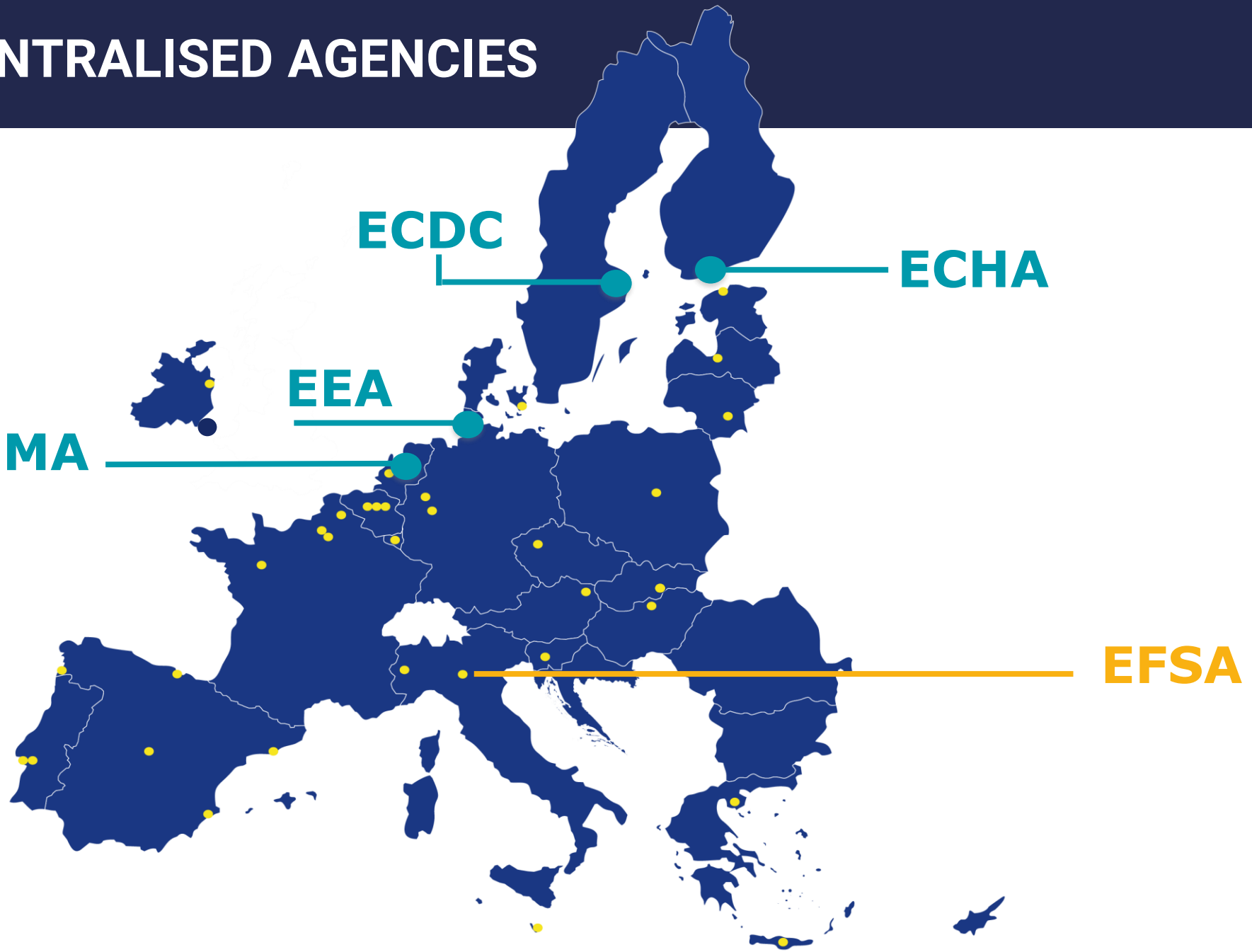
# WHAT IS EFSA?

# EU DECENTRALISED AGENCIES



# HEADQUARTERS

## in the heart of Parma

EFSA was established under EU law in 2002 following a series of food crises

## TO

**Improve** the EU food safety system

**Help ensure** a high level of consumer protection

**Restore and maintain** confidence in the EU food supply

**Clearly separate** risk assessment and risk management functions

ESTABLISHED

# 2002

**539** staff

**650** experts

**1,600** virtual meetings / year

**9,300** scientific outputs since 2003

# LEGAL FRAMEWORK

## EU Food Law
(Regulation (EC) No 178/2002, as amended)

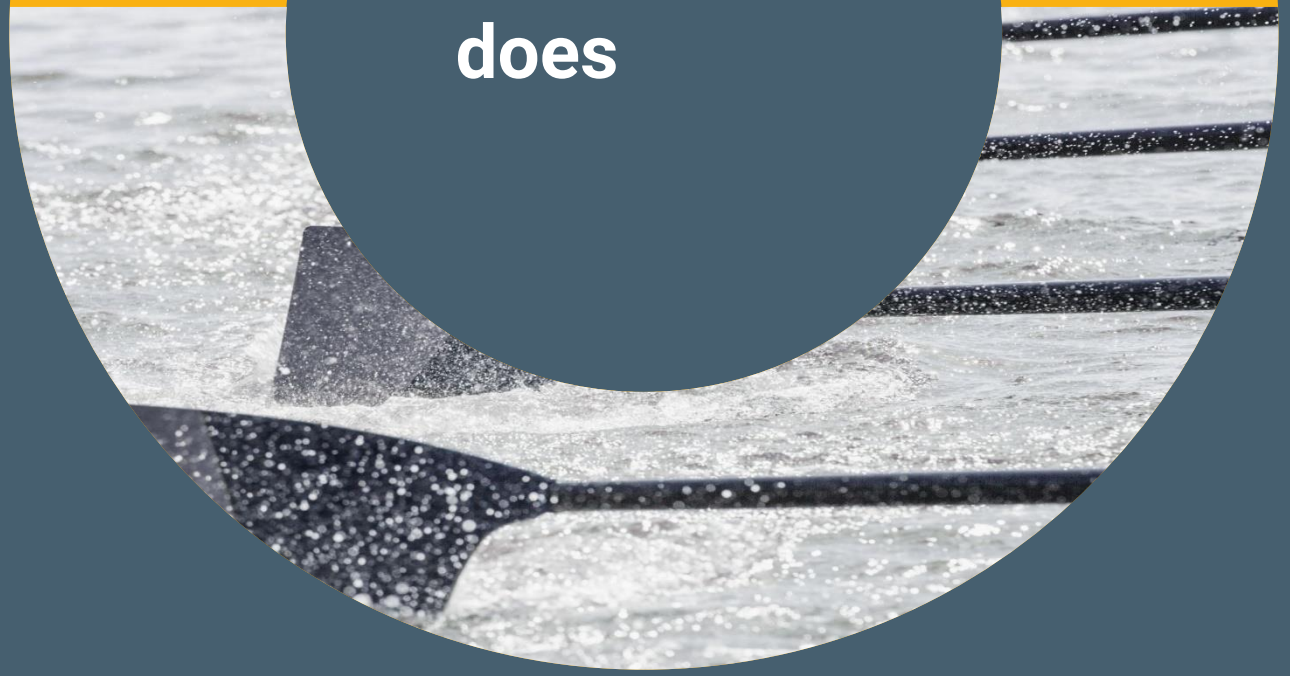
- Risk analysis and risk communication at the core of EU Food Law
- Regulatory science informing EU Food Law decision making
- Transparency
- Independence (legal, financial, regulatory)
- Emergency/crisis procedures

