EXTERNAL SCIENTIFIC REPORT

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# Third report on the update and maintenance of EFSA's Chemical Hazards Database

## S-IN Soluzioni Informatiche

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## Abstract

The present document is a summary of the update and maintenance of the EFSA's Chemical Hazards Database that has been established few years ago to map the hazard data as collected from the EFSA opinions, statements and conclusions; more specifically the repository holds summary data on chemical identification, document descriptors, hazard identification, and hazard characterisation/ risk characterisation. The repository includes data extracted from opinions and statements adopted by a number of EFSA panels including NDA (vitamins and minerals, novel foods, dietetic products), CONTAM (contaminants in the food chain, contaminants in the feed chain), FEEDAP (feed additives-application linked to 1381/2003, feed additives-application under to 1381/2003, feed additives-other), AFC (food additives, food contact materials, nutrient sources, processing aids, flavourings), CEF (food contact materials, food manufacturing processes, processing aids, flavourings), ANS (food additives, nutrient sources) and PPR (pesticides). Substances which do not fall within the category of chemicals (e.g., microorganisms and enzymes) are excluded from the EFSA's Chemical Hazards Database.



**Key words:** EFSA's chemical hazards database, data model, critical study, hazard assessment, safety assessment.

**Question number:** EFSA-Q-2015-00172

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## Summary

EFSA's Chemical Hazards Database aims at mapping the hazard data included in the documents (opinions, statements, conclusions) on risk assessments in food and feed published by EFSA (European Food Safety Authority). The database covers the work of many units and panels, including ANS (Food Additives and Nutrient Sources Added to Food), CEF (Food Contact Materials, Enzymes, Flavourings and Processing Aids), CONTAM (Contaminants in the Food Chain), FEEDAP (Additives and Products or Substances used in Animal Feed), PPR panel and PRAPeR unit (Plant Protection Products and their Residues), NDA (Dietetic Products, Nutrition and Allergies). It was created some years ago to summarise hazard data for chemicals assessed by EFSA since its creation.

The repository stores summary data on the chemical entity, the document details, the hazard identification, and the hazard characterisation/risk characterisation. The latest update and maintenance of the database has involved extraction, collection and collation of relevant data included in the EFSA documents that were adopted (and then published) by the Scientific Panels in the past year (until March 2017); additional quality check activities have also been carried out on the database.

The entire database includes data as extracted from the screening of nearly 1700 documents (opinions, statements, conclusions) published from 2003 to 2017, holding more than 9000 assessements for about 4500 chemicals. The assessements are classified based on well-defined categories (e.g. pesticides, flavourings, sensory additives, nutrient sources). For example, the repository stores: nearly 5600 assessments related to flavourings (about 2110 substances) as collected from the screening of 287 EFSA documents (opinions and statements); about 1190 assessments related to pesticides (nearly 1000 substances) as collected from the screening of 463 EFSA documents (conclusions); about 250 assessments related to food additives (about 200 substances) as collected from the screening of about 150 EFSA documents (opinions and statements); nearly 400 assessments related to sensory additives (396 substances) as collected from the screening of 60 EFSA documents (opinions and statements).

A suitable *ad hoc* accessory IT platform is used to aid and support the data extraction and collation workflow. This IT infrastructure, that makes use of a web application, provides the means for organizing the data in a temporary local database, that is then exported and submitted to EFSA in due time.

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# 1. Introduction

## 1.1. Background and Terms of Reference as provided by the requestor

The European Food Safety Authority (EFSA) is the keystone of European Union (EU) risk assessment regarding food and feed safety. In close collaboration with national authorities and in open consultation with its stakeholders, EFSA provides independent scientific advice and clear communication on existing and emerging risks.

EFSA was set up in January 2002, following a series of food crises in the late 1990s, as an independent source of scientific advice and communication on risks associated with the food chain.

EFSA was created as part of a comprehensive programme to improve EU food safety, ensure a high level of consumer protection and restore and maintain confidence in the EU food supply.

In the European food safety system, risk assessment is done independently from risk management. As the risk assessor, EFSA produces scientific opinions and advice to provide a sound foundation for European policies and legislation and to support the European Commission, European Parliament and EU Member States in taking effective and timely risk management decisions.

EFSA's remit covers food and feed safety, nutrition, animal health and welfare, plant protection and plant health. In carrying out its work, EFSA also considers the possible impact of the food chain on the biodiversity of plant and animal habitats. The Authority performs environmental risk assessments of genetically modified crops, pesticides, feed additives, and plant pests. In all these fields, EFSA's most critical commitment is to provide objective and independent science-based advice and clear communication grounded in the most up-to-date scientific information and knowledge.

In January 2011, the SCER Unit, in collaboration with the SAS and ITS Units, has been assigned the task of designing and developing EFSA's Chemical Hazards Database as an inventory of key information related to EFSA's chemical risk assessments in food and feed. The main objective of the database is to facilitate the work of EFSA's scientific experts and staff in providing scientific advice, particularly in case of emergencies. The establishment of the Chemical Hazards Database will also facilitate the sharing of data with EU Member States, other EU agencies (the European Chemicals Agency (ECHA), the European Medicines Agency (EMA)), international bodies (the Organisation for Economic Co-operation and Development (OECD), the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization of the United Nations (WHO)) and third parties (the United States Environmental Protection Agency (US-EPA)) through the OECD's Global Portal to Information on Chemical Substances (eChemPortal). Thus, the EFSA's Chemical Hazards Database will provide an invaluable tool and source of information for all scientific advisory bodies involved in the risk assessment of chemicals at national (Member States), European and international level and avoid possible duplication of efforts in the area of chemical risk assessments worldwide.

The development of EFSA's Chemical Hazards Database has followed a stepwise approach namely:

(1) Establishment of an internal EFSA Task Force composed of staff members from all EFSA units involved in chemical risk assessment with consultation of experts from EFSA, ECHA, OECD, WHO and US-EPA with expertise in hazard databases and OECD harmonised templates (February-July 2011). Design of a preliminary data model for the database in collaboration with the SAS Unit, taking into consideration the recommendations of the Task Force and the results of the consultations with experts. The data model of the database has been designed using OECD international templates defining the fields and the corresponding pick lists of the database for chemical and hazard information using international standards (February-June 2011).

(2) Launching of a procurement procedure on 'Data collection and data entry for EFSA's Chemical Hazards Database'. In line with the signed contract, the contractor finalised the data model of EFSA's Chemical Hazards Database, submitted the pilot database through the Data Collection Framework (DCF) of EFSA for the CONTAM and NDA Panels (May 2012) and submitted all hazards data for the

NDA, CONTAM, FEEDAP, AFC, ANS and CEF Panels, together with an external report on the database (EFSA, 2013a).

(3) Launching of a procurement procedure on 'Further development and update of EFSA's Chemical Hazards Database'. In line with the signed contract, the contractor has collected all hazard data on pesticides assessed by EFSA since its creation. In addition, the contractor collected all hazard data on flavourings assessed by EFSA, since its creation, and updated all hazard data from EFSA's scientific outputs published between January 2013 and February 2014. The final external report was published on the EFSA website in May 2014 (EFSA, 2014).

(4) In parallel to the data collection and data entry, the SCER Unit is collaborating with the SAS and ITS Units, as well as with the Communications Directorate for the development of a web interface for both internal and external consultation of EFSA's Chemical Hazards Database.

In order to further develop and update EFSA's Chemical Hazards Database, for subsequent dissemination through the EFSA website and the eChemPortal of the OECD, the EFSA Scientific Committee and Emerging Risks (SCER) Unit launched an open Call for tenders for concluding a 4-year single Framework Contract on hazard data collection, entry and transfer into EFSA's Chemical Hazards Database from all current mandates and relevant EFSA opinions adopted by the EFSA Scientific Committee and Scientific Panels involved with chemical risk.

The specific objectives of the framework contract resulting from the present procurement procedure are as follows:

- Objective: Data collection, entry and monthly transfer on the DCF of all hazard data (related to human and animal toxicology, as well as, ecotoxicology) from all relevant EFSA opinions adopted by the EFSA Scientific Committee, Scientific Panels (as well as, the Pesticides Unit of EFSA) involved with chemical risk assessment from May 2014 onwards by using the data model provided in the call for tender.
- Objective: An External Scientific Report for each 12-month period, synthesising, analysing and summarising information on the activities performed, should be submitted to EFSA prior to the end of the respective Specific Contract.

The data are submitted in XML format to the Data Collection Framework (DCF) of EFSA in order to ensure that the dataset is compliant with EFSA IT standards and to enable future sharing of the data with EU Member States, other EU agencies (ECHA, EMA), international bodies (OECD, FAO/WHO) and third parties (US-EPA). Technical assistance regarding IT aspects to optimise the data transfer is provided by EFSA, in particular assistance in the transformation to XML. During the transfer process, the dataset is validated for data type, presence of mandatory fields and compliance with controlled terminologies. EFSA receives a dataset, which passes all validation phases.

This contract was awarded by EFSA to: S-IN, Soluzioni Informatiche srl, Via Ferrari 14 I-36100 Vicenza Italy – VAT registration number: IT 02397280245

Contractor: S-IN Soluzioni Informatiche

Contract: 'Further development and update of EFSA's Chemical Hazards Database'

Contract: OC/EFSA/SCER/2014/01

## 1.2. Interpretation of the Terms of Reference

The overall objective of the underlying project 'Further development and update of EFSA's Chemical Hazards Database' (EFSA, 2015) is the maintenance of the EFSA's Chemical Hazards Database by collecting **all hazard data included in the documents related to the following panels:** ANS (Food Additives and Nutrient Sources Added to Food), CEF (Food Contact Materials, Enzymes, Flavourings and Processing Aids), CONTAM (Contaminants in the Food Chain), FEEDAP (Additives and Products or Substances used in Animal Feed), PPR panel and PRAPeR unit (Plant Protection Products

and their Residues), NDA (Dietetic Products, Nutrition and Allergies). Substances which do not fall within the category of chemicals (e.g., microorganisms and enzymes) are excluded from the EFSA's Chemical Hazards Database. The project entails two activities:

1. Data collection, entry and monthly transfer on the DCF of all hazard data (related to human and animal toxicology, as well as ecotoxicology) from all relevant EFSA opinions adopted by the EFSA Scientific Committee, Scientific Panels (as well as the Pesticides Unit of EFSA) involved with chemical risk assessment in the past year.
2. An External Scientific Report for each 12-month period, synthesising, analysing and summarising information on the activities performed.

## 1.3. EFSA's Chemical Hazards Database

EFSA's Chemical Hazards Database is structured to map the intrinsic properties of the hazard data extracted from the EFSA documents (e.g., opinions, statements, conclusions) and it is organised to store the following information:

- Chemical identification: this section of the database describes the entity that has been assessed in the EFSA opinions or statements or conclusions, and it includes information on nomenclature, chemical formula, and structure (e.g., SMILES).
- Document details: this section contains the description of the document of interest, namely the EFSA opinion or statement or conclusion from which the data has been extracted and stored in the database.
- Hazard identification: the endpoint section of the database reports the critical study from which a reference point was identified to then derive the health-based guidance value or the margin of exposure values or the margin of safety values. More specifically, the database hosts toxicity data on human health, animal (non-target species) health, animal (target species) health, ecotoxicity (soil compartment), and ecotoxicity (water compartment).
- Hazard characterisation/risk characterisation: this section provides the health-based guidance value (hazard characterisation), margin of exposure or the margin of safety (risk characterisation) and environmental standards (hazard characterisation or risk characterisation).

The EFSA's Chemical Hazards Database includes hazard data originating from:

- NDA panel (vitamins and minerals, novel foods, dietetic products);
- CONTAM panel (contaminants in the food chain, contaminants in the feed chain);
- FEEDAP panel (feed additives-application linked to 1381/2003, feed additives-application under to 1381/2003, feed additives-other);
- AFC panel (food additives, food contact materials, nutrient sources, processing aids, favpurings);
- ANS panel (food additives, nutrient sources);
- CEF panel (food contact materials, food manufacturing processes, processing aids, flavourings);
- PPR panel and PRAPeR unit (pesticides).

EFSA opinions and statements related to NDA, ANS, CONTAM, FEEDAP, AFC (including flavourings), and CEF (including flavourings), PPR panel and PRAPeR unit (Conclusions on the peer review of pesticides risk assessment) and published until March 2016 were included in the database in previous procurements (EFSA, 2013a; EFSA, 2014; EFSA, 2015). EFSA opinions and statements published from

April 2016 by NDA, CONTAM, FEEDAP, ANS and CEF (including flavourings) until the first months of 2017 have been processed in the update together with all the conclusions on the peer review of pesticides risk assessment. Substances which do not fall within the category of chemicals (e.g., microorganisms and enzymes) have been excluded from the EFSA's Chemical Hazards Database.

The detailed description of the database (see Figure 1) and the corresponding procedures for data collection, collation and submission are provided in the previous reports 'Data collection and data entry for EFSA's chemical hazards database NP/EFSA/EMRISK/2011/01' (EFSA, 2013a) and 'Further development and update of EFSA's Chemical Hazards Database NP/EFSA/EMRISK/2012/01' (EFSA, 2014). The User Manual for the chemical hazards database is reported in Appendix A.

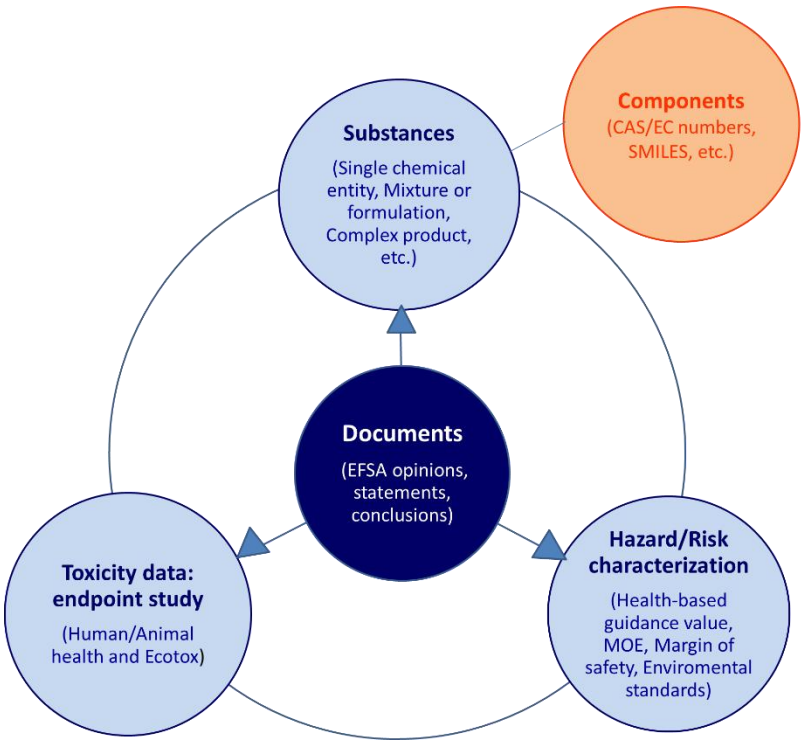


**Figure 1:** Qualitative overview of data organisation in the EFSA's Chemical Hazards Database. Connecting lines between boxes indicate existing relationships between data.

# 2. Methodologies

## 2.1. Data entry

A suitable ad hoc accessory IT platform (developed in-house) aids and supports the activity workflow entailed in the present assignment: data collection, entry and submission (see Figure 2).

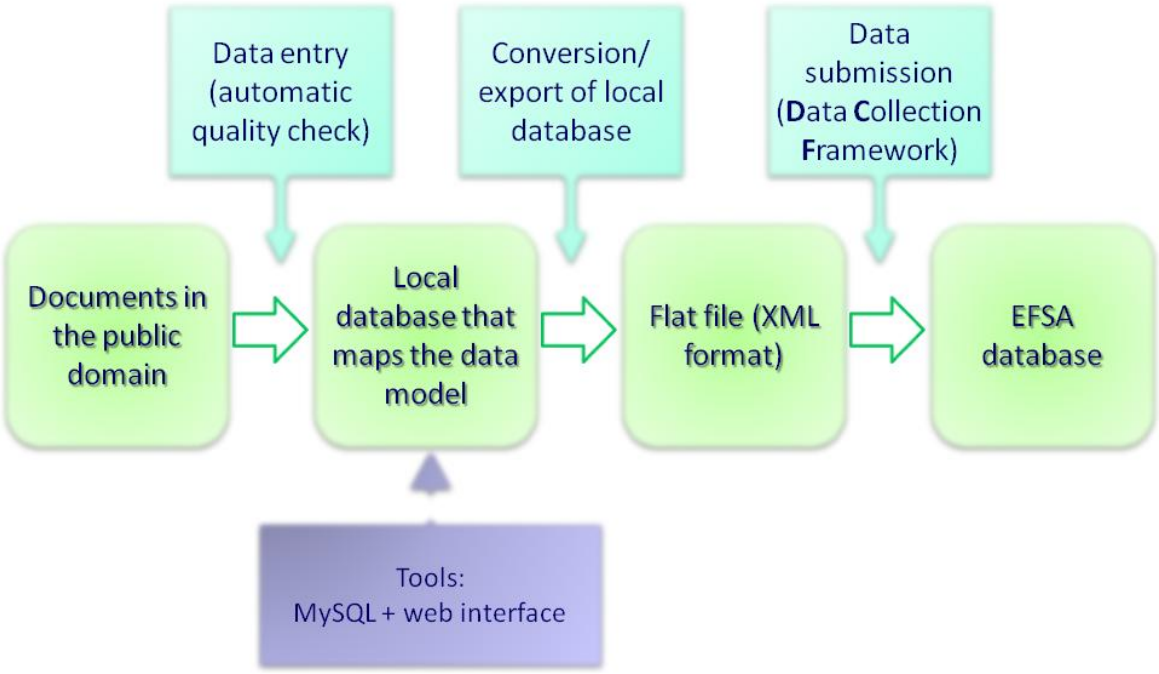


**Figure 2:** Overall workflow for data collection, entry and submission.

## 2.2. Quality check

A number of control mechanisms at the data entry level are automated to guarantee high quality of deliverables and reduce unintended errors (EFSA, 2015):

- Automatic verification of data quality at the data entry level.
- Manual revision of the collected data to be submitted.

## 2.3. Other tools, KNIME and ACD/Name

KNIME, pronounced [naim], is a modern data analytics platform that allows users to perform ETL (extract, transform, load) operations as well as sophisticated statistics and data mining. Its visual workbench combines data access, data transformation, initial investigation, predictive analytics and visualization. KNIME Desktop is open-source and available under GPL license. KNIME is extensively used to process data (e.g., cleaning, data integration) and intended to be uploaded automatically in the EFSA's Chemical Hazards Database. Notably, KNIME includes a number of tools that can deal with molecular structures.

The chemical identification of a substance (e.g., IUPAC name, SMILES, InChI) is sometime missing or poorly reported in the EFSA documents (e.g., the structure is reported as a drawing and not codified

according to standard formats such as SMILES). ACD/Name complements the identification of the chemicals whenever other publicly available resources (e.g., PubChem, ChemSpider) are not enough. ACD/Name generates chemical names according to IUPAC and CAS Index rules, converts names back to structures, and can easily handle challenging areas of nomenclature, such as biological molecules, organometallics, and polymers. The utilities that allow conversion of "name to structure" and "structure to name" prove to be vital in the data entry phase of the chemicals (including identification of stereoisomers).

# 3. Results

## 3.1. Quality check of historical data

A thorough quality check of all the data collected throughout the previous assignments was performed. Particular attention was devoted to the following data:

- Health-based guidance values of pesticides and corresponding critical studies (ADI, ArfD, and AOEL)
- Document conclusions on genotoxicity, mutagenicity and carcinogenicity according to the definitions adopted for the corresponding fields (see below).
- PNEC values with the corresponding compartment and organisms of interest.
- Route of exposure, especially focusing on:
    - Acute and short-term toxicity to birds;
    - Acute contact and dermal toxicity to bees;
    - Mammalian toxicity studies of pesticides;
    - Inhalation toxicity studies, when encountered.
- Study duration, according to the respective test type, as indicated in the opinion. In more details, the following study durations had been agreed for the corresponding test types:
    - ≤ 96 hours for acute toxicity studies;
    - > 90 days, > 3 months, > 13 weeks, and ≥ 1 year for chronic/long-term toxicity studies;
    - from 6 to 28 days for short-term toxicity;
    - from 27 to 90 days, from 1 to 3 months and from 4 to 14 weeks for sub-chronic toxicity studies;
    - variable duration for epidemiological studies.
- Unit of measurements, focusing on those used with a less frequency, e.g. µg/kg bw/day.
- Differences (e.g. effect threshold, unit of measurement, species, duration) noted in the same toxicity studies reported across several opinions published in different years and/or panels for a specific substance.

## 3.2. Clarification on definitions

Six main classification classes were used to report the assessment of mutagenicity (M), genotoxicity (G), and carcinogenicity (C) of chemicals made by EFSA and reported in the relative Opinions of flavourings, food and feed additives, and pesticides. These classes that map the conclusions of the authors on the given endpoint of interest are: Positive, Negative, Ambiguous, No data, Not determined, and Other.

Whilst the three terms Positive/Negative/Ambiguous are characterised by a straightforward meaning, there is a thin line of difference between the terms No data and No determined that could possibly lead to confusion or misinterpretation of the assigned classification as inserted into the Hazard Database. Consequently, a brief description of the categories No data and Not determined is reported below, in order to further clarify the adopted terminology. Lastly, also the category "Other" will be further elucidated:

- **No data.** This term is selected whenever one specific endpoint (e.g. M, G, C) is not mentioned or discussed in the Opinion for that specific substance. Using the endpoint of carcinogenicity, few examples are detailed below:

  i. if no carcinogenicity assessment was made for a pesticide, and this endpoint is also not mentioned in the Opinion, No data is assigned;

  ii. if no carcinogenicity studies of a flavouring compound are available in its CEF Opinion, but the Procedure was reported to be applicable to this flavouring substance (or to its group) since no safety concern was found (with no clear mention to what drives this safety concern), No data is yet assigned. It is very unlikely that the term of No data is used to describe the M and G endpoints of a flavouring, since genotoxicity is usually assessed in all CEF Opinions.

- **Not determined**. This term is selected in the following cases:

  i. when the endpoint under investigation (e.g. M, G, C) was discussed in the Opinion, but no clear conclusion could be reached, because of insufficient data;

  ii. when the endpoint under investigation (e.g. M, G, C) was discussed in the Opinion, but the conclusions do not report a clear assessment;

  iii. when a conclusive assessment of the endpoint at issue was performed in a past Opinion, but the outcome was not clearly reported in the Opinion under evaluation;

  iv. in the CEF Opinions, when it is stated that the Panel concluded that the genotoxicity data available do not preclude the evaluation of the candidate substances through the Procedure, even though no M or G studies were available and there is no discussion about the genotoxicity assessment and potential of the flavouring under investigation. On the other hand, if M or G studies were reported for that flavouring, alongside the above-mentioned EFSA's statement, a Negative classification is assigned to the substance for M and G.

  As this last point iv) is the most challenging and complicated among all of those above-reported, a case-by-case analysis is generally performed. For instance – in some CEF Opinions, substances are separated in chemical classes, where also a representative substance was chosen per chemical group. In these cases, it might be reported that the M or G or C classification assigned to this representative compound can also be extended to the whole group of chemicals, even though no M/G/C data are available for these target compounds. In this case, the term Negative is selected and used for all the substances within the assessed chemical group.

  It should be kept in mind that the use of No data and Not determined aims at reporting only what is clearly stated by EFSA in the Opinion under evaluation, to avoid any sort of (mis)interpretation of the available (or not) data and assessment provided in the EFSA's Opinions.

