EXTERNAL SCIENTIFIC REPORT

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Compilation of a database, specific for the pesticide active substance and their metabolites, comprising the main genotoxicity endpoints

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Abstract

The terminal residues of pesticide active substances in food and feed commodities need to be duly identified following the requirements of Commission Regulation (EU) No 283/2013 in accordance with Regulation (EC) No 1107/2009. This information is necessary to derive the residue definition for the dietary risk assessment. EFSA initiated in 2009 a work programme to support the preparation of scientific guidance on the establishment of the residue definition for risk assessment. In 2012, the Panel on Plant Protection Products and their Residues (PPR Panel) adopted a scientific opinion on the toxicological relevance of pesticide metabolites for dietary risk assessment. In its opinion, the PPR Panel also indicated that the application of integrated approaches including the combination of QSAR models and read across for the genotoxicity assessment of pesticide residues would imply the availability of a robust database specific for pesticide active substances and their metabolites.
The overall objective of the project is the compilation of a database specific for pesticide active substances and their metabolites, which is comprising the different genotoxicity endpoints i.e. point mutations, structural and numerical chromosome aberrations. For each substances and metabolites (and or impurities when available), data collection, data extraction and data entry has been performed according to a methodology agreed by EFSA and the consortium. The database represents a practical tool to complement the in-silico tools i.e. QSAR, grouping and read across for prediction and indication of the genotoxicity hazard. Moreover, the database is expected to increase the specificity and sensitivity of the in-silico tools and to enlarge the chemical domains for their applicability.

Key words: data collection, pesticide residue definition, genotoxicity, point mutations, structural chromosome aberrations.

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Summary

The terminal residues of pesticide active substances in food and feed commodities need to be duly identified following the requirements of Commission Regulation (EU) No 283/2013 in accordance with Regulation (EC) No 1107/2009.

This information is necessary to derive the residue definition for the dietary risk assessment, a key step in the evaluation of the dietary risk for consumers of food commodities containing pesticides residues.

EFSA initiated in 2009 a work programme to support the preparation of scientific guidance on the establishment of the residue definition for risk assessment.

In 2012, the Panel on Plant Protection Products and their Residues (PPR Panel) adopted a scientific opinion on the toxicological relevance of pesticide metabolites for dietary risk assessment, based on the outcome of the outsourced activities.

In its opinion, the PPR Panel also indicated that the application of integrated approaches including the combination of QSAR models and read across for the genotoxicity assessment of pesticide residues would imply the availability of a robust database specific for pesticide active substances and their metabolites, which is comprising the main genotoxicity endpoints.

The overall objective resulting from this project, is the compilation of a database specific for pesticide active substances and their metabolites, which is comprising the different genotoxicity endpoints i.e. point mutations, structural and numerical chromosome aberrations and DNA damage. The database would represent a practical tool to complement the in-silico tools i.e. QSAR, grouping and read across for prediction and indication of the genotoxicity hazard. The availability of a database specific for pesticides active substances and their metabolites is expected to increase the specificity and sensitivity of the in-silico tools and to enlarge the chemical domains for their applicability.

Genotoxicity and chemical information have been collected for 380 active substances (out of 435 listed in Annex 2 of the call for proposal GP/EFSA/PRAS/2014/01) and their metabolites. For the remaining 56 active substances Draft Assessment Report or other report were not available (Appendix E).

Data collection on genotoxicity studies has been retrieved from regulatory toxicological reports as provided by the Rapporteur Member States in support of approval and their evaluations during the pesticide peer review process at European Level.

The database contains information from the studies as reported in the regulatory toxicological reports. The final conclusion by EFSA or EC on the overall genotoxic potential of active substance or metabolites taking into account all studies is not included in the database.

For all pesticide active substances and their metabolites data extraction has been performed to cover all available genotoxicity endpoints (i.e. point mutations, chromosome aberrations and DNA damage). Data have been recorded into an XML format, which has been built according to the agreed data model.

All procedures for data extraction and data entry were associated with Quality Assurance (QA) and Quality Control (QC) methods, before, during and after data extraction and entry.

The process of data extraction and data entry have been divided into two successive phases. During a first step, data were extracted from relevant documents and structured within a predefined Access database template. The second step consisted on the automatic flow of data from the Access DB to the XML format database. The use of this intermediate phase (the Access DB template) significantly facilitated the staff in transforming the unstructured information present in the dossier to a structured database. Indeed, distinct input forms for each study typology were available in order to make the data entry process easier and faster and in order to reduce typing/entry error.

Once the Access database has been filled, it has been converted into XML format to allow tables upload via the EFSA data collection framework. The data submission has been tested regularly during the project to ensure the data being collected is compliant with EFSA data standards. Furthermore, data extraction, collection and collation of the present assignment followed the specific standard operating procedures (SOPs).

It has to be underlined that during the project, chemical comprehensive information (i.e. code/trivial name, , chemical structure, , CAS# when available, Smiles codes, InChi code, IUPAC NAME and molecular formula), were collected for more than 2 thousand of metabolites.

Actually, looking at the whole database, the majority of the components scrutinized were metabolites, in addition, genotoxicity data were collected for more than 6 hundred of metabolites.

The most reported genotoxicity study type is bacterial reverse mutation (for *in vitro* studies), while, for *in vivo* studies, the most described one is mammalian erythrocyte micronucleous test. Considering studies performed on active substance only, 4 type of studies represent the majority of the data package (Bacterial reverse mutation assay, Mammalian erythrocyte micronucleus test, Mammalian cell gene mutation assay and *In vitro* mammalian chromosome aberration test) in line with EU data requirements on pesticides active substances.[1]

Looking at metabolites genotoxicity studies, the most frequently submitted are ***in vitro*** genotoxicity studies as the Bacterial reverse mutation assay and Mammalian cell gene mutation assay.

In the whole database, ambiguous genotoxicity studies results represent only 3% of the total, while more than 80% were negative and less than 15% were positive; separate analysis of the results for the metabolites gave very similar results

However, data extraction encountered some problems, such as the difficulty to retrieve genotoxicity data from some published or confidential studies cited only in the study description.

For the majority of the substances without Appendix B of EFSA conclusion, chemical names and chemical structures of metabolites (tested in genotoxicity studies) were searched in the whole Annex B Vol 3 of the DARs and in several correlated documents (addenda and annexes). EFSA was involved in this specific data search when the consortium was unable to find information, thus leading to a very large and time-consuming activity from both parts.

Retrieving information on confidential data (impurities), slowed down ICPS workflow and increased EFSA staff work load.

Extraction of the data for the chemical information and characterization was the most time-consuming step in the evaluation of the substances due to the workload for data curation and evaluation.

A key recommendation for further work includes:

1. All the genotoxicity data should be entered into the database following the specific SOPs
2. To improve the accessibility and make the data easily available, it would be useful to create a web portal that allows querying the database, according to the different variables present in the database.
3. The actuality of the data should be maintained by performing regular updates of the database. The most recent genotoxicity data present in pesticide dossiers uploaded on EFSA website, should be included.

[1] COMMISSION REGULATION (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market.)

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1. Introduction

1.1. Background as provided by the requestor

The terminal residues of pesticide active substances in food and feed commodities need to be duly identified following the requirements of Commission Regulation (EU) No 283/2013 in accordance with Regulation (EC) No 1107/2009.

This information is necessary to derive the residue definition for the dietary risk assessment, a key step in the evaluation of the dietary risk for consumers of food commodities containing pesticides residues.

General principles to establish the residue definition for risk assessment have been elaborated by the Organisation for Economic Co-operation and Development (OECD) in the guidance document on the definition of residue.

EFSA initiated in 2009 a work programme to support the preparation of scientific guidance on the establishment of the residue definition for risk assessment.

In 2012, the Panel on Plant Protection Products and their Residues (PPR Panel) adopted a scientific opinion on the toxicological relevance of pesticide metabolites for dietary risk assessment, based on the outcome of the outsourced activities.

In its opinion, the PPR Panel also indicated that the application of integrated approaches including the combination of QSAR models and read across for the genotoxicity assessment of pesticide residues would imply the availability of a robust database specific for pesticide active substances and their metabolites, which is comprising the main genotoxicity endpoints.

1.2. Terms of Reference as provided by the requestor

Overall objective:

The overall objective resulting from this project, is the compilation of a database specific for pesticide active substances and their metabolites, which is comprising the different genotoxicity endpoints i.e. point mutations, structural and numerical chromosome aberrations. The database would represent a practical tool to complement the in-silico tools i.e. QSAR, grouping and read across for prediction and indication of the genotoxicity hazard. The Data Model is included in this document (Appendix C-Data Model). The availability of a database specific for pesticides active substances and their metabolites is expected to increase the specificity and sensitivity of the in-silico tools and to enlarge the chemical domains for their applicability. Data retrieval should be comprehensive enough to include information on the endpoints evaluated, the test system used, activity following metabolic activation and the underlying mechanism of genotoxicity.

Specific objectives 1:

The respective data extraction/collection covers all genotoxicity endpoints of the active substances and their metabolites reported in the pesticide dossiers submitted for registration under Directive 91/414/EEC or Regulation (EC) No 1107/2009 (Annex II, point 5.4 for the active substances and point 5.8 for metabolites). Appendix B (List of active substances and Dossier type) of this document contains the list of substances for which genotoxicity data have been retrieved and the dossier type: dossiers A for which peer review was done by EFSA, and dossiers B for which peer review was not done by EFSA.

Specific objectives 2:
The database have been compiled according to the data model in the Appendix C - Data Model, this ensures the data is compliant with EFSA chemical hazards database requirements (Report on "Data collection and data entry for EFSA's chemical hazards database NP/EFSA/EMRISK/2011/01" http://www.efsa.europa.eu/en/supporting/pub/458e.htm). The resulting dataset is exportable in a format to allow horizontal upload into the OECD QSAR toolbox. The resulting tables have been exported in XML format and submitted via the EFSA Data Collection Framework. The submitted data have been subjected to automated validation and only transmissions where all tables have the status "Valid" have been accepted.

This grant was awarded by EFSA to:

Beneficiary: a consortium of the Department of Biomedical and Clinical Sciences of the University of Milan UMIL (Italy) and ASST Fatebenefratelli Sacco/ICPS (Italy).

The tasks and responsibilities have been divided amongst the 2 consortium partners:

- ASST Fatebenefratelli Sacco/ICPS:
    1. Data collection
    2. Data extraction
    3. Data entry
    4. Quality assurance
    5. QualityControl
    6. Data submission
- UMIL:
    1. Data collection
    2. Data extraction
    3. Data entry

Grant title: Compilation of a database, specific for the pesticide active substance and their metabolites, comprising the main genotoxicity endpoints. GP/EFSA/PRAS/2014/01

Grant number: GP/EFSA/PRAS/2014/01

2. Data and Methodologies

The following general methodology has been agreed by EFSA and the consortium in the project outline and complemented by further agreements made between the project team and EFSA.

2.1. Data

2.1.1. Data collection

Data have been retrieved for pesticide active substances listed in the Appendix B (list of active substances and Dossier type). Pesticides in Appendix B can be grouped in two main groups, one (dossiers A) for which peer review was done by EFSA, and the other group (dossiers B) for which the Peer Review was not done by EFSA.

For dossiers A data collection has been retrieved from regulatory toxicological reports provided in support of approval and their evaluations under the peer review process of Directive 91/414/EC and Regulation (EC) 1107/2009 (Draft Assessment Reports, additional reports, addenda, evaluation table and discussion table, EFSA Conclusion, Commission reports) as available in the EFSA journal. The EFSA Data Management System (DMS) was used as an alternative source to collect data.

For dossiers B data collection has been retrieved using European Commission (EC) Review Reports, Draft Assessment Reports or addenda to the Draft Assessment Reports, these last available only in CIRCABC and in DMS.

For some pesticide active substances Draft Assessment Reports are not available in CIRCABC and in DMS. For these substances the data collection has not been performed (see Appendix E).

2.2. Methodologies

2.2.1. Data extraction and data entry

For all pesticide active substances and their metabolites data extraction has been performed to cover all genotoxicity endpoints (i.e. point mutations, chromosome aberrations and DNA damage) in the pesticide dossiers submitted for registration. This included genotoxicity studies reported in section B.6.4 (B.5.4. for some dossiers B) and in section B.6.8 (B.5.8 for some dossiers B) of DARs.

Data and information from genotoxicity studies have been recorded into an XML format, which has been built according to the data model in Appendix C- Data Model, to facilitate data submission via the EFSA data collection framework. The set of data and information included in the database has been those listed below:

- Chemical identifiers (i.e. code/trivial name, chemical name, chemical structure, SMILE notation and codes, CAS# when available) according to the model in Appendix C Table 4 SUBSTANCE_COMPONENT.
- For dossiers A, chemical identifiers to be retrieved in the first place from the EFSA conclusion (Appendix A for active substances and Appendix B for the metabolites in the EFSA conclusion). If chemical identifiers are not available in the EFSA conclusion, the information has been retrieved from the Draft Assessment Report or corresponding Final Addendum.
- For dossiers B, chemical identifiers to be retrieved from the EC Review Report, Draft Assessment Reports or Addendum to the Draft Assessment reports.
- Smiles codes, InChi code, IUPAC NAME and molecular formula have been generated according to the structural formula as drawn in the EFSA conclusion (Appendix A for active substance and Appendix B for the metabolites in the EFSA conclusion). If the formula was not available in the EFSA conclusions, it has been retrieved from DARs or final addendum to the DAR. In order to facilitate these particular type of data insertion, a specific tailored software has been used (ACDb, version C20 H41) that is able to derive the chemical identifiers starting from the simple chemical name instead of drawing manually the structural formula sketch.

- References, data protection and confidentiality have been reported according the model in Appendix C_ Table 3 OPINION.
  For each genotoxicity study, information on whether data protection is claimed or not, have been provided as indicated in the reference list of the Draft Assessment Reports and/or

(Final) Addendum (point B.6.15 or B.5.15). Reference of the source of the genotoxicity data (i.e. Draft Assessment Reports or (Final) Addendum), the Rapporteur Member State (RMS) and year of evaluation and date of the EFSA conclusion or year of the EC review report have been reported. During the implementation of the project, sensitive and confidential data have been treated in compliance with the Data Protection Article 59 and Confidentiality Article 63 as stipulated in Regulation (EC) No 1107/2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC.

- Genotoxicity endpoints has been reported according to the model in Appendix C Table 2 GENOTOX, therefore, information regarding testing method, organism and strain, metabolic activation and result, as well as acceptability of the genotoxicity study according to the RMS assessment has been reported. Relevant remarks have also been included. For example if there was evidence that the test substance contained genotoxic impurities, if there was no proof of tissue exposure in the *in vivo* genotoxicity studies, if in case of equivocal first tier results (*in vitro*), they were addressed with the most appropriate second tier assessment (*in vivo*).

- Relationships have been reported according to the model in Appendix C Table 1 FACT_GENOTOX.

- COMPONENT-SYNONIMS: EFSA requested an additional table during the project: Component Synonym Table, Appendix C Table 5, which characterizes the trade name of the components and substances inserted into the database.

Furthermore, chemical identifiers for metabolites without genotoxicity data listed in the Appendix B of the EFSA conclusions has been retrieved and inserted in the database according to Appendix C Table 4 SUBSTANCE_COMPONENT.

2.2.2. Standard Operating Procedures for data collection, data extraction, data entry and data entry quality check

Data collection

Data collection: performed by both ICPS and UMIL; all partners have formal licence to access CIRCA BC (Interest groups: PLANT PROTECTION PRODUCTS AND THEIR RESIDUES and PPP zonal).
For dossiers A EFSA conclusions have been retrieved from the EFSA journal, while background documents (Draft Assessment Reports or final addendum to the DAR) have been retrieved from EFSA journal and CIRCABC. The EFSA Data Management System (DMS), as an alternative source to collect data, was used during the project.

For dossiers B European Commission review Reports have been retrieved by EU pesticide database portal, while Draft Assessment Reports or final addendum to the DARs have been retrieved from CIRCABC.

Data extraction and data entry

Data extraction and data entry have been divided between ICPS and UMIL and performed by team members.
All procedures for data extraction and data entry were associated with Quality Assurance (QA) and Quality Control (QC) methods. Several protocols have been applied in order to enhance a high quality of the data flow. The process of data extraction and data entry have been divided into two successive phases. During a first step, data were extracted from relevant documents and structured within a predefined Access database template. This last has been tailored on Appendix C data model structure. The second step consisted on the automatic flow of data from the Access DB to the XML format database. The use of this intermediate phase (the Access DB template) significantly facilitated the staff in transforming the unstructured information present in the dossier to a structured database. Indeed, distinct input forms for each study typology were available in order to make the data entry process easier and faster and in order to reduce typing/entry error. The intermediate Access database facilitates data entry both from a human-computer interaction point of view and from an automatic error prevention point of view. The implementation of the Access database and its exportation in XML format have been performed by ICPS. Once XML file has been generated, ICPS ensured the submission via the EFSA data collection framework.

QA and QC procedures have been applied before, during and after data extraction and entry in the database.

QA before data extraction

DB structure

The main focus of QA in this phase was the construction of the Access DB templates. Different templates have been implemented for each study typology, but all data have been organized in one single database (one record for each study). This Access DB include all the fields/tables that need to be filled in the final database (Appendix C-Data Model). To allow data migration via the EFSA data collection framework the Access DB has been exported in XML format.

Coding system

A coding system has been implemented. Each study has been identified by a univocal, automatically generated alphanumeric code. In addition, an incremental numbering (counter) prevented any duplicate.

Staff responsibility

Two/three members of each team have been identified before the start of the data extraction as the people assigned to data extraction and data entry.

QA/QC during data extraction

Practical data extraction

As pesticide dossiers are not formatted with a single style, nor level of information is homogeneously reported, automatic processes for data extraction is unfeasible. Thus, data extraction have been performed directly by staff members while reading all the relevant studies and corresponding

information. However, the influence due to data manipulation by the staff operator has been kept as low as possible.

QA/QC during data entry

DB format

The Access DB template has been formatted in order to decrease the possibility of errors and missing entries. For constrained fields, for which only pre-defined set of values were allowed, drop-down menu have been compiled. Other constraints were on format data type (e.g. no text allowed in numerical entries). In addition, a series of hierarchical menus have been implemented. Choosing one entry in a menu results in a filter of entries into the concatenated dependent menu (e.g.: choosing test type: "bacterial reverse mutation assay" results in OECD guidelines 471 automatically) Also, at the end of the entry process for a study, fields left empty will be highlighted and the user was asked to re-check carefully all of them.

Approaches to minimize errors

Two different approaches have been followed to minimize the errors that might occur during data entry:

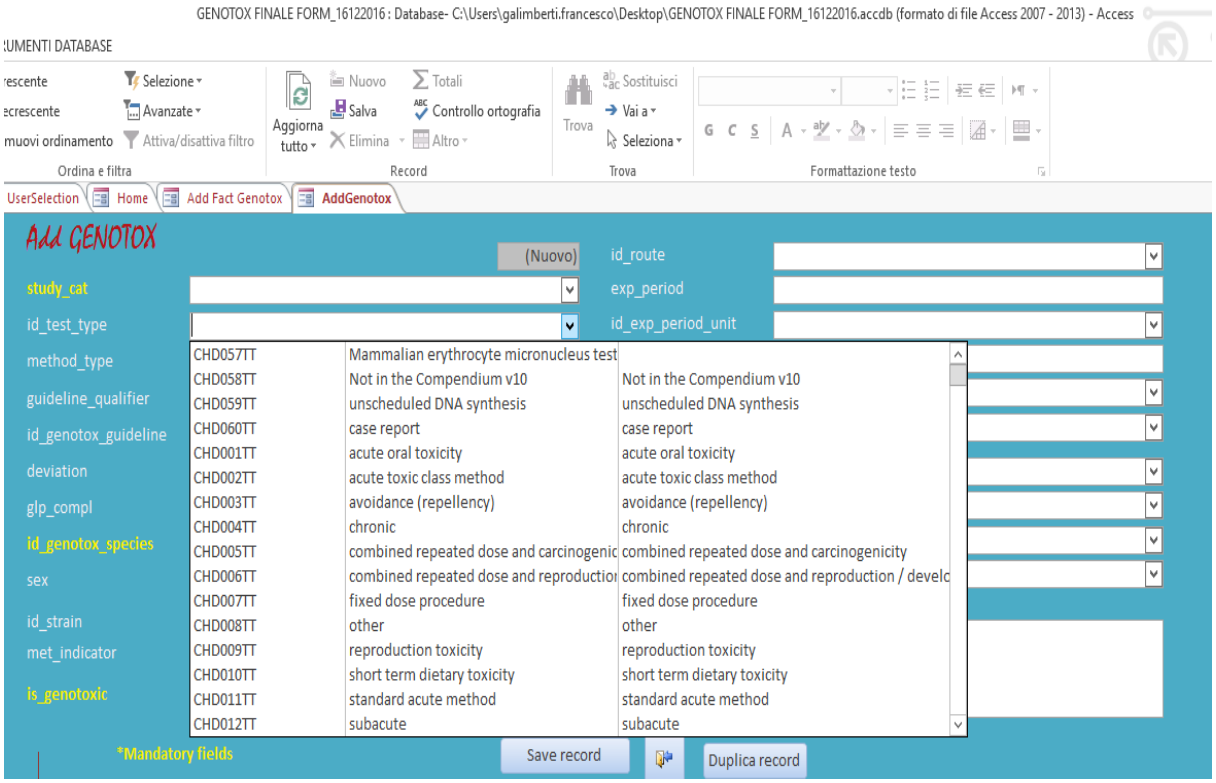
- Automatic verification of data quality at the data entry level.
- Manual revision of the collected data to be submitted.

In the data entry phase, automatically detectable errors can be distinguished in two main categories:

- Structural errors such as: type mismatch, missing values for mandatory fields, wrong format (e.g., dates), and length exceeding the maximum allowed one.
- Logical errors such as: Values that are not part of the "dictionary" in case of fields related to a catalogue. Update or deletion of a parent record without reflecting changes to children records.

For structural errors, the nature itself of the developed database prevented to store wrong data. In fact, in the database creation phase, it was specified for each field its type, length, format and mandatory fields. To facilitate the data insertion, pick lists were developed (see Figure 1).

Figure 1: Example of pick list in the data entry interface.



Metadata

A system of metadata has been implemented in order to keep track of the data flow history. Each study (represented by one record in the Access DB) was associated with:

- the name of the operator(s) who performed the data entry
- the date in which the data entry was performed

This system easily identify the responsibility for the data entry process, and make very easy to trace back the source of the data.

DB Replicates

Few days before each interim data submission, three members of both partners, performed-each other-a complete check of inserted data. A computer-based automatic comparison of the data inserted in the DB replicates has been then performed. Where inconsistencies have been found, an immediate check on the origin of the data has been performed. Wrong entries have been corrected immediately and a record has been added to the Register of amendments (see following text).

Data protection

In order to ensure data protection from informatics failures, an automatic backup system has been adopted. Access to computers where data have been stored were protected by a password.

Data extraction, collection and collation of the present assignment followed the standard operating procedures (SOPs) as defined in Appendix – J.

QC after data entry

Visual check

Few days before each interim data submission, a visual check of the database has been performed. In addition, in-depth controls were performed for a suitable percentage of randomly selected data.

Based on the experience gained on the previous projects, the following general quality check actions were performed for manual revision of the inserted data:

- The data entry team shares issues encountered during data extraction. This allows to define common rules for data entry (SOPs) and to highlight any exceptional case that needs special care or special insertion (Appendix D- Metabolites with Markush structure not inserted in the DB, Appendix G - Details for QU08A and QU09A attribution, Appendix I - Compounds with no chemical identifiers).
- Suitable percentage of gathered data is randomly checked.
- Views of the collected data are analysed to search possible issues/errors. At this stage, a number of empirical and internal rules are followed.

