Literature Review Report
Scientific peer-reviewed open literature for the endocrine disrupting properties of glyphosate

Search period Nov 2016 and Jul 2019

Data Requirements Following EFSA / EFSA-ECHA Guidance Documents

"*Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009*"

and

Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009

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Version history[1]

Date	Data points containing amendments or additions and brief description	Document identifier and version number

[1] It is suggested that applicants adopt a similar approach to showing revisions and version history as outlined in SANCO/10180/2013, Chapter 4 “How to revise an Assessment Report”

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1. SUMMARY

A literature search for glyphosate was carried out according to the requirements stated in the EFSA-ECHA Guidance document "Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009" from June 5, 2019.

All steps in this literature evaluation are based on the EFSA Guidance "Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009", EFSA Journal 2011;9(2):2092.

The objective of this Endocrine Disruptor (ED)-specific literature search was to ascertain whether any scientific peer-reviewed open literature would address the potential endocrine-disrupting properties of glyphosate.

As the previous endocrine disruptor literature search, already evaluated at EU level, covers the publication period between January 2014 and October 2016 (see **Annex A-01** in this document), a new literature search has been conducted in order to extend and update the existing search. This new ED literature search covers the publication period between November 2016 and July 2019.

The literature search has been conducted accessing 11 bibliographic databases: AGRICOLA, BIOSIS, CABA, CAPLUS, EMBASE, ESBIOBASE, MEDLINE, TOXCENTER, FSTA, PQSCITECH, and SCISEARCH via the service provider STN.

After automatic removal of the duplicates, 5036 hits in total were retrieved from the databases.. Applying the search filters for the two technical sections (Ecotoxicology and Toxicology) reduced the number of the hits retrieved to 4692. For these hits a second review and removal of duplicates was performed resulting in 4024 unique references.

From the total of 4024 unique references, 1446 publications could be excluded during the assessment of title and abstract as they were related to topics such as chemical synthesis, efficacy or analytical methods and thus deemed not relevant. Additionally, 2194 publications were considered non-relevant for the evaluation of potential endocrine disrupting properties of glyphosate following assessment of title and abstract as they were caused by exposure to irrelevant compounds, related to acute toxic effects or to non-relevant dossier sections. In total 3640 publications were excluded for the assessment based on their title and abstract.

As a result, 384 publications have been considered relevant for further review in the evaluation of the potential endocrine disrupting properties of glyphosate. According to the work-flow detailed in the EFSA Guidance "Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009" all of these publications were evaluated based on full text information. For the 347 publications considered not relevant following review of the full text, a justification for this assessment has been provided in Table 11 of this document (see below).

The remaining 37 publications were assessed as relevant for the ED assessment following evaluation of their full texts. These relevant publications were subsequently supplemented by 10 publications identified as relevant for ED assessment in the literature assessment according to EFSA Guidance "Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009", EFSA Journal 2011;9(2):2092 (s. Literature Review Report; 108689-CA9-1; KCA 9/01; Anonymous, 2020).

In addition, as required in the EFSA Journal 2011;9(2):2092 "Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009" all

47 publications considered relevant after full text evaluation have been classified in accordance with point 5.4.1 of the guidance document.(Table 12 and Table 13).

For the 17 articles considered to be **relevant AND reliable** and which provided data for establishing / refining risk assessment parameters (EFSA Guidance Document Point 5.4.1 A, for relevance) a summary has been compiled and included in the weight of evidence assessment.

For the 30 articles relevant to the data requirement but in the opinion of the applicant provided only supplementary information that does not alter existing risk assessments justification has been provided (EFSA Guidance Document Point 5.4.1 B) and included in Table 12 and Table 13 of this document.

2. Introduction

A bibliographic literature review has been carried out for the potential endocrine disruptor properties of glyphosate. The search has been conducted via the online service provider STN (www.stn-international.de) which provides access to a broad range of databases and to published research, journal literature, patents, structures, sequences, properties, and other data.

To offer a reliable literature search covering the requirements of the EFSA Guidance Document, 11 databases have been used: AGRICOLA, BIOSIS, CABA, CAPLUS, EMBASE, ESBIOBASE, MEDLINE, TOXCENTER, FSTA, PQSCITECH, and SCISEARCH.

As the number of summary records returned by a “single concept search” was extremely large, a focused search for grouped data requirements have been performed (a combination of a substance search and “search filters” defined for the two relevant sections – ecotoxicology, and toxicology).

Comments, dissertations, editorials, meetings reports, news, patents and press releases have been excluded from the literature search.

The search was conducted on 10 August 2019 and covers the publication period between **November 2016 and July 2019.**

Regarding details of the bibliographic databases used in the literature searches, please refer to the table below.

2.1 Bibliographic databases used in the literature review

Table 1: Bibliographic databases used in the literature review

Data requirement(s) captured in the search	**Details of the search**			
	1. AGRICOLA	**2. BIOSIS**	**3. CABA**	**4. CAPLUS**
Justification for choosing the source:	Provides literature from agriculture and related fields, e.g. biology, biotechnology, botany, ecology etc.	Provides the most comprehensive and largest life science database for literature, e.g. biosciences, biomedicine etc.	Provides literature from agriculture and related sciences, e.g. biotechnology, forestry, veterinary medicine etc.	Provides literature from chemistry and related fields, e.g. biochemistry chemical engineering etc.
Number of records in the database at the time of search:	> 6.1 million (05/2018)	> 27.8 million (04/2019)	> 8.9 million (05/2018)	> 48.7 million (11/2017)
Database update:	Monthly	Weekly	Weekly	Daily updates with biblio. data; weekly updates with indexing data
Date of the search:	10 Aug 2019	10 Aug 2019	10 Aug 2019	10 Aug 2019
Database covers records:	1970-present	1926-present	1973-present	1907-present and more than 180,00 pre-1907
Date of the latest database update:	5 Aug 2019	14 Aug 2019	14 Aug 2019	18 Aug 2019
Language limit:	No	No	No	No
Document types <u>excluded</u> that are not "scientific peer-reviewed open literature":	COMMENT? or DISSERTATION or EDITORIAL or MEETING? or NEWS? or PATENT or PRESS RELEASE	COMMENT? or DISSERTATION or EDITORIAL or MEETING? or NEWS? or PATENT or PRESS RELEASE	COMMENT? or DISSERTATION or EDITORIAL or MEETING? or NEWS? or PATENT or PRESS RELEASE	COMMENT? or DISSERTATION or EDITORIAL or MEETING? or NEWS? or PATENT or PRESS RELEASE
Search strategy:	Details are listed in below.			
Total number of records retrieved:	1284	1445	1702	1527

Table 1 (contd.): Bibliographic databases used in the literature review

Data requirement(s) captured in the search	**Details of the search**		
	5. MEDLINE	**6. EMBASE**	**7. TOXCENTER**
Justification for choosing the source:	Provides literature from every area of medicine.	Provides literature from biomedicinal and pharmaceutical fields, e.g. bioscience, biochemistry, human medicine, forensic science paediatrics, pharmacy, pharmacology, drug therapy, psychiatry, public health, biomedical engineering, environmental science.	Provides literature on pharmacological, biochemical, physiological, and toxicological effects of drugs and other chemicals.
Number of records in the database at the time of search:	> 28.7 million (08/2018)	> 34.3 million (08/2018)	> 13.6 million (08/2018)
Database update:	Six times each week, with an annual reload	Daily	Weekly
Date of the search:	10 Aug 2019	10 Aug 2019	10 Aug 2019
Database covers records:	1946-present	1974-present	1907-present
Date of the latest database update:	18 Aug 2019	16 Aug 2019	12 Aug 2019
Language limit:	No	No	No
Document types excluded that are not "scientific peer-reviewed open literature":	COMMENT? or DISSERTATION or EDITORIAL or MEETING? or NEWS? or PATENT or PRESS RELEASE	COMMENT? or DISSERTATION or EDITORIAL or MEETING? or NEWS? or PATENT or PRESS RELEASE	COMMENT? or DISSERTATION or EDITORIAL or MEETING? or NEWS? or PATENT or PRESS RELEASE
Search strategy:	Details are listed below.		
Total number of records retrieved:	894	738	1886

Table 1 (contd.): Bibliographic databases used in the literature review

Data requirement(s) captured in the search	Details of the search			
	8. FSTA	**9. PQSCITECH**	**10. ESBIOBASE**	**11. SCISEARCH**
Justification for choosing the source:	Provides literature on scientific and technological aspects of the processing and manufacture of human food products, e.g. biotechnology, hygiene and toxicology, engineering etc.	Provides a valuable and huge resource of literature (merge of 25 STN databases) from all science areas and technology; from engineering to lifescience.	Provides comprehensive literature c the entire spectrum of biological an biosciences research, e.g. microbiology, biotechnology, ecological & environmental science genetics, plant and crop science, toxicology and many more.	Provides one of the largest multidisciplinary scientific literatur databases covering a broad field of sciences, technology, and biomedicine.
Number of records in the database at the time of search:	> 1.4 million (07/2018)	> 32 million (07/2017);	> 7.6 million (07/2018)	> 45 million (08/2018)
Database update:	Weekly	Monthly	Weekly	Weekly
Date of the search:	10 Aug 2019	10 Aug 2019	10 Aug 2019	10 Aug 2019
Database covers records:	1969-present	1962-present	1994-present	1974-present
Date of the latest database update:	15 Aug 2019	23 Jul 2019	15 Aug 2019	12 Aug 2019
Language limit:	No	No	No	No
Document types excluded that are not "scientific peer-reviewed open literature":	COMMENT? or DISSERTATION or EDITORIAL or MEETING? or NEWS? or PATENT or PRESS RELEASE	COMMENT? or DISSERTATION or EDITORIAL or MEETING? or NEWS? or PATENT or PRESS RELEASE	COMMENT? or DISSERTATION or EDITORIAL or MEETING? or NEWS? or PATENT or PRESS RELEASE	COMMENT? or DISSERTATION or EDITORIAL or MEETING? or NEWS? or PATENT or PRESS RELEASE
Search strategy:	Details are listed in below.			
Total number of records retrieved:	105	610	988	2067

Table 2: Total number of hits retrieved in the search

After removing duplicates within the databases [A)]	5036
After applying search filters [B)]	4692
Manual removal of duplicates	668
Number of unique publications identified for assessment	4024

[A)] Please note that the STN databases criteria for removing duplicates are very "gentle" in order not to lose valuable data and thus it is necessary to also remove duplicates manually (manual removal of duplicates has been performed in a second round and the final number of hits is reported below).

[B)] Search filters were applied for the two technical sections (toxicology and ecotoxicology). See under Point 2.3.

2.2 Input parameters for literature search

Table 3: Input parameters - Glyphosate

Substance name	Glyphosate (+ salts) Salts: isopropylamine, potassium, ammonium, methylmethanamine
IUPAC / CA name	2-(phosphonomethylamino)acetic acid
CAS number(s)	1071-83-6 Salts: 38641-94-0, 70901-12-1, 39600-42-5, 69200-57-3, 34494-04-7, 114370-14-8, 40465-66-5, 69254-40-6

2.3 Endpoint specific search terms

The approach used for the search was the "focused search" for grouped data requirements, which combines the active substance keywords search in combination with the search filters used in the technical sections (see the following tables below for details).

Table 4: Keywords used for the active substance glyphosate

Gly1: Glyphosate	glyphosat? OR glifosat? OR glyfosat? OR N phosphonomethyl glycine OR phosphonomethyl amino acetic acid OR 1071-83-6 OR 38641-94-0 OR 70901-12-1 OR 39600-42-5 OR 69200-57-3 OR 34494-04-7 OR 114370-14-8 OR 40465-66-5 OR 69254-40-6

Table 5a: Search filters related to the technical section toxicology

Toxicology Gly1 AND the following search filters
TOXI? OR HAZARD OR ADVERSE OR HEALTH OR EFFECT OR NOAEL OR NOEL OR LOAEL OR LOEL OR BMD OR IN VIVO OR IN VITRO OR ACUTE OR SUBACUTE OR SUBCHRONIC OR CHRONIC OR ORAL OR DERMAL OR GAVAGE OR DIET? OR INHAL? OR RAT OR DOG OR RABBIT OR GUINEA PIG OR MOUSE OR MICE OR HAMSTER OR METABOLISM OR METABOLITE OR METABOLIC OR DISTRIBUTION OR ADSORPTION OR EXCRETION OR ELIMINATION OR KINETIC OR PBPK OR CYP OR CYTOCHROME OR ENZYM? OR GEN? OR MUTA? OR CHROMOS? OR CLASTOGEN? OR DNA OR CARCINO? OR CANCER? OR IMMUN? OR NEUR? OR BEHAV? OR ENDOCRIN? OR HORMON? OR REPRODUCT? OR DEVELOPMENT? OR MALFORMATION? OR ANOMAL? OR FERTIL? OR FOET? OR FETO? OR FETUS OR MATERN? OR PREGNAN? OR EMBRYO? OR EPIDEM? OR MEDICAL? OR POISON? OR ESTROGEN? OR ANDROGEN? OR STEROIDOGEN? OR ESTROGEN RECEPTOR? OR ANDROGEN RECEPTOR? OR THYROID OR RECEPTOR? OR AR BIND? OR ER BIND? OR THYROID OR STIMULATING HORMONE OR TSH OR LUTEINIZING HORMONE OR LH(5A)HORM OR ONE OR FOLLICULE STIMULATING HORMONE OR FSH OR ESTRADIOL? OR TESTOSTERONE? OR ACCESSORY GLAND? OR GENITAL? OR COAGULATING OR GLAND? OR PROSTATE? OR TESTIS? OR MOTILITY? OR MAMMARY GLAND? OR CERVIX? OR UTERUS? OR OVARY? OR ANOGENITAL? OR NIPPLE RETENTION? OR PREPUTIAL? OR VAGINA? OR ESTRUS? OR FOLLICULAR? OR ENDOCRINE? OR ENDOCRINE DISRUPT? OR DEVELOPMENTAL? OR REPROT? OR SEXUAL MATURATION? OR OECD 407 OR OECD 408 OR OECD 414 OR OECD 415 OR OECD 421 OR OECD 422 OR OECD 426 OR OECD 451 OR OECD 453 OR OECD 416 OR OECD 443 OR OPPTS 890.1500# OR OPPTS OR 890.1450#

Table 5b: Search filters related to the technical section ecotoxicology

Ecotoxicology Gly1 AND the following search filters
TOXI? OR HAZARD OR ADVERSE OR POISON OR EFFECT? OR IN VIVO OR IN VITRO OR ECOTOXICOLOG? OR AQUATIC OR WILDLIFE OR NON TARGET OR NONTARGET OR POPULATION OR MODEL OR MODE OF ACTION OR ENVIRONMENT OR ENDOCRINE OR DISRUPT? OR ENDOCRIN? OR ABNORMAL? OR SEXUAL OR DEVELOPMENT? OR ADVERS? OR REPRODUCT? OR MALFORMATION? OR ANOMAL? OR FERTIL? OR FECUND? OR INHIBITION OR FSTRA OR BIRD OR MALLARD OR DUCK OR QUAIL OR BOBWHITE OR ANAS? OR COLINUS? OR AVIAN OR VERTEBRAT? OR MAMMAL? OR RAT OR MOUSE OR MICE OR RABBIT OR HARE OR AQUATIC OR FISH OR FATHEAD OR MINNOW OR MEDAKA OR ZEBRAFISH OR STICKLEBACK OR RAINBOW TROUT OR PIMEPHALES PROMELAS OR ORYZIAS LATIPES OR DANIO RERIO OR GASTEROSTEUS ACULEATUS OR ONCORHYNCHUS MYKISS OR SNAIL OR POTAMOPYRGUS ANTIPODARUM OR AMPHIB? OR REPTILE OR XENOPUS OR TADPOLE OR AMA OR LAGDA OR HORMONE OR VITELLOGENIN OR SPIGGIN OR SEX CHARACTERISTICS OR SEX RATIO OR SEX SHIFT OR INTERSEX OR EGG PRODUCTION OR SPAWNING OR GONAD OR THYROID OR HISTOPATHOLOGY OR HISTOLOGY OR AROMATASE OR ANDROGEN OR ESTROGEN OR STEROID? OR ASSAY OR EARLY LIFE STAGE OR LIFE CYCLE OR METAMORPHOSIS OR LARVAL GROWTH OR MALE INDUCTION OR OECD 148 OR OECD 206 OR OECD 210 OR OECD 221 OR OECD 229 OR OECD 230 OR OECD 231 OR OECD 234 OR OECD 236 OR OECD 240 OR OECD 241 OR OECD 225 OR OECD 219 OR OECD 218 OR OECD 242 OR OCSPP 890.2300 OR OCSPP 890.2100 OR EDSP OR SCREENING OR INVERTEBRAT? OR DAPHNI? OR CERIODAPHNI? OR CHIRON? OR SEDIMENT DWELL? OR COPEPOD OR LUMBRICULUS OR ENCHYTREID OR MARIN? OR ESTUARINE OR CRUSTA? OR GASTROPOD? OR MOLLUSK OR BEE? OR API? OR BUMBLE? OR ARTHROPOD? TYPHLODROMUS OR APHIDIUS OR INSECT? OR WORM? OR ?WORM OR EISENIA OR COLLEMBOL? OR MACRO OR ORGANISM OR MACROORGANISM OR FOLSOMIA OR SPRINGTAIL OR MITE? OR HYPOASPIS OR MOLLUSC?

2.4 Relevance assessment

Publicly available scientific literature data were evaluated based upon the new ED identification criteria (Commission Regulation (EU) 2018/605), applicable for plant protection products from 10 November 2018 onwards, and in accordance with the provisions of the ECHA/EFSA "Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009" (EFSA Journal 2018;16(6):5311), Annex F.

According to the European scientific criteria for the determination of endocrine disrupting properties for plant protection products (Commission Regulation (EU) 2018/605), an active substance shall be considered as having endocrine disrupting properties that may cause adverse effects in humans/on non-target organisms if it is a substance that meets all of the following criteria:

(1) it shows an adverse effect in an intact organism or its progeny/non-target organisms;
(2) it has an endocrine mode of action, i.e. it alters the function(s) of the endocrine system;
(3) the adverse effect is a consequence of the endocrine mode of action.

For the literature evaluation concerning endocrine disrupting properties, the publicly available scientific literature was screened in detail for relevant toxicological and ecotoxicological information on potential interaction of the substance with hormonal pathways (Estrogen, Androgen, Thyroid and Steroidogenesis - EATS modalities) and on the adverse effects caused by the exposure to the substance in human/on non-target organisms.

Therefore, data were evaluated following the provisions of the ED Guidance. In the ecotoxicological sections, the ED literature evaluation is focused on non-target aquatic organisms, i.e. fish, reptiles and amphibians, since according to the ED Guidance, information on birds would only be considered in the ED assessment strategy once test methods investigating endocrine specific endpoints are available. However, for the sake of completeness with regard to non-target organisms, the available data on birds have been included, as well as data on invertebrates.

Publications were identified as relevant if endocrine-related (EATS-related) parameters (adversity and/or endocrine activity) were investigated.. This comprises E-, A-, T- or S-related effects in any of the *in vivo* toxicity studies conducted with the substance of concern. Beside this, publications of relevance include toxicity studies investigating relevant parameters for the assessment of potential effects on development and reproduction. Furthermore literature data were considered relevant when investigating effects on reproduction, growth/development, and other relevant effects, including 1

Table 6: Key relevance criteria for the detailed assessment of full-text documents – <u>toxicology only</u>

Criteria for "relevance" - toxicology	
***In vivo* toxicology studies**	***In vitro* toxicology studies**
Exposure to glyphosate acid or its salts only	Exposure to glyphosate acid or its salts only
Use of relevant route of administration	Use of relevant test system
Use of relevant test species	Test concentrations in physiologically acceptable range (<1 mM)
Adequate description of study results	Adequate description of study results

Exposure studies	**Epidemiology studies**
Exposure to glyphosate containing formulations	Exposure to glyphosate containing formulations
Adequate description of exposure circumstances	Adequate description of exposure circumstances
Adequate description of sampling	Adequate description of study population
Adequate description of method of analysis	Adequate description of epidemiological method followed
Overall assessment: Relevant for risk assessment / Relevance uncertain / Not relevant	
Relevance - covering the extent to which data and/or tests are appropriate for a particular hazard identification or risk characterization. Adequacy - defining the usefulness of data for risk assessment purposes. When there is more than one set of data for each effect, the greatest weight is attached to the most reliable and relevant.	

2.5 Reliability assessment

For articles which appeared to be relevant and provided data for establishing / refining risk assessment parameters (EFSA GD Point 5.4.1 A) a reliability assessment has been performed. The reliability criteria for each technical section are summarized in the following tables.

Table 7: Ecotoxicology: Reliability criteria for the detailed assessment of full-text documents

Reliability criteria - ecotoxicology
1. For guideline-compliant studies (GLP studies): OECD, OPPTS, ISO, and others. The validity/quality criteria listed in the corresponding guidelines met.
2. Not previous exposure to other chemicals is documented (where relevant).
3. For aquatic studies, the test substance is dissolved in water or where a carrier is required, it is appropriate (non-toxic) and a carrier control / positive control is considered in the test design.
4. Glyphosate or its metabolites (AMPA and HMPA), is sufficiently documented, and reported (i.e. purity, source, content, storage conditions)
5. For tests including vertebrates, compliance of the batches used in toxicity studies compared to the technical specification
6. Species used in the experimental clearly reported, including source, experimental conditions (where relevant): strain, adequate age/life stage, body weight, acclimatization, temperature, pH, oxygen (dissolved oxygen for aquatic tests) content, housing, light conditions, humidity (terrestrial species) incubation conditions, feeding.
7. The validity criteria from relevant test guidelines can be extrapolated across different species but not necessarily across different test designs. If different, then the nature of the difference and impact should ideally be discussed.
8. Only glyphosate or its metabolites is the test substance (excluding mixture), and information on application of the test substance is described.
9. The endpoint measured can be considered a consequence of glyphosate (or a glyphosate metabolite).
10. Study design / test system is well described, including when relevant: concentration in exposure media (dose rates, volume applied, etc.), dilution/mixture of test item (solvent, vehicle) where relevant.
11. Analytical verifications performed in test media (concentration)/ collected samples, stability of the test substance in test medium should be documented
12. An endpoint can be derived. Findings deliver a regulatory endpoint, and/or is useful as supporting information
13. The test has been tested in several dose levels (at least 3) including a positive/negative control where relevant.
14. Suitable exposure throughout the whole exposure period was demonstrated and reported.

Reliability criteria - ecotoxicology
15. A clear concentration response relationship is reported – in studies where the dose response test design is employed.
16. There is included a sufficient number of animals per group to facilitate statistical analysis: mortality in control groups reported, observations/findings in positive/negative control clearly reported (where relevant).
17. Assessment of the statistical power of the assay is possible with reported data.
18. If statistical methodology was applied for the findings reported, then the data analysis applied is clearly reported (e.g., checking the plots and confidence intervals)
19. Description of the observations (including time-points), examinations, and analyses performed, with (where relevant) dissections being well documented.
20. For terrestrial ecotoxicology studies in the laboratory or the field, the substrates used should be adequately described e.g. nature of substrate i.e. species of leaf or soil type.
20.1. Field locations relevant/comparable to European conditions. Soils not completely matching the OECD criteria but from Europe or to some extent representative of European Agriculture.
20.2. Characterization of soil: texture (sandy loam, silty loam, loam, loamy sand), pH (5.5-8.0), cation exchange capacity, organic carbon (0.5-2-5%), bulk density, water retention, microbial biomass (~1% of organic carbon).
20.3. Other soils where information on characterization by the parameters: pH, texture, CEC, organic carbon, bulk density, water holding capacity, microbial biomass.
20.4. For tests including agricultural soils, the soils should not have been treated with test substance or similar substances for a minimum of 1 year.
20.5. For soil samples, sampling from A-horizon, top 20 cm layers; soils obtained freshly from field preferred (storage max 3 months at 4 +/- 2°C).
20.6. Data on precipitation is recorded.
21. For lab terrestrial studies, the temperature was appropriate to the species being tested and generally should fall within the range between 20-25°C and soil moisture / relative humidity was reported.
22. For bee studies, temperature of the study should be appropriate to species.
23. For lab aquatic studies
23.1. The source and / or composition of the media used should be described
23.2. The temperature of the water should be appropriate to the species being tested and generally fall within the 15-25ºC
24. The residue data can be linked to a clearly described GAP Table appropriate in the context of the renewal of approval of Glyphosate (crop, application method, doses, intervals, PHI).
25. Analytical results present residues measurements which can be correlated with the existing residues definition of glyphosate, and where relevant Its metabolites
26. Analytical methods clearly described and adequate Statement of specificity and sensitivity of the analytical methods is included.
27. Assessment of the ECX for the width of the confidence interval around the median value; and the certainty on the level of protection offered by the median ECX.
Overall assessment: Reliable / Reliable with restrictions / Not reliable
General criteria for relevance considered for all data requirements indicated by the corresponding EU data points as specified in EC Regulation (EU) No 283/2013.

Table 8: Toxicology and Metabolism: Reliability criteria for the detailed assessment of full-text documents – <u>epidemiology and exposure studies</u>

Reliability criteria – toxicology and metabolism

Epidemiology studies	Exposure studies
Guideline-specific	**Guideline-specific**
Study in accordance to valid internationally accepted testing guidelines/practices.	Study in accordance to valid internationally accepted testing guidelines/practices.
Study completely described and conducted following scientifically acceptable standards	Study performed according to GLP
	Study completely described and conducted following scientifically acceptable standards
Test substance	**Test substance**
Exposure to formulations with only glyphosate as a.i.	Exposure to formulations with only glyphosate as a.i.
Exposure to formulations with glyphosate combined with other a.i.	Exposure to formulations with glyphosate combined with other a.i.
Exposure to various formulations of pesticides	Exposure to various formulations of pesticides
Study	**Study**
Study design – epidemiological method followed	Study design clearly described
Description of population investigated	Population investigated sufficiently described
Description of exposure circumstances	Exposure circumstances sufficiently described
Description of results	Sampling scheme sufficiently documented
Have confounding factors been considered	Analytical method described in detail
Statistical analysis	Validation of analytical method reported
	Monitoring results reported
Overall assessment: Reliable / Reliable with restrictions / Reliability not assignable / Not reliable	

Table 9: Toxicology and Metabolism: Reliability criteria for the detailed assessment of full-text documents – *in vitro* and *in vivo* studies

Reliability criteria – toxicology and metabolism	
***In vitro* studies**	***In vivo* studies**
Guideline-specific	**Guideline-specific**
Study in accordance to valid internationally accepted testing guidelines	Study in accordance to valid internationally accepted testing guidelines.
Study performed according to GLP	Study performed according to GLP
Study completely described and conducted following scientifically acceptable standards	Study completely described and conducted following scientifically acceptable standards
Test substance	**Test substance**
Test material (Glyphosate) is sufficiently documented and reported (i.e. purity, source, content, storage conditions)	Test material (Glyphosate) is sufficiently documented and reported (i.e. purity, source, content, storage conditions)
Only glyphosate acid or one of its salts is the tested substance	Only glyphosate acid or one of its salts is the tested substance
AMPA is the tested substance	AMPA is the tested substance
Study	**Study**
Test system clearly and completely described	Test species clearly and completely described
Test conditions clearly and completely described	Test conditions clearly and completely described
Metabolic activation system clearly and completely described	Route and mode of administration described
Test concentrations in physiologically acceptable range	Dose levels reported

(< 1 mM)	
Cytotoxicity tests reported	Number of animals used per dose level reported
Positive and negative controls	Method of analysis described for analysis test media
Complete reporting of effects observed	Validation of the analytical method
Statistical methods described	Analytical verifications of test media
Historical negative and positive control data reported	Complete reporting of effects observed
Dose-effect relationship reported	Statistical methods described
	Historical control data of the laboratory reported
	Dose-effect relationship reported
Overall assessment: Reliable / Reliable with restrictions / Reliability not assignable / Not reliable	

3 SEARCH RESULTS

The full outcome of the literature search is provided below (formatted as recommended in the Appendix to EFSA, 2011 - Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009. EFSA Journal 2011;9(2):2092. 49 pp. doi:10.2903/j.efsa.2011.2092)

Table 6: Summary of the review

	Number	**Justification**
Total number of summary records retrieved from search.	5036	n.a
Total number of summary records retrieved after removing duplicates from all database searches. [a)]	4024	n.a.
Number of summary records excluded after rapid assessment for relevance (by title / abstract).	3640	Irrelevant information for the assessment of the ED potential of Glyphosate
Total number of full-text documents assessed in detail.	384	n.a.
Number of studies excluded from the risk assessment after detailed assessment of full-text documents (*i.e.* not relevant).	347	See table 11
Number of articles not excluded after detailed assessment. [c)]	47 (37 + 10[d)]	See tables 12 & 13
Number of articles / summaries presented in the dossier. [e)]	17	See table 14

[a)] Automatic and manual removal within databases.

[b)] EFSA GD category 5.4.1 a, b and c.

[c)] All articles belonging to the category A, B, C of the Point 5.4.1 (as stated in the EFSA Guidance Document).

[d)] Publication identified as being relevant for ED assessment in the literature assessment according to EFSA Guidance "Submission of of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009",
EFSA Journal 2011;9(2):2092

[e)] Summaries presented in the dossier: articles classified as relevant (EFSA GD, Point 5.4.1, category A) & reliable or relevant (EFSA GD, Point 5.4.1, category A) & reliable with restrictions.

Table 11: Publications excluded from the risk assessment after detailed assessment of full-text documents

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Abalaka M. E. et al.	2015	Effects of pesticides on the micro-flora of loamy soil obtained from biological garden, federal university of technology, minna, Nigeria	Advance in Agriculture and Biology, (2015) Vol. 4, No. 3, pp. 106-113	Not relevant for the assessment of ED effects: Presented data cannot be related to an EU level Annex I risk assessment.
Ecotoxicology	Aguilar-Dorantes K. et al.	2015	Glyphosate Susceptibility of Different Life Stages of Three Fern Species	American fern journal (2015), Vol. 105, No. 3, pp. 131-144	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Considered supplementary as species not relateable to an EU level risk assessment for Annex I renewal.
Ecotoxicology	Alcantara-de la Cruz R. et al.	2017	Side-effects of pesticides on the generalist endoparasitoid Palmistichus elaeisis (Hymenoptera: Eulophidae).	Scientific Reports (2017), Vol. 7, No. 1, 10064 p	Not relevant for the assessment of ED effects: This paper discusses the influence of transgenic crops sprayed with glyphosate on biological control agents. Not relatable to an EU level risk assessment.
Ecotoxicology	Al-Daikh E. B. et al.	2016	Effect of glyphosate herbicide on the behavior of soil arthropods in non-organic tomato system	Advance in Agriculture and Biology (2016), 5(1), 14-19	Not relevant for the assessment of ED effects: Endpoints presented cannot be related to an EU level risk assessment for Annex I renewal.
Ecotoxicology	Alhewairini S. S.	2017	Toxicity of the herbicide glyphosate to non-target species Caenorhabditis elegans.	Journal of Food, Agriculture & Environment (2017), Vol. 15, No. 2, pp. 97-101	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general literature review report (LRR): 5.4.1 case b) Relevant but supplementary information. The aim of the work presented in the paper was to evaluate the impact of glyphosate exposure on a nematode species, by assessing its

Technical section	Author(s)	Year	Title	Source	Justification
					feeding activity on bacteria whilst in the presence of glyphosate. The study has not been conducted according to a recognised test guideline and there are no validity criteria presented. The generated endpoints are not based on direct effects on the nematode, but instead, are based on the optical density related to the density of bacteria present in the NGM agar test cultures. It is unclear if the presented mortality data were due to direct effects of glyphosate in the cultures, or due to indirect effects associated with reduced feeding activity. There was no test substance information presented and glyphosate concentrations were not measured / confirmed during the study. Finally, there were no quantifiable endpoints presented in the paper, that would be considered applicable to an EU level ecotoxicological risk assessment.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Alishahi M. et al.	2016	Acute toxicity evaluation of five herbicides: paraquat, 2,4-dichlorophenoxy acetic acid (2,4-D), trifluralin, glyphosite and atrazine in Luciobarbus esocinus fingerlings.	Iranian Journal of Veterinary Medicine (2016), Vol. 10, No. 4, pp. En319-En330, Pe39	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This article only provides supplementary information for the regulatory risk assessment of glyphosate. The aim of this work was to evaluate the potential acute toxicological effects of glyphosate and other herbicides on native fish in Iran as well as to determine relative potency of frequently used herbicides. Although the study was stated to have been conducted according to a recognised test guideline (OECD 203), no validity criteria was presented. The selected fish species and their approximate origin are described but environmental holding conditions (water quality) for the fish handling prior to and during the study were not included. There was limited test substance information presented, with no rationale presented for the selection of exposure concentrations. Glyphosate concentrations were also not measured/confirmed during the evaluation period. Behavioural observations relating to the lethargy and swimming behaviour are not considered directly relatable to the nominal exposure concentration. The study is considered unreliable.
Ecotoxicology	Allegrini M. et al.	2015	Ecotoxicological assessment of soil microbial community tolerance to glyphosate.	The Science of the total environment, (2015 Nov 15) Vol. 533, pp. 60-8	Not relevant for the assessment of ED effects: Novel test design / approach - not

Technical section	Author(s)	Year	Title	Source	Justification
					relatable to an EU level ecotoxicological risk assessment for Annex I renewal.
Ecotoxicology	Allegrini M. et al.	2017	Repeated glyphosate exposure induces shifts in nitrifying communities and metabolism of phenylpropanoids	Soil biology & biochemistry (2017), Vol. 105, pp. 206-215	Not relevant for the assessment of ED effects: Approaches used cannot be related to an EU level ecotoxicological risk assessment for Annex I renewal.
Ecotoxicology	Anon.	2018	Comparative study of chronic toxicity of herbicides used in South America using a model of Cyprinus carpio	Environmental Science: An Indian Journal, (2018) Vol. 14, No. 5, pp. 175	Not relevant for the assessment of ED effects: When assessing the potential impact of glyphosate on the endocrine system in fish, this study is not considered relevant since no ED related parameters are investigated.
Ecotoxicology	Antunes A. M. et al.	2017	Gender-specific histopathological response in guppies Poecilia reticulata exposed to glyphosate or its metabolite aminomethylphosphonic acid.	Journal of applied toxicology : JAT, (2017 Sep) Vol. 37, No. 9, pp. 1098-1107	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 8.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Babalola O. et al.	2019	Mortality, teratogenicity and growth inhibition of three glyphosate formulations using Frog Embryo Teratogenesis Assay-Xenopus.	Journal of applied toxicology, (2019) Vol. 39, No. 9, pp. 1257-1266	Not relevant for the assessment of ED effects: The formulation used in the assessment is not the representative formulation being considered for the renewal of glyphosate at Annex I, therefore not considered relevant to the ED assessment.
Ecotoxicology	Babalola O. O. et al.	2018	Comparative Early Life Stage Toxicit of the African Clawed Frog, Xenopus laevis Following Exposure to Selected Herbicide Formulations Applied to Eradicate Alien Plants in South Africa	Archives of Environmental Contamination and Toxicology, (1 Jul 2018) Vol. 75, No. 1, pp. 8-16	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: As the composition of the Roundup used in the test cannot be confirmed, the study must be considered as supplementary. Original Roundup contains a POEA surfactant which drives the toxicity of the product.
Ecotoxicology	Bach N. C. et al.	2016	Effect on the growth and development and induction of abnormalities by a glyphosate commercial formulation and its active ingredient during two developmental stages of the South-American Creole frog, Leptodactylus latrans.	Environmental science and pollution research international, (2016 Dec) Vol. 23, No. 23, pp. 23959-23971	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Endpoint data presented for a formulated product other than the representative formualtion for the Annex I. There are data indicated for glyphosate technical material, but this material is not identified in the materials and methods.
Ecotoxicology	Bach N. et al.	2018	Effects of glyphosate and its commercial formulation, Roundup® Ultramax, on liver histology of tadpoles of the neotropical frog, Leptodactylus latrans (amphibia: Anura)	Chemosphere 202 (2018), pp. 289 -297	Not relevant for the assessment of ED effects: The study analyzes short-term effects on growth, development and liver histology of tadpoles of the neotropical frog, Leptodactylus latrans. The effects cannot be regarded as an endocrine mediated effect. Overall, the study cannot be regarded as relevant.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Baier F. et al.	2016	Non-target effects of a glyphosate-based herbicide on Common toad larvae (Bufo bufo, Amphibia) and associated algae are altered by temperature.	PeerJ, (2016) Vol. 4, pp. e2641	Not relevant for the assessment of ED effects: Test item used is not the representative formulation relevant to the EU renewal of glyphosate. Article discusses the impact of temperature on toxicity. Studies conducted for EU renewal are conducted at constant temperature that reflects median temperature in the field. Variable temperature studies are not considered at EU level.
Ecotoxicology	Baier F. et al.	2016	Temperature-Dependence of Glyphosate-Based Herbicide's Effects on Egg and Tadpole Growth o Common Toads.	Frontiers in Environmental Science, (2016) Vol. 4 pp. Article No.: 51	Not relevant for the assessment of ED effects: Test conducted in a formulation not relevant for ED and the renewal of glyphosate.
Ecotoxicology	Berger G. et al	2018	How does changing pesticide usage over time affect migrating amphibians a case study on the use of glyphosate-based herbicides in German agriculture over 20 years.	Frontiers in Environmental Science (2018), Volume 6, Number Feb., 6 p.	Not relevant for the assessment of ED effects: This paper concersn the use of a formulation containing POEA which is not relevant to the representative formulation being considered at Annex I.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Bokony V. et al.	2017	Chronic exposure to a glyphosate-based herbicide makes toad larvae more toxic.	Proceedings. Biological sciences, (2017 Jul 12) Vol. 284, No. 1858	Not relevant for the assessment of ED effects: The article does not report results which can be used for risk assessment and information is insufficient to transfer values into such determinants.
Ecotoxicology	Bokony V. et al.	2018	Endocrine disruptors in breeding ponds and reproductive health of toads in agricultural, urban and natural landscapes.	The Science of the total environment, (2018) Vol. 634, pp. 1335-1345	Not relevant for the assessment of ED effects: Not relevant at full text level as this paper discusses the results of surface water body surveys looking at complex mixtures of chemicals found in the environment from multiple sources. Possible impacts inferred cannot be concluded to be the result of glyphosate exposure despite the higher levels of this compound found in surface waters compared to other chemicals that have a known ED toxicity profile. Ambient monitoring data not considered relevant to an EU level risk assessment for Annex I renewal.
Ecotoxicology	Boone M.	2018	An amphibian with a contracting range is not more vulnerable to pesticides in outdoor experimental communities than common species.	Environmental toxicology and chemistry, (2018) Vol. 37, No. 10, pp. 2699-2704	Not relevant for the assessment of ED effects: this paper concerns the use of a formulation containing POEA which is not relevant to the representative formulation being considered at Annex I.
Ecotoxicology	Boufleuer E. M. S. et al.	2016	Assessment of mortality and reproduction of Daphnia magna subjected to the herbicide glyphosate. Avaliacao da mortalidade e reproducao de Daphnia magna submetida ao herbicida glifosato.	Acta Iguazu (2016), Vol. 5, No. 5, pp. 25-33	Not relevant for the assessment of ED effects: A 48 hour LC50 for Daphnia was determined to be 2.1087 mg/L. Chronic (21 day) study determined effects at 2.1087 mg/L, but no effects at lower concentrations tested. The study was not conducted to GLP or to an acceptable guideline and there are several short comings in the provided report. The test substance used (Polaris 48%) is a Monsanto Brazil product, that is based on the IPA salt

Technical section	Author(s)	Year	Title	Source	Justification
					of Glyphosate. This product also contains a surfactant that is not relevant to the representative formulation, therefore the observed findings are not considered relevant to the renewal and the influence of the co-formulant on the achieved results cannot be excluded. There are no analytical data reported and so the exposure cannot be confirmed.
Ecotoxicology	Bridi D. et al.	2017	Glyphosate and Roundup(®) alter morphology and behavior in zebrafish.	Toxicology, (20171201) Vol. 392, pp. 32-39	Not relevant for the assessment of ED effects: The article does not report results, which can be used for risk assessment and information is insufficient to transfer values into such determinants.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Buck J. C. et a	2015	Effects of pesticide mixtures on host-pathogen dynamics of the amphibian chytrid fungus	PLoS One, (2015) Vol. 10, No. 7, pp. e0132832/1-e0132832/17	Not relevant for the assessment of ED effects: Effects on host pathogen dynamics is not a data requirement for the Annex I submission, therefore, the findings cannot be related to the ecotoxicology risk assessment.
Ecotoxicology	Burella P. et al	2017	Evaluation of Stage-Dependent Genotoxic Effect of RoundupA® (Glyphosate) on Caiman latirostris Embryos	Archives of environmental contamination and toxicology (2017), Vol. 72, Number 1, pp. 50-57	Not relevant for the assessment of ED effects: Work was conducted using a formulation of glyphosate based on the potassium 'K' salt, which is not relevant to the formulation that is the representative formulation for the EU renewal.
Ecotoxicology	Carpenter J. K. et al.	2016	The effect of two glyphosate formulations on a small, diurnal lizard (Oligosoma polychroma).	Ecotoxicology (London, England), (2016 Apr) Vol. 25, No. 3, pp. 548-54	Not relevant for the assessment of ED effects: Contains POEA, therefore not relevant to EU renewal.
Ecotoxicology	Carvalho L. B. et al.	2016	Plant Growth Responses of Apple and Pear Trees to Doses of Glyphosate	Planta Daninha, Vol. 34, No. 4, pp. 815-822, 20161001	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Study investigates the impact of spraying apple and pear saplings at rates up to 720 g/ha and looks at effects on yield. Spraying of sapling trees directly is not on the GAP table as a use, so whilst they may inform on the potential risk via drift, endpoint considered relevant to EU level risk assessment. The endpoints were not established using a test guideline considered relevant to EU renewal.
Ecotoxicology	Carvalho W. et al.	2018	Evaluation of Genotoxic and Mutagenic Effects of Glyphosate Roundup Original® in Dendropsophus minutus Peters, 1872 Tadpoles	South american journal of herpetology (2018), Vol. 13, Number 3, pp. 220-229	Not relevant for the assessment of ED effects: Results of the study are based on a formulation containing POEA - not relevant to EU level renewal of glyphosate as representative formulation does not contain POEA.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Castilho A. F. et al.	2016	The impact of glyphosate herbicides on soil microbial activity from the Carajas National Forest.	Revista de Ciencias Agrarias / Amazonian Journal of Agricultural and Environmental Sciences (2016), Vol. 59, No. 3, pp. 302-309	Not relevant for the assessment of ED effects: Study was a long term monitoring stuyd using multiple Roundup formulations. Roundup original contains POEA and is not therefore relevant. The other Roundup formulations differ in their composition to the representative formulation for the Annex I.
Ecotoxicology	Castro A. d. J. V. et al.	2015	Using a toxicity test with Ruppia maritima (Linnaeus) to assess the effects of Roundup.	Marine pollution bulletin, (2015 Feb 28) Vol. 91, No. 2, pp. 506-10	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This paper presents information on the effects of glyphosate on a saline tolerant species. However, there is no glyphosate exposure presented in the paper so it is very difficult to relate the observed effects to an exposure event / agricultural application.
Ecotoxicology	Cola Zanuncio J. et al.	2017	Glyphosate-based herbicides toxicity on life history parameters of zoophytophagous Podisus nigrispinus (Heteroptera: Pentatomidae)	Ecotoxicology and environmental safety (2017)	Not relevant for the assessment of ED effects: Based on an exposure situation where soldier bugs were exposed to glyphosate resistant crops, which are not relevant to the EU exposure situation.
Ecotoxicology	da Cruz C. et al.	2016	Sensitivity, ecotoxicity and histopathological effects on neotropical fish exposed to glyphosate alone and associated to surfactant	Journal of Environmental Chemistry and Ecotoxicology, (2016) Vol. 8, No. 3, pp. 25-33	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: The study was not conducted to GLP and/or according to a recognized test guideline and there are no validity criteria presented. The authors state that glyphosate alone and in association with Aterbane® BR was classified as practically non-toxic, whereas Aterbane® BR alone was considered moderately toxic for the tested organisms.