## EU food law sectoral legislation

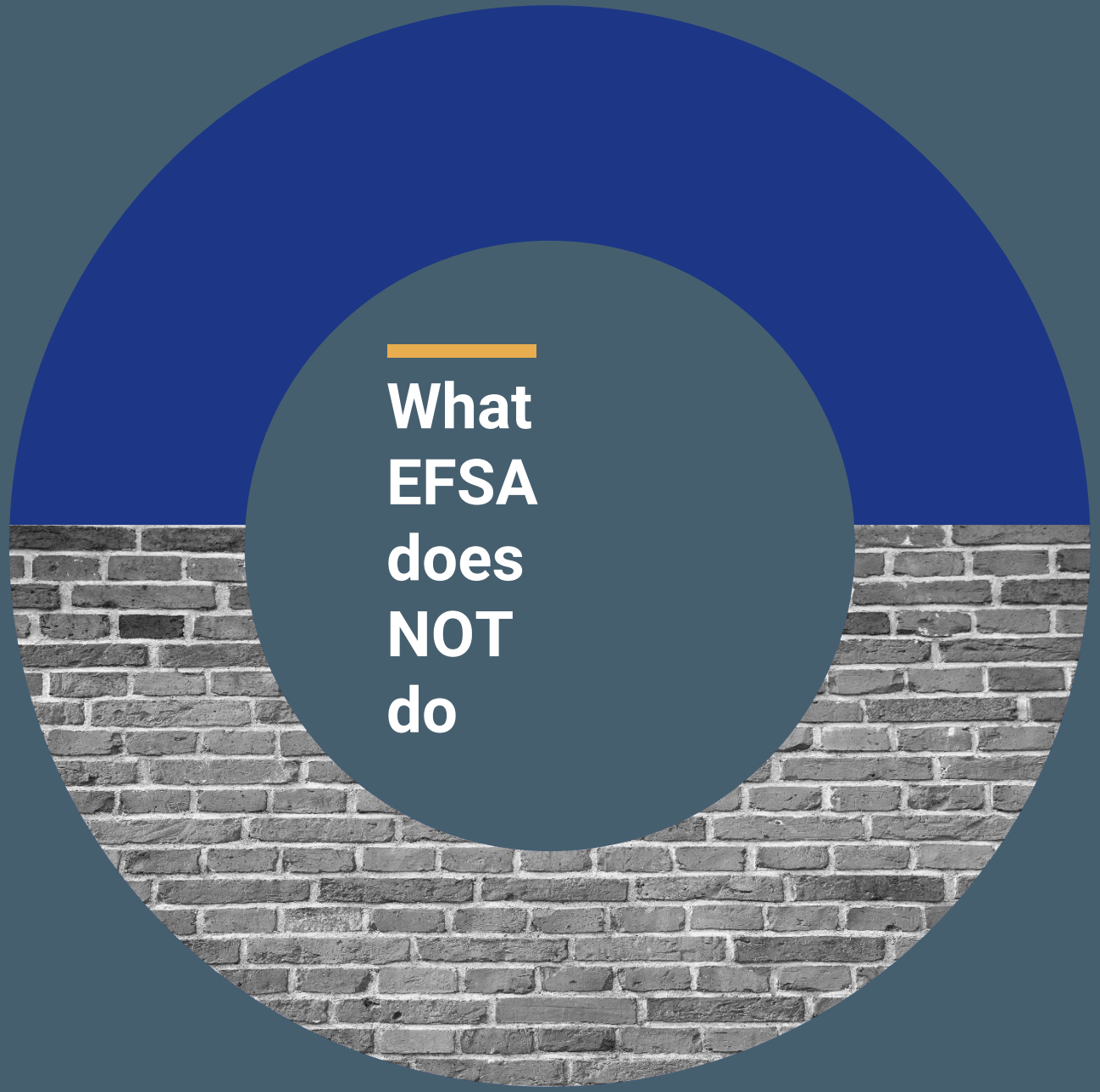
- Review at EU level of products already on the market or authorised for use at national level
- First-time evaluation of new products, prior to their introduction on the market
- Re-evaluation of products due to the expiry of their authorisation

# KEEPING FOOD SAFE IN THE EU

# What EFSA does



- Provides independent scientific advice and support for EU risk managers and policy makers on food and feed safety
- Provides independent, timely risk communication
- Promotes scientific cooperation

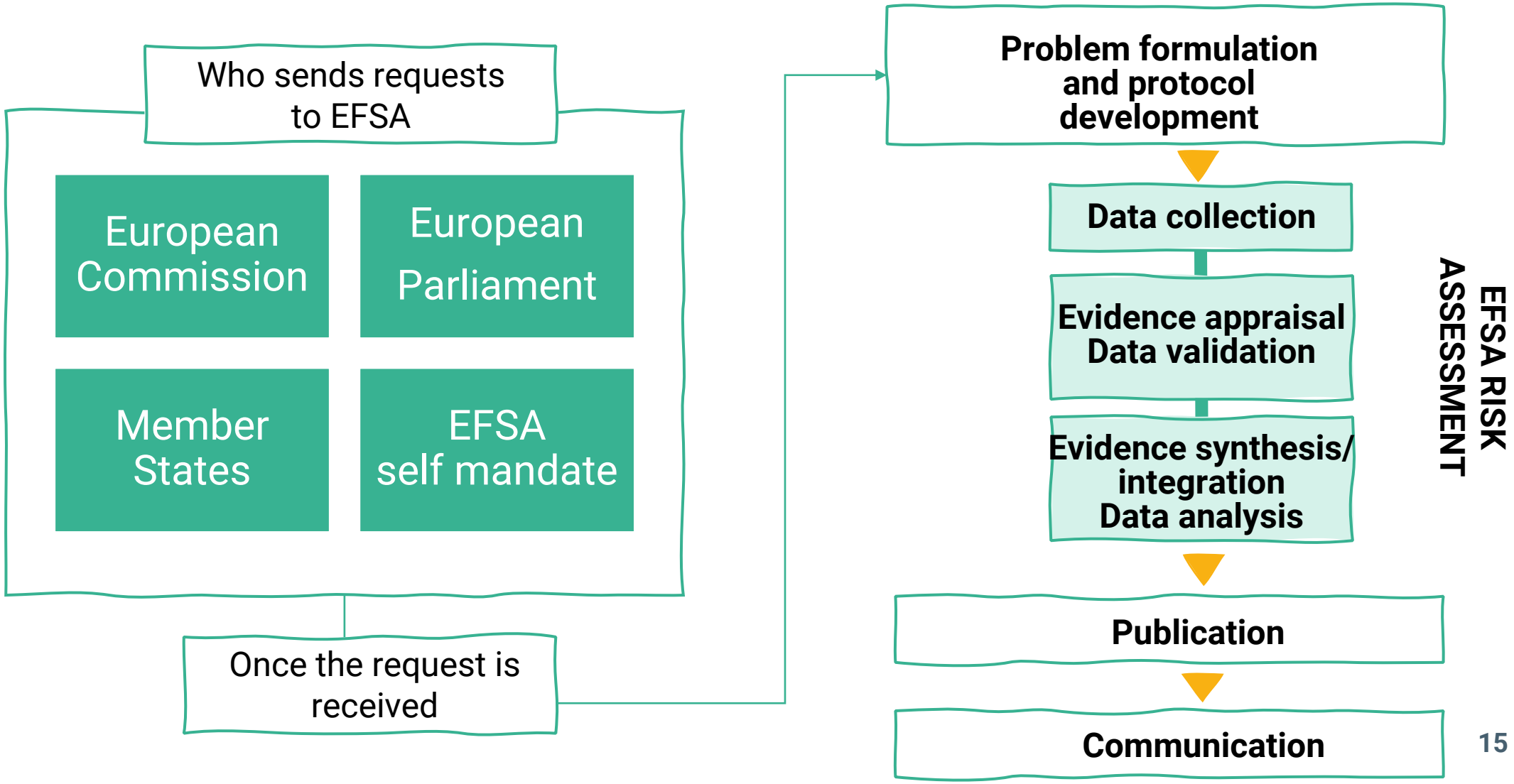


# What EFSA does NOT do

- Develop food safety policies & legislation
- Adopt regulations, authorise marketing of new products
- Enforce food safety legislation