- **Other.** This term is generally used for special cases. In particular:

  i. when a substance is reported to induce co-carcinogenic effects;

  ii. when carcinogenic effects are deemed to be not relevant to human, e.g. when a substance is classified under the CLP Hazard statement H351 Suspected of causing cancer, which corresponds to the former risk phrase R40 Limited evidence of a carcinogenic effect;

  iii. when a substance is reported to be a likely threshold carcinogen.

## 3.3. Data content

The entire database includes data as extracted from the screening of nearly 1700 documents (opinions, statements, conclusions) published from 2003 to 2017; it holds more than 9000 assessements for about 4500 chemicals. About 90% of the chemical records are associated with a representative chemical structure. The assessements are classified based on well-defined categories (e.g. pesticides, flavourings, sensory additives, nutrient sources). For example, the repository stores: nearly 5600 assessments related to flavourings (about 2110 unique substances) as collected from the screening of 287 EFSA documents (opinions and statements); about 1190 assessments related to pesticides (about 1000 unique substances) as collected from the screening of 463 EFSA documents (conclusions); about 250 assessments related to food additives (about 200 unique substances) as collected from the screening of about 150 EFSA documents (opinions and statements); about 400 assessments related to sensory additives (396 unique substances) as collected from the screening of 60 EFSA documents (opinions and statements). Figures 3-9 and Tables 1-7 summarize the content of the database (including the historical data and the data collected in 2017). Data are also provided in excel format in Appendix B. Notably the Figures below highlight the number of documents published each year since 2003.

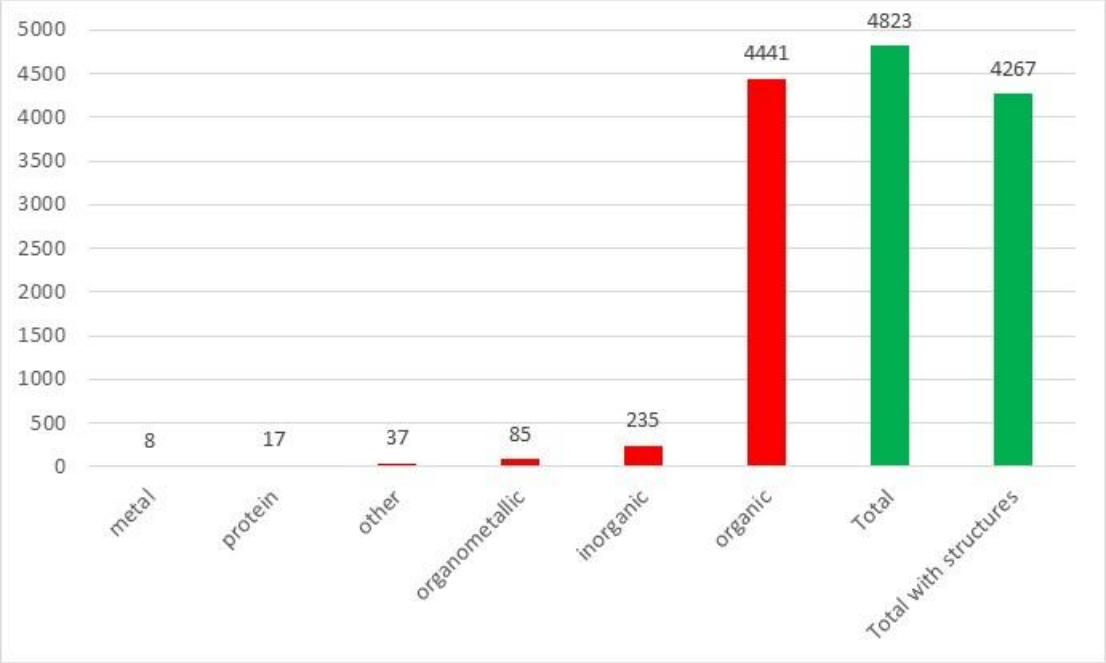


**Figure 3:** Number of components (and their classification) of the substances of the database. Structures in the form of SMILES (if available) are reported for components (exact or representative SMILES).

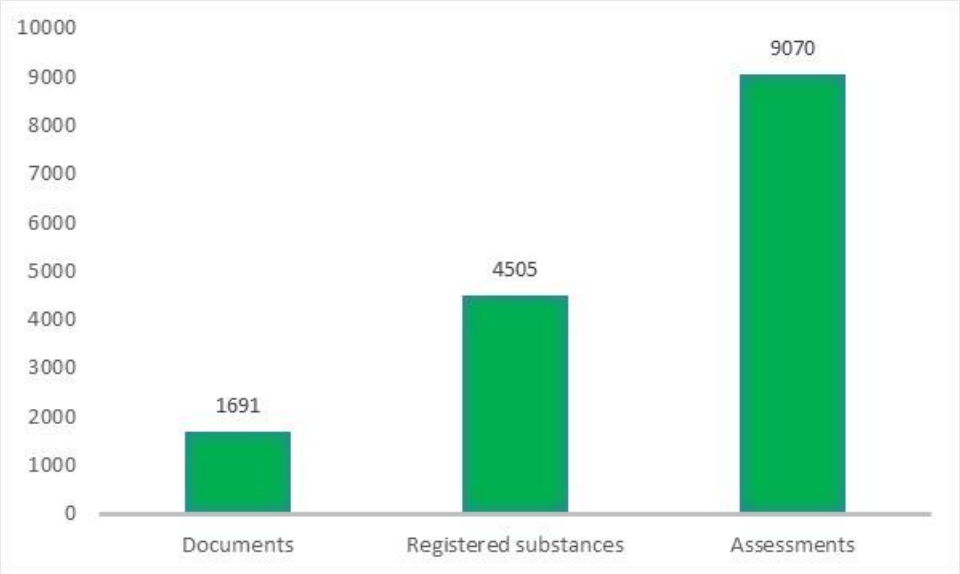


**Figure 4:** Number of documents (opinions/ statements/ conclusions) and substances (substances are formed by one or more components) registered in the database together with the number of assessments of a given substance as discussed in a given EFSA document.

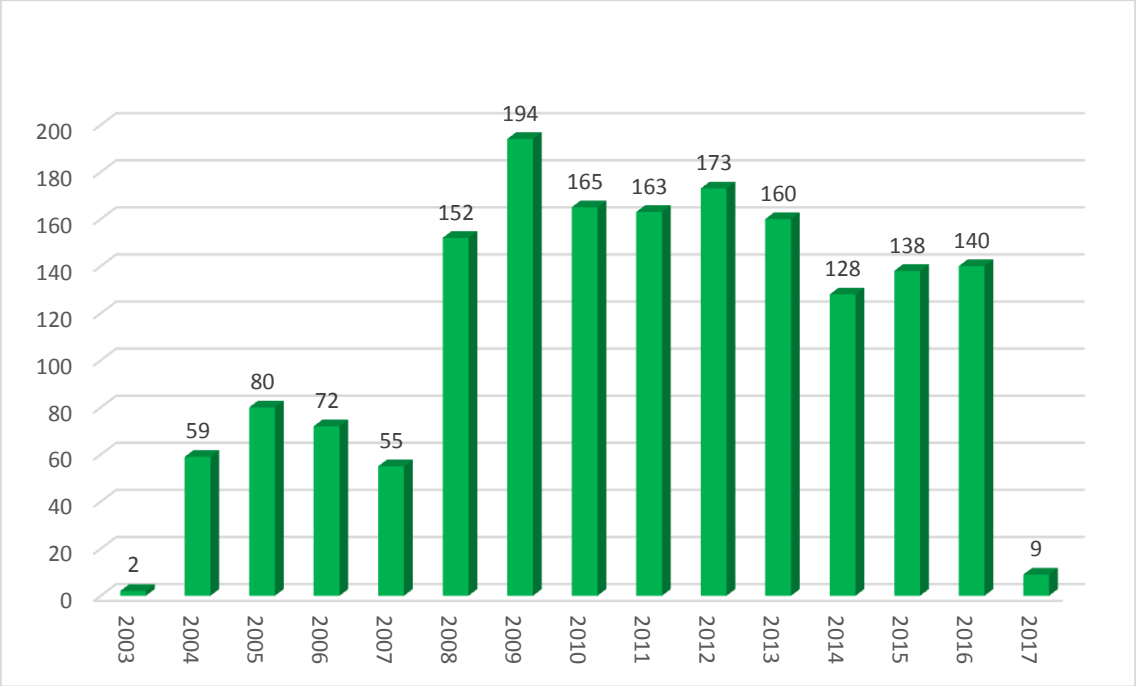


**Figure 5:** Classification of the documents in the database in terms of publication year.

**Table 1:** Classification of the EFSA's documents of the database (only documents for which at least one study exists) in terms of authors (EFSA Panels). The author "EFSA" corresponds to the conclusions on the peer review of the pesticide risk assessment.

| Year of publication | Author | Number of documents |
|---|---|---|
| 2003 | EFSA AFC | 2 |
| 2004 | EFSA AFC | 24 |
| 2004 | EFSA CONTAM | 9 |
| 2004 | EFSA FEEDAP | 17 |
| 2004 | EFSA NDA | 6 |
| 2004 | EFSA PPR | 3 |
| 2005 | EFSA | 15 |
| 2005 | EFSA AFC | 32 |
| 2005 | EFSA CONTAM | 12 |
| 2005 | EFSA FEEDAP | 10 |
| 2005 | EFSA NDA | 10 |
| 2005 | EFSA PPR | 2 |
| 2006 | EFSA | 36 |
| 2006 | EFSA AFC | 21 |
| 2006 | EFSA CONTAM | 4 |
| 2006 | EFSA FEEDAP | 7 |
| 2006 | EFSA NDA | 1 |
| 2006 | EFSA PPR | 3 |
| 2007 | EFSA | 9 |
| 2007 | EFSA AFC | 21 |
| 2007 | EFSA CONTAM | 10 |
| 2007 | EFSA FEEDAP | 11 |
| 2007 | EFSA NDA | 2 |
| 2007 | EFSA PPR | 2 |
| 2008 | EFSA | 37 |
| 2008 | EFSA AFC | 63 |
| 2008 | EFSA ANS | 11 |
| 2008 | EFSA CEF | 4 |
| 2008 | EFSA CONTAM | 22 |
| 2008 | EFSA FEEDAP | 11 |
| 2008 | EFSA GMO | 2 |
| 2008 | EFSA NDA | 4 |
| 2008 | EFSA PPR | 1 |
| 2009 | EFSA | 54 |
| 2009 | EFSA AFC | 20 |
| 2009 | EFSA ANS | 44 |
| 2009 | EFSA CEF | 45 |
| 2009 | EFSA CONTAM | 13 |
| 2009 | EFSA FEEDAP | 13 |
| 2009 | EFSA NDA | 3 |
| 2009 | EFSA PPR | 2 |
| 2010 | EFSA | 66 |
| 2010 | EFSA ANS | 34 |
| 2010 | EFSA CEF | 34 |
| 2010 | EFSA CONTAM | 11 |
| 2010 | EFSA FEEDAP | 13 |
| 2010 | EFSA GMO | 1 |
| 2010 | EFSA NDA | 8 |
| 2011 | EFSA | 35 |
| 2011 | EFSA ANS | 13 |
| 2011 | EFSA CEF | 67 |
| 2011 | EFSA CONTAM | 12 |
| 2011 | EFSA FEEDAP | 31 |

| Year of publication | Author | Number of documents |
|---|---|---|
| 2011 | EFSA NDA | 5 |
| 2012 | EFSA | 49 |
| 2012 | EFSA ANS | 12 |
| 2012 | EFSA CEF | 40 |
| 2012 | EFSA CONTAM | 10 |
| 2012 | EFSA FEEDAP | 54 |
| 2012 | EFSA NDA | 8 |
| 2012 | EFSA PPR | 1 |
| 2013 | EFSA | 42 |
| 2013 | EFSA AHAW | 1 |
| 2013 | EFSA ANS | 19 |
| 2013 | EFSA BIOHAZ | 1 |
| 2013 | EFSA CEF | 35 |
| 2013 | EFSA CONTAM | 4 |
| 2013 | EFSA FEEDAP | 52 |
| 2013 | EFSA NDA | 7 |
| 2013 | EFSA PPR | 1 |
| 2014 | EFSA | 38 |
| 2014 | EFSA ANS | 9 |
| 2014 | EFSA CEF | 34 |
| 2014 | EFSA CONTAM | 4 |
| 2014 | EFSA FEEDAP | 39 |
| 2014 | EFSA NDA | 4 |
| 2015 | EFSA | 32 |
| 2015 | EFSA ANS | 26 |
| 2015 | EFSA CEF | 30 |
| 2015 | EFSA CONTAM | 6 |
| 2015 | EFSA FEEDAP | 36 |
| 2015 | EFSA NDA | 8 |
| 2016 | EFSA | 34 |
| 2016 | EFSA ANS | 22 |
| 2016 | EFSA CEF | 22 |
| 2016 | EFSA CONTAM | 5 |
| 2016 | EFSA FEEDAP | 50 |
| 2016 | EFSA NDA | 7 |
| 2017 | EFSA | 1 |
| 2017 | EFSA ANS | 1 |
| 2017 | EFSA CEF | 3 |
| 2017 | EFSA CONTAM | 2 |
| 2017 | EFSA FEEDAP | 2 |

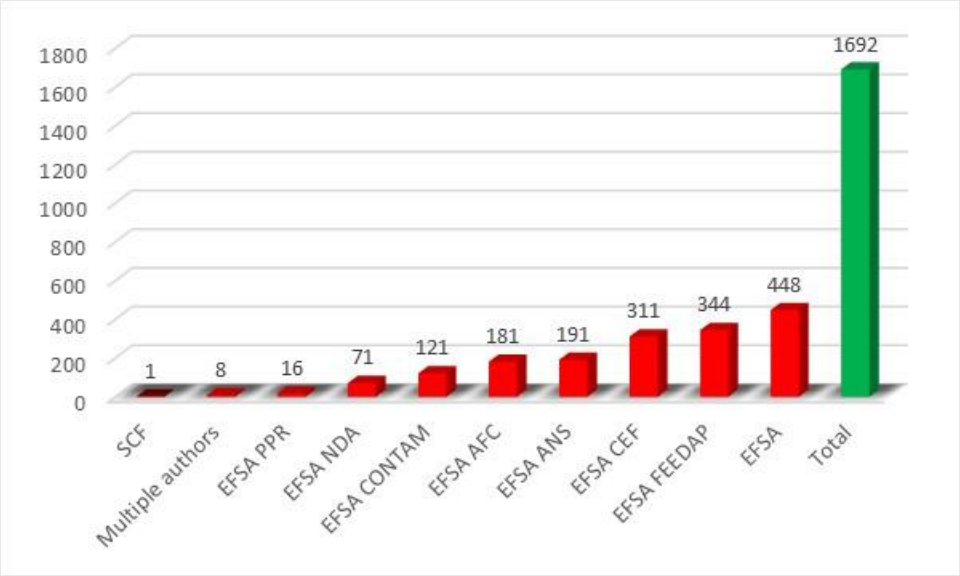


**Figure 6:** Classification of the EFSA's documents of the database in terms of their authors. The author "EFSA" corresponds to the conclusions on the peer review of the pesticide risk assessment.

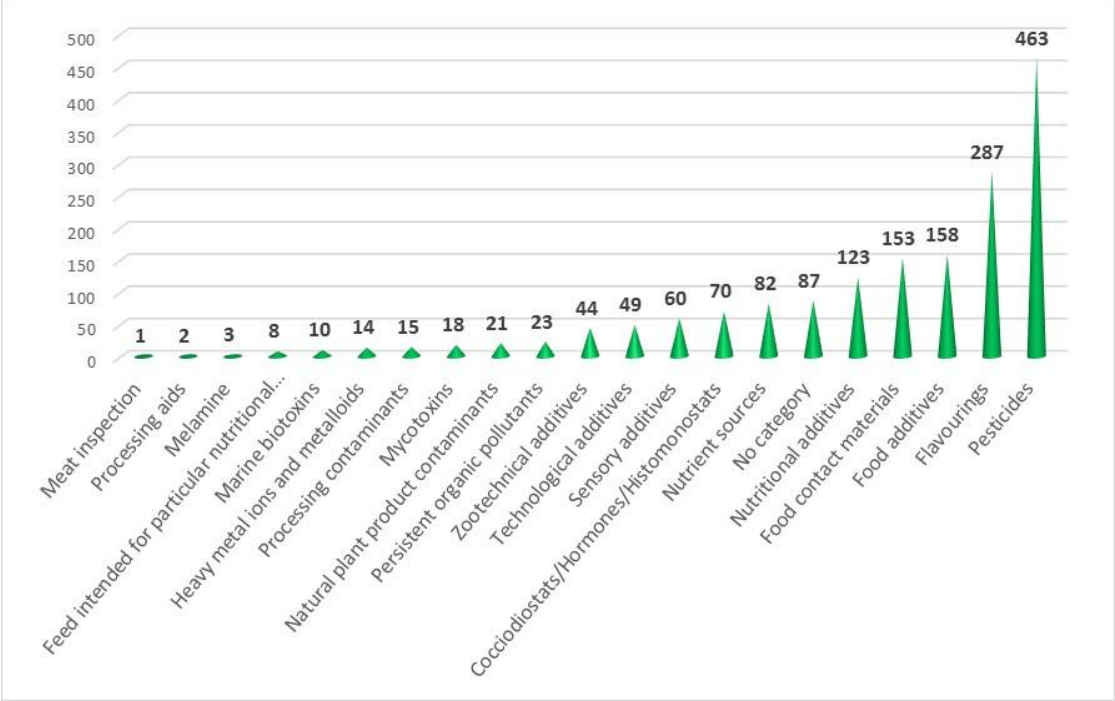


**Figure 7:** Classification of the EFSA's documents of the database in terms of subareas.

**Table 2:** Number of EFSA documents (opinions, statements, conclusions), number of assessments (assessment of a substance in a given opinion), and number of substances for the different subareas. Substances may be discussed and assessed in more than one document; a document of a given subarea may discuss and deal with more than one substance.

| Category | Number of documents | Number of assessments | Number of substances |
|---|---|---|---|
| Cocciodiostats/Hormones/Histomonostats | 70 | 103 | 50 |
| Feed intended for particular nutritional purposes | 8 | 17 | 17 |
| Flavourings | 287 | 5592 | 2111 |
| Food additives | 158 | 252 | 205 |
| Food contact materials | 153 | 374 | 323 |
| Heavy metal ions and metalloids | 14 | 25 | 16 |
| Marine biotoxins | 10 | 67 | 67 |
| Meat inspection | 1 | 31 | 31 |
| Melamine | 3 | 8 | 5 |
| Mycotoxins | 18 | 59 | 54 |
| Natural plant product contaminants | 21 | 32 | 27 |
| No category | 87 | 145 | 126 |
| Nutrient sources | 82 | 243 | 183 |
| Nutritional additives | 122 | 198 | 120 |
| Persistent organic pollutants | 23 | 100 | 91 |
| Pesticides | 463 | 1191 | 1005 |
| Processing aids | 2 | 7 | 7 |
| Processing contaminants | 15 | 99 | 94 |
| Sensory additives | 60 | 404 | 396 |
| Technological additives | 49 | 65 | 46 |
| Zootechnical additives | 44 | 58 | 39 |

**Table 3:** Classification of the registered substances in terms of the different subareas of the assessment. A substance may be classified as belonging to different subareas depending on the assessment approach discussed in a given document. For example, 1856 substances have been assessed **only** as flavourings; 2 substances have been assessed as both pesticides and flavourings in different documents; 7 substances have been assessed as both flavourings and processing contaminants in different documents.

| Category | Number of substances |
|---|---|
| Cocciodiostats/Hormones/Histomonostats | 47 |
| Cocciodiostats/Hormones/Histomonostats, Mycotoxins | 1 |
| Cocciodiostats/Hormones/Histomonostats, Natural plant product contaminants | 1 |
| Cocciodiostats/Hormones/Histomonostats, Processing contaminants | 1 |
| Feed intended for particular nutritional purposes | 4 |
| Feed intended for particular nutritional purposes, Food additives | 2 |
| Feed intended for particular nutritional purposes, Nutrient sources | 1 |
| Feed intended for particular nutritional purposes, Nutrient sources, Nutritional additives | 1 |
| Feed intended for particular nutritional purposes, Nutritional additives | 8 |
| Feed intended for particular nutritional purposes, Zootechnical additives | 1 |
| Flavourings | 1856 |
| Flavourings, Food additives | 6 |
| Flavourings, Food additives, Food contact materials, No category, Pesticides, Sensory additives, Technological additives, Zootechnical additives | 1 |
| Flavourings, Food additives, No category, Sensory additives, Technological additives | 1 |
| Flavourings, Food additives, No category, Technological additives | 1 |

| Category | Number of substances |
|---|---|
| Flavourings, Food additives, Sensory additives | 5 |
| Flavourings, Food additives, Technological additives | 1 |
| Flavourings, Food contact materials | 5 |
| Flavourings, Food contact materials, No category, Sensory additives | 1 |
| Flavourings, Food contact materials, Processing contaminants, Sensory additives | 1 |
| Flavourings, Natural plant product contaminants | 1 |
| Flavourings, Natural plant product contaminants, Processing contaminants | 1 |
| Flavourings, No category | 1 |
| Flavourings, Nutrient sources | 1 |
| Flavourings, Nutrient sources, Nutritional additives | 1 |
| Flavourings, Nutrient sources, Nutritional additives, Sensory additives | 2 |
| Flavourings, Nutrient sources, Sensory additives | 2 |
| Flavourings, Nutritional additives | 3 |
| Flavourings, Nutritional additives, Sensory additives | 4 |
| Flavourings, Pesticides | 2 |
| Flavourings, Pesticides, Sensory additives | 2 |
| Flavourings, Pesticides, Sensory additives, Zootechnical additives | 1 |
| Flavourings, Pesticides, Zootechnical additives | 1 |
| Flavourings, Processing contaminants | 7 |
| Flavourings, Processing contaminants, Sensory additives | 1 |
| Flavourings, Sensory additives | 198 |
| Flavourings, Sensory additives, Zootechnical additives | 3 |
| Flavourings, Technological additives | 1 |
| Flavourings, Technological additives, Zootechnical additives | 1 |
| Food additives | 123 |
| Food additives, Food contact materials | 9 |
| Food additives, Food contact materials, No category, Nutrient sources | 1 |
| Food additives, Food contact materials, Pesticides | 1 |
| Food additives, Natural plant product contaminants | 1 |
| Food additives, Natural plant product contaminants, Nutrient sources, Processing contaminants | 1 |
| Food additives, No category | 3 |
| Food additives, No category, Nutrient sources, Processing contaminants, Zootechnical additives | 1 |
| Food additives, No category, Nutritional additives, Pesticides | 1 |
| Food additives, No category, Processing contaminants, Sensory additives | 1 |
| Food additives, No category, Technological additives | 1 |
| Food additives, Nutrient sources | 2 |
| Food additives, Nutrient sources, Nutritional additives | 1 |
| Food additives, Nutrient sources, Nutritional additives, Zootechnical additives | 1 |
| Food additives, Nutrient sources, Processing contaminants | 1 |
| Food additives, Nutrient sources, Sensory additives | 2 |
| Food additives, Nutritional additives | 2 |
| Food additives, Pesticides | 1 |
| Food additives, Processing aids | 2 |
| Food additives, Processing contaminants | 7 |
| Food additives, Processing contaminants, Sensory additives | 1 |
| Food additives, Processing contaminants, Technological additives | 1 |
| Food additives, Sensory additives | 11 |
| Food additives, Technological additives | 11 |
| Food additives, Zootechnical additives | 2 |
| Food contact materials | 289 |
| Food contact materials, Heavy metal ions and metalloids, No category, Nutrient sources | 1 |
| Food contact materials, Meat inspection | 1 |
| Food contact materials, No category, Nutrient sources | 1 |

| Category | Number of substances |
|---|---|
| Food contact materials, No category, Nutrient sources, Pesticides | 1 |
| Food contact materials, Nutrient sources, Technological additives | 1 |
| Food contact materials, Nutritional additives | 2 |
| Food contact materials, Pesticides | 2 |
| Food contact materials, Processing contaminants | 4 |
| Food contact materials, Technological additives | 2 |
| Heavy metal ions and metalloids | 8 |
| Heavy metal ions and metalloids, Meat inspection, Persistent organic pollutants | 2 |
| Heavy metal ions and metalloids, Natural plant product contaminants, No category, Nutrient sources | 1 |
| Heavy metal ions and metalloids, No category | 1 |
| Heavy metal ions and metalloids, No category, Nutrient sources, Nutritional additives | 1 |
| Heavy metal ions and metalloids, Persistent organic pollutants | 2 |
| Marine biotoxins | 67 |
| Meat inspection | 24 |
| Meat inspection, No category | 1 |
| Meat inspection, No category, Nutrient sources, Nutritional additives | 3 |
| Melamine | 5 |
| Mycotoxins | 53 |
| Natural plant product contaminants | 18 |
| Natural plant product contaminants, No category | 1 |
| Natural plant product contaminants, Processing contaminants | 2 |
| No category | 88 |
| No category, Nutrient sources | 4 |
| No category, Nutrient sources, Nutritional additives | 4 |
| No category, Nutritional additives | 2 |
| No category, Sensory additives | 1 |
| No category, Technological additives | 2 |
| No category, Zootechnical additives | 1 |
| Nutrient sources | 136 |
| Nutrient sources, Nutritional additives | 4 |
| Nutrient sources, Nutritional additives, Processing contaminants | 1 |
| Nutrient sources, Persistent organic pollutants | 1 |
| Nutrient sources, Processing contaminants | 2 |
| Nutrient sources, Sensory additives | 1 |
| Nutrient sources, Technological additives | 2 |
| Nutrient sources, Zootechnical additives | 1 |
| Nutritional additives | 72 |
| Nutritional additives, Pesticides | 5 |
| Nutritional additives, Processing contaminants | 1 |
| Nutritional additives, Sensory additives | 1 |
| Persistent organic pollutants | 83 |
| Persistent organic pollutants, Pesticides | 3 |
| Pesticides | 978 |
| Pesticides, Processing contaminants, Sensory additives | 1 |
| Pesticides, Processing contaminants, Technological additives | 1 |
| Pesticides, Sensory additives | 3 |
| Pesticides, Technological additives | 1 |
| Processing aids | 5 |
| Processing contaminants | 50 |
| Processing contaminants, Sensory additives | 6 |
| Processing contaminants, Technological additives | 2 |
| Sensory additives | 143 |
| Sensory additives, Technological additives | 1 |
| Sensory additives, Zootechnical additives | 2 |

| Category | Number of substances |
|---|---|
| Technological additives | 15 |
| Zootechnical additives | 23 |