Technical section	Author(s)	Year	Title	Source	Justification
					However, due to insufficient explanation of experimental set-up (e.g. test substance, test medium, statistical analysis) and lack of experimental standard procedures (e.g. analytical verification).
Ecotoxicology	da R. J. G. S. e al.	2016	Fish Aversion and Attraction to Selected Agrichemicals.	Archives of environmental contamination and toxicology, (2016 Oct) Vol. 71, No. 3, pp. 415-22	Not relevant for the assessment of ED effects: Paper describes a novel fish avoidance study which is not considered relevant to an EU level risk assessment.
Ecotoxicology	de S. A. S. et al.	2016	Glyphosate sub-lethal toxicity to non-target organisms occurring in Jatropha curcas plantations in Brazil.	Experimental & applied acarology, (2016 Oct) Vol. 70, No. 2, pp. 179-87	Not relevant for the assessment of ED effects: Endpoints not relatable to an EU level ecotoxicologyrisk assessment.
Ecotoxicology	Dominguez A. et al.	2016	Toxicity of AMPA to the earthworm Eisenia andrei Bouche, 1972 in tropical artificial soil.	Scientific reports, (2016 Jan 21) Vol. 6, pp. 19731	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: The aim of the study was to investigate acute and chronic toxicity of the glyphosate metabolite AMPA to earthworm E. andrei in tropical artificial soil. The study is well-documented and performed according to ISO guideline 11268-1 and 11268-2. However, the artificial soil used is not representative for the EU and soil characteristics are only given partly as information on CEC, organic carbon content and bulk density are missing. Additionally, one of the validity criteria for the chronic test was not met (the reported minimum number of control juveniles is too low). Endpoints (NOEC, LC50) were not derived and therefore this study delivers only supplementary information.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Dos S. A. P. R et al.	2017	A glyphosate-based herbicide induces histomorphological and protein expression changes in the liver of the female guppy Poecilia reticulata.	Chemosphere, (2017 Feb) Vol. 168, pp. 933-943	Not relevant for the assessment of ED effects: The paper attempts to establish a proteomic method for detecting sub-lethal impacts of chemicals on fish. Not relevant for risk assessment in the EU, where growth and reproductive parameters achieved in higher tier fish testing are considered. The formulation used is also not the representative formulation for the annex I renewal.
Ecotoxicology	Druille M. et al.	2015	Glyphosate vulnerability explains changes in root-symbionts propagules viability in pampean grasslands	Agriculture, ecosystems & environment (2015), Vol. 202, pp. 48-55	Not relevant for the assessment of ED effects: Findings cannot be related to an EU level ecotoxicologyrisk assessment.
Ecotoxicology	Edge C. et al.	2014	The response of amphibian larvae to exposure to a glyphosate-based herbicide (Roundup WeatherMax) and nutrient enrichment in an ecosystem experiment.	Ecotoxicology and environmental safety, (2014 Nov) Vol. 109, pp. 124-32	Not relevant for the assessment of ED effects: WeatherMax, a non EU representative glyphosate formulated product was used as the test substance. Prior exposure history of the egg masses to other chemicals as well as other organisms within the wetlands was unknown as the study was conducted in a natural environment. Several limitations were observed within the study including lack of exposure history of the local organisms, inability to attribute the results entirely to the test substance, inability to develop a dose-response relationship within the study.Testing conditions were neither documented nor controlled, and representativeness of the test conditions were unknown as the study was not conducted according to a standard guideline.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Erban T. et al.	2017	Detection of the desiccant and plant growth regulator chlormequat in honeybees and comb pollen.	Veterinarni Medicina (2017), Vol. 62, No. 11, pp. 596-603	Not relevant for the assessment of ED effects: Investigation of samples from hives exhibiting poisoning. Analyzed for many pesticides (including glyphosate). No glyphosate detections reported.
Ecotoxicology	Felix F. J. et al	2015	Impact of the herbicide glyphosate roundup (41%) on the haematology of the freshwater fish, Catla catla (Hamilton)	IOSR Journal of Environmental Science, Toxicology and Food Technology, (2015) Vol. 9, No. 4-3, pp. 56-60	Not relevant for the assessment of ED effects: Contains POEA, therefore not relevant to EU renewal.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Ferreira-Junior D. F. et al.	2017	Low Concentrations of Glyphosate-Based Herbicide Affects the Development of Chironomus xanthus	Water, air, and soil pollution (2017), Vol. 228, No 10, 390 p	Not relevant for the assessment of ED effects: The purpose of the study was to test acute and chronic toxicity of Roundup® Original to a tropical fresh water midge. Roundup Original contains POEA surfactant which is not permitted for use in formulations in the EU. The representative formulation (MON 52276) does not contain POEA. The influence of the surfactant on the achieved results in this study cannot be excluded. Due to the test materials not being the representative formulation for the EU renewal, the study is not relevant to the EU level Annex I ecotoxicology risk assessment.
Ecotoxicology	Gagneten A. M. et al.	2014	EFECTOS DEL HERBICIDA RON-DO® SOBRE Cerodaphnia reticulata (CRUSTACEA, CLADOCERA) Y DEGRADABILIDAD DEL GLIFOSATO (N-FOSFOMETILGLICINA) EN CONDICIONES EXPERIMENTALES	Natura Neotropicalis, Vol. 45, No. 1&2, pp. 71-85 20140101, Graphs, Tables, References	Not relevant for the assessment of ED effects: Formulation is not the representative formulation for the Annex I EU renewal.
Ecotoxicology	Gandhi J. and Cecala K.	2016	Interactive effects of temperature and glyphosate on the behavior of blue ridge twoaX80X90lined salamanders (Eurycea wilderae)	Environmental toxicology and chemistry (2016), Vol. 35, Number 9, pp. 2297-2303	Not relevant for the assessment of ED effects: Test conducted in a formulation not relevant for ED and the renewal of glyphosate
Ecotoxicology	Garcia-Perez J A. et al.	2016	Impact of litter contaminated with glyphosate-based herbicide on the performance of Pontoscolex corethrurus, soil phosphatase activities and soil pH	Applied soil ecology (2016)	Not relevant for the assessment of ED effects: relates to a long term monitoring study on earthworms specific to South America.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Garza-Leon C. V. et al.	2017	Toxicity evaluation of cypermethrin, glyphosate, and malathion, on two indigenous zooplanktonic species.	Environmental science and pollution research international, (2017 Aug) Vol. 24, No. 22, pp. 18123-18134	Not relevant for the assessment of ED effects: The tested formulation is not the representative formulation for the Annex I renewal.
Ecotoxicology	Gaupp-Berghausen M et al.	2015	Glyphosate-based herbicides reduce the activity and reproduction of earthworms and lead to increased soil nutrient concentrations.	Scientific reports, (2015 Aug 05) Vol. 5, pp. 1288(	Not relevant for the assessment of ED effects: Paper discusses the indirect impact of nutrient loads in soil after glyphosate based herbicide application. Not relateable to EU ecotoxicologyassessment.
Ecotoxicology	Geyer R. L. et al.	2016	Effects of Roundup formulations, nutrient addition, and Western mosquitofish (Gambusia affinis) on aquatic communities.	Environmental science and pollution research international, (2016 Jun) Vol. 23, No. 12, pp. 11729-39	Not relevant for the assessment of ED effects: Formulations used is not the representative formulation for the Annex I renewal. Effects from co-formulants cannot be excluded.
Ecotoxicology	Giaquinto P. C et al.	2017	Effects of Glyphosate-Based Herbicide Sub-Lethal Concentrations on Fish Feeding Behavior.	Bulletin of environmental contamination and toxicology, (2017 Apr) Vol. 98, No. 4, pp. 460-46	Not relevant for the assessment of ED effects: Test design and endpoints are not used in EU level risk assessment for Annex I renewal.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Givaudan N. et al.	2014	Earthworm tolerance to residual agricultural pesticide contamination: field and experimental assessment of detoxification capabilities.	Environmental pollution (Barking, Essex : 1987), (2014 Sep) Vol. 192, pp. 9-18	Not relevant for the assessment of ED effects: Study provides information on cellular/molecular level and is not an ecotoxicological relevant study
Ecotoxicology	Gomes M. P. et al.	2017	Effects of glyphosate acid and the glyphosate-commercial formulation (Roundup) on Dimorphandra wilsonii seed germination: Interference of seed respiratory metabolism.	Environmental pollution (Barking, Essex : 1987), (2017 Jan) Vol. 220, No. Pt A, pp. 452-459	Not relevant for the assessment of ED effects: Findings are not relatable to an EU level Annex I risk assessment as this species is only found in Brazil.
Ecotoxicology	Gutierrez M. F et al.	2017	Disruption of the hatching dynamics of zooplankton egg banks due to glyphosate application.	Chemosphere, (2017 Mar) Vol. 171, pp. 644-653	Not relevant for the assessment of ED effects: Endpoints based on abundance are used in an EU level ecotoxicology risk assessment. The formulation used is not the representative formulation and therefore impact of co-formulants cannot be excluded. Therefore not relevant to the Annex I renewal.
Ecotoxicology	Hansen L. R. et al.	2016	Behavioral responses of juvenile Daphnia magna after exposure to glyphosate and glyphosate-copper complexes.	Aquatic toxicology (Amsterdam, Netherlands), (2016 Oct) Vol. 179, pp. 36-43	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Paper considers the influence of metals in Daphnia testing and their influence on toxicity. Soils on the toxicity of endpoints considering speciation and enhanced toxicity in the presence of metals are not used in the EU level ecotoxicology risk assessment.
Ecotoxicology	Hasan F. et al.	2016	Ecotoxicological hazards of herbicide on biological attributes of Zygogramma bicolorata Pallister (Coleoptera: Chrysomelidae).	Chemosphere, (2016 Jul) Vol. 154, pp. 398-407	Not relevant for the assessment of ED effects: Novel surface residue exposure study that presents endpoint data that is not relatable to the EU level risk assessment.
Ecotoxicology	Houssou A. M et al.	2017	Lethal and sub-lethal effects of cypermethrin and glyphosate on the freshwater's copepod, Acanthocyclops robustus.	ISJ-Invertebrate Survival Journal, (2017) Vol. 14, pp. 140-148	Not relevant for the assessment of ED effects: The test species selected is also not described and environmental holding conditions (water quality) prior to and during the study were

Technical section	Author(s)	Year	Title	Source	Justification
					not indicated. The formulation (Kumark® (480 g/L) is not the representative formulation for the EU Annex I renewal (MON 52276). The study was not conducted to a guideline, but the acute toxicity test can be considered in-line with OECD guideline 202. According to OECD 202, the validity criteria are not met for Glyphosate (> 10 % mortality in the control). Additionally, there were no quantifiable endpoints presented in the paper to a non-standard species. Due to the test materials not being the representative formulation for the EU renewal, the study is not relevant to the EU level Annex I ecotoxicology risk assessment.
Ecotoxicology	Isaac A. O. et al.	2017	Behavioural and some physiological assessment of glyphosate and paraqua toxicity to juveniles of African catfish Clarias gariepinus.	Pakistan Journal of Zoology (2017), Vol. 49, No. 1, pp. 183-190	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Although the study itself is not directly relatable to an EU level ecotoxicological risk assessment for Annex I renewal purposes, the study was potentially considered as sub-lethal effects on fish behaviour following exposure to glyphosate were described.
Ecotoxicology	Janssens L. et al.	2017	Stronger effects of Roundup than its active ingredient glyphosate in damselfly larvae.	Aquatic toxicology (Amsterdam, Netherlands), (2017 Dec) Vol. 193, pp. 210-216	Not relevant for the assessment of ED effects: Formulation tested contains POEA - not relevant for EU renewal.
Ecotoxicology	Jayawardena U. A. et al.	2017	Effects of agrochemicals on disease severity of Acanthostomum burminis infections (Digenea: Trematoda) in th Asian common toad, Duttaphrynus melanostictus.	BMC Zoology, (SEP 22 2017) Vol. 2	Not relevant for the assessment of ED effects: Discusses results of exposure of nematode infection to multiple a.i. including a glyphosate formulation containing POEA. POEA not relevant to EU level risk assessment.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Jiang JinLin et al.	2017	Influence of commonly used pesticides on acute toxicity to earthworm Eisenia fetida and alteration of antioxidant enzyme activities.	Journal of Agro-Environment Science (2017), Vol 36, No. 3, pp. 466-473	Not relevant for the assessment of ED effects: Acute toxicity to earthworms is not a data requirement in the EU level Annex I ecotoxicology risk assessment.
Ecotoxicology	Jofre D. M. et al.	2015	Acute and chronic toxicity of glyphosate to native fish from San Luis province, Argentina	Current Topics In Toxicology. Vol. 11, pp. 49-54. 2015	Not relevant for the assessment of ED effects: The tested formulation contains POEA and is therefore not relevant to the MON 52276 representative formulation for the Annex I renewal.
Ecotoxicology	Khan A. et al.	2016	Comparative Study of Toxicological Impinge of Glyphosate And Atrazine (Herbicide) on Stress Biomarkers; Blood Biochemical and Haematological Parameters of the Freshwater Common Carp (Cyprinus carpio).	Polish Journal of Environmental Studies, (2016) Vol. 25, No. 5, pp. 1995-2001	Not relevant for the assessment of ED effects: molecular and chemical observations not relevant to traditional ecotoxicology risk assessment. Population level effects may not be inferred from such observations.
Ecotoxicology	Koakoski G. et al.	2014	Agrichemicals chronically inhibit the cortisol response to stress in fish.	Chemosphere, (2014 Oct) Vol. 112, pp. 85-91	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Endpopints based on measured stress hormones are not relevant to an EU level Annex I ecotoxicology risk assessment for renewal.
Ecotoxicology	Kocamaz D. et al.	2017	Adverse effects of roundup, a glyphosate herbicide, on reproductive hormone system and antioxidant enzymes of tilapia, Oreochromisniloticus.	Toxicology Letters, (2017) Vol. 280, Supp. Supplement 1, pp. S176. Abstract Number: P-05-01-11	Not relevant for the assessment of ED effects: Work was conducted using a formulation of glyphosate based on the potassium 'K' salt, which is not relevant to the formulation that is the representative formulation for the EU renewal.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Kondera E. et al.	2018	Effect of glyphosate-based herbicide on hematological and hemopoietic parameters in common carp (Cyprinus carpio L).	Fish physiology and biochemistry, (2018) Vol. 44, No. 3, pp. 1011-1018	Not relevant for the assessment of ED effects: Test conducted in a formulation not relevant for ED and the renewal of glyphosate.
Ecotoxicology	Lance E. et al.	2016	Accumulation and detoxication responses of the gastropod Lymnaea stagnalis to single and combined exposures to natural (cyanobacteria) and anthropogenic (the herbicide RoundUp(®) Flash) stressors.	Aquatic toxicology (Amsterdam, Netherlands), (2016 Aug) Vol. 177, pp. 116-24	Not relevant for the assessment of ED effects: Molecular level results that are not relatable to an EU level ecotoxicologyrisk assessment.
Ecotoxicology	Lanctot C. et al.	2014	Effects of glyphosate-based herbicides on survival, development, growth and sex ratios of wood frog (Lithobates sylvaticus) tadpoles. II: agriculturally relevant exposures to Roundup WeatherMax® and Vision® under laboratory conditions.	Aquatic toxicology (Amsterdam, Netherlands), (2014 Sep) Vol. 154, pp. 291-303	Not relevant for the assessment of ED effects: The tested formulation contains POEA and is therefore not relevant to the MON 52276 representative formulation for the Annex I renewal.
Ecotoxicology	Leccia F. et al.	2016	Disruption of the chemical communication of the European agrobiont groundaX80X90dwelling spider Pardosa agrestis by pesticides	Journal of applied entomology (2016), Vol. 140, No. 8, pp. 609-616	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Endpoints based on the impact of chemicals on spider pheromones are not used in EU level ecotoxicology risk assessment.
Ecotoxicology	Levis N. A. et al.	2016	NonaX80X90adaptive phenotypic plasticity: the effects of terrestrial and aquatic herbicides on larval salamander morphology and swim speed	Biological journal of the Linnean Society (2016), Vol. 118, No. 3, pp. 569-581	Not relevant for the assessment of ED effects: Adaptive phenotypic plasticity is not an endpoint / observed parameter considered in the EU level ecotoxicology risk assessment for Annex I renewal.
Ecotoxicology	Li Jia et al.	2017	Acute toxicity study of glyphosate and cyhalofop-butyl to Daphnia carinata.	Acta Prataculturae Sinica (2017), Vol. 26, No. 9, pp. 148-155	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case c) Relevance cannot be determined: The herbicides evaluated in the study were a 41%

Technical section	Author(s)	Year	Title	Source	Justification
					glyphosate isopropylamine saline water agent. The study was not conducted according to GLP and the test substance source could not be verified. The authors state that glyphosate has an obvious dosage-effect relation to the moving inhibition and fatality rate of Daphnia carinatas, and the routinely used concentration of the two is significantly higher than LC50 and is strongly toxic to Daphnia carinatas. However, given the lack of standard guidelines, an unclear method design and approach, as well as challenges in interpreting the study results make reaching any conclusions arising from the study challenging at best.
Ecotoxicology	Li M. et al.	2017	Metabolic profiling of goldfish (Carassius auratis) after long-term glyphosate-based herbicide exposure.	Aquatic toxicology (Amsterdam, Netherlands), (2017 Jul) Vol. 188, pp. 159-169	Not relevant for the assessment of ED effects: metabolomics approaches to assessing the fate of pesticides in organismss looks specifically at cellular and molecular level based endpoints that are not used in the EU level ecotoxicology risk assessment for Annex I renewal.
Ecotoxicology	Liao L. et al.	2017	Behavioral responses of honey bees (Apis mellifera) to natural and synthetic xenobiotics in food.	Scientific reports, (2017 Nov 21) Vol. 7, No. 1, pp 15924	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Presented data based on preference behaviour of honey bees cannot be directly related to an EU level ecotoxicology risk assessment - may possibly be used to support a lack of effects despite a preference.
Ecotoxicology	Lopes da Silva E. T. et al.	2016	LETHAL CONCENTRATION OF GLYPHOSATE FOR JUVENILES	Boletim Do Instituto De Pesca, (2016) Vol. 42, No. 4, pp. 759-764	Not relevant for the assessment of ED effects: Concerns a formulation of glyphosate

Technical section	Author(s)	Year	Title	Source	Justification
			OF CURIMATA-PACU. Original Title: CONCENTRACAO LETAL DO GLIFOSATO PARA JUVENIS DE CURIMATA-PACU.		(ATANOR®) that is not the representative formulation for the Annex I renewal.
Ecotoxicology	Lopes F. M. et al.	2017	Glyphosate Adversely Affects Danio rerio Males: Acetylcholinesterase Modulation and Oxidative Stress.	Zebrafish, (20170400) Vol. 14, No. 2, pp. 97-105	Not relevant for the assessment of ED effects: Endpoints not relatable to an EU level ecotoxicology risk assessment for Annex I renewal.
Ecotoxicology	Lopes F. M. et al.	2014	Effect of glyphosate on the sperm quality of zebrafish Danio rerio.	Aquatic toxicology (Amsterdam, Netherlands), (2014 Oct) Vol. 155, pp. 322-6	Not relevant for the assessment of ED effects: Endpoint not used in EU level ecotoxicology risk assessment
Ecotoxicology	Louch J. et al.	2017	Potential risks to freshwater aquatic organisms following a silvicultural application of herbicides in Oregon's Coast Range.	Integrated environmental assessment and management, (2017 Mar) Vol. 13, No. 2, pp. 396-409	Not relevant for the assessment of ED effects: This is a specific non-EU monitoring study that cannot be related to an EU level ecotoxicology risk assessment for Annex I renewal.
Ecotoxicology	Lugowska K.	2018	The effects of Roundup on gametes and early development of common carp (Cyprinus carpio L).	Fish physiology and biochemistry, (2018) Vol. 44, No. 4, pp. 1109-1117	Not relevant for the assessment of ED effects: No - formulation not representative forulation being concsidered for the Annex I rnewal.
Ecotoxicology	Ma J. et al.	2015	Alteration in the cytokine levels and histopathological damage in common carp induced by glyphosate.	Chemosphere, (2015 Jun) Vol. 128, pp. 293-8	Not relevant for the assessment of ED effects: Endpoints not relateable to an EU level risk assessment for ANNEX I renewal.
Ecotoxicology	Malecot M. et al.	2013	Specific proteomic response of Unio pictorum mussel to a mixture of glyphosate and microcystin-LR.	Journal of proteome research, (2013 Nov 01) Vol. 12, No. 11, pp. 5281-92	Not relevant for the assessment of ED effects: Observed findings are not relateable to an EU level ecotoxicologyecotoxicologyrisk assessment for Annex I purposes.
Ecotoxicology	Marcano L. et al.	2017	Effects of contaminated natural soil by Glyphosan SL on biochemical responses of the earthworm Eisenia sp	Journal of Toxicology and Environmental Health Sciences, (2017) Vol. 9, No. 10, pp. 92-97	Not relevant for the assessment of ED effects: Test conducted in a formulation not relevant for ED and the renewal of glyphosate

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Marusca T.	2017	Oversowing or resowing of subalpine grassland appointed after the dynamic of floristic composition.	Romanian Journal of Grassland and Forage Crops (2017), No. 15, pp. 45-55	Not relevant for the assessment of ED effects: Study describes ecological succession and not specific effects of glyphosate on NTOs, therefore not relevant to EU level Annex I ecotoxicology risk assessment.
Ecotoxicology	Matozzo V. et al.	2018	Ecotoxicological risk assessment for the herbicide glyphosate to non-target aquatic species: A case study with the mussel Mytilus galloprovincialis.	Environmental pollution (Barking, Essex : 1987), (2018 Feb) Vol. 233, pp. 623-632	Not relevant for the assessment of ED effects: No control data are presented. The concept of up and downregulation of genes folowing exposure to glyphosate within the context of a risk assessment is not relatable to the EU renewal. The purity of the test substance is not presented so dosing cannot be confirmed. The environmental conditions of the exposure phase are not presented other than salinity and temparture. No positive control included.
Ecotoxicology	McVey K. A. et al.	2016	Exposure of C. elegans eggs to a glyphosate-containing herbicide leads to abnormal neuronal morphology.	Neurotoxicology and teratology, (2016 May-Jun) Vol. 55, pp. 23-31	Not relevant for the assessment of ED effects: The article does not report results, which can be used for risk assessment and information is insufficient to transfer values into such determinants.
Ecotoxicology	Medeiros E. V d. et al.	2014	Impact of glyphosate on microbial attributes of soil planted with two species of passion fruit.	Revista Caatinga (2014), Vol. 27, No. 1, pp. 1-8	Not relevant for the assessment of ED effects: non-EU soil based comparitive experiment to establish the impact of glyphosate on bacterial populations in soil for two different species of passion fruit in Brazil. The test design was described without specifc detail on the amount of glyphosate being applied so any impacts could not be related to exposure. Therefore findings cannot be related to an EU level risk assessment for Annex I renewal.
Ecotoxicology	Menendez-Helman R. J. et al.	2015	Subcellular energy balance of Odontesthes bonariensis exposed to a glyphosate-based herbicide.	Ecotoxicology and environmental safety, (2015 Apr) Vol. 114, pp. 157-63	Not relevant for the assessment of ED effects: Molecular level results that are not relatable to an EU level ecotoxicologyrisk assessment.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Mestre Ana P. et al.	2019	Effects of cypermethrin (pyrethroid), glyphosate and chlorpyrifos (organophosphorus) on the endocrine and immune system of Salvator merianae (Argentine tegu).	Ecotoxicology and environmental safety, (2019) Vol. 169, pp. 61-67	Not relevant for the assessment of ED effects: Test conducted in a formulation not relevant for ED and the renewal of glyphosate.
Ecotoxicology	Miko Z. et al.	2017	Effects of a glyphosate-based herbicide and predation threat on the behaviour of agile frog tadpoles.	Ecotoxicology and environmental safety, (2017 Jun) Vol. 140, pp. 96-102	Not relevant for the assessment of ED effects: The results of the study are not based on direct toxic effects of glyphosate to tadpoles, but are based on the interactive effects in the presence of predators. Endpoints of this type are not used in EU level risk assessment for Annex I renewal purposes.
Ecotoxicology	Miko Z. et al.	2017	Standardize or Diversify Experimenta Conditions in Ecotoxicology? A Case Study on Herbicide Toxicity to Larva of Two Anuran Amphibians.	Archives of environmental contamination and toxicology, (2017 Nov) Vol. 73, No. 4, pp. 562-569	Not relevant for the assessment of ED effects: Formulation Glyphogan Classic used in the study contains POEA which is not relevant to an EU level risk assessment for the representative formulattion MON 52276 that does not contain POEA.
Ecotoxicology	Mohamed I. A et al.	2016	Unique efficacy of certain novel herbicides against Culex pipiens (Diptera: Culicidae) mosquito under laboratory conditions	Advances in Environmental Biology, (2016) Vol. 10, No. 8, pp. 104-111	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Important information is missing in the material and methods section. The preparation and application of the test solutions as well as the tested concentration range were not reported. The test items were not adequately specified. It is not clear whether the test concentrations refer to the product or to the active substance. Moreover one active ingredient is given as glyphosate isopropylamine which is formulated as a salt resulting in test concentrations as acid equivalents. In addition, the biological results

Technical section	Author(s)	Year	Title	Source	Justification
					of the test were not sufficiently stated. No mortality data for the test concentrations nor for the controls was provided in order to evaluate the results. Furthermore, there was no analytical verification of test concentrations reported. The study is not to a guideline and is not GLP. The study is considered unreliable.
Ecotoxicology	Mondal S. et al	2017	Phytotoxicity of glyphosate in the germination of Pisum sativum and its effect on germinated seedlings.	Environmental health and toxicology, (2017) Vol. 32, pp. e2017011	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Test design not relevant to EU level ecotoxicology risk assessment for Annex I renewal.
Ecotoxicology	Monquero P. A. et al.	2016	Initial growth of tree species under herbicide drift.	Revista de Ciencias Agrarias / Amazonian Journal of Agricultural and Environmental Sciences (2016), Vol. 59, No. 2, pp. 162-172	Not relevant for the assessment of ED effects: Direct application to trees is not a proposed use of glyphosate and such endpoints are not used in the EU level risk assessment for glyphosate renewal.
Ecotoxicology	Morris A. et al	2016	Effect of two commercial herbicides on life history traits of a human disease vector, Aedes aegypti, in the laboratory setting.	Ecotoxicology (London, England), (2016 Jul) Vol. 25, No. 5, pp. 863-70	Not relevant for the assessment of ED effects: No relevant information on metabolism/residues/background levels of glyphosate. Epidemiology, effect of glyphosate on Aedes aegypti.
Ecotoxicology	Mottier A. et al.	2015	Effects of subchronic exposure to glyphosate in juvenile oysters (Crassostrea gigas): From molecular t individual levels.	Marine pollution bulletin, (2015 Jun 30) Vol. 95, No. 2, pp. 665-77	Not relevant for the assessment of ED effects: Endpoints based on gene expressions are not considered in an Ecotoxicology risk assessment for Annex I renewal.
Ecotoxicology	Murussi C. R. et al.	2016	Exposure to different glyphosate formulations on the oxidative and histological status of Rhamdia quelen	Fish physiology and biochemistry, (2016 Apr) Vo 42, No. 2, pp. 445-55	Not relevant for the assessment of ED effects: Findings cannot be related to an EU level Ecotoxicology risk assessment.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Navarro C. D. C. et al.	2014	Effects of the surfactant polyoxyethylene amine (POEA) on genotoxic, biochemical and physiological parameters of the freshwater teleost Prochilodus lineatus.	Comparative biochemistry and physiology. Toxicology & pharmacology : CBP, (2014 Sep) Vol. 165, pp. 83-90	Not relevant for the assessment of ED effects: Contains POEA, therefore not relevant to EU renewal.
Ecotoxicology	Niemeyer J. et al.	2018	Do recommended doses of glyphosate based herbicides affect soil invertebrates? Field and laboratory screening tests to risk assessment.	Chemosphere, (2018) Vol. 198, pp. 154-160	Not relevant for the assessment of ED effects: Study considers avoidance behaviour in earthworms and reproductive performance of collembolans at field application rate equivalents that are far higher than those considered on the proposed GAP. The maximum rate applied in the assays was the equivalent of 36 kg/ha. At the lowest rates, the reproductive performance of collembolans was not affected. The low rate was equivalent to 4.5 kg/ha. In the avoidance tests, the field application rates were applied at 0.72 g/L in 200 L/ha eqauivalents -which is the same as 144 kga.e /ha. Not relevant for ED assessment
Ecotoxicology	Oliveira C. S. et al.	2014	Exopolysaccharides and abiotic stress tolerance in bacterial isolates from "sabia" nodules.	Revista Caatinga (2014), Vol. 27, No. 4, pp. 240-245	Not relevant for the assessment of ED effects: Paper discusses a novel approach of assessing abiotic stress tolerance in bacterial isolates. Achieved data set is not relatable to an EU level risk assessment.
Ecotoxicology	Oliveira R. d. C. et al.	2016	Assessment of the potential toxicity o glyphosate-based herbicides on the photosynthesis of Nitella microcarpa var. wrightii (Charophyceae)	Phycologia [Phycologia]. Vol. 55, no. 5, 577 p. Sep 2016	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Despite the study using a recognised OECD guideline, the endpoints in terms of respiration rates are not relevant to an EU level risk assessment for Annex I renewal,

Technical section	Author(s)	Year	Title	Source	Justification
					which specifically considers inhibition of glyphosate growth rates. The study considers technical glyphosate, Roundup and AMPA. Despite the techical material being identified, the formulation was not. It is not possible to conclude on the effects caused by the formulation as it was inferred that the product contains POEA. If this is the case then it is not relevant to EU level assessment.
Ecotoxicology	Omran N. E. et al.	2016	The endocrine disruptor effect of the herbicides atrazine and glyphosate on Biomphalaria alexandrina snails.	Toxicology and industrial health, (2016 Apr) Vol. 32, No. 4, pp. 656-65	Not relevant for the assessment of ED effects: Cellular level endpoints are not relatable to an EU level ecotoxicology assessment for AIR 5.
Ecotoxicology	Panda N. et al.	2016	Herbicides impact on Fe and Mn reduction and dehydrogenase activity in an agricultural soil.	Journal of Crop and Weed (2016), Vol. 12, No. 3, pp. 142-149	Not relevant for the assessment of ED effects: comparative effects on Fe and Mn transformation and dehydrogenase activity in soils are not endpoints used in the EU level ecotoxicology risk assessment for Annex I renewal.
Ecotoxicology	Panetto Ottassano S. et al.	2019	The effects of Roundup® in embryo development and energy metabolism of the zebrafish (Danio rerio)	Comparative Biochemistry and Physiology Part - C: Toxicology and Pharmacology (2019) Volume 222, pp. 74-81	Not relevant for the assessment of ED effects: Not relevant to ED evaluation but to be used in the LRR.
Ecotoxicology	Patkowski M. et al.	2016	Response of soil phosphatases to glyphosate and its formulations - Roundup (laboratory conditions).	Plant, Soil and Environment (2016), Vol. 62, No. 6, pp. 286-292	Not relevant for the assessment of ED effects: technical data cannot be related to an EU level Annex I ecotoxicology risk assessment. Formulations used contain POEA
Ecotoxicology	Perez-Iglesias J. M. et al.	2016	Effects of glyphosate on hepatic tissue evaluating melanomacrophages and erythrocytes responses in neotropical anuran Leptodactylus latinasus.	Environmental science and pollution research international, (2016 May) Vol. 23, No. 10, pp. 9852-61	Not relevant for the assessment of ED effects: Presents cellular and morphological level information that cannot be related to an EU level ecotoxicology risk assessment for Annex I renewal.
Ecotoxicology	Pinter I. et al.	2018	TOXICITY TEST OF INDIVIDUAL AND COMBINED TOXIC EFFECTS OF HERBICIDE AMEGA AND	Novenyvdelem, (2018) Vol. 54, No. 11, pp. 476-482	Not relevant for the assessment of ED effects: This paper discusses the impact of a mixture of copper sulphsate + Amega (360 g/L)

Technical section	Author(s)	Year	Title	Source	Justification
			COPPER-SULPHATE ON PHEASANT EMBRYOS. Original Title: AMEGA GYOMIRTO SZER ES A REZ-SZULFAT EGYEDI ES EGYUTTES MEREGHATASANAK VIZSGALATA FACANEMBRIOKBAN.		roundup formulation on pheasent embryos. As this is a mixture assessment, it is not considered relevant for the renewal of a single active containing formulation for Annex I renewal in the EU.
Ecotoxicology	Poletta G. L. et al.	2017	Biomarkers of Environmental Contamination in Reptile Species: The Effect of Pesticide Formulations on Broad-snouted Caiman Caiman latirostris (Crocodilia, Alligatoridae).	Larramendy, ML [	Not relevant for the assessment of ED effects: Cellular and molecular level findings cannot be related to an EU level ecotoxicology risk assessment
Ecotoxicology	Polyakova N. N. et al.	2018	Effect of herbicides application on the soil biological activity in the tree nursery	Agrokhimiya (2018), (12), 35-41	Not relevant for the assessment of ED effects: The paper describes the use of buried linen to establish the activity of microorganisms in the soil during a 2 year monitoring period in a tree nursery. The observations cannot be related to an EU level risk assessment as they are based on visual inspection / qualitative assessment of the amount of apparent breakdown of the linen.
Ecotoxicology	Qin Y. et al.	2017	Toxic effects of glyphosate on diploid and triploid fin cell lines from Misgurnus anguillicaudatus.	Chemosphere, (2017 Aug) Vol. 180, pp. 356-364	Not relevant for the assessment of ED effects: Cellular level endpoints cannot be related to the EcotoxicologyAnnex I renewal risk assessment.
Ecotoxicology	Reddy S. et al.	2018	Disturbances in reproduction and expression of steroidogenic enzymes in aquatic invertebrates exposed to components of the herbicide Roundup	Toxicology Research and Application, Vol. 2, pp 1-10	Not relevant for the assessment of ED effects: No information on the test substance glyphosate is given and only one concentration was tested. Therefore, no ECx values can be derived. Additionally, no analytical measurements of the test substance were performed. No details on snail mortality are shown and further results of the toxicity tests are not described in detail (e.g. no

Technical section	Author(s)	Year	Title	Source	Justification
					standard deviations in protein quantities) and are varying.
Ecotoxicology	Reno U. et al.	2016	Water polluted with glyphosate formulations: effectiveness of a decontamination process using Chlorella vulgaris growing as bioindicator	Journal of applied phycology (2016), Vol. 28, No. 4, pp. 2279-2286	Not relevant for the assessment of ED effects: Study conducted using Roundup ultramx (AKA Mon 78784) that contains surfactants that are different to those used in MON 52276. Therefore findings cannot be related to the ecotoxicology assessment for Annex I renewal for MON 52276.
Ecotoxicology	Reno U. et al.	2016	EFECTOS SUBLETALES DE CUATRO FORMULACIONES DE GLIFOSATO SOBRE Daphnia magn Y Ceriodaphnia dubia (CRUST ACEA, CLADOCERA)	Natura Neotropicalis, Vol. 47, No. 1, pp. 7-20, 20160101, Tables, References, Equations	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: The aim of the study was to compare the chronic toxicity of four different commercially available Glyphosate products to Daphnia magna and Ceriodaphnia dubia. The study was not conducted according to GLP and the study design lacks some details compared with relevant guidelines. The test concentrations are based on nominal and no analytical verification of test item concentrations were conducted (only analysis of stock solutions using an unspecific detector). Although the details of the statistical analyses are reported, the study report only describes where significant differences were found. No detailed results including standard deviations of the investigated parameters are provided. As the study is based on different glyphosate products, the toxicity of glyphosate active substance alone is unknown and therefore endpoints generated from this study are not

Technical section	Author(s)	Year	Title	Source	Justification
					quantifiable and deliver only supplementary information.
Ecotoxicology	Rodriguez-Gil J. L. et al.	2017	Aquatic hazard assessment of MON 0818, a commercial mixture of alkylamine ethoxylates commonly used in glyphosate-containing herbicide formulations. Part 2: Roles of sediment, temperature, and capacity for recovery following a pulsed exposure.	Environmental toxicology and chemistry, (20170200) Vol. 36, No. 2, pp. 512-521	Not relevant for the assessment of ED effects: Contains POEA, therefore not relevant to EU renewal.
Ecotoxicology	Romano-Armada N. et al.	2019	Construction of a combined soil quality indicator to assess the effect of glyphosate application.	The Science of the total environment, (2019 Sep 10) Vol. 682, pp. 639-649	Not relevant for the assessment of ED effects: Paper describes a new approach to establishing the quality of farmland soils by assessing multiple physical, chemical and biological quality factors of soils and attempting to classify these as being of high or low quality based on a known history of glyphosate or no glyphosate application. To this end, the paper does not describe endpoint data that can be related to an EU level Annex I submission.
Ecotoxicology	Roy N. M. et al.	2016	Glyphosate induces neurotoxicity in zebrafish.	Environmental toxicology and pharmacology, (2016 Mar) Vol. 42, pp. 45-54	Not relevant for the assessment of ED effects: Endpoint not used in EU level ecotoxicology risk assessment
Ecotoxicology	Rzymski P. et al.	2013	The effect of glyphosate-based herbicide on aquatic organisms - a case study.	Limnological Review (2013), Vol. 13, No. 4, pp. 215-220	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Information may be relevant to the wider discussion on trophic interactions, but cannot be related to the EU level ecotoxicology risk assessment for Annex I renewal in the EU.
Ecotoxicology	Samanta P. et al.	2014	Biochemical effects of glyphosate based herbicide, Excel Mera 71 on	Ecotoxicology and environmental safety, (2014 Sep) Vol. 107, pp. 120-5	Not relevant for the assessment of ED effects: Cellular level endpoints cannot be related to