# HOW EFSA WORKS

# QUESTIONS AND ANSWERS

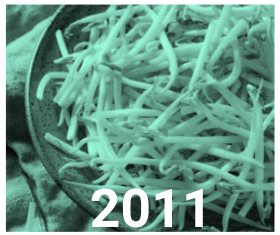


# THE SCIENTIFIC PANELS

# URGENT REQUESTS FOR SCIENTIFIC ADVICE – EXAMPLES


Nicotine in wild mushrooms


Chlormequat in table grapes




STEC in vegetables

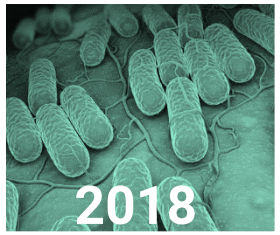

"Schmallenberg" virus


Phenylbutazone in horsemeat


Swine fever


Lumpy skin disease

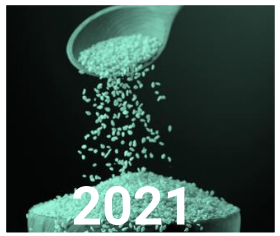

Avian influenza




Salmonella Poona


Listeria monocytogenes


Salmonella and Brazil nuts




Ethylene oxide residues in sesame seeds


Import threshold for pesticide residues

# WHO WE WORK WITH

# OUR PARTNERS

# RISK COMMUNICATION

# RISK COMMUNICATION

## IS

- Bridging the gap between science and the consumer
- Promoting and disseminating consistent messages
- Understanding consumer perception of food and food safety risks

# Coordinated communication with Member States


# SOCIAL RESEARCH

## STRATEGIC

helps us inform communication planning and the choice of topics

## TARGETED

explores a specific topic or an audience to best frame the communication

# RISK COMMUNICATION

efsa JOURNAL

**500**

**PUBLISHED OUTPUTS PER YEAR**

**3.48**

**IMPACT FACTOR**

**4.0M**

**DOWNLOADS FROM ALL OVER THE WORLD IN 2022**

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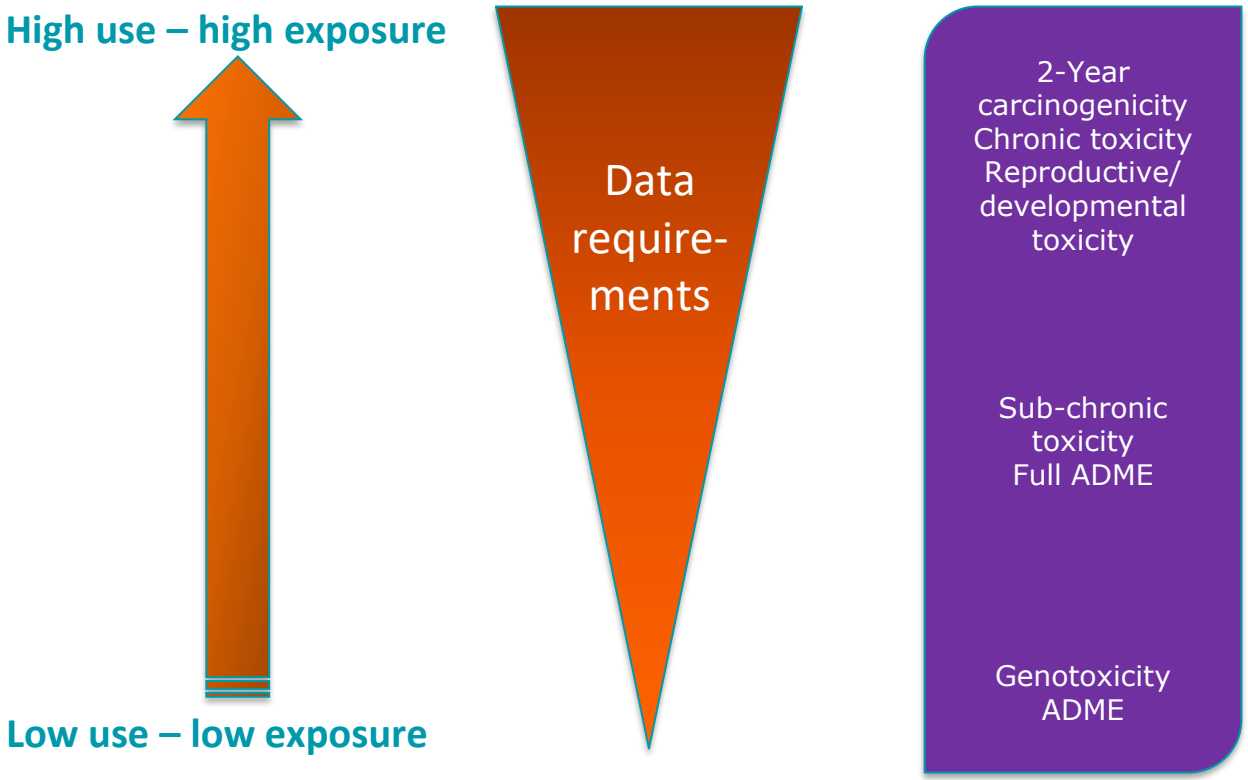
# OVERVIEW – DIFFERENT REGULATIONS AND DIFFERENT DATA REQUIREMENTS!

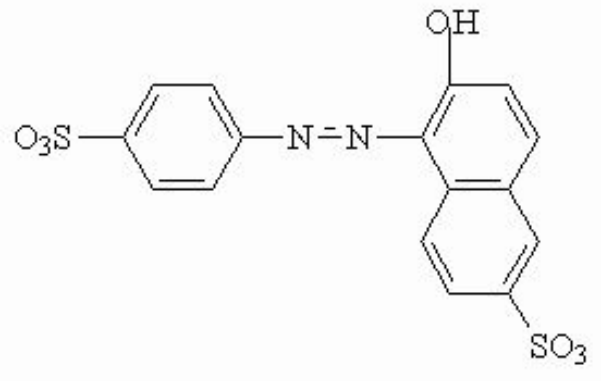
- Environmental pollutants – **No Testing**
- Pharmaceuticals, food additives, plant protection products, biocides – **Extensive testing**
- Other sectors of food and feed safety - **Variable testing depending on exposure**
- Industrial and consumer chemicals (>30K in the EU) – **Variable testing depending on tonnage**
- Cosmetics – **No animal testing**

# DATA FOR RISK ASSESSMENT: GENERAL CONSIDERATIONS



# TYPES OF DATA: 1. CHEMICAL

- Identity
  - Name, CAS No., EINECS No., synonyms, molecular and structural formula
  - Single compound or mixture?
  - Isomers
- Physicochemical properties
  - Molecular mass, particle size (nanoparticles!), lipophilicity, appearance, solubility, ionisation constants, etc. and specifications
- Purity
  - chemical purity, impurities (quantities!), contaminants (quantities!)
  - degradation products, commercial product vs test product



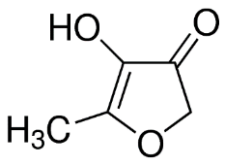

Sunset yellow (E110)

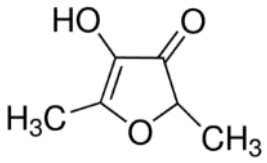
# TYPES OF DATA: 2. BIOASSAY DATA

- ADME – absorption, distribution, metabolism and excretion (toxicokinetics)
- Acute, sub-acute, and sub chronic in vivo studies
- Gene mutation and chromosome damage studies
- Carcinogenicity
- Fertility, development, parturition and post-natal development
- Special studies

# WHAT IF THERE ARE NO DATA: NON-TESTING METHODS

- (Q)SAR (Structure Activity Relationship test)
  - The basic assumption is that similar molecules have similar activities
  - Regression or classification models
  - Activity = f(physiochemical properties and/or structural properties) + error
  - (Q)SAR can predict certain simple endpoints
- Read-across
  - Non-test approach where endpoint information for one chemical (the source chemical) is used to predict the same endpoint for another chemical (the target chemical)
  - May be non-computational or computational



# WHAT IF THERE ARE NO DATA: NON-TESTING METHODS

- Threshold of Toxicological Concern (TTC)
  - Safe exposure levels can be deduced based on structural considerations

| Classification | TTC value in µg/person per day | TTC value in µg/kg bw per day |
|---|---|---|
| Potential DNA-reactive mutagens and/or carcinogens | 0.15 | 0.0025 |
| OPs and carbamates | 18 | 0.3 |
| Cramer Class III | 90 | 1.5 |
| Cramer Class II | 540 | 9.0 |
| Cramer Class I | 1800 | 30 |

**Theophrastus von Hohenheim**
**'Paracelsus'**
**1493 (or 1494) - 1541**

German: 'Alle Ding sind Gift und nichts ohn' Gift; allein die Dosis macht, daß ein Ding kein Gift ist.

English: All things are poison and nothing (is) without poison; only the dose makes that a thing is no poison.