For further details please see SOP attached (Appendix J)

Register of amendments

This register keep track of all the amendments, each record of this register identify:

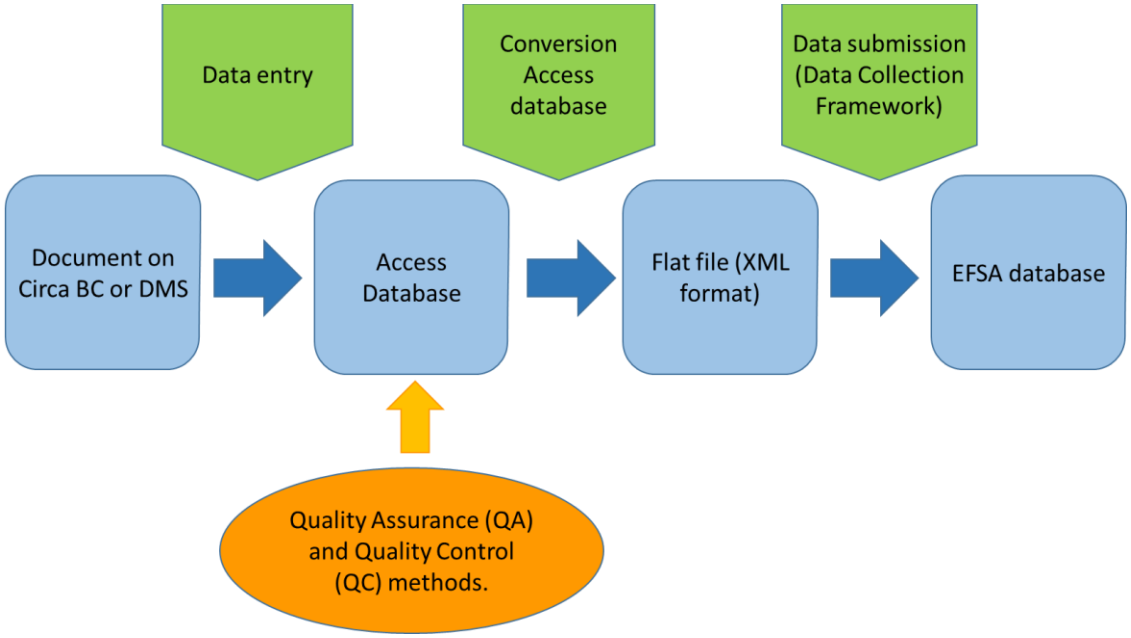
- The substance
- The particular entry
- The part in which the error was found
- The wrong entry and the specific correction
- The operators involved
- The data of the original entry and of its correction

This register has been used to quantify the errors detected in order to assess the efficacy of the adopted QA/QC procedures (see Appendix K).

2.2.3. Data submission

Once the Access database has been filled, it has been converted into XML format to allow tables upload via the EFSA data collection framework. The data submission has been tested regularly during the project to ensure the data being collected is compliant with EFSA data standards. The final submission of the completed database has been done at the end of the project.

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



3. Assessment/Results

ASST Fatebenefratelli Sacco/ICPS and UMIL have performed the data collection, data extraction and data entry while ICPS was responsible for database creation and quality procedure according to agreed SOPs. Moreover, ICPS was in charge for all the interim data submissions and provided the final report together with the final database.

Genotoxicity data from agreed substances (Appendix B- List of Active Substances and Dossier type) were collected and analyzed (see also Appendix F- Date of data dossier collection).

For 56 substances out of the 435 substances to be screened neither Draft Assessment Reports, nor other reports were available (Appendix E- Substances for which the DAR are not available or DAR with no genotoxicity studies).

The data collection table has been filled according to Appendix C- Data Model as was agreed by EFSA and the consortium.

The list of genotoxicity study type is:

1. Bacillus Subtilis Recombination Assay
2. Bacterial Forward Mutation Assay
3. Bacterial Reverse Mutation Assay
4. Chromosome Aberration Assay
5. Dna Damage And Repair Assay, Unscheduled Dna Synthesis In Mammalian Cells *In Vitro*
6. Dominant Lethal Assay
7. Drosophila Slrl Test
8. Heritable Translocation Assay
9. *In Vitro* Gene Mutation Assay In Fungi
10. *In Vitro* Mammalian Cell Micronucleus Test
11. *In Vitro* Mammalian Cell Transformation Assay
12. *In Vitro* Mammalian Chromosome Aberration Test
13. Mammalian Cell Gene Mutation Assay
14. Mammalian Erythrocyte Micronucleus Test
15. Mammalian Germ Cell Cytogenetic Assay
16. Mitotic Recombination In Saccharomyces Cerevisiae
17. Mouse Spot Test
18. Other
19. Single Cell Gel/Comet Assay In Mammalian Cells For Detection Of Dna Damage
20. Sister Chromatid Exchange Assay In Mammalian Cells
21. Somatic Mutation Assay In Drosophila
22. Sos/Umu Test
23. Unscheduled Dna Synthesis
24. Yeast Cytogenetic Assay

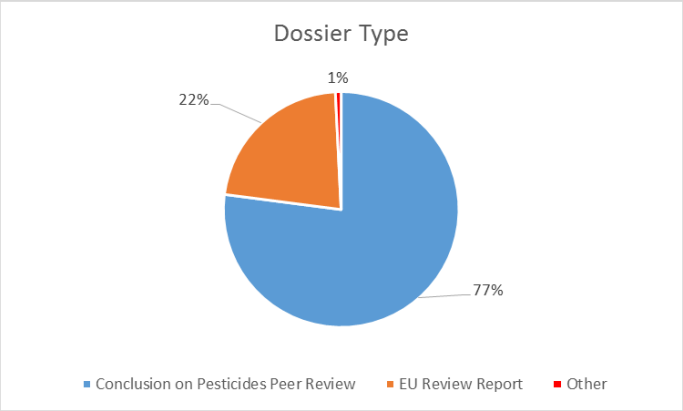
3.1. Results obtained from the data collection

Overview of collected data

From the 380 active substances that were scrutinized (see Appendix A), 292 pesticides were identified as dossier type A (peer review of DARs and finalisation of the risk assessment is done by EFSA),

whereas 84 were identified as dossier type B (Peer Review of the Draft Assessment Reports and the finalization of the risk assessment was not done by EFSA). 3 substances were no identified with a Dossier A or B ("other" in Figure 3) (see Appendix B-List of Active Substances and dossier Type for details).

Figure 3: Dossier type



Regarding substances for which the Draft Assessment Report or other report were not available, all 56 active substances were dossier type B.

For each qualifier, the number is presented in the following table (see Table 1 and Figure 4). The majority of the qualifier scrutinized is represented by metabolites. The number of metabolites not investigated for genotoxicity potential represents the vast majority of the compound recorded. However, metabolites investigated for genotoxicity potential were 664.

Table 1: Total number of substances and correlated qualifiers scrutinized

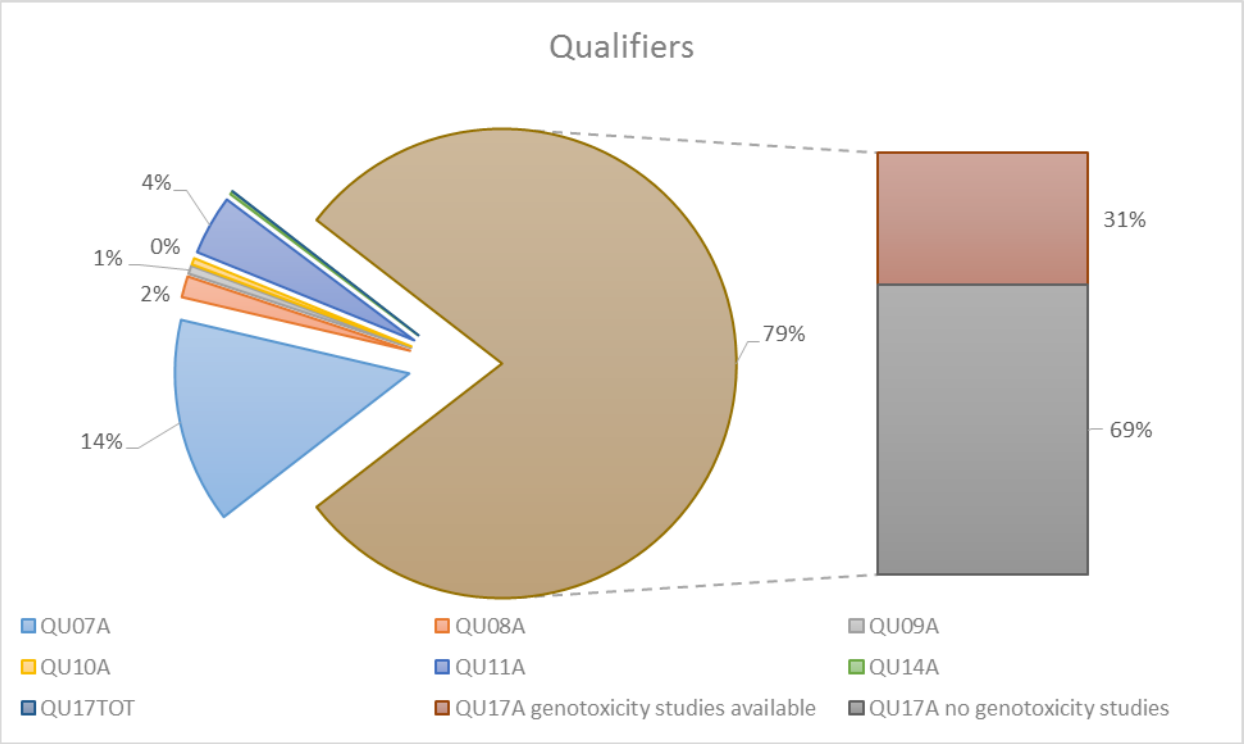
Qualifier		N°	% tot
QU07A		**378***	14
QU08A		36	1
QU09A		18	1
QU10A		12	0
QU11A		**110**	4
QU14A		**6**	0,2
QU17A	a	664	25
	b	1444	54
TOT		2671	100

* two of the 380 active substances are qualified as QU14A

QU07A	Component is identical to the substance
QU08A	Component is part of a group assessment
QU09A	Component is part of a group but not included in the group assessment
QU10A	Component is the active ingredient of the mixture or formulation

QU11A	Component is an impurity in the mixture or formulation
QU14A	Component is part of a mixture or formulation
QU17A	Component is a metabolite of the substance
a	genotoxicity data available
b:	no genotoxicity data performed

Figure 4: Substances, metabolites and other qualifiers



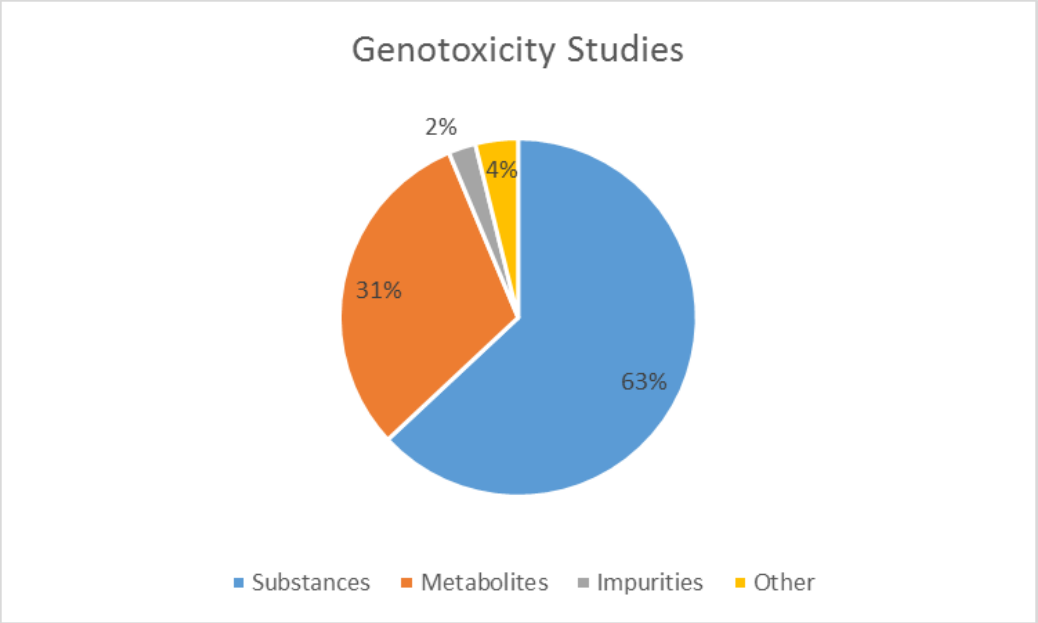
For substances, metabolites and impurities, the number of genotoxicity studies and the number of entries string is presented in the following table (see Table 2). The studies on active substances represent 63% of the total; the studies on metabolites represent 31% of the total, while studies on impurities are only 2% of the total (see Figure 5).

Table 2: Total number of genotoxicity studies for substances and metabolites

	Substances	Metabolites	Impurities	Other*	TOT
N° of studies	3465	1685	136	211	5497
N° of entries string	13132	99294	1125	852	24403
N° of entries considering duplicates	**13173**	**10624**	**1131**	**924**	**25852**

*Q07, Q 08, Q 09, Q 10, Q 14 included

Figure 5: Genotoxicity studies percentage in selected qualifier



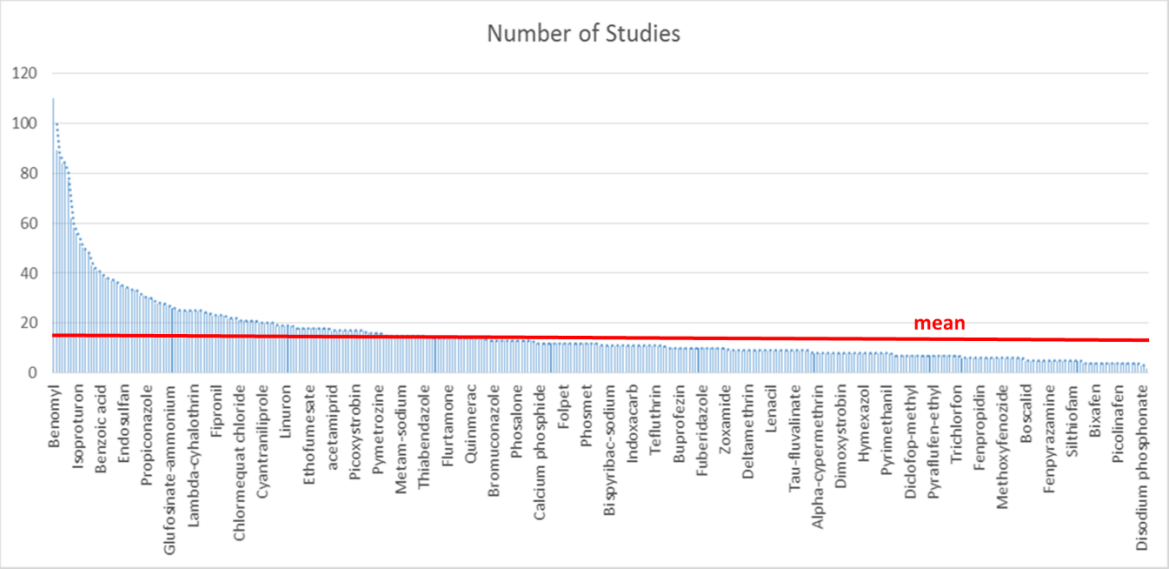
Considering each substance and related metabolites, mean studies for each DAR are presented below (see Table 3 and Figure 6).

The DAR characterized by the minimum number of studies is Ferric phosphate (2 studies), while the substance characterized by the maximum number of studies is Benomyl (110 studies). However in some cases genotoxicity studies could not be retrieved (see Appendix H – List of studies not inserted in the database).

Table 3: DAR genotoxicity studies numbers

	DAR mean	DAR max	DAR min	DAR TOT
N° of studies	15.2	110 (Benomyl)	2 (Ferric phosphate)	5746
N° of entries string	68.2	364 (Mancozeb)	6 (Fenthion)	25795

Figure 6: DAR genotoxicity studies numbers



Considering each genotoxicity study type, percentages from the active substances data package are presented below (see Table 4 and Figure 7).

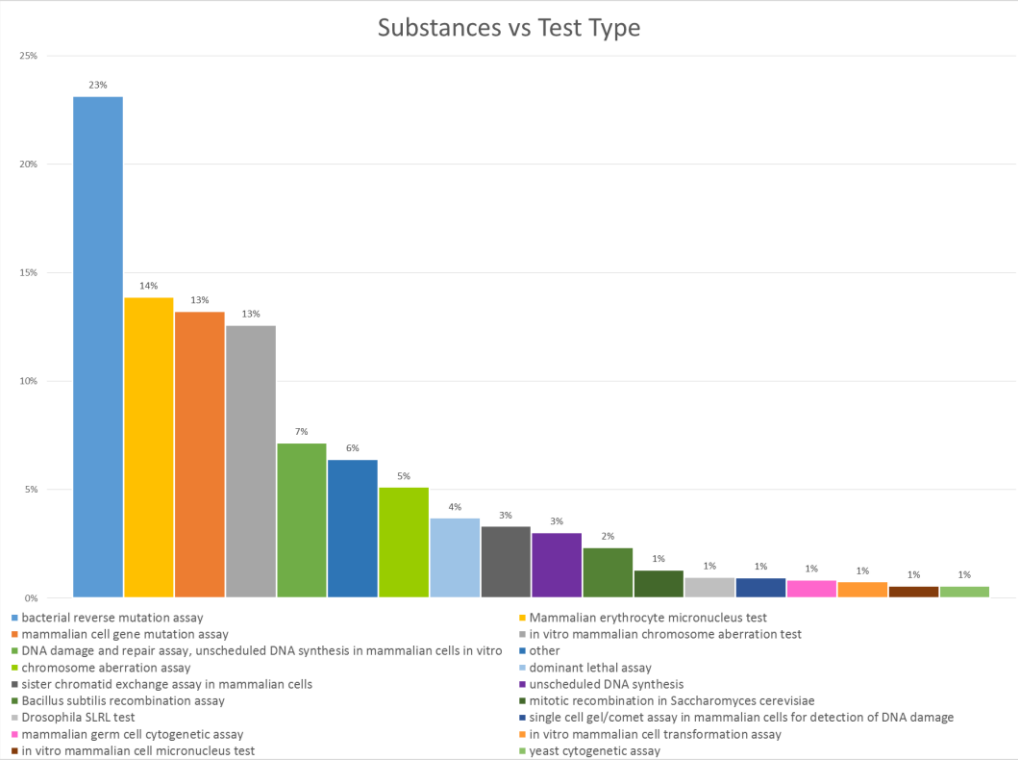
The most frequently submitted one is bacterial reverse mutation considering *in vitro* studies, while for *in vivo* studies the most frequently submitted one is mammalian erythrocyte micronucleous test.

Table 4: test type distribution in active substances

Vitro/vivo	Test type	% TOT
vitro	Bacterial reverse mutation assay	23%
vivo	Mammalian erythrocyte micronucleus test	14%
vitro	Mammalian cell gene mutation assay	13%
vitro	*In vitro* mammalian chromosome aberration test	13%
vitro	DNA damage and repair assay, unscheduled DNA synthesis in mammalian cells *in vitro*	7%
vitro/vivo	Other	6%
vivo	Chromosome aberration assay	5%
vivo	Dominant lethal assay	4%
vitro/vivo	Sister chromatid exchange assay in mammalian cells	3%
vivo	Unscheduled DNA synthesis	3%
vitro	Bacillus subtilis recombination assay	2%
vitro	Mitotic recombination in Saccharomyces cerevisiae	1%
vivo	Drosophila SLRL test	1%

vitro/vivo	**Single cell gel/comet assay in mammalian cells for detection of DNA damage**	**1%**
vivo	**Mammalian germ cell cytogenetic assay**	**1%**
vitro	***In vitro* mammalian cell transformation assay**	**1%**
vitro	***In vitro* mammalian cell micronucleus test**	**1%**
vitro	**Yeast cytogenetic assay**	**1%**

Figure 7: test type distribution in active substances



Considering each genotoxicity study type, percentages from the metabolites data package are presented below (see Table 5 and Figure 8).

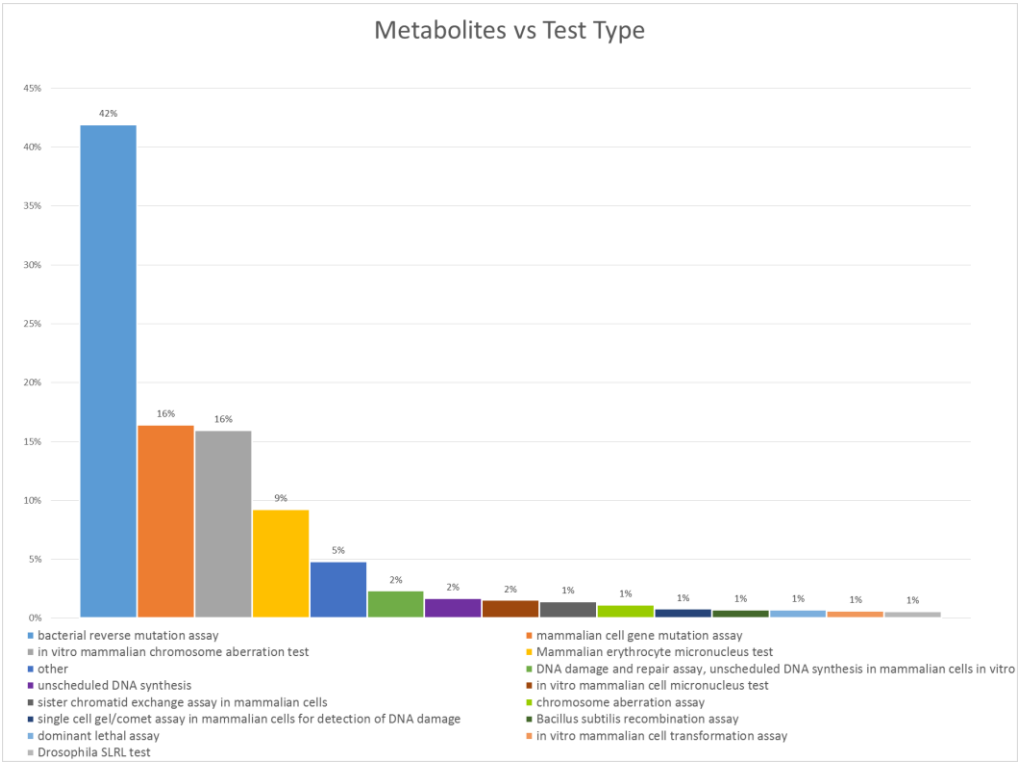
The most representative *in vitro* study is bacterial reverse mutation while, for *in vivo* studies the most representative one is mammalian erythrocyte micronucleous test as for active substances.

Table 5: test type distribution in metabolites

Vitro/vivo	Test type	% tot
vitro	**Bacterial reverse mutation assay**	42%
vitro	**Mammalian cell gene mutation assay**	16%
vitro	***In vitro* mammalian chromosome aberration test**	16%
vivo	**Mammalian erythrocyte micronucleus test**	9%
vitro/vivo	**Other**	5%
Vitro	**Dna damage and repair assay, unscheduled dna synthesis in mammalian cells *in vitro***	2%

Vivo	**Unscheduled dna synthesis**	2%
vitro	***In vitro* mammalian cell micronucleus test**	2%
vitro/vivo	**Sister chromatid exchange assay in mammalian cells**	1%
vivo	**Chromosome aberration assay**	1%
vitro/vivo	**Single cell gel/comet assay in mammalian cells for detection of dna damage**	1%
vitro	**Bacillus subtilis recombination assay**	1%
vivo	**Dominant lethal assay**	1%
vitro	***In vitro* mammalian cell transformation assay**	1%
vivo	**Drosophila slrl test**	1%

Figure 8: test type distribution in metabolites



In the whole database, ambiguous genotoxicity studies results represent only 3% of the total, while 83% were negative and 14% were positive.

Separate analysis of the results for the metabolites- gave very similar results (see Table 6-7-8 and Figure 9-10-11).