Technical section	Author(s)	Year	Title	Source	Justification
			enzyme activities of acetylcholinesterase (AChE), lipid peroxidation (LPO), catalase (CAT), glutathione-S-transferase (GST) and protein content on teleostean fishes.		the ecotoxicology Annex I renewal risk assessment.
Ecotoxicology	Samanta P. et al.	2014	Evaluation of metabolic enzymes in response to Excel Mera 71, a glyphosate-based herbicide, and recovery pattern in freshwater teleostean fishes.	BioMed research international, (2014) Vol. 2014, pp. 425159	Not relevant for the assessment of ED effects: Cellular level endpoints cannot be related to the ecotoxicology Annex I renewal risk assessment.
Ecotoxicology	Sanchez J. A. A. et al.	2017	Effects of Roundup formulations on biochemical biomarkers and male sperm quality of the livebearing Jenynsia multidentata.	Chemosphere, (2017 Jun) Vol. 177, pp. 200-210	Not relevant for the assessment of ED effects: Formulations contain POEA and therefore not relevant to the EU level Aecotoxicology risk assessment for Annex I renewal.
Ecotoxicology	Sani A. et al.	2016	Acute toxicity of herbicide (glyphosate) in Clarias gariepinus juveniles.	Toxicology reports, (2016) Vol. 3, pp. 513-515	Not relevant for the assessment of ED effects: No information on test substance and the test design is not recognised. In addition, the fish were too large for use in the study.
Ecotoxicology	Santric L. et al	2016	Effects of herbicides on growth and number of actinomycetes in soil and i vitro.	Pesticidi i Fitomedicina (2016), Vol. 31, No. 3/4, pp. 121-128	Not relevant for the assessment of ED effects: No endpoints presented that can be used in an EU level ecotoxicology risk assessment for Annex I renewal.
Ecotoxicology	Saska P. et al.	2016	Treatment by glyphosate-based herbicide alters life history parameters of the rose-grain aphid Metopolophium dirhodum.	Scientific reports, (20160615) Vol. 6, pp. 27801	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: The paper does not present endpoints that could be used in an EU level ecotoxicology risk assessment.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Saska P. et al.	2017	Treating Prey With Glyphosate Does Not Alter the Demographic Parameters and Predation of the Harmonia axyridis (Coleoptera: Coccinellidae).	Journal of economic entomology, (20170401) Vol 110, No. 2, pp. 392-399	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Exposure was performed via treated prey, which does not correspond to an adequate route of exposure regarding current test guideline for non-target-arthropods. 2 mL test solution was applied to 50 aphids placed on a filter paper in a petri dish, with dimensions unknown. There is no analytical verification, and the study does not conform to a recognised guideline, nor GLP. The study is well documented, but no endpoints could be derived which can be applied for the risk assessment. Therefore, the study is considered as supplementary only.
Ecotoxicology	Schweizer M. et al.	2019	How glyphosate and its associated acidity affect early development in zebrafish (Danio rerio).	PeerJ, (2019) Vol. 7, pp. e7094. Electronic Publication Date: 19 Jun 2019	Not relevant for the assessment of ED effects: Since only acute teratogenic effects are assessed, this study is not considered as relevant for the assessment of endocrine disrupting properties of glyphosate.
Ecotoxicology	Seguin A. et al	2017	Sub-lethal effects of a glyphosate-based commercial formulation and adjuvants on juvenile oysters (Crassostrea gigas) exposed for 35days.	Marine pollution bulletin, (2017 Apr 15) Vol. 117, No. 1-2, pp. 348-358	Not relevant for the assessment of ED effects: Contains POEA, therefore not relevant to EU renewal.
Ecotoxicology	Sharifi Y. et al	2015	Biodegradation of glyphosate herbicide by Salinicoccus spp isolated from Qom Hoze-soltan lake, Iran	Environmental Health Engineering and Management Journal (2015), 2(1), 31-36	Not relevant for the assessment of ED effects: Paper discusses the potential use of a bacterial strain for biodegrading of glyphosate in a freshwater lake in Iran. Not relevant to the Annex I renewal process in the EU.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Silveira T. et al.	2019	Roundup® Herbicide Decreases Quality Parameters of Spermatozoa of Silversides Odontesthes Humensis	Bulletin of Environmental Contamination and Toxicology (2019) Volume 102, Number 1, DOI: 10.1007/s00128-018-2508-0	Not relevant for the assessment of ED effects: Test conducted in a formulation not relevant for ED and the renewal of glyphosate.
Ecotoxicology	Slaby S. et al.	2018	Effects of glyphosate and a commercial formulation Roundup® exposures on maturation of Xenopus laevis oocytes	Environmental Science and Pollution Research (https://doi.org/10.1007/s11356-019-04596-2)	Not relevant for the assessment of ED effects: The observed effects cannot be traced back to an endocrine mediated effect. It not possible to extrapolate an adverse effect on frog oocyte maturation from this in vitro test.
Ecotoxicology	Smedbol E. et al.	2017	Phytoplankton growth and PSII efficiency sensitivity to a glyphosate-based herbicide (Factor 540(®)).	Aquatic toxicology (Amsterdam, Netherlands), (2017 Nov) Vol. 192, pp. 265-273	Not relevant for the assessment of ED effects: Achieved endpoints are not relateable to an EU level ecotoxicology risk assessment for Annex I renewal.
Ecotoxicology	Smedbol Elise et al.	2017	Effects of low concentrations of glyphosate-based herbicide factor 540A® on an agricultural stream freshwater phytoplankton community	Chemosphere (2017)	Not relevant for the assessment of ED effects: Test substance not glyphosate/metabolite. Paper presented based on a formulation of glyphosate that is not the representative formulation being considered for the Annex I renewal.
Ecotoxicology	Soloneski S. et al.	2016	Genotoxic effect of a binary mixture of dicamba- and glyphosate-based commercial herbicide formulations on Rhinella arenarum (Hensel, 1867) (Anura, Bufonidae) late-stage larvae.	Environmental science and pollution research international, (2016 Sep) Vol. 23, No. 17, pp. 17811-21	Not relevant for the assessment of ED effects: Despite LC50 data being present that could inform on the risk assessment - the formulation used (Credit®) is based on MON 35085, which is a 360 g/L formulation containing MON 0818, which contains POEA. These findings are therefore not relevant to the EU renewal as MON 52276 does not contain POEA.
Ecotoxicology	Stecca C. S. et al.	2016	Side-Effects of Glyphosate to the Parasitoid Telenomus remus Nixon (Hymenoptera: Platygastridae).	Neotropical entomology, (2016 Apr) Vol. 45, No. 2, pp. 192-200	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: The study was conducted in accordance with the protocols proposals by IOBC. The exposure via overspray on egg-cards and

Technical section	Author(s)	Year	Title	Source	Justification
					parasitoid pupae does not correspond to an adequate route of exposure according to current guidelines for testing non-target-arthopods. Regarding the bioassay with adults exposed to dry residues the test design is moderately described; the mortality of parasitoids during exposure is unclear. However, the spray deposit is given. The assessment of the biological endpoints in not exactly reported; day of emergence of parasitoids is not given. As the biological data do not report results in values useful for the risk assessment, there is no analytical verification, and the study is non GLP, the study can be considered as supplementary only.
Ecotoxicology	Sulukan E. et al.	2017	An approach to clarify the effect mechanism of glyphosate on body malformations during embryonic development of zebrafish (Daino rerio).	Chemosphere, (2017 Aug) Vol. 180, pp. 77-85	Not relevant for the assessment of ED effects: Endpoints are not relatable to an EU level risk assessment for Annex 1 renewal.
Ecotoxicology	Sushilkumar et al.	2017	Herbicides effect on fish mortality and water quality in relation to chemical control of alligator weed.	Indian Journal of Weed Science (2017), Vol. 49, No. 4, pp. 396-400	Not relevant for the assessment of ED effects: methods and endpoints not relatable to EU level ecotoxicology assessment for renewal purposes.
Ecotoxicology	Sushilkumar et al.	2017	Chemical control of duck weed and its effect on water quality and residue.	Indian Journal of Weed Science (2017), Vol. 49, No. 1, pp. 105-107	Not relevant for the assessment of ED effects: difficult to relate observed findings to an EU level risk assessment for Annex I renewal.
Ecotoxicology	Thompson H. M. et al.	2014	Evaluating exposure and potential effects on honeybee brood (Apis mellifera) development using glyphosate as an example.	Integrated environmental assessment and management, (2014 Jul) Vol. 10, No. 3, pp. 463-7(	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 8.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Topal A. et al.	2015	Effects of glyphosate on juvenile rainbow trout (Oncorhynchus mykiss) transcriptional and enzymatic analyses of antioxidant defence system, histopathological liver damage and swimming performance.	Ecotoxicology and environmental safety, (2015 Jan) Vol. 111, pp. 206-14	Not relevant for the assessment of ED effects: cellular and molecular level results, not considered relevant to EU level ecotoxicology risk assessment.
Ecotoxicology	Ujszegi J. et al	2016	NO EFFECT OF A GLYPHOSATE-BASED HERBICIDE ON LARVAL DRAGONFLIES (AESHNA CYANEA) AND ADULT NEWTS (LISSOTRITON VULGARIS) IN A LABORATORY-BASED EXPERIMENT.	Acta Zoologica Academiae Scientiarum Hungaricae, (2016) Vol. 62, No. 4, pp. 355-367	Not relevant for the assessment of ED effects: The test substance contains polyethoxylated tallowamine surfactant, which is not permitted in herbicidal formulations in the EU. Due to the test materials not being the representative formulation for the EU renewal, the study is not relevant to the EU level Annex I ecotoxicology risk assessment.
Ecotoxicology	Ulu T. C. et al.	2016	Effects of different pesticides on virulence and mortality of some entomopathogenic nematodes.	ISJ-Invertebrate Survival Journal, (2016) Vol. 13, pp. 111-115	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Nematode mortality and effects on virulence are not endpoints used in EU level ecotoxicology risk assessment for Annex I renewal.
Ecotoxicology	Uren W. T. M. et al.	2014	Effects of glyphosate and its formulation, roundup, on reproduction in zebrafish (Danio rerio).	Environmental science & technology, (2014 Jan 21) Vol. 48, No. 2, pp. 1271-9	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: The test substance Roundup GC is not the representative formulation for the Annex I renewal. There was only a single glyphosate exposure group at 10 mg/L prepared from analytical grade material. The purity of the material was not confirmed, but it was stated to be analytical grade. The study provides no endpoints for glyphosate that could be used in

Technical section	Author(s)	Year	Title	Source	Justification
					the ecotoxicology risk assessment for Annex I renewal. Thus the study is conssidered supplementary only.
Ecotoxicology	Vannini A. et al.	2016	Bioaccumulation, physiological and ultrastructural effects of glyphosate in the lichen Xanthoria parietina (L.) Th. Fr.	Chemosphere, (2016 Dec) Vol. 164, pp. 233-240	Not relevant for the assessment of ED effects: Article discusses the use of lichens as a bioindicator model of glyphosate exposure. Not relatable to an EU level ecotoxicology risk assessment for the renewal of glyphosate onto Annex I in the EU.
Ecotoxicology	Veeraiah K. et al.	2015	Impact of glyphosate on biochemical constituents of the freshwater fish, catla catla	International Journal of Bioassays, (2015) Vol. 4, No. 7, pp. 4139-4144	Not relevant for the assessment of ED effects: the formulation is not the representative formulation for the Annex I renewal.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Velasques R. R. et al.	2016	Roundup(®) in Zebrafish: Effects on Oxidative Status and Gene Expression.	Zebrafish, (20161000) Vol. 13, No. 5, pp. 432-41	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: The data presented demonstrates that in the presence of a toxicant, there are changes in the oxidative status of zebrafish gills and liver tissue. However, these data cannot be related to an Annex I risk assessment for renewal.
Ecotoxicology	von Merey G. et al.	2016	Glyphosate and aminomethylphosphonic acid chronic risk assessment for soil biota	Environmental toxicology and chemistry (2016), pp. 2742-2752	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 8.
Ecotoxicology	Wagner N. et al.	2017	Effects of a commonly used glyphosate-based herbicide formulation on early developmental stages of two anuran species.	Environmental science and pollution research international, (2017 Jan) Vol. 24, No. 2, pp. 1495-1508	Not relevant for the assessment of ED effects: Not the representative formulation for the Annex I renewal. Therefore not relevant to EU renewal.
Ecotoxicology	Wagner N. et al.	2017	Corrigendum [Erratum to document cited in CA166:057881]	Environmental Toxicology and Chemistry, (2017) Vol. 36, No. 1, pp. 276	Not relevant for the assessment of ED effects: This is a corregendium for an article (No. 2248), which is classified as non-relevant.
Ecotoxicology	Wagner N. et al.	2017	Population and life stage specific effects of two herbicide formulations on the aquatic development of European common frogs (Rana temporaria)	Environmental toxicology and chemistry (2017), Volume 36, Number 1, pp. 190-200	Not relevant for the assessment of ED effects: Tested in formulation.
Ecotoxicology	Watts C. et al.	2016	Responses of invertebrates to herbicide in Salix cinerea invaded wetlands: Restoration implications	Ecological management & restoration (2016), Vol 17, No. 3, pp. 243-249	Not relevant for the assessment of ED effects: Non-EU monitoring study. Extrapolation to EU is difficult.
Ecotoxicology	Wu L. et al.	2016	Physiological effects of the herbicide glyphosate on the cyanobacterium Microcystis aeruginosa.	Aquatic toxicology (Amsterdam, Netherlands), (2016 Sep) Vol. 178, pp. 72-9	Not relevant for the assessment of ED effects: Endpoints presented cannot be used in the EU level renewal risk assessment for glyphosate from an ecotoxicology perspective.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Yusof S. et al.	2014	Effect of glyphosate-based herbicide on early life stages of Java medaka (Oryzias javanicus): a potential tropical test fish.	Marine pollution bulletin, (2014 Aug 30) Vol. 85, No. 2, pp. 494-8	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: There is insufficient explanation provided on the analytical verification of the test concentrations, and the test concentrations were high ranging from 100 to 500 ppm. A regulatory endpoint is not available. There is no verification of dose levels, and the study is non guideline and not GLP. The article can be considered as supplementary information only.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Zabaloy M. C. et al.	2016	Soil ecotoxicity assessment of glyphosate use under field conditions: microbial activity and community structure of Eubacteria and ammonia-oxidising bacteria.	Pest management science, (2016 Apr) Vol. 72, No 4, pp. 684-91	Not relevant for the assessment of ED effects: Findings are not relatable to an EU level ecotoxicology risk assessment for Annex I renewal purposes.
Ecotoxicology	Zabotkina E. A. et al.	2016	The changes of the immunocompetent cells ultrastructure in the kidney, spleen and liver in Amur sleeper Perccottus glenii at the influence of pesticide Roundup.	Trudy VNIRO, (2016) Vol. 162, pp. 73-81	Not relevant for the assessment of ED effects: Article cannot be related to an EU level ecotoxicology risk assessment, as exposure levels cannot be confirmed and there are no endpoints presented that could be used in an ecotoxicology assessment. The paper describes sub-lethal effects / morphological changes in the structure of mitochondria.
Ecotoxicology	Zebral Y. et al.	2018	A glyphosate-based herbicide reduces fertility, embryonic upper thermal tolerance and alters embryonic diapause of the threatened annual fish Austrolebias nigrofasciatus.	Chemosphere, (2018) Vol. 196, pp. 260-269	Not relevant for the assessment of ED effects: The formulation used in the assessment is not the representative formulation being considered for the renewal of glyphosate at Annex I, therefore not considered relevant to the ED assessment.
Ecotoxicology	Zhang Q. et al.	2016	Effects of glyphosate at environmentally relevant concentrations on the growth of and microcystin production by Microcysti aeruginosa.	Environmental monitoring and assessment, (2016 Nov) Vol. 188, No. 11, pp. 632	Not relevant for the assessment of ED effects: presents cellular and molecular findings that are not relateable to the EU level ecotoxicology risk assessment for Annex I renewal.
Ecotoxicology	Zhang S. et al.	2017	Biological impacts of glyphosate on morphology, embryo biomechanics and larval behavior in zebrafish (Danio rerio).	Chemosphere, (2017 Aug) Vol. 181, pp. 270-280	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Provides information on a test species that is relied upon in the risk assessment. But endpoints cannot be related to an EU level ecotoxicology risk assessment.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Zhang Z. et al.	2016	Acute toxicity and risk assessment of paraquat aqueous solution and its 9 alternative products to Bombyx mori	Canye Kexue, (2016) Vol. 42, No. 3, pp. 483-487	Not relevant for the assessment of ED effects: The dipping technique for leaf exposure is not a recognised approach for toxicity testing based on the EU approaches. Not relevant to an EU level Annex I ecotoxicology risk assessment.
Ecotoxicology	Zhong G. et al.	2018	Responses of Hydrilla verticillata (L.f.) Royle and Vallisneria natans (Lour.) hara to glyphosate exposure	Chemosphere, (2018 Feb) Vol. 193, pp. 385-393	Not relevant for the assessment of ED effects: The paper describes enzymatic levels in aquatic plants that cannot be related to an EU level risk assessment for EU renewal.
Ecotoxicology	Zhu X. et al.	2016	Herbicides interfere with antigrazer defenses in Scenedesmus obliquus.	Chemosphere, (2016 Nov) Vol. 162, pp. 243-51	Not relevant for the assessment of ED effects: This paper discusses sub-lethal impacts of glyphosate on colonising activity of scenedesmus. The endpoints are not releatable to the EU level ecotoxicology risk assessment for Annex I renewal.

Technical section	Author(s)	Year	Title	Source	Justification
Ecotoxicology	Zhu Y. C. et al	2017	Feeding toxicity and impact of imidacloprid formulation and mixture with six representative pesticides at residue concentrations on honey bee physiology (Apis mellifera).	PloS one, (2017) Vol. 12, No. 6, pp. e0178421	Not relevant for the assessment of ED effects: No effects on bees from glyphosate exposure alone. When mixed with other pestcides, effects are observed, however as based on mixtures, not relevant to EU level ecotoxicology risk assessment for a single active containing formulation for Annex I renewal in the EU.
Toxicology	Acquavella J. et al.	2016	Glyphosate epidemiology expert pane review: a weight of evidence systematic review of the relationship between glyphosate exposure and non Hodgkin's lymphoma or multiple myeloma.	Critical reviews in toxicology, (2016 Sep) Vol. 46 No. sup1, pp. 28-43	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: review, secondary source.
Toxicology	Ait B. Y. et al.	2017	Behavioral and Immunohistochemical Study of the Effects of Subchronic an Chronic Exposure to Glyphosate in Mice.	Frontiers in behavioral neuroscience, (2017) Vol. 11, pp. 146	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Formulation tested (Roundup, 486 g/L isopropylamine salt, 360 g/L a.e.) in vivo.
Toxicology	Almeida L. L. d. et al.	2017	Effects of melatonin in rats in the initial third stage of pregnancy exposed to sub-lethal doses of herbicides.	Acta histochemica, (2017 Apr) Vol. 119, No. 3, pp. 220-227	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Formulation tested at high doses of 500 mg/kg bw/day (Roundup).
Toxicology	Anifandis G. e al.	2017	The In Vitro Impact of the Herbicide Roundup on Human Sperm Motility and Sperm Mitochondria.	Toxics, (2017 Dec 21) Vol. 6, No. 1	Not relevant for the assessment of ED effects: Formulation tested in vitro (Roundup, not characterized)
Toxicology	Anon.	2017	Erratum to: Transcriptome profile analysis reflects rat liver and kidney damage following chronic ultra-low dose Roundup exposure (Environmental Health: A Global	Environmental Health: A Global Access Science Source, (23 Mar 2017) Vol. 16, No. 1. arn. 28	Not relevant for the assessment of ED effects: This is erratum to Roy_2016.

Technical section	Author(s)	Year	Title	Source	Justification
			Access Science Source (2015) 14:70 DOI: 10.1186/s12940-015-0056-1).		
Toxicology	Anon.	2017	Some organophosphate insecticides and herbicides.	IARC Monographs on the Evaluation of Carcinogenic Risks to Humans (2017), Vol. 112, VII + 452 p	Not relevant for the assessment of ED effects: secondary source of infomation.
Toxicology	Avgerinou C. et al.	2017	Occupational, dietary, and other risk factors for myelodysplastic syndrome in Western Greece.	Hematology (Amsterdam, Netherlands), (2017 Aug) Vol. 22, No. 7, pp. 419-429	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information. A case-control study with non-blinded interviewers is compromised both by potential recall bias and interviewer bias.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Avila-Vazquez M. et al.	2015	Cancer and detrimental reproductive effects in an Argentine agricultural community environmentally exposed to glyphosate	Journal of Biological Physics and Chemistry, (2015) Vol. 15, No. 3, pp. 97-110. CODEN: JBPCAJ.	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate with relation to ED because the general population followed was exposed to multiple environmental factors making it impossible to establish a causal relationship between exposure to glyphosate and reproductive disorders.
Toxicology	Avila-Vazquez M. et al.	2018	Environmental exposure to glyphosate and reproductive health impacts in agricultural population of Argentina.	Journal of Environmental Protection (2018), Vol. 9, Number 3, pp. 241-253	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate in relation to ED because the general population followed was exposed to multiple environmental factors making it impossible to establish a causal relationship between exposure to glyphosate and reproductive disorders.
Toxicology	Baier C. J. et al.	2017	Behavioral impairments following repeated intranasal glyphosate-based herbicide administration in mice.	Neurotoxicology and teratology, (2017 Nov) Vol. 64, pp. 63-72	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Formulation tested via intra-nasal administration.
Toxicology	Beecham J. E. et al.	2015	The possible link between autism and glyphosate acting as glycine mimetic - a review of evidence from the literature with analysis	Journal of Molecular and Genetic Medicine, (2015) Vol. 9, No. 4, pp. 1000197/1-1000197/16	Not relevant for the assessment of ED effects: This publication is considered not relevant for glyphosate risk assessment because it is not based on experimental work and no epidemiologic methodology was followed.
Toxicology	Beranger R. et al.	2018	Multiple pesticide analysis in hair samples of pregnant French women: Results from the ELFE national birth cohort.	Environment International, (2018) Vol. 120, pp. 43-53	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate with relation to ED because glyphosate was not

Technical section	Author(s)	Year	Title	Source	Justification
					monitored in this multi-pesticide exposure study.
Toxicology	Bernieri T. et al.	2019	Occupational exposure to pesticides and thyroid function in Brazilian soybean farmers.	Chemosphere, (2019) pp. 425-429	Not relevant for the assessment of ED effects: This study is considered not relevant for the risk assessment of glyphosate with relation to ED because there was exposure to multiple pesticides with no quantitative estimate of exposure to glyphosate.
Toxicology	Berry C.	2013	Comments on "Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize".	Food and Chemical Toxicology, (MAR 2013) Vol 53, pp. 430-431	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Letter to Editor

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Bhardwaj K. et al.	2019	Effective attenuation of glyphosate-induced oxidative stress and granulosa cell apoptosis by vitamins C and E in caprines	Molecular reproduction and development, (2019) Vol. 86, No. 1, pp. 42-52	Not relevant for the assessment of ED effects: This publication is found not relevant for the risk assessment of glyphosate because it is not clear that either glyphosate or a glyphosate formulation was tested and the effects investigated were only found at concentrations beyond a concentration range that is physiologically possible (> 1mM).
Toxicology	Bonvallot N. et al.	2018	Metabolome disruption of pregnant rats and their offspring resulting from repeated exposure to a pesticide mixture representative of environmental contamination in Brittany	PLoS One, (2018) Vol. 13, No. 6, pp.	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate in relation to ED because the rats in this study were orally exposed to a mixture of 8 pesticides including glyphosate.
Toxicology	Brusick D. et al.	2016	Genotoxicity Expert Panel review: weight of evidence evaluation of the genotoxicity of glyphosate, glyphosate-based formulations, and aminomethylphosphonic acid.	Critical reviews in toxicology, (2016 Sep) Vol. 46 No. sup1, pp. 56-74	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: review, secondary source
Toxicology	Burstyn I. et al	2017	Visualizing the heterogeneity of effects in the analysis of associations of multiple myeloma with glyphosate use. comments on sorahan, t. multiple myeloma and glyphosate use: A re-analysis of us agricultural health study (AHS) data. int. j. environ. res. public health 2015, 12, 1548-1559.	International Journal of Environmental Research and Public Health, (January 2017) Vol. 14, No. 1. arn. 5	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Reanalysis of old data, no stastically significant glyphosate findings.
Toxicology	Bus J. S.	2017	IARC use of oxidative stress as key mode of action characteristic for facilitating cancer classification: Glyphosate case example illustrating a lack of robustness in interpretative implementation.	Regulatory toxicology and pharmacology : RTP, (2017 Jun) Vol. 86, pp. 157-166	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: review, secondary source.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Caganova B. et al.	2017	Caustic effects of chemicals: risk factors for complications and mortality in acute poisoning	Monatshefte fuer Chemie, (2017) Vol. 148, No. 3, pp. 497-503	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This article discusses caustic injury in suicide attempts and therefore should not impact registration decisions.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Caganova B. et al.	2017	Caustic ingestion in the elderly: influence of age on clinical outcome	Molecules, (2017) Vol. 22, No. 10, pp. 1726/1-1726/11	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This article compares outcomes of caustic ingestions in elderly to younger patients and unsurprisingly demonstrates that there is a higher mortality in the older group. Glyphosate is mentioned in a table where there were 9 ingestions with no fatalities in the younger group and 2 fatalities in the elderly. This article discusses suicidal ingestions of caustic substances and should therefore not impact re-registration.
Toxicology	Cai W. et al.	2017	Effects of glyphosate exposure on sperm concentration in rodents: A systematic review and meta-analysis.	Environmental toxicology and pharmacology, (2017 Oct) Vol. 55, pp. 148-155	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Re-evaluation of pooled literature data.
Toxicology	Caloni F. et al.	2018	In vitro effects of two environmental toxicants, beauvericin and glyphosate in Roundup, on cell proliferation and steroidogenesis using a novel bovine whole ovarian cell culture system	JOURNAL OF VETERINARY PHARMACOLOGY AND THERAPEUTICS, (2018) Vol. 41, Supp. [1], Sp. iss. SI, pp. 103-104	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate with relation to ED because cells in culture were exposed to a glyphosate formulation which is not appropriate because of the presence of surfactant.
Toxicology	Caloni F. et al.	2016	Suspected poisoning of domestic animals by pesticides.	The Science of the total environment, (2016 Jan 01) Vol. 539, pp. 331-336	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Review article on domestic animal poisonings by pesticides.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Camacho A. et al.	2017	The health consequences of aerial spraying illicit crops: The case of Colombia.	Journal of health economics, (2017 Jul) Vol. 54, pp. 147-160	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate because it is too general and no specific epidemiological method was followed to establish an association between the application of glyphosate and disease outcome.
Toxicology	Caramello C. S. et al.	2017	Evaluation of herbicide glyphosate effects in the fish Prochilodus lineatus using chromosome aberration test.	Revista Veterinaria (2017), Vol. 28, No. 1, pp. 65-68	Not relevant for the assessment of ED effects: Formulation tested (Roundup Full II), not representative for the renewal.
Toxicology	Cattani D. et al	2017	Developmental exposure to glyphosate-based herbicide and depressive-like behavior in adult offspring: Implication of glutamate excitotoxicity and oxidative stress.	Toxicology, (20170715) Vol. 387, pp. 67-80	Not relevant for the assessment of ED effects: Formulation tested (Roundup Original, Brazil, 360 g/L glyphosate), not-representative for the renewal.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Cattani D. et al	2014	Mechanisms underlying the neurotoxicity induced by glyphosate-based herbicide in immature rat hippocampus: involvement of glutamate excitotoxicity.	Toxicology, (2014 Jun 05) Vol. 320, pp. 34-45	Not relevant for the assessment of ED effects: Formulation tested (Roundup Original, Brazil, 360 g/L glyphosate), not-representative for the renewal.
Toxicology	Cattelan M. et al.	2018	Occupational exposure to pesticides in family agriculture and the oxidative, biochemical and hematological profile in this agricultural model	Life Sciences, (2018) Vol. 203, pp. 177-183	Not relevant for the assessment of ED effects: Related to epidemiology section of dossier, but not relevant to ED.
Toxicology	Chang E. T. et al.	2016	Systematic review and meta-analysis of glyphosate exposure and risk of lymphohematopoietic cancers.	Journal of environmental science and health. Part. B, Pesticides, food contaminants, and agricultural wastes, (2016) Vol. 51, No. 6, pp. 402-34	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: The glyphosate meta-RRs took the results from the available studies at face value. The authors had no way to correct for recall bias, confounding, etc. Therefore, the meta-RRs are in error to the extent that the studies included in the meta-analysis are in error. Chang and Delzell (2016) are clear on this point in their meta-analysis article. Accordingly, p values and confidence intervals for the meta-RRs cannot be taken at face value because they incorporate systematic error or bias. Thus, the argument about the statistical significance (or not) of the meta-RR for glyphosate is inconsequential. You cannot calculate a valid p value when there is uncontrolled systematic error (Greenland S. Randomization, statistics, and causal inference. Epidemiology 1990; 1:421-429).

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Chlopecka M. et al.	2014	Glyphosate affects the spontaneous motoric activity of intestine at very low doses - in vitro study.	Pesticide biochemistry and physiology, (2014 Jul) Vol. 113, pp. 25-30	Not relevant for the assessment of ED effects: novel ex-vivo model not relevant to 1107/2009 review.
Toxicology	Chlopecka M. et al.	2017	The effect of glyphosate-based herbicide Roundup and its co-formulant, POEA, on the motoric activity of rat intestine - In vitro study	Environmental toxicology and pharmacology, (2017 Jan) Vol. 49, pp. 156-162	Not relevant for the assessment of ED effects: Formulation and mixtures of glyphosate and surfactant tested in vitro (Roundup ULTRA 170 SL; 170 g isopropylamine salt/L).
Toxicology	Clark P. A. et al.	2016	Chronic kidney disease in Nicaraguan sugarcane workers: A historical, medical, environmental analysis and ethical analysis.	Internet Journal of Third World Medicine, (2016) Vol. 12, No. 1	Not relevant for the assessment of ED effects: This publication is considered not relevant for glyphosate risk assessment because no systematic epidemiological approach was followed with no figures reported on workers observed with their exposure patterns.
Toxicology	Clausing P.	2017	Cancer risk by glyphosate: The "Weight of Evidence Approach" of BfR. Krebsgefahr durch Glyphosat: Der "Weight of Evidence Approach" des BfR.	Umweltmedizin Hygiene Arbeitsmedizin (2017), Vol. 22, No. 1, pp. 27-34	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate because it is not based on experimental work.
Toxicology	Connolly A. et al.	2017	Exposure assessment using human biomonitoring for glyphosate and fluroxypyr users in amenity horticulture.	International journal of hygiene and environmenta health, (20170800) Vol. 220, No. 6, pp. 1064-1073	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 5
Toxicology	Conrad A. et a	2017	Glyphosate in German adults - Time trend (2001 to 2015) of human exposure to a widely used herbicide	International journal of hygiene and environmenta health, (2017 Jan) Vol. 220, No. 1, pp. 8-16	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 5
Toxicology	Coullery R. P. et al.	2016	Neuronal development and axon growth are altered by glyphosate through a WNT non-canonical signaling pathway.	Neurotoxicology, (2016 Jan) Vol. 52, pp. 150-61	Not relevant for the assessment of ED effects: High in vitro doses >10 mM

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Cremonese C. et al.	2017	Occupational exposure to pesticides, reproductive hormone levels and sperm quality in young Brazilian men	Reproductive Toxicology, (2017) Vol. 67, pp. 174-185	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Due to exposure/outcome temporal ambiguity and failure to control for other exposures in the evaluation of specific exposures.
Toxicology	Dar A. M. et al	2015	Single and interactive toxic potential of Rroundup and ammonium nitrate on Haemato-biochemical parameters in wistar rats	Journal of Cell and Tissue Research, (2015) Vol. 15, No. 3, pp. 5295-5299	Not relevant for the assessment of ED effects: High dose of glyphosate based herbicide administered to rats in drinking water.
Toxicology	de Araujo J. et al.	2016	Glyphosate and adverse pregnancy outcomes, a systematic review of observational studies.	BMC public health, (20160606) Vol. 16, pp. 472	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Review of literature
Toxicology	de Aguiar L.. e al.	2016	Glyphosate-based herbicide exposure causes antioxidant defence responses in the fruit fly Drosophila melanogaster.	Comparative biochemistry and physiology. Toxicology & pharmacology : CBP, (2016 Jul-Aug) Vol. 185-186, pp. 94-101	Not relevant for the assessment of ED effects: Tested formulation (Roundup Original) for cellular mechanisms in houseflies, not directly relevant to human health risk assessment.
Toxicology	de Avila Renato I. et al.	2017	In vitro assessment of skin sensitization, photosensitization and phototoxicity potential of commercial glyphosate-containing formulations.	Toxicology in vitro : an international journal published in association with BIBRA, (2017 Dec) Vol. 45, No. Pt 3, pp. 386-392	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Non-validated model confirms glyphosate non-sensitized and is a non-photosensitizer. Formulation data inconsistent in non-validated model.
Toxicology	de Moura F. et al.	2017	Effects of glyphosate-based herbicide on pintado da Amazonia: Hematology histological aspects, metabolic parameters and genotoxic potential.	Environmental toxicology and pharmacology, (2017 Dec) Vol. 56, pp. 241-248	Not relevant for the assessment of ED effects: high doses of glyphosate based herbicide to aquatic species.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	de Souza. J. et al.	2017	Perinatal exposure to glyphosate-based herbicide alters the thyrotrophic axis and causes thyroid hormone homeostasis imbalance in male rats.	Toxicology, (20170215) Vol. 377, pp. 25-37	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate because a glyphosate formulation (Roundup Transorb) was used instead of glyphosate.
Toxicology	Dechartes J. et al.	2019	Glyphosate and glyphosate-based herbicide exposure during the peripartum period affects maternal brain plasticity, maternal behaviour and microbiome	Journal of Neuroendocrinology, (2019) pp. Ahead of Print. CODEN: JOUNE2. ISSN: 0953-8194.	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate in relation to ED as no effects were studied related to endocrine organs.
Toxicology	Dedeke Gabrie A. et al.	2018	Comparative Assessment on Mechanism Underlying Renal Toxicity of Commercial Formulation of Roundup Herbicide and Glyphosate Alone in Male Albino Rat.	International journal of toxicology, (2018) Vol. 37 No. 4, pp. 285-295	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate with relation to ED as no ED related endpoints were investigated in this study.
Toxicology	Defarge N. et al.	2016	Co-Formulants in Glyphosate-Based Herbicides Disrupt Aromatase Activity in Human Cells below Toxic Levels.	International journal of environmental research an public health, (2016 Feb 26) Vol. 13, No. 3	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: In vitro results not significant for glyphosate vs multiple formulations or mixtures.
Toxicology	Diken M. E. et al.	2017	In vitro effects of some pesticides on glutathione-s transferase activity.	Fresenius Environmental Bulletin (2017), Vol. 26, No. 12A, pp. 8023-8029	Not relevant for the assessment of ED effects: excessively high in vitro doses in the mM range.
Toxicology	Dung Le Tien et al.	2013	Comments on "Long term toxicity of Roundup herbicide and a Roundup-tolerant genetically modified maize".	Food and Chemical Toxicology, (MAR 2013) Vol 53, pp. 428-429	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Letter to Editor
Toxicology	Fagan J. et al.	2015	The Seralini affair: degeneration of Science to Re-Science?	Environmental Sciences Europe (2015), Vol. 27, No. 19, (29 August 2015) p	Not relevant for the assessment of ED effects: Commentary of Seralini paper retraction.
Toxicology	Faria M. A.	2015	Glyphosate, neurological diseases - and the scientific method	Surgical neurology international, (2015) Vol. 6, pp. 132	Not relevant for the assessment of ED effects: LETTER -> Comments on Samsel and Seneff (ref 2324, rated not relevant for RA)

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Feldman V.	2014	Neurodevelopmental toxicity: Still more questions than answers.	The Lancet Neurology, (July 2014) Vol. 13, No. 7 pp. 645-646	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Letter to Editor
Toxicology	Fluegge K. et al.	2017	Exploring the potential confounder of nitrogen fertilizers in the relationship between pesticide exposures and risk of leukemia: a Poisson regression with two-way fixed-effects analysis	Chinese Journal of Cancer, Vol. 36, 20170101	Not relevant for the assessment of ED effects: Letter to editor, focuses on nitrogen fertilizers.
Toxicology	Fluegge K. et al.	2017	Exposure to ambient PM10 and nitrogen dioxide and ADHD risk: A reply to Min & Min (2017).	Environment International, (JUN 2017) Vol. 103, pp. 109-110	Not relevant for the assessment of ED effects: No new data.
Toxicology	Fluegge K. et al.	2016	Glyphosate Use Predicts Healthcare Utilization for ADHD in the Healthcare Cost and Utilization Project net (HCUPnet): A Two-Way Fixed-Effects Analysis.	Polish Journal of Environmental Studies, (2016) Vol. 25, No. 4, pp. 1489-1503	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: No new information without clear relevance for the risk assessment.
Toxicology	Fluegge K. R. et al.	2015	Glyphosate Use Predicts ADHD Hospital Discharges in the Healthcare Cost and Utilization Project Net (HCUPnet): A Two-Way Fixed-Effects Analysis.	PloS one, (2015) Vol. 10, No. 8, pp. e0133525	Not relevant for the assessment of ED effects: Retracted publication.
Toxicology	Ford B. et al.	2017	Mapping Proteome-wide Targets of Glyphosate in Mice.	Cell chemical biology, (2017 Feb 16) Vol. 24, No. 2, pp. 133-140	Not relevant for the assessment of ED effects: This publication is considered not relevant because intraperitoneal injection was used which is an inappropriate route of administration for the occupational and food risk assessment of glyphosate.
Toxicology	Fortes C. et al.	2016	Occupational Exposure to Pesticides With Occupational Sun Exposure Increases the Risk for Cutaneous Melanoma	Journal of occupational and environmental medicine, (2016 Apr) Vol. 58, No. 4, pp. 370-5	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information:

Technical section	Author(s)	Year	Title	Source	Justification
					No specific analyses for glyphosate. Interviewers were not impartial. Recall bias may produce spurious positive associations.
Toxicology	Freddo N. et al	2019	Isoflavone quantitation in soymilk: Genistein content and its biological effect	CYTA – JOURNAL OF FOOD 2019, VOL. 17, NO. 20-24	Not relevant for the assessment of ED effects: This publication is not relevant for the risk assessment of glyphosate in relation to ED as it mainly concerns the development of a bioanalytical method for the analysis of genistein and glyphosate in soymilk. The biological endpoint selected (anxiety) and the test system used (elevated plus maze test) are not suitable for regulatory use.
Toxicology	Gallegos C. E. et al.	2016	Exposure to a glyphosate-based herbicide during pregnancy and lactation induces neurobehavioral alterations in rat offspring.	Neurotoxicology, (2016 Mar) Vol. 53, pp. 20-28	Not relevant for the assessment of ED effects: Formulation tested in vivo via drinking water (Glifloglex, 48% glyphosate, Gleba S.R.L., Argentina)
Toxicology	De Castilhos Ghisi N. et al.	2016	Does exposure to glyphosate lead to an increase in the micronuclei frequency? A systematic and meta-analytic review.	Chemosphere, (2016 Feb) Vol. 145, pp. 42-54	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: No new data presented, only a compilation of pooled glyphosate and formulated product meta-anslysis is provided.
Toxicology	Goldstein D. A et al.	2014	Neurodevelopmental toxicity: Still more questions than answers.	The Lancet Neurology, (July 2014) Vol. 13, No. 7 pp. 645	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Letter to Editor

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Good Peter	2018	Evidence the U.S. autism epidemic initiated by acetaminophen (Tylenol) is aggravated by oral antibiotic amoxicillin/clavulanate (Augmentin) and now exponentially by herbicide glyphosate (Roundup).	Clinical nutrition ESPEN, (20180200) Vol. 23, pp 171-183	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case c) Relevance cannot be determined: Potential effects on gut microbes are not part of the risk assessments and suitable scientific approaches to assess these effects are not specified, thus relevance of these effects remained unclear. This paper contains no new data. It uses computer algor=ithms to make associations that are not proved. It claims that glyphosate impacts methionine and tryptophan and ignores that these amino acids are essential for human diet as microbially derived amino acids are only available via coprophagy.
Toxicology	Gress S. et al.	2016	Dig1 protects against locomotor and biochemical dysfunctions provoked by Roundup.	BMC complementary and alternative medicine, (2016 Jul 22) Vol. 16, pp. 234	Not relevant for the assessment of ED effects: A glyphosate based herbicide was administered to rats in drinking water.
Toxicology	Grunewald W. et al.	2013	Comment on "Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize" by Seralini et al.	Food and Chemical Toxicology, (2013) Vol. 53, pp. 447-448	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Letter to Editor
Toxicology	Guerrero S. M. et al.	2017	Neonatal exposure to a glyphosate based herbicide alters the developmen of the rat uterus.	Toxicology, (2017 Feb 01) Vol. 376, pp. 2-14	Not relevant for the assessment of ED effects: Formulation tested in vivo via sub-cutaneous injection (Roundup FULL II, 66.2% potassium salt).
Toxicology	Guilherme S. e al.	2014	Are DNA-damaging effects induced by herbicide formulations (Roundup® and Garlon®) in fish transient and reversible upon cessation of exposure?.	Aquatic toxicology (Amsterdam, Netherlands), (2014 Oct) Vol. 155, pp. 213-21	Not relevant for the assessment of ED effects: A glyphosate based herbicide was tested in aquatic species.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Haggard D. et al.	2018	High-throughput H295R steroidogenesis assay: utility as an alternative and a statistical approach t characterize effects on steroidogenesis	Toxicological Sciences, (2018) Vol. 162, No. 2, pp. 509-534	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate in terms of ED as it concerns the validation of the high-throughput H295R steroidogenesis assay.
Toxicology	Halwachs S. et al.	2016	Assessment of ABCG2-mediated transport of pesticides across the rabbit placenta barrier using a novel MDCKII in vitro model.	Toxicology and applied pharmacology, (20160815) Vol. 305, pp. 66-74	Not relevant for the assessment of ED effects: No adverse effects, no relevance to human health risk assessment.
Toxicology	Hamdaoui L. e al.	2016	Nephrotoxicity of Kalach 360 SL: biochemical and histopathological findings.	Toxicology mechanisms and methods, (2016 Nov) Vol. 26, No. 9, pp. 685-691	Not relevant for the assessment of ED effects: Formulation tested (Kalach 360 SL) in vivo.
Toxicology	Hammond B. e al.	2013	A Comment on "Seralini, G.-E., et al., Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food Chemical Toxicol. (2012)," http://dx.doLorg/10.1016/j.fct.2012.08 .005.	Food and Chemical Toxicology, (MAR 2013) Vol 53, pp. 444-449	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Letter to Editor
Toxicology	Han J. et al.	2016	Determination of glyphosate and its metabolite in emergency room in Korea.	Forensic science international, (2016 Aug) Vol. 265, pp. 41-6	Not relevant for the assessment of ED effects: Analytical method development in human blood
Toxicology	Haskovi E. et al.	2016	Effects of Glyphosate on Enzyme Activity and Serum Glucose in Rats Rattus norvegicus	Acta veterinaria (2016), Vol. 66, No. 2, pp. 214-221	Not relevant for the assessment of ED effects: Only liver enzymes measured after 15 days dermal application of formulated product (Total 480 SL, Croatia)
Toxicology	Heritier L. et al.	2017	Oxidative stress induced by glyphosate-based herbicide on freshwater turtles.	Environmental toxicology and chemistry, (20171200) Vol. 36, No. 12, pp. 3343-3350	Not relevant for the assessment of ED effects: GBH tested on turtles.
Toxicology	Hong Y. et al.	2017	Effects of glyphosate on immune responses and haemocyte DNA damage of Chinese mitten crab, Eriocheir sinensis.	Fish & shellfish immunology, (2017 Dec) Vol. 71, pp. 19-27	Not relevant for the assessment of ED effects: high doses of GBH to crabs

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Hoppin J. A. et al.	2017	Pesticides are Associated with Allergic and Non-Allergic Wheeze among Male Farmers.	Environmental health perspectives, (20170400) Vol. 125, No. 4, pp. 535-543	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: The exposure and outcome data were concurrent, so a temporal relationship could not be established. The extraordinary number of positive statistically significant findings mitigates against interpreting any one finding as likely to be causal.
Toxicology	Hua J. et al.	2018	Differential microRNA expression in the prefrontal cortex of mouse offspring induced by glyphosate exposure during pregnancy and lactation.	Experimental and therapeutic medicine, (2018) Vol. 15, No. 3, pp. 2457-2467	Not relevant for the assessment of ED effects: Formulation is not relevant for the ED risk assessment
Toxicology	Ilyushina N. et al.	2019	Maximum tolerated doses and erythropoiesis effects in the mouse bone marrow by 79 pesticides' technical materials assessed with the micronucleus assay.	Toxicology Reports, (2019) Vol. 6, pp. 105-110	Not relevant for the assessment of ED effects: Releated to genotoxicity, not relevant to ED.
Toxicology	Indirakshi J. et al.	2017	Toxic Epidermal Necrolysis and Acut Kidney Injury due to Glyphosate Ingestion.	Indian journal of critical care medicine : peer-reviewed, official publication of Indian Society of Critical Care Medicine, (2017 Mar) Vol. 21, No. 3 pp. 167-169	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Glyphosate based formulations are not known to cause TEN which is a t-cell mediated type IV hypersensitivity reaction. >1% of glyphosate is absorbed through the skin and large ingestions have caustic effects on th GI tract which can result in multiorgan failure.
Toxicology	Ingaramo P. I. et al.	2017	Neonatal exposure to a glyphosate-based herbicide alters uterine decidualization in rats.	Reproductive toxicology (Elmsford, N.Y.), (2017 Oct) Vol. 73, pp. 87-95	Not relevant for the assessment of ED effects: Formulation tested in vivo via subcutaneous injection (undisclosed brand, 66.2% potassium salt; 54% glyphosate acid).