# INTEGRATION OF DATA

## Qualitative

- Qualitative assessment of hazard information
- The United Nations, IARC and ECHA use qualitative classification of animal bioassay results.
- This approach is at the **basis to C&L** (Classification and Labelling of Chemicals).
- This is Hazard Identification (characterisation) and not Risk Assessment

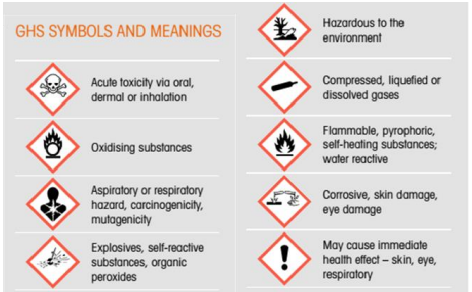
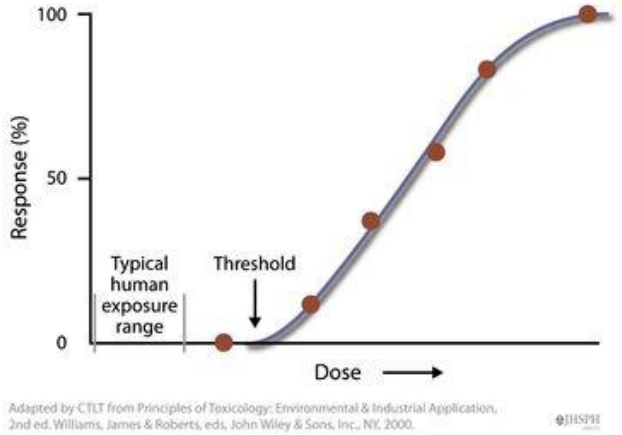



Figure 3.6.1: Hazard categories for carcinogens

| | |
|---|---|
| CATEGORY 1: | **Known or presumed human carcinogens**<br>The placing of a substance in Category 1 is done on the basis of epidemiological and/or animal data. An individual substance may be further distinguished: |
| Category 1A: | **Known to have carcinogenic potential for humans; the placing of a substance is largely based on human evidence.** |
| Category 1B: | **Presumed to have carcinogenic potential for humans; the placing of a substance is largely based on animal evidence.**<br>Based on strength of evidence together with additional considerations, such evidence may be derived from human studies that establish a causal relationship between human exposure to a substance and the development of cancer (known human carcinogen). Alternatively, evidence may be derived from animal experiments for which there is sufficient evidence to demonstrate animal carcinogenicity (presumed human carcinogen). In addition, on a case by case basis, scientific judgement may warrant a decision of presumed human carcinogenicity derived from studies showing limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals.<br>**Classification**: Category 1 (A and B) Carcinogen |
| CATEGORY 2: | **Suspected human carcinogens**<br>The placing of a substance in Category 2 is done on the basis of evidence obtained from human and/or animal studies, but which is not sufficiently convincing to place the substance in Category 1. Based on strength of evidence together with additional considerations, such evidence may be from either limited evidence of carcinogenicity in human studies or from limited evidence of carcinogenicity in animal studies.<br>**Classification**: Category 2 Carcinogen |

## Quantitative

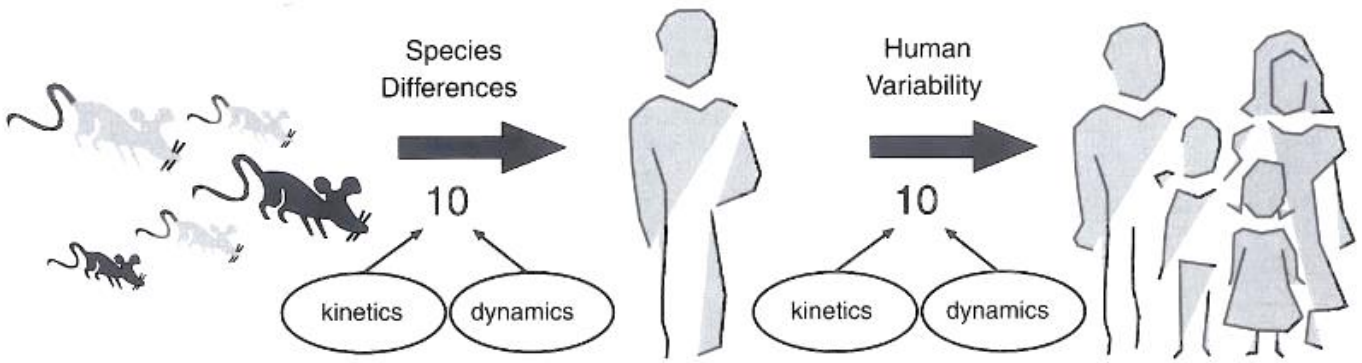
- Involves **dose-response** assessments
- Need to distinguish **threshold** approaches versus **non-threshold** approaches
- Traditionally threshold approaches are applied to **non-cancer endpoint** and non-threshold approaches for cancer endpoints.
  - Exception: non-genotoxic carcinogens and indirect-acting genotoxic agents