Table 6: Genotoxicity test result distribution in all qualifiers

ALL QUALIFIERS

Results	Studies%
Negative	83
Ambiguous / Inconclusive	3
Positive	14
TOTAL	**100**

Figure 9: Genotoxicity test result distribution in all qualifiers

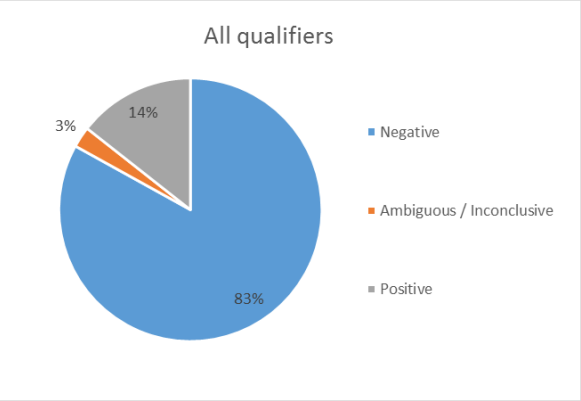


Table 7: Genotoxicity test result distribution in active substances

ACTIVE SUBSTANCES

Results	Studies %
Negative	82
Ambiguous / Inconclusive	3
Positive	15
TOTAL	**100**

Figure 10: Genotoxicity test result distribution in active substances

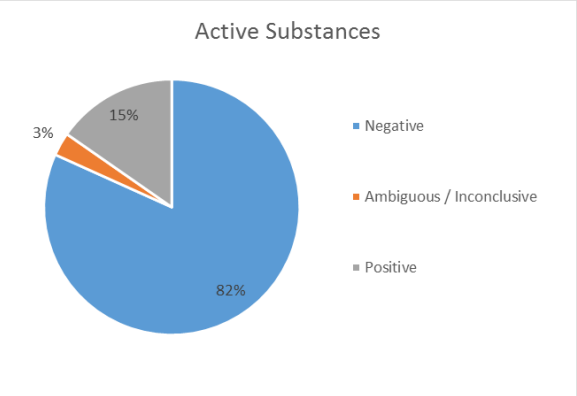
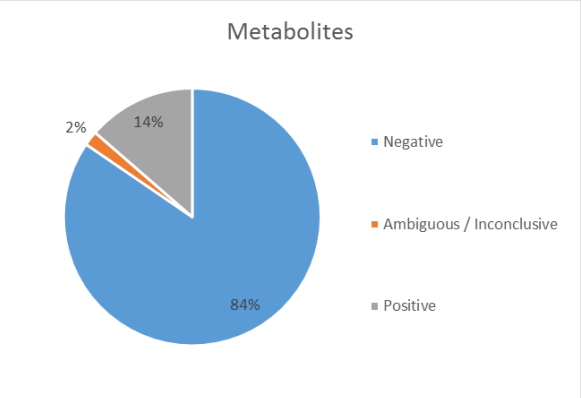


Table 8: Genotoxicity test result distribution in metabolites

METABOLITES

Results	Studies %
Negative	85
Ambiguous / Inconclusive	2
Positive	14
TOTAL	**100**

Figure 11: Genotoxicity test result distribution in metabolites

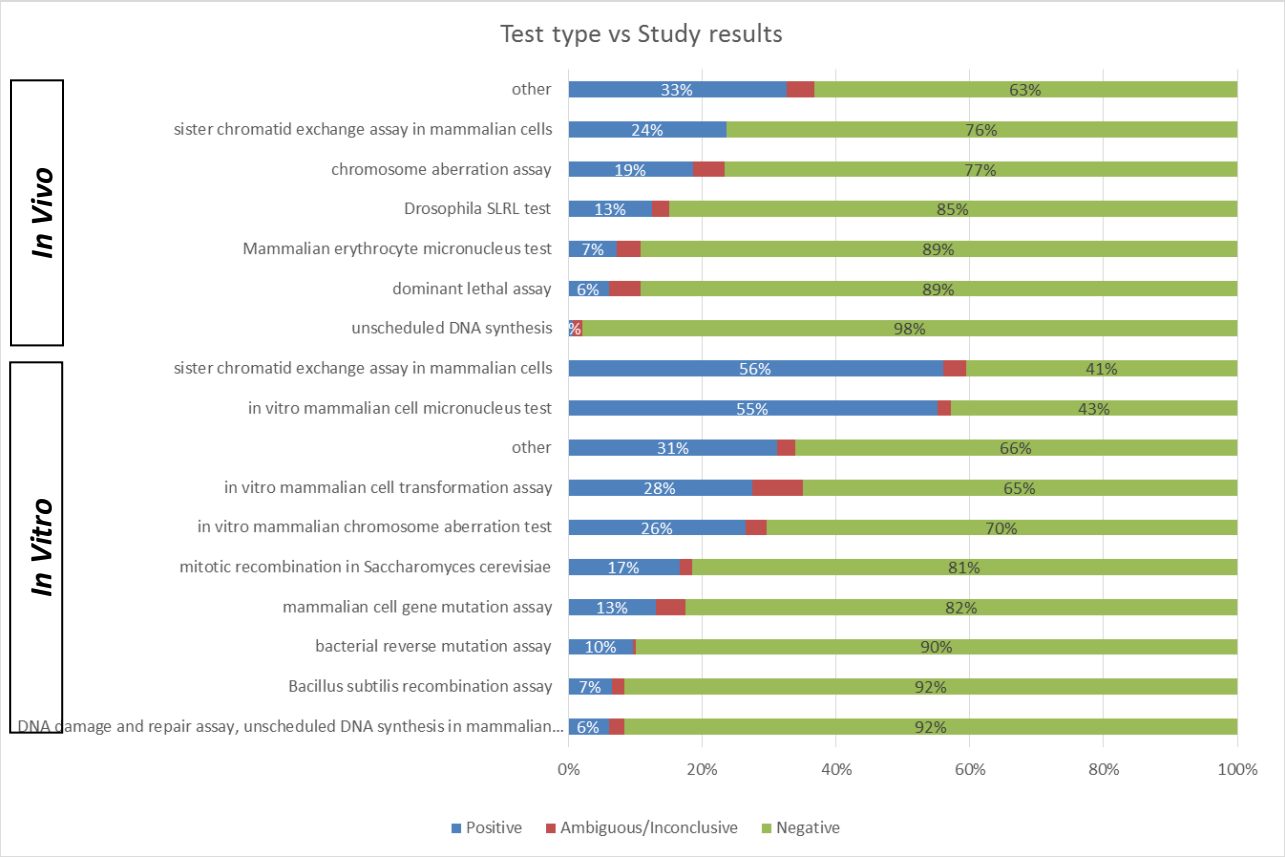


Results percentage (positive, ambiguous/inconclusive and negative) have been reported (see Table 9 and Figure 12) for each type of study. The Sister chromatid exchange assay in mammalian cells *in vitro* present the higher percentage of positive results, 56 % were positive out of 116 SCE studies. On the contrary, the DNA damage and repair assay, unscheduled DNA synthesis in mammalian cells *in vitro* gave only 6% of positive results studies out of 311 studies.

Table 9: test type results

test type	method_type	Positive	Ambiguous/ Inconclusive	Negative
sister chromatid exchange assay in mammalian cells	*in vitro*	56%	3%	41%
in vitro mammalian cell micronucleus test	*in vitro*	55%	2%	43%
other	*in vitro*	31%	3%	66%
in vitro mammalian cell transformation assay	*in vitro*	28%	8%	65%
in vitro mammalian chromosome aberration test	*in vitro*	26%	3%	70%
mitotic recombination in Saccharomyces cerevisiae	*in vitro*	17%	2%	81%
mammalian cell gene mutation assay	*in vitro*	13%	4%	82%
bacterial reverse mutation assay	*in vitro*	10%	0%	90%
Bacillus subtilis recombination assay	*in vitro*	7%	2%	92%
DNA damage and repair assay, unscheduled DNA synthesis in mammalian cells *in vitro*	*in vitro*	6%	2%	92%
other	*in vivo*	33%	4%	63%
sister chromatid exchange assay in mammalian cells	*in vivo*	24%	0%	76%
chromosome aberration assay	*in vivo*	19%	5%	77%
Drosophila SLRL test	*in vivo*	13%	3%	85%
Mammalian erythrocyte micronucleus test	*in vivo*	7%	3%	89%
dominant lethal assay	*in vivo*	6%	5%	89%
unscheduled DNA synthesis	*in vivo*	1%	1%	98%

Figure 12: test type results



In vitro studies and *in vivo* studies are shown, separately for active substances and metabolites, in figure 13 and 14.

Genotoxicity potential in active substances is mostly investigated using *in vitro* test. *In vivo* test represent a minor part of the data package (some exceptions: Metiram and Dichlorvos).

Figure 13: *in vitro* and *in vivo* studies in active substances

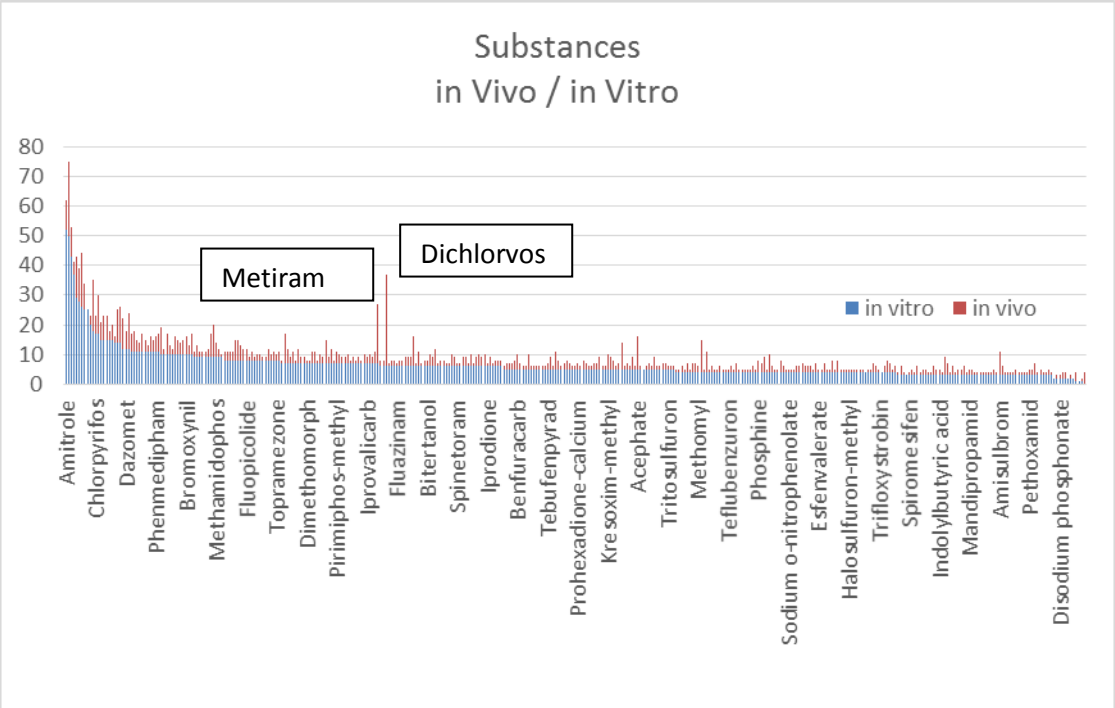
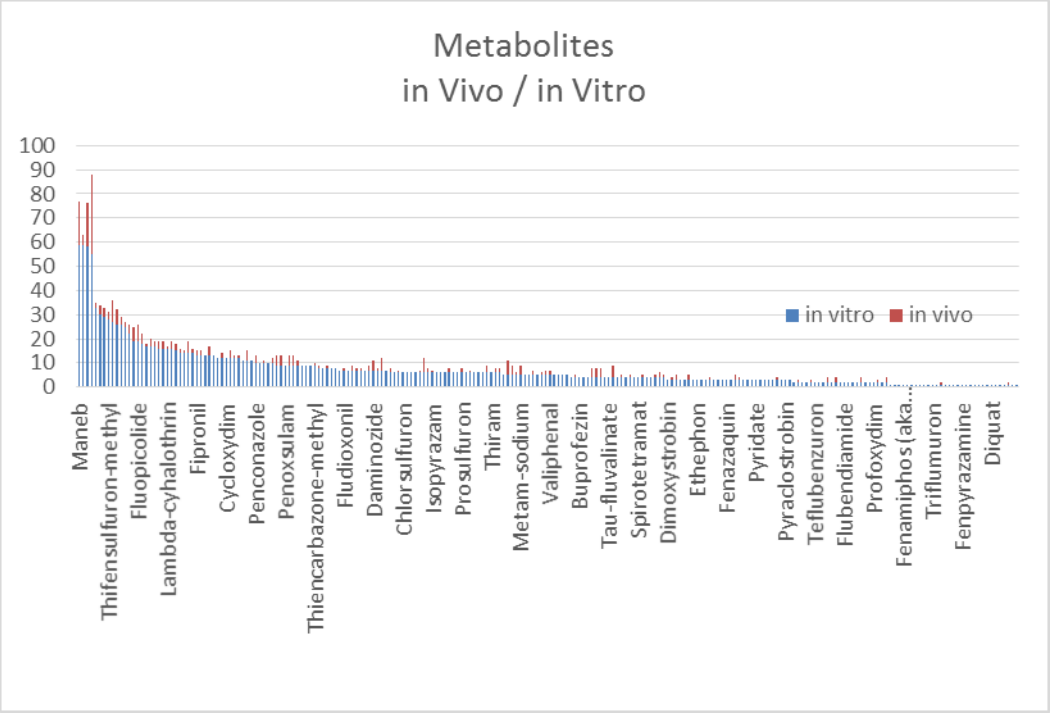


Figure 14: *in vitro* and *in vivo* studies in metabolites



4. Conclusions

This project and related database represent an extensive genotoxicity data collection on more than 350 active substances. Moreover during the project, chemical comprehensive information (i.e. code/trivial name, chemical name, chemical structure, SMILE notation and codes, CAS# when available, Smiles codes, InChi code, IUPAC NAME and molecular formula), were collected for more than 2 thousand of metabolites.

Actually, looking at the whole database the majority of the components scrutinized were metabolites, in addition genotoxicity data were collected for more than 6 hundred of metabolites.

The most reported genotoxicity study type, is bacterial reverse mutation (for *in vitro* studies), while for *in vivo* studies the most described one is mammalian erythrocyte micronucleous test. Considering studies performed on active ingredient only, 4 types of studies represent the majority of the data package (Bacterial reverse mutation assay, Mammalian erythrocyte micronucleus test, Mammalian cell gene mutation assay *In vitro* mammalian chromosome aberration test).

In the whole database, ambiguous genotoxicity studies results represent only 3% of the total, while more than 80% were negative and less than 15% were positive;separate analysis of the results for the metabolites- gave very similar results.

Genotoxicity potential in active substances is mostly investigated using *in vitro* test. *In vivo* test represent a minor part of the data package (some exceptions: Metiram and Dichlorvos).

Considering metabolites, the most representative *in vitro* study is bacterial reverse mutation while, for *in vivo* studies, the most representative one is mammalian erythrocyte micronucleous test as for active substances.

4.1. Structure of the database

During the first half of the project, the structure of the database was modified to satisfy new EFSA request of additional information on Genotoxicity endpoints and to optimize the reliability of the data. The database includes new fields regarding the MN test *in vivo* (see Appendix C- Data Model).
Furthermore, differently from first Data Model, each study was split in several field for each different entry points: metabolic_activation (with and without), strain (one entry point for each strain), exposure time (one entry point for each time endpoint of exposure).

4.2. Problem encountered

However, data extraction encountered some problems, such as the difficulty to retrieve genotoxicity data from some published or confidential studies cited only in the study description.

For the majority of the substances without Appendix B of EFSA conclusion, chemical names and chemical structures of metabolites (tested in genotoxicity studies) were searched in the whole Annex B Vol 3 of the DARs and in several correlated documents (addenda and annexes). EFSA team was involved in this specific data search when the consortium was unable to find information, leading to a very large and time-consuming activity from both parts.

Retrieving information on confidential data (impurities), slowed down ICPS workflow and increased EFSA staff work load.

Extraction of the data for the chemical information and characterization was the most time-consuming step in the evaluation of the substances due to the workload for data curation and evaluation.

5. Recommendations

5.1. Enter genotoxicity data

The genotoxicity data should be entered into the database following the specific SOPs (Appendix-J). The data would allow detailed analyses of the substances and metabolites scrutinized. The stored information on several active substances, together with chemical and genotoxicity information on their metabolites will help to provide solid background for in-silico tools i.e. QSAR, grouping and read across for prediction and indication of the genotoxicity hazard.

5.2. Accessibility of the database

To improve the accessibility and make the data easily available, it would be useful to create a web portal that allows querying the database, according to the different variables present in the database.

5.3. Information update

The actuality of the data should be maintained by performing regular updates of the database. The most recent genotoxicity data present in pesticide dossiers uploaded on EFSA website should be included.

References

1) Commission Regulation (EU) No 283/2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market
2) Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EC and 91/414/EEC. Official Journal L 309, 1-50. 24 November 2009
3) OECD, Guidance document on the definition of residue (as revised in 2009), Series on testing and assessment Nr. 63, Series on Pesticides Nr. 31, 28-Jul-2009
4) http://www.efsa.europa.eu/en/supporting/pub/44e.htm
5) http://www.efsa.europa.eu/en/supporting/pub/50e.htm
6) http://www.efsa.europa.eu/en/efsajournal/doc/49e.pdf
7) http://www.efsa.europa.eu/en/supporting/pub/169e.htm
8) EFSA Panel on Plant Protection Products and their Residues (PPR); Scientific Opinion on Evaluation of the Toxicological Relevance of Pesticide Metabolites for Dietary Risk Assessment. EFSA Journal 2012;10(07): 2799. [187pp.] doi:10.2903/j.efsa.2012.2799. Available online: www.efsa.europa.eu/efsajournal

Glossary and Abbreviations

ASST	Azienda Socio Sanitaria Territoriale
CAS number	Unique numerical identifier assigned by Chemical Abstracts Service (CAS) to every chemical substance described in the open scientific literature
CIRCABC	Platform for managing internal documents between European Union Reference Laboratories (EURLs), National Reference Laboratories (NRLs), Official Laboratories (OfLs)
DB	database
EC	European Commission
EFSA	European Food Safety Authority
EEC	European Economic Community
EU	European Union
ICPS	International Centre for Pesticides and Health Risk Prevention
InChI	The IUPAC International Chemical Identifier (InChI) is a textual identifier for chemical substances to encode molecular information.
IUPAC name	systematic method of naming organic chemical compounds as recommended by the International Union of Pure and Applied Chemistry (IUPAC)
OECD	Organisation for Economic Co-operation and Development
PPR	EFSA Scientific Panel on Plant Protection Products and their Residues
QA	Quality Assurancemethods.
QC	Quality Control methods.
QSAR	Quantitative structure–activity relationship
SCE	Sister chromatid exchange assay
SLRL test	sex-linked recessive lethal test
SMILES	The Simplified Molecular Input Line Entry System (SMILES) is a specification in form of a line notation for describing the structure of molecules using short ASCII strings.
SOPs	Standard operating procedures

SOS/umu test	genotoxicity assay evaluates the primary DNA damage caused by chemicals from the β-galactosidase activity of S. typhimurium.
UMIL	University of Milan
XML	Extensible Markup Language

Appendix A – Final Report

1. Active substances and number of related studies

Sub_name	Total N° studies (active substance and related compounds)
1,4-Dimethylnaphthalene	6
1-Methylcyclopropene	15
1-Naphthylacetic acid	16
2-(1-Naphthyl)acetamide	8
2,4,6,8-Tetramethyl-1,3,5,7-tetraoxacyclooctane	6
2,4-D	18
2,4-DB	18
2-Phenylphenol	41
6-Benzyladenine	8
8-Hydroxyquinoline	13
Abamectin	6
Acephate	16
Acequinocyl	7
acetamiprid	17
Acibenzolar-S-methyl	18
Aclonifen	6
Acrinathrin	11
Aldicarb	17
Alpha-cypermethrin	8
Aluminium ammonium sulphate dodecahydrate	11
Aluminium phosphide	13
Aluminium sulphate	10
Amidosulfuron	8
Aminopyralid	4
Amisulbrom	12
Amitraz	14
Amitrole	62
Anthraquinone	7
Azadirachtin A	12
Azimsulfuron	10
azinphos-methyl	14
Azoxystrobin	7
Beflubutamid	4
Benalaxyl	18
Benalaxyl-M	28
Benfluralin	8
Benfuracarb	37
Benomyl	110

Bensulfuron-methyl	10
Bentazone	33
Benthiavalicarb-isopropyl	35
Benzoic acid	35
beta-Cyfluthrin	10
Beta-Cypermethrin	4
Bifenazate	4
Bifenox	11
Bifenthrin	14
Bispyribac-sodium	11
Bitertanol	23
Bixafen	4
Boscalid	5
Bromadiolone	4
Bromoxynil	22
Bromuconazole	13
Bupirimate	11
Buprofezin	10
Cadusafos	8
Calcium phosphide	12
Captan	17
Carbaryl	7
Carbendazim	87
Carbetamide	8
Carbofuran	36
Carbosulfan	52
Carboxin	10
Carfentrazone-ethyl	43
Chlorantraniliprole	12
Chlorfenapyr	9
Chloridazon	24
Chlormequat chloride	21
Chlorothalonil	50
Chlorotoluron	5
Chlorpropham	48
Chlorpyrifos	25
Chlorsulfuron	12
Chlorthal-dimethyl	17
Chromafenozide	20
Clethodim	26
Clodinafop-propargyl	7

Clofentezine	9
Clomazone	7
Clopyralid	9
Clothianidin	25
Copper	15
Cyantraniliprole	20
Cyazofamid	9
Cyclanilide	9
Cycloxydim	31
Cyflufenamid	12
Cyflumetofen	13
Cyfluthrin	18
Cyhalofop-butyl	8
Cymoxanil	11
Cypermethrin	19
Cyproconazole	15
Cyprodinil	12
Cyromazine	9
Daminozide	21
Dazomet	28
Deltamethrin	9
Desmedipham	13
Diazinon	5
Dicamba	58
Dichlorprop-P	8
Dichlorvos	37
Diclofop-methyl	7
Dicloran	6
Dicofol	5
Didecyldimethylammonium chloride	4
Diethofencarb	6
Difenoconazole	27
Diflubenzuron	5
Diflufenican	9
Dimethachlor	20
Dimethenamid-P	18
Dimethoate	25
Dimethomorph	8
Dimoxystrobin	8
Dinocap	16
Diphenylamine	5

Diquat	9
Disodium phosphonate	3
Dithianon	22
Diuron	20
Dodemorph acetate	4
Dodine	8
Emamectin	5
Endosulfan	35
Epoxiconazole	6
Esfenvalerate	7
Ethametsulfuron methyl	33
Ethephon	8
Ethofumesate	18
Ethoprophos	11
Etofenprox	8
Etoxazole	8
Etridiazole	15
Eugenol	22
Famoxadone	11
Fenamidone	15
Fenamiphos (aka phenamiphos)	10
Fenarimol	8
Fenazaquin	12
Fenbuconazole	39
Fenbutatin oxide	9
Fenhexamid	9
Fenitrothion	12
Fenoxaprop-P-ethyl	14
Fenoxycarb	5
Fenpropidin	6
Fenpropimorph	10
Fenpyrazamine	5
Fenpyroximate	6
Fenthion	4
Ferric phosphate	2
Fipronil	23
Flazasulfuron	25
Flonicamid	16
Florasulam	13
Fluazifop-P-butyl	9
Fluazinam	14

Flubendiamide	6
Fludioxonil	19
Flufenoxuron	12
Flumioxazin	6
Fluometuron	18
Fluopicolide	38
Fluopyram	11
Fluoxastrobin	13
Flupyrsulfuron-methyl-sodium	18
Fluquinconazole	10
Flurochloridone	10
Fluroxypyr-meptyl	6
Flurtamone	14
Flusilazole	8
Flutolanil	6
Flutriafol	10
Fluxapyroxad	18
Folpet	12
Foramsulfuron	5
Forchlorfenuron	8
Formetanate hydrochloride	11
Fosetyl-aluminium	10
Fuberidazole	10
Geraniol	7
Gibberellins	9
Glufosinate-ammonium	27
Glyphosate	77
Halosulfuron-methyl	9
Haloxyfop-P	15
Hexythiazox	7
Hymexazol	8
Imazalil	11
Imazamox	12
Imazaquin	7
Imazosulfuron	10
Imidacloprid	28
Indolylbutyric acid	5
Indoxacarb	11
Iodosulfuron-methyl-sodium	11
Ioxynil	20
Ipconazole	4

Iprodione	25
Iprovalicarb	10
Iron sulfate anhydrous	10
Isoproturon	56
Isopyrazam	14
Isoxaben	17
Isoxaflutole	12
Kresoxim-methyl	14
Lambda-cyhalothrin	25
L-ascorbic acid	9
Lenacil	9
Lindane	34
Linuron	19
Lufenuron	10
Magnesium phosphide	13
Malathion	23
Maleic hydrazide	15
Mancozeb	90
Mandipropamid	14
Maneb	84
MCPA	31
MCPB	5
Mecoprop	7
Mecoprop-P	9
Mepanipyrim	25
Mepiquat chloride	9
Meptyldinocap	4
Mesosulfuron-methyl	14
Mesotrione	12
Metaflumizone	17
Metalaxyl	9
Metalaxyl-M	35
Metamitron	18
Metam-sodium	15
Metazachlor	49
Metconazole	12
Methamidophos	14
Methiocarb	9
Methomyl	6
Methoxyfenozide	6
Metiram	84

Metobromuron	7
Metosulam	12
Metrafenone	5
Metribuzin	18
Metsulfuron-methyl	24
Milbemectin	12
Myclobutanil	21
Napropamide	20
Nicosulfuron	25
Nicotine	3
Orange oil	15
Orthosulfamuron	19
Oryzalin	8
Oxadiazon	8
Oxamyl	6
Oxasulfuron	8
Oxydemeton-methyl	21
Oxyfluorfen	11
Paclobutrazol	12
Parathion	13
Parathion-methyl	23
Penconazole	19
Pencycuron	14
Pendimethalin	33
Penflufen	13
Penoxsulam	13
Penthiopyrad	28
Permethrin	4
Pethoxamid	8
Phenmedipham	17
Phosalone	13
Phosmet	12
Phosphine	10
Picloram	5
Picolinafen	4
Picoxystrobin	17
Pinoxaden	21
Pirimicarb	15
Pirimiphos-methyl	11
Potassium phosphonates	6
Prochloraz	18