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Ingaramo P. I. et al.	2016	Effects of neonatal exposure to a glyphosate-based herbicide on female rat reproduction.	Reproduction (Cambridge, England), (20161100) Vol. 152, No. 5, pp. 403-15	Not relevant for the assessment of ED effects: Formulation tested in vivo (66.2%, potassium salt)
Toxicology	Iummato M. M. et al.	2017	Effect of glyphosate acid on biochemical markers of periphyton exposed in outdoor mesocosms in the presence and absence of the mussel Limnoperna fortunei.	Environmental toxicology and chemistry, (20170700) Vol. 36, No. 7, pp. 1775-1784	Not relevant for the assessment of ED effects: endpoints not relevant to human health.
Toxicology	Iwai K. et al.	2014	Utility of upper gastrointestinal endoscopy for management of patient with roundup poisoning.	Journal of Clinical Toxicology (2014), Vol. 4, No. 6, 1000218 p	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This article discusses the use of endoscopy to treat formulated glyphosate overdose and medical management of suicidal ingestions and therefore should not impact registration decisions.
Toxicology	Jayasumana C. et al.	2014	Glyphosate, hard water and nephrotoxic metals: are they the culprits behind the epidemic of chronic kidney disease of unknown etiology in Sri Lanka?.	International journal of environmental research an public health, (2014 Feb 20) Vol. 11, No. 2, pp. 2125-47	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Presents a hypothesis which is not tested, only discussed.
Toxicology	Jayasumana C. et al.	2015	Simultaneous exposure to multiple heavy metals and glyphosate may contribute to Sri Lankan agricultural nephropathy.	BMC nephrology, (2015 Jul 11) Vol. 16, pp. 103	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Presents a hypothesis which is not tested, only discussed
Toxicology	Jomichen J. et al.	2017	Australian work exposures studies: occupational exposure to pesticides.	Occupational and environmental medicine, (20170100) Vol. 74, No. 1, pp. 46-51	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Occupational exposure survey.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Jovic-Stosic J. et al.	2016	Intravenous lipid emulsion in treatment of cardiocirculatory disturbances caused by glyphosate-surfactant herbicide poisoning.	Vojnosanitetski pregled, (2016 Apr) Vol. 73, No. 4, pp. 390-2	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Medical case of intentional ingestion.
Toxicology	Kasuba V. et al.	2017	Effects of low doses of glyphosate on DNA damage, cell proliferation and oxidative stress in the HepG2 cell line	Environmental science and pollution research international, (2017 Aug) Vol. 24, No. 23, pp. 19267-19281	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 5

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Kawagashira Y. et al.	2017	Vasculitic Neuropathy Following Exposure to a Glyphosate-based Herbicide.	Internal medicine (Tokyo, Japan), (2017) Vol. 56, No. 11, pp. 1431-1434	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This article discussed the development of painful discoloration of the toes and feet 4 months after the patient sprayed formulated glyposate to crops. Interestingly enough, the patient was taking warfarin therapeutically, which can cause the well-described "purple toe syndrome". There is not a mechanism by which sprayed formulated glyphosate can be absorbed by the skin and directly impact small vasculature or neurons in the feet.
Toxicology	Kim E. et al.	2016	Patterns of drugs & poisons in southern area of South Korea in 2014.	Forensic Science International, (1 Dec 2016) Vol. 269, pp. 50-55	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This is an article describing the chemicals/pharmaceuticals that were used in fatal overdoses that were forensically evaluated at the Busan Institute of National Forensic Services. Out of 606 fatalities, agricultural chemicals were involved in 5 and glyphosate was detected in 2 of the cases.
Toxicology	Kim Y. H. et al.	2014	Heart rate-corrected QT interval predicts mortality in glyphosate-surfactant herbicide-poisoned patients	The American journal of emergency medicine, (2014 Mar) Vol. 32, No. 3, pp. 203-7	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This article discusses the utility of the QTc interval to predict mortality in suicidal ingestions of glyphosate-based formulations. It is not unexpected for critically ill patients to develop a long QTc.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Kim Y. H. et al.	2016	Prognostic Factors in Emergency Department Patients with Glyphosate Surfactant Intoxication: Point-of-Care Lactate Testing.	Basic & clinical pharmacology & toxicology, (2016 Dec) Vol. 119, No. 6, pp. 604-610	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This study evaluated the use of lactate as a predictor of mortality and found a statistically significant association between a serum lactate of 4.7mmol/L and mortality in formulated glyphosate overdoses. This is not surprising as caustic injury due to detergent-like surfactants will cause cell death and thereby increase lactate levels. This article discusses predictors of mortality in suicidal ingestions and therefore should not impact registration decisions.
Toxicology	Knudsen L. E. et al.	2017	Biomonitoring of Danish school children and mothers including biomarkers of PBDE and glyphosate.	Reviews on environmental health, (2017 Sep 26) Vol. 32, No. 3, pp. 279-290	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: All glyphosate levels many orders of magnitude lower than the ADI.
Toxicology	Kongtip P. et al.	2017	Glyphosate and Paraquat in Maternal and Fetal Serums in Thai Women.	Journal of agromedicine, (2017) Vol. 22, No. 3, pp. 282-289	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 5
Toxicology	Kubsad D. et al.	2019	Assessment of Glyphosate Induced Epigenetic Transgenerational Inheritance of Pathologies and Sperm Epimutations: Generational Toxicology	Scientific Reports, (2019) Vol. 9, No. 1, pp. 1-17	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate with relation to ED because of the use of an inappropriate route of administration (intraperitoneal injection).

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Kumar S. et al.	2014	Glyphosate-rich air samples induce IL-33, TSLP and generate IL-13 dependent airway inflammation	Toxicology, (2014 Nov 05) Vol. 325, pp. 42-51	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 5
Toxicology	Kurenbach B. et al.	2017	Herbicide ingredients change Salmonella enterica sv. Typhimurium and Escherichia coli antibiotic responses.	Microbiology (Reading, England), (2017 Nov 17)	Not relevant for the assessment of ED effects: high doses to an in vitro system.
Toxicology	Kurenbach B. et al.	2015	Sublethal exposure to commercial formulations of the herbicides dicamba, 2,4-dichlorophenoxyacetic acid, and glyphosate cause changes in antibiotic susceptibility in Escherichia coli and Salmonella enterica serovar Typhimurium.	mBio, (2015 Mar 24) Vol. 6, No. 2	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Endpoints at doses tested not relevant to residue levels or to human health.
Toxicology	Kwiatkowska M. et al.	2014	The effect of metabolites and impurities of glyphosate on human erythrocytes (in vitro).	Pesticide biochemistry and physiology, (2014 Feb) Vol. 109, pp. 34-43	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate because the in vitro concentrations used are in the mM range and the impurities were tested at the same concentrations as glyphosate which will never occur in practice.
Toxicology	Kwiatkowska M. et al.	2016	The Impact of Glyphosate, Its Metabolites and Impurities on Viability, ATP Level and Morphological changes in Human Peripheral Blood Mononuclear Cells.	PloS one, (2016) Vol. 11, No. 6, pp. e0156946	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate because the in vitro concentrations used are in the mM range and the impurities were tested at the same concentrations as glyphosate which will never occur in practice.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Landrigan P.	2018	Pesticides and Human Reproduction.	JAMA Internal Medicine, (2018) Vol. 178, No. 1, pp. 26-27	Not relevant for the assessment of ED effects: Secondary source of information not related to ED
Toxicology	Larsen K. E. et al.	2016	The herbicide glyphosate is a weak inhibitor of acetylcholinesterase in rats.	Environmental toxicology and pharmacology, (2016 Jul) Vol. 45, pp. 41-4	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate because the concentrations used for in vitro testing were all in the mM range.
Toxicology	Larsen K. et al	2014	Effects of Sublethal Exposure to a Glyphosate-Based Herbicide Formulation on Metabolic Activities of Different Xenobiotic-Metabolizing Enzymes in Rats.	International journal of toxicology, (20140700) Vol. 33, No. 4, pp. 307-318	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Formulation tested in vivo via drinking water (Roundup FULL II, 662 g/L potassium salt).
Toxicology	Le Tien D. et al.	2013	Comments on "Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize"	Food and Chemical Toxicology, (2013) Vol. 53, pp. 443-444	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Letter to Editor
Toxicology	Lee D. H. et al	2017	Severe glyphosate-surfactant intoxication: Successful treatment with continuous renal replacement therapy.	Hong Kong Journal of Emergency Medicine, (January 2017) Vol. 24, No. 1, pp. 40-44	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This is a report about multiorgan failure and the use of dialysis after suicidal ingestion of formulated glyphosate and should not impact re-registration.
Toxicology	Lemma T. et al	2019	Combined effect of glyphosphate, saccharin and sodium benzoate on rats	Biophysical chemistry, (2019 Jul) Vol. 250, pp. 106176	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Novel assays and endpoints not applicable/reliable for risk assessment.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Leveroni F. A. et al.	2017	Genotoxic response of blood, gill and liver cells of Piaractus mesopotamicus after an acute exposure to a glyphosate-based herbicide	Caryologia (2017), Vol. 70, No. 1, pp. 21-28	Not relevant for the assessment of ED effects: Formulation tested in aquatic species (Roundup Full II; 66.2% glyphosate potassium salt; CAS no. 70901-12-1)
Toxicology	Lewis M. M. e al.	2017	Lateralized basal ganglia vulnerability to pesticide exposure in asymptomatic agricultural workers	Toxicological Sciences, (2017) Vol. 159, No. 1, pp. 170-178	Not relevant for the assessment of ED effects: Results not correlated to exposure to glyphosate
Toxicology	Li M. et al.	2016	Multi-tissue metabolic responses of goldfish (Carassius auratus) exposed to glyphosate-based herbicide.	Toxicology Research, (2016) Vol. 5, No. 4, pp. 1039-1052	Not relevant for the assessment of ED effects: glyphosate based herbicide tested on goldfish. Endpoints not relevant to human health risk assessment

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Lieshchova M. A. et al.	2018	Combined effect of glyphosphate, saccharin and sodium benzoate on rats.	Regulatory Mechanisms in Biosystems (2018), Vol. 9, No. 4, pp. 591-597, many ref	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Substantially lower water consumption in glyphosate only group confounds data and makes endpoint comparisons meaningless.
Toxicology	Loomba R. S.	2016	Prevalence of isomerism from a European registry: Live births, fetal deaths, and terminations of pregnancy	Congenital Anomalies, (NOV 2016) Vol. 56, No. 6, pp. 256-257	Not relevant for the assessment of ED effects: No mention of glyphosate or AMPA.
Toxicology	Lopez G. E. C. et al.	2017	Micronuclei and other nuclear abnormalities on Caiman latirostris (Broad-snouted caiman) hatchlings after embryonic exposure to different pesticide formulations.	Ecotoxicology and environmental safety, (2017 Feb) Vol. 136, pp. 84-91	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This study looks at the impact of pesticide formulations on the nuclear developments of Caimen embryos via topical application to their eggs shells after laying. The endpoints achieved cannot be related to EU risk assessment.
Toxicology	Luaces J. P. et al.	2017	Genotoxic effects of Roundup Full II® on lymphocytes of Chaetophractu villosus (Xenarthra, Mammalia): In vitro studies.	PloS one, (2017) Vol. 12, No. 8, pp. e0182911	Not relevant for the assessment of ED effects: Formulation tested in vivo (Roundup Full II, 66.2% glyphosate, Argentina)
Toxicology	Luna S and Rosso S.	2019	Glyphosate exposure impairs neurona connectivity and spatial learning in rats.	ASN Neuro, (2019) Vol. 11, pp. 52-53. Abstract Number: P65. Meeting Info: 33rd Congress of the Argentine Society for Research in Neuroscience. Cordoba, Argentina. 24 Oct 2018-26 Oct 2018	Not relevant for the assessment of ED effects: related to neurotoxicity, not ED
Toxicology	Luo L. et al.	2017	In vitro cytotoxicity assessment of roundup (glyphosate) in L-02 hepatocytes.	Journal of environmental science and health. Part. B, Pesticides, food contaminants, and agricultural wastes, (2017 Jun 03) Vol. 52, No. 6, pp. 410-417	Not relevant for the assessment of ED effects: Formulation tested in vitro (Roundup, 41% isopropylamine salt; Belgium). Effects due to high dosing of surfactant in vitro.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Malagoli C. et al.	2016	Passive exposure to agricultural pesticides and risk of childhood leukemia in an Italian community.	International journal of hygiene and environmenta health, (20161100) Vol. 219, No. 8, pp. 742-748	Not relevant for the assessment of ED effects: No specific analyses for glyphosate. Very small case control study with a very speculative exposure variable
Toxicology	Mao Q. et al.	2018	The Ramazzini Institute 13-week pilo study on glyphosate and Roundup administered at human-equivalent dose to Sprague Dawley rats: effects on the microbiome	Environmental Health , Vol. 17, (2018) pp. 12940	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate in relation to ED because no ED related endpoint was investigated (gut microbiome in dams and offspring).
Toxicology	Mao Y. et al.	2015	Effect of glyphosate on serum biochemical indices of exposed workers	Zhongguo Gongye Yixue Zazhi, (2015) Vol. 28, No. 5, pp. 362-364	Not relevant for the assessment of ED effects: The worker protections and manufacturing processes in China do not likely reflect Western occupational exposure scenarios.
Toxicology	Marcoccia D. et al.	2017	Food components and contaminants a (anti)androgenic molecules.	Genes and Nutrition, (16 Feb 2017) Vol. 12, No. 1 arn. 6	Not relevant for the assessment of ED effects: Discusses some glyphosate literature, but no new data
Toxicology	Martens M. et al.	2019	Toxicology and human health risk assessment of polyethoxylated tallow amine surfactant used in glyphosate formulations.	Regulatory toxicology and pharmacology (2019) Vol. 107, pp. 104347	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate in relation to ED as the surfactant used in glyphosate formulations was tested and evaluated instead of glyphosate.
Toxicology	Martini C. N. e al.	2016	Glyphosate Inhibits PPAR Gamma Induction and Differentiation of Preadipocytes and is able to Induce Oxidative Stress.	Journal of biochemical and molecular toxicology, (2016 Aug) Vol. 30, No. 8, pp. 404-13	Not relevant for the assessment of ED effects: Formulation tested in vitro at a single high dose in the mM range (Glifosato Atanor, 48% isopropylamine salt, 35.6% glyphosate, Argentina)
Toxicology	Mesnage R. et al.	2015	Transcriptome profile analysis reflects rat liver and kidney damage following chronic ultra-low dose Roundup exposure.	Environmental health : a global access science source, (2015 Aug 25) Vol. 14, pp. 70	Not relevant for the assessment of ED effects: Formulation tested (Grand Travaux Plus (450 g/L, Belgium) for non-validated endpoints.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Mesnage R. et al.	2015	Potential toxic effects of glyphosate and its commercial formulations below regulatory limits.	Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, (2015 Oct) Vol. 84, pp. 133-53	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: review, secondary source.
Toxicology	Mesnage R. et al.	2017	Facts and Fallacies in the Debate on Glyphosate Toxicity.	Frontiers in public health, (2017) Vol. 5, pp. 316	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: review, secondary source
Toxicology	Mesnage R. et al.	2017	Multiomics reveal non-alcoholic fatty liver disease in rats following chronic exposure to an ultra-low dose of Roundup herbicide.	Scientific reports, (20170109) Vol. 7, pp. 39328	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Formulation tested (Roundup, composition not described). Livers obtained from research of republished reteated Seralini rat study.
Toxicology	Mesnage R. et al.	2014	Major pesticides are more toxic to human cells than their declared active principles.	BioMed research international, (2014) Vol. 2014, pp. 179691	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: In vitro cytotoxicity data at high doses not informative for hazard characterization.
Toxicology	Mesnage R. et al.	2018	Ignoring Adjuvant Toxicity Falsifies the Safety Profile of Commercial Pesticides	FRONTIERS IN PUBLIC HEALTH, (22 JAN 2018) Vol. 5	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 5

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Mills P. J. et al	2017	Excretion of the Herbicide Glyphosate in Older Adults Between 1993 and 2016.	JAMA, (20171024) Vol. 318, No. 16, pp. 1610-1611	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Not relevant for EU toxicology risk assessment but supplementary information on human exposure.
Toxicology	Mohamed F. et al.	2016	Mechanism-specific injury biomarkers predict nephrotoxicity early following glyphosate surfactant herbicide (GPSH) poisoning.	Toxicology letters, (2016 Sep 06) Vol. 258, pp. 1-10	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This article discusses the use of biomarkers to predict kidney damage in formulated glyphosate overdose and predictors of nephrotoxicity in suicidal ingestions and therefore should not impact registration decisions.
Toxicology	Moon J. M. et al.	2016	The characteristics of emergency department presentations related to acute herbicide or insecticide poisoning in South Korea between 2011 and 2014.	Journal of toxicology and environmental health. Part A, (2016) Vol. 79, No. 11, pp. 466-76	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This study showed a decrease in the case fatality rate of suicidal pesticide ingestions between 2011-2014 in South Korea. This clearly demonstrates that herbicides with a lower acute toxicity profile are associated with lower mortality in suicidal ingestions.
Toxicology	Nakae H. et al.	2015	Paralytic ileus induced by glyphosate intoxication successfully treated using Kampo medicine.	Acute medicine & surgery, (20150700) Vol. 2, No 3, pp. 214-218	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This article describes alternative medicine therapies that were used to treat a Japanese woman with a paralytic ileus after glyphosate

Technical section	Author(s)	Year	Title	Source	Justification
					ingestion. It is not uncommon for patients in a critical care setting to develop an ileus. These tend to resolve on their own without intervention. It cannot be commented on whether this intervention increases GI motility. This should not impact re-registration.
Toxicology	Nardi J. et al.	2017	Prepubertal subchronic exposure to soy milk and glyphosate leads to endocrine disruption.	Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, (2017 Feb) Vol. 100, pp. 247-252	Not relevant for the assessment of ED effects: Formulation co-dosed with phytoestrogen containing vehicle.
Toxicology	Naz S. et al.	2019	Effect of glyphosate on hematological and biochemical parameters of Rabbit (Oryctolagus cuniculus)	Pure and Applied Biology (2019), Vol. 8, No. 1, pp. 78-92	Not relevant for the assessment of ED effects: Not relevant: Tested formulation 48%IPA (36.6% a.e.) . Only hematology and clinical chemistry values reported.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Nielsen L. N. c r. et al.	2017	Glyphosate has limited short-term effects on commensal bacterial community composition in the gut environment due to sufficient aromati amino acid levels	Environmental pollution (2017)	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case c) Relevance cannot be determined: The investigation of potential effects on the gut microbiome of ruminants is not a data requirement for the approval of pesticides and suitable test protocols to assess these effects are not specified in the form of official guidance documents. Therefore, the relevance of the publication is unclear.
Toxicology	Owagboriaye F. O. et al.	2017	Reproductive toxicity of Roundup herbicide exposure in male albino rat.	Experimental and toxicologic pathology : official journal of the Gesellschaft fur Toxikologische Pathologie, (2017 Sep 05) Vol. 69, No. 7, pp. 461-468	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Formulation tested in vivo (Roundup 441 g/L potassium salt, 360 g/L a.e.)
Toxicology	Ozaki T. et al.	2017	Severe Glyphosate-Surfactant Intoxication Successfully Treated With Continuous Hemodiafiltration and Direct Hemoperfusion: Case Report.	Therapeutic apheresis and dialysis : official peer-reviewed journal of the International Society for Apheresis, the Japanese Society for Apheresis, the Japanese Society for Dialysis Therapy, (20170600 Vol. 21, No. 3, pp. 296-297	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This article discusses the use of haemodialysis and haemofiltration in formulated glyphosate overdoses.This article discusses medical management of suicidal ingestions and therefore should not impact registration decisions.
Toxicology	Parajuli K. R. et al.	2015	Aminomethylphosphonic acid and methoxyacetic acid induce apoptosis in prostate cancer cells.	International journal of molecular sciences, (2015 May 22) Vol. 16, No. 5, pp. 11750-65	Not relevant for the assessment of ED effects: Therapeutic use of AMPA evaluated.
Toxicology	Park S. et al.	2016	Concurrent Hemoperfusion and Hemodialysis in Patients with Acute Pesticide Intoxication.	Blood Purification, (1 Dec 2016) Vol. 42, No. 4, pp. 329-336	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information:

Technical section	Author(s)	Year	Title	Source	Justification
					This article describes the use of haemodialysis and haemoperfusion in pesticide overdoses. Out of 383 pesticide ingestions 110 were glyphosate formulations. Of the 80 deaths reported 12 of them were glyphosate. This article describes a possibly beneficial modality of treating severe pesticide overdose and should not impact re-registration.
Toxicology	Parks C. G. et al.	2016	Rheumatoid Arthritis in Agricultural Health Study Spouses: Associations with Pesticides and Other Farm Exposures.	Environmental health perspectives, (2016 Nov) Vol. 124, No. 11, pp. 1728-1734	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Lack of information about glyphosate frequency of use and timing of use.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Perego M. C. et al.	2017	Influence of a Roundup formulation on glyphosate effects on steroidogenesis and proliferation of bovine granulosa cells in vitro.	Chemosphere, (2017 Dec) Vol. 188, pp. 274-279	Not relevant for the assessment of ED effects: In vitro formulation effects only, not glyphosate alone.
Toxicology	Perez-Torres I. et al.	2017	Beneficial Effects of the Amino Acid Glycine.	Mini reviews in medicinal chemistry, (2017) Vol. 17, No. 1, pp. 15-32	Not relevant for the assessment of ED effects: No glyphosate data
Toxicology	Picetti E. et al.	2017	Glyphosate ingestion causing multiple organ failure: A near-fatal case report.	Acta Biomedica, (2017) Vol. 88, No. 4, pp. 533-536	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This is a report concerning multiorgan failure following suicidal ingestion of formulated glyphosate and should not impact re-registration.
Toxicology	Portier C. J. et al.	2016	Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA).	Journal of epidemiology and community health, (20160800) Vol. 70, No. 8, pp. 741-5	Not relevant for the assessment of ED effects: This publication is considered not relevant because it is not based on experimental data.
Toxicology	Portier C. J. et al.	2017	Re: Tarazona et al. (2017): Glyphosat toxicity and carcinogenicity: a review of the scientific basis of the European Union assessment and its differences with IARC. doi: 10.1007/s00204-017-1962-5.	Archives of toxicology, (20170900) Vol. 91, No. 9, pp. 3195-3197	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: letter to editor, ref to Tarazona_2017
Toxicology	Pouokam G. B et al.	2017	A Pilot Study in Cameroon to Understand Safe Uses of Pesticides in Agriculture, Risk Factors for Farmers' Exposure and Management of Accidental Cases.	Toxics, (2017 Nov 01) Vol. 5, No. 4	Not relevant for the assessment of ED effects: No informative data on glyphosate
Toxicology	Ramsden J. J.	2017	Assaults on health.	Journal of Biological Physics and Chemistry, (2017) Vol. 17, No. 1, pp. 3-7	Not relevant for the assessment of ED effects: Commentary on various threats to human health.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Rebai O. et al.	2017	Morus alba leaf extract mediates neuroprotection against glyphosate-induced toxicity and biochemical alterations in the brain.	Environmental science and pollution research international, (2017 Apr) Vol. 24, No. 10, pp. 9605-9613	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Formulation administered via i.p. injection (described as a commercial formulation registered in the Tunisian Ministry of Agriculture).
Toxicology	Ren X. et al.	2019	Effects of chronic glyphosate exposur to pregnant mice on hepatic lipid metabolism in offspring.	Environmental pollution, (2019) Vol. 254, pp. 112906	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate in the context of ED as effects were investigated on hepatic lipid metabolism in offspring which are not considered in an EATS assessment.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Rendon-von O J. et al.	2017	Glyphosate Residues in Groundwater, Drinking Water and Urine of Subsistence Farmers from Intensive Agriculture Localities: A Survey in Hopelchen, Campeche, Mexico.	International journal of environmental research an public health, (20170603) Vol. 14, No. 6	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: No new information without clear relevance for the risk assessment
Toxicology	Roongruangch i J. et al.	2018	The teratogenic effects of glyphosate based herbicide (GBH) on the development of chick embryos.	Siriraj Medical Journal (2018), Volume 70, Number 5, pp. 419-428	Not relevant for the assessment of ED effects: Test substance was a glyphosate based formulation not relevant for the risk assessment
Toxicology	Roustan A. et al.	2014	Genotoxicity of mixtures of glyphosate and atrazine and their environmental transformation product before and after photoactivation	Chemosphere, (2014 Aug) Vol. 108, pp. 93-100	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 5
Toxicology	Samsel A. et al	2013	Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intolerance.	Interdisciplinary toxicology, (2013 Dec) Vol. 6, No. 4, pp. 159-84	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate because it is not based on experimental work and no epidemiologic methodology was followed.
Toxicology	Samsel A. et al	2015	Glyphosate, pathways to modern diseases III: Manganese, neurological diseases, and associated pathologies.	Surgical neurology international, (2015) Vol. 6, pp. 45	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate because it is not based on experimental work and no epidemiologic methodology was followed.
Toxicology	Samsel A. et al	2015	Glyphosate, pathways to modern diseases IV: cancer and related pathologies.	Journal of Biological Physics and Chemistry, (2015) Vol. 15, No. 3, pp. 121-159	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate because it is not based on experimental work and no epidemiologic methodology was followed.
Toxicology	Samsel A. et al	2016	Glyphosate pathways to modern diseases V: Amino acid analogue of glycine in diverse proteins.	Journal of Biological Physics and Chemistry, (2016) Vol. 16, No. 1, pp. 9-46	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate because it is

Technical section	Author(s)	Year	Title	Source	Justification
					not based on experimental work and no epidemiologic methodology was followed.
Toxicology	Samsel A. et al	2017	Glyphosate pathways to modern diseases VI: Prions, amyloidoses and autoimmune neurological diseases.	Journal of Biological Physics and Chemistry, (2017) Vol. 17, No. 1, pp. 8-32	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate because it is not based on experimental work and no epidemiologic methodology was followed.
Toxicology	Schaumburg L G. et al.	2016	Genotoxicity induced by Roundup® (Glyphosate) in tegu lizard (Salvator merianae) embryos.	Pesticide biochemistry and physiology, (2016 Jun) Vol. 130, pp. 71-78	Not relevant for the assessment of ED effects: A glyphosate based herbicide tested in lizard eggs.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Schinasi L. et al.	2014	Non-Hodgkin lymphoma and occupational exposure to agricultural pesticide chemical groups and active ingredients: a systematic review and meta-analysis.	International journal of environmental research an public health, (2014 Apr 23) Vol. 11, No. 4, pp. 4449-527	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case c) Relevance cannot be determined: The relevance of this paper is considered uncertain because it concerns a meta-analysis where the results were taken from available studies at face value. The authors had no way to correct for recall bias, confounding, etc. Therefore, the meta-RRs are in error to the extent that the studies included in the meta-analysis are in error.
Toxicology	Seneff S. et al.	2015	Death as a drug side effect in FAERS: is glyphosate contamination a factor?	Agricultural Sciences (2015), Vol. 6, No. 12, pp. 1472-1501	Not relevant for the assessment of ED effects: Hypothesis discussed without any empirical data
Toxicology	Seneff S. et al.	2017	Can glyphosate's disruption of the gut microbiome and induction of sulfate deficiency explain the epidemic in gout and associated diseases in the industrialized world?.	Journal of Biological Physics and Chemistry, (2017) Vol. 17, No. 2, pp. 53-76	Not relevant for the assessment of ED effects: Not relevant as the study is not based upon experimental work and no epidemiologic methodology was followed. Results and proposed mode of actions are pure speculation without any experimental proof.
Toxicology	Seralini G. et al.	2014	Republished study: long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modifie maize.	Environmental sciences Europe, (2014) Vol. 26, No. 1, pp. 14	Not relevant for the assessment of ED effects: This publication is considered not relevant for risk assessment of glyphosate a a glyphosate formulation was used instead of glyphosate.
Toxicology	Shaw W.	2017	Elevated Urinary Glyphosate and Clostridia Metabolites With Altered Dopamine Metabolism in Triplets With Autistic Spectrum Disorder or Suspected Seizure Disorder: A Case Study.	Integrative medicine (Encinitas, Calif.), (2017 Feb Vol. 16, No. 1, pp. 50-57	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This is a limited case study of 3 individuals, with minimal data on glyphosate exposure.
Toxicology	Shehata A. A. et al.	2014	Neutralization of the antimicrobial effect of glyphosate by humic acid in vitro.	Chemosphere, (2014 Jun) Vol. 104, pp. 258-61	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case

Technical section	Author(s)	Year	Title	Source	Justification
					c) Relevance cannot be determined: The investigation of potential effects on the gut microbiome of ruminants is not a data requirement for the approval of pesticides and suitable test protocols to assess these effects are not specified in the form of official guidance documents. Therefore, the relevance of the publication is unclear. In the absence of a suitable dossier datapoint it was allocated to point KCA 6.4 since it concerns livestock. However, it is important to note that it is not a residue study and does not provide any data on the transfer of residues from feed to food of animal origin.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Solomon K.	2017	WHAT IS THE PROBLEM WITH GLYPHOSATE?	Outlooks on Pest Management, Vol. 28, No. 4, pp. 173-174, 20170801	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Review of IARC deficiencies.
Toxicology	Solomon K. R.	2016	Glyphosate in the general population and in applicators: a critical review of studies on exposures.	Critical reviews in toxicology, (2016 Sep) Vol. 46 No. sup1, pp. 21-27	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: review, secondary source
Toxicology	Sorahan T.	2015	Multiple myeloma and glyphosate use a re-analysis of US Agricultural Health Study (AHS) data.	International journal of environmental research an public health, (2015 Jan 28) Vol. 12, No. 2, pp. 1548-59	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 5
Toxicology	Sorahan T.	2017	Visualising and thinking and interpreting. Response to the burstyn and de roos comments on sorahan, t. multiple myeloma and glyphosate use A re-analysis of us agricultural health study (AHS) data. Int. j. environ. res. public health 2015, 12, 1548-1559	International Journal of Environmental Research and Public Health (1 Jan 2017) Vol. 14, No. 1, arn 6	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Letter to Editor
Toxicology	Stipicevic S.	2017	Some organophosphate insecticides and herbicides	Arhiv Za Higijenu Rada i Toksikologiju, Vol. 68, No. 2, pp. A10-A11, 20170401	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Commentary on IARC evaluation.
Toxicology	Stur E. et al.	2019	Glyphosate-based herbicides at low doses affect canonical pathways in estrogen positive and negative breast cancer cell lines.	PloS one, (2019) Vol. 14, No. 7, pp.	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate with relation to ED because AMPA was tested at concentrations in vitro that are physiologically not feasible in vivo (10 mM).

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Suarez-Larios K. et al.	2017	Screening of Pesticides with the Potential of Inducing DSB and Successive Recombinational Repair	Journal of Toxicology, 20170101	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 5.
Toxicology	Szabo R. et al.	2017	Studies on joint toxic effects of a glyphosate herbicide (Fozat 480) and heavy metal (cadmium) on chicken embryos.	AGROFOR International Journal (2017), Vol. 2, No. 3, pp. 37-43	Not relevant for the assessment of ED effects: A glyphosate based herbicide applied to fertilized chicken eggs, not relevant to human health risk assessment.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Szemeredy Geza et al.	2016	TOXICITY TEST OF INDIVIDUAL AND COMBINED TOXIC EFFECTS OF HERBICIDE GLIALKA STAR AND LEAD-ACETATE ON CHICKEN EMBRYOS. Original Title: GLIALKA STAR GYOMIRTO SZER ES AZ OLOM-ACETAT EGYEDI ES INTERAKCIOS TOXICITASANAK VIZSGALATA MADAREMBRIOKBAN.	Novenyvdelem, (OCT 2016) Vol. 52, No. 10, pp. 483-487	Not relevant for the assessment of ED effects: Formulation tested via injection to chicken embryos.
Toxicology	Tang J. et al.	2017	Ion Imbalance Is Involved in the Mechanisms of Liver Oxidative Damage in Rats Exposed to Glyphosate.	Frontiers in physiology, (2017) Vol. 8, pp. 1083	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 5.
Toxicology	Tarazona J. V. et al.	2017	Glyphosate toxicity and carcinogenicity: a review of the scientific basis of the European Union assessment and its differences with IARC.	Archives of toxicology, (2017 Aug) Vol. 91, No. 8 pp. 2723-2743	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Comparison of EU regulatory review with IARC evaluation.
Toxicology	Tarazona J. V. et al.	2017	Response to the reply by C. J. Portier and P. Clausing, concerning our review "Glyphosate toxicity and carcinogenicity: a review of the scientific basis of the European Union assessment and its differences with IARC".	Archives of toxicology, (20170900) Vol. 91, No. 9, pp. 3199-3203	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: letter to editor, ref to Tarazona_2017.
Toxicology	Tincher C. et al.	2017	The Glyphosate-Based Herbicide Roundup Does not Elevate Genome-Wide Mutagenesis of Escherichia coli	G3 (Bethesda, Md.), (2017 Oct 05) Vol. 7, No. 10, pp. 3331-3335	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate because a glyphosate formulation was used instead of glyphosate for in vitro testing.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Townsend M. et al.	2017	Evaluation of various glyphosate concentrations on DNA damage in human Raji cells and its impact on cytotoxicity.	Regulatory toxicology and pharmacology : RTP, (2017 Apr) Vol. 85, pp. 79-85	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case a) relevant and provides data for the risk assessment: Summary is provided in MCA 5.
Toxicology	Tribe D.	2013	Serious inadequacies regarding the pathology data presented in the paper by Seralini et al. (2012).	Food and Chemical Toxicology, (MAR 2013) Vol 53, pp. 452-457	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Letter to Editor
Toxicology	Upadhyay J. et al.	2019	Biomarker responses (serum biochemistry) in pregnant female wistar rats and histopathology of their neonates exposed prenatally to pesticides.	Brazilian Journal of Pharmaceutical Sciences, (2019) Vol. 55. http://www.bcq.usp.br/revista_brasileira_de_cienc as.htm. ISSN: 1984-8250. E-ISSN: 2175-9790.	Not relevant for the assessment of ED effects: Formulation is not relevant for the ED risk assessment
Toxicology	Vandenberg L. N. et al.	2017	Is it time to reassess current safety standards for glyphosate-based herbicides?.	Journal of epidemiology and community health, (2017 Jun) Vol. 71, No. 6, pp. 613-618	Not relevant for the assessment of ED effects: This publication is considered not relevant because it is not based on experimental work.
Toxicology	Vinceti M. et al.	2017	Pesticide exposure assessed through agricultural crop proximity and risk of amyotrophic lateral sclerosis.	Environmental Health: A Global Access Science Source, (29 Aug 2017) Vol. 16, No. 1. arn. 91	Not relevant for the assessment of ED effects: No correlations wih glyphosate use and effect.
Toxicology	Von Ehrenstein O. et al.	2019	Prenatal and infant exposure to ambient pesticides and autism spectrum disorder in children: Population based case-control study	BMJ (Online) (2019) Volume 364, DOI: 10.1136/bmj.l962	Not relevant for the assessment of ED effects: This publication is not relevant for the risk assessment of glyphosate in relation to ED as the pathology investigated is not ED related (autism spectrum disorder in children).
Toxicology	Williams G. M et al.	2016	A review of the carcinogenic potential of glyphosate by four independent expert panels and comparison to the IARC assessment.	Critical reviews in toxicology, (2016 Sep) Vol. 46 No. sup1, pp. 3-20	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: review, secondary source
Toxicology	Williams G. M et al.	2016	Glyphosate rodent carcinogenicity bioassay expert panel review.	Critical reviews in toxicology, (2016 Sep) Vol. 46 No. sup1, pp. 44-55	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case

Technical section	Author(s)	Year	Title	Source	Justification
					b) Relevant but supplementary information: review, secondary source
Toxicology	Youness E. R. et al.	2016	The protective effect of orange juice on glyphosate toxicity in adult male mice.	Journal of Chemical and Pharmaceutical Research (2016), Vol. 8, No. 3, pp. 13-28	Not relevant for the assessment of ED effects: Excessively high gavage doses to rats
Toxicology	Yu G. C. et al.	2017	The clinical analytics of 10 patients with acute glyphosate poisoning	Zhonghua lao dong wei sheng zhi ye bing za zhi = Zhonghua laodong weisheng zhiyebing zazhi = Chinese journal of industrial hygiene and occupational diseases, (2017 May 20) Vol. 35, No 5, pp. 382-383	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This is a case series describing the clinical course of 10 patients who drank formulated glyphosate. All 10 patients survived the ingestion with no long-lasting sequelae. These were suicdal ingestions and should not impact re-registration.
Toxicology	Yu Ning T. et al.	2018	Circular RNA expression profiles in hippocampus from mice with perinata glyphosate exposure.	Biochemical and biophysical research communications, (2018) Vol. 501, No. 4, pp. 838-845	Not relevant for the assessment of ED effects: This publication is considered not relevant for risk assessment of glyphosate in relation to ED as a non-ED related endpoint was investigated (circular RNA expression profiles in the hippocampus).
Toxicology	Zhang C. et al.	2016	Health effect of agricultural pesticide use in China: implications for the development of GM crops	Scientific reports, (20161010) Vol. 6, pp. 34918	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Results likely valid for glyphosate under the exposure circumstances of the study, but not an appropriate design for chronic health effects. Short follow-up and limited exposure histories.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Zhang F. et al.	2017	Study of the effect of occupational exposure to glyphosate on hepatorena function.	Zhonghua yu fang yi xue za zhi [Chinese journal of preventive medicine], (2017 Jul 06) Vol. 51, No. 7, pp. 615-620	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: Very poorly described study design, methods, and analysis. Seemingly cross-sectional in time orientation precluding causal evaluation.
Toxicology	Zhang L. et al.	2019	Exposure to glyphosate-based herbicides and risk for non-Hodgkin lymphoma: A meta-analysis and supporting evidence.	Mutation research, (2019) Vol. 781, pp. 186-206	Not relevant for the assessment of ED effects: This publication is considered not relevant for the risk assessment of glyphosate in relation to ED as a non-ED related pathology was investigated in this study (non-Hodgkin lymphoma).
Toxicology	Zoccali C.	2017	Causal mechanism and component causes in Mesoamerican-Sri Lankan nephropathy: the moderator's view	NEPHROLOGY DIALYSIS TRANSPLANTATION, (APR 2017) Vol. 32, No. 4, pp. 607-610	Not relevant for the assessment of ED effects: no glyphosate specific information
Toxicology	Zouaoui K. et al.	2013	Determination of glyphosate and AMPA in blood and urine from humans: about 13 cases of acute intoxication.	Forensic science international, (2013 Mar 10) Vol. 226, No. 1-3, pp. e20-5	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This is a report on a series of formulated glyphosate overdoses that found that higher blood and urine concentrations of glyphosate were associated with a poorer outcome. This is not surprising, as it reflects that patients drank a larger volume. Larger volumes of formulated product are associated with more toxicity due to the caustic nature of the surfactant, not the amount of active ingredient. All of the laboratory parameters are expected in critically ill patients. As these were suicidal ingestions, this paper should not impact re-registration.