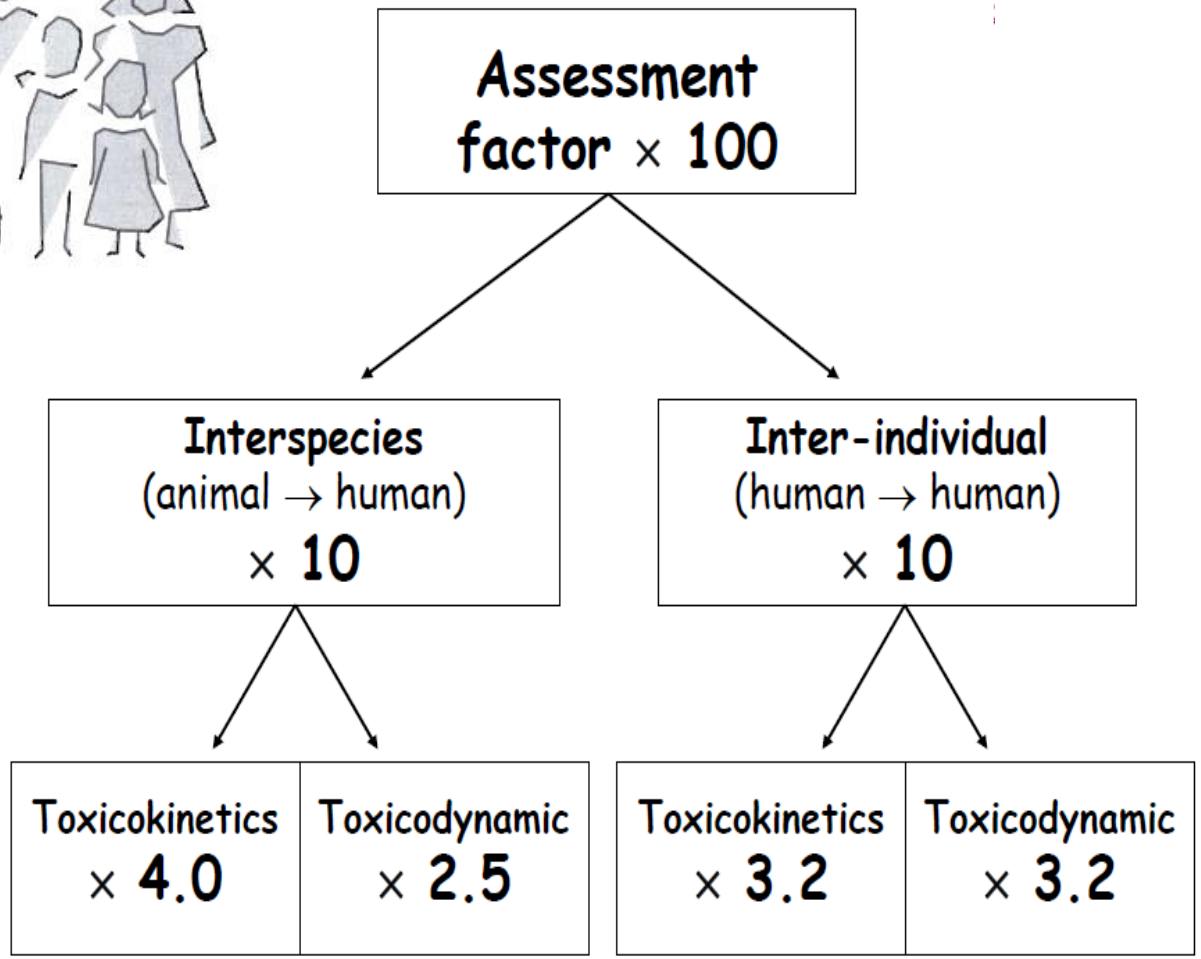



Point of departure:
NOAEL or BMDL

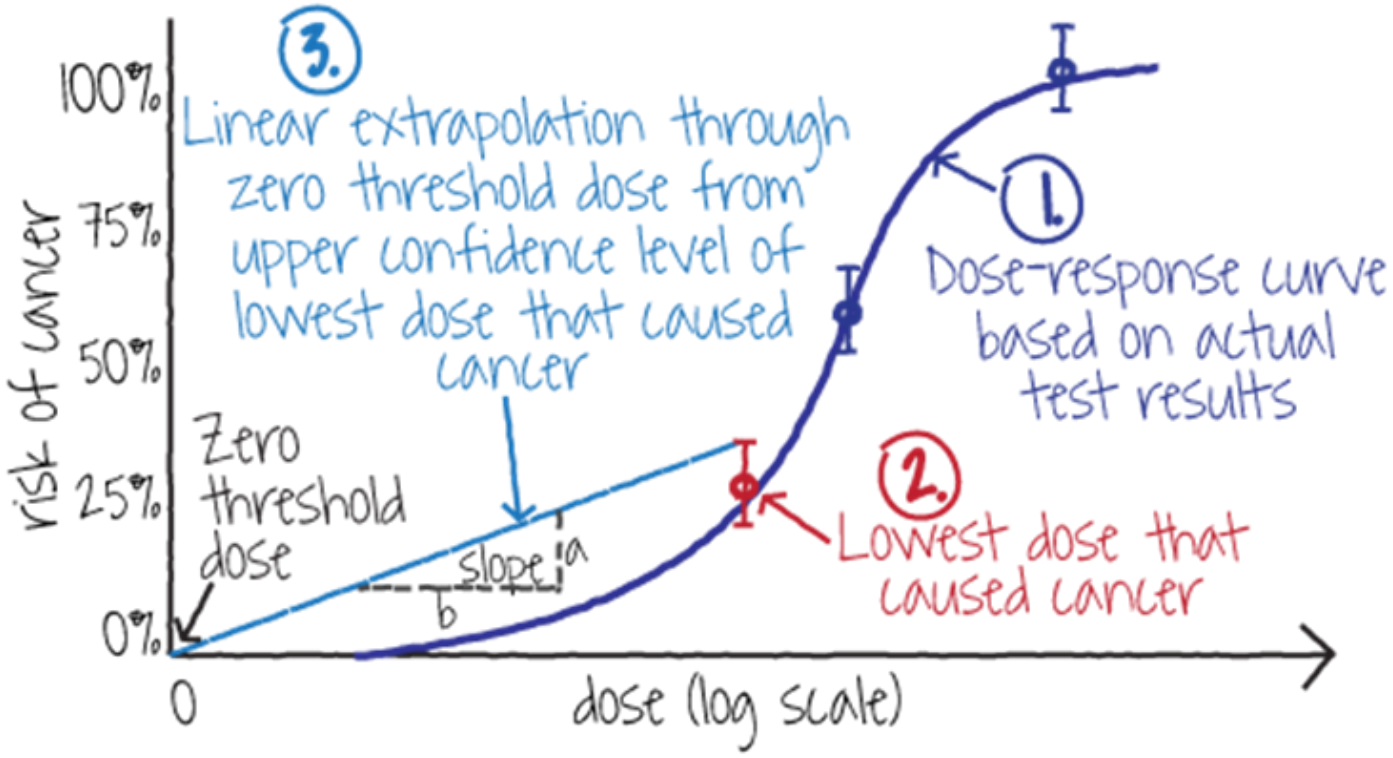
HBGV:
ADI=NOAEL/UF

# DOSE-RESPONSE ASSESSMENTS

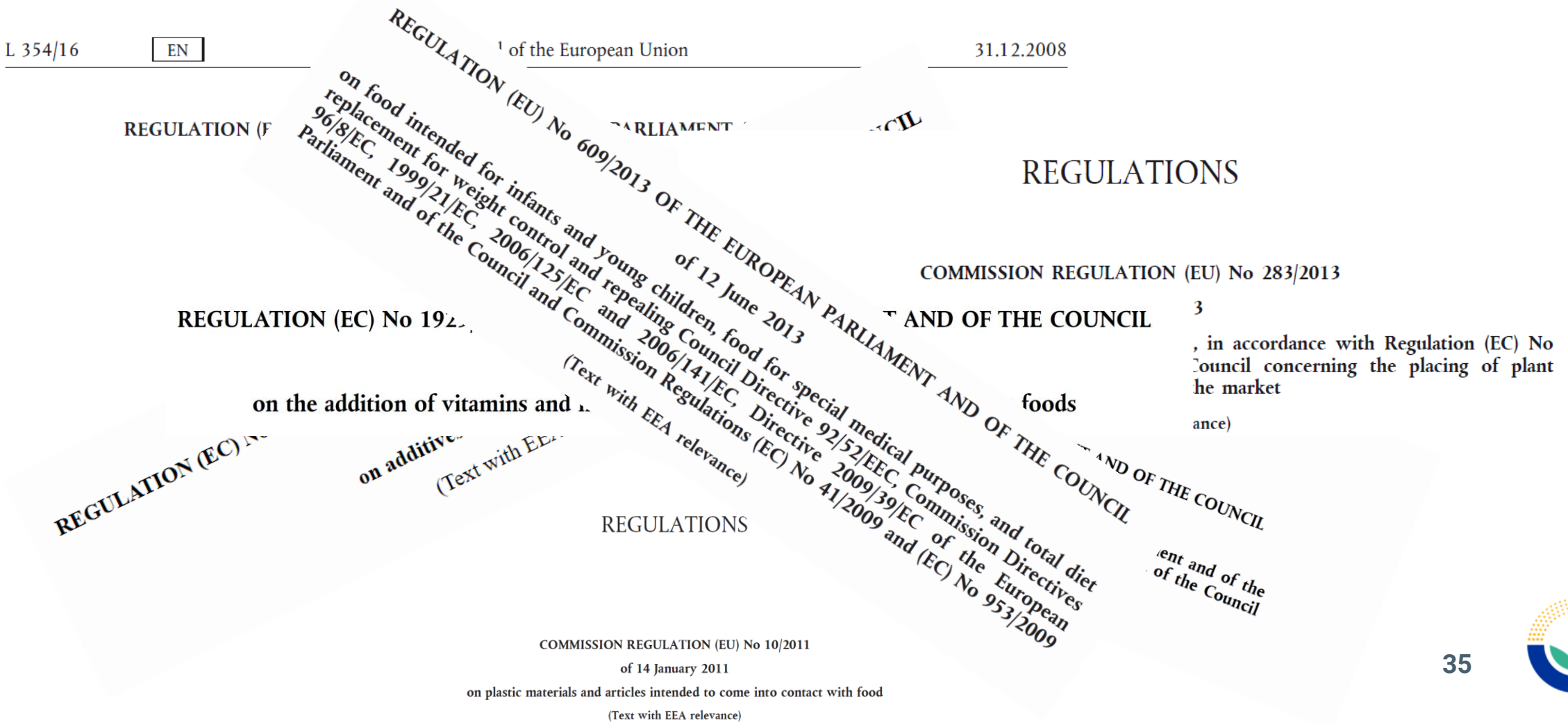


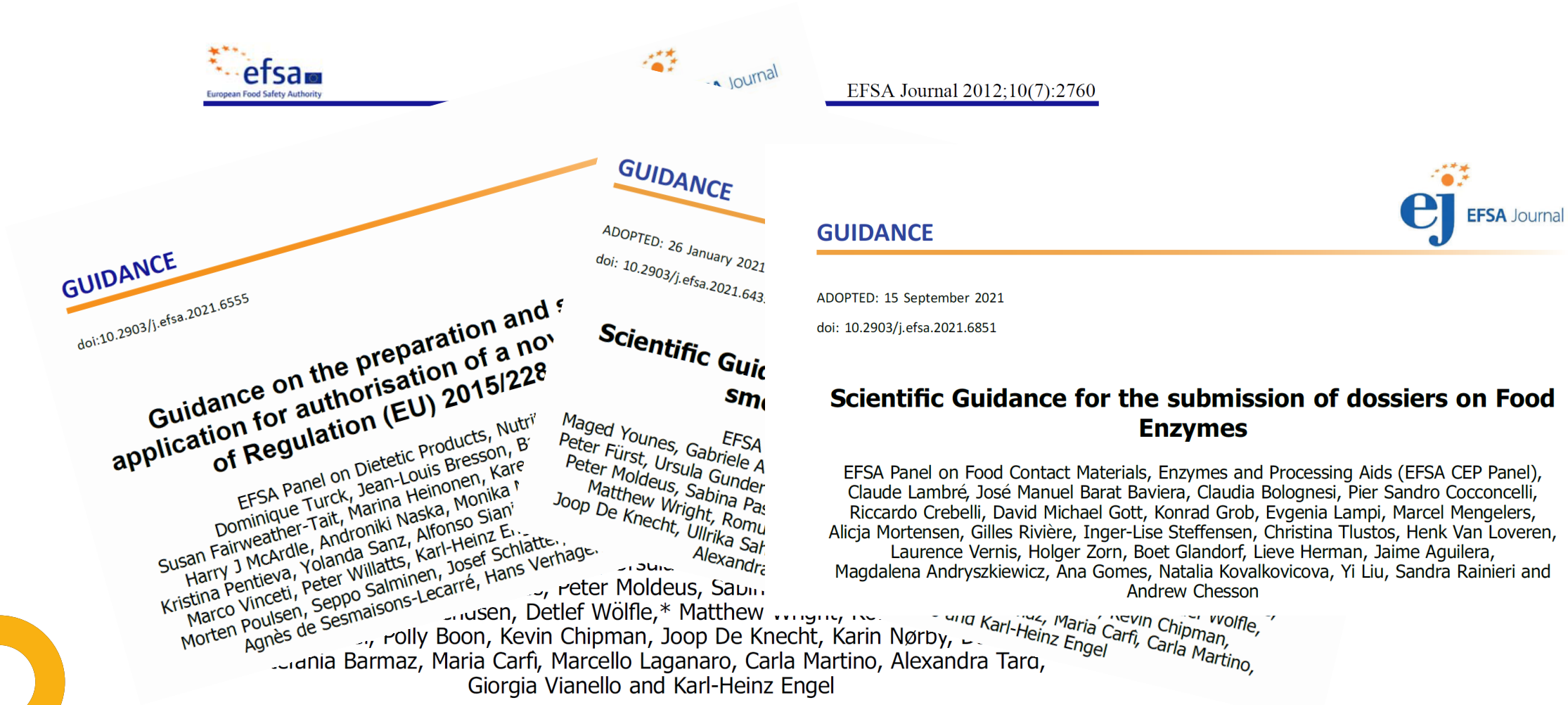
# INTEGRATION OF DATA: GENOTOXIC CARCINOGENS



# SETTING THE EFSA SCENE (II)



# SETTING THE EFSA SCENE (III)



# DATA REQUIREMENTS FOR FOOD SAFETY: PPPS

REGULATIONS

**COMMISSION REGULATION (EU) No 283/2013**

**of 1 March 2013**

**setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market**

**(Text with EEA relevance)**

INTRODUCTION

**Information to be submitted, its generation and its presentation**

1. The information submitted shall meet the following requirements.

1.1. The information shall be sufficient to evaluate the foreseeable risks, whether immediate or delayed, which the active substance may entail for humans, including vulnerable groups, animals and the environment and contain at least the information and results of the studies referred to in this Annex.

# DATA REQUIREMENTS FOR FOOD SAFETY: PPPS

SECTION 5. ***Toxicological and metabolism studies***

Introduction

5.1. Studies on absorption, distribution, metabolism and

5.1.1. Absorption, distribution, metabolism and excretion

5.1.2. Absorption, distribution, metabolism and excretion

5.2. Acute toxicity

5.2.1. Oral

5.2.2. Dermal

5.2.3. Inhalation

5.2.4. Skin irritation

5.2.5. Eye irritation

5.2.6. Skin sensitisation

5.2.7. Phototoxicity

5.3. Short-term toxicity

5.3.1. Oral 28-day study

5.3.2. Oral 90-day study

5.3.3. Other routes

5.4. Genotoxicity testing

5.4.1. *In vitro* studies

5.4.2. *In vivo* studies in somatic cells

5.4.3. *In vivo* studies in germ cells

5.5. Long-term toxicity and carcinogenicity

5.6. Reproductive toxicity

5.6.1. Generational studies