**Table 4:** Examples of multiple classifications for some substances. The number of substances together with their names are reported for a given combination of subareas. The complete list of multiple classifications is given in Appendix C.

| Multiple Classification | Number of substances | Substances |
|---|---|---|
| Flavourings, Food additives | 6 | 5-Hydroxymethyl-2-furfural, Butyl 4-hydroxybenzoate, Ethyl 4-hydroxybenzoate, L-Cysteine hydrochloride, Methyl methacrylate, Steviol glycosides |
| Flavourings, Pesticides | 2 | Dec-3-en-2-one, Tetradecan-1-ol |
| Flavourings, Pesticides, Sensory additives | 2 | 1,2-Dimethoxy-4-(prop-1-enyl)-benzene, Geraniol |
| Flavourings, Processing contaminants | 7 | Butane-1,3-diol, Butane-2,3-diol, Cyclohexanol, Cyclohexanone, Limonene, Propylene glycol, sec-Butyl acetate |
| Food additives, Pesticides | 1 | Calcium carbonate |
| Pesticides, Sensory additives | 3 | Allyl mercaptan, Methyl nonyl ketone, Trimethylamine hydrochloride |

**Table 5:** Number of toxicity studies (including critical studies used to derive health-based guidance values) in the database. The endpoint column lists the endpoints collected for a given class of endpoint study. The number of toxicity studies for a given endpoint is given in parenthesis. A substance may be assessed multiple times.

| Assessments | Number of toxicity studies | Endpoint |
|---|---|---|
| Animal (non-target species) health | 2819 | NOEL (296), dose level(42), LD50 (1392), LC50 (400), NOEC (294), NOAEL (341), LOEL (4), LOAEL (9), NOAEC (8), LDLo (1), LDD50 (Lethal Dietary Dose)(22), LC10 (2), LOEC (1), BMDL(1), NOEDD(1), NOAEDD(1), conc. Level(3), BMDL05 (1) |
| Animal (target species) health | 262 | LOEL (2), dose level(131), LOAEL (27), NOAEL (92), NOEL (4), LD50 (4), BMDL05 (1), BMDL10 (1) |
| Ecotox (soil compartment) | 1994 | NOEC (431), EC50 (35), LR50 (318), ER50(204), LC50 (364), LD50 (494), NOEL (8), dose level(114), EC25(2), conc. Level(2), LDD50 (Lethal Dietary Dose)(7), EC10 (12), EL50 (1), NOED(2) |
| Ecotox (water compartment) | 2579 | LC50 (479), EC50 (1147), NOEC (914), EC5(2), LOEC (1), EC10 (23), IC50 (2), NOEL (2), EL50 (1), NOAEC (4), EC15(2), LD50 (2) |
| Human health | 1802 | conc. Level(3), NOAEL (1416), NOEL (87), dose level(31), LOAEL (64), LD50 (8), T5(1), BMDL10 |

| Assessments | Number of toxicity studies | Endpoint |
|---|---|---|
| | | (43), BMDL01(7), LOEL (3), TEF(75), BMDL05 (18), NOAEC (3), BMDL(2), RPF(40), T25 (1) |

**Table 6:** Summary of the hazard/risk characterization records with focus on populations.

| Population | Types of hazard/risk assessment | Total number of records |
|---|---|---|
| Human | ADI , ARfD , MOE , TDI , critical study not identified, group TDI, margin of safety, RfD, TTC Cramer Class I, TTC Cramer Class II, TTC Cramer Class III, group ADI, ADI, provisional, MTDI, TWI, UL , TDI, provisional (PTDI), TDI, provisional maximum (PMTDI), TWI, provisional (PTWI), maximum safe intake/maximum safe concentration in feed, TTC genotoxicity, group ARfD, OSL, UL, provisional (PUL), MoBB, group TWI, AAOEL, AOEC, provisional, AOEL , AOEL, provisional | 10995 |
| Terrestrial Vertebrates | margin of safety, maximum safe intake/maximum safe concentration in feed, maximum tolerated level/dose, critical study not identified, TDI , TDI, provisional (PTDI), TTC Cramer Class I, TTC Cramer Class II, TTC Cramer Class III | 2733 |
| Aquatic Vertebrates | margin of safety, maximum safe intake/maximum safe concentration in feed, critical study not identified, maximum tolerated level/dose, TTC Cramer Class I, TTC Cramer Class II, TTC Cramer Class III | 476 |
| Aquatic Invertebrates | margin of safety | 2 |
| Soil compartment | PNEC | 46 |
| Aquatic compartment | PNEC | 57 |
| Terrestrial Plants | PNEC | 1 |

**Table 7:** Summary of the hazard/risk characterization records with focus on the assessment type. The total number of assessments for each assessment type is reported with the total number of unique substances. The population of the hazard/risk assessment is also reported.

| Assessment type | Total number of assessments | Total number of unique substances | Population |
|---|---|---|---|
| AAOEL | 5 | 5 | Human |
| ADI | 711 | 513 | Human |
| ADI, provisional | 6 | 5 | Human |
| AOEC, provisional | 3 | 2 | Human |
| AOEL | 397 | 340 | Human |
| AOEL, provisional | 5 | 3 | Human |
| ARfD | 445 | 357 | Human |
| MOE | 162 | 36 | Human |
| MTDI | 3 | 3 | Human |
| MoBB | 16 | 7 | Human |

| Assessment type | Total number of assessments | Total number of unique substances | Population |
|---|---|---|---|
| OSL | 1 | 1 | Human |
| PNEC | 104 | 53 | Soil compartment, Aquatic compartment, Terrestrial Plants |
| RfD | 4 | 3 | Human |
| TDI | 66 | 53 | Human, Terrestrial Vertebrates |
| TDI, provisional (PTDI) | 14 | 11 | Human, Terrestrial Vertebrates |
| TDI, provisional maximum (PMTDI) | 14 | 6 | Human |
| TTC Cramer Class I | 3161 | 1246 | Human, Terrestrial Vertebrates, Aquatic Vertebrates |
| TTC Cramer Class II | 1510 | 503 | Human, Aquatic Vertebrates, Terrestrial Vertebrates |
| TTC Cramer Class III | 702 | 318 | Human, Aquatic Vertebrates, Terrestrial Vertebrates |
| TTC genotoxicity | 2 | 2 | Human |
| TWI | 20 | 9 | Human |
| TWI, provisional (PTWI) | 6 | 5 | Human |
| UL | 303 | 41 | Human |
| UL, provisional (PUL) | 3 | 1 | Human |
| critical study not identified | 1434 | 889 | Human, Terrestrial Vertebrates, Aquatic Vertebrates |
| group ADI | 39 | 30 | Human |
| group ARfD | 2 | 2 | Human |
| group TDI | 23 | 19 | Human |
| group TWI | 6 | 3 | Human |
| margin of safety | 2737 | 1066 | Human, Terrestrial Vertebrates, Aquatic Vertebrates, Aquatic Invertebrates |
| maximum safe intake/maximum safe concentration in feed | 2312 | 326 | Human, Terrestrial Vertebrates, Aquatic Vertebrates |
| maximum tolerated level/dose | 94 | 16 | Terrestrial Vertebrates, Aquatic Vertebrates |

# 4. Conclusions

The EFSA's Chemical Hazards Database includes summary hazard data originating from scientific opinions, statements and conclusions published by:

- NDA panel (vitamins and minerals, novel foods, dietetic products);
- CONTAM panel (contaminants in the food chain, contaminants in the feed chain);
- FEEDAP panel (feed additives-application linked to 1381/2003, feed additives-application under to 1381/2003, feed additives-other);
- AFC panel (food additives, food contact materials, nutrient sources, processing aids, falvourings);
- ANS panel (food additives, nutrient sources);
- CEF panel (food contact materials, food manufacturing processes, processing aids, flavourings);
- PPR panel and PRAPeR unit (pesticides).

The database is constantly updated and maintained and hazard data together with chemical information are added as collected from the documents (opinions, statements, conslusions) published by EFSA. Substances which do not fall within the category of chemicals (e.g., microorganisms and enzymes) are generally excluded from the EFSA's Chemical Hazards Database. An extract of the collected data is available in Appendix B in the format of excel sheets. The database, which is structured to map the intrinsic properties of the hazard data taken from the EFSA documents (e.g., opinions, statements, conclusions), is organised to store the following features:

- Chemical identification: this section of the database describes the entity that has been assessed in the EFSA opinions or statements or conclusions, and it includes information on nomenclature, chemical formula, and structure (e.g., SMILES).
- Document details: this section contains the description of the document of interest, namely the EFSA opinion or statement or conclusion from which the data has been extracted and stored in the database.
- Hazard identification: the endpoint section of the database reports the critical study from which a reference point was identified to then derive the health-based guidance value or the margin of exposure values or the margin of safety values. More specifically, the database hosts toxicity data on human health, animal (non-target species) health, animal (target species) health, ecotoxicity (soil compartment), and ecotoxicity (water compartment).
- Hazard characterisation/risk characterisation: this section provides the health-based guidance value (hazard characterisation), margin of exposure or the margin of safety (risk characterisation) and environmental standards (hazard characterisation or risk characterisation).

Currently the update and maintenance of the EFSA's Chemical Hazards Database is carried out by manual data extraction from the pdf documents and manual data insertion (with aid of a proper IT platform) in the repository. In the future, a more automated procedure could be envisaged by developing proper table templates to be published together with the EFSA opinions, statements and conclusions. Table templates mirroring the data structure of the database may guide the opinion's authors to summarise the relevant hazard data (e.g. critical study, HBGV for the substance of interest) thus providing all the requested details for the database in authoritative and exhaustive ways using a well-defined onthology. Such pdf tables could then be uploaded in the database with an automated procedure.

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# Abbreviations

| | |
|---|---|
| **ADI** | Acceptable Daily Intake |
| **AFC** | Former EFSA panel on food Additives, Flavourings, processing aids and materials in Contact with food |
| **ANS** | EFSA panel on food Additives and Nutrient Sources added to food |
| **ARfD** | Acute Reference Dose |
| **BMD** | Benchmark Dose |
| **BMDL** | Benchmark Dose Level |
| **CAS** | Chemical Abstract Service |
| **CEF** | EFSA panel on food Contact materials, Enzymes, Flavourings and processing aids |
| **CONTAM** | EFSA panel on Contaminants in the food chain |
| **DCF** | Data Collection Framework |
| **EER** | Enhanced Entity-relationship |
| **FEEDAP** | EFSA panel on additives and products or substances used in animal feed. |
| **InChI** | IUPAC International Chemical Identifier |
| **LOAEL** | Lowest observed adverse effect level |
| **LOEL** | Lowest observed effect level |
| **MeSH** | Medical Subject Headings |
| **MOE** | Margin of Exposure |
| **NDA** | EFSA panel on Dietetic products, Nutrition and allergies including vitamins and minerals |
| **NOAEL** | No Observed Adverse Effect Level |
| **NOEC** | No Observed Adverse Effect Concentration |
| **NOEL** | No Observed Effect Level |
| **OECD** | Organisation for Economic Co-operation and Development |
| **PNEC** | Predicted No Effect Concentration |

| | |
|---|---|
| **PPR** | The Pesticides Unit and the Panel on Plant Protection Products and their Residues |
| **SMILES** | Simplified Molecular Input Line Entry System |
| **SOP** | Standard Operating Procedure |
| **TDI** | Tolerable Daily Intake |
| **TEF** | Toxicity Equivalency Factor |
| **TTC** | Threshold of Toxicological Concern |

# Appendix A – User Manual of the EFSA's Chemical Hazards Database

The following paragraphs provide a description and a guidance on the procedure to collect data from the EFSA documents and on the protocols to compile the EFSA's Chemical Hazards Database (EFSA, 2013a; EFSA, 2014). Original names of the fields and field types (e.g., string, number) are reported in parenthesis. Some terms of the catalogues/picklists are also reported here with the corresponding definitions. EFSA owns and holds all the most recent catalogues and definitions.

## A.1. Content of the EFSA's Chemical Hazards Database

The EFSA's Chemical Hazards Database hosts the following records:

- Substances that are discussed in the EFSA documents (i.e., opinions, statements, conclusions); substances are included together with information on nomenclature, chemical formula and structure.
- Documents reporting the substance hazard assessment: each record summarises the corresponding bibliographic details.
- Details of the critical study/toxicity study (endpoint section of the database) used to either derive health-based guidance values, margin of exposure values for human health, reference point or toxicity value for animal health or environmental standards or margin of safety values for human or animal health.
- Details on genotoxicity (including mutagenicity) if the substance is genotoxic (or mutagenic).
- Health-based guidance values including TTC (hazard/risk characterisation section of the database).
- Margin of exposure, margin of safety and environmental standard values (hazard/risk characterisation section of the database).

## A.2. General remarks

While compiling the database, special care should be paid to following issues:

- Special characters: care should be paid to special characters including:
  - Carriage return (i.e., setting a new line in the free text fields) should be avoided unless necessary.
  - Special characters such as α, β, γ, are preferably reported as alpha, beta, gamma, respectively.
  - Other special characters (e.g., the trademark character ®) are either omitted (e.g., the trademark character ® is usually omitted) or reported in a more extensive way.

- Identification numbers (IDs): an ID number is allocated to each record inserted in the database. For example, each document is associated with an ID; similarly each term of a catalogue list is associated with an ID. The ID numbers are unique for each group of records and are usually automatically assigned by the system during the data entry process.

- Fields that are not mandatory (see EFSA, 2013a) are left blank if the document does not provide the corresponding relevant information. Mandatory fields report terms such as "No data"/"Not applicable"/"Not reported" if the document does not provide the corresponding relevant information.

- Many fields can host only a single value/term. Only in some cases multiple values are allowed.

## A.3. Bibliographic details

The details of the documents (EFSA opinions, EFSA statements, EFSA conclusions) containing relevant data to be entered in the EFSA's Chemical Hazards Database are stored in the opinion section. The bibliographic details include:

- Title of the document (title, free text): the title of the document as reported in the published document (PDF file) is reported. Information such as the header "SCIENTIFIC OPINION" or the panel author(s) is generally not included in the title field.

- Reference type (op_type, picklist): whether the document is an EFSA opinion or statement or conclusion on Pesticides Peer Review is reported.

- Owner (owner, picklist): the sponsor body of the report is identified; for all the documents inserted in the EFSA's Chemical Hazards Database, the value has always been set to EFSA.

- Adoption Date (adoption_date, date): the adoption date of the opinion/statement/conclusion is reported. The format is yyyy-mm-dd. The date is taken from the EFSA register of questions website.

- Publication Date (publication_date, date): the publication date of the opinion/statement/conclusion is reported. The format is yyyy-mm-dd. The date is taken from the EFSA register of questions.

- Bibliographic source (doi, free text): the reference Doi is reported. The Doi is taken from the EFSA register of questions (e.g., doi:10.2903/j.efsa.2008.730).

- Status 1 (status1, picklist): the status of the document (current or deprecated) is reported. This is also the status of health guideline value included. For the current assignment the status is always current.

- Status 2 (status 2, picklist): some documents are only partially disclosed (only summary is available) and this field reports whether the opinion is disclosed, undisclosed or partially disclosed.

- Regulation (regulation, picklist): the regulation triggering the assessment of the opinion is reported. Only one regulation can be entered and sometimes a choice must be made on which regulation to report if more than one regulation is associated with the assessment described in the document. The most significant regulation is chosen and it may happen that the choice is skewed by the data-entry personnel. The general approach is to identify the regulation from the data that can be downloaded from the "Register of Questions" (e.g., the subarea field of the downloaded csv usually reports the corresponding regulation). Alternatively, the regulation is sought in the Abstract and/or Summary of the EFSA document. If no regulation is mentioned in these sections, then the regulation is chosen from the Background section of the opinion. The Terms of Reference section of the opinion is consulted at last. Notably, many opinions are associated with Regulation 178/2002 that lays down the general principles and requirements of food law, establishes the European Food Safety Authority, and lays down procedures in matters of food safety. The Regulation 178/2002 is assigned to documents that do not mention any regulation in the text.

- Author (panel, picklist): This field reports the panel (or panels) who authored the opinion. If the author is ambiguous, the corresponding author as cited in the opinions is chosen. More than one author can be entered and it can be chosen from:

- EFSA NDA panel: vitamins and minerals.
- EFSA PRAPeR panel: plant protection products and their residues.
- EFSA CEF panel: food contact materials, enzymes, flavourings and processing aids.
- EFSA ANS panel: food additives and nutrient sources added to food.
- EFSA FEEDAP panel: additives and products or substances used in animal feed.
- EFSA CONTAM panel: contaminants in the food chain.
- EFSA AFC panel: former panel on food additives, flavourings, processing aids and materials in contact with food.
- EFSA, that is used for Conclusions on Pesticides Peer Review.

- Question (question, picklist). The question number associated with the opinion (as reported in the EFSA webpage of the document or csv file downloaded from the EFSA register of questions) is reported. This field may host more than one value and the corresponding picklist is continuously refreshed. Example: EFSA-Q-2007-140.

## A.4. Substance details

A substance registered in the EFSA's Chemical Hazards Database is every entity (chemical entity or product) that is assessed in an EFSA opinion/statement/conclusion; for each substance registered in the database one or more of the following information is reported in the opinions and thus entered in the database:

- Hazard identification: the EFSA document defines a critical study from which a reference point (e.g., NOAEL, LOAEL, BMDL) is identified for that substance. The reference point is described in the EFSA documents and used to derive health-based guidance values, margin of exposure values for human health, margin of safety values for human or animal health. The opinion may also discuss a reference point or toxicity values for animal health or environmental standards. Likewise the opinion may discuss mutagenicity, and/or genotoxicity and/or carcinogenicity of the substance.

- Hazard characterisation/risk characterisation: the EFSA document provides a health-based guidance value, margin of safety values or margin of exposure values, and/or environmental standards.

A substance is registered and included in the database if one or more of the points listed above are discussed by the authors of the EFSA document. When only information regarding exposure is provided, the substance is not registered and the corresponding opinion is not included in the database. In summary, registered substances are entities which have been assessed for its hazards in the EFSA documents.

It should be noted that the substance is either a chemical entity (compound or mixture or formulation) or a food product (as in the case of the NDA opinions). A substance may also be a group of compounds undergoing a group assessment, as for example the saxitoxin group (EFSA, 2009b) whose components are characterized by a Toxicity Equivalency Factor (TEF) or the caramels group for which a group ADI is provided. In general, substances which do not fall within the category of chemicals (e.g., microorganisms and enzymes) have been excluded from the EFSA's Chemical Hazards Database. Complex products (e.g., natural products) are exceptions included in the database. The relevant EFSA documents usually assess one of the following (chemical) entities (i.e., substances):

- A defined chemical compound
- In general an element contained in food
- A group of chemical compounds

- A food product (e.g., chia seeds)

It should be noted that the nature of the substances registered in the EFSA's Chemical Hazards Database is different from the substance definition according to article 3 of REACH: "A chemical element and its compounds in the natural state or obtained by any manufacturing process, including any additive necessary to preserve its stability and any impurity deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition."

The substance assessed in the relevant EFSA documents (and that qualifies for inclusion in the EFSA hazards database, see above) is described by information on the molecules that are either retrieved from the corresponding EFSA documents or complemented with chemical data obtained from publicly available resources such as:

- ChemIDPlus: http://chem.sis.nlm.nih.gov/chemidplus/
- PubChem: https://pubchem.ncbi.nlm.nih.gov/
- ChemSpider: http://www.chemspider.com/
- ECHA CHEM: https://echa.europa.eu/information-on-chemicals

The following details are usually reported for a substance registered in the database:

EFSA substance ref number (rns_efsa, picklist). The substance is associated whenever possible to the PARAM substance definition as provided in the standard sample description (EFSA, 2013b). The EFSA DB substance is matched with the EFSA PARAM substance and if the matching cannot be identified, the "not in the list" PARAM value is selected.

Substance name (name, free text). The substance name is taken from the substance description of the corresponding documents. If multiple names for the same substances are reported, the most specific (or most common) is reported. No synonyms are foreseen for the substance name. The name of the substance follows these standard operating procedures:

- The name starts with a capital letter.
- If the substance is the element for which an overall assessment is made, then the element is reported as: Element (total) as for example Calcium (total). This type of substance is usually defined as group (see below).
- If the substance is a group (or a general mixture) including well-defined components, the substance is named specifying the components when this helps to distinguish it from similar entities as for example: "Organotin compounds (including n-octyltin compounds)" or "Organotin compounds (including TBT, DBT, TPT and DOT)".
- Substance Type (sub_type, picklist). An EFSA DB substance is tagged according to a classification resembling the one reported by the EFSA Panel on Food Additives and Nutrient Sources added to Food (EFSA, 2012b):

    - Single chemical entity. Chemical entity that cannot be clearly decomposed in terms of other defined chemical entities. The component of a single entity is the substance itself. The single entity includes single substances (e.g., sorbic acid, sodium ascorbate, propyl gallate, EFSA, 2012b).
    - Mixture or formulation. Substance that can be decomposed in terms of different chemical entities which are described in the component table. The components of a mixture or formulation are the chemical compounds forming the mixture or formulation.
    - Complex product: derived from botanical sources. Products or complex mixtures derived from botanical sources (e.g., steviol glycosides from Stevia, or rosemary extracts, EFSA, 2012b).