Technical section	Author(s)	Year	Title	Source	Justification
Toxicology	Zyoud S. H. et al.	2017	Global research production in glyphosate intoxication from 1978 to 2015: A bibliometric analysis.	Human & experimental toxicology, (2017 Oct) Vol. 36, No. 10, pp. 997-1006	Not relevant for the assessment of ED effects, but relevant for the general literature review. Assessment for the general LRR: 5.4.1 case b) Relevant but supplementary information: This article analyzes the reports of increase in glyphosate intoxications from the early 1970s-2016. Given the increase in use over the same time period it is not surprising that there has been an increase in reporting. This should not impact re-registration.

Table 7: Relevant studies included in a dossier/Assessment Report after detailed assessment of full-text documents for relevance: sorted by data requirement(s)

KCA Datapoint	Author(s)	Year	Title	Source	Classification according to EFSA Guidance 2092 Point 5.4.1
Toxicology					
KCA 5.8.3	Kongtip P. et al.	2019	Thyroid Hormones in Conventional and Organic Farmers in Thailand.	International journal of environmental research and public health, (2019) Vol. 16, No. 15. Electronic Publication Date: 29 Jul 2019	5.4.1 case b) Relevant but supplementary information. This publication is considered relevant but supplementary for the risk assessment of glyphosate du to the higher incidence of thyroid disease in women (more numerous in organic farming), no data on the menopausal status of the women (change in thyroid hormones), the collection of data with diaries of the farmers may be incomplete, the exposure of farmers to pesticides prior to the study and prior to starting organi farming, and the results for glyphosate should have bee examined for confounding from other pesticides that were correlated with glyphosate use. Moreover, the use rate and bioavailability (Acquavella et al. (2004)

KCA Datapoint	Author(s)	Year	Title	Source	Classification according to EFSA Guidance 2092 Point 5.4.1
					Environmental Health Perspectives Vol. 112(3), 321-326; Acquavella et al. (2006) Epidemiology, Vol. 17(1) 69-74) of glyphosate was lower than that of the other pesticides used. Since the determination of serum thyroid hormone levels is key in this study, the methods of analysis should have been better documented.
KCA 5.8.3	Parvez S. et al.	2018	Glyphosate exposure in pregnancy and shortened gestational length: a prospective Indiana birth cohort study	Environmental Health, (2018) Vol. 17, pp. 23	5.4.1 case b) Relevant but supplementary information. This publication is considered relevant but supplementary for the risk assessment of glyphosate as the number of pregnancies followed was too low and no data are available on urinary concentrations of other pesticides and environmental chemicals.
KCA 5.8.3	Pinto L. et al.	2018	Identification of candidate reference chemicals for in vitro steroidogenesis assays	Toxicology In Vitro, (2018) Vol. 47, pp. 103-119	5.4.1 case b) Relevant but supplementary information. Relevant secondary information
KCA 5.8.3	Rappazzo K. et al	2019	Maternal residential exposure to specific agricultural pesticide active ingredients and birth defect in a 2003-2005 North Carolina birth cohort.	Birth defects research, (2019) Vol. 111, No. 6, pp. 312-323	5.4.1 case b) Relevant but supplementary information This publication is considered relevant but supplementary for the risk assessment of glyphosate because of the small number of specific birth defects. Although confounding by co-occurring pesticides has been considered in this study the potential for confounding by joint pesticide exposures and other environmental factors cannot be excluded.
KCA 5.8.3	Shrestha S. et al.	2018	Incident thyroid disease in female spouses of private pesticide applicators.	Environment International, (September 2018) Vol. 118, pp. 282-292	5.4.1 case b) Relevant but supplementary information. Not a glyphosate specific study.
KCA 5.8.3	Shrestha S. et al.	2018	Pesticide use and incident hypothyroidism in pesticide applicators in the agricultural health study	Environmental Health Perspectives (2018) Volume 126, Number 9, 11 p.	5.4.1 case b) Relevant but supplementary information. Not a glyphosate specific study. Self-reporting had inconsistencies at age of diagnosis, moreover only 32% of self-reported disease was confirmed by medical records.
KCA 5.3	Owagboriaye F. et al.	2019	Comparative studies on endogenic stress hormones, antioxidant, biochemical and hematological	Environmental science and pollution research international, (2019) Vol. 26, No. 14, pp. 14502-14512	5.4.1 case b) Relevant but supplementary information Considering this study represent a repeated-exposure, 90-day study desing, several deviations can be

KCA Datapoint	Author(s)	Year	Title	Source	Classification according to EFSA Guidance 2092 Point 5.4.1
			status of metabolic disturbance in albino rat exposed to roundup herbicide and its active ingredient glyphosate.		identified from the guidance document: 1. no proper identification of the test substance presented 2. no proper description of the animals, housing conditions are reported 3. number of animals used in the dose groups is less than suggested 4. no pathology were performed 5. no historical control data mentioned 6. no clinical findings or body weight measurements recorded.
KCA 5.4	De Almeida L. et al.	2018	Moderate levels of glyphosate and its formulations vary in their cytotoxicity and genotoxicity in a whole blood model and in human cell lines with different estrogen receptor status	3 BIOTECH, (2018) Vol. 8, No. 10. ISSN: 2190-572X.	5.4.1 case b) Relevant but supplementary information. Mixed study design: in the Comet assay only 2 doses were established.
KCA 5.4	Defarge N. et al.	2018	Toxicity of formulants and heavy metals in glyphosate-based herbicides and other pesticides.	Toxicology reports, (2018) Vol. 5, pp. 156-163	5.4.1 case b) Relevant but supplementary information Article is not glyphosate specific. Concentration groups are not properly described, moreover the chosen concentrations are high for in vitro studies and not applicable to test aromatase inhibition.
KCA 5.6	Dai P. et al.	2016	Effect of glyphosate on reproductive organs in male rat.	Acta Histochemica 118 (2016) 519–526	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.6	Forgacs A. et al.	2012	BLTK1 murine Leydig cells: a novel steroidogenic model for evaluating the effects of reproductive and developmental toxicants.	TOXICOLOGICAL SCIENCES 127 (2), 391–402 (2012)	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.6	Johansson H. et al	2018	Exposure to a glyphosate-based herbicide formulation, but not glyphosate alone, has only minor effects on adult rat testis.	Reproductive toxicology(2018) Vol. 82, pp. 25-31	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.6	Manservisi F. et al.	2019	The Ramazzini Institute 13-week pilot study glyphosate-based herbicides administered at human-	Environmental health : a global access science source, (2019) Vol. 18, No. 1, pp 15	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment

KCA Datapoint	Author(s)	Year	Title	Source	Classification according to EFSA Guidance 2092 Point 5.4.1
			equivalent dose to Sprague Dawley rats: effects on development and endocrine system.		
KCA 5.6	Panzacchi S. et al.	2018	The Ramazzini Institute 13-week study on glyphosate-based herbicides at humanequivalent dose in Sprague Dawley rats: study design and first in-life endpoints evaluation	Environmental Health, (2018) Vol. 17, pp. 52	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.6	Perego M. et al.	2016	Evidence for direct effects of glyphosate on ovarian function: glyphosate influences steroidogenesis and proliferation of bovine granulosa but not theca cells in vitro.	Journal of applied toxicology (2017) Vol 37, No. 6, pp. 692-698	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.6	Pham T. et al.	2019	Perinatal Exposure to Glyphosate and a Glyphosate-Based Herbicid Affect Spermatogenesis in Mice.	Toxicological sciences(2019) Vol. 169, No. 1, pp. 260-271	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.6	Ren X. et al.	2018	Effects of glyphosate on the ovarian function of pregnant mice the secretion of hormones and the sex ratio of their fetuses.	Environmental pollution (2018) Vol. 243 No. Pt B, pp. 833-841	5.4.1 case b) Relevant but supplementary information. Substance was not sufficiently characterized, moreover only one dose was considered as glyphosate and as RoundUp exposure group.
KCA 5.6	Sritana N. et al.	2018	Glyphosate induces growth of estrogen receptor alpha positive cholangiocarcinoma cells via non-genomic estrogen receptor/ERK1/2 signaling pathway.	Food and chemical toxicology (2018) Vol. 118, pp. 595-607	5.4.1 case b) Relevant but supplementary information. No replicates had been used in the study, the incubation time was an extended 40 h, the active substance identification is not entirely complete, moreover the cel line selection is not explained.
KCA 5.6	Wrobel M. et al.	2018	Glyphosate affects the secretion o regulators of uterine contractions in cows while it does not directly impair the motoric function of myometrium in vitro.	Toxicology and applied pharmacology, (2018) Vol. 349, pp. 55-61	5.4.1 case b) Relevant but supplementary information This publication is considered relevant but supplementa for the risk assessment of glyphosate as the glyphosate used is not sufficiently characterized and the analysis o

KCA Datapoint	Author(s)	Year	Title	Source	Classification according to EFSA Guidance 2092 Point 5.4.1
					glyphosate, hormones and prostaglandins is not sufficiently documented.
KCA 5.6	Gorga A. et al.	2019	In vitro effects of glyphosate and Roundup on Sertoli cell physiology.	Toxicology in vitro : an international journal published in association with BIBRA,Electronic Publication Date: 15 Oct 2019 Journal code: 8712158. E-ISSN: 1879-3177. L-ISSN: 0887-2333.	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.6	Zhang J. et al.	2019	The toxic effects and possible mechanisms of glyphosate on mouse oocytes.	Chemosphere, (2019) Vol. 237, pp. 124435	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.7	Gallegos C. et al.	2018	Perinatal Glyphosate-Based Herbicide Exposure in Rats Alters Brain Antioxidant Status, Glutamate and Acetylcholine Metabolism and Affects Recognition Memory.	Neurotoxicity research, (2018) Vol. 34, No. 3, pp. 363-374	5.4.1 case b) Relevant but supplementary information Not relevant as only a glyphosate based herbicide was used as test material, in two established doses. As supportive information can be transferred to the general LRR.
KCA 5.8.3	Brennan JC. et al.	2016	Development of a recombinant human ovarian (BG1) cell line containing oestrogen receptor alpha and beta for improved detection of oestrogenic/ Antioestrogenic chemicals; study supplementary	Environ Toxicol Chem. (2016) 35:91-100.	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.8.3	Defarge N. et al.	2016	Coformulants in glyphosate-based herbicides disrupt aromatase activity in human cells below toxi levels; study supplementary	Int J Environ Res Public Health. 2016 Feb 26;13(3).	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.8.3	George A. et al.	2018	The effect of glyphosate on human sperm motility and sperm DNA fragmentation	International Journal of Environmental Research and Public Health (2018) Vol. 15, 1117	5.4.1 case b) Relevant but supplementary information This publication is considered relevant but supplementa as the glyphosate used is not characterized, only one tes concentration was used, no positive control was considered and the results obtained are not corroborated by in vivo regulatory reproductive toxicology studies with much higher systemic levels of glyphosate.

KCA Datapoint	Author(s)	Year	Title	Source	Classification according to EFSA Guidance 2092 Point 5.4.1
KCA 5.8.3	Gigante P. et al.	2018	Glyphosate affects swine ovarian and adipose stromal cell functions	Animal reproduction science, (2018) Vol 195, pp. 185-196	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.8.3	Martina B. et al.	2019	Quizalofop-p-Ethyl Induces Adipogenesis in 3T3-L1 Adipocytes	TOXICOLOGICAL SCIENCES, 170, (2019), 452–461	5.4.1 case a) relevant and provides data for the risk assessment: This publication is considered relevant for the risk assessment of glyphosate and reliable without restrictions.
KCA 5.8.3	Mesnage R. et al.	2017	Evaluation of estrogen receptor alpha activation by glyphosate-based herbicide constituents.	Food and Chemical Toxicology 108 (2017) 30-42	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.8.3	Sakpa C. et al.	2018	Effects of glyphosate on sperm parameters and pregnancy success rate in Wistar rats.	Annals of Biomedical Sciences (2018), Volume 17, Number 2, pp. 156-164	5.4.1 case b) Relevant but supplementary information This publication is considered relevant but supplementary for the risk assessment of glyphosate because the glyphosate used is not sufficiently characterized, only two dose levels were tested and the number of animals used per dose level was too low.
KCA 5.8.3	Santos R. et al.	2019	Thyroid and reproductive hormones in relation to pesticide use in an agricultural population i Southern Brazil.	Environmental Research, (2019) pp. 221-231	5.4.1 case b) Relevant but supplementary information. Exposure related information based on biased recall data.
KCA 5.8.3	Thongprakaisang S. et al.	2013	Glyphosate induces human breast cancer cells growth via estrogen receptors.	Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, (2013) Vol. 59, pp. 129-36.	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.8.3	Vanlaeys A. et al.	2018	Formulants of glyphosate-based herbicides have more deleterious impact than glyphosate on TM4 Sertoli cells.	Toxicology in vitro : an international journal published in association with BIBRA, (2018) Vol. 52, pp. 14-22	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
KCA 5.8.3	Zhao H. et al.	2018	Effects of Glyphosate on Testosterone Synthesis in Male Rats.	Asian Journal of Ecotoxicology, (2018) Vol. 13, No. 5, pp. 242-247	5.4.1 case b) Relevant but supplementary information This publication is considered relevant but supplementa for the risk assessment of glyphosate but reliable with restrictions because the reporting of the experimental conditions is not complete.

KCA Datapoint	Author(s)	Year	Title	Source	Classification according to EFSA Guidance 2092 Point 5.4.1
Ecotoxicology					
KCA 8.1.4	Verderame M. et al.	2019	How Glyphosate Impairs Liver Condition in the Field Lizard Podarcis siculus (Rafinesque-Schmaltz, 1810): Histological and Molecular Evidence.	BioMed research international, (2019) Vol. 2019, pp. 4746283	5.4.1 case b) Relevant but supplementary information Whilst the product was idenitifed, the details of the environmental considitons under which the sperm were assessed is not clearly stated, therefore the influence of factors other than glyphosate are not considered. pH an co-formulant toxicity should be have been considered i the assessment. Only two doses were tested, therefore no dose-dependent ECx values can be determined. Histological results were not statistically analysed and results from the expression analysis do not follow a clear dose-response relationship. Additionally, no verification of the test substance was performed. This assessment is considered supplementary to the ED assessment as specific endpoints relevant to ESFA GD approach for ED evaluation are not considered.
KCA 8.2.1	Druate C. et al.	2017	A full life-cycle bioassay with Cantareus aspersus shows reproductive effects of a glyphosate-based herbicide suggesting potential endocrine disruption.	Environmental pollution, (2017) Vol. 226, pp. 240-249	5.4.1 case b) Relevant but supplementary information The test design is novel and the achieved endpoints cannot be related to an EU level ecotoxicology risk assessment for an Annex I renewal.
KCA 8.2.2	Fiorino E. et al.	2018	Effects of glyphosate on early life stages: comparison between Cyprinus carpio and Danio rerio.	Environmental science and pollution research international, (2018) Vol. 25, No. 9, pp. 8542-8549	5.4.1 case b) Relevant but supplementary information. No detailed information on the test substance is given and the results are not compliant with given validity criteria for the hatching rate after 96 h (< 80%).
KCA 8.2.2	Le Mer C. et al.	2013	Effects of chronic exposures to th herbicides atrazine and glyphosate to larvae of the threespine stickleback (Gasterosteus aculeatus).	Ecotoxicol. Environ. Saf. 89: 174-181.	5.4.1 case a) relevant and provides data for the risk assessment: Summary of the publication is provided with the ED assessment
KCA 8.2.2	Maskey E. et al.	2019	Disruption of oocyte maturation by selected environmental chemicals in zebrafish.	Toxicology in vitro : an international journal published in association with BIBRA, (2019) Vol. 54, pp. 123-129	5.4.1 case b) Relevant but supplementary information The findings in the study consider exposure concentrations that are much higher than would be

KCA Datapoint	Author(s)	Year	Title	Source	Classification according to EFSA Guidance 2092 Point 5.4.1
					expected following a field application at the max gap application rate. No analytical measurements of the test substance were performed. The test conditions of the toxicity tests (e.g. pH) are not described in detail. Supplemental information.
KCA 8.2.2	Smith C. et al.	2019	Developmental and epigenetic effects of Roundup and glyphosat exposure on Japanese medaka (Oryzias latipes).	Aquatic toxicology, (2019) Vol. 210, pp. 215-226	5.4.1 case b) Relevant but supplementary information. Test conditions such as duration are only generally described (e.g.100-120 days). Only one test concentration was tested, therefore no ECx values coul be derived. Additionally, no verification of the test substance was performed and the influence of the different co-formulants on the results cannot be elucidated in the study. Therefore this paper is considered supplementary.
KCA 8.2.2	Zhang S. et al.	2017	Biological impacts of glyphosate on morphology, embryo biomechanics and larval behavior in zebrafish (Dartio rerio).	Chemosphere, (2017) Vol. 181, pp. 270-280	5.4.1 case b) Relevant but supplementary information. Results of control mortality (graphic) donot seem to meet validity criteria from OECD 236, which is similar to the test design at this time point of the study. Possibl effects due to a lower pH caused by higher glyphosate concentrations cannot be excluded. Additionally, no analytical measurements of the test substance were performed and no effect concentrations were derived fo glyphosate. Therefore, the study is considered supplementary only.
KCA 8.2.3	Xie L. et al.	2005	Evaluation of Estrogenic Activities of Aquatic Herbicides and Surfactants Using an Rainbow Trout Vitellogenin Assay	Toxicol. Sci. (2005) 87:91-8.	5.4.1 case b) Relevant but supplementary information. The results of this study demonstrate that glyphosate di not induce production of VTG, providing additional evidence that glyphosate does not have oestrogenic activity.
KCA 8.2.8	Avigliano L. et al.	2018	Effects of Glyphosate on Somatic and Ovarian Growth in the Estuarine Crab Neohelice granulata, During the Pre-Reproductive Period	Water, air, and soil pollution (2018), Volume 229, Number 2, 44 p.	5.4.1 case b) Relevant but supplementary information. The documentation of the results is not described in detail and influence of a lower pH caused by glyphosat cannot be excluded. Therefore, the study cannot be regarded as reliable .

KCA Datapoint	Author(s)	Year	Title	Source	Classification according to EFSA Guidance 2092 Point 5.4.1
KCA 8.2.8	Bonfanti P. et al.	2018	A glyphosate micro-emulsion formulation displays teratogenicity in Xenopus laevis.	Aquatic toxicology, (2018) Vol. 195, pp. 103-113	5.4.1 case b) Relevant but supplementary information. The study analyses teratogenic effects and abnormalities (e.g. oedema (cardiac, abdominal, facial), blisters, craniofacial defects) after short term exposure of frog embryos. The study was not performed under GLP with minor deviations from the guidance (ASTM 1438). Scientific value for the ED assessment is reduced by missing analytical measurements of the test substance. Supplemental information .
KCA 8.2.8	Canosa I. et al.	2019	Imbalances in the male reproductive function of the estuarine crab Neohelice granulata, caused by glyphosate	Ecotoxicology and Environmental Safety 182 (2019) 109405	5.4.1 case b) Relevant but supplementary information. Results of the analytical measurements indicate a high variation of exposure concentration (80 – 166%). Additionally, no results on pH values from the exposure media are presented. Due to the acidic properties of glyphosate, an influence of a potentially lower pH compared to the control exposure groups cannot be excluded from the available data.
KCA 8.2.8	de Brito Rodrigue L. et al.	2019	Impact of the glyphosate-based commercial herbicide, its components and its metabolite AMPA on non-target aquatic organisms.	Mutation research, (2019 Jun) Vol. 842, pp. 94-101	5.4.1 case b) Relevant but supplementary information The findings in the study for AMPA and glyphosate are relevant to the Annex I level renewel discussion, but as there was no analytical supporting data for the analysis of glyphosate and AMPA in the exposure media, the data can only be considered as supplementary.
KCA 8.2.8	Howe C.M. et al.	2004	Toxicity of Glyphosate-based pesticides to four American frog species	Environmental Toxicology and Chemistry, Vol. 23, No. 8, pp. 1928–1938	5.4.1 case b) Relevant but supplementary information The test design is not well described. The mortality rate of the control group during the experiment was 38%, which is clearly above suggested validity criteria from guidelines comparable to this study (≤ 20% mortality specified in OECD 241). Furthermore, no references were given to prove that this result is “not unexpected” or to verify that other endpoints e.g. the developmental time to be acceptable.

KCA Datapoint	Author(s)	Year	Title	Source	Classification according to EFSA Guidance 2092 Point 5.4.1
KCA 8.2.8	Quassinti L. et al.	2015	Toxicity of Cupside 480SL® Spray Mixture Formulation Of Glyphosate To Aquatic Organism	Pesticide Biochemistry and Physiology, Vol. 93, pp. 91-95	5.4.1 case b) Relevant but supplementary information. No information on the test substance is given and no analytical measurements of the test substance were performed. The exposure conditions (especially pH values) are not described in detail. A positive control should have been tested to verify the suitability and to assess test validity of the test. Additionally, it is difficul to extrapolate effects from this in vitro test to exposed whole organisms. Therefore, the study is regarded as not reliable.

Table 8: Relevant studies included in the dossier/Assessment Report after detailed assessment of full-text documents for relevance: sorted by author(s)

Author(s)	Title	Source	Year	Sanco datapoint (KCA)	Classification according to EFSA Guidance 2092 Point 5.4.1
Ecotoxicology					
Avigliano L. et al.	Effects of Glyphosate on Somatic and Ovarian Growth in the Estuarine Crab Neohelice granulata, During the Pre-Reproductive Period	Water, air, and soil pollution (2018), Volume 229, Number 2, 44 p.	2018	KCA 8.2.8	5.4.1 case b) Relevant but supplementary information. The documentation of the results is not described in detail and influence of a lower pH caused by glyphosate cannot be excluded. Therefore, the study cannot be regarded as reliable .
Bonfanti P. et al.	A glyphosate micro-emulsion formulation displays teratogenicity in Xenopus laevis.	Aquatic toxicology, (2018) Vol. 195, pp. 103-113	2018	KCA 8.2.8	5.4.1 case b) Relevant but supplementary information. The study analyzes teratogenic effects and abnormalities (e.g. oedema (cardiac, abdominal, facial), blisters, craniofacial defects) after short term exposure of frog embryos. The study was not performed under GLP with minor deviations from the guidance (ASTM 1438). Scientific value for the ED assessment is reduced by missing analytical measurements of the test substance. Supplemental information

Author(s)	Title	Source	Year	Sanco datapoint (KCA)	Classification according to EFSA Guidance 2092 Point 5.4.1
Canosa I. et al.	Imbalances in the male reproductive function of the estuarine crab Neohelice granulata, caused by glyphosate	Ecotoxicology and Environmental Safety 182 (2019) 109405	2019	KCA 8.2.8	5.4.1 case b) Relevant but supplementary information. Results of the analytical measurements indicate a high variation of exposure concentration (80 – 166%). Additionally, no results on pH values from the exposure media are presented. Due to the acid properties of glyphosate, an influence of a potentially lower pH compared to the control exposure groups cannot be excluded from the available data.
de Brito Rodrigues L. et al.	Impact of the glyphosate-based commercial herbicide, its components and its metabolite AMPA on non-target aquatic organisms.	Mutation research, (2019 Jun) Vol. 842, pp. 94-101	2019	KCA 8.2.8	5.4.1 case b) Relevant but supplementary information. The findings in the study for AMPA and glyphosate are relevant to the Annex I level reneweal discussion, but as there was no analytical supporting data for the analysis of glyphosate and AMPA in the exposure media, the data can only be considered as supplementary.
Druate C. et al.	A full life-cycle bioassay with Cantareus aspersus shows reproductive effects of a glyphosate-based herbicide suggesting potential endocrine disruption.	Environmental pollution, (2017) Vol. 226, pp. 240-249	2017	KCA 8.2.1	5.4.1 case b) Relevant but supplementary information The test design is novel and the achieved endpoints cannot be related to an EU level ecotoxicologyrisk assessment for an Annex I renewal.
Fiorino E. et al.	Effects of glyphosate on early life stages: comparison between Cyprinus carpio and Danio rerio.	Environmental science and pollution research international, (2018) Vol. 25, No. 9, pp. 8542-8549	2018	KCA 8.2.2	5.4.1 case b) Relevant but supplementary information. No detailed information on the test substance is given and the results are not compliant with given validity criteria for the hatching rate after 96 h (< 80%).
Howe C.M. et al.	Toxicity of Glyphosate-based pesticides to four American frog species	Environmental Toxicology and Chemistry, Vol. 23, No. 8 pp. 1928–1938	2004	KCA 8.2.8	5.4.1 case b) Relevant but supplementary information The test design is not well described. The mortality rate of the control group during the experiment was 38%, which is clearly above suggested validity criteria from guidelines comparable to this study (≤ 20% mortality specified in OECD 241). Furthermore, no references were given to prove that this result is “not unexpected” or to verify that other endpoints e.g. the developmental time to be acceptable.

Author(s)	Title	Source	Year	Sanco datapoint (KCA)	Classification according to EFSA Guidance 2092 Point 5.4.1
Le Mer C. et al.	Effects of chronic exposures to the herbicides atrazine and glyphosate to larvae of the threespine stickleback (Gasterosteus aculeatus).	Ecotoxicol. Environ. Saf. 89: 174-181.	2013	KCA 8.2.2	5.4.1 case a) relevant and provides data for the risk assessment: Summary of the publication is provided with the ED assessment
Maskey E. et al.	Disruption of oocyte maturation by selected environmental chemicals in zebrafish.	Toxicology in vitro : an international journal published in association with BIBRA, (2019) Vol. 54, pp. 123-129	2019	KCA 8.2.2	5.4.1 case b) Relevant but supplementary information. The findings in the study consider exposure concentrations that are much higher than would be expected following a field application at the max gap application rate. No analytical measurements of the test substance were performed. The test conditions of the toxicity tests (e.g. pH) are not described in detail. Supplemental information.
Quassinti L. et al.	Toxicity of Cupside 480SL® Spray Mixture Formulation Of Glyphosate To Aquatic Organisms	Pesticide Biochemistry and Physiology, Vol. 93, pp. 91-95	2015	KCA 8.2.8	5.4.1 case b) Relevant but supplementary information No information on the test substance is given and no analytical measurements of the test substance were performed. The exposure conditions (especially pH values) are not described in detail. A positive control should have been tested to verify the suitability and to assess test validity. Additionally, it is difficult to extrapolate effects from this in vitro test to exposed whole organisms. Therefore, the study is regarded as not reliable.
Smith C. et al.	Developmental and epigenetic effects of Roundup and glyphosate exposure on Japanese medaka (Oryzias latipes).	Aquatic toxicology, (2019) Vol. 210, pp. 215-226	2019	KCA 8.2.2	5.4.1 case b) Relevant but supplementary information. Test conditions like duration are only approximately described (e.g.100-120 days). Only one test concentration was tested, therefore no ECx values could be derived. Additionally, no verification of the test substance was performed and the influence of the different co-formulants on the results cannot be elucidated in the study. Therefore this paper is considered supplementary.

Author(s)	Title	Source	Year	Sanco datapoint (KCA)	Classification according to EFSA Guidance 2092 Point 5.4.1
Verderame M. et al.	How Glyphosate Impairs Liver Condition in the Field Lizard Podarcis siculus (Rafinesque-Schmaltz, 1810): Histological and Molecular Evidence.	BioMed research international, (2019) Vol. 2019, pp. 4746283	2019	KCA 8.1.4	5.4.1 case b) Relevant but supplementary information Whilst the product was identifed, the details of the environmental condidtions under which the sperm were assessed is not clearly stated, therefore the influence of factors other than glyphosate are not considered. pH and co-formulant toxicity should be have been considered in the assessment. Only two doses were tested, therefore no dose-dependent ECx values can be determined. Histological results were not statistically analysed and results from the expression analysis do not follow a clear dose-response relationship. Additionally, no verification of the test substance was performed. This assessment is considered supplementary to the ED assessment as sp[ecific endpoints relevant to ESFA GD approach for ED evaluation are not considered.

Author(s)	Title	Source	Year	Sanco datapoint (KCA)	Classification according to EFSA Guidance 2092 Point 5.4.1
Xie L. et al.	Evaluation of Estrogenic Activities of Aquatic Herbicides and Surfactants Using an Rainbow Trout Vitellogenin Assay	Toxicol. Sci. (2005) 87:91-8.	2005	KCA 8.2.3	5.4.1 case b) Relevant but supplementary information The results of this study demonstrate that glyphosate did not induce production of VTG, providing additional evidence that glyphosate does not have estrogenic activity.
Zhang S. et al.	Biological impacts of glyphosate on morphology, embryo biomechanics and larva behavior in zebrafish (Dartio rerio).	Chemosphere, (2017) Vo 181, pp. 270-280	2017	KCA 8.2.2	5.4.1 case b) Relevant but supplementary information. Results of control mortality (graphic) don´t seem to meet validity criteria from OECD 236, which is similar to the test design at this time point of the study. Possible effects due to a lower pH caused by higher glyphosate concentrations cannot be excluded. Additionally, no analytical measurements of the test substance were performed and no effect concentrations were derived for glyphosate. Therefore, the study is considered supplementary only
Toxicology					
Brennan JC. et al.	Development of a recombinant human ovarian (BG1) cell line containing oestrogen receptor alpha and beta for improved detection of oestrogenic/ Antioestrogenic chemicals; study supplementary	Environ Toxicol Chem. (2016) 35:91-100.	2016	KCA 5.8.3	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
Dai P. et al.	Effect of glyphosate on reproductive organs in male rat.	Acta Histochemica 118 (2016) 519–526	2016	KCA 5.6	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
De Almeida L. et al.	Moderate levels of glyphosate and its formulations vary in their cytotoxicity and genotoxicity in a whole blood model and in human cell lines with different estrogen receptor status	3 BIOTECH, (2018) Vol. 8, No. 10. ISSN: 2190-572X.	2018	KCA 5.4	5.4.1 case b) Relevant but supplementary information. Mixed study design: in the Comet assay only 2 doses were established.
Defarge N. et al.	Coformulants in glyphosate-based herbicides disrupt aromatase activity in human cells below toxic levels; study supplementary	Int J Environ Res Public Health. 2016 Feb 26;13(3).	2016	KCA 5.8.3	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.

Author(s)	Title	Source	Year	Sanco datapoint (KCA)	Classification according to EFSA Guidance 2092 Point 5.4.1
Defarge N. et al.	Toxicity of formulants and heavy metals in glyphosate-based herbicides and other pesticides.	Toxicology reports, (2018) Vol. 5, pp. 156-163	2018	KCA 5.4	5.4.1 case b) Relevant but supplementary information. Article is not glyphosate specific. Concentration groups are not properly described , moreover the chosen concentrations are high for in vitro studies and not applicable to test aromatase inhibition.
Forgacs A. et al.	BLTK1 murine Leydig cells: a novel steroidogenic model for evaluating the effects of reproductive and developmental toxicants.	TOXICOLOGICAL SCIENCES 127 (2), 391–402 (2012)	2012	KCA 5.6	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
Gallegos C. et al.	Perinatal Glyphosate-Based Herbicide Exposure in Rats Alters Brain Antioxidant Status, Glutamate and Acetylcholine Metabolism and Affects Recognition Memory.	Neurotoxicity research, (2018) Vol. 34, No. 3, pp 363-374	2018	KCA 5.7	5.4.1 case b) Relevant but supplementary information Not relevant as only a glyphosate based herbicide was used as test material, in two established doses. As supportive information can be transferred to the general LRR.

Author(s)	Title	Source	Year	Sanco datapoint (KCA)	Classification according to EFSA Guidance 2092 Point 5.4.1
George A. et al.	The effect of glyphosate on human sperm motility and sperm DNA fragmentation	International Journal of Environmental Research and Public Health (2018) Vol. 15, 1117	2018	KCA 5.8.3	5.4.1 case b) Relevant but supplementary information. This publication is considered relevant but supplemental as the glyphosate used is not characterized, only one test concentration was used, no positive control was considered and the results obtained are not corroborated by in vivo regulatory reproductive toxicology studies with much higher systemic levels of glyphosate.
Gigante P. et al.	Glyphosate affects swine ovarian and adipose stromal cell functions.	Animal reproduction science, (2018) Vol. 195, pp. 185-196	2018	KCA 5.8.3	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
Gorga A. et al.	In vitro effects of glyphosate and Roundup or Sertoli cell physiology.	Toxicology in vitro : an international journal published in association with BIBRA,Electronic Publication Date: 15 Oct 2019 Journal code: 8712158. E-ISSN: 1879-3177. L-ISSN: 0887-2333.	2019	KCA 5.6	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
Johansson H. et al.	Exposure to a glyphosate-based herbicide formulation, but not glyphosate alone, has only minor effects on adult rat testis.	Reproductive toxicology(2018) Vol. 82 pp. 25-31	2018	KCA 5.6	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
Kongtip P. et al.	Thyroid Hormones in Conventional and Organic Farmers in Thailand.	International journal of environmental research and public health, (2019) Vol. 16, No. 15. Electronic Publication Date: 29 Jul 2019	2019	KCA 5.8.3	5.4.1 case b) Relevant but supplementary information. This publication is considered relevant but supplementary for the risk assessment of glyphosate due to the higher incidence of thyroid disease in women (more numerous in organic farming), no data on the menopausal status of the women (change in thyroid hormones), the collection of data with dairies of the farmers may be incomplete, the exposure of farmers to pesticides prior to the study and prior to starting organic farming, and the results for glyphosate

Author(s)	Title	Source	Year	Sanco datapoint (KCA)	Classification according to EFSA Guidance 2092 Point 5.4.1
					should have been examined for confounding from other pesticides that were correlated with glyphosate use. Moreover, the use rate and bioavailability (Acquavella et al. (2004) Environmental Health Perspectives Vol. 112(3), 321-326; Acquavella et al. (2006) Epidemiology, Vol. 17(1), 69-74) of glyphosate was lower than that of the other pesticides used. Since the determination of serum thyroid hormone levels is key in this study, the methods of analysis should have been better documented.
Manservisi F. et al	The Ramazzini Institute 13-week pilot study glyphosate-based herbicides administered at human-equivalent dose to Sprague Dawley rats: effects on development and endocrine system.	Environmental health : a global access science source, (2019) Vol. 18, No. 1, pp. 15	2019	KCA 5.6	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
Martina B. et al.	Quizalofop-p-Ethyl Induces Adipogenesis in 3T3-L1 Adipocytes	TOXICOLOGICAL SCIENCES, 170, (2019), 452–461	2019	KCA 5.8.3	5.4.1 case a) relevant and provides data for the risk assessment: This publication is considered relevant for the risk assessment of glyphosate and reliable without restrictions.
Mesnage R. et al.	Evaluation of estrogen receptor alpha activation by glyphosate-based herbicide constituents.	Food and Chemical Toxicology 108 (2017) 30-42	2017	KCA 5.8.3	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
Owagboriaye F. et al.	Comparative studies on endogenic stress hormones, antioxidant, biochemical and hematological status of metabolic disturbance in albino rat exposed to roundup herbicide and its active ingredient glyphosate.	Environmental science and pollution research international, (2019) Vol. 26, No. 14, pp. 14502-14512	2019	KCA 5.3	5.4.1 case b) Relevant but supplementary information. Considering this study represent a repeated-exposure, 90-day study desing, several deviations can be identified from the guidance document: 1. no proper identification of the test substance presented 2. no proper description of the animals, housing conditions are reported 3. number of animals used in the dose groups is less than suggested 4. no pathology were performed 5. no historical control data mentioned 6. no clinical findings or body weight measurements recorded

Author(s)	Title	Source	Year	Sanco datapoint (KCA)	Classification according to EFSA Guidance 2092 Point 5.4.1
Panzacchi S. et al.	The Ramazzini Institute 13-week study on glyphosate-based herbicides at humanequivalent dose in Sprague Dawley rats: study design and first in-life endpoints evaluation	Environmental Health, (2018) Vol. 17, pp. 52	2018	KCA 5.6	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
Parvez S. et al.	Glyphosate exposure in pregnancy and shortened gestational length: a prospective Indiana birth cohort study	Environmental Health, (2018) Vol. 17, pp. 23	2018	KCA 5.8.3	5.4.1 case b) Relevant but supplementary information This publication is considered relevant but supplementary for the risk assessment of glyphosate because the number of pregnancies followed was too low and no data are available on urinary concentrations of other pesticides and environmental chemicals.
Perego M. et al.	Evidence for direct effects of glyphosate on ovarian function: glyphosate influences steroidogenesis and proliferation of bovine granulosa but not theca cells in vitro.	Journal of applied toxicology (2017) Vol. 37 No. 6, pp. 692-698	2016	KCA 5.6	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
Pham T. et al.	Perinatal Exposure to Glyphosate and a Glyphosate-Based Herbicide Affect Spermatogenesis in Mice.	Toxicological sciences(2019) Vol. 169, No. 1, pp. 260-271	2019	KCA 5.6	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
Pinto L. et al.	Identification of candidate reference chemicals for in vitro steroidogenesis assays	Toxicology In Vitro, (2018) Vol. 47, pp. 103-119	2018	KCA 5.8.3	5.4.1 case b) Relevant but supplementary information Relevant secondary information
Rappazzo K. et al.	Maternal residential exposure to specific agricultural pesticide active ingredients and birth defects in a 2003-2005 North Carolina birth cohort.	Birth defects research, (2019) Vol. 111, No. 6, pp. 312-323	2019	KCA 5.8.3	5.4.1 case b) Relevant but supplementary information This publication is considered relevant but supplementary for the risk assessment of glyphosate because of the small number of specific birth defects. Although confounded by co-occurring pesticides has been considered in this study the potential for confounding by joint pesticide exposures and other environmental factors cannot be excluded.
Ren X. et al.	Effects of glyphosate on the ovarian function of pregnant mice, the secretion of hormones and the sex ratio of their fetuses.	Environmental pollution (2018) Vol. 243, No. Pt B pp. 833-841	2018	KCA 5.6	5.4.1 case b) Relevant but supplementary information Substance was not sufficiently characterized, moreover only one dose was considered as glyphosate and as RoundUp exposure group.