5.6.2. Developmental toxicity studies

5.7. Neurotoxicity studies

5.7.1. Neurotoxicity studies in rodents

5.7.2. Delayed polyneuropathy studies

5.8. Other toxicological studies

5.8.1. Toxicity studies of metabolites

# DATA REQUIREMENTS FOR FOOD SAFETY: ADDITIVES

L 354/16 EN Official Journal of the European Union 31.12.2008

**REGULATION (EC) No 1333/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL**

**of 16 December 2008**

**on food additives**

**(Text with EEA relevance)**

(7) Food additives should be approved and used only if they fulfil the criteria laid down in this Regulation. Food additives must be safe when used, there must be a technological need for their use, and their use must not mislead the consumer and must be of benefit to the consumer. Mis-

# DATA REQUIREMENTS FOR FOOD SAFETY: ADDITIVES

efsa European Food Safety Authority

EFSA Journal 2012;10(7):2760

**SCIENTIFIC OPINION**

## Guidance for submission for food additive evaluations[1]

**EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS)[2, 3]**

European Food Safety Authority (EFSA), Parma, Italy

# IMPORTANCE OF EXPOSURE

- EFSA “shall search for, collect, collate, analyse and summarise relevant scientific and technical data in the fields within its mission. This shall involve in particular the collection of data relating to food consumption and the exposure of individuals to risks related to the consumption of food”;

- EFSA “shall work in close cooperation with all organisations operating in the field of data collection, including those from applicant countries, third countries or international bodies”.

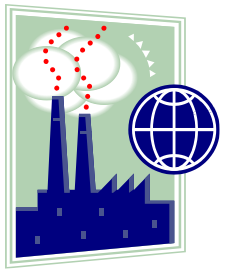
## REGULATION (EC) N° 178/2002

# DATA PROVIDERS

Member States
European Commission

efsa
European Food Safety Authority

Industry



Consumers associations

University, academia, etc.