Procymidone	12
Profoxydim	8
Prohexadione-calcium	7
Propamocarb hydrochloride	15
Propaquizafop	17
Propargite	4
Propiconazole	30
Propineb	24
Propoxycarbazone-sodium	23
Propyzamide	8
Proquinazid	9
Prosulfocarb	6
Prosulfuron	15
Prothioconazole	12
Pymetrozine	16
Pyraclostrobin	9
Pyraflufen-ethyl	7
Pyrazophos	6
Pyrethrins	4
Pyridaben	8
Pyridalyl	14
Pyridate	12
Pyrimethanil	8
Pyriofenone	7
Pyriproxyfen	5
Pyroxsulam	13
Quinmerac	14
Quinoclamine	5
Quintozene	7
Quizalofop-P-ethyl	9
Quizalofop-P-tefuryl	6
Rimsulfuron	10
S-abscisic acid	4
Sedaxane	12
Silthiofam	5
Sintofen (aka cintofen)	9
Sodium 5-nitroguaiacolate	5
Sodium hypochlorite	7
Sodium o-nitrophenolate	5
Sodium p-nitrophenolate	5
Sodium silver thiosulfate	4

Spinetoram	10
Spinosad	7
Spirodiclofen	4
Spiromesifen	4
Spirotetramat	11
Spiroxamine	14
Sulcotrione	15
Sulfosulfuron	11
Sulfoxaflor	17
Sulfuryl fluoride	6
Tau-fluvalinate	9
Tebuconazole	11
Tebufenozide	15
Tebufenpyrad	11
Tecnazene	4
Teflubenzuron	7
Tefluthrin	11
Tembotrione	15
Tepraloxydim	9
Terbuthylazine	42
Tetraconazole	21
Thiabendazole	15
Thiacloprid	13
Thiamethoxam	14
Thiencarbazone-methyl	14
Thifensulfuron-methyl	40
Thiodicarb	11
Thiophanate-methyl	8
Thiram	13
Thymol	11
Tolclofos-methyl	7
Tolylfluanid	26
Topramezone	13
Tralkoxydim	9
Triadimenol	30
Tri-allate	15
Triasulfuron	7
Triazoxide	9
Tribenuron-methyl	6
Trichlorfon	7
Triclopyr	16

Trifloxystrobin	14
Triflumizole	7
Triflumuron	9
Trifluralin	17
Triflusulfuron-methyl	18
Trinexapac-ethyl	13
Triticonazole	9
Tritosulfuron	22
Valiphenal	11
Vinclozolin	21
Zeta-cypermethrin	6
Zinc phosphide	14
Ziram	25
Zoxamide	10
Totale	**5739***

* Notice that the number of studies reported does not correspond to the number of id_rep in the opinion table. This mismatch is due to the presence of common studies among different substances

Appendix B – List of Active Substances and Dossier type

SUB_NAME	Peer Review by	Dossier type
1,4-Dimethylnaphthalene	EFSA	A
1-Methylcyclopropene	EFSA	A
2-(1-Naphthyl)acetamide	EFSA	A
1-Naphthylacetic acid	EFSA	A
2,4-D	EFSA	A
2,4-DB	EFSA	A
2-Phenylphenol	EFSA	A
6-Benzyladenine	EFSA	A
8-Hydroxyquinoline	EFSA	A
Abamectin	EFSA	A
Acephate	EC	B
Acequinocyl	EFSA	A
Acetamiprid	EC	B
Acibenzolar-S-methyl	EFSA	A
Aclonifen	EFSA	A
Acrinathrin	EFSA	A
Aldicarb	EC	B
Alpha-cypermethrin	EC	B
Aluminium ammonium sulphate dodecahydrate	EFSA	A
Aluminium phosphide	EFSA	A
Aluminium sulphate	EFSA	A
Amidosulfuron	EFSA	A
Aminopyralid	EFSA	A
Amisulbrom	EFSA	A
Amitraz	EC	B
Amitrole	EFSA	A
Anthraquinone	EC	B
L-ascorbic acid	EFSA	A
Azadirachtin A	EFSA	A
Azimsulfuron	EFSA	A
Azinphos-methyl	No EC and/or no EFSA Conclusions*	
Azoxystrobin	EFSA	A
Beflubutamid	EC	B
Benalaxyl	EFSA	A
Benalaxyl-M	EFSA	A
Benfluralin	EFSA	A
Benfuracarb	EFSA	A
Benomyl	EC	B
Bensulfuron-methyl	EFSA	A
Bentazone	EFSA	A

Benthiavalicarb-isopropyl	EFSA	A
Benzoic acid	EC	B
Beta-Cyfluthrin	EC	B
Beta-Cypermethrin	EFSA	A
Bifenazate	EC	B
Bifenox	EFSA	A
Bifenthrin	EFSA	A
Bispyribac-sodium	EFSA	A
Bitertanol	EFSA	A
Bixafen	EFSA	A
Boscalid	EC	B
Bromadiolone	EFSA	A
Bromoxynil	EC	B
Bromuconazole	EFSA	A
Bupirimate	EFSA	A
Buprofezin	EFSA	A
Cadusafos	EFSA	A
Calcium phosphide	EFSA	A
Captan	EFSA	A
Carbaryl	EFSA	A
Carbendazim	EFSA	A
Carbetamide	EFSA	A
Carbofuran	EFSA	A
Carbosulfan	EFSA	A
Carboxin	EFSA	A
Carfentrazone-ethyl	EFSA	A
Chlorantraniliprole	EFSA	A
Chlorfenapyr	No EC and/or no EFSA Conclusions*	
Chloridazon	EFSA	A
Chlormequat chloride	EFSA	A
Chlorothalonil	EC	B
Chlorotoluron	EC	B
Chlorpropham	EC	B
Chlorpyrifos	Substance with studies not referring to current EFSA Conclusion**	A
	EFSA	
Chlorsulfuron	EFSA	A
Chlorthal-dimethyl	EFSA	A
Chromafenozide	EFSA	A
Clethodim	EFSA	A

Clodinafop-propargyl	EFSA	A
Clofentezine	EFSA	A
Clomazone	EFSA	A
Clopyralid	EFSA	A
Clothianidin	EC	B
Copper	EFSA	A
Cyantraniliprole	EFSA	A
Cyazofamid	EC	B
Cyclanilide	EC	B
Cycloxydim	EFSA	A
Cyflufenamid	EFSA	A
Cyflumetofen	EFSA	A
Cyfluthrin	EC	B
Cyhalofop-butyl	EFSA	A
Cymoxanil	EFSA	A
Cypermethrin	EFSA	A
Cyproconazole	EFSA	A
Cyprodinil	EFSA	A
Cyromazine	EFSA	A
Daminozide	EC	B
Dazomet	EFSA	A
Deltamethrin	EC	B
Desmedipham	EC	B
Diazinon	EFSA	A
Dicamba	EFSA	A
Dichlorprop-P	EFSA	A
Dichlorvos	EFSA	A
Diclofop-methyl	EFSA	A
Dicloran	EFSA	A
Dicofol	EC	B
Didecyldimethylammonium chloride	EFSA	A
Diethofencarb	EFSA	A
Difenoconazole	EFSA	A
Diflubenzuron	EFSA	A
Diflufenican	EFSA	A
Dimethachlor	EFSA	A
Dimethenamid-P	EC	B
Dimethoate	EFSA	A
Dimethomorph	EFSA	A
Dimoxystrobin	EFSA	A
Dinocap	EC	B

Diphenylamine	EFSA	A
Diquat	EFSA	A
Disodium phosphonate	EFSA	A
Dithianon	Substance with studies not referring to current EFSA Conclusion**	A
	EFSA	
Diuron	EFSA	A
Dodemorph acetate	EFSA	A
Dodine	EFSA	A
Emamectin	EFSA	A
Endosulfan	EC	B
Epoxiconazole	EFSA	A
Esfenvalerate	EFSA	A
Ethametsulfuron methyl	EFSA	A
Ethephon	EFSA	A
Ethofumesate	EFSA	A
Ethoprophos	EFSA	A
Etofenprox	EFSA	A
Etoxazole	EC	B
Etridiazole	Substance with studies not referring to current EFSA Conclusion**	A
	EFSA	
Eugenol	EFSA	A
Famoxadone	EFSA	A
Fenamidone	EFSA	A
Fenamiphos (aka phenamiphos)	EFSA	A
Fenarimol	EC	B
Fenazaquin	EFSA	A
Fenbuconazole	EFSA	A
Fenbutatin oxide	EFSA	A
Fenhexamid	EFSA	A
Fenitrothion	EFSA	A
Fenoxaprop-P-ethyl	EFSA	A
Fenoxycarb	EFSA	A
Fenpropidin	EFSA	A
Fenpropimorph	EFSA	A
Fenpyrazamine	EFSA	A
Fenpyroximate	EFSA	A
Fenthion	EC	B
Ferric phosphate	EFSA	A

Fipronil	EFSA	A
Flazasulfuron	EC	B
Flonicamid	EFSA	A
Florasulam	EFSA	A
Fluazifop-P-butyl	EFSA	A
Fluazinam	EFSA	A
Flubendiamide	EFSA	A
Fludioxonil	EFSA	A
Flufenoxuron	EFSA	A
Flumioxazin	EFSA	A
Fluometuron	Substance with studies not referring to current EFSA Conclusion**	A
	EFSA	
Fluopicolide	EFSA	A
Fluopyram	EFSA	A
Fluoxastrobin	EFSA	A
Flupyrsulfuron-methyl-sodium	EFSA	A
Fluquinconazole	EFSA	A
Flurochloridone	EFSA	A
Fluroxypyr-meptyl	EFSA	A
Flurtamone	EFSA	A
Flusilazole	EC	B
Flutolanil	EFSA	A
Flutriafol	EFSA	A
Fluxapyroxad	EFSA	A
Folpet	EFSA	A
Foramsulfuron	EFSA	A
Forchlorfenuron	EC	B
Formetanate hydrochloride	EFSA	A
Fosetyl-aluminium	EFSA	A
Fuberidazole	EFSA	A
Geraniol	EFSA	A
Gibberellins	EFSA	A
Glufosinate-ammonium	EFSA	A
Glyphosate	EFSA	A
Halosulfuron-methyl	EFSA	A
Haloxyfop-P	EFSA	A
Hexythiazox	EFSA	A
Hymexazol	EFSA	A
Imazalil	EFSA	A
Imazamox	EC	B

Imazaquin	EFSA	A
Imazosulfuron	EC	B
Imidacloprid	EFSA	A
Indolylbutyric acid	Substance with studies not referring to current EFSA Conclusion**	A
	EFSA	
Indoxacarb	EC	B
Iodosulfuron-methyl-sodium	EC	B
Ioxynil	EC	B
Ipconazole	EFSA	A
Iprodione	EC	B
Iprovalicarb	EFSA	A
Iron sulfate anhydrous	EFSA	A
Isoproturon	EFSA	A
Isopyrazam	EFSA	A
Isoxaben	EFSA	A
Isoxaflutole	EFSA	A
Kresoxim-methyl	EFSA	A
Lambda-cyhalothrin	EFSA	A
Lenacil	EFSA	A
Lindane	EC	B
Linuron	EC	B
Lufenuron	EFSA	A
Magnesium phosphide	EFSA	A
Malathion	EFSA	A
Maleic hydrazide	EC	B
Mancozeb	EC	B
Mandipropamid	EFSA	A
Maneb	EC	B
MCPA	EC	B
MCPB	EC	B
Mecoprop	EC	B
Mecoprop-P	EC	B
Mepanipyrim	EC	B
Mepiquat chloride	EFSA	A
Meptyldinocap	EFSA	A
Mesosulfuron-methyl	EC	B
Mesotrione	EFSA	A
Metaflumizone	EFSA	A
Metalaxyl	EC	B
Metalaxyl-M	EFSA	A

2,4,6,8-Tetramethyl-1,3,5,7-tetraoxacyclooctane	EFSA	A
Metam-sodium	EFSA	A
Metamitron	EFSA	A
Metazachlor	EFSA	A
Metconazole	EFSA	A
Methamidophos	EC	B
Methiocarb	EFSA	A
Methomyl	EFSA	A
Methoxyfenozide	EC	B
Metiram	EC	B
Metobromuron	EFSA	A
Metosulam	EFSA	A
Metrafenone	EFSA	A
Metribuzin	EFSA	A
Metsulfuron-methyl	EFSA	A
Milbemectin	EC	B
Myclobutanil	EFSA	A
Napropamide	EFSA	A
Nicosulfuron	EFSA	A
Nicotine	EC	B
Orange oil	EFSA	A
Orthosulfamuron	EFSA	A
Oryzalin	EFSA	A
Oxadiazon	EFSA	A
Oxamyl	EFSA	A
Oxasulfuron	EC	B
Oxydemeton-methyl	EFSA	A
Oxyfluorfen	EFSA	A
Paclobutrazol	EFSA	A
Parathion	EC	B
Parathion-methyl	EC	B
Penconazole	EFSA	A
Pencycuron	EFSA	A
Pendimethalin	EC	B
Penflufen	EFSA	A
Penoxsulam	EFSA	A
Penthiopyrad	Substance with studies not referring to current EFSA Conclusion** EFSA	A
Permethrin	EC	B
Pethoxamid	EC	B

Phenmedipham	EC	B
Phosalone	EFSA	A
Phosmet	EFSA	A
Phosphine	EFSA	A
Picloram	EFSA	A
Picolinafen	EFSA	A
Picoxystrobin	EC	B
Pinoxaden	EFSA	A
Pirimicarb	EFSA	A
Pirimiphos-methyl	EFSA	A
Potassium phosphonates	EFSA	A
Prochloraz	EFSA	A
Procymidone	EC	B
Profoxydim	EC	B
Prohexadione-calcium	EFSA	A
Propamocarb hydrochloride	EFSA	A
Propaquizafop	EFSA	A
Propargite	EFSA	A
Propiconazole	EC	B
Propineb	EC	B
Propoxycarbazone-sodium	EC	B
Propyzamide	EC	B
Proquinazid	EFSA	A
Prosulfocarb	EFSA	A
Prosulfuron	EFSA	A
Prothioconazole	EFSA	A
Pymetrozine	EFSA	A
Pyraclostrobin	EC	B
Pyraflufen-ethyl	EFSA	A
Pyrazophos	EC	B
Pyrethrins	EFSA	A
Pyridaben	EFSA	A
Pyridalyl	EFSA	A
Pyridate	EFSA	A
Pyrimethanil	EFSA	A
Pyriofenone	EFSA	A
Pyriproxyfen	EFSA	A
Pyroxsulam	EFSA	A
Quinmerac	EFSA	A
Quinoclamine	EFSA	A
Quintozene	EC	B

Quizalofop-P-ethyl & Quizalofop-P-tefuryl	EFSA	A
Rimsulfuron	EFSA	A
S-abscisic acid	EFSA	A
Sedaxane	EFSA	A
Silthiofam	EC	B
Sintofen (aka cintofen)	EFSA	A
Sodium 5-nitroguaiacolate	EFSA	A
Sodium hypochlorite	EFSA	A
Sodium o-nitrophenolate	EFSA	A
Sodium p-nitrophenolate	EFSA	A
Sodium silver thiosulfate	EFSA	A
Spinetoram	EFSA	A
Spinosad	EC	B
Spirodiclofen	EFSA	A
Spiromesifen	EFSA	A
Spirotetramat	EFSA	A
Spiroxamine	EFSA	A
Sulcotrione	EFSA	A
Sulfosulfuron	EFSA	A
Sulfoxaflor	EFSA	A
Sulfuryl fluoride	EFSA	A
Tau-fluvalinate	EFSA	A
Tebuconazole	EFSA	A
Tebufenozide	EFSA	A
Tebufenpyrad	EFSA	A
Tecnazene	EC	B
Teflubenzuron	EFSA	A
Tefluthrin	EFSA	A
Tembotrione	EFSA	A
Tepraloxydim	EC	B
Terbuthylazine	Substance with studies not referring to current EFSA Conclusion** EFSA	A
Tetraconazole	EFSA	A
Thiabendazole	EFSA	A
Thiacloprid	EC	B
Thiamethoxam	EFSA	A
Thiencarbazone-methyl	EFSA	A
Thifensulfuron-methyl	EFSA	A
Thiodicarb	EFSA	A
Thiophanate-methyl	EC	B

Thiram	EC	B
Thymol	EFSA	A
Tolclofos-methyl	EFSA	A
Tolylfluanid	Substance with studies not referring to current EFSA Conclusion**	A
	EFSA	
Topramezone	EFSA	A
Tralkoxydim	EFSA	A
Triadimenol	EFSA	A
Tri-allate	EFSA	A
Triasulfuron	EFSA	A
Triazoxide	EFSA	A
Tribenuron-methyl	EFSA	A
Trichlorfon	EFSA	A
Triclopyr	EFSA	A
Trifloxystrobin	EC	B
Triflumizole	EFSA	A
Triflumuron	EFSA	A
Trifluralin	EFSA	A
Triflusulfuron-methyl	EFSA	A
Trinexapac-ethyl	EFSA	A
Triticonazole	EFSA	A
Tritosulfuron	EC	B
Valiphenal	EFSA	A
Vinclozolin	No EC and/or no EFSA Conclusions*	
Zeta-cypermethrin	EFSA	A
Zinc phosphide	EFSA	A
Ziram	EC	B
Zoxamide	EC	B

*no EC or EFSA Conclusion (referring to date of data collection)

**data inserted in the database refer to both EFSA conclusion and to a subsequent DAR not yet peer reviewed at the date of data collection.

Please note that, due to the constrained choices, Owner, Author and the Publication date Fields are made-up (e.g.: publication_date = 19000101; Author = EFSA; Owner = EFSA).

Appendix C – Data Model

In this annex the data model agreed at the kickoff meeting and its following updates is presented.

TABLE NAME	COLUMN NAME	TYPE	LENGTH	MANDATORY	DESCRIPTION	CONTROLLED TERMINOLOGY	INCLUDED IN ANNEX 3 OF EFSA KICK-OFF MEETING
COMPONENT	**Name and identifier of the components**						N
	ID_Com	Numeric	Integer	Y	Primary Key	N	N
	Com_name	String	255	Y	Name of the Component	N	N
	DateTime	Date	16	N	Field Insertion Date	N	N
COMPONENT SYNONYMS	**Trade name of the components**						N (agreed to be added in December 2015)
	ID_SUB_COM	Numeric	Integer	Y	Trivial Name of the Substance or Component	N	N
	Type	String	255	Y	Type of additional information	Y (TYPE_COM_SYN Table)	N
	Description	String	Memo	Y	Additional Information	N	N
	Definition	String	Memo	N	Definition	N	N
	ID_SYNON	Numeric	Integer	Y	Primary Key	N	N
D_GENOTOX (TABLE 2)	**Genotoxicity characterization of the Studies**						Y
	Id_genotox	Numeric	Integer	Y	Primary Key	N	Y
	Study_cat	String	255	Y	Category of the study	Y (Genotoxicity; Mutagenicity)	Y
	Id_test_type	String	255	N	Classification of type of test according to OECD phraselist	Y (termDesc_TESTTYPE Table)	Y
	Method_type	String	255	N	Classification of method type either in vivo or in vitro	Y (in vivo; in vitro)	Y
	Guideline_qualifier	String	255	N	Qualifier of the guideline followed by the study	Y (According to"; Equivalent or similar to; No guideline followed; No guideline available; No guideline required)	Y
	Id_genotox_guideline	String	255	N	Identifier of the followed	Y (termDesc_GUIDELINE	Y

TABLE NAME	COLUMN NAME	TYPE	LENGTH	MANDATORY	DESCRIPTION	CONTROLLED TERMINOLOGY	INCLUDED IN ANNEX 3 OF EFSA KICK-OFF MEETING
					guideline	Table)	
	Deviation	String	255	N	Any deviation from the guideline	Y (Yes; No; No data; Not applicable)	Y
	Glp_compl	String	255	N	GLP Compliance	Y (Yes; No; No data; Not applicable)	Y
	Id_genotox_species	String	255	Y	Organism/cell culture used in the endpoint study	Y (termDesc_MTX Table)	Y
	Id_strain	String	255	N	The strain of the organism tested	Y (termDesc_STRAIN Table)	Y
	Sex	String	255	N	Gender	Y (Female; Male; Male/Female; No data)	Y
	Met_indicator	String	255	N	Metabolic activation whether exogenous metabolic activation was applied or not	Y (with; with and without; without; not applicable; no data)	Y
	Id_route	String	255	N	Route of exposure	Y (termDesc_ROUTE Table)	Y
	Exp_period	Numeric	Integer	N	Exposure duration	N	Y
	Id_exp_period_unit	String	255	N	Unit of exposure duration	Y (termDesc_Unit Table)	Y
	Number_individuals	Numeric	Integer	N	The number of organisms dosed at each dose level of the in vivo genotoxicty study	N	Y
	Control	String	255	N	Indication whether and what type of concurrent control groups were used in the in vivo genotoxicity study	Y (yes; yes, concurrent no treatment; yes, concurrent vehicle; yes, plain diet; yes, sham-exposed; yes, historical; no; no data)	Y
	Genotox_endpoint	String	255	N	Type of genotoxicity endpoint	Y (gene mutation; chromosome aberration; DNA damage and/or repair; genome mutation)	Y
	Is_genotoxic	String	255	Y	Summarize the result of the endpoint study	Y (Positive; Negative; Ambiguous; Not determined; Not applicable; No data; Other; Inconclusive)	Y

TABLE NAME	COLUMN NAME	TYPE	LENGTH	MANDATORY	DESCRIPTION	CONTROLLED TERMINOLOGY	INCLUDED IN ANNEX 3 OF EFSA KICK-OFF MEETING
	Remarks	String	Memo	N	Remarks on genotoxicity study	N	Y
	Acceptability	String	255	N	Acceptability of the study according to the Rapporteur Member State opinion	Y (Acceptable; Not Acceptable)	Y
	mouseLymphTest	String	255	N	information regarding the size of colony mutant	Y (small colonies; large colonies; no information)	N (agreed to be added during the project duration)
	InvivoTissueExp	String	255	N	to indicate for in vivo micronucleus test whether there was	direct evidence-cytotoxicity; indirect evidence-systemic toxicity; indirect-toxicokinetic investigations; no evidence; direct evidence-cytotoxicity$indirect evidence-systemic toxicity; direct evidence-cytotoxicity$indirect-toxicokinetic investigations; indirect evidence-systemic toxicity$indirect-toxicokinetic investigations; direct evidence-cytotoxicity$indirect evidence-systemic toxicity$indirect-toxicokinetic	N (agreed to be added during the project duration)
	Id_target_tissue	String	255	N	field for the tissue/target organ investigated in the in vivo test	N	N (agreed to be added during the project duration)
	DATETIME	Date	16	N	Field Insertion Date	N	N
	DATETIMECK	Date	16	N	Field checked Date	N	N
D_SUBSTANCE_COMPONENT (TABLE 4)	**Characterization of the substances and their metabolites, impurities (component)**						Y
	Id_sub_com	Numeric	Integer	Y	Primary Key	N	Y
	Id_sub	Numeric	Integer	N	Unique Substance	N	Y

TABLE NAME	COLUMN NAME	TYPE	LENGTH	MANDATORY	DESCRIPTION	CONTROLLED TERMINOLOGY	INCLUDED IN ANNEX 3 OF EFSA KICK-OFF MEETING
					Identifier		
	Sub_name	String	255	N	Substance name	N	Y
	Sub_type	String	255	N	Enumerated list to describe components comprising the substance	Y (mixture or formulation; single chemical entity; complex product: derived from botanical sources; polymer; complex product: microorganisms or derived from microorganisms; group, open; group, closed; complex mixtures: not derived from botanical sources)	Y
	sub_ecSubInventEntryRef	String	255	N	The EC reference number as defined by ESIS	N	Y
	sub_casNumber	String	255	N	Chemical Abstracts Service number	N	Y
	Sub_description	String	255	N	Short description	N	Y
	sub_rns_efsa	String	255	N	EFSA PARAM code to allow linkage with existing EFSA datasets, referring to substance name or its metabolite name	Y (termDesc_PARAM Table)	Y
	Id_qualifier	String	255	N	alphanumeric code to define the composition of the substance in terms of components	Y (termDesc_QUALIFIER Table)	Y
	Id_com	Numeric	Integer	N	Unique Component Identifier	N	Y
	Com_name	String	255	N	Component name	N	Y
	comp_value	String	255	N	Numeric value (in percentage) of the composition applicable for formulations	N	Y
	Comp_type	String	255	N	OECD substance description	Y (inorganic; metal; organic; organometallic; other;	Y