- Complex product: microorganisms or derived from microorganisms. Microorganisms or products (or complex mixtures) derived from microorganisms.
- Complex mixtures: not derived from botanical sources. Complex mixtures not derived from botanical sources (e.g., mineral hydrocarbons, beeswax, shellac, EFSA, 2012b).
- Polymer. Substances that are polymers (e.g., e.g., anionic methacrylate, agar, alginate and xanthan gums, pectins, modified starches, celluloses, polyvinylpyrrolidone, EFSA, 2012a).
- Group. A group of substances undergoing a group assessment (e.g., assessments involving TEF or group ADI). A substance that is defined as a group may also fulfill the definition of complex mixture. The classification of group or complex mixture strongly depends on the interpretation of the information provided on the substance and on the type of assessment described in the opinion. The group may be of two types:
    - Group, closed: the components of the group are well defined, and the assessment refers only to the well defined components of the closed group. An example is PAH2 which is composed only by Benzo[a]pyrene and Chrysene (EFSA, 2008a).
    - Group, open: the components of the group are not well defined and the assessment refers to the generic definition of this group. The restriction of an open group may be achieved by other means of the database, as for example the group equivalency concept (see below).

- EC ref number (ecSubInventEntryRef, free text). The EC reference number of the substance is reported. The EC number is retrieved from the EFSA documentation or by browsing publicly available databases such as: ECHA CHEM or ChemIDPlus. From ChemIDplus other databases can be reached for cross-checking (e.g., PubChem (Bolton, 2008)).

- CAS number (casNumber, free text). The Chemical Abstract Service registration number of the substance is reported. The CAS number is retrieved from the EFSA documentation or by browsing publicly available databases such as: ECHA CHEM, ChemIDPlus. From ChemIDPlus other databases can be reached for cross-checking (e.g., PubChem (Bolton, 2008)).

- Substance description (description, free text). Summary of the substance description as derived from opinions. The description may usually be amended and refined when the substance is selected multiple times to report the toxicity and hazard data.

Importantly, before entering any new substance, the user checks whether the same substance has already been registered in the database searching the substance repository by name, CAS number or more rarely EC number. This procedure is vital to avoid duplicates.

## A.5. Components

The substance is entered in the database with reference to its chemical components (whenever possible) which are then individually described. The EFSA database component (EFSA DB component) is any chemical entity that is identified as part of the EFSA DB substance. Chemical entity usually refers to a specific chemical compound; they may also be a broader chemical species (e.g., tocopherols) or complex mixtures/products (see below).

The details of the chemical identification of the EFSA DB components may not be readily available in the EFSA documents, and the data is then retrieved from publicly available resources such as ChemSpider and ChemIDPlus; from ChemIDPlus other databases can be reached for cross-checking (e.g., PubChem (Bolton, 2008)):

- ChemIDPlus: http://chem.sis.nlm.nih.gov/chemidplus/
- PubChem: https://pubchem.ncbi.nlm.nih.gov/
- ChemSpider: http://www.chemspider.com/
- ECHA CHEM: https://echa.europa.eu/information-on-chemicals

In the special case of substances which are defined as "Group" (see above), the components are intended as components of the group. For example the saxitoxin group (the saxitoxin group is entered as a substance) is made up by saxitoxin (synonym: STX), neosaxitoxin (synonym: NEO), gonyautoxin 2 (synonym: GTX2), gonyautoxin 4 (GTX4) and other compounds (EFSA, 2009b).

The component record is described by the following fields:

- EFSA component ref number (rnc_efsa, picklist). The component is associated with the PARAM substance definition as provided in the standard sample description (EFSA, 2013b). The chemical component is matched with the EFSA PARAM substance and if the component is not available, the "not in the list" PARAM value is selected.

- Component name (name, free text). The component name as derived from the corresponding EFSA documents is reported. If more than one name is reported in the opinion (excluding IUPAC name), then the most common or most specific name is reported as component name.

- Component type (com_type, picklist). The chemical entities included as components of the EFSA DB substance are classified according to a number of chemical types. The majority of the chemical types are extracted from the OECD picklist (OECD, 2012):

    - Element: the chemical is an element (see element definition in the substance type).
    - Inorganic: the chemical is classified as inorganic.
    - Metal: the chemical is a metal (note: if it is a metallic element, then the chemical is classified as element and not metal). Not applicable: the chemical description is not possible within this classification scheme.
    - Organic: the chemical is classified as organic.
    - Organometallic: the chemical is classified as organometallic.
    - Protein: the chemical is a protein (enzyme).
    - Other: the chemical is not described by the present classification scheme.

- EC ref number (ecSubInventEntryRef, free text). The EC reference number of the component is reported. The EC number is retrieved from the EFSA documentation or by browsing publicly available databases such as: ECHA CHEM, ChemIDPlus. From ChemIDplus other databases can be reached for cross-checking (e.g., PubChem (Bolton, 2008)).

- CAS number (casNumber, free text). The Chemical Abstract Service registration number of the component is reported. The CAS number is retrieved from the EFSA documentation or by browsing publicly available databases such as: ECHA CHEM, ChemIDPlus. From ChemIDplus other databases can be reached for cross-checking (e.g., PubChem (Bolton, 2008)).

- IUPAC name (iupacName, free text). The IUPAC (International Union of Pure and Applied Chemistry) name is reported. The IUPAC name is retrieved from the EFSA documentation or by browsing publicly available databases, in particular PubChem (Bolton, 2008). Other tools can be used to generate the name of the chemical such as ACD/Name.

- Molecular formula (molecularFormula, free text). The molecular formula is reported. The molecular formula is retrieved from the EFSA documentation or by browsing publicly available databases in particular PubChem (Bolton, 2008).

- Structure shown of component (com_structureShown, picklist). This field is used to specify the nature of the structure as compared to the component name; for example: the structure of the compound itself, the structure of the monomer if the compound is a polymer, the structure of an isomer, or no structure at all.

- SMILES notation (smilesNotation, free text). The SMILES (Simplified Molecular Input Line Entry Specification) for the compound is reported. The coded structure is retrieved from the EFSA documentation (very rarely), by browsing publicly available databases such as: PubChem, ChemIDPlus and ChemSpider. The structure code can be also obtained by manually drawing the structure in popular chemical drawing programs that allow for the SMILES generation.

- SMILES notation source (smilesNotationSource, picklist). The source used to get the SMILES notation is reported. The source can be for example PubChem or ChemIDPlus.

- International Chemical Identifier (inchi, free text). The International Chemical Identifier (InChI) is reported. The coded structure is retrieved from the EFSA documentation (very rarely), by browsing publicly available databases such as: PubChem, ChemIDPlus and ChemSpider. The structure code can also obtained by manually drawing the structure in popular chemical drawing programs that allow for the InChI generation.

- InChI notation source (inchi_notationSource, picklist). The source used to retrieve the InChI notation is reported. The source can be for example PubChem or ChemIDplus.

- Synonyms (com_syn, free text). Multiple synonyms (or alternative naming in general) of the chemical compounds can be reported. For flavourings, for example the flavis number is reported with other available identifiers such as the JECFA-no, the CoE-no, FEMA-no.

- Synonym type (syn, picklist). The synonym field is associated with a type of synonym:

    - CAS: Alternative CAS as found in the documents.
    - Name: Synonym of the component as reported in the various opinions. For example, Aflatoxin B1 is the component name and AFB1 is a synonym (type: name). The name type for the synonym is broadly used to include anything that may help to trace back the compounds.
    - Flavis number. Each flavouring substance is attributed a FLAVIS-number (FL-number) and all substances are divided into 34 chemical groups. Substances within a group should have some metabolic and biological behaviour in common.
    - Other types of synonyms can be included if necessary.

- Pharmacological classification (pharma_class, picklist). The pharmacological classes of a chemical compound is reported as retrieved from the Medical Subject Headings (MeSH, 2014a; MeSH 2014b). The classes are, for example:

    - Antifungal Agents: Substances that destroy fungi by suppressing their ability to grow or reproduce. They differ from fungicides, industrial because they defend against fungi present in human or animal tissues.
    - Antiprotozoal Agents: Substances that are destructive to protozoans.
    - Coccidiostats: Agents useful in the treatment or prevention of coccidiosis in man or animals.
    - Ionophores: Chemical agents that increase the permeability of biological or artificial lipid membranes to specific ions. Most ionophores are relatively small organic molecules that act as mobile carriers within membranes or coalesce

to form ion permeable channels across membranes. Many are antibiotics, and many act as uncoupling agents by short-circuiting the proton gradient across mitochondrial membranes.
- Enzyme Inhibitor: Compounds or agents that combine with an enzyme in such a manner as to prevent the normal substrate-enzyme combination and the catalytic reaction.

- OECD QSAR Toolbox classification (toolbox_class, picklist). The chemical is classified according to the OECD QSAR Toolbox profile which includes 227 organic functional groups defined by the Laboratory of Mathematical Chemistry (LMC), Bourgas, Bulgaria (OECD QSAR Toolbox version 3.0). A chemical is part of one or more classes which are, for example:

  - Alcohol
  - Alkane, branched with tertiary carbon
  - Carboxylic acids
  - Ether
  - Ether (Cyclic)
  - Heterocyclic fragment
  - Ketal
  - Methyl
  - Methylene

  The OECD QSAR Toolbox classification is generated by processing the compound in the OECD QSAR toolbox; more specifically the procedure is:

  - Import the structure of interest (Input section of the program). It is possible to process a single compound or a list of compounds.
  - Open the profiling section and select the Empiric – Organic Functional Groups from the Profiling Methods.
  - Click apply profiling.
  - The profile of the chemical is shown. If a list of compounds has been processed, it is possible to export the output from the export button in the Endpoint section.

  It has been common practice to run the OECD QSAR Toolbox classification in batch: many components are processed altogether (after careful inspection of the SMILES code). The list of components is inputed in the OECD QSAR toolbox as SMILES associated with the component ID. The classification of the list is then added into the database.

Importantly, before entering any new component into the EFSA's hazards database, the user checks if the same chemical has already been registered by searching the component repository by name, synonym, CAS number or more rarely EC number. This procedure is important to avoid duplicates.

## A.6. Composition of a substance

Each substance is described in terms of its chemical composition with reference to the chemical components. More specifically, the data model includes the information regarding how a registered substance is constituted by different components.

As mentioned above, the definition of substance for the present data model (e.g., entity which has been assessed for its hazards in the EFSA documents) leads to the fact that a registered substance is not necessarily a well-defined chemical entity but it can also be a food product or food ingredient (e.g., chia seeds).

Each registered substance is related to a component and the relationship (i.e., the composition of a substance with respect to the components) is given in terms of the following descriptors:

- Composition qualifier (comp, picklist). Qualifiers to define the composition of the EFSA DB substance in terms of the EFSA DB components. The qualifier may point to a quantitative description (% composition) or to a qualitative description and the following terms are proposed:

    - < : Less than (in this case the % composition field is also filled in, see below).
    - <= : Up to (in this case the % composition field is also filled in, see below).
    - = : Equal to (in this case the % composition field is also filled in, see below).
    - > : More than (in this case the % composition field is also filled in, see below).
    - >= : More or equal than (in this case the % composition field is also filled in, see below).
    - ca: About (in this case the % composition field is also filled in, see below).
    - as such: this refers to substance which is identical to the corresponding chemical component.
    - group assessment: component: a component of the group assessment.
    - group assessment: possible component: a possible component of the group.
    - active ingredient: this is the active (or functional) ingredient of the mixture/formulation and quantitative composition may be complex and thus not reported. This term is usually employed in the case of pesticides.
    - impurity: this is an impurity of the mixture/formulation and quantitative composition may be complex and thus not reported.
    - additive: this is an additive added in the mixture/formulation and quantitative composition may be complex and thus not reported.
    - in the mixture or formulation. a component of the mixture and quantitative composition is complex and thus not reported.
    - in the mixture or formulation, possibly: a possible component of the mixture and quantitative composition is not reported.
    - Composition % (comp_value, number): The percentage composition (mass) of the EFSA DB substance in terms of the component in question. The information is obtained only from the EFSA documents.

The following standard operating procedures are followed to set the composition of a substance:

1. A single chemical entity is identical to the corresponding component. The composition is set "as such". The common descriptors of the substance and the corresponding component are identical (name, CAS number, EC number).

2. A substance which is a mixture or formulation and for which the (major) components can be identified, is described by (the major) components in the composition section.

3. A substance which is a mixture or formulation and for which the composition is complex or poorly defined is classified as "Complex product: derived from botanical sources" or "Complex product: microorganisms or derived from microorganisms" or "Complex mixtures: not derived from botanical sources". For these types of substances the composition is either provided (e.g., the major components are reported if significant and/or available) or described "as such" in the composition section. In the latter case, it follows that the complex mixture is entered as component as well.

4. A polymer (or copolymer) is usually described "as such" in the composition section. It follows that the polymer is entered as component as well.

5. A closed group is described in terms of its components which are usually listed as "group assessment: component".

6. An open group is described in terms of its components which are usually listed as either "group assessment: possible component" or "group assessment: component".

7. When the assessment is about the total element (i.e., Calcium (total)), then it is chosen to identify the substance as group (open). The composition of this type of group is retrieved from the opinion reporting relevant compounds (e.g., compounds included in food, test compounds in the toxicity studies).

8. For mixtures and groups, the composition may include the mixture or group itself if this is for example present in the component table.

## A.7. Toxicity data and hazard/risk characterisation

A substance qualifies to be registered in the database if there exists one of the following information/data: conclusion on mutagenicity and/or genotoxicity and/or carcinogenicity; identification of a critical study used to derive a health-based guidance value; health-based guidance values, margin of exposure values for human health, margin of safety values for human or animal health; reference point or toxicity values for animal health or environmental standards. If either one of this type of information or data is included in the EFSA documents, then the substance is entered in the database together with the bibliographic details of the corresponding opinion.

The registered substance and the corresponding opinion of the assessment make up a unique couple, also referred to as study. Two substances assessed in the same opinion makes up two different studies; the same substance assessed in two different opinions also makes up two different studies. A study may contain:

- Summary data on mutagenicity, genotoxicity, carcinogenicity (e.g., positive, negative, ambiguous).

- Details on genotoxicity studies (if available) if the panel concludes that the substance is mutagenic/genotoxic.

- Details on toxicity (including ecotoxicity) studies, and more specifically: critical study to derive the health-based guidance values or other relevant toxicity studies on sensitive animals.

- Hazard data including health-based guidance values, margin of safety, margin of exposure (MOE). For sensitive animals maximum safe intake/maximum safe concentration in feed is also reported.

- The relationship existing between the critical study and the assessment (e.g., TDI, ADI).

## A.8. Toxicity data and hazard/risk characterisation: identification of key information

The relevant information summarised in the EFSA's Chemical Hazards Database is identified by means of the following procedures.

1. Abstract, summary, and conclusions are explored to identify key information to be reported.

2. Summary information on the conclusions drawn by the document's authors on mutagenicity, genotoxicity, carcinogenicity (e.g., positive/negative/no data) is retrieved. This summary information is usually reported in the abstract, summary, and/or conclusions.

3. For human-health, the critical study identified by the panel to derive the health-based guidance value is singled out. Abstract, summary and/or conclusions are usually reporting summary data (e.g., NOAEL) on the critical study. The study usually involves laboratory animals, but it may also be an epidemiological study. The details on the toxicity study as retrieved from the document are then collected.

4. For animal health, the most sensitive animals (i.e., animals for which the authors of the document mention toxicity effects) are identified from the abstract, summary and/or conclusions. These procedures guide the collection of toxicity data for sensitive animals:

    - The studies for sensitive animals collated in the database are those usually mentioned in the abstract, summary and/or conclusions (further details on the toxicity study are then collected from the corresponding sections of the documents).
    - If the abstract/summary/conclusion sections do not single out any specific toxicity study for sensitive animals (but they do mention a number of sensitive animals), then the details on the toxicity study are sought in the corresponding sections of the document. If only one study for the selected sensitive animal is reported, then the details on this study is reported in the endpoint section. If several studies are reported, the choice cannot be made and no hazard identification is included in the database.

5. Details on the ecotoxicity studies used to derive predicted no effect concentrations (e.g., PNEC) are reported in the endpoint section of the database.

6. The hazard characterisation/risk characterisation is reported in the hazard section of the database. Abstract, summary and/or conclusions usually provide useful hints to identify key information to report.

7. If the substance is genotoxic or mutagenic, then the details of the genotoxicity and/or mutagenicity study are sought inside the document.

## A.9. Toxicity data and hazard/risk characterisation: data collection

Data on toxicity of chemicals and about their hazard/risk characterisation are collected and collated according to the following procedures:

1. Details on the critical studies are reported in the hazard identification section.

2. Details on toxicity studies (if available) on the selected sensitive animal species are reported in the endpoint section of the database.

3. Details on the ecotoxicity studies used to derive predicted no effect concentrations (e.g., PNEC) are reported in the endpoint section of the database.

4. Whether a substance is mutagenic or genotoxic, then details on selected genotoxicity/mutagenicity studies are reported in the genotoxicity section. The selection of the toxicity study to report follows this procedure:

    - The EFSA documents usually include conclusive paragraphs which summarizes the conclusions on specific topics. In the conclusive paragraphs regarding genotoxicity/ mutagenicity/

carcinogenicity, the authors usually mention specific studies proving the genotoxicity and/or mutagenicity. Details of the selected studies are retrieved and included in the database.

- If conclusive paragraphs do not allow one to identify the toxicity study to report, then the in vivo studies are prioritized. It may happen than more than one in vivo study are extracted from a given document and reported in the database.

- If conclusive paragraphs do not allow one to identify the toxicity study and in vivo studies are missing, then the popular Ames test is reported.

- It may happen that for substances classified as genotoxic and/or mutagenic, the genotoxicity details are not provided. Most of the time this mirrors the lack of data in the opinion.

5. Information on the hazard characterisation is reported in the corresponding hazard characterisation/risk characterisation section of the database. Information on risk characterisation may also be included (e.g., margin of exposure or margin of safety). These procedures guide the collection and collation of hazard assessment (and sometimes risk) data from the EFSA documents:

    - The health-based guidance value (e.g., ADI, TDI) derived by the authors of the document is reported and then linked to the corresponding reference dose (if available), namely the critical study as reported in the endpoint section of the database.

    - MOE values are reported in the hazard section for key populations; MOE values are also linked to the corresponding critical study (if available). It may be the case that MOE numerical values are not reported and a qualitative evaluation is reported (e.g., MOE is of low concern).

    - A numerical margin of safety is given when a reference dose and the exposure levels are compared. Numerical values of the margin of safety (for human population or for sensitive animals) are reported in the hazard section and linked to the corresponding critical study (if available). It may be the case that margin of safety numerical values are not reported and a qualitative evaluation is reported (e.g., margin of safety is large and of low concern).

    - Whether the document does not derive any health-based guidance value and the authors endorse (or make use of) a health-based guidance value derived from other bodies (e.g., JECFA, SCF), this external health-based guidance value is included in the database and tagged accordingly (e.g., health-based guidance value not derived from EFSA). The choice of the external health-based guidance value to report is guided by any of these points: a) the authors use the external health-based guidance value in the risk assessment; b) the health-based guidance value is mentioned in the abstract/summary/conclusions; c) the authors seem to support the use of the health-based guidance value. The most recent health-based guidance value is reported giving preference to SCF and JECFA references. For external health-based guidance values, the corresponding critical study is not reported in the database because the details are usually unavailable. In the special cases of ADI "not specified" by external bodies (SCF and/or JECFA), the hazard section reports that "no critical study" has been identified by the external bodies. The remark field of the hazard section provide additional details (e.g., no/low concern).

    - The hazard section reports that no critical study has been reported for human health in the opinion if the authors do not identify any critical study because: a) the substance does not raise concern (similarly to the ADI "not specified" case); b) available data are insufficient or inadequate to derive a health-based guidance value or in general to carry out a risk assessment; c) the assessment makes reference to a previous evaluation by EFSA (if the

evaluation refers to other bodies such as JECFA or SCF, the assessment is tagged accordingly (see above).

- When the conclusion of the opinion is that the substance does not raise concern at the use levels (or proposed used levels) or in relation to some exposure levels or in relation to a specific use, the hazard section qualitatively reports that the "margin of safety" is of "no concern"/"low concern"/"some concern". Notably, in such cases the document does not usually single out a critical study associated with this conclusion.

- For sensitive animal species, values such as maximum safe intake/maximum safe concentration in feed, margin of safety, maximum tolerated level/dose are reported.

- For ecotoxicity, the PNEC is reported in the hazard section and linked to the corresponding reference dose (if any) listed in the endpoint section of the database.

- The hazard assessment may refer to multiple reference doses (e.g., well-defined NOAELs, range of NOAELs). The multiple critical studies are reported in the endpoint section (and linked to the corresponding hazard assessment) if the authors of the document clearly describe such studies.

- Whether the toxicity studies used to derive the reference dose for the hazard assessment are not well described in the documents (the description of the experiment is very limited), the hazard assessment section reports the experiment description as free text.

- Special care is taken to collate data on pesticides and flavourings as summarised in the paragraph below.

- Special care should be taken when reporting a group ADI or TDI as reported in detail in the paragraph below that discusses groups.

## A.10. Summary data on mutagenicity, genotoxicity, carcinogenicity

A substance registered in the database together with its specific composition is associated with the bibliographic details of corresponding document reporting its assessment. A summary section is dedicated to summarise data on mutagenicity, genotoxicity and carcinogenicity of the substance including the following fields:

- Substance (id_sub, picklist): reference to the substance which is the subject of the assessment. The substance is described in detail in the substance section of the database (see above).

- Document (id_op, picklist): reference to the opinion/document reporting the assessment being collated in the database. The bibliographic details of the document are reported in the opinion section (see above).

- Class (sub_op_class, picklist); classification of the substance as assessed in the corresponding EFSA document. Each category aims at grouping assessments of the same type. The category is either suggested by EFSA experts (if available) or it can be retrieved from the "Register of Questions", which provides a csv file including useful information for the classification. More specifically, some fields of the csv file (e.g., subarea field) classify the opinions in terms categories (e.g., Technological additives/Sensory additives/Nutritional additives/Zootechnical additives/Coccidiostats and histomonostats). The following classes are available in the class picklist of the database:

- Cocciodiostats/Hormones/Histomonostats
- Feed intended for particular nutritional purposes
- Flavourings
- Food additives
- Food contact materials
- Food manufacturing processes
- Heavy metal ions and metalloids
- Marine biotoxins
- Meat inspection
- Melamine
- Mycotoxins
- Natural plant product contaminants
- No category
- Nutrient sources
- Nutritional additives
- Persistent organic pollutants
- Pesticides
- Processing aids
- Processing contaminants
- Sensory additives
- Technological additives
- Zootechnical additives

The No category list is usually selected when no category could be identified. For example all the studies from the NDA opinions are tagged as "no category".