# FROM CHAOS …. TO ORDER

Standardisation & harmonisation

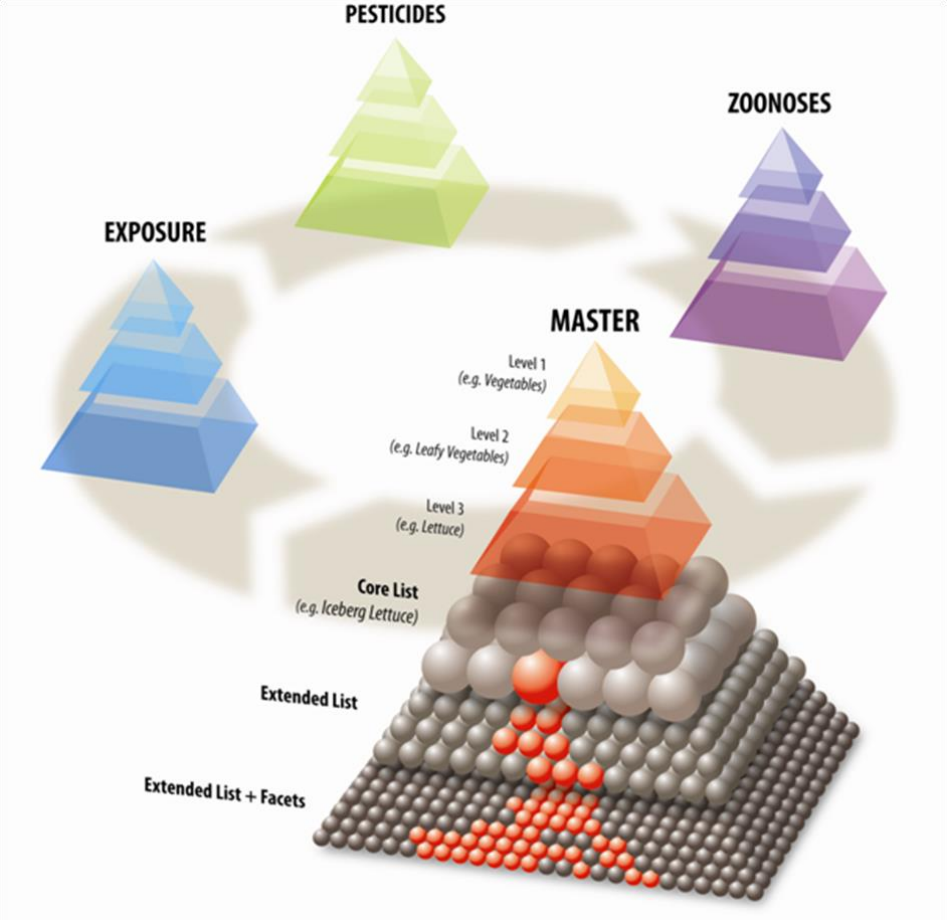

Coordinated approaches
Standard protocols
Compatible systems

# FOODEX2

**The food classification and description system of EFSA**

The common
'language'
between national datasets

and between the
**Food consumption**
and
**Occurrence data**



# EFSA OPEN-SOURCE TOOLS FOR EXPOSURE ASSESSMENT

## Assessment calculation tools

**Food Enzyme Intake Model (FEIM)**

**Food Additives Intake Model 2.1 (FAIM)**

**Dietary Exposure tool (DietEx)**

**Rapid Assessment of Contaminant Exposure (RACE)**

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Environment International

journal homepage: www.elsevier.com/locate/envint

Review article

### European Food Safety Authority open access tools to estimate dietary exposure to food chemicals

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*European Food Safety Authority, Via Carlo Magno, 1A, Parma 43126, Italy*

ARTICLE INFO

Handling Editor: Martí Nadal

*Keywords:*
EFSA
Dietary exposure tools
Open access
Food chemicals
FoodEx2
Food consumption

ABSTRACT

The European Food Safety Authority (EFSA) has developed a suite of open access tools to estimate dietary exposure to food-borne chemical hazards. The tools are tailored to several regulatory domains within EFSA's remit (e.g. food and feed additives, pesticide residues, contaminants and food enzymes) and are intended for use by EFSA experts, industry applicants of regulatory product dossiers, researchers or any stakeholder with an interest in estimating dietary exposure using European food consumption data. The majority of the tools are based on FoodEx2, EFSA's food classification and description system as well as the EFSA Comprehensive European food consumption database. This paper provides an overview of these open access tools, the regulatory framework in which they were developed as well as data sources used.

**1. Introduction**

The European Food Safety Authority (EFSA) provides independent scientific advice on risks associated with the food chain. EFSA's scientific advice helps to protect consumers, animals and the environment from food related risks by informing EU risk management measures.

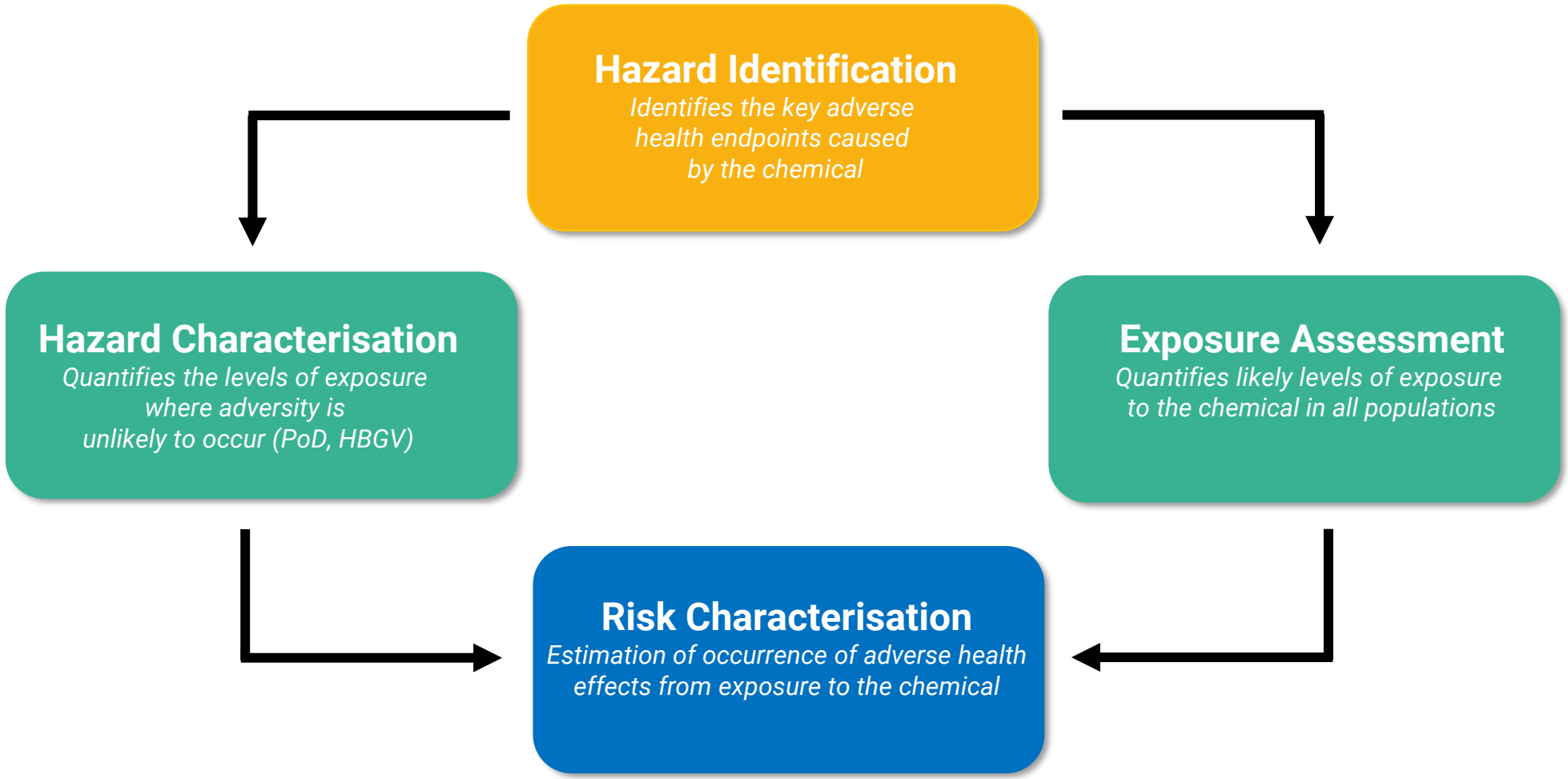
Dietary exposure to hazards is a key component of the food chemical data. Exposure estimates are compared with health-based guidance values (hazard characterisation) to estimate risk.