Author(s)	Title	Source	Year	Sanco datapoint (KCA)	Classification according to EFSA Guidance 2092 Point 5.4.1
Sakpa C. et al.	Effects of glyphosate on sperm parameters and pregnancy success rate in Wistar rats.	Annals of Biomedical Sciences (2018), Volume 17, Number 2, pp. 156-164	2018	KCA 5.8.3	5.4.1 case b) Relevant but supplementary information This publication is considered relevant but supplementary for the risk assessment of glyphosate because the glyphosate used is not sufficiently characterized, only two dose levels were tested and the number of animals used per dose level was too low.
Santos R. et al.	Thyroid and reproductive hormones in relation to pesticide use in an agricultural population in Southern Brazil.	Environmental Research, (2019) pp. 221-231	2019	KCA 5.8.3	5.4.1 case b) Relevant but supplementary information. Exposure related information based on biased recall data.
Shrestha S. et al.	Incident thyroid disease in female spouses of private pesticide applicators.	Environment International, (September 2018) Vol. 118, pp. 282-292	2018	KCA 5.8.3	5.4.1 case b) Relevant but supplementary information Not a glyphosate specific study.
Shrestha S. et al.	Pesticide use and incident hypothyroidism in pesticide applicators in the agricultural health study	Environmental Health Perspectives (2018) Volume 126, Number 9, 11 p.	2018	KCA 5.8.3	5.4.1 case b) Relevant but supplementary information Not a glyphosate specific study. Self reporting had inconsistencies at age of diagnosis, moreover only 32% of self-reported disease was confirmed by medical records.
Sritana N. et al.	Glyphosate induces growth of estrogen receptor alpha positive cholangiocarcinoma cells via non-genomic estrogen receptor/ERK1/2 signaling pathway.	Food and chemical toxicology (2018) Vol. 118, pp. 595-607	2018	KCA 5.6	5.4.1 case b) Relevant but supplementary information No replicates had been used in the study, the incubation time was an extended 40 h, the active substance identification is not entirely complete, moreover the cell line selection is not explained.
Thongprakaisang S. et al.	Glyphosate induces human breast cancer cell growth via estrogen receptors.	Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, (2013) Vol. 59, pp. 129-36.	2013	KCA 5.8.3	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment

Author(s)	Title	Source	Year	Sanco datapoint (KCA)	Classification according to EFSA Guidance 2092 Point 5.4.1
Vanlaeys A. et al.	Formulants of glyphosate-based herbicides have more deleterious impact than glyphosate on TM4 Sertoli cells.	Toxicology in vitro : an international journal published in association with BIBRA, (2018) Vol. 52, pp. 14-22	2018	KCA 5.8.3	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
Wrobel M. et al.	Glyphosate affects the secretion of regulators of uterine contractions in cows while it does not directly impair the motoric function of myometrium in vitro.	Toxicology and applied pharmacology, (2018) Vol. 349, pp. 55-61	2018	KCA 5.6	5.4.1 case b) Relevant but supplementary information. This publication is considered relevant but supplemental for the risk assessment of glyphosate because the glyphosate used is not sufficiently characterized and the analysis of glyphosate, hormones and prostaglandins is not sufficiently documented.
Zhang J. et al.	The toxic effects and possible mechanisms of glyphosate on mouse oocytes.	Chemosphere, (2019) Vo 237, pp. 124435	2019	KCA 5.6	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment
Zhao H. et al.	Effects of Glyphosate on Testosterone Synthesis in Male Rats.	Asian Journal of Ecotoxicology, (2018) Vol. 13, No. 5, pp. 242-247	2018	KCA 5.8.3	5.4.1 case b) Relevant but supplementary information This publication is considered relevant but supplemental for the risk assessment of glyphosate but reliable with restrictions because the reporting of the experimental conditions is not complete.

Table 9: Relevant studies included in a dossier/Assessment Report after detailed assessment of full-text documents for relevance: sorted by data requirement(s)

SANCO datapoint (KCA)	Autor	Year	Title	Source	Classification according to EFSA Guidance 2092 Point 5.4.1
Toxicology					
KCA 5.6	Dai P. et al.	2016	Effect of glyphosate on reproductive organs in male rat.	Acta Histochemica 118 (2016) 519–526	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
KCA 5.6	Forgacs A. et al.	2012	BLTK1 murine Leydig cells: a novel steroidogenic model for evaluating the effects of reproductive and developmenta toxicants.	TOXICOLOGICAL SCIENCES 127 (2), 391–402 (2012)	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
KCA 5.6	Johansson H. et al	2018	Exposure to a glyphosate-based herbicide formulation, but not glyphosate alone, has only minor effects on adult rat testis.	Reproductive toxicology(2018) Vol. 82, pp. 25-31	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
KCA 5.6	Manservisi F. et al.	2019	The Ramazzini Institute 13-week pilot study glyphosate-based herbicides administered at human-equivalent dose to Sprague Dawley rats: effects on development and endocrine system.	Environmental health : a global access science source, (2019) Vol 18, No. 1, pp. 15	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
KCA 5.6	Panzacchi S. et al.	2018	The Ramazzini Institute 13-week study of glyphosate-based herbicides at humanequivalent dose in Sprague Dawley rats: study design and first in-life endpoints evaluation	Environmental Health, (2018) Vol. 17, pp. 52	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
KCA 5.6	Perego M. et al.	2016	Evidence for direct effects of glyphosate on ovarian function: glyphosate influences steroidogenesis and proliferation of bovine granulosa but not theca cells in vitro.	Journal of applied toxicology (2017) Vol. 37, No. 6, pp. 692-698	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
KCA 5.6	Pham T. et al.	2019	Perinatal Exposure to Glyphosate and a Glyphosate-Based Herbicide Affect Spermatogenesis in Mice.	Toxicological sciences(2019) Vol 169, No. 1, pp. 260-271	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessmen.t

SANCO datapoint (KCA)	Autor	Year	Title	Source	Classification according to EFSA Guidance 2092 Point 5.4.1
KCA 5.6	Gorga A. et al.	2019	In vitro effects of glyphosate and Roundup on Sertoli cell physiology.	Toxicology in vitro : an international journal published in association with BIBRA,Electronic Publication Date: 15 Oct 2019 Journal code: 8712158. E-ISSN: 1879-3177. L-ISSN: 0887-2333.	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
KCA 5.6	Zhang J. et al.	2019	The toxic effects and possible mechanisms of glyphosate on mouse oocytes.	Chemosphere, (2019) Vol. 237, pp. 124435	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.

SANCO datapoint (KCA)	Autor	Year	Title	Source	Classification according to EFSA Guidance 2092 Point 5.4.1
KCA 5.8.3	Brennan JC. et al.	2016	Development of a recombinant human ovarian (BG1) cell line containing oestrogen receptor alpha and beta for improved detection of oestrogenic/ Antioestrogenic chemicals; study supplementary	Environ Toxicol Chem. (2016) 35:91-100.	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
KCA 5.8.3	Defarge N. et al.	2016	Coformulants in glyphosate-based herbicides disrupt aromatase activity in human cells below toxic levels; study supplementary	Int J Environ Res Public Health. 2016 Feb 26;13(3).	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
KCA 5.8.3	Gigante P. et al.	2018	Glyphosate affects swine ovarian and adipose stromal cell functions.	Animal reproduction science, (2018) Vol. 195, pp. 185-196	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
KCA 5.8.3	Martina B. et al.	2019	Quizalofop-p-Ethyl Induces Adipogenesi in 3T3-L1 Adipocytes	TOXICOLOGICAL SCIENCES, 170, (2019), 452–461	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
KCA 5.8.3	Mesnage R. et al.	2017	Evaluation of estrogen receptor alpha activation by glyphosate-based herbicide constituents.	Food and Chemical Toxicology 108 (2017) 30-42	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
KCA 5.8.3	Thongprakaisang S. et al.	2013	Glyphosate induces human breast cancer cells growth via estrogen receptors.	Food and chemical toxicology : a international journal published fo the British Industrial Biological Research Association, (2013) Vol 59, pp. 129-36.	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
KCA 5.8.3	Vanlaeys A. et al.	2018	Formulants of glyphosate-based herbicides have more deleterious impact than glyphosate on TM4 Sertoli cells.	Toxicology in vitro : an international journal published in association with BIBRA, (2018) Vol. 52, pp. 14-22	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.
Ecotoxicology					
KCA 8.2.2	Le Mer C. et al.	2013	Effects of chronic exposures to the herbicides atrazine and glyphosate to larvae of the threespine stickleback (Gasterosteus aculeatus).	Ecotoxicol. Environ. Saf. 89: 174- 181.	5.4.1 case a) relevant and provides data for the risk assessment: Summary is provide in the ED WoE assessment.

Appendix: ORIGINAL SEARCH QUERY

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            ---------
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              GLYFOSAT? OR N PHOSPHONOMETHYL GLYCINE OR PHOSPHONOMETHYL
              AMINO ACETIC ACID OR 1071-83-6 OR 38641-94-0 OR 70901-12-1 OR
              39600-42-5 OR 69200-57-3 OR 34494-04-7 OR 114370-14-8 OR
              40465-66-5 OR 69254-40-6
            ---------
L2         3220 SEA SPE=ON  ABB=ON  PLU=ON  GLYPHOSAT? OR GLIFOSAT? OR
              GLYFOSAT? OR N PHOSPHONOMETHYL GLYCINE OR PHOSPHONOMETHYL
              AMINO ACETIC ACID OR 1071-83-6 OR 38641-94-0 OR 70901-12-1 OR
              39600-42-5 OR 69200-57-3 OR 34494-04-7 OR 114370-14-8 OR
              40465-66-5 OR 69254-40-6
L3          915 SEA SPE=ON  ABB=ON  PLU=ON  L2 AND ED>20161031
L4          894 SEA SPE=ON  ABB=ON  PLU=ON  L3 NOT (COMMENT? OR DISSERTATION
              OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/D
              T
              SAVE L4 GLYMEDL/A

    FILE 'AGRICOLA' ENTERED AT 13:35:01 ON 19 AUG 2019
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              GLYFOSAT? OR N PHOSPHONOMETHYL GLYCINE OR PHOSPHONOMETHYL
              AMINO ACETIC ACID OR 1071-83-6 OR 38641-94-0 OR 70901-12-1 OR
              39600-42-5 OR 69200-57-3 OR 34494-04-7 OR 114370-14-8 OR
              40465-66-5 OR 69254-40-6
L6         1284 SEA SPE=ON  ABB=ON  PLU=ON  L5 AND ED>20161031
L7         1284 SEA SPE=ON  ABB=ON  PLU=ON  L6 NOT (COMMENT? OR DISSERTATION
              OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/D
              T
              SAVE L7 GLYAGRI/A

    FILE 'BIOSIS' ENTERED AT 13:39:34 ON 19 AUG 2019
CHARGED TO COST=110517
L8        10110 SEA SPE=ON  ABB=ON  PLU=ON  GLYPHOSAT? OR GLIFOSAT? OR
              GLYFOSAT? OR N PHOSPHONOMETHYL GLYCINE OR PHOSPHONOMETHYL
              AMINO ACETIC ACID OR 1071-83-6 OR 38641-94-0 OR 70901-12-1 OR
              39600-42-5 OR 69200-57-3 OR 34494-04-7 OR 114370-14-8 OR
              40465-66-5 OR 69254-40-6
L9         1672 SEA SPE=ON  ABB=ON  PLU=ON  L8 AND ED>20161031
L10        1445 SEA SPE=ON  ABB=ON  PLU=ON  L9 NOT (COMMENT? OR DISSERTATION
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              GLYFOSAT? OR N PHOSPHONOMETHYL GLYCINE OR PHOSPHONOMETHYL
              AMINO ACETIC ACID OR 1071-83-6 OR 38641-94-0 OR 70901-12-1 OR
              39600-42-5 OR 69200-57-3 OR 34494-04-7 OR 114370-14-8 OR
              40465-66-5 OR 69254-40-6
L12        1703 SEA SPE=ON  ABB=ON  PLU=ON  L11 AND ED>20161031
L13        1702 SEA SPE=ON  ABB=ON  PLU=ON  L12 NOT (COMMENT? OR DISSERTATION
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              T
              SAVE L13 GLYCABA/A

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              GLYFOSAT? OR N PHOSPHONOMETHYL GLYCINE OR PHOSPHONOMETHYL
              AMINO ACETIC ACID OR 1071-83-6 OR 38641-94-0 OR 70901-12-1 OR
              39600-42-5 OR 69200-57-3 OR 34494-04-7 OR 114370-14-8 OR
              40465-66-5 OR 69254-40-6
L15         108 SEA SPE=ON  ABB=ON  PLU=ON  L14 AND ED>20161031
L16         105 SEA SPE=ON  ABB=ON  PLU=ON  L15 NOT (COMMENT? OR DISSERTATION
              OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/D
              T
              SAVE L16 GLYFSTA/A

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              GLYFOSAT? OR N PHOSPHONOMETHYL GLYCINE OR PHOSPHONOMETHYL
              AMINO ACETIC ACID OR 1071-83-6 OR 38641-94-0 OR 70901-12-1 OR
              39600-42-5 OR 69200-57-3 OR 34494-04-7 OR 114370-14-8 OR
              40465-66-5 OR 69254-40-6
L18         698 SEA SPE=ON  ABB=ON  PLU=ON  L17 AND ED>20161031
L19         610 SEA SPE=ON  ABB=ON  PLU=ON  L18 NOT (COMMENT? OR DISSERTATION
              OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/D
              T
              SAVE L19 GLYPQSCI/A