- Mutagenicity (is_mutagenic, picklist)/genotoxicity (is_genotoxic, picklist)/carcinogenicity (is_carcinogenic, picklist): the conclusions of the authors on the mutagenicity, genotoxicty and carcinogenicity of a substance are summarized using three different fields that in turn can make use of the following catalogue:

  - Ambiguous
  - Negative
  - No data
  - Not applicable
  - Not determined
  - Other
  - Positive

  The term "Ambiguous" is selected if the conclusions of the authors (or the studies mentioned in the document) are indeed ambiguous. Whether the authors conclude that a substance is negative or positive, then the corresponding terms are selected. For groups of substances (or mixtures) the field may not be applicable (term: "Not applicable"): the substance may include different component which may give different results in the genotoxicity/mutagenicity/carcinogenicity studies (e.g., a component of the group is mutagenic while another one is not mutagenic). If the opinion does not report any information, then the term "No data" is selected from the list. If the document reports that there are limited (or not relevant) studies in the literature to determine genotoxicity/mutagenicity/carcinogenicity then the term "Not determined" is selected. "Other" was also selected for special cases as for example: the substance induces co-carcinogenic effects; carcinogenic effects are not relevant to human; carcinogenicity would be thresholded.

- Remarks (remarks_study, free text). The purpose of the assessment discussed in the opinion is reported as free text. This is usually copied from the first sentences of the summary or the background section of the document.

- Trade name (trade, picklist): trade name of the substance being discussed in the opinion. Multiple values are permitted for this field.

## A.11. Hazard identification: toxicity study/critical study

A substance is registered in the database when one or more of the following points are discussed in the EFSA documents. The opinion defines a critical study from which a reference point (e.g., NOAEL, LOAEL, BMDL) is identified for that substance. The reference point is described in the EFSA documents and used to derive health-based guidance values, margin of exposure values for human health, margin of safety values for human or animal health . The opinion may also discuss a reference point or toxicity value for animal health or environmental standards. Likewise the opinion may discuss mutagenicity, and/or genotoxicity and/or carcinogenicity of the substance.

Details on selected (eco)toxicity studies (see above) are entered (if necessary and if available in the documents) in the database in the hazard identification section. For human health, this toxicity data form the basis for the hazard characterisation/risk characterisation leading to a health-based guidance value or margin of exposure values or margin of safety. In the case of animal health, relevant toxicity data for sensitive animals (see above) are also entered (if available). In the case of ecotoxicty, relevant data leading to the effect assessment (e.g., PNEC) is registered.

In particular, the toxicity data are described by a number of fields.

- Toxicity type (study_cat, picklist): indication on whether the record refers to the hazard identification for:
    - Human health
    - Animal (non-target species) health
    - Animal (target species) health
    - Ecotox (soil compartment)
    - Ecotox (water compartment)

- Overall remarks on toxicity study (remarks, free text): free text on hazard identification (as taken from the corresponding document) including (if necessary): 1) short explanation on how the study has been carried on; 2) any relevant remarks on the hazard identication.

- Test substance description (testsubstance, free text): a description (free text) of the sample used in the toxicity study being reported. The substance is for example Polybrominated biphenyls but the toxicity study refers to "Technical PBBs mixtures (FireMaster FF-1): hexaBBs (main PBB congeners) and 2-5% tetraBBs".

- Test type (test_type, picklist): a reference to the test type of the toxicity study being reported such as acute oral toxicity, chronic, epidemiological/study with volunteers, subchronic.

- Limit test (limit_test, picklist): indicator (yes/no) that the critical study was a limit test.

- Guideline Qualifier (guideline_qualifier, picklist): indicator signifying how strict the guideline given in the subsequent field 'Guideline' was followed or whether no guideline was used or available/required. The catalogue includes these terms:
    - According to
    - Equivalent or similar to
    - No guideline followed
    - No guideline available
    - No guideline required

- Guideline (guideline, picklist): name of the guideline followed in performing the toxicity study or to which the method used can be compared. A list of relevant guidelines is included in the corresponding picklist.

- Deviations from guideline (deviation, picklist): indication (yes/no) that the toxicity study being reported contains deviations from the standard test protocol.

- GLP compliance (glp_compl, picklist): indication (yes/no) whether a GLP certificate or compliance statement is available.

- Species (species, picklist): species of the animal/organism/cell culture used in the toxicity study. The picklist that includes common names has been integrated with latin names. A "Not reported" term is also available in the species picklist. This may turn out to be useful when the toxicity study is referring "Microorganisms" or when the species is not reported (e.g., in the case of some TEFs).

- Strain (strain, picklist): strain of the animal tested.

- Sex (sex, picklist): sex of the tested animals (female/male/male&female).

- Route of administration (routeh, picklist): indicator on how the chemical was administered to the test animals/organisms. The catalogue includes terms such as: dermal, implantation, infusion, inhalation, inhalation: aerosol, inhalation: dust, inhalation: gas, inhalation: vapour, intramuscular, intraperitoneal, intracheal, intraveneous, oral: capsule, oral: drinking water, oral: feed, oral: gavage, oral: unspecified, subcutaneous.

- Duration of treatment/exposure (duration, number): exposure duration (unit is given in another field).

- Duration unit (duration_unit, picklist): corresponding unit of the duration of treatment/exposure field (e.g., year, day, week, month).

- Number individuals (number_individuals, integer): number of animals/organisms dosed at each dose level of the toxicity study being reported.

- Control group (control, picklist): indication on whether and what type of concurrent control groups were used. Since this is not a mandatory fields, it is left blank if the corresonding data is not available in the EFSA documents. The catalogue includes terms such as: yes; yes, concurrent no treatment; yes, concurrent vehicle ; yes, plain diet ; yes, sham-exposed; yes, historical; no.

- Endpoint (endpoint, picklist): type of endpoint (e.g., NOAEL) of the toxicity study being reported. Most of the values have been extracted from the OECD picklist as for example: BMDL05 conc. level, dose level, EC50, IC50, LC50, LD50, LOAEL, LOEL, NOAEC, NOAEL, NOEL, T25, TEF.

- Effect level qualifier (qualifier, picklist): the qualifier (e.g., =, >, <, ca) for the effect corresponding to the endpoint specified in the endpoint field.

- Effect level (lovalue, number): actual value of the endpoint.

- Unit of dose (dose_unit, picklist): unit of the numeric value of the endpoint. This field is complemented by the component-dependent unit in the case of group assessments (if necessary; see subsequent section on group assessment).

- Toxicity target (toxicity, picklist): classification of the toxicity target has been devised according to the EFSA input.

    - Systemic
    - Hepatotoxicty
    - Nephrotoxicity
    - Neurotoxicity
    - Reproductive
    - Teratogenic
    - Developmental
    - Pulmonary and cardiac
    - Immunotoxicty
    - Hemopoietic
    - Irritation
    - Endocrine
    - Musclo-Skeletal
    - None
    - Not applicable
    - Not reported

  The list should cover all the toxicity targets for human/animal health. Ecotoxicity studies are usually associated with the "Not applicable" term. The "None" term most of the time refers to cases where no effects (see subquente field regarding the basis effects) are observed. Being a mandatory field, the "Not reported" term is sometimes used if the document does not allow one to identify the toxicity target.

- Target tissue (target-tissue, picklist). the toxicity is classified according to the OECD Harmonised Template for Gross Necropsy:

    - Adrenal Glands
    - Aorta
    - Brain
    - Bone Marrow
    - Caecum
    - Colon
    - Duodenum
    - Epididymides
    - Esophagus
    - Eyes
    - Gall Bladder
    - Glandular: Mammary Gland
    - Heart
    - Ileum
    - Jejunum
    - Kidneys
    - Lachrymal Glands
    - Larynx
    - Liver
    - Lung
    - Lymph Nodes
    - Muscle, Skeletal
    - Nasal Cavity
    - Nerve, Peripheral
    - Overay and oviduct
    - Pancreas

- Periphreal Nerve
- Pituitary
- Pharynx
- Prostate
- Rectum
- Salivary Glands (Mandibular, Sublingual)
- Seminal Vesicles
- Skin/subcutis
- Spinal Cord
- Spleen
- Sternum
- Stomach
- Testis
- Thymus
- Thyroid/parathyroid
- Tongue
- Trachea
- Urinary Bladder
- Uterus
- Vagina

- Basis effects (basis, picklist): information on the effect parameter of the endpoint observation. Only a single value can be selected from the picklist. If multiple effects are reported in an opinion, then the most significant one is chosen. The catalogue includes terms such as behaviour, biomass, body weight, clinical chemistry, clinical signs, development, food consumption, food efficiency, frond number, gross pathology, growth, haematology, histopathology neoplastic, histopathology non neoplastic, immunology, mobility, morphology, mortality, neurology, not reported, no effect, no adverse effect observed at single/highest dose, ophthalmoscopic examination, organ weights, reproduction, seedling emergence, time to swim, time to hatch, urinalysis, other. As a general rule (most of the time satisfied), the basis effect "No effect" is associated with the toxicity target term: "None" (see above). Being a mandatory field, the "not reported" is also used if the basis effects are not cleraly reported.

- Effect description (effec_descr, free text): free text to further describe (if necessary) effects observed in the toxicity study.

It should be noted that in some cases the unit refers to a reference substance which is different from the substance being assessed (e.g., this happens for example for groups as illustrated in the group section of the document). For example the substance under assessment is a salt (e.g., Calcium L-threonate) and the corresponding NOAEL is provided in terms of the anionic compound (e.g., L-threonate). The units can thus be fully specified using two additional fields on top the unit field: a reference to the component (as taken from the component list of the database) which the unit refers to (L-threonate); indication on whether the unit refers to the mass or the (toxicity) equivalents of the reference substance as compared to the substance of the toxicity study; general remarks (free text) are also allowed.

## A.12. Hazard identification: genotoxicity

Details of the genotoxicity (or mutagenicity) study proving the genotoxicity (or mutagenicity) of the substance are also entered (and stored in the genotoxicity section of the database). The preference for the study to report is given according to prioritization rules (see above): a) any specific study mentioned in conclusive paragraphs by the authors is preferred above all; b) if authors do not single out a given genotoxicity/mutagenicity study, then the *in vivo* studies are sought; c) if *in vivo* studies

are missing, the popular Ames test is reported. The genotoxicity/mutagenicity study is described according to a number of fields.

- Toxicity type (study_cat, picklist): indication on whether the study refers to mutagenicity or genotoxicity.
- Overall remarks on toxicity study (remarks, free text): free text reporting any useful information (if needed) on the study.
- Is Positive/Negative (is_genotoxic, picklist): indication on whether the substance is genotoxic/mutagenic according to the study being reported. Only studies proving that a substance is genotoxic and/or mutagenic have been entered so far.
- Genotoxicity Guideline Qualifier (guideline_qualifier, picklist): indicator signifying how strict the guideline given in the subsequent field 'Guideline' was followed or whether no guideline was used or available/required.
- Genotoxicity Guideline (genotox_guideline, picklist): name of the guideline followed in performing the genotoxic study or to which the method used can be compared. The supplementary remarks field (see above) may provide indication of guideline version or title if deviating from the picklist value, or of additional test guidelines cited.
- Deviations from genotoxicity guideline (yn_deviation, picklist): indication (yes/no) that the toxicity study being reported contains deviations from the standard test protocol.
- Genotoxicity GLP compliance (yn_glp, picklist): indication (yes/no) on whether a GLP certificate or compliance statement is available.
- Genotoxicity Species (genotox_species, picklist): species of the animal/organism/cell culture used in the genotoxicity study. The species catalogue is the same as the one discussed above.
- Genotoxicity Strain (strain, picklist): strain of the animal tested in *in vivo* genotoxicity study.
- Genotoxicity Sex (sex, picklist): sex of the tested animals (female/male/male&female) in *in vivo* genotoxicity study.
- Metabolic activation (met_indicator, picklist): indicator specifying whether exogenous metabolic activation was applied or not (*in vitro* studies only).
- Genotoxicity route of administration (routeh, picklist): how the chemical was administered to the test animals in *in vivo* genotoxicity studies (the picklist is the same described above for toxicity studies in the toxicity study section).
- Genotoxicity duration of treatment/exposure (exp_period, number): exposure duration for *in vivo* genotoxicity studies.
- Genotoxicity duration unit (exp_period_unit, picklist): unit of exposure duration (e.g., week, day) for *in vivo* genotoxicity studies.
- Genotoxicity number of animals per dose group (number_individuals, number): number of organisms dosed at each dose level of the *in vivo* genotoxicty study.
- Genotoxicity control animals (control, picklist): indication on whether and what type of concurrent control groups were used in *in vivo* genotoxicity study (picklist as control group of the Toxicity study).

## A.13. Hazard/risk characterisation

On top of the hazard identification section, the EFSA's Chemical Hazards accomodates the quantitative description of the hazard characterisation/risk characterisation. Hazard characterisation correponds to dose-response assessment and the derivation of a health-based guidance value or enviromental standards. Risk characterisation corresponds to the derivation of margion of exposure or margin of safety. The hazard characterisation/risk characterisation is summarised using a number of fields described below.

- Study (study, picklist): reference to which substance and which opinion (study), the safety/risk value is being reported.

- Hazard/risk characterisation type (assessment_type, picklist): this indicates the type of health-based guidance value or environmental standard being reported. Alternatively it indicates the risk assessment type (e.g., margin of exposure or margin of safety) entered in the database. Some of the available terms are reported below:

    - AAOEL: Acute Acceptable Operator Exposure Level (AAOEL): a term used to describe a reference value against which acute non-dietary exposures (i.e. those that might be incurred in a single day) could be assessed. This would be relevant only to those plant protection products for which such exposures might produce significant toxicity.
    - ADI: Acceptable Daily Intake (ADI): estimated maximum amount of an agent, expressed on a body mass basis, to which an individual in a (sub)population may be exposed daily over its lifetime without appreciable health risk. To calculate the daily intake per person, a standard body mass of 60 kg is used. The ADI is normally used for food additives, while the tolerable daily intake (TDI) is used for contaminants (van Leeuwen, 2007).
    - AOEL: Acceptable Operator Exposure Level (AOEL): maximum amount of active substance to which the operator may be exposed without any adverse health effects. The Acceptable Operator Exposure Level (AOEL) is applied in the assessment and review of pesticides and biocides within Europe.
    - ARfC: Acute Reference Concentration (ARfC): an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for an acute duration (24 hours or less) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments (EPA, 2011).
    - ARfD: Acute Reference Dose: an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure for an acute duration (24 hours or less) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments (EPA, 2011).
    - BMDL05: Benchmark Dose Lower confidence limit (BMDL): the benchmark dose (BMD) is defined as the dose that corresponds to a specific change in an adverse response compared to the response in unexposed subjects, and the lower 95% confidence limit is termed the benchmark dose level (BMDL). BMDL01, BMDL05, and BMDL10 are the lower 95% confidence bounds on the

Benchmark Dose (BMD) corresponding to extra risks of 1%, 5%, and 10%, respectively.

- critical study not identified
- group ADI: Acceptable Daily Intake (ADI) for a group
- group TDI: Tolerable Daily Intake (TDI) for a group
- group TWI: Tolerable Weekly Intake (TWI) for a group
- margin of safety: for some experts the margin of safety has the same meaning as the margin of exposure (ratio of the dose-response output (e.g., NOAEL, BMDL) for the critical effect from animal characterization to the theoretical, predicted or estimated dose or concentration, i.e., exposure); for other experts the margin of safety means the margin between the reference dose and the actual exposure dose or concentration.
- maximum safe intake/maximum safe concentration in feed: this value represents the safety values for animals either expressed as intake (e.g., mg/kg bw/day or mg/day) or as maximum safe concentration in feed (mg/kg) (van Leeuwen, 2007 and IPCS/OECD, 2004)
- maximum tolerated level/dose: In a toxicity study, the highest dose that does not produce unacceptable toxicity (FDA, 2005).
- MOE: Margin Of Exposure (MOE): ratio of the dose-response output (e.g., NOAEL, BMDL) for the critical effect from animal characterization to the theoretical, predicted or estimated dose or concentration, i.e., exposure (van Leeuwen, 2007 and IPCS/OECD, 2004). The MOE approach compares the margin between a dose or an exposure causing cancer in animals or humans with the estimated human exposure to that substance. It uses a reference point, usually taken from an animal cancer bioassay in which the substance has been administered for most of the animal's life span. The reference point corresponds to a daily dose causing a low but measurable increase in the incidence of tumors. This reference point (also called a point of departure) is then divided by the estimate of human dietary exposure to the substance to give a dimensionless ratio that is the MOE (ILSI, 2009). Accordingly EFSA (EFSA, 2005a) defines the margin of exposure as the ratio between a defined point on the dose-response curve for the adverse effect and the human intake. The MOE approach uses a reference point, often taken from an animal study and corresponding to a dose that causes a low but measurable response in animals. This reference point is then compared with various dietary intake estimates in humans, taking into account differences in consumption patterns. Several MOEs can be calculated for an individual substance if estimates of exposure vary within the human population.
- PNEC: Predicted No Effect Concentration (PNEC): environmental concentration which is regarded as a level below which the balance of probability is that an unacceptable effect will not occur (van Leeuwen, 2007).
- RfD: Reference dose: the RfD is a benchmark dose operationally derived from the NOAEL by consistent application of generally order-of-magnitude uncertainty factors (UFs) that reflect various types of data sets used to estimate RfDs. For example, a valid chronic animal NOAEL is normally divided by an UF of 100. In addition, a modifying factor (MF), is sometimes used which is based on a professional judgment of the entire data base of the chemical (EPA, 1993).
- TDI: Tolerable Daily Intake (TDI): analogous to an acceptable daily intake. The term tolerable is used for agents which are not deliberately added such as contaminants (van Leeuwen, 2007).
- TDI, provisional (PTDI): Provisional Tolerable Daily Intake (definition according to the document/organization reporting the value).

- TDI, provisional maximum (PMTDI): Provisional Maximum Tolerable Daily Intake (PMTDI) (definition according to the document/organization providing the value).
- TTC Cholinesterase Activity: Threshold of toxicological concern (TTC): three groups or classes of chemicals have been originally proposed and are classified as Cramer Classes and expressed in micrograms/kg bw/day for a 60 kg adult according to their toxicity: namely Low toxicity (Group I: 30 micrograms/kg bw/day), intermediate (Group II: 9 micrograms/kg bw/day) and high toxicity (Group III: 1.5 micrograms/kg bw/day). For genotoxic carcinogens (excluding aflatoxin-like substances, azoxy- and nitroso-compounds), a TTC of 0.0025 micrograms/kg bw/day has also been suggested by Kroes et al. (Kroes, 2004) based on linear extrapolation of bioassay data (cancer risk of 1 in $10^6$) for structurally-related substances (Renwick, 2005). The new EFSA evaluation by the Scientific Committee refined Cramer classes according to the following human exposure threshold values (in micrograms/kg body weight per day): 0.0025 for substances with a structural alert for genotoxicity, 0.3 for organophosphates and carbamates with anti-cholinesterase activity, 1.5 for Cramer Class III and Cramer Class II substances, and 30 for Cramer Class I (EFSA, 2012c). TTC Cholinesterase Activity = 0,3 Micrograms per kilogram body weight per day.
- TTC Cramer Class I: Threshold of toxicological concern (TTC): three groups or classes of chemicals have been originally proposed and are classified as Cramer Classes and expressed in micrograms/kg bw/day for a 60 kg adult according to their toxicity: namely Low toxicity (Group I: 30 micrograms/kg bw/day), intermediate (Group II: 9 micrograms/kg bw/day) and high toxicity (Group III: 1.5 micrograms/kg bw/day). For genotoxic carcinogens (excluding aflatoxin-like substances, azoxy- and nitroso-compounds), a TTC of 0.0025 micrograms/kg bw/day has also been suggested by Kroes et al. (Kroes, 2004) based on linear extrapolation of bioassay data (cancer risk of 1 in $10^6$) for structurally-related substances (Renwick, 2005). The new EFSA evaluation by the Scientific Committee refined Cramer classes according to the following human exposure threshold values (in micrograms/kg body weight per day): 0.0025 for substances with a structural alert for genotoxicity, 0.3 for organophosphates and carbamates with anti-cholinesterase activity, 1.5 for Cramer Class III and Cramer Class II substances, and 30 for Cramer Class I (EFSA, 2012c). TTC Cramer Class I = 30 Micrograms per kilogram body weight per day.
- TTC Cramer Class II: Threshold of toxicological concern (TTC): three groups or classes of chemicals have been originally proposed and are classified as Cramer Classes and expressed in micrograms/kg bw/day for a 60 kg adult according to their toxicity: namely Low toxicity (Group I: 30 micrograms/kg bw/day), intermediate (Group II: 9 micrograms/kg bw/day) and high toxicity (Group III: 1.5 micrograms/kg bw/day). For genotoxic carcinogens (excluding aflatoxin-like substances, azoxy- and nitroso-compounds), a TTC of 0.0025 micrograms/kg bw/day has also been suggested by Kroes et al. (Kroes, 2004) based on linear extrapolation of bioassay data (cancer risk of 1 in $10^6$) for structurally-related substances (Renwick, 2005). The new EFSA evaluation by the Scientific Committee refined Cramer classes according to the following human exposure threshold values (in micrograms/kg body weight per day): 0.0025 for substances with a structural alert for genotoxicity, 0.3 for organophosphates and carbamates with anti-cholinesterase activity, 1.5 for Cramer Class III and Cramer Class II substances, and 30 for Cramer Class I (EFSA, 2012c). TTC Cramer Class II = 9 Micrograms per kilogram body weight per day.

- TTC Cramer Class III: Threshold of toxicological concern (TTC): three groups or classes of chemicals have been originally proposed and are classified as Cramer Classes and expressed in micrograms/kg bw/day for a 60 kg adult according to their toxicity: namely Low toxicity (Group I: 30 micrograms/kg bw/day), intermediate (Group II: 9 micrograms/kg bw/day) and high toxicity (Group III: 1.5 micrograms/kg bw/day). For genotoxic carcinogens (excluding aflatoxin-like substances, azoxy- and nitroso-compounds), a TTC of 0.0025 micrograms/kg bw/day has also been suggested by Kroes et al. (Kroes, 2004) based on linear extrapolation of bioassay data (cancer risk of 1 in $10^6$) for structurally-related substances (Renwick, 2005). The new EFSA evaluation by the Scientific Committee refined Cramer classes according to the following human exposure threshold values (in micrograms/kg body weight per day): 0.0025 for substances with a structural alert for genotoxicity, 0.3 for organophosphates and carbamates with anti-cholinesterase activity, 1.5 for Cramer Class III and Cramer Class II substances, and 30 for Cramer Class I (EFSA, 2012c). TTC Cramer Class III = 1.5 Micrograms per kilogram body weight per day.
- TTC genotoxicity: Threshold of toxicological concern (TTC): three groups or classes of chemicals have been originally proposed and are classified as Cramer Classes and expressed in micrograms/kg bw/day for a 60 kg adult according to their toxicity: namely Low toxicity (Group I: 30 micrograms/kg bw/day), intermediate (Group II: 9 micrograms/kg bw/day) and high toxicity (Group III: 1.5 micrograms/kg bw/day). For genotoxic carcinogens (excluding aflatoxin-like substances, azoxy- and nitroso-compounds), a TTC of 0.0025 micrograms/kg bw/day has also been suggested by Kroes et al. (Kroes, 2004) based on linear extrapolation of bioassay data (cancer risk of 1 in $10^6$) for structurally-related substances (Renwick, 2005). The new EFSA evaluation by the Scientific Committee refined Cramer classes according to the following human exposure threshold values (in micrograms/kg body weight per day): 0.0025 for substances with a structural alert for genotoxicity, 0.3 for organophosphates and carbamates with anti-cholinesterase activity, 1.5 for Cramer Class III and Cramer Class II substances, and 30 for Cramer Class I (EFSA, 2012c). TTC Genotoxicity = 0.0025 Micrograms per kilogram body weight per day.
- TWI: Tolerable Weekly Intake (TWI).
- TWI, provisional (PTWI): Provisional Tolerable Weekly Intake (PTWI).
- UL: Tolerable Upper Intake Level (UL): the maximum level of total chronic daily intake of a nutrient (from all sources) judged to be unlikely to pose a risk of adverse health effects to humans. 'Tolerable intake' in this context connotes what is physiologically tolerable and is a scientific judgment as determined by assessment of risk, i.e., the probability of an adverse effect occurring at some specified level of exposure. ULs may be derived for various life stage groups in the population. The UL is not a recommended level of intake. It is an estimate of the highest level of intake which carries no appreciable risk of adverse health effects. To establish whether an exposed population is at risk requires a risk assessment to determine what is the fraction (if any) of the population whose intake exceeds the UL and the magnitude and duration of the excessive intake (EFSA, 2006a).
- UL, Provisional (PUL): Provisional Tolerable Upper Level.