TABLE NAME	COLUMN NAME	TYPE	LENGTH	MANDATORY	DESCRIPTION	CONTROLLED TERMINOLOGY	INCLUDED IN ANNEX 3 OF EFSA KICK-OFF MEETING
						protein)	
	Com_rns_efsa	String	255	N	EFSA PARAM code to allow linkage with existing EFSA datasets, referring to substance name or its metabolite name	Y (termDesc_PARAM Table)	Y
	com_ecSubInventEntryRef	String	255	N	The EC reference number as defined by ESIS	N	Y
	com_casNumber	String	255	N	Chemical Abstracts Service number	N	Y
	iupacName	String	Memo	N	International Union of Pure and Applied Chemistry name	N	Y
	molecularFormula	String	255	N	Molecular formula	N	Y
	com_structureShown	String	255	N	indication on what type of structure	Y (compound; monomer of polymer; no structure; representative compound; representative isomer)	Y
	smilesNotation	String	Memo	N	simplified molecular input line entry specification for the substance (com_name) tested	N	Y
	smilesNotationSource	String	255	N	source of the smiles notation	Y (compound; monomer of polymer; no structure; representative compound; representative isomer)	Y
	inchi	String	Memo	N	Internation Chemical Identifier	N	Y
	inchi_notationSource	String	255	N	source of the InChi notation	Y (Other; ChemIDPlus; DSSTox; OECD QSAR Toolbox; PubChem InChI)	Y
	DATETIME	Date	16	N	Field Insertion Date	N	N
	DATETIMECK	Date	16	N	Field checked Date	N	N
	NOEFSA	String	255	N	Rows not be considered in the DB, data coming	N	N

TABLE NAME	COLUMN NAME	TYPE	LENGTH	MANDATORY	DESCRIPTION	CONTROLLED TERMINOLOGY	INCLUDED IN ANNEX 3 OF EFSA KICK-OFF MEETING
					from Provisional Substance_Component DataHazDB		
	Subs	String	255	N	Identifier of Active Substances, Metabolites with and without genotoxicity characterization	N	N
	ID_EFSA	Numeric	Integer	N	Identifier of the substances in the Annex2	N	N
DAR / OPINION / EFSAOPINION (TABLE 3)	**Characterization of the Dossier and the Studies**						Y
	Id_op(id_dar, id_rep, id_op)	Numeric	Integer	Y	Primary Key	N	Y
	Op_type	String	255	Y	type of source reference	Y (termDesc_REFTYPE Table)	Y
	Owner	String	255	N	the name of data owner	N	Y
	author	String	255	N	author	N	Y
	Title	String	Memo	Y	title of the document	N	Y
	Adoption_date	Numeric	12	N	complete date of the adoption of the document	N	Y
	Publication_date	Numeric	12	Y	complete date of the publication of the document	N	Y
	journal_title	String	255	N	title of the journal or the editor	N	Y
	Id_language	String	255	N		N	Y
	Doi	String	255	N	Digital Object Identifier	N	Y
	internation_unique_number	String	255	N	International Standard Book Number (ISBN) or International Standard Serial Number (ISSN)	N	Y
	URL	String	Memo	N	uniform resource locator	N	Y

TABLE NAME	COLUMN NAME	TYPE	LENGTH	MANDATORY	DESCRIPTION	CONTROLLED TERMINOLOGY	INCLUDED IN ANNEX 3 OF EFSA KICK-OFF MEETING
	citation	String	Memo	N	reference to a book, article, web page, or other published item	N	Y
	status1	String	255	N		Y (Current; Deprecated)	Y
	Id_regulation	String	255	N		Y (termDesc_LegRef Table)	Y
	DATETIME	Date	16	N	Field Insertion Date	N	N
	DATETIMECK	Date	16	N	Field checked Date	N	N
FACT GENOTOX (TABLE 1)	**Characterizes the relationship between SubstanceComponent, Genotox, Opinion and ComponentSynonyms**						Y
	Id_fact	Numeric	Integer	Y	Primary Key	N	Y
	Id_genotox	Numeric	Integer	Y	Unique identifier of genotox table	N	Y
	Id_sub_com	Numeric	Integer	Y	Unique identifier of substance component table	N	Y
	Id_op	Numeric	Integer	Y	Unique identifier of EFSA Document or EC	N	Y
	Id_dar	Numeric	Integer	Y	Unique identifier of DAR	N	Y
	Id_rep	Numeric	Integer	Y	Unique identifier of Studies	N	N
	Dataprotection	String	1	Y	Data protection	Y (Y;N;U)	Y
	Id_sub	Numeric	Integer	N	Unique identifier of the Substances	N	N
	User	Numeric	Integer	N	Unique identifier of the user	N	N
	Datatime	Date	16	N	Date and time of the data insertion	N	N
	Id_EFSA	Numeric	Integer	N	Identifier of the substances in the Annex2	N	N
ID_EFSA	**Substances and their identificator in the DB and as requested by EFSA in the call**						N
	ID_SUBdb	Numeric	Integer	Y	Id_sub of the Substance_component Table	N	N

TABLE NAME	COLUMN NAME	TYPE	LENGTH	MANDATORY	DESCRIPTION	CONTROLLED TERMINOLOGY	INCLUDED IN ANNEX 3 OF EFSA KICK-OFF MEETING
	SUB_Db	String	255	Y	Sub_name of the substance_component Table	N	N
	ID_EFSA	Numeric	Integer	Y	Identifier of the substances in the Annex2	N	N
	SUB_EFSA	String	255	Y	Name of the substances in Annex2	N	N
LOGINS	**LOG TABLE**						N
	ID	Numeric	Integer	Y	Primary Key	N	N
	ID_User	Numeric	Integer	N	Identifier of the User	N	N
	DateTime	Date	16	N	Logged time and date	N	N
SUBSTANCES	**Name and identifier of the**						N
	Id_sub	Numeric	Integer	Y	Unique identifier of the substances	N	N
	Sub_name	String	255	Y	Substance name	N	N

Appendix D – Metabolites with Markush structure not inserted in the DB

Sub_name	Com_name
Bifenox	5-(2,4-dichloro-?-hydroxy-phenoxy)-2-nitrobenzoic acid
Bixafen	N-{3',4'-dichloro-5-fluoro-x-[(6-O-sulfo-β-D-glucopyranosyl)oxy]biphenyl-2-yl}-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide
Dicloran	dibenzofuran
Dicloran	polychlorinated biphenyl
Dicloran	polychlorinated dibenzo-p-dioxin
Diphenylamine	n-hydroxydiphenylamine
Diphenylamine	O-glucose ester conjugate of diphenylamine
Penoxsulam	N-(carbamimidoylcarbamoyl)-2-(3,3,3-trifluoropropyl)benzenesulfonamide
Propargite	4-[4-(2-methyl-2-propanyl)phenoxy]-1,xcyclohexanediol
	4-[4-(1-hydroxy-2-methyl-2-propanyl)phenoxy]-1,x-cyclohexanediol
	2-{4-[(2,xdihydroxycyclohexyl)oxy]phenyl}-2-methylpropanoic acid
	2-methyl-2-{4-[(2,x,ytrihydroxycyclohexyl) oxy]phenyl}propanoic acid
Prosulfocarb	glucose conjugate of prosulfocarb
Spirodiclofen	2,4-dichloro-mandelic acid hydroxy-cyclohexyl ester
Spiromesifen	dihydroxy spiromesifen enol (4,x,y-trihydroxy-3-mesityl-1-oxaspiro[4.4]non-3-en-2-one)
Fenhexamid	1-methyl-N-(2,3,4-trihydroxyphenyl)cyclohexanecarboxamide
Fenamidone	γ-glutamyl-S-{4-methyl-1-[(4-nitrophenyl)amino]-5-oxo-4-phenyl-4,5-dihydro-1H-imidazol-2-yl}cysteinylglycine
Fluometuron	Hydroxylated di-desmethyl fluometuron
Azoxystrobin	4-{[6-(2-cyanophenoxy)pyrimidin-4-yl]oxy}-3-[(1E)-1,3-dimethoxy-3-oxoprop-1-en-2-yl]phenyl glucopyranuronic acid
	methyl (2E)-2-(2-{[6-(2- cyanophenoxy)pyrimidin-4-yl]oxy}-xhydroxyphenyl)-3-methoxyprop-2-enoate
	S-(2-cyano-x-hydroxyphenyl)cysteine

	2-{[6-(2-cyanophenoxy)pyrimidin-4-yl]oxy}-x-hydroxybenzoic acid
Fluoxastrobin	HEC5725-hydroxy carboxylic acid
	HEC5725-OH-phenoxy-amino-PMD

Appendix E - Substances for which the DAR are not available or DAR with no genotoxicity studies

1. Substances with no DAR available

Substances
2-Chloroethanol
Ametoctradin
Azinphos-ethyl
Benzalkonium chloride (BAC)
Bromide ion
Bromopropylate
Camphechlor
Carvone
Chlordane
Chlorfenvinphos
Chlorobenzilate
Chlorpyrifos-methyl
Cinidon ethyl
DDT
Dichlofluanid
Dicrotophos
Dieldrin
Dinotefuran
DNOC
Emamectin benzoate
Endrin
EPN
Ethion
Ethoxysulfuron
Ethylene oxide
Fenpropathrin
Fenvalerate
Fluazifop
Flufenacet (formerly fluthiamide)
Fonofos
Fosthiazate
HCH
Heptachlor
Hexachlorobenzene
Hexaconazole
Isoprocarb
Methidathion

Methoxychlor
Molinate
Monocrotophos
Omethoate (metabolite of dimethoate)
Oxadiargyl
Oxadixyl
Phenthoate
Phoxim
Profenofos
Prothiofos
Quinoxyfen
Resmethrin
S-Metolachlor
Tetradifon
Tetramethrin
Tolfenpyrad
Triazophos
2-Chloroethanol

2. DAR with no genotoxicity studies

Maltodextrin

Appendix F - Date of data dossier collection

Active Substance	Date of data dossier collection
1,4-Dimethylnaphthalene	07/09/2015
1-Methylcyclopropene	07/09/2015
1-Naphthylacetamide (1-NAD)	07/09/2015
1-Naphthylacetic acid (1-NAA)	07/09/2015
2,4-D	14/10/2015
2,4-DB	14/10/2015
2-Phenylphenol (incl. sodium salt orthophenyl phenol)	21/07/2016
6-Benzyladenine	07/09/2015
8-Hydroxyquinoline (incl. Oxyquinoleine)	07/09/2015
Abamectin (aka avermectin)	08/09/2015
Acephate	03/03/2016
Acequinocyl	08/09/2015
Acetamiprid	08/09/2015
Acibenzolar-S-methyl	07/09/2015
Aclonifen	20/10/2015
Acrinathrin	20/10/2015
Aldicarb	27/07/2016
alpha-Cypermethrin (aka alphamethrin)	22/10/2015
Aluminium ammonium sulphate	26/10/2015
Aluminium phosphide	26/10/2015
Aluminium sulphate	28/10/2015
Amidosulfuron	28/10/2015
Aminopyralid	02/11/2015
Amisulbrom	03/11/2015
Amitraz	05/11/2015
Amitrole (aminotriazole)	15/07/2016
Anthraquinone	21/03/2016
Ascorbic acid	09/11/2016
Azadirachtin	09/11/2015
Azimsulfuron	16/11/2015
Azinphos-methyl	17/11/2015
Azoxystrobin	04/11/2015
Beflubutamid	05/11/2015
Benalaxyl	11/12/2015
Benalaxyl-M	18/04/2016
Benfluralin	19/11/2015
Benfuracarb	14/03/2016
Benomyl	18/03/2016

Bensulfuron	20/11/2015
Bentazone	23/11/2015
Benthiavalicarb	16/12/2015
Benzoic acid	10/06/2016
beta-Cyfluthrin	26/11/2015
beta-Cypermethrin	26/11/2015
Bifenazate	16/06/2016
Bifenox	27/11/2015
Bifenthrin	04/03/2016
Bispyribac	23/03/2016
Bitertanol	04/03/2016
Bixafen	16/12/2015
Boscalid (formerly nicobifen)	27/07/2015
Bromadiolone	27/07/2015
Bromoxynil	05/07/2016
Bromuconazole	27/07/2015
Bupirimate	27/07/2015
Buprofezin	27/07/2015
Cadusafos	27/07/2015
Calcium phosphide	07/03/2016
Captan	11/03/2016
Carbaryl	08/07/2016
Carbendazim	20/06/2016
Carbetamide	02/11/2015
Carbofuran	02/05/2016
Carbosulfan	28/04/2016
Carboxin	14/01/2016
Carfentrazone-ethyl	27/05/2016
Chlorantraniliprole	26/04/2016
Chlorfenapyr	02/07/2016
Chloridazon (aka pyrazone)	06/05/2016
Chlormequat	09/05/2106
Chlorothalonil	25/06/2016
Chlorotoluron	10/02/2016
Chlorpropham	25/05/2016
Chlorpyrifos	15/06/2016
Chlorsulfuron	07/01/2016
Chlorthal-dimethyl	18/04/2016
Chromafenozide	09/05/2016
Clethodim	25/03/2016
Clodinafop	07/01/2016
Clofentezine	22/01/2016

Clomazone	07/01/2016
Clopyralid	11/01/2016
Clothianidin	16/05/2016
Copper compounds	29/07/2016
Cyantraniliprole	21/04/2016
Cyazofamid	16/02/2016
Cyclanilide	16/02/2016
Cycloxydim	31/05/2016
Cyflufenamid	12/02/2016
Cyflumetofen	23/05/2016
Cyfluthrin	24/05/2016
Cyhalofop-butyl	12/01/2016
Cymoxanil	27/01/2016
Cypermethrin	04/08/2016
Cyproconazole	12/02/2016
Cyprodinil	15/02/2016
Cyromazine	18/01/2016
Daminozide	11/05/2016
Dazomet	11/07/2016
Deltamethrin	22/02/2016
Desmedipham	23/02/2016
Diazinon	21/01/2016
Dicamba	04/02/2016
Dichlorprop-P	15/01/2016
Dichlorvos	17/08/2016
Diclofop	09/01/2016
Dicloran	20/01//2016
Dicofol	18/02/2016
Didecyldimethylammonium chloride (DDAC)	20/01/2016
Diethofencarb	23/02/2016
Difenoconazole	21/08/2016
Diflubenzuron	12/01/2016
Diflufenican	18/01/2016
Dimethachlor	19/02/2016
Dimethenamid-P	20/07/2016
Dimethoate	24/08/2016
Dimethomorph	17/02/2016
Dimoxystrobin	24/02/2016
Dinocap	13/05/2016
Diphenylamine	22/03/2016
Diquat (dibromide)	29/01/2016
Disodium phosphonate	25/02/2016

Dithianon	10/04/2016
Diuron	30/05/2016
Dodemorph	02/02/2016
Dodine	02/02/2016
Emamectin	22/03/2016
Endosulfan	17/06/2016
Epoxiconazole	03/02/2016
Esfenvalerate	05/02/2016
Ethametsulfuron	05/04/2016
Ethephon	12/01/2016
Ethofumesate	14/06/2016
Ethoprophos	13/04/2016
Etofenprox	24/02/2016
Etoxazole	26/02/2016
Etridiazole	08/02/2016
Eugenol	26/04/2016
Famoxadone	25/05/2016
Fenamidone	17/06/2016
Fenamiphos (aka phenamiphos)	01/07/2016
Fenarimol	21/06/2016
Fenazaquin	06/07/2016
Fenbuconazole	12/08/2016
Fenbutatin oxide	02/07/2016
Fenhexamid	14/06/2016
Fenitrothion	04/07/2016
Fenoxaprop-P	04/08/2016
Fenoxycarb	22/06/2016
Fenpropidin	12/07/2016
Fenpropimorph	05/07/2016
Fenpyrazamine	30/08/2016
Fenpyroximate	08/07/2016
Fenthion	13/08/2016
Ferric phosphate	06/08/2016
Fipronil	22/08/2016
Flazasulfuron	19/07/2016
Flonicamid (IKI-220)	07/07/2016
Florasulam	12/09/2016
Fluazifop-P	14/07/2016
Fluazinam	16/06/2016
Flubendiamide	06/07/2016
Fludioxonil	19/07/2016
Flufenoxuron	01/08/2016

Flumioxazin	15/07/2016
Fluometuron	03/08/2016
Fluopicolide	30/08/2016
Fluopyram	10/08/2016
Fluoxastrobin	11/07/2016
Flupyrsulfuron-methyl	16/08/2016
Fluquinconazole	14/07/2016
Flurochloridone	21/07/2016
Fluroxypyr	05/08/2016
Flurtamone	29/09/2016
Flusilazole	22/07/2016
Flutolanil	09/08/2016
Flutriafol	29/08/2016
Fluxapyroxad	02/09/2016
Folpet	09/09/2016
Foramsulfuron	29/05/2016
Forchlorfenuron	01/08/2016
Formetanate	02/08/2016
Fosetyl-Al	14/07/2016
Fuberidazole	03/08/2016
Geraniol	08/07/2016
Gibberellin	29/07/2016
Glufosinate	26/08/2016
Glyphosate (incl trimesium aka sulfosate)	05/09/2016
Halosulfuron methyl	27/08/2016
Haloxyfop-P (Haloxyfop-R)	05/09/2016
Hexythiazox	11/08/2015
Hymexazol	23/08/2015
Imazalil (aka enilconazole)	03/08/2015
Imazamox	03/09/2015
Imazaquin	07/09/2015
Imazosulfuron	08/02/2016
Imidacloprid	10/09/2015
Indolylbutyric acid	07/01/2016
Indoxacarb	07/03/2016
Iodosulfuron	10/03/2016
Ioxynil	13/05/2016
Ipconazole	17/09/2015
Iprodione	07/04/2016
Iprovalicarb	10/10/2015
Iron sulphate	02/11/2015
Isoproturon	20/01/2016

Isopyrazam	06/11/2015
Isoxaben	02/11/2015
Isoxaflutole	24/06/2016
Kresoxim-methyl	22/11/2015
lambda-Cyhalothrin	20/05/2016
Lenacil	03/11/2015
Lindane	25/05/2016
Linuron	27/05/2016
Lufenuron	15/04/2016
Magnesium phosphide	07/03/2016
Malathion	19/11/2015
Maleic hydrazide	22/03/2016
Mancozeb	22/07/2016
Mandipropamid	22/03/2016
Maneb	21/07/2016
MCPA	02/08/2016
MCPB	22/03/2016
Mecoprop	19/04/2016
Mecoprop-P	17/06/2016
Mepanipyrim	11/09/2016
Mepiquat	27/01/2016
Meptyldinocap	25/01/2016
Mesosulfuron	11/02/2016
Mesotrione	27/08/2016
Metaflumizone	22/04/2016
Metalaxyl	11/04/2016
Metalaxyl-M	08/06/2016
Metaldehyde	08/01/2016
Metam (incl. -potassium and -sodium)	29/08/2016
Metamitron	25/03/2016
Metazachlor	18/08/2016
Metconazole	26/08/2016
Methamidophos	03/09/2016
Methiocarb (aka mercaptodimethur)	24/02/2016
Methomyl	12/02/2016
Methoxyfenozide	02/02/2016
Metiram	23/02/2016
Metobromuron	11/01/2016
Metosulam	15/04/2016
Metrafenone	15/02/2016
Metribuzin	14/06/2016
Metsulfuron-methyl	07/09/2016

Milbemectin	08/07/2016
Myclobutanil	16/08/2016
Napropamide	30/08/2016
Nicosulfuron	09/09/2016
Nicotine	28/08/2016
Orange oil	01/09/2016
Orthosulfamuron	06/07/2016
Oryzalin	11/05/2016
Oxadiazon	22/02/2016
Oxamyl	03/02/2016
Oxasulfuron	26/02/2016
Oxydemeton-methyl	19/07/2016
Oxyfluorfen	05/07/2016
Paclobutrazol	06/07/2016
Parathion	14/07/2016
Parathion-methyl	12/09/2016
Penconazole	24/08/2016
Pencycuron	01/07/2016
Pendimethalin	23/02/2016
Penflufen	04/07/2016
Penoxsulam	29/04/2016
Penthiopyrad	12/07/2016
Permethrin	05/02/2016
Pethoxamid	08/02/2016
Phenmedipham	11/07/2016
Phosalone	02/07/2016
Phosmet	07/07/2016
Phosphane	07/03/2016
Picloram	13/01/2016
Picolinafen	12/01/2016
Picoxystrobin	19/02/2016
Pinoxaden	29/06/2016
Pirimicarb	21/06/2016
Pirimiphos-methyl	21/06/2016
Potassium phosphonates (formerly potassium phosphite)	16/07/2016
Prochloraz	17/06/2016
Procymidone	07/06/2016
Profoxydim	17/06/2016
Prohexadione	16/02/2016
Propamocarb	07/06/2016
Propaquizafop	07/06/2016
Propargite	15/01/2016

Propiconazole	17/06/2016
Propineb	31/05/2016
Propoxycarbazone	07/06/2016
Propyzamide	31/05/2016
Proquinazid	17/02/2016
Prosulfocarb	18/01/2016
Prosulfuron	29/04/2016
Prothioconazole	28/04/2016
Pymetrozine	27/05/2016
Pyraclostrobin	09/02/2016
Pyraflufen-ethyl	10/02/2016
Pyrazophos	17/06/2016
Pyrethrins	09/03/2016
Pyridaben	20/01/2016
Pyridalyl	10/05/2016
Pyridate	03/05/2016
Pyrimethanil	18/02/2016
Pyriofenone	19/01/2016
Pyriproxyfen	14/01/2016
Pyroxsulam	26/04/2016
Quinmerac	18/07/2016
Quinoclamine	20/05/2016
Quintozene	07/01/2016
Quizalofop-P (including -ethyl and -tefuryl)	26/05/2016
Rimsulfuron (aka renriduron)	26/04/2016
S-Abscisic acid	22/01/2016
Sedaxane	08/08/2016
Silthiofam	22/01/2016
Sintofen (aka Cintofen)	20/04/2016
Sodium 5-nitroguaiacolate	31/05/2016
Sodium hypochlorite	26/01/2016
Sodium o-nitrophenolate	01/06/2016
Sodium p-nitrophenolate	03/06/2016
Sodium silver thiosulphate	17/05/2016
Spinetoram	18/05/2016
Spinosad	19/05/2016
Spirodiclofen	04/06/2016
Spiromesifen	10/06/2016
Spirotetramat	15/06/2016
Spiroxamine	13/06/2016
Sulcotrione	04/02/2016
Sulfosulfuron	05/02/2016

Sulfoxaflor	19/07/2016
Sulfuryl fluoride	03/02/2016
tau-Fluvalinate	30/05/2016
Tebuconazole	08/02/2016
Tebufenozide	18/08/2016
Tebufenpyrad	17/02/2016
Tecnazene	18/02/2016
Teflubenzuron	25/08/2016
Tefluthrin	20/08/2016
Tembotrione	01/09/2016
Tepraloxydim	26/08/2016
Terbuthylazine	30/07/2016
Tetraconazole	29/08/2016
Thiabendazole	19/02/2016
Thiacloprid	25/08/2016
Thiamethoxam	05/09/2016
Thiencarbazone	22/05/2016
Thifensulfuron-methyl	02/09/2016
Thiodicarb	22/02/2016
Thiophanate-methyl	17/08/2016
Thiram	08/07/2016
Thymol	27/02/2016
Tolclofos-methyl	03/03/2016
Tolylfluanid	06/06/2016
Topramezone	04/03/2016
Tralkoxydim	22/04/2016
Triadimenol	24/08/2016
Tri-allate	21/05/2016
Triasulfuron	21/04/2016
Triazoxide	09/03/2016
Tribenuron (aka metometuron)	10/03/2016
Trichlorfon	11/03/2016
Triclopyr	14/03/2016
Trifloxystrobin	15/03/2016
Triflumizole	16/03/2016
Triflumuron	23/05/2016
Trifluralin	19/04/2016
Triflusulfuron	06/09/2016
Trinexapac (aka cimetacarb ethyl)	05/04/2016
Triticonazole	07/04/2016
Tritosulfuron	12/06/2016
Valifenalate (formerly valiphenal)	08/04/2016

Vinclozolin	23/08/2016
zeta-Cypermethrin	17/03/2016
Zinc phosphide	07/03/2016
Ziram	04/04/2016
Zoxamide	16/01/2016