    FILE 'TOXCENTER' ENTERED AT 13:45:54 ON 19 AUG 2019
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L20       13864 SEA SPE=ON  ABB=ON  PLU=ON  GLYPHOSAT? OR GLIFOSAT? OR
              GLYFOSAT? OR N PHOSPHONOMETHYL GLYCINE OR PHOSPHONOMETHYL
```

AMINO ACETIC ACID OR 1071-83-6 OR 38641-94-0 OR 70901-12-1 OR
39600-42-5 OR 69200-57-3 OR 34494-04-7 OR 114370-14-8 OR
40465-66-5 OR 69254-40-6
L21 2617 SEA SPE=ON ABB=ON PLU=ON L20 AND ED>20161031
L22 1886 SEA SPE=ON ABB=ON PLU=ON L21 NOT (COMMENT? OR DISSERTATION
OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/D
T
SAVE L22 GLYTOXC/A

FILE 'EMBASE' ENTERED AT 13:47:36 ON 19 AUG 2019
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L23 3875 SEA SPE=ON ABB=ON PLU=ON GLYPHOSAT? OR GLIFOSAT? OR
GLYFOSAT? OR N PHOSPHONOMETHYL GLYCINE OR PHOSPHONOMETHYL
AMINO ACETIC ACID OR 1071-83-6 OR 38641-94-0 OR 70901-12-1 OR
39600-42-5 OR 69200-57-3 OR 34494-04-7 OR 114370-14-8 OR
40465-66-5 OR 69254-40-6
L24 743 SEA SPE=ON ABB=ON PLU=ON L23 AND ED>20161031
L25 738 SEA SPE=ON ABB=ON PLU=ON L24 NOT (COMMENT? OR DISSERTATION
OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/D
T
SAVE L25 GLYEMBA/A

FILE 'ESBIOBASE' ENTERED AT 13:49:01 ON 19 AUG 2019
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GLYFOSAT? OR N PHOSPHONOMETHYL GLYCINE OR PHOSPHONOMETHYL
AMINO ACETIC ACID OR 1071-83-6 OR 38641-94-0 OR 70901-12-1 OR
39600-42-5 OR 69200-57-3 OR 34494-04-7 OR 114370-14-8 OR
40465-66-5 OR 69254-40-6
L27 992 SEA SPE=ON ABB=ON PLU=ON L26 AND ED>20161031
L28 988 SEA SPE=ON ABB=ON PLU=ON L27 NOT (COMMENT? OR DISSERTATION
OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/D
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GLYFOSAT? OR N PHOSPHONOMETHYL GLYCINE OR PHOSPHONOMETHYL
AMINO ACETIC ACID OR 1071-83-6 OR 38641-94-0 OR 70901-12-1 OR
39600-42-5 OR 69200-57-3 OR 34494-04-7 OR 114370-14-8 OR
40465-66-5 OR 69254-40-6
L30 3780 SEA SPE=ON ABB=ON PLU=ON L29 AND ED>20161031
L31 1527 SEA SPE=ON ABB=ON PLU=ON L30 NOT (COMMENT? OR DISSERTATION
OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/D
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SAVE L31 GLYHCAP/A

FILE 'SCISEARCH' ENTERED AT 13:52:15 ON 19 AUG 2019
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GLYFOSAT? OR N PHOSPHONOMETHYL GLYCINE OR PHOSPHONOMETHYL
AMINO ACETIC ACID OR 1071-83-6 OR 38641-94-0 OR 70901-12-1 OR
39600-42-5 OR 69200-57-3 OR 34494-04-7 OR 114370-14-8 OR
40465-66-5 OR 69254-40-6
L33 2120 SEA SPE=ON ABB=ON PLU=ON L32 AND ED>20161031
L34 2067 SEA SPE=ON ABB=ON PLU=ON L33 NOT (COMMENT? OR DISSERTATION
OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/D
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EMBASE, ESBIOBASE, HCAPLUS, SCISEARCH' ENTERED AT 13:56:36 ON 19 AUG 2019
CHARGED TO COST=110517
L35 5036 DUP REM L4 L7 L10 L13 L16 L19 L22 L25 L28 L31 L34 (8210 DUPLICA
ANSWERS '1-893' FROM FILE MEDLINE
ANSWERS '894-1802' FROM FILE AGRICOLA
ANSWERS '1803-2369' FROM FILE BIOSIS
ANSWERS '2370-3125' FROM FILE CABA
ANSWERS '3126-3159' FROM FILE FSTA
ANSWERS '3160-3514' FROM FILE PQSCITECH
ANSWERS '3515-3910' FROM FILE TOXCENTER
ANSWERS '3911-4109' FROM FILE EMBASE
ANSWERS '4110-4191' FROM FILE ESBIOBASE
ANSWERS '4192-4516' FROM FILE HCAPLUS
ANSWERS '4517-5036' FROM FILE SCISEARCH
D SAVE
SAVE L35 GLYSUBST/A

FILE 'MEDLINE' ENTERED AT 16:33:18 ON 19 AUG 2019
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L36 QUE SPE=ON ABB=ON PLU=ON TOXI? OR HAZARD OR ADVERSE OR
HEALTH OR EFFECT OR NOAEL OR NOEL OR LOAEL OR LOEL OR BMD OR
IN VIVO OR IN VITRO OR ACUTE OR SUBACUTE OR SUBCHRONIC OR
CHRONIC OR ORAL OR DERMAL OR GAVAGE OR DIET? OR INHAL?
L37 QUE SPE=ON ABB=ON PLU=ON RAT OR DOG OR RABBIT OR GUINEA PIG
OR MOUSE OR MICE OR HAMSTER OR METABOLISM OR METABOLITE OR
METABOLIC OR DISTRIBUTION OR ADSORPTION OR EXCRETION OR
ELIMINATION OR KINETIC OR PBPK OR CYP OR CYTOCHROME OR ENZYM?
L38 QUE SPE=ON ABB=ON PLU=ON GEN? OR MUTA? OR CHROMOS? OR
CLASTOGEN? OR DNA OR CARCINO? OR CANCER? OR IMMUN? OR NEUR? OR
BEHAV? OR ENDOCRIN? OR HORMON? OR REPRODUCT? OR DEVELOPMENT?
OR MALFORMATION?
L39 QUE SPE=ON ABB=ON PLU=ON ANOMAL? OR FERTIL? OR FOET? OR
FETO? OR FETUS OR MATERN? OR PREGNAN? OR EMBRYO? OR EPIDEM? OR
MEDICAL? OR POISON? OR ESTROGEN? OR ANDROGEN? OR STEROIDOGEN?
OR ESTROGEN RECEPTOR? OR ANDROGEN RECEPTOR? OR THYROID
RECEPTOR?

L40 QUE SPE=ON ABB=ON PLU=ON AR BIND? OR ER BIND? OR THYROID STIMULATING HORMONE OR TSH OR LUTEINIZING HORMONE OR LH(5A)HORM ONE OR FOLLICULE STIMULATING HORMONE OR FSH OR ESTRADIOL? OR TESTOSTERONE? OR ACCESSORY GLAND? OR GENITAL? OR COAGULATING GLAND?
L41 QUE SPE=ON ABB=ON PLU=ON PROSTATE? OR TESTIS? OR MOTILITY? OR MAMMARY GLAND? OR CERVIX? OR UTERUS? OR OVARY? OR ANOGENITAL ? OR NIPPLE RETENTION? OR PREPUTIAL? OR VAGINA? OR ESTRUS? OR FOLLICULAR?
L42 QUE SPE=ON ABB=ON PLU=ON ENDOCRINE? OR ENDOCRINE DISRUPT? OR DEVELOPMENTAL? OR REPROT? OR SEXUAL MATURATION?
L43 QUE SPE=ON ABB=ON PLU=ON OECD 407 OR OECD 408 OR OECD 414 OR OECD 415 OR OECD 421 OR OECD 422 OR OECD 426 OR OECD 451 OR OECD 453 OR OECD 416 OR OECD 443 OR OPPTS 890.1500# OR OPPTS 890.1450#
L44 QUE SPE=ON ABB=ON PLU=ON (L36 OR L37 OR L38 OR L39 OR L40 OR L41 OR L42 OR L43)
SAVE L44 EDTOX/Q

ACT EDECOTOX/Q

L45 QUE SPE=ON ABB=ON PLU=ON TOXI? OR HAZARD OR ADVERSE OR POISON OR EFFECT? OR IN VIVO OR IN VITRO OR ECOTOXICOLOG? OR AQUATIC OR WILDLIFE OR NON TARGET OR NONTARGET OR POPULATION OR MODEL OR MODE OF ACTION OR ENVIRONMENT OR ENDOCRINE DISRUPT?
L46 QUE SPE=ON ABB=ON PLU=ON ENDOCRIN? OR ABNORMAL? OR SEXUAL OR DEVELOPMENT? OR ADVERS? OR REPRODUCT? OR MALFORMATION? OR ANOMAL? OR FERTIL? OR FECUND? OR INHIBITION OR FSTRA
L47 QUE SPE=ON ABB=ON PLU=ON BIRD OR MALLARD OR DUCK OR QUAIL OR BOBWHITE OR ANAS? OR COLINUS? OR AVIAN OR VERTEBRAT? OR MAMMAL? OR RAT OR MOUSE OR MICE OR RABBIT OR HARE OR AQUATIC OR FISH OR FATHEAD OR MINNOW OR MEDAKA OR ZEBRAFISH OR STICKLEBACK
L48 QUE SPE=ON ABB=ON PLU=ON RAINBOW TROUT OR PIMEPHALES PROMELAS OR ORYZIAS LATIPES OR DANIO RERIO OR GASTEROSTEUS ACULEATUS OR ONCORHYNCHUS MYKISS OR SNAIL OR POTAMOPYRGUS ANTIPODARUM OR AMPHIB? OR REPTILE OR XENOPUS OR TADPOLE OR AMA OR LAGDA
L49 QUE SPE=ON ABB=ON PLU=ON HORMONE OR VITELLOGENIN OR SPIGGIN OR SEX CHARACTERISTICS OR SEX RATIO OR SEX SHIFT OR INTERSEX OR EGG PRODUCTION OR SPAWNING OR GONAD OR THYROID OR HISTOPATHO LOGY OR HISTOLOGY OR AROMATASE OR ANDROGEN OR ESTROGEN OR STEROID?
L50 QUE SPE=ON ABB=ON PLU=ON ASSAY OR EARLY LIFE STAGE OR LIFE CYCLE OR METAMORPHOSIS OR LARVAL GROWTH OR MALE INDUCTION
L51 QUE SPE=ON ABB=ON PLU=ON OECD 148 OR OECD 206 OR OECD 210 OR OECD 221 OR OECD 229 OR OECD 230 OR OECD 231 OR OECD 234 OR OECD 236 OR OECD 240 OR OECD 241 OR OECD 225 OR OECD 219 OR OECD 218 OR OECD 242 OR OCSPP 890.2300 OR OCSPP 890.2100 OR EDSP OR SCREENING
L52 QUE SPE=ON ABB=ON PLU=ON INVERTEBRAT? OR DAPHNI? OR CERIODAPHNI? OR CHIRON? OR SEDIMENT DWELL? OR COPEPOD OR LUMBRICULUS OR ENCHYTREID OR MARIN? OR ESTUARINE OR CRUSTA? OR GASTROPOD? OR MOLLUSK OR BEE? OR API? OR BUMBLE? OR ARTHROPOD?
L53 QUE SPE=ON ABB=ON PLU=ON TYPHLODROMUS OR APHIDIUS OR INSECT? OR WORM? OR ?WORM OR EISENIA OR COLLEMBOL? OR MACRO ORGANISM OR MACROORGANISM OR FOLSOMIA OR SPRINGTAIL OR MITE? OR HYPOASPIS OR MOLLUSC?
L54 QUE SPE=ON ABB=ON PLU=ON (L45 OR L46 OR L47 OR L48 OR L49 OR L50 OR L51 OR L52 OR L53)

FILE 'MEDLINE, AGRICOLA, BIOSIS, CABA, FSTA, PQSCITECH, TOXCENTER, EMBASE, ESBIOBASE, HCAPLUS, SCISEARCH' ENTERED AT 16:36:59 ON 19 AUG 2019
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L55 4253 SEA SPE=ON ABB=ON PLU=ON L35 AND L44
SAVE L55 GLYEDTOX/A
L56 4400 SEA SPE=ON ABB=ON PLU=ON L35 AND L54
SAVE L56 GLYEDECOTOX/A
L57 4692 SEA SPE=ON ABB=ON PLU=ON L55 OR L56
SAVE L57 GLYED/A

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 17:14:26 ON 19 AUG 2019

ANNEX A-01:

Endocrine Disruptor literature search report
Search period Jan 2014 and Oct 2016

Literature Search on
Glyphosate

Focus of the search:

Data Requirements Following EFSA Guidance Document

"Submission of scientific peer-reviewed open literature
for the approval of pesticide active substances
under Regulation (EC) No 1107/2009"

(EFSA Journal 2011; 9(2):2092)

Date of search: 10 October 2016

TABLE OF CONTENTS

TABLE OF TABLES

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http://www.stn-international.de/sum_sheets.html

Disclaimer

The information contained herein has been obtained from sources believed to be the most reliable. Every effort has been made to ensure completeness of data. However, no database search can be completely comprehensive, and it is possible that relevant documents have been omitted.

CA 9.0 INTRODUCTION

EFSA has been requested to assess the available information on potential endocrine activity of glyphosate, and conclude whether the data gap set in the EFSA Conclusion published on 12 November 2015 (EFSA Journal 2015;13(11):4302) is addressed.

Following the authority request, the search focussed in:

- ✓ Data according to the Endocrine Disruptor Screening Programme (EDSP) or the Level 2 and 3 tests indicated in the Organisation for Economic Co-operation and Development (OECD) Conceptual Framework, as outlined in the EFSA Conclusion
- ✓ Any other study that may be suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion, in particular with regard to the studies evaluated by the EDSP

Based on the above search, an update on the scientific peer-reviewed open literature in accordance with the EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092) was prepared.

The STN search was performed by the service provider of literature search: FIZ Karlsruhe – Leibniz Institute for Information Infrastructure[1]. The requested timeframe: January 2014- October 2016

In September 2014 the Glyphosate Task Force submitted an update of the literature review at request of the Authority, therefore the time window for this literature review was limited to January 2014 –October 2016.

Following the EFSA request, the search was limited to those studies that have not been submitted to EFSA and the Member States in the course of the peer review for renewal of glyphosate under Commission Regulation (EU) No 1141/2010. In order to get an overview of the studies already assessed under the peer review for renewal of glyphosate, we kindly ask you to consult the Background Documents to the EFSA Conclusion. The relevant study lists are available in the Final Addendum from electronic page 1422 to page 1511 (Volume 3, chapter B.6 on toxicology and metabolism).

Also, other document types have been excluded during the screening title/abstract in line with the EFSA guidance on "Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009." Details for exclusion during the first selection process are provided in this EFSA guidance in Appendix C (page 46 ff). The document types that have been excluded:

COMMENT
COMMENTARY
DISSERTATION
EDITORIAL
MEETING ABSTRACT(S)
MEETING POSTER
MEETING SLIDE
MEETING SUMMARY
NEWS
NEWS ANNOUNCEMENT
NEWS BRIEF
NEWSPAPER ARTICLE
PATENT
PRESS RELEASE
SHORT COMMUNICATION

CA 9.1 Relevance criteria

For this public literature search, the specific request to consider information on potential endocrine activity of glyphosate has been requested, in order to assess the available information on that topic.

[1] www.fiz-karlsruhe.de: Order number: 15206: Entry date: 07.10.2016 - Delivery date: 10.10.2016

Therefore, in frame of the request, the relevance criteria guide the selection of literature dealing only with potential endocrine activity. Non-GLP studies in open literature may be considered relevant if the design and execution of the study is consistent with generally accepted scientific practice and guidelines. Clearly non-relevant studies are excluded.

Table 1 lists the selection criteria applied to the results of the search for peer reviewed open literature relevant to glyphosate and its metabolites.

Table 1
Relevance criteria

EFSA Request[2]	Criteria for relevance
POTENTIAL ENDOCRINE ACTIVITY OF GLYPHOSATE	1. Description of the observations, examinations, analysis performed, or necropsy are well described. 2. The endpoints addressed should be according to or equivalent to tests listed under EDSP or OECD CF. 3. Testing results have to be based on the active ingredient rather than products/formulations.

CA 9.2 Search criteria

Reasonable effort was taken to locate all sources of relevant peer reviewed open literature concentrated on comprehensive databases containing worldwide coverage of biology, chemistry, biomedical, agricultural and environmental fields.

A search profile for glyphosate was setup, containing synonyms, trade names and CAS Registry numbers.

- A restricting keyword search profile was setup, containing the following terms: hormon?, endocrin?, thyroid?, androgen?, estrogen?, steroido?, aromatase, cytochrome p450 and intersex?

- The search profiles were linked and searched in the databases TOXCENTER, HCAPLUS, MEDLINE, BIOSIS, EMBASE, CABA and AGRICOLA

- Results were restricted to the non-patent literature and a publication date greater than 2013

- Duplicates were eliminated

The search by STN retrieved 115 references. **Table 3** lists the literature search details: search statements and search strategy.

[2] Request for Data from EFSA: Ref. JT/MT/ml (2016)-out-16219711

Table 2
Databases used

Data requirement(s) captured in the search	**Details of the searches**			
	AGRICOLA	*BIOSIS*	*CABA*	*CAPLUS*
Justification for choosing the source:	Agriculture Online Access is a bibliographic database containing selected worldwide literature of agriculture and related fields. More than 5.2 million records (01/2016)	The largest and most comprehensive life science database in the world, BIOSIS covers original research reports, reviews, and selected U.S. patents in biological and biomedical areas, with subject coverage ranging from aerospace biology to zoology. More than 24.8 million records (02/2016)	The CAB Abstracts database covers worldwide literature from all areas of agriculture and related sciences including biotechnology, forestry, and veterinary medicine. More than 8.0 million records (01/2016)	Chemical Abstracts Plus (CAplusSM) provides current and comprehensive worldwide coverage of chemistry and related scientific disciplines. CAplus covers international journals, patents, patent families, technical disclosures, technical reports, books, conference proceedings, dissertations, electronic-only journals, and web pre-prints from all areas of chemistry, biochemistry, chemical engineering, and related sciences from 1907 to the present.
Date of the search	10 October 2016	10 October 2016	10 October 2016	10 October 2016
File covers	1970 to date	1926 to date	1973 to date	1907 - 10 October 2016
File last updated:	5 October 2016	5 October 2016	5 October 2016	9 October 2016
Language limit:	No	No	No	No
Document types excluded that are not "scientific peer-reviewed open literature":	PATENT	PATENT	PATENT	PATENT
Search strategy:	Details are listed in Table 3			
Total number of records retrieve	**1**	**3**	**36**	**8**

Table 2
Databases used (continued)

Data requirement(s) captured in the search	**Details of the searches**		
	MEDLINE	*EMBASE*	TOXCENTER
Justification for choosing the source:	MEDLINE contains information on every area of medicine. More than 25.3 million records (01/2016)	The Excerpta Medica database, covers worldwide literature in the biomedical and pharmaceutical fields, including biological science, biochemistry, human medicine, forensic science, pediatrics, pharmacy, pharmacology and drug therapy, pharmacoeconomics, psychiatry, public health, biomedical engineering and instrumentation, and environmental science. More than 31.2 million records (01/2016).	TOXCENTER (Toxicology Center) is a bibliographic database that covers the pharmacologi-cal, biochemical, physiological, and toxicological effects of drugs and other chemicals.
Date of the search	10 October 2016	10 October 2016	10 October 2016
File covers	1946 to date	Embase-originated material 1947 to 7 Oct 2016 (20161007/ED) Unique MEDLINE content 1948 to present Emtree thesaurus last updated September 2016.	1907 to 3 October 2016
File last updated:	5 October 2016	-	-
Language limit:	No	No	No
Document types excluded that are not "scientific peer-reviewed open literature":	PATENT	PATENT	PATENT
Search strategy:	Details are listed in Table 3		
Total number of summary records retrieved	**7**	**11**	**49**
Total number of summary records retrieved after removing duplicates[3]			**N= 115**
Total number of summary records retrieved after removing duplicates			**N= 104**

[3] The service provider of the STN search, inidicated that the duplicates were removed. However, duplicates articles (n=11) were identified (e.g. initial versus full authors names)

Table 3
Details of the Search strategy

Search strategy
- A search profile for [glyphosate] was setup, containing synonyms, trade names and CAS Registry numbers. - A restricting keyword search profile was setup, containing the following terms: hormon?, endocrin?, thyroid?, androgen?, estrogen?, steroido?, aromatase, cytochrome p450 and intersex? - The search profiles were linked and searched in the databases TOXCENTER, HCAPLUS, MEDLINE, BIOSIS, EMBASE, CABA and AGRICOLA. - Results were restricted to the non-patent literature and a publication date greater than 2013. - Duplicates were eliminated.
The following terms were used for the search: - Hormone - Endocrine (- system, - disruption, - mediated mode of action,…) - Thyroid (-effects, -pathway,-inhibition) - Androgen* (- system, - disruption, - mediated mode of action,…) - Estrogen* (-effects, -pathway,-inhibition) - Steroido* - Aromatase (-effects, -pathway,-inhibition) - Cytochrome P450 (-effects, -pathway,-inhibition) - Intersex (effects, symptoms,…)

CA 9.3 Relevant study selection-results of the selection process

As first step, the rapid assessment was performed by expert reviewers based on summary records (title/abstracts).
Summary records clearly related to one of the following topics were classified as **obviously irrelevant:**

- Publications in non-EU language without English abstract
- Abstract refers to a conference contribution and does not contain data, full text not available
- Test substance was not the active ingredient glyphosate, but products/formulations only.
- Study is not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion as the information given in the summary records does not bear reference to "Endocrine Disruptor Screening Programme (EDSP)" or the Level 2 and 3 tests indicated in the Organisation for Economic Co-operation and Development (OECD) Conceptual Framework.

Obviously non-relevant studies in open literature search were excluded by applying the relevance criteria previously defined in Table 1 of this document. A total of **104 summary records** were reviewed; of these **99 were not relevant**. After reviewing the 7 potentially relevant studies, the 5 articles have been considered for Tier II summaries in Appendix 1.

Table 4 summarize the results of the selection process including the number of summary records and full text documents assessed.

Table 4
Literature search results

Data requirement(s) captured in the search	Number
Total number of summary records retrieved after all searches of peer-reviewed literature (excluding duplicates)	104
Number of summary records excluded from the search results after rapid assessment for relevance	97
Total number of full-text documents assessed in detail	7
Number of studies excluded from further consideration after detailed assessment for relevance	2
Number of studies not excluded for relevance after detailed assessment	5

CA 9.4 Literature included in the dossier after detailed assessment

Literature included as Tier II summaries are summarized and evaluated (e.g., Klimisch evaluation) in the Appendix 1).

Copies of the full text documents, abiding applicable copyright laws, are attached in Appendix 1. The list of literature excluded by rapid assessment is presented in Appendix 2.

Table 5 contain the bibliographic references for all relevant studies included as Tier II summaries.

Reliability assessments for each relevant study are included in this report at the end of each Tier II summary. There were not articles/literature excluded after detailed assessment, all relevant articles were subject of evaluation at full text level (see Appendix 1).

Table 5
Literature to be included after detailed assessment

N°	Author(s)	Year	Title	Source
1	Brennan, Jennifer C.; Bassal, Arzoo; He, Guochun; Denison, Michael S.	2016	Development of a recombinant human ovarian (BG1) cell line containing estrogen receptor alpha and beta for improved detection of estrogenic/antiestrogenic chemicals	Environmental toxicology and chemistry / SETAC. Volume 35, Number 1, Pages 91–100
2	Dai, Pengyuan; Hu, Ping; Tang, Juan; Li, Yansen; Li, Chunmei	2016	Effect of glyphosate on reproductive organs in male rat	Acta histochemical Volume 118, Issue 5, June 2016, Pages 519–526
3	Defarge, Nicolas; Takacs, Eszter; Lozano, Veronica Laura; Mesnage, Robin; Spiroux de Vendomois, Joel; Seralini, Gilles-Eric; Szekacs, Andras	2016	Co-Formulants in Glyphosate-Based Herbicides Disrupt Aromatase Activity in Human Cells below Toxic Levels	International journal of environmental research and public health. Vol 13.
4	Lanctot, C.; Navarro-Martin, L.; Robertson, C.; Park, B.; Jackman, P.; Pauli, B. D.; Trudeau, V. L.	2014	Effects of glyphosate-based herbicides on survival, development, growth and sex ratios of wood frog (Lithobates sylvaticus) tadpoles. II: agriculturally relevant exposures to Roundup WeatherMax(R) and Vision(R) under laboratory conditions	Aquatic toxicology (Amsterdam, Netherlands). Volume 154, September 2014, Pages 291–303
5	Uren Webster, Tamsyn M.; Laing, Lauren V.; Florance, Hannah; Santos, Eduarda M.	2014	Effects of glyphosate and its formulation, roundup, on reproduction in zebrafish (Danio rerio)	Environmental science & technology. Volume 48, Number 2, Pages 1271–1279

APPENDIX 1
TIER II SUMMARIES AND EVALUATION OF ARTICLES EVALUATED AT FULL TEXT LEVEL

1. Brennan, J., *et al.*, 2016: Development of a recombinant human ovarian (BG1) cell line containing estrogen receptor alpha and beta for improved detection of estrogenic/antiestrogenic chemicals.

Report: Brennan, J.C.; Bassal, A.; He, G.; Denison, M.S. (2016); Development of a recombinant human ovarian (BG1) cell line containing estrogen receptor alpha and beta for improved detection of estrogenic/antiestrogenic chemicals.

Source: Environmental Toxicology and Chemistry, 35 (1): 91-100

Abstract: Estrogenic endocrine-disrupting chemicals are found in environmental and biological samples, commercial and consumer products, food, and numerous other sources. Given their ubiquitous nature and potential for adverse effects, a critical need exists for rapidly detecting these chemicals. The authors developed an estrogen-responsive recombinant human ovarian (BG1Luc4E2) cell line recently accepted by the US Environmental Protection Agency (USEPA) and Organisation for Economic Co-operation and Development (OECD) as a bioanalytical method to detect estrogen receptor (ER) agonists/antagonists. Unfortunately, these cells appear to contain only 1 of the 2 known ER isoforms, ERa but not ERb, and the differential ligand selectivity of these ERs indicates that the currently accepted screening method only detects a subset of total estrogenic chemicals. To improve the estrogen screening bioassay, BG1Luc4E2 cells were stably transfected with an ERb expression plasmid and positive clones identified using ERb-selective ligands (genistein and Br-ERb-041). A highly responsive clone (BG1LucERbc9) was identified that exhibited greater sensitivity and responsiveness to ERb-selective ligands than BG1Luc4E2 cells, and quantitative reverse-transcription polymerase chain reaction confirmed the presence of ERb expression in these cells. Screening of pesticides and industrial chemicals identified chemicals that preferentially stimulated ERb-dependent reporter gene expression. Together, these results not only demonstrate the utility of this dual-ER recombinant cell line for detecting a broader range of estrogenic chemicals than the current BG1Luc4E2 cell line, but screening with both cell lines allows identification of ERa- and ERb-selective chemicals

Comment: The publication on *in vitro* estrogen receptor agonistic activity of pesticides in Environmental Toxicology and Chemistry, 35 (1): 91-100 is being submitted for the first time in this submission and has been conducted with glyphosate. A review of this publication indicates that even though it doesn't follow a defined guideline, the study is well documented and is scientifically sound. Therefore, the study is reliable and is relevant for risk assessment.

MATERIALS AND METHODS

A. MATERIALS

1. Test material: Glyphosate
   Purity: not provided
   CAS #: not provided

2. Control materials
   Vehicle control: Dimethyl sulphoxide (DMSO) (no data on purity).
   Positive control: 17β-Estradiol (E2; no data on purity)

3. Cell line and cell culture conditions

BG1Luc4E2 and BG1LucERβc9 cell lines were used in the studies with glyphosate. The BG1Luc4E2 cell line was developed by the authors and is used and accepted by USEPA and OECD for determination of ER agonists/antagonists. The BG1LucERβc9 was produced by stable transfection of the BG1LucERβc9 cells with ERβ/pcDNA3.1^{+}Zeo. For routine maintenance, cells were grown in α-minimal essential medium containing 10% fetal bovine serum and additional 600 mg/L Zeocin for the BG1LucERβc9 cells.

4. Stable transfection

To produce the stable BG1LucERβ cell line, human ovarian carcinoma (BG1Luc4E2) cells containing a stably transfected estrogen-responsive luciferase plasmid were transfected with ERβ/pcDNA3.1^{+}Zeo using FuGene6 transfection reagent according to the manufacturer's recommendation. After 24 h incubation in regular medium, the transfected cells were split 1 to 15 and replated into selective medium containing the antibiotic Zeocin (600 mg/L) which was replaced every 3 d with fresh Zeocin-containing medium. After approximately 3 weeks of growth, 28 individual cell colonies were isolated, their ERβ responsiveness was determined, and those clones exhibiting the greatest induction by ERβ-selective ligands (Br-ERβ-04 [31.6 nM] and genistein [10 nM]), were selected for further evaluation.

B. STUDY DESIGN AND METHODS

1. RNA isolation and RT-PCR

Cells in 10-cm plates (4 replicates per cell line) were grown in maintenance medium with the addition of Zeocin for the BG1LucERβc9 cells. Total RNA was isolated using RNeasy (Qiagen) according to the manufacturer's instructions (β-mercaptoethanol was added to the lysis buffer immediately before use, and cells were homogenized using QIAshredder homogenizer). Complementary DNA (cDNA) was generated from 2 mg RNA using a high-capacity cDNA Reverse Transcription kit (Applied Biosystems) with random primers followed by a 1:10 dilution with RNAse/DNAse-free water. Real-time quantitative polymerase chain reactions (20 mL) were performed with TaqMan Fast Universal PCR Master Mix and TaqMan Gene Expression assays (Applied Biosystems). The ERα and ERβ messenger RNA (mRNA) levels were quantitated, normalized to β-actin (internal control), and results presented relative to levels in BG1Luc4E2 cells (set to value of 1.0). Primers or probes for human ERb (ESR2, Hs01100353_m1), human ERa (ESR1, Hs00174860_m1), and human b-actin (ACTB, Hs999999031_m1) were obtained from Applied Biosystems.

2. Incubation and luciferase analysis

BG1LucERβ cells were switched from maintenance medium to estrogen-stripped medium, containing 10% charcoal-stripped fetal bovine serum and incubated 3 d before plating into white, clear-bottomed 96-well tissue culture plates at a density of 750 000 cells/mL. Cells were allowed to attach for 24 h and then were incubated with carrier solvent DMSO (1% final solvent concentration) or 10 µM glyphosate for 24 h at 37°C with triplicate wells per chemical and controls. After incubation, cells were rinsed twice with phosphate-buffered saline, lysed with Promega cell lysis buffer, and shaken for 20 min at room temperature to allow complete cell lysis. Luciferase activity in each well was measured by a microplate luminometer. For comparative purposes, luciferase induction values were normalized to maximal luciferase induction obtained with 1 nM E2 in each plate (set at 100%). Values represented the mean ± standard deviation (SD) of triplicate incubations in the single screening analysis of the chemical compound.

3. Data analysis

Significant differences between results were determined using one-way analysis of variance (i.e., Student's t test, 2-tailed, type 2, $p<0.05$). Luciferase activity of control (solvent-treated) cells was subtracted from that of treated cells to obtain final induced activity (relative light units [RLU]). Final RLU values less than 0 were set at 0 RLUs. Half-maximal concentrations induced (50% effective concentration [EC_{50}]) or repressed (50% inhibitory concentration [IC_{50}]) by chemical or extract were determined using SigmaPlot (Ver. 12) by the concentration of chemical that induced exactly 50% of maximal E2-induced luciferase activity.

II. RESULTS AND DISCUSSION

Estrogenic effects of glyphosate

Glyphosate had no estrogenic effect in both BG1LucERβ and BG1LucERβ cells. The induction of luciferase activity was in the range of the solvent control (DMSO). The relative luciferase activities after treatment with DMSO, E2 and glyphosate are provided in the following table (DMSO was set to 0% and E2 was set to 100%):

Compound	Activity [%] BG1Luc4E2	Activity [%] BG1LucERβc9
DMSO	0	0
Glyphosate	6 ± 2	2 ± 4
E2	100	100

III. CONCLUSION

Glyphosate did not show any estrogenic activity at a concentration of 10 µM in two cell lines or via the two human estrogen receptor (hER) subtypes, hERα and hERβ. Based on the OECD 455 guideline for the BG1 assay, relative activity for the test substance that is <20% of the response of a maximally inducing concentration of E2 is considered to be negative. Therefore, glyphosate is conlcluded to have no ERα, ERβ agonistic activities, *in vitro*.

(Brennan, J.C.; Bassal, A.; He, G.; Denison, M.S., 2016)

KLIMISCH EVALUATION

1. RELIABILITY OF STUDY:	**Reliable with restrictions**
Comment:	• No purity of test substance is provided. • No information about analytical verification of dosing/stability in solvent is provided but this has not been a requiremtn for these Level 2 assays. • Only few numbers/raw data were provided, which restricted a comprehensive assessment. • No GLP and no specific guideline followed. However, the methods were overall very comparable with the established and validate OECD 455 test guideline.
2. RELEVANCE OF STUDY:	Relevant with restrictions
Comment:	The information provided in the study is considered to be acceptable as supplementary data used for a weight of evidence approach for evaluation of endocrine disruption. Although no specific guideline was followed and no GLP was applied, the study is considered mechanistically and functionally similar to US EPA (Tier I) or OECD CF (Tier II) screening studies. The results from this study are in agreement with results from other mechanistically and functionally similar assays and are discussed in the Monsanto weight of evidence paper, including an estrogen receptor binding assay which is the gold standard for assessing whether a compound is a ligand for the estrogen receptor.
3. KLIMISCH CODE:	Klimisch rating of 2

2. Dai, P., *et al*, 2016: Effect of glyphosate on reproductive organs in male rat.

Report: Dai, P.; Hu, P.; Tang, J.; Li, Y.; Li, C. (2016); Effect of glyphosate on reproductive organs in male rat.

Source: Acta Histochemica, 118: 519-526

Abstract: Glyphosate as an active ingredient of Roundup®, which is thought to be one of the most popular herbicide was used worldwide. Many studies have focused on reproductive toxicity on glyphosate-based herbicide, but few evidence exists to imply the male reproductive toxicity of glyphosate alone in vivo. In this study SD rats were lavaged with glyphosate at doses of 5, 50, 500 mg/kg to detect the toxicity of glyphosate on rat testis. Glyphosate significantly decreased the average daily feed intake at dose of 50 mg/kg, and theweight of seminal vesicle gland, coagulating gland as well as the total sperm count at dose of 500 mg/kg. Immunohistochemistry of androgen receptor (AR) has no difference among all groups. As to testosterone, estradiol, progesterone and oxidative stress parameters, the level of them has no differences amidst all doses. Taken together, we conclude that glyphosate alone has low toxicity on male rats reproductive system.

Comment: The publication on glyphosate effects on male reproductive organs in SD rats in Acta Histohemica, 118 (2016) is being submitted for the first time in this submission and has been conducted with glyphosate. A review of this publication indicates that even though it doesn't follow a defined guideline and was not performed under GLP, the study is well documented and is scientifically sound. As deficits it could be mentioned that no detailed discussion concerning the relationship of parental toxicity (reduction of body weight gain and body weight) and effects observed in the reproductive organs was given. Furthermore, presentation of raw data of hormone levels would be helpful for further evaluation. In conclusion, the study is considered reliable and relevant for risk assessment and could be used as supplementary data.

MATERIALS AND METHODS

A. MATERIALS

1. Test material: Glyphosate (isopropylamine salt of n-phosphonomethylglycine)
   Purity: 90%
   CAS #: not provided

2. Control materials
   Vehicle control: Dimethyl sulphoxide (DMSO) (no data on purity).
   Positive control: 17β-Estradiol (E2; no data on purity)

3. Animals
   Strain: Sprague-Dawley rats
   Sex: male
   Age: 56 days old (sexually mature)
   Diet: balanced mixture pelleted food and water
   Environmental conditions:
   Air changes: not specified (air-conditioned room)
   Temperature: 21°
   Lighting: 12h/12h light/dark cycle

B. STUDY DESIGN AND METHODS

1. Experimental design

32 SD rats were divided into four groups randomly, three groups were lavaged with glyphosate which is diluted in a watery suspension and administered once a day between 8 a.m and 9 a.m. Control group was treated in the same way with deionized water. The applied doses were 5, 50, 500 mg/kg bw, respectively. All rats were lavaged with glyphosate or deionized water for 5 weeks continuously. After gavage, testis, epididymis, prostate gland and seminal vesicle were removed and weighed. Absolute weight and relative weight in comparison with total body of those organs were recorded. The right testis and epididymis were cut and stored at -20°C until the experiment was performed. The entire left testis were conserved overnight in 4% paraformaldehyde, and then

embedded in paraffin blocks prior to hematoxylin and eosin staining (HE) and immunohistochemical examination. The entire left epididymis were stored in normal saline at -20°C until calculating the total sperm count.

2. Endpoints determined

Epididymal sperm parameters
After sacrifice, the epididymis was weighed and then minced in PBS. The minced epididymis was filtered using a nylon mesh screen, and the filtrate was treated with 10 mL PBS. The number of sperm ount in term of standard hemo-cytometric method.

Hormone measurement
The serum hormones were measured by radioimmunoassay using a ^{125}I-labeled radio ligand double-antibody RIA Kit for total testosterone, estradiol and progesterone. The minimum sensitivity was 0.02 ng/mL, and intra- and inter-assay coefficients of variation (CV) was <10% for testosterone, and less than 0.2 ng/mL and a CV < 10%for progesterone, and less than 5 pg/mL and a CV < 10% for estradiol.

Testicular, epididymal and seminal vesicle gland histology
Following fixation of the tissues, the fixed samples were passed through a graded series of ethanol and xylene solutions and embedded in paraffin wax. Paraffin-embedded tissues were serially sectioned (5 μm thickness). For each rat, two non-serial sections were stained with hematoxylin and eosin (HE) using standard procedures for morphological analysis.

Antioxidant status analysis
The levels of catalase (CAT, U/mg protein), superoxide dismutase (SOD, U/mg protein) and malondialdehyde (MDA, μmol/g protein) were determined by the absorbance of samples in multiskan spectrum. SOD activity was detected by an SOD assay kit and the activity was supervised at 560 nm. As to CAT, the activity was determined by the consumption of H_2O_2 (μmol/g protein), and the absorbance was measured at 405 nm. MDA, produced by lipid-peroxidation, is determined by TBA (absorbance measured at 532 nm).

Immunohistochemistry
The sections of testis were deparaffinized with xylene and rehydrated in graded ethanol before being washed with twice-distilled water. To increase epitope exposure, the sections were heated for 15 min in sodium citrate buffer (0.01 M, pH 6.0) in a microwave oven. The sections were then cooled and washed with 0.01 M PBS, pH 7.2, and then blocked with 10% bovine serum albumin (BSA) in TBST (20 mMTris-buffered saline, 0.05% Tween 20, pH 7.5) for 1 h at room temperature. The sections were incubated overnight at 4°C with diluted (1:400) polyclonal antibodies against androgen receptor (rabbit anti-human AR) and the secondary antibody goat anti-rabbit IgG. The binding of the antibodies were visualized using an SABC Kit Elite and 0.05% 3,3-diaminobenzidine tetra-chloride in 0.01 M PBS, pH 7.2,containing 0.01% H_2O_2 for 2 min. The sections were counterstained with hematoxylin and mounted with coverslips. The specificity of the antibody was examined using 1% BSA rather than the primary antibody.

3. Data analysis

All results are means ± SEM. When multiple comparisons were performed, evaluation was done using one-way ANOVA followed by Tukey's multiple comparison test. Significant differences with controls were considered when $p < 0.05$.

II. RESULTS AND DISCUSSION

Body weight, body weight gain and average daily feed intake
Daily exposure to glyphosate dilution caused a significant decrease in average daily feed intake at the dose of 50 mg/kg bw but no dose-dependency was observed. There were no significant differences between experimental groups and control group about average daily gain, but the decrease of that was dose-dependent. No statistically significant effects on final body weights were observed although a slight reduction of the mean body weights of the 50 and 500 mg/kg bw groups was observed.

Reproductive organ weights and sperm parameters
The analysis of the absolute weights of the seminal vesicle gland and coagulating gland showed a significant and dose-dependent reduction. No significant difference was observed in other absolute organ weight or other

relative organ weight. The total sperm count in the 500 mg/kg experimental group was significantly decreased by about 25% comparing to that in control group, lacking a clear dose-dependent effect.

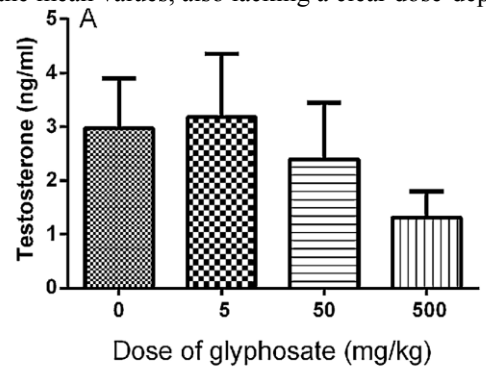
Absolute and relative (to body weight) weight parameters of investigated organs

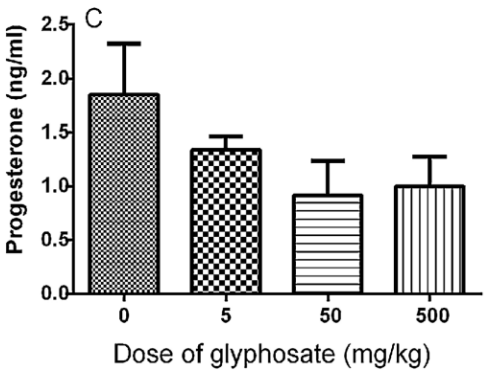
	Dose group [mg kg/bw]			
Weight parameters	**0**	**5**	**50**	**500**
Body weight				
abs. [g]	389 ± 7	404 ± 6	352 ± 21	352 ± 8
Testis				
abs. [g]	3.1 ± 0.11	3.04 ± 0.10	2.59 ± 0.22	3.06 ± 0.19
rel. [%]	0.83 ± 0.05	0.75 ± 0.02	0.73 ± 0.05	0.87 ± 0.04
Epididymis				
abs. [g]	1.09 ± 0.04	1.13 ± 0.03	0.98 ± 0.09	1.07 ± 0.05
rel. [%]	0.29 ± 0.01	0.28 ± 0.01	0.28 ± 0.02	0.30 ± 0.01
Prostate				
abs. [g]	0.45 ± 0.03	0.45 ± 0.02	0.39 ± 0.06	0.40 ± 0.05
rel. [%]	0.12 ± 0.01	0.11 ± 0.01	0.011 ± 0.01	0.011 ± 0.01
Seminal vesicle and coagulating gland				
abs. [g]	**1.58 ± 0.25**[a]	**1.49 ± 0.20**[ab]	**1.23 ± 0.48**[ab]	**1.10 ± 0.29**[b]
rel. [%]	0.42 ± 0.02	0.37 ± 0.02	0.34 ± 0.04	0.31 ± 0.03

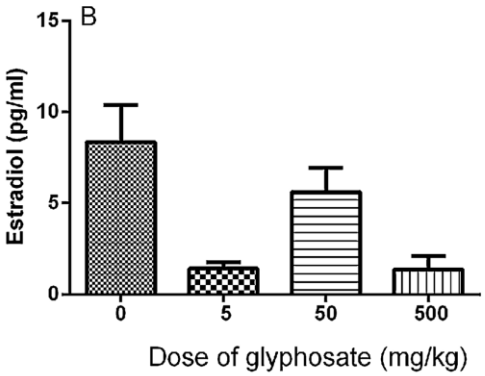
Data are means ± SEM (n=8,8,8,6)
characters a/b indicate significant differences between the compared groups ($p<0.05$)

Serum hormone levels

Glyphosate treatment did not lead to significant changes in the concentration of testosterone, estradiol and progesterone in serum between control group and treated groups. But testosterone levels seem to be decreased at 500 mg/kg bw by about 50%. Estradiol levels are decreased to approximately 25%, 75%, and 25% of the control values for the 5, 50, and 500 mg/kg bw dose group, respectively, lacking a clear dose-dependent trend. Progesterone seems to be slightly decreased to 40-60% of the control values at all three dose levels regarding the mean values, also lacking a clear dose-dependent trend.



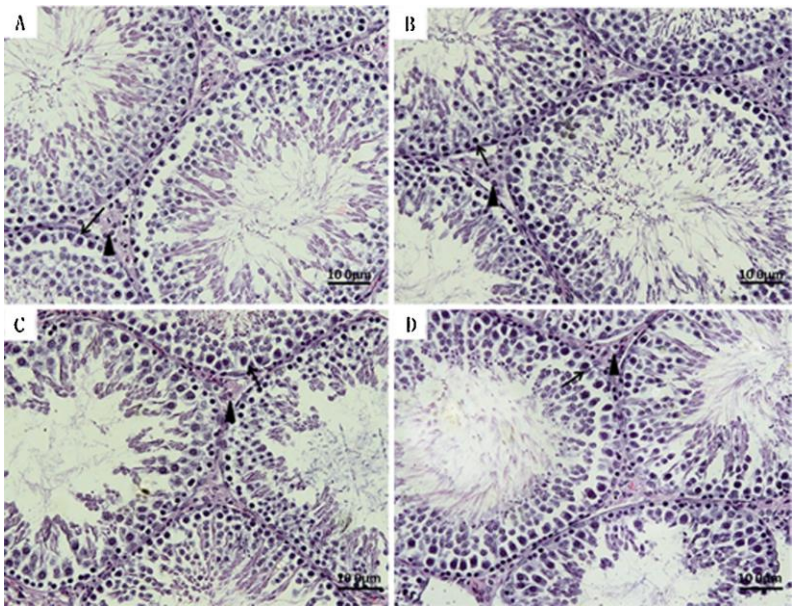




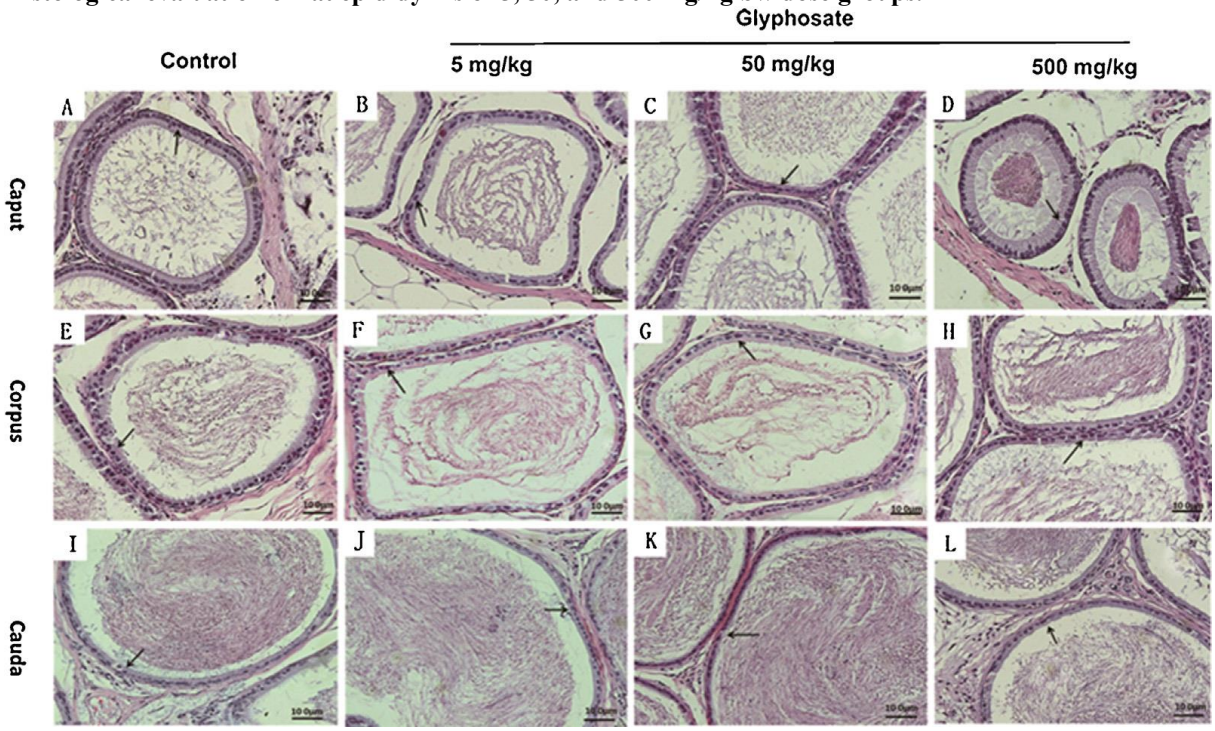
Effects of glyphosate on SOD and CAT activity, H_2O_2 and MDA level in testis
No significant differences within dose groups on SOD or CAT activity, as well as H_2O_2 and MDA levels in rat testis was observed.

Histology evaluation
No significant differences were observed in the testis, caput of epididymis, corpus or cauda of the epididymis, and seminal vesicle gland within any dose group.

Histological evaluation of rat testis of 5, 50, and 500 mg/kg bw dose groups.



Histological evaluation of rat epididymis of 5, 50, and 500 mg/kg bw dose groups.



Immunohistochemical localization of androgen receptor in testis
Androgen receptor (AR) immunoreactivity was localized in the nuclei of cells, including Sertoli cells, peritubular myoid cells and Leydig cells. There was no difference among all groups.

III. CONCLUSION

Glyphosate, when given to SD rats at 5, 50, and 500 mg/kg bw, respectively, significantly decreased the average daily feed intake at dose of 50 mg/kg bw, and the weight of seminal vesicle gland, coagulating gland as well as the total sperm count at a dose of 500 mg/kg bw. Immunohistochemistry of androgen receptor (AR) has no difference among all groups. As to testosterone, estradiol, progesterone and oxidative stress parameters, no significant effects were detected

(Dai, P.; Hu, P.; Tang, J.; Li, Y.; Li, C., 2016)

KLIMISCH EVALUATION

1. RELIABILITY OF STUDY:	**Reliable with restrictions**
Comment:	• No information about analytical verification of dosing/stability in solvent is provided. • No GLP and no guideline followed. • Data are available in a summarized format, as typical for a scientific publication. Therefore, a detailed re-evaluation is difficult to perform.
2. RELEVANCE OF STUDY:	Relevant with restrictions
Comment:	The information provided in the study is supposed to be acceptable as supplementary data used for evaluation of reproductive effects of glyphosate in male rats. Although no guideline was followed and no GLP was applied, the study is considered similar to US EPA (Tier I) or OECD CF (Tier IV) screening studies.
3. KLIMISCH CODE:	Klimisch rating of 2

3. Defarges, N., Takacs, E., Lozano, V.L., Mesnage, R., Spiroux de Vendomois, J., Seralini, G.E., Szekacs, A. (2016); Co-formulants in glyphosate-based herbicides disrupt aromatase activity in human cells below toxic levels.

Report: Defarges, N., Takacs, E., Lozano, V.L., Mesnage, R., Spiroux de Vendomois, J., Seralini, G.E., Szekacs, A. (2016); Co-formulants in glyphosate-based herbicides disrupt aromatase activity in human cells below toxic levels.

Source: International Journal of Environmental Research and Public Health, 13 (264): 1-17

Abstract: Pesticide formulations contain declared active ingredients and co-formulants presented as inert and confidential compounds. We tested the endocrine disruption of co-formulants in six glyphosate-based herbicides (GBH), the most used pesticides worldwide. All co-formulants and formulations were comparably cytotoxic well below the agricultural dilution of 1% (18–2000 times for co-formulants, 8–141 times for formulations), and not the declared active ingredient glyphosate (G) alone. The endocrine-disrupting effects of all these compounds were measured on aromatase activity, a key enzyme in the balance of sex hormones, below the toxicity threshold. Aromatase activity was decreased both by the co-formulants alone (polyethoxylated tallow amine—POEA and alkyl polyglucoside—APG) and by the formulations, from concentrations 800 times lower than the agricultural dilutions; while G exerted an effect only at 1/3 of the agricultural dilution. It was demonstrated for the first time that endocrine disruption by GBH could not only be due to the declared active ingredient but also to co-formulants. These results could explain numerous in vivo results with GBHs not seen with G alone; moreover, they challenge the relevance of the acceptable daily intake (ADI) value for GBHs exposures, currently calculated from toxicity tests of the declared active ingredient alone.

NOTE: This study tested formulations, coformulants and glyphosate alone. The focus of this assessment is on the glyphosate alone data.

MATERIALS AND METHODS

A. MATERIALS

1. Test material: Glyphosate (isopropylamine salt of n-phosphonomethylglycine);
   Purity: not provided
   CAS #: 1071-83-6
   Soure: Lamberti S.p.A, Abizzate, Italy
2. Control materials
   Negative control: not further specified
   Positive control: Formestan (4-hydroxyandrost-4-ene-3,17-dione; no data on purity)

Further test materials were used in this study and are listed in the following table for the sake of completeness, but are not discussed in detail in the summary:

	Products	**Trade Name (Manufacturer, Country)**	**Declared Active Ingredient (dAI)**
Co-formulants			
	POEA	Emulson AG GPE 3SS (Lamberti, Ita)	Polyethoxylated tallow amine
	POEA/F	Emulson AG GPE 3/SSM (Lamberti, Ita)	Polyethoxylated tallow amine
	QAC	Emulson AG CB 30 (Lamberti, Ita)	Quaternary ammonium compound
	POE-APE	Rolfen Bio (Lamberti, Ita)	POE alkyl phosphate ether
	APG	Plantapon LGC (The Soap kitchen, UK)	Alkyl polyglucoside
Formulations Glyphosate-based herbicides (GBH)			

	Products	Trade Name (Manufacturer, Country)	Declared Active Ingredient (dAI)
	RWMAX)	Roundup WeatherMAX (Monsanto, Can)	Potassium (660
	Glyfos	Glyfos (Cheminova, Hun)	IPA (486)
	R Classic	Roundup Classic (Monsanto, Hun)	IPA (486)
	Kapazin	Kapazin (Arysta, Hun)	IPA (486)
	Total	Total (Sinon Corporation, Hun)	IPA (486)
	Medallon	Medallon Premium (Syngenta, Hun)	diammonium (433)

B. STUDY DESIGN AND METHODS

1. Cell culture

JEG3 cells (human placental choriocarcinoma cells) used in these assays are well-characterized and validated as useful models to test toxicities of pesticides, corresponding to what is observed in fresh tissue or primary cells. They were reported to be partly less sensitive than primary cells and therefore do not overestimate cellular toxicity.

JEG3 cells were grown in phenol red-free Eagle's minimum essential medium (EMEM) containing 2 mM glutamine, 1% non-essential amino acid, 100 U/mL of antibiotics (a mixture of penicillin, streptomycin, and fungizone), 10 mg/mL of liquid kanamycin and 10% fetal bovine serum. JEG3 cells were supplemented with 1 mM sodium pyruvate. Cells were grown with this medium at 37°C (5% CO_2, 95% air) during 48 h to 80% confluence, then washed and exposed 24 h with serum-free EMEM to glyphosate (G), GBH formulations and their co-formulants. Before treatment, all the G, GBH, and co-formulants were diluted in serum-free medium and adjusted to a similar pH.

2. Cell treatment and cytotoxicity biomarkers

Confluent cells (80% of confluence) were washed with serum-free EMEM and then exposed to various concentrations of G, GBHs, and co-formulants in EMEM serum-free medium for 24 h. After treatments, cytotoxicity was determined by means of MTT assay (optical density measured at 570 nm). The bioluminescent Toxilight bioassay (Lonza, Saint Beauzire, France) was applied for the membrane degradation assessment by intracellular adenylate kinase (AK) release in the medium that is described as a necrosis marker. Glyphosate was tested from 1 to 10000 ppm [mg/L].

3. Determination of aromatase activity

Aromatase activity was evaluated according to the tritiated water release assay. This method is based on the stereo-specific release of 1β-hydrogen from the androstenedione substrate, which forms tritiated water during aromatization.

JEG3 cells were exposed for 22 h at 37°C (5% CO_2, 95% air) to 700 µL of non-toxic doses of different xenobiotics. Formestane, a well-known aromatase inhibitor, was used as a positive control. Then 50 µL of 200 nM [1β-^{3}H] androstenedione was added, and incubation went on for 120 min more. The reaction was stopped by placing the plates at 4°C for 10 min. Cell fragments were removed by 5 min centrifugation at 2000 rpm at 4°C and by addition of 1 mL of chloroform to the 500 µL supernatant. After 5 min centrifugation at 4000 rpm at 4°C, 0.5 mL of charcoal/dextran (0.25%/0.025%) was added. The mixture was gently agitated, rested at 4°C for 10 min, and centrifuged at 4000 rpm for 10 min at 4°C. Supernatant fractions (500 µL) were harvested in 6 mL vials and 4 mL Ultima Gold LLT was added. The mixture was assessed for radioactivity by a double 5 min scintillation counting. Glyphosate was tested at non-toxic doses in the aromatase assay (16 ppm [mg/L])

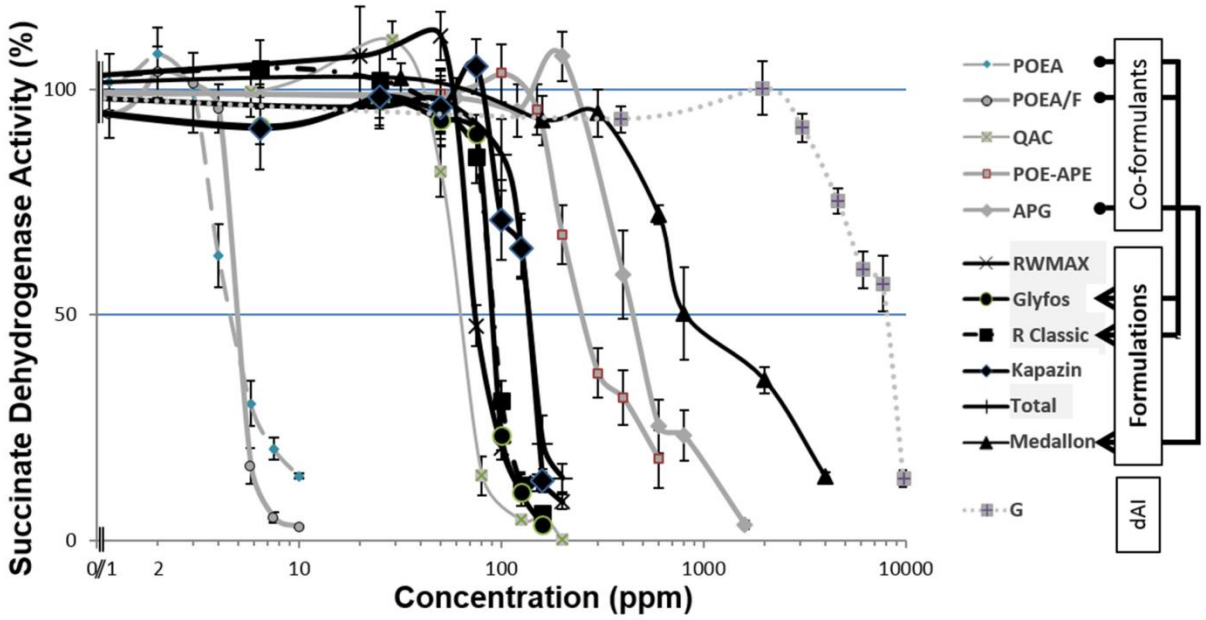
4. Data analysis

All results are means ± SEM. Three independent experiments were performed using triplicate cultures each. In MTT assays, LC_{50} values were the best-fitted value of a non-linear regression using asymmetric (5-parameters) equation with GraphPad Prism 5 (GraphPad software, La Jolla, CA, USA). Statistical differences were determined by a non-parametric Wilcoxon (Mann–Whitney) rank-sum test or, in case of more than two samples, a non-parametric Kruskal–Wallis test followed by a Dunn's post hoc test for multiple comparisons, using GraphPad Prism 5 (GraphPad software, La Jolla, CA, USA). Significant levels were reported with $p < 0.05$ (*), $p < 0.01$ (**) and $p < 0.001$ (***).