- Hazard/risk characterisation type qualifier (risk_qualifier, picklist): qualifier (e.g., +, -, <, >) of the hazard/risk characterisation value (e.g., health-based guidance value or margin of exposure, TTC, PNEC).

- Hazard/risk characterisation type value (risk_value, number): the hazard/risk characterisation numerical value (e.g., health-based guidance value or margin of exposure, TTC, PNEC).

- Hazard/risk characterisation unit (risk_unit, picklist): unit of the hazard/risk characterisation value (e.g., health-based guidance value or margin of exposure, TTC, PNEC). This field is complemented by the component-dependent unit in the case of group assessments (if necessary, see section on group assessment).

- Uncertainty factor (safety_factor, number): uncertainty factor used to derive the health-based guidance value or environmental standards.

- Population (population, picklist): population of the health-based guidance value or more in the hazard/risk characterisation value. The current picklist includes various terms:Aquatic compartment, Aquatic Invertebrates, Aquatic other organisms, Aquatic Plants, Aquatic Vertebrates, Human, Soil compartment, Terrestrial Invertebrates, Terrestrial Plants, Terrestrial Vertebrates.

- Subgroup (subgroup, picklist): subgroup of the population for which health-based guidance (HBG) value applies or for which more in general the hazard/rissk characterisation applies. Some of the terms of the subgroup catalogue are listed below. It should be noted that the subgroup definition can be further refined by specifying the age (see subsequent class field) as in the case of calves or lambs (subgroup: cattle and class: juvenile).

    - Animal, food producing - unspecified
    - Animal, non-food producing - unspecified
    - Aquatic organisms - unspecified
    - Birds - unspecified
    - Cattle - for meat production
    - Cattle - for milk production
    - Cattle - for reproduction
    - Cattle - unspecified
    - Chickens - broilers
    - Chickens - for egg production
    - Consumers
    - Consumers, High
    - Consumers, Mean
    - Consumers, Median
    - Consumers, P50
    - Consumers, P90
    - Consumers, P95
    - Consumers, P97.5
    - Crustaceans
    - Ducks - unspecified
    - Equine - unspecified
    - Fish - unspecified
    - Goats - for meat production
    - Goats - for milk production
    - Goats - for reproduction
    - Goats - unspecified
    - Guinea fowls - unspecified
    - Horses
    - Livestock
    - Mammals - unspecified
    - Minks

- Pets - cats
- Pets - dogs
- Pets - unspecified
- Pheasants - unspecified
- Pigs - for meat production
- Pigs - for reproduction
- Pigs - unspecified
- Poultry - unspecified
- Rabbits - for meat production
- Rabbits - for reproduction
- Rabbits - unspecified
- Rodents - unspecified
- Ruminants - unspecified
- Salmons
- Sheep - for meat production
- Sheep - for milk production
- Sheep - for reproduction
- Sheep - unspecified
- Soil macroorganims - arthropods (except honeybees)
- Soil macroorganims - honeybees
- Soil macroorganisms - earthworms
- Trouts
- Turkeys - for meat production
- Turkeys - for reproduction
- Turkeys
- Workers

- Class (age, picklist): class of the subgroup. Most of the values (age class) have been retrieved from the EFSA Comprehensive European Food Consumption Database. The current catalogue includes:

  - Adolescents: age 10-17 years
  - Adults for humans: age 18-64 years
  - All age groups
  - Children: age 36 months - 9 years (unless specified)
  - Elderly: age 65-74 years
  - Infants: age up to 11 months
  - Juvenile: young animals (e.g., calves, lambs, kids)
  - Toddlers: age 12-35 months
  - Very elderly: age from 75 years
  - Women, lactating
  - Women, pregnant

  The class, subgroup and population fields must report compatible values as for example: a) Terrestrial Vertebrates/Chickens-for egg production/Adults; b) Human/Consumers, P97.5/Adults, c) Terrestrial Vertebrates/Pigs-for meat production/Juvenile. Additionally it should be pointed out that adequate combinations of subgroup and age mirrors specific groups: Calves for fattening correspond to Cattle-for meat production/Juvenile; Piglets weaned correspond to Pigs-for meat production/Juvenile. The Adult class is used when the document makes reference to adult animal species or adult humans.

- Remarks on hazard/risk characterisation. This field provides additional information regarding the assessment particularly when no health-based guidance value (e.g., ADI, TDI) is provided in the hazard characterisation/risk characterisation section. It can be regarded as a catalogue-based remark on the assessment type (see above). The field does not aim at summarising the

risk assessment unless the health-based guidance value or MOE values or margin of safety values are lacking.

- additional data required
- insufficient data
- low-quality data
- no additional data, reference to previous assessment
- health-based guidance value (HBGV) not from EFSA committees/panels
- no concern
- low concern
- some concern

Relationships hold between the actual hazard characterisation/risk characterisation type and the assessment term. For example, the "additional data required" term is associated with the term "critical study not identified". ADI and TDI values do not require that this field is filled in unless ADI/TDI are derived from other bodies than EFSA (e.g., SCF, JECFA). A list of relationships is provided in a subsequent paragraph. The choice of the terms (e.g., no concern, some concern) aims at mirroring the document wording.

- Overall remarks (remarks, free text): additional information on the assessment as deemed useful.

As in the case of the toxicity study, it should be noted that in some cases the unit refers to a reference substance which is different from the substance being assessed (e.g., this happens for example for groups as illustrated in the group section of the document). For example the substance under assessment is a mixture and the unit of the corresponding health-based guidance value is provided in terms of the one of its components. The units can thus be fully specified using two additional fields on top the unit field (the same unit field of the toxicity study section described above):

- A reference to the component (as taken from the component list of the database).
- The indication on whether the unit refers to the mass or the (toxicity) equivalents of the reference substance as compared to the substance of the toxicity study.
- General remarks (free text) are also allowed.

## A.14. Relationships between data

A number of relationships hold for data stored in the hazard characterisation/risk characterisation section. Some of database relationships are intrinsic to the data model structure (the hazard characterisation may be associated with its corresponding critical study described in the endpoint section). Some relationships between terms are empirical rules that have been devised based on the scope of the database, which aims at summarizing hazards data. Notably, exceptions to the rules are allowed for special cases, most of the time documented in the free text remarks. A summary of the relationships/rules are provided below:

- Each hazard characterisation/risk characterisation record may be referenced to the corresponding toxicity test that has been identified as critical study and fully described in the hazard identification section (endpoint section). The critical study (or critical studies) used to derive the health-based guidance value or margin of exposure or the margin of safety (or in general the hazard/risk characterisation) may belong to the same substance or to a different substance (in the opinion under investigation or in another opinion). The hazard/risk characterisation can be linked to multiple toxicity studies; in turn a toxicity study can be linked to multiple hazard/risk characterisation records.

- When a numerical value is provided in the hazard/ risk characterisation section (as for example: ADI, TDI, MOE), then the remarks on hazard/risk characterisation field is usually null (it does not contain any term) since the scope of the database is a collection of hazards data. The risk assessment which implies a well-defined exposure scenario is out of the scope of the database. In some cases, the remarks on hazard/risk characterisation field may include information such as:

    - The hazard characterisation/risk characterisation (e.g., ADI, TDI, MOE) was not performed by EFSA panels ("HBGV not from EFSA committees/panels"). As reported above, hazard/risk characterisation values derived by other bodies other than EFSA (e.g., SCF, JECFA) are included in the database because the authors of the documents seem to support this conclusibe value (or it is the only value available in the document).

    - The hazard characterisation/risk characterisation includes limited information (e.g., the critical study is not described) and it makes reference to a previous assessment of EFSA. This also happens when the substance is re-evaluated. For such situations, the remarks on hazard/risk characterisation field includes the following term: "no additional data, reference to previous assessment".

- For TTC assessments (Threshold of Toxicological Concern), the hazard characterisation is usually not linked to any critical study; the hazard characterisation type field is set to the corresponding TTC class (e.g., TTC Cramer Class, TTC Cramer Class II, TTC Cramer Class III). The corresponding TTC value is entered in the hazard/risk characterisation value field:

| | | | | |
|---|---|---|---|---|
| - | TTC Genotoxicity | = | 0.0025 | µg/kg bw/day |
| - | TTC Cramer Class I | = | 30 | µg/kg bw/day |
| - | TTC Cramer Class II | = | 9 | µg/kg bw/day |
| - | TTC Cramer Class III | = | 1.5 | µg/kg bw/day |
| - | TTC Cramer Class II and III | = | 1.5 | µg/kg bw/day |
| - | TTC Cholinesterase Activity | = | 0.3 | µg/kg bw/day |

- The remark picklist on the hazard characterisation/risk characterisation mirrors the conclusions when dealing with flavourings as for example: "no concern" or "HBGV not from EFSA committees/panels" (the TTC is a derivation from a body other than EFSA; "additional data required" (the exposure values or other considerations require additional data for the assessment of the substance).
- When the conclusion of the document is that the compound cannot be assessed because suitable data is not available then the hazard characterisation/risk characterisation type is set to "critical study not identified". The remarks on the hazard characterisation/risk characterisation field explains why a critical study was not identified: "additional data required", "insufficient data", "low-quality data". The remarks on hazard/risk characterisation field may host a single value, and in some few cases more than one term fits the assessment framework as for example when reporting that for a substance the ADI is set to "ADI not specified" by another body (e.g., SCF, JECFA). SCF and JECFA refers to ADI "not specified" for food additives when the (food) substances have very low toxicity which, on the basis of the available data (chemical, biochemical, toxicological, and other), of the total dietary intake of the substance arising from its use at the levels necessary to achieve the desired effect and from its acceptable background in food, does not represent a hazard to health. The EFSA document may support the ADI not specified and the database reports that the critical study was not identified; the remarks on hazard characterisation/risk characterisation field may either report that the conclusion comes from bodies other than EFSA ("HBGV not from EFSA

committees/panels") or that the substance is of "no concern". The "no concern" term is usually preferred in such cases.

- It happens that the authors of the documents concludes on the safety of the chemical of interest without identification of any critical study as reference point. Two possible scenarios occur. The hazard characterisation/risk characterisation type is set to "critical study not identified". The remarks on hazard characterisation/risk characterisation field corresponds to risk characterisation and reports that the substance does not raise concern regarding its safety. If conclusion is however related to use levels, specific applications, maximum residue limits, or in general to some kind of exposure of the population, then the hazard characterisation/ risk characterisation type is set to "margin of safety" instead of "critical study not identified", and the "no concern" term is reported in the remarks on hazard characterisation/risk characterisation field.

- A margin of exposure (MOE) may be provided since for non threshold effects (e.g., compounds that are genotoxic and carcinogenic) a MOE approach is used in the EFSA opinions. In this approach the estimated human exposure is divided by the reference point (the dose that does not result in biologically significant effects), usually BMDL10. In this specific case, the hazard characterisation/risk characterisation type is risk characterisation and is set to "MOE" values, which are referenced to the corresponding toxicity study (or studies) in laboratory animals selected as critical study. The same structure holds for the margin of safety.

- When the document implicitly or explicitly makes reference to a qualitative margin of safety or margin of exposure (e.g., high margin of safety), then the remarks on hazard characterisation/risk characterisation field is necessarily reporting the conclusions regarding the safety of the substance ("no concern", low concern" "some concern").

## A.15. Special cases: pesticides and flavourings

Given the wealth of information included in the EFSA documents dealing with flavourings and pesticides, data collection of such groups require special care

For the flavourings substances, data on toxicity and hazard/risk characterisation are summarised according to the following procedures (more details on these procedures are reported in the previous chapters of this Appendix). Notably, the flavourings opinions usually include summary tables that prove to be very useful to identify relevant data.

- Genotoxicity, mutagenicity, carcinogenicity are summarised by means of the available terms: Ambiguous, Negative, No data, Not applicable, Not determined, Other, Positive. Notably, the flavourings opinions aim at evaluating genotoxicity, mutagenicity and carcinogenicity in relation to the application of the risk assessment procedure used for flavourings (EC, 2000; SCF, 1999). It follows that in many cases the conclusion on genotoxicity, mutagenicity and carcinogenicity refers to the fact that the risk assessment procedure can be applied since available data (which may also be rather limited) do not indicate any concern/evidence/proof for genotoxicity/mutagenicity/carcinogenicity. In these cases, a conservative approach was adopted: the fields for mutagenicity and genotoxicity were set to "not determined".

- The TTC structural class (population=human and subgroup=consumer) is reported together with the corresponding value in the hazard/risk characterisation section of the EFSA's Chemical Hazards Database. The TTC assessment is complemented with the following terms in the Remarks on risk/safety value:

- additional data required: EFSA concludes that additional toxicity data are needed (e.g., to provide a margin of safety from the use of the candidate substance as flavouring substance).
- HBGV not from EFSA committees/panels: safety evaluation is performed by JEFCA and the EFSA Scientific Panel could conclude that has reservations (only USA production volumes are available and/or missing data on specifications and/or isomerism/composition).
- No concern: EFSA concludes that the estimated level of intake does not exceed the TTC.

The field "Overall remarks" usually in the Hazard/risk characterisation section includes the EFSA conclusions on metabolism, genotoxicity, the outcome on the name compound, and outcome on the material of commerce.

- In some cases, identification of a critical study is required for the assessment. Available NOAELs (for the candidate substance under evaluation or for a structurally related substance) are reported and linked to the corresponding margin of safety which is expressed numerically (preferably) or qualitatively. The field "Overall remarks" in this hazard/risk characterisation section usually includes the same remarks as those reported for the corresponding hazard TTC Cramer Class.

- Lack of the adequate NOAEL required by the risk assessment procedure is summarised by entering: a) the term "critical study not identified" (in addition to the corresponding TTC Cramer Class) as Risk/Safety assessment Type; b) the term "additional data required" as Remarks on risk/safety value.

- Whenever the panel does not evaluate the substance because for example the substance raises concerns regarding genotoxicity, the TTC is reported (if available) in the hazard/risk characterisation section and complemented by the term "Insufficient data".

For the pesticide chemicals, data on toxicity and hazard/risk characterisation are summarised according to the following procedures (more details on these procedures are reported in the previous chapters of this report). Notably, "Conclusions on Pesticides Peer Review" typically contain summary appendix table on the toxicity data reviewed by EFSA; the appendices help to identify relevant data to collect.

- Data on the active substance is usually preferred. On top of the data on the active substance, data on formulations may also be included in the database if relevant. In these cases, the formulation is registered in the database having the corresponding active substance as component.
- Human health hazard data usually include acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD), with associated critical studies (e.g., NOAEL values).
- Ecotoxicity data include the effects on terrestrial vertebrates (non-target species); data usually regards acute and reproductive toxicity to mammals and acute, dietary and reproductive toxicity to birds (EFSA, 2009a).
- Ecotoxicity data include the effects on aquatic species (fish, aquatic invertebrates, algae, aquatic plants and sediment organisms ) and terrestrial species (earthworms, other soil macro-organisms, bees, arthropods other than bees, terrestrial plants). The risk assessment (RA) endpoints as identified by EFSA are summarised in the database.

## A.16. Hazard characterisation for groups

Group assessment is sometimes carried out in EFSA; for example there are documents establishing a health-based guidance value for a group (e.g., saxitoxin group) such as: "an acute reference dose (ARfD) of 0.5 µg STX equivalents/kg b.w." (EFSA, 2009b); in these cases the EFSA opinions discuss the toxicity of the components of the group in terms of relative toxicity (TEF, toxicity equivalency factors). More specifically, such group assessments including TEF are stored in the database in this way (see Figure A1 sketching an example on how groups with TEF are stored in the database):

- The group is registered as a substance (e.g., STX group)

| COMPOSITION | |
|---|---|
| EFSA DB Substance | EFSA DB Components |
| STX group | STX, GTX1, GTX2 (group components) |
| STX | STX (as such) |
| GTX1 | GTX1 (as such) |
| GTX2 | GTX2 (as such) |

| EFSA DB STUDY | |
|---|---|
| EFSA DB Substance | Opinion |
| STX group | The EFSA Journal (2009) 1019, 48-76 |
| STX | The EFSA Journal (2009) 1019, 48-76 |
| GTX1 | The EFSA Journal (2009) 1019, 48-76 |
| GTX2 | The EFSA Journal (2009) 1019, 48-76 |

| ENDPOINT STUDY | | | | | |
|---|---|---|---|---|---|
| EFSA DB Study | Endpoint | Qualifier | Endpoint value | Endpoint UNIT | |
| | | | | UNIT | GROUP Unit |
| STX group (assessment by opinion 1019) | NOAEL | = | 0,5 | µg/kg bw | STX equivalents |
| Substance STX (assessment by opinion 1019) | TEF | = | 1 | dimensionless | |
| Substance GTX1 (assessment by opinion 1019) | TEF | = | 1 | dimensionless | |
| Substance GTX2 (assessment by opinion 1019) | TEF | = | 0,4 | dimensionless | |

| GROUP EQUIVALENCY TOX | |
|---|---|
| Toxicity data | Reference toxicity data |
| TEF of STX as reported in opinion 1019 | NOAEL of STX group as reported in opinion 1019 |
| TEF of GTX1 as reported in opinion 1019 | NOAEL of STX group as reported in opinion 1019 |
| TEF of GTX2 as reported in opinion 1019 | NOAEL of STX group as reported in opinion 1019 |

| HAZARD | | | | | |
|---|---|---|---|---|---|
| EFSA DB Study | Safety assessment type | Qualifier | Assessment type value | Assessment type UNIT | |
| | | | | UNIT | GROUP Unit |
| Group substance: STX group (assessment by opinion 1019) | ARfD | = | 0,5 | µg/kg bw | STX equivalents |

**Figure A1:** Example of how information is stored in the case of group assessment including TEF values.

- The substance being a group is assigned the following descriptions:

- The EFSA DB components of the group are the compounds included in the group by the corresponding opinion (e.g., STX, GTX, NeoGTX).
- The substance (group) is related to the corresponding opinion discussing the assessment. Genotoxicity, mutagenicity and carcinogenicity information ("*Is genotoxic*", "*Is mutagenic*", "*Is carcinogenic*") usually cannot be assigned to a group because the compounds making up the group can have different profiles.
- The substance (group) is provided with a threshold level (e.g., NOAEL) including the full unit (e.g., µg STX equivalents/kg bw). Additional fields in the endpoint section of the database have been devised to properly store the component-dependent unit for the toxicity data. The full unit is made up by three fields:
  - The unit field (the same field of the toxicity study section described above) which includes for example µg/kg bw.
  - A reference to the component (as taken from the component list of the database) which the unit refers to (for example STX).
  - The indication on whether the unit refers to the mass or the (toxicity) equivalents of the reference substance as compared to the substance of the toxicity study.

- The reference point (critical study included in the Hazard identification) for the group is linked to the health-based guidance value of the group itself. As for the toxicity study, the unit of the health-based guidance value may be component dependent (e.g., an acute reference dose (ARfD) of 0.5 µg STX equivalents/kg bw). Also in this case the units are additionally defined by reporting the reference substance.

- The constituents of the group for which an assessment is provided are also registered as substances. It follows that the group constituents are registered as substances and components of the group substance.

- Each constituent of the group is provided with a TEF value (dimensionless), that needs to be linked to the reference group threshold level or health-based guidance value. A relationship is established between the threshold level of the group substance (e.g., NOAEL of the STX group) and the TEF of the constituents of the group for which a TEF is provided (see Figure 1).

For group assessments where GROUP ADI is for example provided, there are two choices to report the health-based guidance value:

- The single entities making up the group or mixtures are entered as single substances, the group ADI/TDI is reported for each of the substances and the corresponding remarks (free text) include a note specifying the substances the group ADI/TDI refers to.

- The substance is entered in the database as group or mixture, defined in terms of its components, and linked to the corresponding group TDI/ADI. In some of these cases summary genotoxicity/mutagenicity/carcinogenicity summary data may refer (or be valid) only for single components. If this is the case, then also the single components of the group/mixture are entered as substances and the genotoxicity/ mutagenicity/ carcinogenicity summary data are reported accordingly.

Usually for groups/mixtures formed by many chemical entities, the latter choice is preferable. The former choice would better fit data in some other cases where for example the group ADI/TDI refers only to two well-defined chemicals.

# Appendix B – EFSA's Chemical Hazards Database, supporting material (excel sheets)

The present report is complemented with a number of attachments in the format of excel sheets including summary data as exctrated from the local repository.

# Appendix C – EFSA's Chemical Hazards Database, supporting material (tables)

The following table reports additional details regarding the data included in the local repository and submitted to EFSA via DCF.