Appendix G – Details for QU08A and QU09A attribution

1. QU08A - Component is part of a group assessment

id_sub_com	sub_name	com_name
1710	Triclopyr	Triclopyr-butoxyethyl ester
1723	Haloxyfop-P	Haloxyfop-P-methyl ester
1741	Fenoxaprop-P-ethyl	Fenoxaprop-ethyl
15310	Bentazone	bentazone sodium
15783	Benzoic acid	Sodium benzoate
15831	Bromoxynil	Bromoxynil octanoate
15840	Geraniol	Geranyl acetate
15891	Dimethenamid-P	Racemic dimethenamid
15894	2-Phenylphenol	2-Phenylphenol sodium salt
15903	Copper	Copper (I) oxide
15905	Copper	Bordeaux mixture
15906	Copper	Tribasic copper sulfate
15907	Copper	Copper oxychloride
15908	Copper	Oxine copper
15909	Copper	Copper chloride
15910	Copper	Copper nitrate
15911	Copper	Copper II sulphate pentahydrate
15923	Cypermethrin	Alpha-Cypermethrin
15924	Dichlorvos	Desmethyl dichlorvos
16074	Benalaxyl-M	Benalaxyl
16130	2,4-D	2,4-D dimethyl amine salt
16133	Bromoxynil	Bromoxynil butyrate
35251	Metaflumizone	Z-isomer of metaflumizone
35393	Ioxynil	Ioxynil octanoate
35562	MCPA	MCPA thioethyl
35626	Orange oil	d-limonene
35629	Orange oil	β-myrcene
35630	Orange oil	Linalool
35668	Nicosulfuron	Nicosulfuron leachate (lysimeter product)
35732	Maleic hydrazide	Maleic hydrazide (potassium salt)
55671	Glyphosate	MON 8080
55672	Glyphosate	MON 0818
55673	Glyphosate	Dodigen 4022
55674	Glyphosate	Glyphosate isopropyl amine salt
55704	Emamectin	Emamectin benzoate
55705	Emamectin	Emamectin Hydrochloride

2. QU09A - Component is part of a group but not included in the group assessment

Id_sub_com	Sub_name	Com_name	note
15310	Aluminium phosphide	Magnesium phosphide	Calcium phosphide is a phosphine generator. Other examples of phosphine (IUPAC name phosphane) Generators are magnesium, aluminium phosphide and zinc phosphide. Phosphides in contact with moisture readily decompose to metal hydroxides and phosphine. In the meeting of experts it was agreed that due to the decomposition by moisture other metal phosphides can be regarded as adequate model compounds for the evaluation of calcium phosphide because phosphine is the toxicologically active component.
15783	Calcium phosphide	Magnesium phosphide	
15806	Calcium phosphide	Aluminium phosphide	
15831	Magnesium phosphide	Aluminium phosphide	
15840	Zinc phosphide	Magnesium phosphide	
15891	Zinc phosphide	Aluminium phosphide	
15894	Phosphine	Magnesium phosphide	
15898	Phosphine	Aluminium phosphide	
16033	Folpet	Captan	The study performed with Captan was included in the folpet dossier because the reactive trichloromethylthio side chain of folpet is the same as in captan and metabolism studies have shown that the properties are very similar.
16058	Aluminium ammonium sulphate dodecahydrate	Aluminium sulphate	Most of the data submitted by the notifier are published reviews performed by third parties on different aluminium salts.
16059	Aluminium ammonium sulphate dodecahydrate	Aluminium chloride	
16060	Aluminium ammonium sulphate dodecahydrate	Aluminium oxide	
16061	Aluminium ammonium sulphate dodecahydrate	Aluminium potassium sulphate	
16062	Aluminium ammonium	Aluminum	

	sulphate dodecahydrate		
15898	Aluminium sulphate	Sodium aluminium sulphate	The toxicological assessment of aluminium sulfate is essentially based on studies reported in the public literature that were partly carried out with other aluminium salts.
15899	Aluminium sulphate	Aluminium potassium sulphate	
15900	Aluminium sulphate	Aluminum	
55724	Carbendazim	Thiophanate-methyl	They are closely related compounds

Appendix H – List of studies not inserted in the database

1. List of published papers/references not found

Substance	Reference	Published	EFSA conclusion	Note
Lufenuron	Ashby J and Tennant RW (1991) Definitive relationships among chemical structure, carcinogenicity and mutagenicity for 301 chemicals tested by the U.S. NTP., Mutation Research, 257, 229-306	Yes	Yes	Addendum 1 May 2008: Annex B pag. 23
Orange oil	US EPA (2005) Polymers; Exemption from the Requirement of a Tolerance. ENVIRONMENTAL PROTECTION AGENCY; 40 CFR Part 180 [OPP-2005-0110; FRL-7710-3]; May 18, 2005 (Volume 70, Number 95).	Unknown	Yes	Revised DAR 2012: Annex B, B.6.8.2.3 pag. 72-73: "Genotoxicity study summaries indicated no evidence of mutagenicity in several Salmonella typhimurium reverse mutation assays, one unscheduled DNA assay, and one sister chromatid exchange assay."
	Rockwell et al. (1979) A mutagenic screening of various herbs, spices and food additives. Nutrition and Cancer 1:10-15	Yes	Yes	Revised DAR 2012: Annex B, B.6.8.2.4 pag. 73: "…numerous in vitro genotoxicity studies indicate it is non-genotoxic (Sasaki et al., 1989; Rockwell et al., 1979)."
Napropamide	IUCLID (2003) Data summaries for 1-naphthol. Document no. 201 – 4623B. Bayer	Unknown	Yes	Addendum January 2008 (Follow-up to PRAPeR meetings October 2007 Non-Peer Reviewed information Mammalian toxicology): pag. 4/23: "A range of in vitro and in vivo genotoxicity studies showed that 1-naphthol is non genotoxic overall (Suter and Jaeger, 1982; IUCLID, 2003)."
Metsulfuron-methyl	California EPA, 2003; WHO, 1981; Scientific Committee for Food, 1997)	Unknown	Yes	DAR September 2014: Annex B 2013: B.6.8.1/01 pag 99-100 "The weight-of-evidence from numerous published studies indicates that saccharin is non-genotoxic Saccharin has been subjected to genotoxicity screening in the following tests: in vitro mutation in bacteria (Ames test) and mammalian cells (CHO/HGPRT); chromosome aberration tests in

				vitro and in vivo, including tests in germ cells; DNA binding assay; tests for DNA damage (e.g., Unscheduled DNA synthesis and Comet assays); and DNA gene expression studies. With the exception of tests conducted at excessive doses (i.e., doses toxic to the test system or that greatly increase the ionic strength of the test media), e.g. the in vitro chromosomal aberration test, all tests were negative. The weight-of-evidence from the battery of tests confirms saccharin to be non-genotoxic"
Aluminium ammonium sulphate	Karlik SJ, Eichhorn GL, & Crapper McLachlan DR (1980) Molecular interactions of aluminum with DNA. Neurotoxicology, 1: 83-88	Yes	Yes	Pag 90 Aluminium and ammonium sulphate_DAR_Vol3_B1-B6 (2008). Paper is retrived from IPCS EHC 194
	Rao KSJ & Divakar S (1993) Spectroscopic studies on the effects of aluminum ion on calf-thymus DNA. Bull Environ Contam Toxicol, 50: 92-99	Yes	Yes	Pag 90 Aluminium and ammonium sulphate_DAR_Vol3_B1-B6 (2008). Paper is retrived from IPCS EHC 194
	Tarkka T, Yli-Mäyry N, Mannermaa RM, Majamaa K, & Oikarinen J (1993) Specific non-enzymatic glycation of the rat histone H1 nucleotide binding site in vitro in the presence of AlF4 -. A putative mechanism for impaired chromatin function. Biochim Biophys Acta, 1180: 294-298	yes	Yes	Pag 90 Aluminium and ammonium sulphate_DAR_Vol3_B1-B6 (2008). Paper is retrieved from IPCS EHC 194
	Altmann P, Dhanesha U, Hamon C, Cunningham J, Blair J, & Marsh F (1989) Disturbance of cerebral function by aluminium in haemodialysis patients without overt aluminium toxicity. Lancet, 2: 7-12	yes	yes	Pag 90 Aluminium and ammonium sulphate_DAR_Vol3_B1-B6 (2008). Paper is retrived from IPCS EHC 194
	Crapper McLachlan DR, Dam TV, Farnell BJ, & Lewis PN (1983) Aluminum inhibition of ADP-ribosylation in vivo and in vitro. Neurobehav Toxicol Teratol, 5: 645-647.	yes	yes	Pag 90 Aluminium and ammonium sulphate_DAR_Vol3_B1-B6 (2008). Paper is retrived from IPCS EHC 194

Bentazone	Moriya M, 1983 Further mutagenicity studies on pesticides in bacterial reversion assay systems. Mutation research, 116, (1983), pp185-216	yes	yes	Bentazone – Volume 3 B6 - Annex B –January 2015 - page 101
	Shirasu Y, 1981 Mutagenicity screening studies on pesticides. Environ, Mutagens, Carcinogens, Proc. Int. Cons., 3, (1981), pp331-335	yes	yes	Bentazone – Volume 3 B6 - Annex B –January 2015 - page 101
	Jeang CL and Li GC, 1978 Screening of pesticides for mutagenicity in the microbial systems. Progress in sciences, 6, (1978), pp 770-778	yes	yes	Bentazone – Volume 3 B6 - Annex B –January 2015 - page 101
	Jeang CL and Li GC, 1978 Screening of pesticides for mutagenicity in the microbial systems II. With mammalian microsomal activation. Natl. Sci. Counc. Monthly, ROC, 8, 6, (1980), pp 551-559	yes	yes	Bentazone – Volume 3 B6 - Annex B –January 2015 - page 101
Aminopyralid	It is reassuring that clear negative genotoxicity results were obtained in in vitro assays (Ames, chromosome aberration and CHO-HPRT assays) with aminopyralid containing enhanced levels of three impurities		Yes	(see C.1.4.4 in Vol 4 April 2013) – pag 976 Final Addendum July 2013
Cyromazine	Melamine is not considered to be genotoxic agent based on a complete battery of genotoxicity studies conducted in vitro and in vivo.		yes	Pag 180 Cyromazine-Volume 3; Annex B-6: Toxicology and Metabolism 2007

2. Annex C not available

substance	note	EFSA CONCLUSION
Cyhalofop-butyl	EFSA conclusion pag 8 (The metabolite diacid was tested in vitro for its genotoxic potential, and was not shown to induce neither chromosomal aberrations, nor gene mutations in bacterial or mammalian cells)	yes
Diquat	EFSA conclusion pag 8 (The impurities 1,2-dibromoethane (genotoxic carcinogen), 2,2'-bipyridine (Ames positive, and potential teratogen) and total terpyridines (sum of 2,2':6',2"terpyridine and related isomers; very acutely toxic) are considered relevant impurities based on their hazard profiles)	yes
Emamectin	DAR 2011, B.6.8.3 Studies with impurities in technical material (pag 198). Ames test	yes
Acrinathrin	DAR 2010, B.6.8.3. Supplementary studies on impurities (pag 178). Ames test has been conducted with impurity 7 and the results are available (see confidential information Vol 4 revised)	yes
Carbetamide	B.6.8.2. Discussion on a specific impurity. The possible health impact of a certain impurity of Carbetamide technical is further discussed in vol 4 Annex C.	yes
Metam	Document Circabc: Metam-sodium_DAR_Vol3_B1-B7_doc.zip B.6.8.1.2 toxicity studies on impurities (Annex II A 5.8.1) See confidential part of the DAR (Vol 4, Annex C)	Yes

3. Studies with not sufficient details

Substance	Reference	Published	EFSA concl	Note
Dicamba	Table 6.4.1-1 Overview of reported results of in vitro and in vivo mutagenicity assays		Yes	pag 99 Final addendum November 2010 For some studies it is reported a positive result regarding the entire study without specifying the particular results for strains and metabolic activation. We are not able to retrieve the original paper (titles

				of the studies are not reported in the DAR)
Napropamide	Purchase, I. F.H., E. Longstaff, j. Ashby, J.A. Styles, D. Anderson, P.A. Lefevre and F.R. Westwood (1978) An evaluation of 6 short-term tests for detecting organic chemical carcinogens, Br. J. Cancer, 37, 873-959 Reference included in the article "Comparative evaluation of different pairs of DNA repair-deficient and DNA repair-proficient bacterial tester strains for rapid detection of chemical mutagens and carcinogens, W. Suter and J. Jaeger, 1982, Mut. Research, 97 (1982), 1-18" cited in the DAR	Yes	Yes	Addendum January 2008 (Follow-up to PRAPeR meetings October 2007 Non-Peer Reviewed information Mammalian toxicology): For this study it is reported a positive result regarding the entire study without specifying the particular results for strains and metabolic activation.
Ziram	Table 6.5.4.4-6 Test for mitotic recombinant	yes	no	pag 108 DAR_May 1998 For some studies it is reported a positive result regarding the entire study without specifying the particular results at treat. time: 48h, 72h, 96h. We are not able to retrieved the original paper ("Genotoxicity of ziram established through wing, eye and female germ-line mosaic assays and the sex-linked recessive lethal test in Drosophila melanogaster" Mutat Res. 1989 Oct;224(2):161-9. Tripathy NK1, Majhi B, Dey L, Das CC)

4. Substance THIRAM

B.6.4.4. Additional information from the open literature, pag. 43

In vitro genotoxicity tests	
	Reference
Table 1: Tests for gene mutations in vitro	Hedenstedt et al., 1979
	Zdzienicka et al., 1979
	Zdzienicka et al., 1981a,b
	Moriya et al.,1983
	Rannug and Rannug. 1984
	Rannug,et al 1984
	Crebelli et al.,1985
	Crebelli et al.,1992
	Franekic et al,1994
	Donner et al , 1983
	Paschin and Bakhitova, 1985
	Zdzienicka et al.,1981a,b
Table 2: Tests for chromosome damage	Mosesso et al., 1994
	Mosesso et al., 1994
Table 3: Sister chromatid exchanges	Pienkowska and Zielenska, 1990
	Perocco et al., 1989
	Donner et al., 1983
Table 4: Repairable DNA damage: UDS	Perocco et al., 1989
	Rocchi et al.,1980
Table 5: Tests for aneuploidy	Franekic et al.1994
	Upshall and Johnson, 1981
Table 6: Other indicators of genetic damage	Franekic, J., 1994
	Zdzienicka et al., 1981a,b
	Rosenkranz and Leifer, 1980
	Dulout et al., 1982
	Kada et al., 1974
In vivo genotoxicity tests	
	Reference
Table 7: Sex-linked recessive lethal test (gene mutations and small deletions in germ cells)	Donner, M.1981
	Donner et al., 1983
Table 8: Micronucleus test	Dulout et al., 1982
	Crebelli et al., 1992
	Paik and Se Young Lee, 1977
	Paschin and Bakhitova, 1985
	Donner et al., 1983
Table 9: Morphological sperm abnormalities	Zdzienicka et al., 1982
	Prasad et al., 1987
	Hemavathi and Rahiman, 1993

Appendix I - Compounds with no chemical identifiers

id_sub_com	id_sub	sub_name	id_qualifier	id_com	com_name	NOTE*
35526	35046	Milbemectin	QU07A	50511	Milbemectin	Milbemectin is a mixture of Milbemycin A3 and Milbemycin A4
35625	35055	Orange oil	QU07A	50580	Orange oil	Orange oil is a blend of many molecules mainly monoterpenes including the major compound D-limonene
15891	15054	Dimethenamid-P	QU08A	15819	Racemic dimethenamid	it is a racemic mixture
35668	1152	Nicosulfuron	QU08A	50614	Nicosulfuron leachate (lysimeter product)	It is a lysimeter product; the test material was mixed soil leachates
55671	85028	Glyphosate	QU08A	75589	MON 8080	It is a surfactant contained in glyphosate
55672	85028	Glyphosate	QU08A	75590	MON 0818	It is a surfactant contained in glyphosate
55673	85028	Glyphosate	QU08A	75591	Dodigen 4022	It is a surfactant contained in glyphosate
55705	15038	Emamectin	QU08A	75612	Emamectin Hydrochloride	The chemical structure could not be retrieved
55666	85028	Glyphosate	QU10A	75584	Glyphosate formulation (Rodeo)	formulation
55667	85028	Glyphosate	QU10A	75585	Glyphosate formulation (MON 2139)	formulation
55668	85028	Glyphosate	QU10A	75586	Glyphosate formulation (MON 14445t)	formulation
55669	85028	Glyphosate	QU10A	75587	Glyphosate formulation (Glifos)	formulation
55670	85028	Glyphosate	QU10A	75588	Glyphosate formulation (Roundup)	formulation
55675	85028	Glyphosate	QU10A	75593	Glyphosate formulation (Percozyd 10 SL)	formulation
55676	85028	Glyphosate	QU10A	75594	Glyphosate formulation (Herbazed)	formulation
15573	1217	Benthiavalicarb-isopropyl	QU11A	15537	KIF-230-I4	the software could not recognized the name or the component could not be retrieved

id_sub_com	id_sub	sub_name	id_qualifier	id_com	com_name	NOTE*
15697	3707	Chromafenozide	QU11A	15631	N“-tert-butyl-N“-benzoyl)-5-methyl-6-chromancarbohydrazide	the software could not recognized the name or the component could not be retrieved
15698	3707	Chromafenozide	QU11A	15632	N“-tert-butyl-N“-(3-methylbenzoyl)-5-methyl-6-chromancarbohydrazide	the software could not recognized the name or the component could not be retrieved
15700	3707	Chromafenozide	QU11A	15634	N“-tert-butyl-N“-(3,5-dimethyl-6-chromancarbonyl)-5-methyl-6-chroman-carbohydrazide	the software could not recognized the name or the component could not be retrieved
15701	3707	Chromafenozide	QU11A	15635	N“-tert-butyl-N“-(3,5-dimethylbenzoil)-3,5-dimethylbenzohydrazide	the software could not recognized the name or the component could not be retrieved
15702	3707	Chromafenozide	QU11A	15636	N“-tert-butyl-N“-(3,5-dimethylbenzoyl)-8-chloro-5-methyl-6-chromancarbohydrazide	the software could not recognized the name or the component could not be retrieved
15723	15040	Clothianidin	QU11A	15657	CCMT	the software could not recognized the name or the component could not be retrieved
15724	15040	Clothianidin	QU11A	15658	BZT	the software could not recognized the name or the component could not be retrieved
15763	1244	Cycloxydim	QU11A	15695	3-propyl-6-(3-thianyl)-4,5,6,7-tetrahydrobenzisoxazol-4-one	the software could not recognized the name or the component could not be retrieved
15769	1244	Cycloxydim	QU11A	15701	Reg. No. 230 845	the software could not recognized the name or the component could not be retrieved
15815	15049	Chlorothalonil	QU11A	15747	2,4,5,6-tetrachloro-dibenzamide	the software could not recognized the name or the component could not be retrieved
16025	1239	Carbendazim	QU11A	15930	5-hydroxy carbendazim	the software could not recognized the name or the component could not be retrieved
16087	1162	Bromuconazole	QU11A	15975	LS880226	the software could not recognized the name or the component could not be retrieved
16088	1162	Bromuconazole	QU11A	15976	RPA405516	the software could not recognized the name or the component could not be retrieved
16089	1162	Bromuconazole	QU11A	15977	RPA405517	the software could not recognized the name or the component could not be retrieved

id_sub_com	id_sub	sub_name	id_qualifier	id_com	com_name	NOTE*
16132	15051	Bromoxynil	QU11A	16014	AE 0652991	the software could not recognized the name or the component could not be retrieved
16139	1144	Chloridazon	QU11A	16021	Impurity #4	the software could not recognized the name or the component could not be retrieved
35394	35034	Ioxynil	QU11A	50393	2,6-diiodo-4-(octanoyl-carbamoy)phenyl octanoate	the software could not recognized the name or the component could not be retrieved
35445	1128	Propamocarb hydrochloride	QU11A	50443	N,N-dimethyl-, dihydrochloride 1,3-propanediamine	the software could not recognized the name or the component could not be retrieved
35447	1128	Propamocarb hydrochloride	QU11A	50445	di-n-propyl-carbonate	the software could not recognized the name or the component could not be retrieved
35482	1106	Phosalone	QU11A	2035	Phosalone impurity (AE C500659/RPA 13515)	the software could not recognized the name or the component could not be retrieved
35483	1106	Phosalone	QU11A	2036	Phosalone impurity (AE F073749/RPA 590184)	the software could not recognized the name or the component could not be retrieved
35597	35031	Mesotrione	QU11A	50556	R287463	the software could not recognized the name or the component could not be retrieved
35598	35031	Mesotrione	QU11A	50557	Imp 4	the software could not recognized the name or the component could not be retrieved
16129	15013	Benomyl	QU14A	16011	Benlate	part of a mixture or formulation
55665	1137	Haloxyfop-P	QU14A	75583	Racemic Haloxyfop	part of a mixture or formulation
15699	3707	Chromafenozide	QU17A	15633	N"-tert-butyl-N"-(5-methyl-6-chromancarbonyl)-5-methyl-6-chroman-carbohydrazide	the software could not recognized the name or the component could not be retrieved
15753	15043	Carfentrazone-ethyl	QU17A	15685	Carfentrazone ethyl lysimeter percolate	the software could not recognized the name or the component could not be retrieved
15817	15049	Chlorothalonil	QU17A	15749	2,5,6-trichloro-4-thio-isophthalonitrile	the software could not recognized the name or the component could not be retrieved
15819	15049	Chlorothalonil	QU17A	15751	5-(2,4-dicyano-3,5,6-trichlorophenyl) glutathione	the software could not recognized the name or the component could not be retrieved
15820	15049	Chlorothalonil	QU17A	15752	5-chloro-2,4-6-	the software could not recognized the name or

id_sub_com	id_sub	sub_name	id_qualifier	id_com	com_name	NOTE*
					trismercaptoisophthalonitrile	the component could not be retrieved
15821	15049	Chlorothalonil	QU17A	15753	S,S1-(2,4-dicyano-3,6-dichlorophenyl) dicysteine	the software could not recognized the name or the component could not be retrieved
15822	15049	Chlorothalonil	QU17A	15754	S,S,S1- (2,4-dicyano-6-chlorophenyl) tricysteine	the software could not recognized the name or the component could not be retrieved
16019	1451	Thiamethoxam	QU17A	15924	NOA 459602	the software could not recognized the name or the component could not be retrieved
35497	1461	Penflufen	QU17A	50487	-	the software could not recognized the name or the component could not be retrieved
35737	1323	Oxyfluorfen	QU17A	50669	2-amino-5-[2-chloro-4-(trifluoromethyl)phenoxy]phenol-conjugate	the software could not recognized the name or the component could not be retrieved
55098	85008	Trifloxystrobin	QU17A	75089	NOA 414412	the software could not recognized the name or the component could not be retrieved
55398	1110	Fenamiphos (aka phenamiphos)	QU17A	75343	des-isopropylamino fenamiphos sulfoxide	the software could not recognized the name or the component could not be retrieved
16053	15008	acetamiprid	QU17A	15952	2(N2-carbamoyl-N1-[(6-chloro-3-pyridyl)methyl]-N1-methylacetamidine)	the software could not recognized the name or the component could not be retrieved
16057	15008	acetamiprid	QU17A	15956	N2-cyano-N1-methyl-N1-[(2-aza-3-oxobicyclo[2,2,0]hex-5-en-6-yl]-acetamidine	the software could not recognized the name or the component could not be retrieved
16077	15016	beta-Cyfluthrin	QU17A	15969	3(4'-hydroxy-phenoxy)-4-fluoro-benzoic acid	the software could not recognized the name or the component could not be retrieved
16079	15016	beta-Cyfluthrin	QU17A	15970	3-phenoxy-4-fluoro-benzoic acid amide	the software could not recognized the name or the component could not be retrieved
16090	3429	Chlorantraniliprole	QU11A	15978	IN-G2S78	the software could not recognized the name or the component could not be retrieved
16091	3429	Chlorantraniliprole	QU11A	15979	IN-E8S90	the software could not recognized the name or the component could not be retrieved
16078	15041	Cyfluthrin	QU17A	15969	3(4'-hydroxy-phenoxy)-4-fluoro-benzoic acid	the software could not recognized the name or the component could not be retrieved

id_sub_com	id_sub	sub_name	id_qualifier	id_com	com_name	NOTE*
16080	15041	Cyfluthrin	QU17A	15970	3-phenoxy-4-fluoro-benzoic acid amide	the software could not recognized the name or the component could not be retrieved
55699	1230	Flonicamid	QU11A	75610	TFNG-CAM	the software could not recognized the name or the component could not be retrieved
35682	35058	Mepanipyrim	QU17A	50625	2-(2-hydroxyanilino)-4-(ethyhyl)-6-methylpyrimidine	the software could not recognized the name or the component could not be retrieved
35685	35058	Mepanipyrim	QU11A	50628	impurity I3	the software could not recognized the name or the component could not be retrieved
35527	35046	Milbemectin	QU17A	50512	8,9Z-MA3	the software could not recognized the name or the component could not be retrieved
35528	35046	Milbemectin	QU17A	50513	8,9Z-MA4	the software could not recognized the name or the component could not be retrieved
35556	1135	Oxydemeton-methyl	QU11A	50531	O,O,S-trimethyl-phosphorothioate	the software could not recognized the name or the component could not be retrieved
35706	1135	Oxydemeton-methyl	QU17A	50642	2-hydroxy-3-[(2-ethylsulfinyl-2-ethyl)-thio]propionic acid	the software could not recognized the name or the component could not be retrieved
35707	1135	Oxydemeton-methyl	QU17A	50643	2-hydroxy-3-[(2-ethylsulfonyl-2-ethyl)-thio]propionic acid	the software could not recognized the name or the component could not be retrieved
35708	1135	Oxydemeton-methyl	QU17A	50644	2-hydroxy-3-[(2-ethylsulfonyl-2-ethyl)-sulfinyl]propionic acid	the software could not recognized the name or the component could not be retrieved
35710	1135	Oxydemeton-methyl	QU17A	50646	2-ethylthio ethane sulfonic acid	the software could not recognized the name or the component could not be retrieved
35444	1128	Propamocarb hydrochloride	QU11A	50442	HOE 131392 (AE B131392)	the software could not recognized the name or the component could not be retrieved
55408	1167	Fenpropimorph	QU11A	75352	Fenpropimorph impurity 116453	the software could not recognized the name or the component could not be retrieved
55439	1215	Fluoxastrobin	QU11A	75382	Fluoxastrobin impurity 15	the software could not recognized the name or the component could not be retrieved
55564	1305	Tebufenozide	QU17A	75500	N-tert-butyl-N'-{[4-(1-hydroxyethyl)phenyl]carbonyl}-3-(hydroxymethyl)-5-methylbenzohydrazide conjugates	the structure is present on EFSA conclusion without specifying the conjugates residue

id_sub_com	id_sub	sub_name	id_qualifier	id_com	com_name	NOTE*
4493	3686	Sodium silver thiosulfate	QU07A	6115	Sodium silver thiosulfate (in solution with a ratio of at least 1 to 8 silver to thiosulfate ions)	Not applicable (please refer to EFSA Journal 2013; 11(3):3136)
1996	1391	Prochloraz	QU10A	1916	Prochloraz-Copper	the software could not recognized the name or the component could not be retrieved.
15676	1141	Carbosulfan	QU10A	15620	Carbosulfan formulation	formulation

Please note that these substances and compounds have no SMILE notation and no INCHI notation.