The outcome of the hazard characterisation step, which may relate to an acute or chronic toxicological end point, drives the type of dietary exposure assessment (e.g. acute versus chronic dietary exposure) (Kroes et al., 2002). In the case of pesticide residues, where acute toxicological effects are observed, acute dietary exposure is typically estimated

https://www.sciencedirect.com/science/article/pii/S0160412020323126

Find more at https://www.efsa.europa.eu/en/science/tools-and-resources

# FROM HAZARD CHARACTERISATION TO RISK CHARACTERISATION



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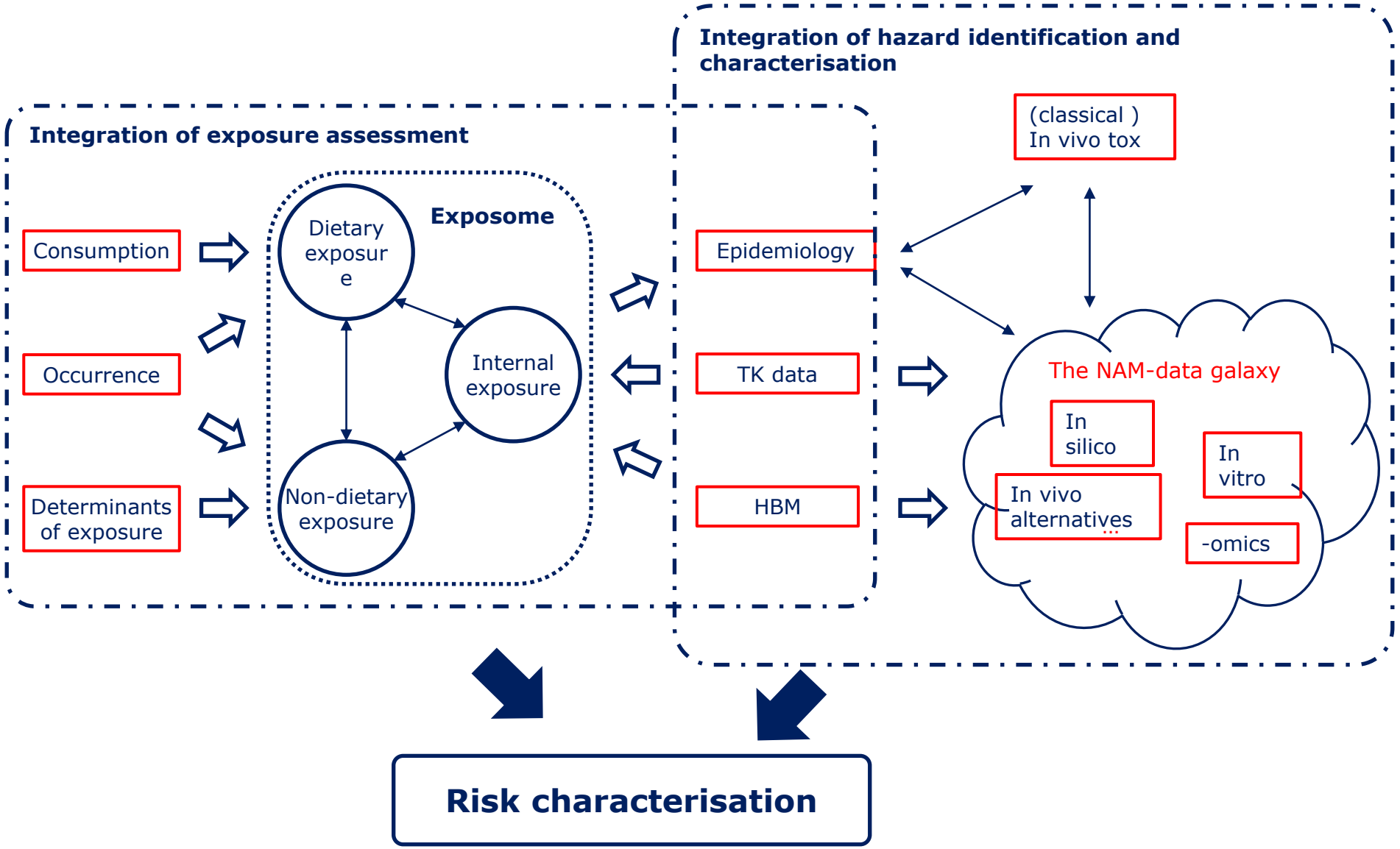
4. Where do we go from here?

# MAIN SOURCES AND TYPES OF DATA RECEIVED BY EFSA

| | |
|---|---|
| In vivo biological studies | • ADME studies<br>• Following OECD TG and GLP criteria |
| In vivo toxicological studies | • Sub-chronic, chronic, repro-dev studies<br>• Following OECD TG and GLP criteria<br>• Traditional Tox parameters |
| In vitro studies | • Mainly for genotoxicity and metabolism<br>• Following OECD TG and GLP criteria |

- **Traditional chemical risk assessment relies mainly on animal bioassays**
- **The future: NGRA - AOPs, NAMS, IATAs**

# 3R AND EFSA: OUR VISION – SHORT TO MEDIUM TERM



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# CHANGING THE WAY TO DO RISK ASSESSMENT: EC POLICIES

EUROPEAN
COMMISSION

Brussels, 14.10.2020
COM(2020) 667 final

**Safety testing and chemical risk assessment** need to innovate in order to reduce dependency on animal testing but also to improve the quality, efficiency and speed of chemical hazard and risk assessments.

**COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL, THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE AND THE COMMITTEE OF THE REGIONS**

**Chemicals Strategy for Sustainability**
**Towards a Toxic-Free Environment**

**SCIENCE-POLICY INTERFACE**

The Commission will:

- foster multidisciplinary research and digital innovations for **advanced tools, methods and models, and data analysis capacities**[102] to also move away from animal testing;

European Commission

Commission's response to the European citizens' initiative

# SAVE CRUELTY-FREE COSMETICS - COMMIT TO A EUROPE WITHOUT ANIMAL TESTING

July 2023
#EUTakeTheInitiative

European Citizens' Initiative

mb210624-a2

# EFSA Strategy 2027

Science
Safe food
Sustainability

Adopted at the Management Board meeting
held in virtual modality on 24 June 2021
For EFSA's Management Board
[SIGNED]
Raymond O'Rourke
Chair of the Management Board

efsa
European Food Safety Authority

# STRATEGIC OBJECTIVE 2

## Ensure preparedness for future risk analysis needs

2.1.3 The quality of scientific guidance and methodologies, with the necessary risk assessment capabilities is improved to address future challenges. Within its risk assessment approaches, EFSA will develop and integrate new scientific developments focusing on NAM-based methods and the minimisation of animal testing, innovations in food systems, data, and technology, and strive to meet One health policy needs.

### Expected Operational Result 2.1.3

**The quality of scientific guidance and methodologies, with the necessary risk assessment capabilities, is improved to address future challenges**

### KEY ACTIONS

- Develop and integrate new approach methodologies (NAMs) and omics for regulatory risk assessment

# NEW CHALLENGES AND THREATS

**Environmental risks**

- multiple stressors and bees

**Evaluation of the safety of new products**

- novel foods
- nanomaterials (e.g. nano-pesticides)

**Development of new assessment methods**

- NAMs (in vitro, in chemico, in silico)
- '-omics', less animal testing

**Chemical mixtures/ combined toxicity of substances in food**

**Antimicrobial resistance**

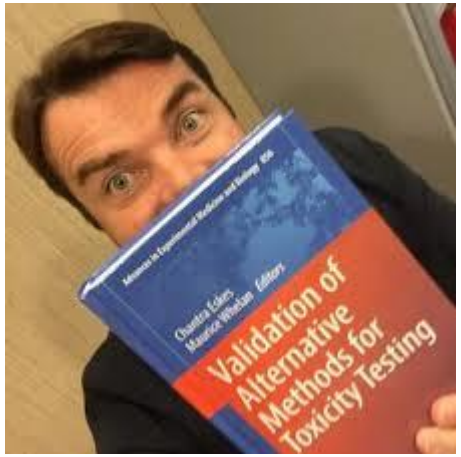
**Hazards linked to globalisation**

- plant pests, animal diseases, vector-borne diseases

# EFSA'S ENGAGEMENT: EU LANDSCAPE

PARC

EURL ECVAM
European Union Reference Laboratory for Alternatives to Animal Testing




ASPIS Consortium
(RISK-HUNT3R, ONTOX and PrecisionTOX)

efsa

epaa
The European Partnership for Alternative Approaches to Animal Testing

EUTOXRISK

# EFSA'S ENGAGEMENT: INTERNATIONAL LANDSCAPE


OECD

efsa

World Health Organization

**Food safety agencies**

**ILMERAC**

Global Coalition for Regulatory Science Research

# THE CHALLENGES

## Lack of NAM data submitted to EFSA

- ✓ Guidance documents are ‘young’
- ✓ NAM-based data remain optional

## Need for confidence building

- ✓ Validated NAMs: performance standards, right chemicals, reproducibility, etc…
- ✓ Change in concept: NAMs are not a 1-to-1 replacement of a 90-d study
- ✓ Benchmarking and coverage of potential adversity
- ✓ Fit-for-purpose and ready-to-use
- ✓ Identification of low toxicity compounds

# HOW CAN WE PROGRESS ANIMAL-FREE RISK ASSESSMENT?

Global blueprint

Working together

Efficient validation process

Adhere to MAD principle

1S1A

Capacity building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