**Table C.1.** Extended list of multiple classifications for the substances registered in the database. The number of substances together with their name (and the documents in which they are assessed) are reported for a given combination of subareas.

| Multiple Classification | Number of substances | Substances | Documents |
|---|---|---|---|
| Food additives, Sensory additives | 11 | Allura Red AC, Brilliant Blue FCF, Canthaxanthin, Carmoisine, Erythrosine, Indigo Carmine, Iron oxides and hydroxides (E 172), Monosodium L-glutamate, Paprika extract, Quinoline Yellow, Tartrazine | doi:10.2903/j.efsa.2009.1327, doi:10.2903/j.efsa.2013.3234, doi:10.2903/j.efsa.2012.2675, doi:10.2903/j.efsa.2015.4270, doi:10.2903/j.efsa.2010.1853, doi:10.2903/j.efsa.2013.3288, doi:10.2903/j.efsa.2010.1852, doi:10.2903/j.efsa.2007.507, doi:10.2903/j.efsa.2014.3527, doi:10.2903/j.efsa.2009.1332, doi:10.2903/j.efsa.2013.3234, doi:10.2903/j.efsa.2012.2570, doi:10.2903/j.efsa.2011.1854, doi:10.2903/j.efsa.2011.2447, doi:10.2903/j.efsa.2014.3768, doi:10.2903/j.efsa.2015.4108, doi:10.2903/j.efsa.2015.4317, doi:10.2903/j.efsa.2016.4482, doi:10.2903/j.efsa.2015.3981, doi:10.2903/j.efsa.2014.3670, doi:10.2903/j.efsa.2015.4320, doi:10.2903/j.efsa.2006.386, doi:10.2903/j.efsa.2009.1329, doi:10.2903/j.efsa.2015.4070, doi:10.2903/j.efsa.2013.3320, doi:10.2903/j.efsa.2009.1331, doi:10.2903/j.efsa.2013.3234, doi:10.2903/j.efsa.2016.4613 |
| Food additives, Technological additives | 11 | All-rac-alpha-tocopherol, Ascorbyl palmitate, Calcium propionate, Cassia gum (Cassia tora and Cassia obtusifolia), Citric acid, Complexation product of sodium tartrates and iron(III) chloride, Hexamethylene tetramine, Potassium sorbate, Rosemary extract liquid of natural origin, Sodium ascorbate, Sodium propionate | doi:10.2903/j.efsa.2015.4247, doi:10.2903/j.efsa.2012.2784, doi:10.2903/j.efsa.2015.4289, doi:10.2903/j.efsa.2013.3104, doi:10.2903/j.efsa.2014.3779, doi:10.2903/j.efsa.2011.2446, doi:10.2903/j.efsa.2006.389, doi:10.2903/j.efsa.2014.3899, doi:10.2903/j.efsa.2014.3900, doi:10.2903/j.efsa.2014.3901, doi:10.2903/j.efsa.2014.3902, doi:10.2903/j.efsa.2016.4599, doi:10.2903/j.efsa.2015.4009, doi:10.2903/j.efsa.2015.4010, doi:10.2903/j.efsa.2015.3980, doi:10.2903/j.efsa.2015.4114, doi:10.2903/j.efsa.2014.3696, doi:10.2903/j.efsa.2015.4014, doi:10.2903/j.efsa.2015.4144, doi:10.2903/j.efsa.2012.2735, doi:10.2903/j.efsa.2013.3283, doi:10.2903/j.efsa.2014.3792, doi:10.2903/j.efsa.2015.4090, doi:10.2903/j.efsa.2012.2526, doi:10.2903/j.efsa.2010.1942, doi:10.2903/j.efsa.2015.4087, doi:10.2903/j.efsa.2013.3104, doi:10.2903/j.efsa.2014.3779, doi:10.2903/j.efsa.2016.4546, |

| Multiple Classification | Number of substances | Substances | Documents |
|---|---|---|---|
| | | | doi:10.2903/j.efsa.2011.2446 |
| Food additives, Food contact materials | 9 | 1,2-Benzisothiazolin-3-one, Boric acid, Butylated hydroxyanisole, Carbon Black, Copolymer of ethyl acrylate, methyl methacrylate, Methyl acrylate, Polyethylene waxes oxidised, Polyvinyl alcohol, Vinyl acetate | doi:10.2903/j.efsa.2007.416, doi:10.2903/j.efsa.2007.555, doi:10.2903/j.efsa.2013.3407, doi:10.2903/j.efsa.2012.2642, doi:10.2903/j.efsa.2011.2392, doi:10.2903/j.efsa.2012.2759, doi:10.2903/j.efsa.2012.2592, doi:10.2903/j.efsa.2005.248a, doi:10.2903/j.efsa.2012.2643, doi:10.2903/j.efsa.2010.1655, doi:10.2903/j.efsa.2009.1196, doi:10.2903/j.efsa.2011.2464, doi:10.2903/j.efsa.2010.1656, doi:10.2903/j.efsa.2013.3154, doi:10.2903/j.efsa.2015.4145, doi:10.2903/j.efsa.2009.1028, doi:10.2903/j.efsa.2006.294, doi:10.2903/j.efsa.2008.601, doi:10.2903/j.efsa.2013.3303, doi:10.2903/j.efsa.2014.3555 |
| Feed intended for particular nutritional purposes, Nutritional additives | 8 | Guanidinoacetic acid, L-Tryptophan, Manganese chelate of amino acids, hydrate, Manganous oxide, Manganous sulphate monohydrate, Selenium sulfide, Sodium selenate, Sodium selenite | doi:10.2903/j.efsa.2016.4394, doi:10.2903/j.efsa.2009.988, doi:10.2903/j.efsa.2016.4444, doi:10.2903/j.efsa.2013.3368, doi:10.2903/j.efsa.2014.3673, doi:10.2903/j.efsa.2015.4015, doi:10.2903/j.efsa.2015.4238, doi:10.2903/j.efsa.2016.4343, doi:10.2903/j.efsa.2016.4395, doi:10.2903/j.efsa.2013.3324, doi:10.2903/j.efsa.2016.4395, doi:10.2903/j.efsa.2013.3325, doi:10.2903/j.efsa.2013.3435, doi:10.2903/j.efsa.2016.4395, doi:10.2903/j.efsa.2013.3435, doi:10.2903/j.efsa.2016.4398, doi:10.2903/j.efsa.2016.4442 |
| Heavy metal ions and metalloids | 8 | Arsenic (total), Arsenic, organic derivates, Fluorine, Inorganic mercury, Mercuric chloride, Methylmercuric chloride, Methylmercury, Uranium (total) | doi:10.2903/j.efsa.2005.180, doi:10.2903/j.efsa.2004.100, doi:10.2903/j.efsa.2008.654, doi:10.2903/j.efsa.2012.2985, doi:10.2903/j.efsa.2012.2985, doi:10.2903/j.efsa.2004.34, doi:10.2903/j.efsa.2008.654, doi:10.2903/j.efsa.2012.2985, doi:10.2903/j.efsa.2009.1018 |
| Flavourings, Processing contaminants | 7 | Butane-1,3-diol, Butane-2,3-diol, Cyclohexanol, Cyclohexanone, Limonene, Propylene glycol, sec-Butyl acetate | doi:10.2903/j.efsa.2005.246, doi:10.2903/j.efsa.2009.934, doi:10.2903/j.efsa.2011.2164, doi:10.2903/j.efsa.2012.2563, doi:10.2903/j.efsa.2011.2482, doi:10.2903/j.efsa.2005.166, doi:10.2903/j.efsa.2008.493, doi:10.2903/j.efsa.2011.1170, doi:10.2903/j.efsa.2014.3888, doi:10.2903/j.efsa.2009.1391, doi:10.2903/j.efsa.2005.165, doi:10.2903/j.efsa.2009.927, doi:10.2903/j.efsa.2010.1454, doi:10.2903/j.efsa.2011.2396, doi:10.2903/j.efsa.2012.2836, doi:10.2903/j.efsa.2014.3865, doi:10.2903/j.efsa.2015.4243, doi:10.2903/j.efsa.2009.1391, doi:10.2903/j.efsa.2008.855, doi:10.2903/j.efsa.2012.2636, doi:10.2903/j.efsa.2016.4338, doi:10.2903/j.efsa.2009.1391, doi:10.2903/j.efsa.2011.2177, doi:10.2903/j.efsa.2015.4069, |

| Multiple Classification | Number of substances | Substances | Documents |
|---|---|---|---|
| | | | doi:10.2903/j.efsa.2012.2703, doi:10.2903/j.efsa.2010.1453, doi:10.2903/j.efsa.2011.2482, doi:10.2903/j.efsa.2005.164, doi:10.2903/j.efsa.2008.722, doi:10.2903/j.efsa.2009.1020, doi:10.2903/j.efsa.2010.1845, doi:10.2903/j.efsa.2012.2899, doi:10.2903/j.efsa.2012.2984 |
| Food additives, Processing contaminants | 7 | Beeswax, Calcium lignosulphonate (40-65), Candelilla wax, Carnauba wax, Chlorate, Furan, Microcrystalline wax | doi:10.2903/j.efsa.2007.615, doi:10.2903/j.efsa.2012.2703, doi:10.2903/j.efsa.2010.1525, doi:10.2903/j.efsa.2011.2319, doi:10.2903/j.efsa.2011.2482, doi:10.2903/j.efsa.2017.4656, doi:10.2903/j.efsa.2012.2946, doi:10.2903/j.efsa.2012.2984, doi:10.2903/j.efsa.2012.2880, doi:10.2903/j.efsa.2012.2984, doi:10.2903/j.efsa.2016.4388, doi:10.2903/j.efsa.2015.4135, doi:10.2903/j.efsa.2011.2004, doi:10.2903/j.efsa.2004.137, doi:10.2903/j.efsa.2013.3146, doi:10.2903/j.efsa.2012.2984 |
| Flavourings, Food additives | 6 | 5-Hydroxymethyl-2-furfural, Butyl 4-hydroxybenzoate, Ethyl 4-hydroxybenzoate, L-Cysteine hydrochloride, Methyl methacrylate, Steviol glycosides | doi:10.2903/j.efsa.2005.215, doi:10.2903/j.efsa.2010.1403, doi:10.2903/j.efsa.2011.2313, doi:10.2903/j.efsa.2011.2314, doi:10.2903/j.efsa.2011.2004, doi:10.2903/j.efsa.2008.637, doi:10.2903/j.efsa.2004.83, doi:10.2903/j.efsa.2006.296, doi:10.2903/j.efsa.2009.976, doi:10.2903/j.efsa.2010.1405, doi:10.2903/j.efsa.2011.2176, doi:10.2903/j.efsa.2012.2994, doi:10.2903/j.efsa.2004.83, doi:10.2903/j.efsa.2008.790, doi:10.2903/j.efsa.2006.390, doi:10.2903/j.efsa.2005.204, doi:10.2903/j.efsa.2008.643, doi:10.2903/j.efsa.2010.1400, doi:10.2903/j.efsa.2010.1513, doi:10.2903/j.efsa.2010.1655, doi:10.2903/j.efsa.2010.1656, doi:10.2903/j.efsa.2011.2181, doi:10.2903/j.efsa.2010.1537, doi:10.2903/j.efsa.2011.1972, doi:10.2903/j.efsa.2014.3639, doi:10.2903/j.efsa.2015.4146, doi:10.2903/j.efsa.2015.4316 |
| Processing contaminants, Sensory additives | 6 | Butan-2-one, Ethyl acetate, Isobutanol, Isobutyl acetate, Methyl acetate, Propyl acetate | doi:10.2903/j.efsa.2012.2703, doi:10.2903/j.efsa.2015.4268, doi:10.2903/j.efsa.2011.2482, doi:10.2903/j.efsa.2013.3169, doi:10.2903/j.efsa.2009.1391, doi:10.2903/j.efsa.2012.2927, doi:10.2903/j.efsa.2012.2984, doi:10.2903/j.efsa.2012.2927, doi:10.2903/j.efsa.2017.4656, doi:10.2903/j.efsa.2013.3169, doi:10.2903/j.efsa.2012.2703, doi:10.2903/j.efsa.2013.3169 |
| Flavourings, Food additives, Sensory additives | 5 | Allyl isothiocyanate, Benzene-1,3-diol, Ethyl acrylate, L-Cysteine, L-Glutamic acid | doi:10.2903/j.efsa.2008.813, doi:10.2903/j.efsa.2010.1943, doi:10.2903/j.efsa.2013.3208, doi:10.2903/j.efsa.2008.711, doi:10.2903/j.efsa.2010.1411, doi:10.2903/j.efsa.2012.2573, doi:10.2903/j.efsa.2010.1401, doi:10.2903/j.efsa.2010.1655, doi:10.2903/j.efsa.2013.3169, doi:10.2903/j.efsa.2008.870, |

| Multiple Classification | Number of substances | Substances | Documents |
|---|---|---|---|
| | | | doi:10.2903/j.efsa.2006.390, doi:10.2903/j.efsa.2014.3670, doi:10.2903/j.efsa.2014.3625, doi:10.2903/j.efsa.2015.3981, doi:10.2903/j.efsa.2014.3670 |
| Flavourings, Food contact materials | 5 | 2,3,6-Trimethylphenol, 3-Phenylpropan-1-ol, Benzophenone, Dodecyldimethylamine, Phenol | doi:10.2903/j.efsa.2008.711, doi:10.2903/j.efsa.2009.1196, doi:10.2903/j.efsa.2009.1032, doi:10.2903/j.efsa.2009.1028, doi:10.2903/j.efsa.2008.869, doi:10.2903/j.efsa.2009.1104, doi:10.2903/j.efsa.2009.243r, doi:10.2903/j.efsa.2009.964, doi:10.2903/j.efsa.2007.555, doi:10.2903/j.efsa.2008.857, doi:10.2903/j.efsa.2013.3189 |
| Melamine | 5 | Ammelide, Ammeline, Cyanuric acid, Melamine, Melamine (total) | doi:10.2903/j.efsa.2010.1573, doi:10.2903/j.efsa.2007.1047, doi:10.2903/j.efsa.2010.1573, doi:10.2903/j.efsa.2007.1047, doi:10.2903/j.efsa.2008.807, doi:10.2903/j.efsa.2010.1573, doi:10.2903/j.efsa.2007.1047 |
| Nutritional additives, Pesticides | 5 | Dicopper chloride trihydroxide, Iron sulfate heptahydrate, Iron sulfate monohydrate, Potassium iodide, Urea | doi:10.2903/j.efsa.2011.2355, doi:10.2903/j.efsa.2008.187r, doi:10.2903/j.efsa.2013.3235, doi:10.2903/j.efsa.2014.3566, doi:10.2903/j.efsa.2016.4396, doi:10.2903/j.efsa.2012.2521, doi:10.2903/j.efsa.2014.3607, doi:10.2903/j.efsa.2016.4396, doi:10.2903/j.efsa.2012.2521, doi:10.2903/j.efsa.2013.3099, doi:10.2903/j.efsa.2013.3101, doi:10.2903/j.efsa.2012.2923, doi:10.2903/j.efsa.2012.2624, doi:10.2903/j.efsa.2012.2523 |
| Processing aids | 5 | Chlorine, Dimethyl ether, Peroxyacid solution, Sodium chlorite, Trisodium phosphate | doi:10.2903/j.efsa.2006.297, doi:10.2903/j.efsa.2015.4174 |
| Feed intended for particular nutritional purposes | 4 | 6-Phytase formulation (RONOZYME HiPhos), 6-Phytase formulation (RONOZYME NP), Manganese chelate of glycine, hydrate, Manganous chloride tetrahydrate | doi:10.2903/j.efsa.2016.4393, doi:10.2903/j.efsa.2016.4392, doi:10.2903/j.efsa.2016.4395 |
| Flavourings, Nutritional additives, Sensory additives | 4 | L-Arginine, L-Methionine, L-Tyrosine, L-Valine | doi:10.2903/j.efsa.2008.870, doi:10.2903/j.efsa.2011.1924, doi:10.2903/j.efsa.2007.473, doi:10.2903/j.efsa.2016.4345, doi:10.2903/j.efsa.2014.3670, doi:10.2903/j.efsa.2008.790, doi:10.2903/j.efsa.2013.3428, doi:10.2903/j.efsa.2014.3670, doi:10.2903/j.efsa.2008.870, doi:10.2903/j.efsa.2013.3310, doi:10.2903/j.efsa.2014.3670, doi:10.2903/j.efsa.2008.790, doi:10.2903/j.efsa.2014.3625, doi:10.2903/j.efsa.2008.695, doi:10.2903/j.efsa.2008.872, doi:10.2903/j.efsa.2013.3429, doi:10.2903/j.efsa.2014.3795, doi:10.2903/j.efsa.2015.4110, doi:10.2903/j.efsa.2014.3670 |

| Multiple Classification | Number of substances | Substances | Documents |
|---|---|---|---|
| Food contact materials, Processing contaminants | 4 | 1,4-Butanediol, Epoxidised soybean oil, Hydrogen peroxide, Water | doi:10.2903/j.efsa.2004.109, doi:10.2903/j.efsa.2011.2482, doi:10.2903/j.efsa.2004.64, doi:10.2903/j.efsa.2006.332, doi:10.2903/j.efsa.2011.2482, doi:10.2903/j.efsa.2013.3153, doi:10.2903/j.efsa.2009.1391, doi:10.2903/j.efsa.2012.2643, doi:10.2903/j.efsa.2012.2703 |
| No category, Nutrient sources | 4 | Molybdenum (total), Potassium (total), Vitamin B6, Vitamin E | doi:10.2903/j.efsa.2013.3408, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2005.193, doi:10.2903/j.efsa.2009.1088, doi:10.2903/j.efsa.2013.3408, doi:10.2903/j.efsa.2008.760, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2013.3408, doi:10.2903/j.efsa.2008.640, doi:xx.xxxx/x.xxxx.xxxx.xxxx |
| No category, Nutrient sources, Nutritional additives | 4 | Folic acid, Nicotinamide, Nicotinic acid, Vitamin A | doi:10.2903/j.efsa.2013.3408, doi:10.2903/j.efsa.2004.135, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2012.2674, doi:10.2903/j.efsa.2013.3408, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2012.2731, doi:10.2903/j.efsa.2012.2781, doi:10.2903/j.efsa.2012.2788, doi:10.2903/j.efsa.2012.2789, doi:10.2903/j.efsa.2012.2885, doi:10.2903/j.efsa.2013.3408, doi:10.2903/j.efsa.2008.887, doi:10.2903/j.efsa.2009.949, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2012.2731, doi:10.2903/j.efsa.2012.2781, doi:10.2903/j.efsa.2012.2788, doi:10.2903/j.efsa.2012.2789, doi:10.2903/j.efsa.2012.2885, doi:10.2903/j.efsa.2013.3408, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2009.873 |
| Nutrient sources, Nutritional additives | 4 | Copper(II) oxide, D-(+)-biotin, L-Carnitine L-tartrate, L-Selenomethionine | doi:10.2903/j.efsa.2009.1089, doi:10.2903/j.efsa.2015.4057, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2012.2925, doi:10.2903/j.efsa.2012.2926, doi:10.2903/j.efsa.2003.19, doi:10.2903/j.efsa.2012.2676, doi:10.2903/j.efsa.2009.1082, doi:10.2903/j.efsa.2013.3219 |
| Flavourings, Nutritional additives | 3 | L-Cystine, L-Lysine, d,l-Methionine | doi:10.2903/j.efsa.2006.373, doi:10.2903/j.efsa.2008.790, doi:10.2903/j.efsa.2013.3173, doi:10.2903/j.efsa.2008.870, doi:10.2903/j.efsa.2011.1924, doi:10.2903/j.efsa.2013.3365, doi:10.2903/j.efsa.2014.3895, doi:10.2903/j.efsa.2016.4346, doi:10.2903/j.efsa.2008.870, doi:10.2903/j.efsa.2012.2623 |
| Flavourings, Sensory additives, Zootechnical additives | 3 | Benzyl salicylate, Isopentyl salicylate, Vanillin | doi:10.2903/j.efsa.2008.637, doi:10.2903/j.efsa.2012.2785, doi:10.2903/j.efsa.2012.2620, doi:10.2903/j.efsa.2008.637, doi:10.2903/j.efsa.2012.2785, doi:10.2903/j.efsa.2010.1633 |
| Food additives, No category | 3 | Alpha-tocopherol-containing oil suspension of lycopene (Blakeslea trispora), Butylated | doi:10.2903/j.efsa.2005.275, doi:10.2903/j.efsa.2005.212, doi:10.2903/j.efsa.2012.2588, doi:10.2903/j.efsa.2013.3423, doi:10.2903/j.efsa.2008.674, doi:10.2903/j.efsa.2010.1444, doi:10.2903/j.efsa.2010.1676, |

| Multiple Classification | Number of substances | Substances | Documents |
|---|---|---|---|
| | | hydroxytoluene, Lycopene | doi:10.2903/j.efsa.2008.676, doi:10.2903/j.efsa.2015.3955 |
| Meat inspection, No category, Nutrient sources, Nutritional additives | 3 | Copper (total) , Selenium (total), Zinc (total) | doi:10.2903/j.efsa.2013.3263, doi:10.2903/j.efsa.2013.3408, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2012.2969, doi:10.2903/j.efsa.2013.3107, doi:10.2903/j.efsa.2014.3796, doi:10.2903/j.efsa.2013.3263, doi:10.2903/j.efsa.2013.3408, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2016.4442, doi:10.2903/j.efsa.2013.3263, doi:10.2903/j.efsa.2013.3408, doi:10.2903/j.efsa.2006.391a, doi:10.2903/j.efsa.2007.495, doi:10.2903/j.efsa.2008.761, doi:10.2903/j.efsa.2009.1113, doi:10.2903/j.efsa.2009.1187, doi:10.2903/j.efsa.2009.924, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2012.2970, doi:10.2903/j.efsa.2013.3038, doi:10.2903/j.efsa.2014.3668 |
| Persistent organic pollutants, Pesticides | 3 | Dieldrin, Endosulfan, Gamma-hexachlorocyclohexane | doi:10.2903/j.efsa.2005.285, doi:10.2903/j.efsa.2007.554, doi:10.2903/j.efsa.2005.234, doi:10.2903/j.efsa.2011.2131, doi:10.2903/j.efsa.2012.2799, doi:10.2903/j.efsa.2005.236, doi:10.2903/j.efsa.2005.250, doi:10.2903/j.efsa.2012.2799 |
| Pesticides, Sensory additives | 3 | Allyl mercaptan, Methyl nonyl ketone, Trimethylamine hydrochloride | doi:10.2903/j.efsa.2012.2496, doi:10.2903/j.efsa.2013.3208, doi:10.2903/j.efsa.2012.2495, doi:10.2903/j.efsa.2015.4268, doi:10.2903/j.efsa.2012.2503, doi:10.2903/j.efsa.2012.2679 |
| Feed intended for particular nutritional purposes, Food additives | 2 | Cu-chlorophyllins E 141(ii), Cu-chlorophylls E 141(i) | doi:10.2903/j.efsa.2016.4391, doi:10.2903/j.efsa.2015.4151 |
| Flavourings, Nutrient sources, Nutritional additives, Sensory additives | 2 | Taurine, Thiamine hydrochloride | doi:10.2903/j.efsa.2008.870, doi:10.2903/j.efsa.2011.1924, doi:10.2903/j.efsa.2009.935, doi:10.2903/j.efsa.2012.2736, doi:10.2903/j.efsa.2014.3670, doi:10.2903/j.efsa.2008.875, doi:10.2903/j.efsa.2013.3455, doi:10.2903/j.efsa.2008.864, doi:10.2903/j.efsa.2011.2411, doi:10.2903/j.efsa.2011.2413, doi:10.2903/j.efsa.2016.4441 |
| Flavourings, Nutrient sources, Sensory additives | 2 | 4-Hydroxy-2,5-dimethylfuran-3(2H)-one, L-Aspartic acid | doi:10.2903/j.efsa.2009.1061, doi:10.2903/j.efsa.2011.1841, doi:10.2903/j.efsa.2012.2901, doi:10.2903/j.efsa.2013.3390, doi:10.2903/j.efsa.2015.4117, doi:10.2903/j.efsa.2015.4286, doi:10.2903/j.efsa.2011.2395, doi:10.2903/j.efsa.2012.2786, doi:10.2903/j.efsa.2008.870, doi:10.2903/j.efsa.2008.883, doi:10.2903/j.efsa.2014.3670 |
| Flavourings, Pesticides | 2 | Dec-3-en-2-one, Tetradecan-1-ol | doi:10.2903/j.efsa.2012.2992, doi:10.2903/j.efsa.2015.3932, doi:10.2903/j.efsa.2008.709, doi:10.2903/j.efsa.2014.3524 |
| Flavourings, Pesticides, Sensory additives | 2 | 1,2-Dimethoxy-4-(prop-1-enyl)-benzene, Geraniol | doi:10.2903/j.efsa.2010.1899, doi:10.2903/j.efsa.2012.2518, doi:10.2903/j.efsa.2012.2678, doi:10.2903/j.efsa.2009.1081, doi:10.2903/j.efsa.2010.1402, |