Appendix J – Standard Operating Procedure (SOPs)

GP/EFSA/PRAS/2014/01:

COMPILATION OF A DATABASE, SPECIFIC FOR THE PESTICIDE ACTIVE SUBSTANCE AND THEIR METABOLITES, COMPRISING THE MAIN GENOTOXICITY ENDPOINTS

STANDARD OPERATING PROCEDURES

DATA COLLECTION, DATA EXTRACTION, DATA ENTRY AND DATA QUALITY EVALUATION.

Table of Contents

Scope

This document describes the standard operating procedures for data collection, data extraction, data entry and data quality evaluation in the Efsa Project GP/EFSA/PRAS/2014/01: Compilation of a database, specific for the pesticide active substance and their metabolites, comprising the main genotoxicity endpoints.

It is to be used as a document for each users operating in the project

Objective

The objective of this SOP is to standardize and harmonize the data collection and quality controls within the Efsa Project GP/EFSA/PRAS/2014/01 in order to ensure that the quality of the data is high and the data insertion across the different users are comparable. This document describes generally the specific aspects on which data collection procedures and quality controls, should be conducted by each user. This document may serve the user for defining specific procedures and instruction for each kind of data to be collected and inserted: during the data collection, during the data extraction, during the data entry, in the data check and cleaning phase, and the data-handling phase. Insight in the quality of the results is essential for the interpretation and comparison of the results.

1. STANDARD OPERATING PROCEDURES

1.1. Data Entry Procedure

The data compilation of a database specific for pesticide active substances and their metabolites to be achieved through the following procedural steps:

- Dossier collection
- Data extraction
- Data quality evaluation
- Data entry (Annex 3 database)
- Quality Control of data entry

Hereafter a brief description on the methods applied to accomplish these steps.

1.2. Dossier collection

Data to be retrieved for pesticide active substances listed in the Annex 2 of the call (GP/EFSA/PRAS/2014/01: Compilation of a database, specific for the pesticide active substance and their metabolites, comprising the main genotoxicity endpoints).

An additional list of active substances as described in Annex 2 was provided by EFSA. Further information has been included to indicate whether the peer review was conducted by EFSA or not, whether a renewal, post approval, article 21 or confirmatory data on the field of mammalian toxicology is available for those substances.

For those substances that have not been peer reviewed by EFSA in the first evaluation at EU level there is a need for the contractor to check if the substance is under renewal because the most updated source of

information for data collection should be the renewal assessment report. This is indicated in the table by the term AIR.

For those substances that have been peer reviewed by EFSA there is also a need for the contractor to check if the substance has been subject to other procedures (renewal, confirmatory data, article 21, post approval) since further information relevant for data collection could be found in addendum or renewal assessment report under these procedures.

Please note that for confirmatory data an EFSA conclusion might not be available but there should be an EC review report available or a previous published EFSA document (coded in the Opinion Table as 32774) unless the confirmatory data is on-going.

Please note that the final EFSA conclusion or EC review report might not be available because the procedure is on-going (e.g. AIR III substances – coded in the Opinion Table as 32773).

Since the contractor has access to the EFSA DMS platform, the contractor should retrieve data for each substances both in DMS and in CIRCABC.

Dossier A

Peer Review of the Draft Assessment Reports and the finalization of the risk assessment done by EFSA (dossiers A).

Type of document to be collected:

- Draft Assessment Reports
- Additional reports
- Addenda
- Evaluation table and discussion table
- EFSA Conclusion
- Commission reports

Source of information:

- EFSA journal
  http://www.efsa.europa.eu/en/publications/efsajournal.htm

- CIRCABC
https://circabc.europa.eu/faces/jsp/extension/wai/navigation/container.jsp

- EFSA DMS platform.
https://dms.efsa.europa.eu/otcs/llisapi.dll?func=ll&objId=9512479&objAction=browse&sort=name

Dossier B

Peer Review of the Draft Assessment Reports and the finalization of the risk assessment not done by EFSA (dossiers B)

Type of document to be collected:

- European Commission (EC) Review Reports
- Draft Assessment Reports or addenda

Source of information:

- EFSA journal
http://www.efsa.europa.eu/en/publications/efsajournal.htm

- CIRCABC
https://circabc.europa.eu/faces/jsp/extension/wai/navigation/container.jsp

- EU Pesticides Database
http://ec.europa.eu/sanco_pesticides/public/index.cfm?event=activesubstance.selection&language=EN

Information regarding the genotoxicity of active substances and their metabolites to be retrieved from Draft Assessment Report (dossier A and dossier B). EFSA documents (dossier A) and EC Review Reports to be consulted to look for conclusions which differ from those reported in the Draft Assessment Report.

For some pesticide active substances, Draft Assessment Reports are not available in CIRCABC and in DMS. For these substances the data collection not to be performed.

Original studies only to be consulted when these sources of information would include insufficient details to perform the compilation of the database (mandatory fields).

Original studies report to be asked for the Italian Ministry of Health. Amended by EFSA: when original study report could not be retrieved, to include a list at the end of each interim report. It will be an action for EFSA to provide these studies.

For each substance, an electronic folder containing all the downloaded documents to be created.

In the MS Excel file provided by EFSA it should be reported if data dossier collection has been done for a specific substance, the date of data dossier collection and if not, the reason.

1.3. Data extraction

Set of data and information for pesticide active substances and their metabolites to be included in the database according to the data model provided in the Annex 3 of this call.

Exclusion criteria:

- Study considered not acceptable as a conclusion of the peer review process (e.g. study considered not acceptable by RMS in the first step, but considered acceptable in the EFSA conclusion or Review report, to be inserted in the database).

- Study performed on substance different from the active ingredient or its metabolites not to be included.

The data extraction procedures are given below to cover the following data categories:

- GENOTOX (characterizes the genotoxicity end point study)
- OPINION (divided into three different sub-tables):
    - Opinion REPORT referring to the references of the studies;
    - Opinion DAR with information on DARs
    - Opinion EFSA and EC Documents
- SUBSTANCE_COMPONENT (characterizes active substances and metabolites)
- COMPONENT SYNONIM (characterizes the alternative names of the substance i.e. trivial names).

GENOTOX

For the GENOTOX table, data extraction from the specified source of the Draft Assessment Report or (Final) Addendum to be performed for these fields:

- **id_genotox**: numerical key generated automatically;

- **id_study_cat**: type of genotoxicity; data to be extracted from Section B.6.4 "Genotoxicity" (Annex IIA.5.4) Vol 3 of DAR for active substances and Section B.6.8.1 "Genotoxicity studies of metabolites" (Annex IIA 5.8.1) Vol 3 of DAR for the metabolites. "Genotoxicity" is the default entry;

- **id_test_type:** classification of type of test according to OECD phrase list, included in EFSA_TEST_TYPE catalogue; data reported in the title of the study in Section B.6.4 for active substances and Section B.6.8.1 for metabolites (see Figure 15);

- **method_type:** classification of testing method (*in vitro*, *in vivo*); data reported in the title of the study, in Section B.6.4 (B.6.4.1 *In vitro* studies; B.6.4.2 *In vivo* studies) for active substances and Section B.6.8.1.2 for metabolites;

- **id_genotox_species:** organism or cell culture used, included in EFSA_MATRIX catalogue; data to be extracted from the "Materials & methods" of the study in Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites (see Figure 15);

- **id_strain:** strain of the organism tested, included in EFSA_STRAIN catalogue; data to be extracted from the "Materials & methods" of the study in Section B.6.4 for active substances (see Figure 15) and Section B.6.8.1.2 for metabolites.
Where the test is performed on more than one strain, a record in the database to be created for each strain tested;

- **met_indicator:** whether exogenous metabolic activation was applied or not in the study; data to be extracted from the "Materials & methods" of the study in Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites.
The most commonly used system is a cofactor-supplemented post-mitochondrial fraction (S9) prepared from the livers of rodents treated with enzyme-inducing agents such as Aroclor 1254. When the test is performed *with* and *without* metabolic activation, a record in the database to be created for each metabolic activation status;

- **id_route:** the route of administration; only for *in vivo* studies, data to be extracted from the "Materials & methods" of the study in Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites.
Where the test is performed using more than one route, a record in the database to be created for each route used;

- **id_ genotox_endpoint:** type of genotoxicity endpoint covered by the study (i.e: gene mutation, chromosome aberration, DNA damage and/or repair, genome mutation); data reported in the subtitle or extracted from the "Objective" Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites.

Table 1: Most commonly used methods and related endpoint

Most commonly used *in vitro* methods	Studies to investigate gene (point) mutation	Bacterial reverse mutation test in Salmonella typhimurium and Escherichia coli (OECD TG 471)

		In vitro mammalian cell gene mutation test (OECD TG 476)
	Studies to investigate chromosome aberrations:	In vitro mammalian chromosomal aberration test (OECD 473)
		In vitro mammalian cell micronucleus test (OECD TG 487)
Most commonly used *in vivo* methods	Studies to investigate gene mutations:	Transgenic rodent somatic and germ cell gene mutation assays (OECD TG 488)
	Studies to investigate chromosome aberrations	Mammalian erythrocyte micronucleus test (OECD TG 474)
		Mammalian bone marrow chromosome aberration test (OECD TG 475)
	Studies to investigate primary DNA damage	*In Vivo* Mammalian Alkaline Comet Assay (OECD TG 489)
		Unscheduled DNA synthesis (UDS) test with mammalian liver cells *in vivo* (OECD TG 486)

- **is_ genotoxic:** the result of the study; data to be extracted from the "Conclusion" or "Results & discussion" in Section B.6.4 for active substances and B.6.8.1.2 for metabolites;

- **remarks:** all relevant information on genotoxicity study to be extracted from Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites in the text of the study.
It should be structured as follows (if feasible):

1. deviations from the guideline (e.g: four strains were tested instead of five strains)
2. statistical evaluation (e.g.: no statistical analysis was performed)
3. doses (e.g.: dose range: from 100 to 1000 µg/ml without S9 mix - from 10 to 250 µg/ml with S9 mix)
4. additional remarks (e.g.: the study is acceptable as additional information)
5. potential presence of genotoxic impurities
6. indicate if the aneugenic potential was investigated for those substances positive in vitro and *in vivo* MN test.

- **acceptability:** whether genotoxicity study is considered acceptable or not according to RMS assessment; data reported in "Acceptability" at the beginning of the study in Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites (see figure 15); if the study is acceptable, enter the data "Acceptable" in the corresponded field; if the study is not acceptable, check in the review report or EFSA conclusion if there is a mention of revised acceptability of that specific study: if not, exclude the study from data entry, if yes, put "Acceptable" in the corresponded field and add in the remarks the following reference "the study is considered not acceptable in the DAR, but re-assessed as acceptable in the review report or in the EFSA

conclusion"; if the study is acceptable as additional information, enter the data "Acceptable" in the corresponding field and add in the remarks the following reference "the study is acceptable as additional information".

- **guideline_qualifier:** whether Guideline was followed or not in the study; data to be extracted from Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites;

- **id_genotox_guideline:** Guideline number followed in the study, included in EFSA_GUIDELINE catalogue; data reported in the "Guideline" at the beginning of the study in Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites (see Figure 15) ;

- **deviation:** whether the study contains deviations from the standard test protocol; data reported in the "Deviation" at the beginning of the study in Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites (see Figure 15) ;

- **glp_compl:** whether a GLP certificate or compliance statement is available; data reported in the "GLP compliance" at the beginning of the study to be extracted from Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites (see Figure 15) or from Section B.6.15 "References relied on";

- **sex:** sex of the tested organisms for *in vivo* studies; data to be extracted from the "Materials & methods" of the study in Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites;

- **exp_period:** exposure duration for *in vivo* studies; data to be extracted from the "Materials & methods" of the study in Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites;

- **number_individuals**: the number of organisms dosed at each dose level of the *in vivo* genotoxicity study; data to be extracted from the "Materials & methods" of the study in Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites;

- **id_duration_unit:** unit of exposure duration for *in vivo* studies; data to be extracted from the "Materials & methods" of the study in Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites;
This field refers to the exp_period reported previously;

- **control:** whether and what type of concurrent negative control group were used in the *in vivo* and *in vitro* studies; data to be extracted from the "Materials & methods" and "Results & discussion" of the study in Section B.6.4 for active substances and Section B.6.8.1.2 for metabolites.
Note that for same studies also positive controls are present. In this field only negative controls are considered;

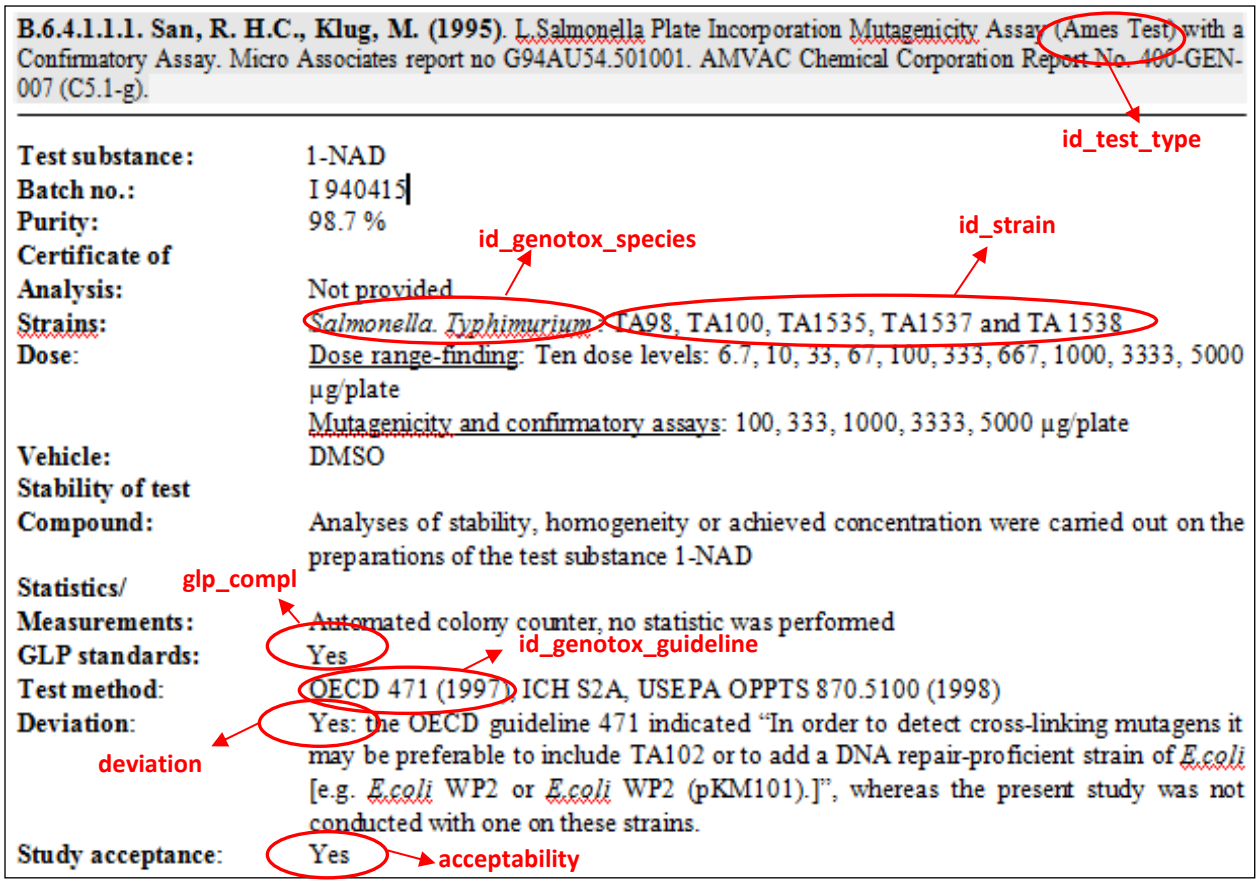
- **mouseLymphTest:** information regarding the size of colony mutant. It is required only for "In Vitro Mammalian Cell Gene Mutation Assays Using the Thymidine Kinase Gene".
There are three alternatives:
1. small colonies
2. large colonies
3. no information available

- **Target_Tissue-Exposure:** to indicate for *in vivo* micronucleus test whether there was:

1. direct evidence-cytotoxicity: evidence of exposure of the bone marrow to the test substance indicated as a decrease of the ratio of polychromatic erythrocytes (PCE) to normochromatic erythrocytes (NCE) or the ratio of polychromatic erythrocytes (PCE) to the total number of erythrocytes.
2. indirect evidence-systemic toxicity: if there is an indication of clinical systemic signs (i.e. death, dyspnoea, ataxia etc.)
3. indirect-toxicokinetic investigations: evidence of exposure of the bone marrow to the test substance can be extracted from Section B.6.1 "Administration, distribution, metabolism and excretion". Studies are performed in rodents at similar concentrations
4. no evidence

- **id_target_tissue:** field for the tissue/target organ investigated in the *in vivo* test.

Figure 15: example of section B.6.4 (for active substances)



B.6.4.1.1.1. San, R. H.C., Klug, M. (1995). L Salmonella Plate Incorporation Mutagenicity Assay (Ames Test) with a Confirmatory Assay. Micro Associates report no G94AU54.501001. AMVAC Chemical Corporation Report No. 400-GEN-007 (C5.1-g).

id_test_type

Test substance:	1-NAD
Batch no.:	I 940415
Purity:	98.7 %
Certificate of Analysis:	Not provided
Strains:	*Salmonella. Typhimurium*: TA98, TA100, TA1535, TA1537 and TA 1538
Dose:	Dose range-finding: Ten dose levels: 6.7, 10, 33, 67, 100, 333, 667, 1000, 3333, 5000 µg/plate Mutagenicity and confirmatory assays: 100, 333, 1000, 3333, 5000 µg/plate
Vehicle:	DMSO
Stability of test Compound:	Analyses of stability, homogeneity or achieved concentration were carried out on the preparations of the test substance 1-NAD
Statistics/ Measurements:	Automated colony counter, no statistic was performed
GLP standards:	Yes
Test method:	OECD 471 (1997), ICH S2A, USEPA OPPTS 870.5100 (1998)
Deviation:	Yes: the OECD guideline 471 indicated "In order to detect cross-linking mutagens it may be preferable to include TA102 or to add a DNA repair-proficient strain of *E.coli* [e.g. *E.coli* WP2 or *E.coli* WP2 (pKM101).]", whereas the present study was not conducted with one on these strains.
Study acceptance:	Yes

id_genotox_species

id_strain

glp_compl

id_genotox_guideline

deviation

acceptability

OPINION-REPORT

For the OPINION-REPORT table, data extraction from the specified source of the Draft Assessment Report or (Final) Addendum to be performed for these fields:

- **id_rep:** numerical key generated automatically;

- **op_type:** type of source reference, included in EFSA_REFTYPE catalogue; the correct EFSA catalogue terminology is “Report” (code RT006ART);

- **id_owner:** the name of data owner (in some cases this might be the company); information will to extracted from Section B.6.15 “References relied on” – sixth column (see Figure 16);

- **author:** list of authors of the report (for ease of sorting and searchability use following convention: Surname, Initial (Example 1: White D, Ruehl KJ, Borman SA & Little J. Example 2: Hartley M & Murray W (avoid unnecessary full-stops, commas). If no individuals are cited as authors, enter name of company or organization or 'Anon.' as appropriate);

- **title:** the entire title of the study as described in the DAR or addendum; information to be extracted from Section B.6.15 “References relied on” – fourth column (see Figure 16) . In case of unpublished studies, Report No in fourth column (see Figure 16) , to be also added in this field;

- **adoption_date:** complete date of the adoption of the document;

- **publication_date:** year of the publication of the document; date to be reported as yyyy.

- **journal_title:** title of the journal or the editor. Information to be extracted from Section B.6.15 “References relied on” in the fourth column, when column “owner” is blank or with the word “public” (published study) (see Figure 16) ;

- **doi:** Digital Object Identifier, a permanent character string (a "digital identifier") used to uniquely identify an object such as an electronic document, source the study report or publication, URL or EFSA Journal;

- **international_unique_number:** International Standard Book Number (ISBN) or International Standard Serial Number (ISSN) is a unique numeric commercial book identifier or periodical publications such as magazines (if published report);

- **URL:** uniform resource locator, specific character string that constitutes a reference to a resource in internet.
E.g.:http://www.ncbi.nlm.nih.gov/pubmed/?term=Metabolites+of+the+biocide+ophenylphenol+generate+oxidative+DNA+lesions+in+V+79+cells;

- **citation:** reference to a book, article, web page, or other published item (if published report). Information to be extracted from Section B.6.15 “References relied on”- fourth column (see Figure 16);

Figure 16: example for data extraction from section B.6.15 (for active substances)

B.6.15 Refence relied on

OECD data point number / reference number	Author(s)	Year	Title Source (where different from company) Company name, Report No., Date, GLP status (where relevant), published or not	Data protect. claimed	Owner*
IIA 5.4.1/01	San, R.H.C. and Springfield, K.A.	1989	Salmonella/Mammalian-Microsome Plate Incorporation Mutagenicity Assay (Ames Test). Bayer AG, Report No. C141,501017, Date: 1989-12-22, GLP, unpublished	Yes	LAN
IIA 5.4.1/02	Pagano, G., Cipollaro, M., Corsale, G., Della Morte, R., Esposito, A., Giordano, G.G., Micallo, G., Quinto, I. and Staiano, N.	1988	Comparative Toxicity of Diphenyl, Diphenyl Ether, and Some of their Hydroxy Derivatives. Istituto Nazionale Tumori, Fondazione Pascale, Naples, Italy *Med. Biol. Environ.* 16, pp. 291-297, 1988, Non-GLP, published	No	–

UNPUBLISHED STUDY

PUBLISHED STUDY

title

id_owner

Title_Report No.

title

Journal_title

citation

OPINION-DAR

For the OPINION-DAR table, data extraction from the specified source of the Draft Assessment Report or (Final) Addendum to be performed for these fields:

- **id_dar**: numerical key generated automatically;

- **op_type:** type of source reference, included in EFSA_REFTYPE catalogue; the correct EFSA catalogue terminology is “Report from national authority” (code RT002IZS);

- **id_owner:** the name of data owner;

- **author**: list of authors of the document (i.e. RMS and CoRMS if present, i.e. RMS: Belgium - CoRMS: Lithuania); data to be extracted from the cover page - Vol 1 of DAR (see Figure 17);

- **title:** title of the DAR; data to be extracted from the cover page - Vol 1 of DAR (see Figure 17); if an addendum of the DAR is present, the title to report to be extracted from the cover page – Vol 1 of DAR and to be reported in a uniform way (i.e. Imazalil (Addendum)).