| Multiple Classification | Number of substances | Substances | Documents |
|---|---|---|---|
| | | | doi:10.2903/j.efsa.2013.3392, doi:10.2903/j.efsa.2012.2915, doi:10.2903/j.efsa.2016.4512 |
| Food additives, Nutrient sources | 2 | D-delta-Tocopherol, D-gamma-Tocopherol | doi:10.2903/j.efsa.2015.4247, doi:10.2903/j.efsa.2009.1116 |
| Food additives, Nutrient sources, Sensory additives | 2 | Beta-apo-8'-carotenal, Lutein | doi:10.2903/j.efsa.2012.2499, doi:10.2903/j.efsa.2014.3492, doi:10.2903/j.efsa.2012.2593, doi:10.2903/j.efsa.2009.1098, doi:10.2903/j.efsa.2010.1678, doi:10.2903/j.efsa.2011.2144, doi:10.2903/j.efsa.2012.2589, doi:10.2903/j.efsa.2007.315, doi:10.2903/j.efsa.2009.1098 |
| Food additives, Nutritional additives | 2 | Polyoxyethylene sorbitan monooleate, Thaumatin | doi:10.2903/j.efsa.2015.4152, doi:10.2903/j.efsa.2016.4443, doi:10.2903/j.efsa.2015.4290, doi:10.2903/j.efsa.2011.2354 |
| Food additives, Processing aids | 2 | Chlorine dioxide, Chlorite | doi:10.2903/j.efsa.2016.4388, doi:10.2903/j.efsa.2006.297 |
| Food additives, Zootechnical additives | 2 | Riboflavin-5'-phosphate sodium, Sodium benzoate | doi:10.2903/j.efsa.2013.3357, doi:10.2903/j.efsa.2016.4349, doi:10.2903/j.efsa.2016.4433, doi:10.2903/j.efsa.2011.2005, doi:10.2903/j.efsa.2011.2443, doi:10.2903/j.efsa.2012.2779 |
| Food contact materials, Nutritional additives | 2 | All-rac-alpha-tocopheryl acetate, D-alpha-tocopheryl acetate | doi:10.2903/j.efsa.2016.4412, doi:10.2903/j.efsa.2010.1635 |
| Food contact materials, Pesticides | 2 | Ethylene, Sulphur | doi:10.2903/j.efsa.2014.3555, doi:10.2903/j.efsa.2012.2508, doi:10.2903/j.efsa.2012.2643, doi:10.2903/j.efsa.2009.221r |
| Food contact materials, Technological additives | 2 | Bentonite, Clinoptilolite | doi:10.2903/j.efsa.2012.2904, doi:10.2903/j.efsa.2011.2007, doi:10.2903/j.efsa.2011.2276, doi:10.2903/j.efsa.2012.2787, doi:10.2903/j.efsa.2013.3179, doi:10.2903/j.efsa.2013.3155, doi:10.2903/j.efsa.2013.3039 |
| Heavy metal ions and metalloids, Meat inspection, Persistent organic pollutants | 2 | Cadmium (total), Lead (total) | doi:10.2903/j.efsa.2004.72, doi:10.2903/j.efsa.2009.980, doi:10.2903/j.efsa.2011.1975, doi:10.2903/j.efsa.2013.3263, doi:10.2903/j.efsa.2005.236, doi:10.2903/j.efsa.2010.1570, doi:10.2903/j.efsa.2013.3263, doi:10.2903/j.efsa.2005.236 |
| Heavy metal ions and metalloids, Persistent organic pollutants | 2 | Arsenic, inorganic derivates, Mercury (total) | doi:10.2903/j.efsa.2005.180, doi:10.2903/j.efsa.2009.1351, doi:10.2903/j.efsa.2005.236, doi:10.2903/j.efsa.2004.34, doi:10.2903/j.efsa.2008.654, doi:10.2903/j.efsa.2005.236 |
| Natural plant product contaminants, Processing contaminants | 2 | (-)-Scopolamine, Atropine | doi:10.2903/j.efsa.2008.691, doi:10.2903/j.efsa.2013.3386 |
| No category, Nutritional additives | 2 | Betaine, Vitamin D | doi:10.2903/j.efsa.2005.191, doi:10.2903/j.efsa.2013.3209, doi:10.2903/j.efsa.2013.3210, doi:10.2903/j.efsa.2013.3211, doi:10.2903/j.efsa.2010.1609, doi:10.2903/j.efsa.2012.2813, doi:10.2903/j.efsa.2013.3408, doi:10.2903/j.efsa.2014.3520, doi:10.2903/j.efsa.2012.2968, doi:10.2903/j.efsa.2013.3289, doi:10.2903/j.efsa.2014.3568 |
| No category, Technological additives | 2 | Kofa Grain pH5, Potassium diformate | doi:10.2903/j.efsa.2006.408, doi:10.2903/j.efsa.2011.2357, doi:10.2903/j.efsa.2012.2681, |

| Multiple Classification | Number of substances | Substances | Documents |
|---|---|---|---|
| | | (aqueous solution) | doi:10.2903/j.efsa.2004.140, doi:10.2903/j.efsa.2012.2530 |
| Nutrient sources, Processing contaminants | 2 | Mineral oil with medium and low viscosity (class I), Silicon dioxide | doi:10.2903/j.efsa.2009.1387, doi:10.2903/j.efsa.2008.1049, doi:10.2903/j.efsa.2012.2984, doi:10.2903/j.efsa.2009.1132, doi:10.2903/j.efsa.2012.2703 |
| Nutrient sources, Technological additives | 2 | Calcium L-ascorbate dihydrate, Calcium acetate | doi:10.2903/j.efsa.2009.994, doi:10.2903/j.efsa.2013.3104, doi:10.2903/j.efsa.2009.1088, doi:10.2903/j.efsa.2012.2571 |
| Processing contaminants, Technological additives | 2 | Formic acid, Sodium hydroxide | doi:10.2903/j.efsa.2012.2703, doi:10.2903/j.efsa.2014.3827, doi:10.2903/j.efsa.2015.4113, doi:10.2903/j.efsa.2012.2703, doi:10.2903/j.efsa.2012.2882 |
| Sensory additives, Zootechnical additives | 2 | Tannic acid, Trans-anethole | doi:10.2903/j.efsa.2014.3828, doi:10.2903/j.efsa.2016.4472, doi:10.2903/j.efsa.2011.2440, doi:10.2903/j.efsa.2012.2620, doi:10.2903/j.efsa.2016.4351 |
| Cocciodiostats/Hormones/Histomonostats, Mycotoxins | 1 | Zearalenone | doi:10.2903/j.efsa.2016.4425, doi:10.2903/j.efsa.2004.89, doi:10.2903/j.efsa.2011.2197 |
| Cocciodiostats/Hormones/Histomonostats, Natural plant product contaminants | 1 | Cyanogenic glycosides | doi:10.2903/j.efsa.2016.4424, doi:10.2903/j.efsa.2007.434 |
| Cocciodiostats/Hormones/Histomonostats, Processing contaminants | 1 | 3-Monochloropropane-1,2-diol fatty acid esters | doi:10.2903/j.efsa.2016.4426, doi:10.2903/j.efsa.2008.1048 |
| Feed intended for particular nutritional purposes, Nutrient sources | 1 | Manganese (total) | doi:10.2903/j.efsa.2016.4395, doi:xx.xxxx/x.xxxx.xxxx.xxxx |
| Feed intended for particular nutritional purposes, Nutrient sources, Nutritional additives | 1 | Selenious acid | doi:10.2903/j.efsa.2016.4398, doi:10.2903/j.efsa.2009.1009, doi:10.2903/j.efsa.2016.4442 |
| Feed intended for particular nutritional purposes, Zootechnical additives | 1 | Zeolite A | doi:10.2903/j.efsa.2004.160, doi:10.2903/j.efsa.2007.523 |
| Flavourings, Food additives, Food contact materials, No category, Pesticides, Sensory additives, Technological additives, Zootechnical additives | 1 | Benzoic acid | doi:10.2903/j.efsa.2008.835, doi:10.2903/j.efsa.2009.1025, doi:10.2903/j.efsa.2016.4433, doi:10.2903/j.efsa.2009.961, doi:10.2903/j.efsa.2006.408, doi:10.2903/j.efsa.2016.4657, doi:10.2903/j.efsa.2012.2785, doi:10.2903/j.efsa.2016.4353, doi:10.2903/j.efsa.2005.290, doi:10.2903/j.efsa.2007.457, doi:10.2903/j.efsa.2011.2005, doi:10.2903/j.efsa.2011.2358, doi:10.2903/j.efsa.2012.2620, doi:10.2903/j.efsa.2012.2775, doi:10.2903/j.efsa.2015.4157 |
| Flavourings, Food additives, No category, Sensory additives, Technological additives | 1 | Lactic acid | doi:10.2903/j.efsa.2009.975, doi:10.2903/j.efsa.2011.1924, doi:10.2903/j.efsa.2013.3144, doi:10.2903/j.efsa.2008.234r, doi:10.2903/j.efsa.2012.2928, doi:10.2903/j.efsa.2015.4198 |
| Flavourings, Food additives, No category, Technological additives | 1 | Formaldehyde | doi:10.2903/j.efsa.2010.1337, doi:10.2903/j.efsa.2007.415, doi:10.2903/j.efsa.2004.96, doi:10.2903/j.efsa.2014.3561, doi:10.2903/j.efsa.2014.3562, doi:10.2903/j.efsa.2014.3790 |
| Flavourings, Food additives, Technological additives | 1 | (E,E)-Hexa-2,4-dienoic acid | doi:10.2903/j.efsa.2009.1205, doi:10.2903/j.efsa.2011.1924, doi:10.2903/j.efsa.2015.4144, doi:10.2903/j.efsa.2014.3792 |
| Flavourings, Food contact materials, No category, Sensory additives | 1 | Acetaldehyde | doi:10.2903/j.efsa.2010.1337, doi:10.2903/j.efsa.2014.3555, doi:10.2903/j.efsa.2013.3423, |

| Multiple Classification | Number of substances | Substances | Documents |
|---|---|---|---|
| | | | doi:10.2903/j.efsa.2013.3169 |
| Flavourings, Food contact materials, Processing contaminants, Sensory additives | 1 | 2-Ethylhexanol | doi:10.2903/j.efsa.2009.929, doi:10.2903/j.efsa.2009.934, doi:10.2903/j.efsa.2011.2164, doi:10.2903/j.efsa.2012.2563, doi:10.2903/j.efsa.2009.961, doi:10.2903/j.efsa.2011.2482, doi:10.2903/j.efsa.2012.2927 |
| Flavourings, Natural plant product contaminants | 1 | Theobromine | doi:10.2903/j.efsa.2009.741, doi:10.2903/j.efsa.2008.725 |
| Flavourings, Natural plant product contaminants, Processing contaminants | 1 | Hydrogen cyanide | doi:10.2903/j.efsa.2004.105, doi:10.2903/j.efsa.2007.434, doi:10.2903/j.efsa.2007.551 |
| Flavourings, No category | 1 | Caffeine | doi:10.2903/j.efsa.2009.741, doi:10.2903/j.efsa.2015.4102 |
| Flavourings, Nutrient sources | 1 | 4-Hydroxy-5-methylfuran-3(2H)-one | doi:10.2903/j.efsa.2009.1061, doi:10.2903/j.efsa.2011.1841, doi:10.2903/j.efsa.2012.2901, doi:10.2903/j.efsa.2013.3390, doi:10.2903/j.efsa.2015.4117, doi:10.2903/j.efsa.2015.4286, doi:10.2903/j.efsa.2011.2395 |
| Flavourings, Nutrient sources, Nutritional additives | 1 | L-Lysine monohydrochloride | doi:10.2903/j.efsa.2006.373, doi:10.2903/j.efsa.2008.790, doi:10.2903/j.efsa.2008.761, doi:10.2903/j.efsa.2013.3365, doi:10.2903/j.efsa.2014.3895, doi:10.2903/j.efsa.2016.4471 |
| Flavourings, Pesticides, Sensory additives, Zootechnical additives | 1 | Eugenol | doi:10.2903/j.efsa.2009.965, doi:10.2903/j.efsa.2012.2506, doi:10.2903/j.efsa.2012.2914, doi:10.2903/j.efsa.2011.2440, doi:10.2903/j.efsa.2012.2620, doi:10.2903/j.efsa.2015.4273 |
| Flavourings, Pesticides, Zootechnical additives | 1 | Thymol | doi:10.2903/j.efsa.2008.711, doi:10.2903/j.efsa.2012.2916, doi:10.2903/j.efsa.2012.2620, doi:10.2903/j.efsa.2016.4351 |
| Flavourings, Processing contaminants, Sensory additives | 1 | Benzyl alcohol | doi:10.2903/j.efsa.2008.835, doi:10.2903/j.efsa.2009.1025, doi:10.2903/j.efsa.2011.2482, doi:10.2903/j.efsa.2012.2785 |
| Flavourings, Technological additives | 1 | Sodium diacetate | doi:10.2903/j.efsa.2011.2163, doi:10.2903/j.efsa.2012.2571 |
| Flavourings, Technological additives, Zootechnical additives | 1 | Ammonium chloride | doi:10.2903/j.efsa.2009.955, doi:10.2903/j.efsa.2011.1925, doi:10.2903/j.efsa.2012.2738, doi:10.2903/j.efsa.2012.2569, doi:10.2903/j.efsa.2016.4352 |
| Food additives, Food contact materials, No category, Nutrient sources | 1 | Magnesium (total) | doi:10.2903/j.efsa.2016.4599, doi:10.2903/j.efsa.2014.3637, doi:10.2903/j.efsa.2013.3408, doi:10.2903/j.efsa.2006.391a, doi:10.2903/j.efsa.2007.495, doi:10.2903/j.efsa.2008.761, doi:10.2903/j.efsa.2009.1088, doi:10.2903/j.efsa.2009.1118, doi:10.2903/j.efsa.2009.1146, doi:10.2903/j.efsa.2009.1187, doi:10.2903/j.efsa.2009.924, doi:10.2903/j.efsa.2009.947, doi:xx.xxxx/x.xxxx.xxxx.xxxx |
| Food additives, Food contact materials, Pesticides | 1 | Aluminium (total) | doi:10.2903/j.efsa.2008.754, doi:10.2903/j.efsa.2011.2157, doi:10.2903/j.efsa.2011.1999, doi:10.2903/j.efsa.2012.2904, doi:10.2903/j.efsa.2012.2906, doi:10.2903/j.efsa.2013.3401, doi:10.2903/j.efsa.2014.3637, doi:10.2903/j.efsa.2010.1889 |
| Food additives, Natural plant product contaminants | 1 | Nitrite | doi:10.2903/j.efsa.2010.1538, doi:10.2903/j.efsa.2008.689, |

| Multiple Classification | Number of substances | Substances | Documents |
|---|---|---|---|
| | | | doi:10.2903/j.efsa.2009.1017 |
| Food additives, Natural plant product contaminants, Nutrient sources, Processing contaminants | 1 | Nitrate | doi:10.2903/j.efsa.2010.1538, doi:10.2903/j.efsa.2008.689, doi:10.2903/j.efsa.2010.1935, doi:10.2903/j.efsa.2009.1111, doi:10.2903/j.efsa.2009.1391 |
| Food additives, No category, Nutrient sources, Processing contaminants, Zootechnical additives | 1 | Calcium (total) | doi:10.2903/j.efsa.2011.2318, doi:10.2903/j.efsa.2010.1609, doi:10.2903/j.efsa.2012.2814, doi:10.2903/j.efsa.2013.3408, doi:10.2903/j.efsa.2004.112, doi:10.2903/j.efsa.2004.135, doi:10.2903/j.efsa.2004.20, doi:10.2903/j.efsa.2006.391a, doi:10.2903/j.efsa.2007.491, doi:10.2903/j.efsa.2007.495, doi:10.2903/j.efsa.2008.761, doi:10.2903/j.efsa.2008.814, doi:10.2903/j.efsa.2008.866, doi:10.2903/j.efsa.2009.1088, doi:10.2903/j.efsa.2009.1146, doi:10.2903/j.efsa.2009.1187, doi:10.2903/j.efsa.2009.924, doi:10.2903/j.efsa.2016.4488, doi:10.2903/j.efsa.2009.1391, doi:10.2903/j.efsa.2007.504 |
| Food additives, No category, Nutritional additives, Pesticides | 1 | Ascorbic acid | doi:10.2903/j.efsa.2015.4087, doi:10.2903/j.efsa.2004.59, doi:10.2903/j.efsa.2013.3103, doi:10.2903/j.efsa.2013.3104, doi:10.2903/j.efsa.2013.3197 |
| Food additives, No category, Processing contaminants, Sensory additives | 1 | Methanol | doi:10.2903/j.efsa.2013.3496, doi:10.2903/j.efsa.2013.3423, doi:10.2903/j.efsa.2011.2482, doi:10.2903/j.efsa.2013.3169 |
| Food additives, No category, Technological additives | 1 | Propionic acid | doi:10.2903/j.efsa.2014.3779, doi:10.2903/j.efsa.2006.408, doi:10.2903/j.efsa.2011.2446 |
| Food additives, Nutrient sources, Nutritional additives | 1 | Beta-carotene | doi:10.2903/j.efsa.2012.2953, doi:10.2903/j.efsa.2016.4434, doi:10.2903/j.efsa.2012.2593, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2012.2737 |
| Food additives, Nutrient sources, Nutritional additives, Zootechnical additives | 1 | Riboflavin | doi:10.2903/j.efsa.2013.3357, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2014.3531, doi:10.2903/j.efsa.2016.4349 |
| Food additives, Nutrient sources, Processing contaminants | 1 | White mineral oil with high viscosity (kinematic viscosity at 100 °C not less than 11 mm²/s) | doi:10.2903/j.efsa.2013.3073, doi:10.2903/j.efsa.2009.1387, doi:10.2903/j.efsa.2008.1049, doi:10.2903/j.efsa.2012.2984 |
| Food additives, Pesticides | 1 | Calcium carbonate | doi:10.2903/j.efsa.2011.2318, doi:10.2903/j.efsa.2011.2298 |
| Food additives, Processing contaminants, Sensory additives | 1 | Propan-2-ol | doi:10.2903/j.efsa.2005.202, doi:10.2903/j.efsa.2012.2703, doi:10.2903/j.efsa.2015.4268 |
| Food additives, Processing contaminants, Technological additives | 1 | Phosphoric acid | doi:10.2903/j.efsa.2013.3444, doi:10.2903/j.efsa.2011.2482, doi:10.2903/j.efsa.2013.3043 |
| Food contact materials, Heavy metal ions and metalloids, No category, Nutrient sources | 1 | Boron (total) | doi:10.2903/j.efsa.2012.2642, doi:10.2903/j.efsa.2013.3401, doi:10.2903/j.efsa.2005.237, doi:10.2903/j.efsa.2004.80, doi:10.2903/j.efsa.2005.1044 |
| Food contact materials, Meat inspection | 1 | 4,4'-Diaminodiphenyl sulphone | doi:10.2903/j.efsa.2005.248a, doi:10.2903/j.efsa.2013.3263 |
| Food contact materials, No category, Nutrient sources | 1 | Phosphorus (total) | doi:10.2903/j.efsa.2013.3245, doi:10.2903/j.efsa.2005.233, doi:10.2903/j.efsa.2010.1584 |

| Multiple Classification | Number of substances | Substances | Documents |
|---|---|---|---|
| Food contact materials, No category, Nutrient sources, Pesticides | 1 | Iron (total) | doi:10.2903/j.efsa.2008.628, doi:10.2903/j.efsa.2012.2906, doi:10.2903/j.efsa.2004.125, doi:10.2903/j.efsa.2006.299, doi:10.2903/j.efsa.2007.495, doi:10.2903/j.efsa.2009.1187, doi:10.2903/j.efsa.2010.1584, doi:10.2903/j.efsa.2010.1585, doi:10.2903/j.efsa.2015.3973 |
| Food contact materials, Nutrient sources, Technological additives | 1 | Malic acid | doi:10.2903/j.efsa.2009.961, doi:10.2903/j.efsa.2006.391a, doi:10.2903/j.efsa.2009.1088, doi:10.2903/j.efsa.2014.3563 |
| Heavy metal ions and metalloids, Natural plant product contaminants, No category, Nutrient sources | 1 | Fluoride | doi:10.2903/j.efsa.2004.100, doi:10.2903/j.efsa.2005.237, doi:10.2903/j.efsa.2010.1593, doi:10.2903/j.efsa.2005.192, doi:10.2903/j.efsa.2013.3408, doi:10.2903/j.efsa.2008.882, doi:10.2903/j.efsa.2008.886 |
| Heavy metal ions and metalloids, No category | 1 | Nickel (total) | doi:10.2903/j.efsa.2015.4002, doi:10.2903/j.efsa.2005.146 |
| Heavy metal ions and metalloids, No category, Nutrient sources, Nutritional additives | 1 | Iodine (total) | doi:10.2903/j.efsa.2006.1046, doi:10.2903/j.efsa.2013.3408, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2005.168, doi:10.2903/j.efsa.2013.3099, doi:10.2903/j.efsa.2013.3100, doi:10.2903/j.efsa.2013.3101, doi:10.2903/j.efsa.2013.3178 |
| Meat inspection, No category | 1 | 3-Amino-oxazolidone-2 | doi:10.2903/j.efsa.2013.3263, doi:10.2903/j.efsa.2015.4140 |
| Natural plant product contaminants, No category | 1 | Delta9-Tetrahydrocannabinol | doi:10.2903/j.efsa.2015.4141, doi:10.2903/j.efsa.2011.2011 |
| No category, Sensory additives | 1 | Zeaxanthin | doi:10.2903/j.efsa.2012.2891, doi:10.2903/j.efsa.2009.1098 |
| No category, Zootechnical additives | 1 | Potassium diformate | doi:10.2903/j.efsa.2004.139, doi:10.2903/j.efsa.2006.325, doi:10.2903/j.efsa.2009.1315 |
| Nutrient sources, Nutritional additives, Processing contaminants | 1 | Chromium(III) | doi:10.2903/j.efsa.2008.887, doi:10.2903/j.efsa.2009.1111, doi:10.2903/j.efsa.2009.1112, doi:10.2903/j.efsa.2009.1113, doi:10.2903/j.efsa.2009.1187, doi:10.2903/j.efsa.2010.1882, doi:10.2903/j.efsa.2010.1883, doi:xx.xxxx/x.xxxx.xxxx.xxxx, doi:10.2903/j.efsa.2009.1043, doi:10.2903/j.efsa.2014.3595 |
| Nutrient sources, Persistent organic pollutants | 1 | Organotin compounds (including TBT, DBT, TPT and DOT) | doi:10.2903/j.efsa.2005.1063, doi:10.2903/j.efsa.2004.102, doi:10.2903/j.efsa.2005.236 |
| Nutrient sources, Sensory additives | 1 | Choline chloride | doi:10.2903/j.efsa.2009.948, doi:10.2903/j.efsa.2011.2353 |
| Nutrient sources, Zootechnical additives | 1 | Calcium disodium EDTA | doi:10.2903/j.efsa.2010.1414, doi:10.2903/j.efsa.2016.4472 |
| Nutritional additives, Processing contaminants | 1 | Chromium (VI) | doi:10.2903/j.efsa.2014.3532, doi:10.2903/j.efsa.2014.3595 |
| Nutritional additives, Sensory additives | 1 | Ethyl ester of beta-apo-8'-carotenoic acid | doi:10.2903/j.efsa.2016.4439, doi:10.2903/j.efsa.2009.1098 |
| Pesticides, Processing contaminants, Sensory additives | 1 | Ethanol | doi:10.2903/j.efsa.2009.215r, doi:10.2903/j.efsa.2011.2482, doi:10.2903/j.efsa.2013.3169 |
| Pesticides, Processing contaminants, Technological additives | 1 | Acetic acid | doi:10.2903/j.efsa.2013.3060, doi:10.2903/j.efsa.2012.2703, doi:10.2903/j.efsa.2012.2571 |
| Pesticides, Technological additives | 1 | Ethoxyquin | doi:10.2903/j.efsa.2010.1710, doi:10.2903/j.efsa.2012.2799, doi:10.2903/j.efsa.2015.4272 |

| Multiple Classification | Number of substances | Substances | Documents |
|---|---|---|---|
| Sensory additives, Technological additives | 1 | Fumaric acid | doi:10.2903/j.efsa.2012.2928, doi:10.2903/j.efsa.2013.3102 |