- **adoption_date:** complete date of the adoption of the document ;

- **publication_date:** year of the publication of the document; data to be extracted from the cover page - Vol 1 of DAR (see Figure 17); date to be reported as yyyy.

- **journal_title:** title of the journal or the editor; the title to be reported as entire title

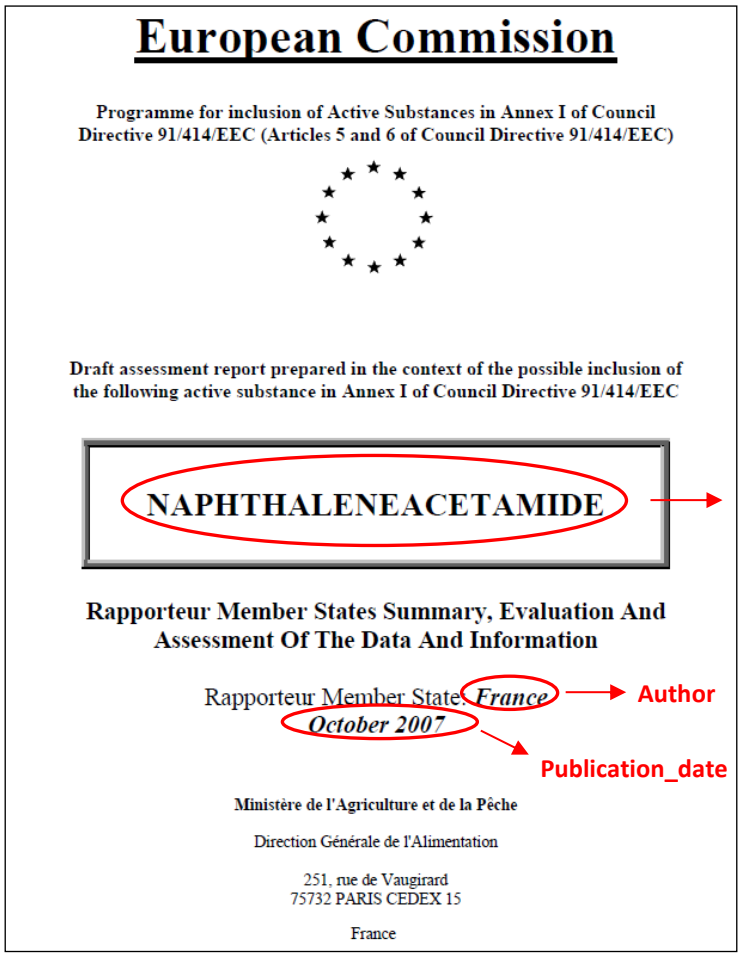
- **doi:** Digital Object Identifier, a permanent character string (a "digital identifier") used to uniquely identify an object such as an electronic document, source the study report or publication, URL or EFSA Journal;

- **international_unique_number:** International Standard Book Number (ISBN) or International Standard Serial Number (ISSN) is a unique numeric commercial book identifier or periodical publications such as magazines (if published report);

- **URL:** uniform resource locator, specific character string that constitutes a reference to a resource in internet;

- **citation:** reference to a book, article, web page, or other published item; it will be reported the entire title of the reference

Figure 17: example for data extraction from the cover page –Vol 1 of DAR



European Commission

Programme for inclusion of Active Substances in Annex I of Council Directive 91/414/EEC (Articles 5 and 6 of Council Directive 91/414/EEC)

Draft assessment report prepared in the context of the possible inclusion of the following active substance in Annex I of Council Directive 91/414/EEC

NAPHTHALENEACETAMIDE → Title

Rapporteur Member States Summary, Evaluation And Assessment Of The Data And Information

Rapporteur Member State: *France* → Author

October 2007 → Publication_date

Ministère de l'Agriculture et de la Pêche

Direction Générale de l'Alimentation

251, rue de Vaugirard
75732 PARIS CEDEX 15

France

OPINION-EFSA and EC DOCUMENT

For the OPINION-EFSA and EC DOCUMENT table, data extraction from the specified source of the EFSA document (e.g. Conclusion, Peer-review) and EC document (e.g. Review Report) to be performed for these fields:

- **id_op**: numerical primary key of EFSA documents. Information to be extracted from "EFSAOutputsPesticides.xls" (second column) provided by EFSA. For documents not present in the catalogue or for EU Commission Reports, a prefix to the ID_OP will be added in order to keep track of new insertion against data already provided by EFSA. The EFSAOutputsPesticides.xls file was integrated into the operational database.

- **op_type:** type of source reference, included in EFSA_REFTYPE catalogue; for EFSA documents the correct EFSA catalogue terminology is "Conclusion on Pesticides Peer Review" (code RT004HAZ); for information retrieved from EU Commission Reports the correct EFSA catalogue terminology is "EU Review Report" (code RT007HAZ);

- **id_owner:** the name of data owner; for EFSA documents the owner is EFSA, for EU Commission Reports the owner is EC;

- **author**: author of the EFSA documents is EFSA; author of the EU Commission Reports is EC

- **title:** title of the document; for EFSA documents the title to be extracted from http://www.efsa.europa.eu/it/publications.htm (see Figure 18); for EU Commission Reports, the title to be extracted from the cover page of the document (see Figure 19);

- **adoption_date:** the date will be extracted from http://www.efsa.europa.eu/it/publications.htm (see Figure 18). Date should be reported as yyyymmdd;

- **publication_date:** for EFSA documents the date will be extracted from http://www.efsa.europa.eu/it/publications.htm (see Figure 18) for EU Commission Reports, the date will be extracted from the cover page of the document. Date should be reported as yyyymmdd

- **journal_title:** title of the journal is EFSA Journal;

- **doi:** Digital Object Identifier, a permanent character string (a "digital identifier") used to uniquely identify an object such as an electronic document, source the study report or publication, URL or EFSA Journal. The doi will be extracted from http://www.efsa.europa.eu/it/publications.htm (see Figure 18);

- **international_unique_number:** International Standard Book Number (ISBN) or International Standard Serial Number (ISSN) is a unique numeric commercial book identifier or periodical publications such as magazines (if published report); for EFSA Journal the ISSN is 1831 – 4732.

- **URL:** uniform resource locator, specific character string that constitutes a reference to a resource in internet. E.g.: http://www.efsa.europa.eu/it/efsajournal/pub/2019.htm;

- **citation:** reference to a book, article, web page, or other published item; information will be extracted from http://www.efsa.europa.eu/it/publications.htm (see Figure 18);

Figure 18: example for data extraction from http://www.efsa.europa.eu/it/publications.htm

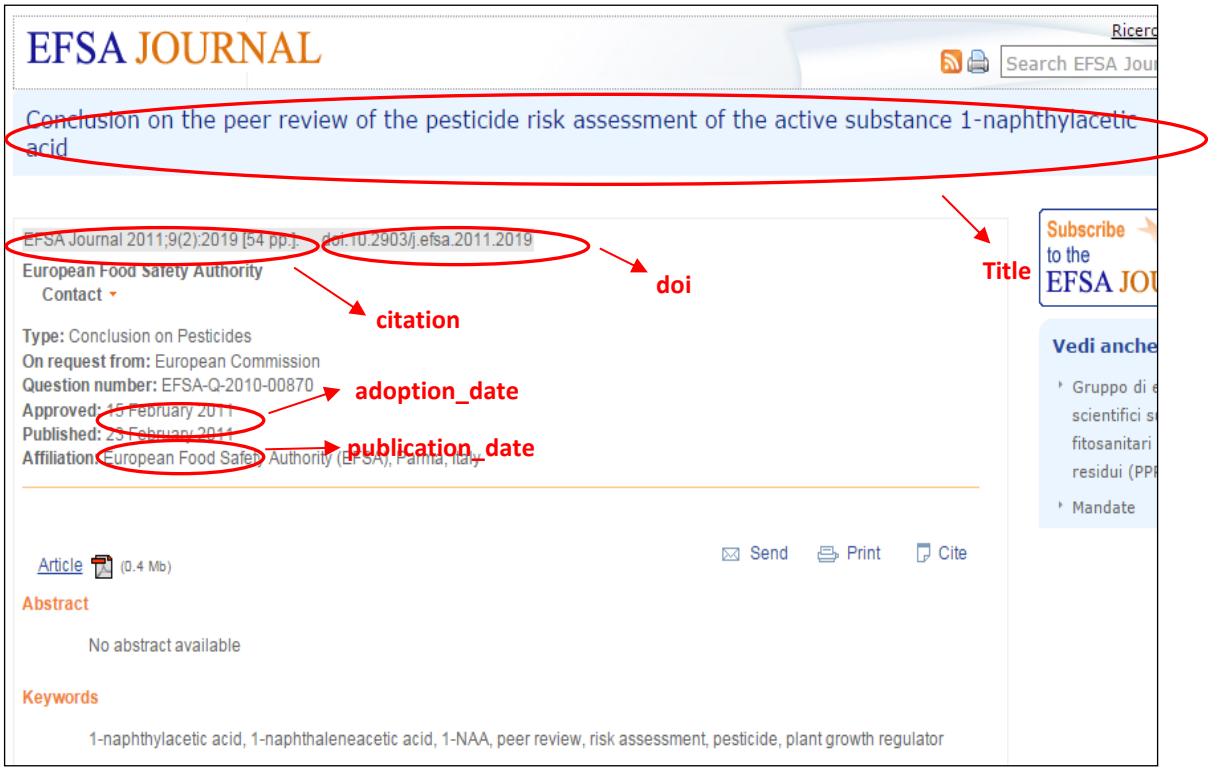
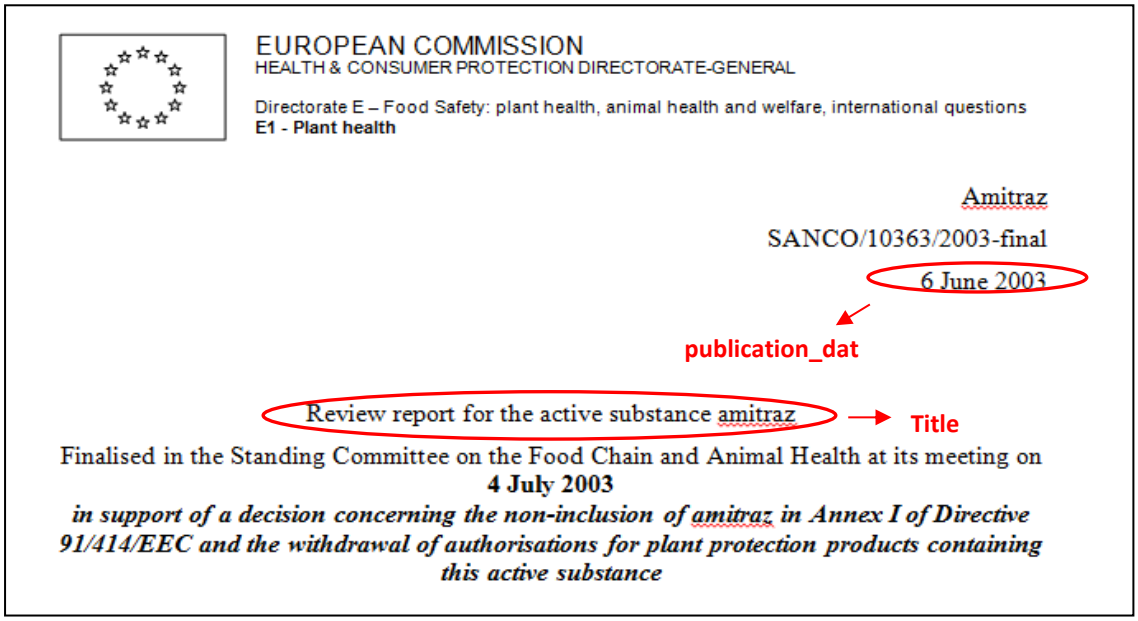


Figure 19*:* example for data extraction from European Commission



EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate E – Food Safety: plant health, animal health and welfare, international questions
E1 - Plant health

Amitraz

SANCO/10363/2003-final

6 June 2003

publication_dat

Review report for the active substance amitraz → Title

Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on **4 July 2003**

in support of a decision concerning the non-inclusion of amitraz in Annex I of Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing this active substance

SUBSTANCE-COMPONENT

For the SUBSTANCE_COMPONENT table, data extraction for the characteristics of active substances and metabolites tested to be performed for these fields:

- **id-sub-com:** numerical key generated automatically;

- **id_sub:** numerical primary key of the substance data corresponding to active substance name as reported in the dossier list of Annex 2 of this call. For new substances, a prefix to the ID_SUB to be added in order to keep track of new insertion against data already provided by EFSA;

- **sub_name:** active substance name as reported in the dossier list of Annex 2 of this call;

- **id_com:** numerical primary key of the component. For new substances, a prefix to the ID_COM to be added in order to keep track of new insertion against data already provided by EFSA;

- **sub_type:** description of components comprising the substance (mixture or formulation, single chemical entity, polymer) data extracted from EFSA conclusion or European Commission (EC) Review Reports in the active substance description chapter;

- **id_qualifier:** alphanumeric code to define the composition of the substance in terms of components and allows the linkage of metabolites, or impurities… to active substances, included in EFSA_QUALIFIER catalogue. Data extracted from EFSA conclusion or European Commission (EC) Review Reports in the active substance description chapter.
Codes to be inserted as follow:

1. QU07A: component is identical to the substance
2. QU08A: component is part of a group assessment
3. QU09A: component is part of a group but not included in the group assessment
4. QU10A: component is the active ingredient of the mixture or formulation
5. QU11A: component is an impurity in the mixture or formulation
6. QU14A: component is part of a mixture or formulation
7. QU15A: component maybe part of a mixture or formulation
8. QU17A: component is a metabolite of the substance

- **comp_value:** numeric value (in percentage) of the composition applicable for formulations; data extracted from List of End Points, Volume 1-Appendix 3, “Identity, Physical and Chemical Properties, Details of Uses, Further Information” or Appendix A from EFSA conclusion;

- **com_name:** chemical name test Substance / ISO common name. For active substance, information to be extracted from Section B.1.1.3 “Common name or ISO-accepted, and synonyms” (annex IIA 1.3) Vol 1 of

DAR (see Figure) or Appendix A from EFSA conclusion. For active substances the value “com_name” is the same one of “sub_name”.
For metabolites, information to be extracted from Appendix B and/or C (used compound code(s)) of EFSA conclusion. (see Figure);

- **com_type:** OECD substance description (element, inorganic, metal, not applicable, organic, organometallic, other); according the following:

1. inorganic: a compound that does not contain hydrocarbon groups

2. metal: The following elements have been considered metals based on their position in the periodic table:
- alkaline elements (first main group) with the exception of H;
- alkaline earth elements (second main group);
- transition elements (or d-group elements);
- rare earth elements (or f-group elements), subdivided into the lanthanide series (including La) and the actinide series (including Ac);
- Some p-group elements, namely: Al, Ga, In, Sn, Tl, Pb and Bi

3. organic: a compound containing hydrocarbon groups

4. organometallic: consisting of a metal combined with an organic radical, used particularly for a compound in which the metal is linked directly to a carbon atom

5. other than point 1, 2, 3 and 4

- **com_rns_efsa:** EFSA PARAM code to allow linkage with existing EFSA datasets, referring to substance name or its metabolite name. If the PARAM code cannot be matched for a substance or a component it should be reported the code RF-XXXX-XXX-XXX;

- **com_ecSubInventEntryRef:** the EC reference number as defined by ESIS (European Substances Information System). Information to be retrieved from the EC reference list by ECHA (http://echa.europa.eu/documents/10162/13643/substance_id_en.pdf). For older documents this will be retrieved from ECHA/IUCLID;

- **com_casNumber:** Chemical Abstracts Service number. Information to be extracted from Section B.1.1.6 “CAS, EC and CIPAC numbers” (annex IIA 1.6) Vol 1 of DAR (see **Figure**20) or Appendix A from EFSA conclusion; if the information is not provided in the DAR/EFSA/EU report, information to be extracted from PubChem (if the CAS number exists);

- **iupacName:** International Union of Pure and Applied Chemistry name; data to be extracted from Section B.1.1.4 “Chemical Name” (annex IIA 1.4) Vol 1 of DAR or Appendix A from EFSA conclusion (see Figure20); if the information is not provided in the DAR/EFSA/EU report, information to be extracted from PubChem or ChemSketch.

- **molecularFormula:** molecular formula using format specified in the EC reference list. Information to be extracted from Section B.1.1.7 "Molecular and structural formulae, molecular mass"(annex IIA, 1.7) Vol 1 of DAR or Appendix A from EFSA conclusion (see Figure); if the information is not provided in the DAR/EFSA/EU report, information to be extracted from PubChem.

- **com_structureShown:** indication on what type of structure (either SMILES or InChI). It should always represent the substance (com_name) tested in the genotoxicity study. There are five alternatives: compound, monomer of polymer, no structure, representative compound and representative isomer;

- **smilesNotation:** simplified molecular input line entry specification for the substance (com_name) tested, generated according to the structural formula as drawn in PubChem or ChemSketch or ChemDraw.
If CAS number, IUPAC name or common name are available, information to be extracted from PubChem (https://pubchem.ncbi.nlm.nih.gov/). Otherwise information to be extracted from ChemSchetch or ChemDraw;

- **smilesNotationSource:** source of the smiles notation. It will be retrieved from PubChem (PubChem isomeric SMILES or PubChem canonical SMILES) or ChemSketch or ChemDraw (Other);

- **inchi:** Internation Chemical Identifier. If CAS number, IUPAC name or common name are available, information to be extracted from PubChem (https://pubchem.ncbi.nlm.nih.gov/). Otherwise information to be extracted from ChemSchetch or ChemExper Chemical Directory database (http://www.chemexper.com/);

- **inchi_notation Source:** source of the InChi notation. to be retrieved from PubChem (PubChem InChI) or ChemSketch or ChemExper Chemical Directory database (Other);

COM_SYNONYMS

- **type**: the type of synonym being reported (CAS, name, EC enzyme number, trade name or other component classification type). Default entry: Name.

- **description:** code/trivial name; information to be extracted from the appendix B and/or C -Used Compound codes from EFSA conclusions (see Figure), when a EFSA conclusion is not available, the code/trivial name to be extracted from the draft assessment report. All code/trivial name reported in the appendix B and/or C of the EFSA conclusion have to be included.

Figure 20: example of active substances

B.1. IDENTITY

B.1.1. IDENTITY OF THE ACTIVE SUBSTANCE (ANNEX IIA 1)

B.1.1.3. Common name proposed or iso accepted, and synonyms

1-naphthylacetamide (1-NAD) → Com_Name

B.1.1.4. Chemical name (IUPAC and CA nomenclature)

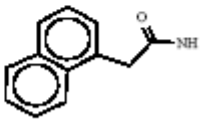
IUPAC: 2-(1-naphthyl)acetamide → iupacName
CA: 1-Naphthaleneacetamide

B.1.1.6. CAS, EEC and CIPAC numbers (if available)

CAS: 86-86-2 → Com_casNumber
EINECS: 201-704-2
CIPAC: 282

B.1.1.7. Molecular and structural formula, molecular mass

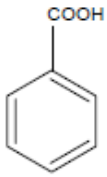
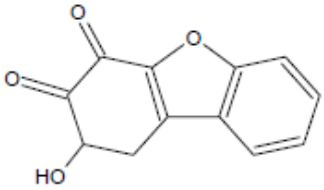
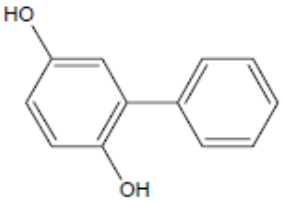
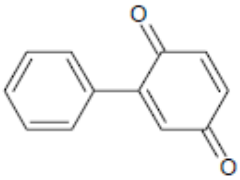
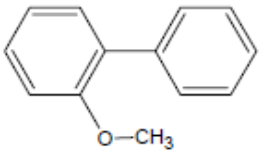
Formula: $C_{12}H_{11}NO$ → molecularFormula
Structural Formula:



Molecular Mass: 185.2

Figure 21: example for metabolites

APPENDIX C – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
Benzoic acid Code_Trival_name	Benzoic acid Com_name	
Diketohydroxy-compound	2-Hydroxy-1,2-dihydrodibenzo[b,d]furan-3,4-dione	
Phenylhydroquinone PHQ	2-Phenylhydroquinone 2,5-Dihydroxybiphenyl	
Phenylbenzoquinone PBQ	–	
2-Methoxybiphenyl 2-MBP	–	

Moreover, data regarding the majority fields for SUBSTANCE_COMPONENT table, will be also available in the List of End Points, Volume 1-Appendix 3, "Identity, Physical and Chemical Properties, Details of Uses, Further Information", Identity (Annex IIA, point 1) in the DAR or Appendix A from EFSA conclusion.

Furthermore, data regarding all fields indicated above for SUBSTANCE_COMPONENT for all the metabolites listed in the Appendix B of the EFSA conclusions (even ones without genotoxicity study), have to be scrutinized and inserted in the database.

1.4. Data entry (Annex 3 database)

- A structured database were provided according to the general scheme and data models as presented in the kickoff meeting of 17 Janury 2015. Different updates and upgrades occurred during the work flow: additional fields were inserted (e.g. mouseLymphTest.); some conceptual data schemes were completely rebuilt (relationship between Opinion and Genotox; firstly a onetoone relation were created and then onetomany relation; the Opinion Table at the beginning of the project contained only information on study reports, during the project the opinion Table was divided into three different tables with different CODES). The Component synonym Table were added in the middle of the project; a continuous update of the catalogue versions were performed during the project.

- Every update or upgrade, depending from a decision taken into a teleconference, mail or internal meeting was shared with the group and tested in the database.

- In order to facilitate the insertion and check of the data, different database SOPs were developed: predefined aggregations between variables were created so that, once a variable was chosen from a menu, the subsequent related menu excluded values that were of no consistency.

1.5. Data quality evaluation – Data Check

- Most of the fields to be implemented in combo boxes. This means no possibility to add additional values to what is already inserted in the combo boxes. For all fields with enumeration or a catalogue a drop down list to be provided

- Where textual values are expected, consistency value operations to be performed at the end of the data insertion.

- Metadata to be implemented to keep track of the operator and the date/time of the entries.

- Three single operators have been selected for the data entry procedures. The operators were chosen according to their experiences in previous data managing activities, as can be recognized from their CV. Each operator to work on his own database. Then to switch the databases within the operators: Operator A to check database B; Operator B to check database C … Where inconsistencies were found, an immediate check on the origin of the data to be performed. Wrong entries to be corrected immediately and a record to be added to the Register of amendments (manual insertion). After this phase, a computer-based automatic comparison of the data inserted before and after the data check to be performed (ICPS Automatic Register of amendments).

The register of the amendments to keep tracks of any error or problem belonging from the data entry control check, and in particular:

- The relevant study
- The part in which the error was found
- The wrong entry and the specific correction
- The operators involved
- The data of the original entry and of its correction

This register to be used to quantify the errors detected in order to assess the efficacy of the adopted QA/QC procedures.

Appendix K – Register of Amendments

Submission1	Submission2	Corrections	Numb.Rows	Numb.Columns	Numb.CompiledFields	Error%	Date
07/07/2015	28/08/2015	30	42	88	3696	0.8%	28/08/2015
28/08/2015	09/09/2015	42	41	88	3608	1.2%	09/09/2015
09/09/2015	01/10/2015	1818	876	88	77088	2.4%	01/10/2015
01/10/2015	10/12/2015	3384	1433	88	126104	2.7%	10/12/2015
10/12/2015	26/01/2016	515	2674	88	235312	0.2%	26/01/2016
26/01/2016	01/03/2016	4871	3578	88	314864	1.5%	01/03/2016
01/03/2016	31/03/2016	31002	5603	88	493064	6.3%	31/03/2016
31/03/2016	12/05/2016	38197	6948	88	611424	6.2%	12/05/2016
12/05/2016	27/06/2016	1227	9773	88	860024	0.1%	27/06/2016
27/06/2016	14/09/2016	4844	13991	88	1231208	0.4%	14/09/2016
19/09/2016	16/12/2016	150099	23805	88	2094840	7.2%	16/12/2016
In addition to the 19/09/2016 Submission there are 2106 new records