II. RESULTS AND DISCUSSION

Toxicity tests

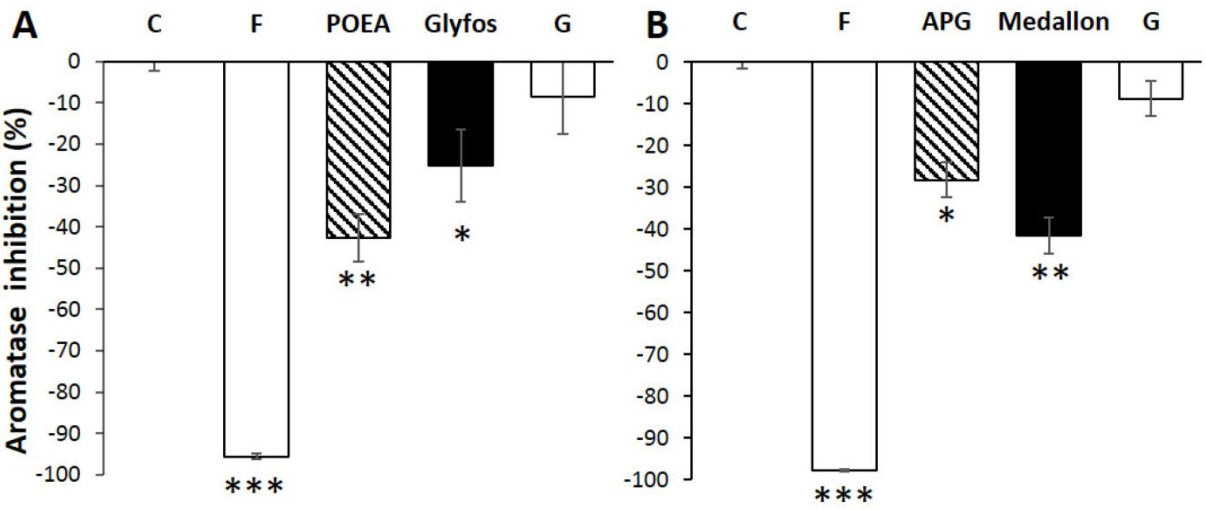
The lowest concentration exerting a significant toxic effect (LOEC) was considered to be the toxicity threshold. The highest concentration without significant cytotoxic effect (NOEC) was also reported. LC50, NOEC, and LOEC values of 7878, 3100, and 4600 ppm [mg/L] were determined for glyphosate. Glyphosate showed cytotoxic effects at high doses only, whereas the co-formulants or formulations were more toxic by a factor 10-1000 (see the following table):



The adenylate kinase activity, which was determined as a marker for necrosis, was not influenced by glyphosate when compared to the negative control.

Aromatase activity

Glyphosate had no effect on the aromatase activity when tested at concentrations used in the formulations (16 – 146 ppm [mg/L]). At very high doses of 3000 ppm a significant aromatase inhibition was observed by glyphosate (-51%; data not shown in article and 3000 ppm which is equivalent to 17,740 µM glyphosate). In the following figure the effects of glyphosate (G) on the aromatase activity is exemplary shown (A: POEA, 2.5 ppm; Glyfos, 25 ppm; G, 16 ppm; B: APG, 120 ppm; Medallon, 300 ppm; G, 146 ppm):



III. CONCLUSION

Glyphosate showed low toxicity in JEG3 cells. At non-toxic concentrations (up to approximately 2000 ppm [mg/L]) glyphosate had no effect on the aromatase activity. At 3000 ppm [mg/L; equivalent to 17,741 µM glyphosate] a reduction of aromatase activity by glyphosate was observed. In conclusion, the reported data showed that glyphosate did significantly inhibit aromatase inhibition.

(Defarges, N., Takacs, E., Lozano, V.L., Mesnage, R., Spiroux de Vendomois, J., Seralini, G.E., Szekacs, A., 2016)

KLIMISCH EVALUATION

1. RELIABILITY OF STUDY:	**Not Reliable**
Comment:	• No data on purity. • No information about analytical verification of dosing/stability in solvent is provided. • Non GLP and no guideline followed. Tested glyphosate concentrations greater than the aromatase assay has been validated to assess.
2. RELEVANCE OF STUDY:	**Not Relevant**
Comment:	Although no guideline was followed and no GLP was applied, the assays that tested glyphosate is considered similar to US EPA (Tier I) or OECD CF (Tier II) screening studies. The maximum glyphosate concentration tested of 3000 ppm, where inhibition was reported but not shown, is equivalent to a concentration of 17,741 µM. The highest concentration that is required to be tested under the EPA guideline is 1000 µM, which still represents a highly supraphysiological concentration. No effect at the lower concentrations (e.g., 2,000 ppm) anf this result is consistent with the result for the aromatase assay in the Tier 1 EDSP battery where glyphosate did not inhibit aromatase activity up to 1000 µM and was concluded to not be a aromatase inhibitor. No indication of aromatase inhibition was observed in any of the *in vitro* or *in vivo* Tier 1 EDSP assays (i.e., steroidogenesis, Hershberger, male and female pubertals, fish short term reproduction).
3. KLIMISCH CODE:	Klimisch rating of 3

4. Lanctot, C., *et al*, 2014: Effects of glyphosate-based herbicides on survival, development, growth and sex ratios of wood frog (Lithobates sylvaticus) tadpoles. II: agriculturally relevant exposures.

Report: Lanctot, C., Navarro-Martin, L., Robertson, C., Park, B., Jackman, P., Pauli, B.D., Trudeau, V.L. (2014); Effects of glyphosate-based herbicides on survival, development, growth and sex ratios of wood frog (Lithobates sylvaticus) tadpoles. II: Agriculturally relevant exposures to Roundup WeatherMax® and Vision® under laboratory conditions.

Source: Aquatic Toxicology, 154:291-303

Abstract: Glyphosate-based herbicides are currently the most commonly used herbicides in the world. They have been shown to affect survival, growth, development and sexual differentiation of tadpoles under chronic laboratory exposures but this has not been investigated under more environmentally realistic conditions. The purpose of this study is (1) to determine if an agriculturally relevant exposure to Roundup WeatherMax®, a relatively new and understudied formulation, influences the development of wood frog tadpoles (Lithobates sylvaticus) through effects on the mRNA levels of genes involved in the control of metamorphosis; (2) to compare results to the well-studied Vision® formulation (containing the isopropylamine salt of glyphosate [IPA] and polyethoxylated tallowamine [POEA] surfactant) and to determine which ingredient(s) in the formulations are responsible for potential effects on development; and (3) to compare results to recent field studies that used a similar experimental design. In the present laboratory study, wood frog tadpoles were exposed to an agriculturally relevant application (i.e., two pulses) of Roundup WeatherMax® and Vision® herbicides as well as the active ingredient (IPA) and the POEA surfactant of Vision®. Survival, development, growth, sex ratios and mRNA levels of genes involved in tadpole metamorphosis were measured. Results show that Roundup WeatherMax® (2.89 mg acid equivalent (a.e.)/L) caused 100% mortality after the first pulse. Tadpoles treated with a lower concentration of Roundup WeatherMax® (0.21 mg a.e./L) as well as Vision® (2.89 mg a.e./L), IPA and POEA had an increased condition factor (based on length and weight measures in the tadpoles) relative to controls at Gosner stage (Gs) 36/38. At Gs42, tadpoles treated with IPA and POEA had a decreased condition factor. Also at Gs42, the effect on condition factor was dependent on the sex of tadpoles and significant treatment effects were only detected in males. In most cases, treatment reduced the normal mRNA increase of key genes controlling development in tadpoles between Gs37 and Gs42, such as genes encoding thyroid hormone receptor beta in brain, glucocorticoid receptor in tail and deiodinase enzyme in brain and tail. We conclude that glyphosate-based herbicides have the potential to alter mRNA profiles during metamorphosis. However, studies in natural systems have yet to replicate these negative effects, which highlight the need for more ecologically relevant studies for risk assessment.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material[4]:: 540 g a.e. /L (WeatherMax®); 356 g a.e./L (Vision ®)
   Purity: Source for IPA or POAE not stated
   CAS #: 1071-83-6
   Source of test substance: Monsanto, Winnipeg, MB, CAN

2. Control materials
   Positive control: none

3. Test organism

   Tadpoles in Gosner stage 25 reared from fertilized *L. sylvaticus* egg masses collected from natural wetlands in New Brunswick, Canada (45◦401N, 66◦291W).

[4] a.e.: acid equivalent

B. STUDY DESIGN AND METHODS

1. Test organism treatment and study design

Tadpoles (n = 50) were placed into 50-liter glass aquaria (1 tadpole/L) and divided into seven treatment groups (3 replicates per treatment): control, Roundup WeatherMax® (0.21 and 2.89 mg a.e./L), Vision® (2.89 mg a.e./L), isopropylamine (IPA) salt of glyphosate (2.89 mg a.e./L), polyethoxylated tallowamine (POEA, 1.43 mg/L, pulse exposure) and POEA Chronic (1.43 mg/L, continuous exposure until tadpoles reached Gs42). Tadpoles were fed a combination of boiled kale and Ward's dry tadpole food daily ad libitum, supplemented with algal pellets weekly.

Treatments were added to experimental aquaria twice except for POEA Chronic. The first application took place when tadpoles reached Gs25, which corresponds approximately to the developmental stage that *L. sylvaticus* tadpoles would reach when the first pulse application would be applied for agriculture. The second application took place 2 weeks later (~Gs30). Each pulse exposure was carried out over 4 consecutive days with full water renewal each day. During each 4-day pulse, nominal concentrations were decreased by 25% each day to mimic natural degradation of the herbicide. After the fourth day, tadpoles were transferred to and remained in clean water until they reached Gs42. Water renewals were performed three times per week between and after each pulse exposure. The POEA Chronic treatment was maintained at a target concentration of 1.43 mg/L POEA until tadpoles reached Gs42 and POEA treatment was renewed at the same time as the pulse treatments. Water samples (1 L) were taken on each day of the 4-day exposure and additionally on day 5 for each pulse to determine glyphosate concentrations. Samples were maintained at ~6 ◦C and analyzed within 11 days. Aqueous glyphosate concentrations were measured using a liquid chromatography/mass spectrometry method. Temperature, dissolved oxygen and pH measurements were recorded regularly (approximately 3–5 times per week).

Survival was assessed regularly throughout the experiment.

Tadpoles were sampled for analysis of mRNA levels when the median developmental stage within each aquarium reached Gs31 (pre-metamorphosis), Gs37 (pro-metamorphosis) and Gs42 (metamorphic climax). For each developmental stage, tadpoles were sampled and morphometrics were measured from one aquarium per treatment (i.e., Gs31, Gs37, Gs42 were sampled from different aquaria). Subsequently, tadpoles were dissected and whole brain and tail tissues were preserved in RNAlater (Ambion), a reagent used to stabilize RNA.

Five males and three females per treatment were randomly selected for histological assessment to determine presence of testicular oocytes, inhibited gonadal development, oocyte atresia or other potential abnormalities. Mesonephrosgonad complexes were embedded in paraffin blocks and oriented in transverse plane for sectioning. Paraffin sections were cut at 6 µm and stained with haematoxylin–eosin following conventional histological procedures.

Total RNA from whole brain and tail tissue from Gs37 and Gs42 tadpoles was isolated using Qiagen RNeasy Micro Kit, or a combined protocol of TRIzol (Invitrogen) and Qiagen RNeasy Mini Kit, respectively. The concentrations of total RNA, the ratio of absorbance at 260 and 280 nm and the ratio of absorbance at 260 and 230 nm were determined using a spectrophotometer. Total cDNA of brain and tail samples was synthesized from 1 and 3 µ,g of total RNA, respectively.

Real-time RT- PCR was performed using SYBR Green I for trˇ, grII, crf and rpl8, and fluorogenic 51 nuclease chemistry for dio2 and dio3. NORMA-Gene, a data driven normalization algorithm, was used to normalize mRNA level data. Normalization was performed using 6 target genes analyzed for each tissue. Fold change in normalized mRNA relative to control Gs37 was then calculated for each sample. Biological replicates were averaged to obtain mean fold change in mRNA levels ± standard error of the mean (SEM).

2.1 Data analysis

Differences in growth measurements (SVL, tail length, weight and condition factor) between treatments were analyzed for significance using non-parametric Kruskal–Wallis test with pairwise multiple comparisons. At Gs42 analysis for alterations in sex ratios of the treated groups relative to the control and relative to an equal proportion of males and females was performed using the Chi-

Square test. In addition, differences between sexes in SVL, tail length, weight, condition factor (k) and time to metamorphosis were analyzed by Mann–Whitney U test. Levels of mRNA were analyzed for normality (Kolmogorov–Smirnov) and homogeneity of variance (Levene's test) and log10 transformed to meet parametric assumptions. Two- way ANOVA was performed with treatment and developmental Gosner stage as independent factors and mRNA levels as the dependent variables. Tukey's HSD post hoc multiple comparisons were used to analyze for statistical differences between treatments and developmental stages. Analyses were performed using SPSS 20.0.0 (IBM Corp.) and differences were considered to be significant when $p < 0.05$.

II. RESULTS AND DISCUSSION

A. GROWTH, SURVIVAL AND DEVELOPMENT

16 days after the first exposure to Roundup WeatherMax® (2.89 mg a.e./L) survival was 5.3% and complete mortality was observed before the second pulse (day 18). Similarly, in the chronic POEA (1.43 mg/L) treatment, survival was 11.3% at 16 days after the beginning of the exposure (approximately 8 times lower than control), and by day 23, all test specimens died. By the end of the experiment (after 2 pulses), survival was 78% in control, 86% in Roundup WeatherMax® (0.21 mg a.e./L), 68% in Vision® (2.89 mg a.e./L), 86% in IPA (2.89 mg a.e./L) and 70% in POEA pulse (1.43 mg/L).

At Gs31, no significant differences in SVLm tail length or condition of tadpoles were observed. Tadpoles exposed to one pulse of Roundup WeatherMax® (0.21 mg a.e./L), Vision (2.89 mg a.e./L), IPA (2.89 mg a.e./L) and POEA (1.43 mg/L) weighed 7.9, 7.1, 12.9 and 6.4% more than control tadpoles, respectively. Tadpoles exposed to two pulses of Roundup WeatherMax® (0.21 mg a.e./L), Vision® (2.89 mg a.e./L), IPA (2.89 mg a.e./L), and POEA (1.43 mg/L) had 11.3, 5.8, 8.4, 5.8% smaller SVL than control tadpoles, respectively. Tadpoles exposed to two pulses of POEA (1.43 mg/L) also had a 7.4% increase in tail length relative to control. No significant differences in tail length were observed in the Roundup WeatherMax® (0.21 mg a.e./L), Vision® (2.89 mg a.e./L) and IPA (2.89 mg a.e./L) treatments relative to controls. In addition, tadpoles exposed to Roundup WeatherMax® (0.21 mg a.e./L), Vision® (2.89 mg a.e./L), IPA (2.89 mg a.e./L), and POEA (1.43 mg/L) had 32.3, 18.8, 34.7, 22.6% higher condition factor than control, respectively. At metamorphic climax (Gs42), no significant differences in SVL, weight or tail length were observed between treatments. Tadpoles exposed to IPA (2.89 mg a.e./L) and POEA (1.43 mg/L) had 28.0 and 22.2% lower condition factor than controls, respectively. There were no treatment related differences in time to metamorphosis.

B. SEX RATIOS AND GONADAL MORPHOLOGY

There were no differences for sex ratios between control and treatment groups except for the IPA (2.89 mg a.e./L) treatment, with an increase in the proportion of females to 55.2%, compared to 41.1% in the control group. However, a Chi-Square test was performed to detect any possible deviation of sex ratios from the theoretical expected equal proportion of males and females (50:50). Results showed no significant differences compared to the predicted 50:50 sex ratio in any case (Chi-Square test, $p > 0.05$). Intersex (presence of both ovarian and testicular tissue in the same individual) was not observed in this study. In addition, there were no anomalies observed in the gonads.

C. MRNA LEVELS IN BRAIN AND TAIL

The effect of treatment in brain was significant for crf, tr, and dio3 but was not significant for grII . Tadpoles exposed to IPA (2.89 mg a.e./L) had significantly less tr mRNA than all other treatments. Although two-way ANOVA showed significant differences for crf and dio3, Tukey post hoc tests did not detect significant differences between treatments. Significant interactions between Gosner stage and treatment were detected for dio2 and rpl8 in the brain. rpl8 mRNA levels were significantly increased by Roundup WeatherMax® (0.21 mg a.e./L) and reduced by POEA (1.43 mg/L) treatment at Gs42. No interactions were detected for all other genes (tr˘, dio3, crf and grII).

In tail tissue, a two-way ANOVA analysis also revealed stage and treatment differences, and significant stage treatment interactions for some of the genes analyzed. Simple main effects analysis showed significant differences between Gosner developmental stage for crf, dio2, and dio3. Specifically, an increase in dio2 and dio3 mRNA levels and a decrease in crf mRNA levels between Gs37 and Gs42 was

observed. Tadpoles exposed to IPA (2.89) had significantly less dio2 mRNA than did tadpoles exposed to Roundup WeatherMax® (0.21 mg a.e./L) and POEA (1.43 mg/L) ($p < 0.05$), but they did not differ from control and Vision® (2.89 mg a.e./L) groups. Tadpoles exposed to IPA (2.89 mg a.e./L) also had significantly less dio3 mRNA than control and Vision® (2.89 mg a.e./L) but did not differ from Roundup WeatherMax® (0.21 mg a.e./L) and POEA (1.43 mg/L) ($p > 0.05$). Significant interactions between Gosner stage and treatment were detected for trˇ, grII and rpl8. For these 3 genes, the normal developmental changes in mRNA levels between Gs37 and Gs42 observed in the control group were altered by treatment. At Gs42, trˇ mRNA levels were reduced by Roundup WeatherMax® (0.21 mg a.e./L) and IPA (2.89 mg a.e./L) treatment. Similarly, grII mRNA levels were also reduced by Roundup WeatherMax® (0.21 mg a.e./L) treatment at Gs42. For rpl8, mRNA levels were reduced by both IPA (2.89 mg a.e./L) and POEA (1.43 mg/L) treatment at Gs42.

III. CONCLUSION

The current laboratory study shows that exposures of wood frog tadpoles to Roundup WeatherMax® alter the mRNA levels of genes involved in the control of metamorphosis. These effects were observed at an exposure concentration of 0.21 mg a.e./L applied at two 4-day pulses, but concentrations were not high enough to translate into clear phenotypic or developmental changes. Time to metamorphic climax (Gs42) was not affected. Furthermore, exposure to Roundup WeatherMax® and chronic exposure to POEA (1.43 mg/L) is highly toxic to *L. sylvaticus* tadpoles under laboratory conditions. Survival, growth and mRNA results also indicate that Roundup WeatherMax® has greater toxicity than Vision® formulation containing the POEA surfactant. Furthermore, pulse exposure to POEA (1.43 mg/L) did not cause a greater disruption of growth, development, or mRNA abundance of thyroid-dependent genes than the active ingredient (IPA).

In the discussion section, differences between laboratory and field studies are discussed. It is concluded that the effects of glyphosate-based herbicides are exaggerated in laboratory studies.

(Lanctot, C., Navarro-Martin, L., Robertson, C., Park, B., Jackman, P., Pauli, B.D., Trudeau, V.L. 2014)

KLIMISCH EVALUTION

1. RELIABILITY OF STUDY: **Not reliable**

Comment:

- The paper is well documented laboratory assays , data about test conditions are reported; however, application scheme (pulse dosing) is unrealistic for agricultural applications, dosing is very high. Variability of test concentrations very high (as reported)
- No reliable, growth-stage specific, and exposure time relevant LC50 values determined to justify the testing range, ahead of performing the study on ED endpoints.

The test items IPA and POEA are not reported as to their source or purity.

No reference test item was used to demonstrate that ED endpoints could be measured reliably in the test system.

2. RELEVANCE OF STUDY: **Not relevant**

Comment:

The design of this study does not follow an established and validated protocol to evaluate potential impacts to tadpoles. Under EPA's EDSP, glyphosate was tested following the amphibian metamorphosis guideline (OECD 231). This study showed that glyphosate did not to interfere with the normal function of the HPT axis of African clawed frog tadpoles up to a concentraton 90 mg glyphosate a.e./L.

Excessive mortality was observed in treatment groups, hence it cannot be excluded that any metabolic changes are due to overt toxicity.

3. KLIMISCH CODE: Klimisch rating of 3

5. Uren, T., et al, 2014: Effects of glyphosate and its formulation, roundup, on reproduction in zebrafish (*Danio rerio*) - Results from a fish full life cycle study with the fathead minnow

Report: Uren Webster, T.M., Laing, L.V., Florance, H., Santos, E.M. (2014); Effects of glyphosate and its formulation, Roundup, on reproduction in zebrafish (*Danio rerio*).

Source: Journal of Toxicology and Environmental Health, Part A, 77:405–414

Abstract: Roundup and its active ingredient glyphosate are among the most widely used herbicides worldwide and may contaminate surface waters. Research suggests both Roundup and glyphosate induce oxidative stress in fish and may also cause reproductive toxicity in mammalian systems. We aimed to investigate the reproductive effects of Roundup and glyphosate in fish and the potential associated mechanisms of toxicity. To do this, we conducted a 21-day exposure of breeding zebrafish (*Danio rerio*) to 0.01, 0.5, and 10 mg/L (glyphosate acid equivalent) Roundup and 10 mg/L glyphosate. 10 mg/L glyphosate reduced egg production but not fertilization rate in breeding colonies. Both 10 mg/L Roundup and glyphosate increased early stage embryo mortalities and premature hatching. However, exposure during embryogenesis alone did not increase embryo mortality, suggesting that this effect was caused primarily by exposure during gametogenesis. Transcript profiling of the gonads revealed 10 mg/L Roundup and glyphosate induced changes in the expression of cyp19a1 and esr1 in the ovary and hsd3b2, cat, and sod1 in the testis. Our results demonstrate that these chemicals cause reproductive toxicity in zebrafish, although only at high concentrations unlikely to occur in the environment, and likely mechanisms of toxicity include disruption of the steroidogenic biosynthesis pathway and oxidative stress.

I. MATERIALS AND METHODS

A. MATERIALS

1.	Test material:	Roundup GC liquid glyphosate concentrate containing 120 g/L and separately glyphosate acid
	Purity:	Commercial MON formulation Purity not stated
	Source of test substance	Formulation: Commercial MON formulation Glyphosate: Analytical grade; Molekula, Wimborne, U.K
2.	Control materials	
	Positive control:	Another test substance
	Source of test substance	Molekula, Wimborne, U.K.

3. Test organism

4 male and4 female WIK strain *D. rerio* at an age of 20 weeks were kept15 L glass vessels and allowed to breed naturally during a 7 day acclimation period. The mean mass and length of male and female fish were 375.0 ± 6.3 mg/32.6 ± 0.2 mm and 402.6 ± 9.3 mg/31.7 ± 0.2 mm, respectively. Each tank was aerated and supplied with a water flow rate of 48 L /day. The aquarium water supply was reverse-osmosis treated tap water reconstituted with salts to produce standardized synthetic freshwater, and maintained at 28 ± 0.5 °C and pH 7-7.5. Fish were kept under a 12h light:dark cycle (with 30 minute dawn/dusk transitional periods) and fed twice daily with live *Artemia* nauplii and flake food.

B. STUDY DESIGN AND METHODS

1. Test organism treatment and study design

Experiments were carried out using a flow-through test system for a period of 21 days, preceded by a 10 day pre-exposure period. The treatment groups consisted of three concentrations of Roundup; 0.01, 0.5, and 10 mg/L glyphosate acid equivalent, 10 mg/L glyphosate, and a control group. Each treatment group was comprised of three replicate breeding colonies (4 males and 4 females) in 15 L tanks. Water samples were collected from each tank on days 7, 14, and 21 of the exposure period and stored at −20 °C prior to chemical analysis. Eggs were collected 1 h post fertilization (hpf), rinsed thoroughly to remove detritus and incubated in water containing the same chemical exposure concentrations as their tank of origin, at 28 °C.

2. Reproductive test and embryo exposures

Eggs from each colony were examined using light microscopy between 2 1/2 and 3 1/2 h after dawn, when all fertilized eggs had reached at least the 16-cell stage during early cleavage, and the total number of fertilized and unfertilized eggs were quantified on each day throughout the pre-exposure and exposure periods. During the 21-day chemical exposure, fertilized eggs displaying cellular necrosis were counted and recorded as early stage mortalities (<3.5 hpf). Fifty fertilized eggs from each tank were selected randomly and incubated in 50 mL exposure water until 72 hpf. During this period, embryo mortality was recorded at 24, 54, and 72 hpf and embryo hatching was recorded at 54 and 72 hpf. To determine if the observed effects of Roundup and glyphosate on embryos were because of the effects of exposure during gametogenesis or during embryogenesis, embryos collected from a control population were exposed concurrently to a range of concentrations of glyphosate and Roundup. Chemical treatment was initiated between 10 and 20 min post fertilization. In addition to the exposure concentrations used for the adult exposures, embryos were also treated with higher concentrations (50, 100, 250, 500, and 1000 mg/L a.e. Roundup and glyphosate) to determine the concentration thresholds for embryo mortalities and developmental toxicity. Experiments were conducted in triplicate; each replicate contained 50 embryos.

3. Histological analysis and transcript profiling

Wet weight and fork length were recorded and the condition factor (k = (weight (g) × 100)/(fork length (cm)3)) was calculated for individual fish. Livers were dissected and weighed, and the hepatosomatic index (HSI) was determined for individual fish. Gonads were dissected and weighed. Gonads for histological analysis were fixed in Bouin'solution. The gonadosomatic index (GSI; gonad weight (mg)/total weight (mg)) × 100)) was determined for both males and females. Transcript profiling of genes encoding steroidogenic enzymes, sex steroid receptors and antioxidant enzymes, was conducted using real time quantitative PCR (RT-QPCR) in the gonads of exposed fish. Primers for each target gene were designed with Beacon Designer 3.0 software using zebrafish NCBI refseq sequences. Primer specificity throughout the range of detection was confirmed by the observation of single amplification products of the expected size and Tm, and optimised by performing a standard curve for each primer pair. RNA was extracted from the gonads of eight male and eight female fish from each treatment group. RNA concentration and purity were assessed from 2 µg of total RNA treated with RQ1 DNase. cDNA was diluted (ovary 1:4, testis 1:2) and RT-QPCR was performed in duplicate in an iCycler iQ Real-time Detection System using SYBR Green chemistry. A template-minus negative control was run in duplicate on each plate to verify the absence of cDNA contamination. Efficiency-corrected relative expression levels were determined by normalizing to a control gene, ribosomal protein l8 (rpl8), which was previously shown to have consistent expression in ovaries and testis.

4. Data analysis

Statistical analyses were conducted with SigmaStat (version 12.0). Before analysis, proportional data (embryo survival and hatching) were subjected to variance-stabilizing square-root or arcsine transformations as appropriate. All reproductive output and sampling data met assumptions of normality and equal variance. Outliers in transcript expression data were identified and removed according to Chauvenet's criterion41 prior to statistical analysis. Transcript expression data that did not meet normally distributed criteria was log transformed before statistical analysis. All data was analyzed using single factor one way analysis of variance (ANOVA), followed by the Holm−Sidak post hoc test using a pairwise comparison method. Data were considered to be significant when $P < 0.05$.

II. RESULTS AND DISCUSSION

A. MORPHOMETRY AND REPRODUCTION

There were no significant differences in size or condition factor (mean 1.08 and 1.25 for males and females, respectively) between treatment groups. No alteration of general health or behaviour was observed in any colony. The GSI of females was significantly lower in the fish treated with 10 mg/L glyphosate compared to the control group. There was no significant difference in the GSI of males between treatment groups, or in the HSI of males or females.

In terms of reproduction, during the 10 day pre-exposure period, there was no difference in cumulative egg production between the treatment groups. During the exposure period, colonies in the control group consistently spawned the greatest number of eggs per female, while those treated with 10 mg/L glyphosate spawned the least. From day 10 of the exposure period, cumulative egg production was significantly reduced in colonies exposed to 10 mg/L glyphosate compared to the controls, and this difference intensified throughout the remainder of the exposure period. At the end of the 21 day exposure, cumulative egg production was significantly lower in colonies exposed to 10 mg/L glyphosate compared to the control, and also compared to the 10 and 0.01 mg/L Roundup groups. Fertilisation rate remained consistently high throughout the exposure period with no significant differences between treatment groups and an overall mean value of 83.4%.

There was a significant increase in embryo mortalities occurring before 3.5 hpf in embryos from both the 10 mg/L Roundup and glyphosate treatment groups. Additionally, there was a significant correlation between early embryo mortality and the concentration of Roundup. There were no significant differences between treatments in embryo mortality between the start of epiboly (3.5 hpf) and the end of somitogenesis at 24 hpf. However, there was a significant increase in the percentage of embryos that had hatched at 54 hpf in groups treated with 10 mg/L Roundup and 10 mg/L glyphosate compared to the control group. For embryos originating from a control population, exposure to glyphosate and Roundup at the concentrations used in the adult reproductive test (0, 0.01, 0.5, and 10 mg/L Roundup and 10 mg/L glyphosate) did not result in increased mortality rate at either 3.5 hpf or 24 hpf, but there was a significant increase in 3.5−24 hpf mortality in embryos exposed to concentrations ≥100 mg/L glyphosate and ≥500 mg/L Roundup.

B. GONAD TRANSCRIPT PROFILING AND HISTOLOGY

In the ovary, the transcript encoding aromatase (cyp19a1) was significantly up-regulated in the 10 mg/L Roundup treatment group compared to the controls. Estrogen receptor 1 (esr1) in the 10 mg/L Roundup group was significantly up-regulated compared to the 10 mg/L glyphosate group. There were similar, but not statistically significant, decreasing trends in expression of other steroido- genic enzymes including cytochrome P450, subfamilies 17 and 11 (cyp17a1, cyp11a1) and 3β-hydroxysteroid dehydrogenase (hsd3b2) in groups exposed to both Roundup and glyphosate. In contrast, for the antioxidants glutathione peroxidase (gpx1a), catalase (cat) and glutathione-S-transferase pi (gstp1) non- significant, increasing trends in transcript expression were observed.

In the testis, hsd3b2 was significantly up-regulated following exposure to 10 mg Roundup/L compared to all other treatment groups. The expression pattern of steroidogenic acute regulatory protein (star), cyp17a1, cyp11a1, and the androgen receptor (ar) additionally appeared to follow an expression pattern similar to hsd3b2 across treatment groups. cat was significantly up-regulated in groups exposed to both 10 mg/L Roundup and 10 mg/L glyphosate compared to those treated with 0.5 mg/L Roundup. In addition, sod1 was significantly up- regulated in the 10 mg/L compared to 0.5 mg/L Roundup groups.

Histological examination of females from all treatment groups showed that the ovaries of all individuals contained oocytes at all stages of development (oogonia, primary oocytes, cortical alveoli stage oocytes, secondary oocytes, and mature vitellogenic oocytes) and the majority contained recent postovulatory follicles. Evidence of ovarian abnormalities was reported in 9.1%, 18.2%, 9.1%, 50.0%, and 63.6% of females in the control, 0.01 mg/L Roundup, 0.5 mg/L Roundup, 10 mg/L Roundup and 10 mg/L glyphosate treatment groups, respectively. The majority of abnormalities were relatively mild and included accumulation of eosinophilic fluid and presence of abnormal tissue. In addition, the proportion of fish containing atretic oocytes in their ovaries also appeared to be increased. Histological examination of males showed that testes of all individuals from all treatment groups contained germ cells at all stages of spermatogenesis (including spermatogonia, sperma- tocytes, spermatids, and mature spermatozoa). There were no abnormalities and no differences between stages of development between treatment groups.

III. CONCLUSION

Reduction in the number of eggs of zebra fish exposed to concentrations (10 mg/L) of glyphosate was observed. No obvious signs of developmental toxicity at exposure concentrations up to 10 mg/L Roundup or glyphosate were reported. Evidence of developmental delay in embryos exposed to concentrations ≥50 mg/L glyphosate and ≥250 mg/L Roundup was attributed to greater acidity of glyphosate than the buffered Roundup formulation. In conclusion, only extremely high concentrations of Roundup and glyphosate induce developmental toxicity in zebrafish.

(Uren Webster, T.M., Laing, L.V., Florance, H., Santos, E.M., 2014)

KLIMISCH EVALUTION

1. RELIABILITY OF STUDY: **Not reliable**

Comment:

- Well documented laboratory assays , data about test conditions are reported. However, it is unclear which surfactant was used in the formulated product.

- Important information on the glyphosate application procedure are missing to reconstruct the actual dosing.

Test concentrations exceeded 20% variance from the target concentration, it is hence not clear how these variations were accounted for (88-140%). The lowest test concentration was not measureable with the analytical method, hence <LOQ (0.05 mg/L), which makes the study highly unreliable.

Positive control absent hence not demonstrated that the effects were observed excluding overt toxicity.

Overt toxicity cannot be excluded for the highest test concentration (10 mg/L).

Decrease in pH due to glyphosate addition at very high concentrations could have been prevented with addition of buffer. At 3.8 the pH is clearly too low to allow for normal fish development.

Prevalence of atresia (20%) and irregular tissue (10%) in ovaries of control group oserved via histopathology suggest that there were sub-optimal test conditions for Zebra fish. Temperature in the test was 28±0.5 C, when guideline recommendation states 26±2 C (OECD 229) or 25±2 (OECD 210). dissolved oxygen not measured. Aeration not recommended unless oxygenation falls below 60% of saturation.

Recommended hatching success should be 70% at 30 days post-hatch (OECD 210). Hatching rate in the control (20%) was reported only 54h post-hatch hence the endpoint is not reliable.

2. RELEVANCE OF STUDY: Not relevant

Comment: As noted by the authors, the concentration at which effects on reproduction were observed is unrealistically high (10 mg/L) and therefore at this point the study doesn't provide any additional information. Although there was decreased egg production at 10 mg/L it is not possible to conclude that tis occured through an endocrine mechanism. The results from a 21-day short-term

	reproduction assay of glyphosate with the fathead minnow (*Pimephales promelas*) conducted for the US EPA showed no effects on gonad histopathology were evident up to the highest concentration of 33 mg glyphosate/L. In addition, there were no effects on survival, growth, reproduction, secondary sex characteristics, GSI, or vitellogenin in male or female fish exposed to glyphosate for 21 days. Results from a fish full life cycle study with the fathead minnow. Continuous exposure of aquatic biota to concentrations at 10 mg/L is highly unlikely (as stated by the author). No effects observed at concentrations up to 0.5 mg/L which is in the range of the highest ever measured surface water concentration in the EU based on long-term monitoring programs for glyphosate. The most frequent measurements of glyphosate in the EU do not exceed 0.1 ug/L (0.0001 mg/L).
3. KLIMISCH CODE:	Klimisch rating of 3

RESULTS FROM A FISH FULL LIFE CYCLE STUDY WITH THE FATHEAD MINNOW:

The fish full life-cycle study is the highest Tier of fish ecotoxicology testing and typically performed with the fathead minnow as a freshwater test species. In the study, the entire life-cycle is exposed; therefore, de facto the most sensitive life-stage to any toxicant (including endocrine active compounds) is encompassed by the test design. Parameters evaluated of relevance to the endocrine system include hatchability, percent survival, total length and wet weight, number of spawnings, eggs per female and eggs per spawn, and percentages of live fry hatching

APPENDIX 2
LITERATURE EXCLUDED BY RAPID ASSESSMENT

Obviously non-relevant studies in open literature search were excluded by applying the relevance criteria previously defined in Table 1 of this document. A list of this non-relevant literature is given below.

Table 6 contain the bibliographic references for the literature excluded by rapid assessment.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Abarikwu, Sunny O.; Akiri, Oghenetega F.; Durojaiye, Mojisola A.; Adenike, Alabi	2015	Combined effects of repeated administration of Bretmont Wipeout (glyphosate) and Ultrazin (atrazine) on testosterone, oxidative stress and sperm quality of Wistar rats	Toxicology mechanisms and methods Vol 25 pag 70-80	Paper is based on finding of a commercialized product containing glyphosate in Nigeria and not on the active substance. The specifications, and the co-formulants of that product cannot be verified or extrapolated to the one used in the EU.
Aguiar, Lais Mattos de; Figueira, Fernanda Hernandes; Gottschalk, Marco Silva; da Rosa, Carlos Eduardo	2016	Glyphosate-based herbicide exposure causes antioxidant defence responses in the fruit fly Drosophila melanogaster	Comparative biochemistry and physiology. Vol 185-186, pag 94-101.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Almeida, Lécio L. de; Teixeira, Álvaro A.C.; Bezerra, Natallyanea S.; Wanderley-Teixeira, Valéria	2016	Efeito protetor da melatonina sobre intoxicações por herbicidas	Pesq. Vet. Bras. (Pesquisa Veterinária Brasileira) Vol 36, pag 174-180.	No new primary data with Glyphosate. Review of existing publications.
Américo, Gabriela Helena Pinê; Furlani Junior, Enes; Santos, Danilo Marcelo Aires; Américo, Juliana Heloisa Pinê; Pinto, Carolina Cipriano	2015	Glyphosate and cotton growth regulator sub-doses systems application	RBHerbicidas (Revista Brasileira de Herbicidas). Vol 14, pag 54.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Asif Tanveer; Abdul Khaliq; Ali, H. H.; Gulshan Mahajan; Chauhan, B. S.	2015	Interference and management of parthenium: the world's most important invasive weed	Crop Protection (2015), Volume 68, pp. 49-59	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Avigliano, L.; Fassiano, A. V.; Medesani, D. A.; Rios de Molina, M C; Rodriguez, E. M.	2014	Effects of glyphosate on growth rate, metabolic rate and energy reserves of early juvenile crayfish, Cherax quadricarinatus M	Bulletin of environmental contamination and toxicology. Vol 92 pag 631 - 635	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Avigliano, Luciana; Alvarez, Natalia; Loughlin, Camila Mac; Rodriguez, Enrique Marcelo	2014	Effects of glyphosate on egg incubation, larvae hatching, and ovarian rematuration in the estuarine crab Neohelice granulata	Environmental toxicology and chemistry / SETAC. Vol 33, pag 1879–1884.	Toxicology investigation in crab. Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Bal, J. S.	2016	Proceedings of the III International Jujube Symposium	Twenty-ninth International Horticultural Congress IHC2014. Vol 1116	Conference proceeding. Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Baldwin, C. M.; Brede, A. D.; Mayer, J. J.	2015	Growth regulation and tank mixing associated with a glyphosate-tolerant perennial ryegrass cultivar	HortTechnology (2015), Volume 25, Number 2, pp. 214-220	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Bishop, Patricia L.; Willett, Catherine E.	2014	The use and acceptance of Other Scientifically Relevant Information (OSRI) in the U.S. Environmental Protection Agency (EPA) Endocrine Disruptor Screening Program	Birth defects research. Part B, Developmental and reproductive toxicology. Vol 101, pag 3 – 22.	Only a summary of EDSP screening tests and therefore only secondary data.
Caloni, F.; Albonico, M.; Schutz, L. F.; Cortinovis, C.; Spicer, L. J.	2015	In vitro effects of glyphosate on cell proliferation and steroid production by bovine granulosa cells	Toxicology Letters: Univ Milan, Dept Hlth Anim Sci and Food Safety VESPA, Milan, Italy	Meeting abstract. Full-text not available.
Cassault-Meyer, Estelle; Gress, Steeve; Seralini, Gilles-Eric; Galeraud-Denis, Isabelle	2014	An acute exposure to glyphosate-based herbicide alters aromatase levels in testis and sperm nuclear quality	Environmental toxicology and pharmacology. Vol 38, pag 131–140.	Not relevant for evaluation of active ingredient as only a formulation was tested. Subacute rat treatment and ED relevant parameters were investigated. No focus on ED.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Chahoud, I.; Grote, K.	2016	Is there a need in regulatory toxicity testing for evaluating chemicals at doses eliciting general toxicity?	Toxicology Vol 363 – 364, pag 46-47	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Chiamolera, Maria Izabel; Kisys, Marina M.L.; Sena-Souza, Nina I.; Romano, Renata M. Ortiga-Carvalho, Tania Maria Maciel, Rui M.B. Giannocco, Gisele Da Silva, Magnus R. Dias Romano, Marco A.	2014	Glyphosate mimics tecidual hypothyroidism in perinatally treated rats	Endocrine Reviews, (2014) Vol. 35, Supp. SUPPL. 3.	Not relevant for evaluation of active ingredient as only a formulation was tested.
Colquhoun, Jed B.; Heider, Daniel J.; Rittmeyer, Richard A.	2014	Relationship between Visual Injury from Synthetic Auxin and Glyphosate Herbicides and Snap Bean and Potato Yield	Weed Technology Vol 28 No. 4, pag 671–678	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Corniani, Natalia; Velini, Edivaldo D.; Silva, Ferdinando M. L.; Nanayakkara, N. P. Dhammika; Witschel, Matthias; Dayan, Franck E.	2014	Novel bioassay for the discovery of inhibitors of the 2-C-methyl-D-erythritol 4-phosphate (MEP) and terpenoid pathways leading to carotenoid biosynthesis	PloS one. Journal Article Research Support, Non-U.S. Gov't	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Costa, N. V.; Zobiole, L. H. S.; Scariot, C. A.; Pereira, G. R.; Moratelli, G.	2014	Glyphosate tolerant volunteer corn control at two development stages	Planta Daninha (2014), Volume 32, Number 4, pp. 675-682	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Dabrowski, James Michael; Shadung, Justinus Madimetja; Wepener, Victor	2014	Prioritizing agricultural pesticides used in South Africa based on their environmental mobility and potential human health effects	Environment international Vol 62, pag 31-40.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Dinalli, R. P.; Buzetti, S.; Gazola, R. de N.; Castilho, R. M. M. de; Celestrino, T. de S.; Dupas, E.; Teixeira Filho, M. C. M.; Lima, R. C.; S. Celestrino, T. de; de Castilho, R. M. M.	2015	Application of herbicides as growth regulators of emerald Zoysia grass fertilized with nitrogen	Bookseller catalog	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Dittmar, P. J.; Ferrell, J. A.; Fernandez, J. V.; Smith, H.	2016	Effect of glyphosate and dicamba drift timing and rates in bell pepper and yellow squash	Weed Technology (2016), Volume 30, Number 1, pp. 217-223	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
D'Mello, J. P. Felix	2016	Amino acids in higher plants	The British Library Chapter 24 (Page no: 461)	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Dogramac, M.; Gramig, G. G.; Anderson, J. V.; Chao, W. S.; Foley, M. E.	2016	Field application of glyphosate induces molecular changes affecting vegetative growth processes in leafy spurge (Euphorbia esula)	Weed Science (2016), Volume 64, Number 1, pp. 87-100	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Dogramaci, Munevver; Foley, Michael E.; Horvath, David P.; Hernandez, Alvaro G.; Khetani, Radhika S.; Fields, Christopher J.; Keating, Kathleen M.; Mikel, Mark A.; Anderson, James V.	2015	Glyphosate's impact on vegetative growth in leafy spurge identifies molecular processes and hormone cross-talk associated with increased branching	BMC genomics Vol 16	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Doğramacı, Münevver; Anderson, James V.; Chao, Wun S.; Foley, Michael E.	2014	Foliar Application of Glyphosate Affects Molecular Mechanisms in Underground Adventitious Buds of Leafy Spurge (*Euphorbia esula*) and Alters Their Vegetative Growth Patterns	Weed Science Vol 62 No. 2, pag 217 - 229	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
European Teratology Society	2016	44th Annual Conference of the European-Teratology-Society, Dublin, IRELAND, September 11 -14, 2016	Reproductive Toxicology, (SEP 2016) Vol. 64, No. Sp. Iss. SI, pp. 12-49	Conference data. Full-text or comprehensive information not available.
Fernandez-Garcia, Jose C.; Arrebola, Juan P.; Gonzalez-Romero, Stella; Soriguer, Federico; Olea, Nicolas; Tinahones, Francisco J.	2014	Diabetic ketoacidosis following chlorothalonil poisoning	Occupational and environmental medicine. Case Reports Letter	Poisoning case without link to quantitative glyphosate exposure. No relevant ED endpoints.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Fluegge, Keith	2016	Does environmental exposure to the greenhouse gas, N2O, contribute to etiological factors in neurodevelopmental disorders? A mini-review of the evidence	Environmental toxicology and pharmacology. Vol 47, pag 6-18.	Review article - Secondary source only.
Forster, W. A.; Pathan, A. K.; Kimberley, M. O.; Steele, K. D.; Gaskin, R. E.	2014	The Relative Influence of Retention, Uptake, and Translocation on the Bioefficacy of Glyphosate	American Chemical Society Vol 171 pag 111 - 139	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Garg, Bharti; Vaid, Neha; Tuteja, Narendra	2014	In-silico analysis and expression profiling implicate diverse role of EPSPS family genes in regulating developmental and metabolic processes	BMC research notes. Research Support, Non-U.S. Gov't. Vol 7.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Gazola, R. P. D.; Buzetti, S.; Gazola, R. de N.; Castilho, R. M. M. de; Celestrino, T. de S.; S. Celestrino, T. de; de Castilho, R. M. M.	2015	Nitrogen fertilization and herbicides as growth regulators in micronutrient concentrations of zoysiagrass.	Revista Agrotecnologia (2015), Volume 6, Number 1, pp. 27-44	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Gazola, Raíssa Pereira Dinalli; Buzetti, Salatiér; Gazola, Rodolfo de Niro; Castilho, Regina Maria Monteiro de; Teixeira Filho, Marcelo Carvalho Minhoto; Celestrino, Thiago de Souza; Dupas, Elisângela	2016	Nitrogen dose and type of herbicide used for growth regulation on the green coloration intensity of Emerald grass	Cienc. Rural (Ciência Rural) Vol 46 No. 6, pag 984 - 990	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Gress, Steeve; Laurant, Claire; Defarge, Nicolas; Travert, Carine; Seralini, Gilles-Eric	2016	Dig1 protects against locomotor and biochemical dysfunctions provoked by Roundup	BMC complementary and alternative medicine. Vol 16	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Guerrero Schimpf, Marlise; Milesi, Maria M.; Ingaramo, Paola I.; Luque, Enrique H.; Varayoud, Jorgelina	2016	Neonatal exposure to a glyphosate based herbicide alters the development of the rat uterus	Toxicology 2016 Jun 7. Epub 2016 Dec 7.	Not relevant for evaluation of active ingredient as only a formulation was tested.
Gupta, Ramesh C.	2011	Reproductive and developmental toxicology	The British Library, pag 503–521	Book chapter. Secondary data only.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Gurikar Chennappa; Adkar-Purushothama, C. R.; Umdale Suraj; Tamilvendan, K.; Sreenivasa, M. Y.; Chennappa, G.; Suraj, U.	2014	Pesticide tolerant Azotobacter isolates from paddy growing areas of northern Karnataka, India	World Journal of Microbiology & Biotechnology (2014), Volume 30, Number 1, pp. 1-7, 23	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Halwachs, S.; Kuhnert, L.; Giantin, M.; Dacasto, M.; Honscha, W.	2015	ABCG2-pesticide interactions in the bovine mammary gland and pesticide-mediated induction of ABCG2 efflux activity by the arylhydrocarbon receptor	Journal of Veterinary Pharmacology and Therapeutics, (JUL 2015) Vol. 38.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Huang, Yong-lu; Liu, Xiao-liang; Tang, Wen-wei; Zeng, Dong-qiang	2014	Field trials of 18% 2,4-D micro-emulsion against Mikania micrantha in non-cultivated land	Nanfang Nongye Xuebao (2014), 45(3), 406-409	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Huang ShaoWen; Liu ChunHong; Huang, S. W.; Liu, C. H.	2015	Toxic effects and exposure risk assessment of glyphosate	Journal of Food Safety and Quality (2015), Volume 6, Number 3, pp. 880-885	Secondary data only.
Hulin, M.; Bemrah, N.; Nougadere, A.; Volatier, J. L.; Sirot, V.; Leblanc, J. C.	2014	Assessment of infant exposure to food chemicals: the French Total Diet Study design	Food additives & contaminants. Part A, Chemistry, analysis, control, exposure & risk assessment. Vol 31, pag 1226–1239.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Ingaramo, Paola I.; Varayoud, Jorgelina; Milesi, Maria M.; Schimpf, Marlise Guerrero; Munoz-de-Toro, Monica; Luque, Enrique H.	2016	Effects of neonatal exposure to a glyphosate-based herbicide on female rat reproduction	Reproduction (Cambridge, England). Vol 152, pag 403-415.	Not relevant for evaluation of active ingredient as only a formulation was tested.
Jamkhande, Prasad Govindrao; Chintawar, Kalyani Diliprao; Chandak, Prakash Gopaldas	2014	Teratogenicity: A mechanism based short review on common teratogenic agents	Asian Pacific Journal of Tropical Disease. Vol 4, pag 421-432.	Secondary data only.
Karmollachaab, A.; Bakhshandeh, A.; MoradiTlavat, M. R.; Moradi, F.; Shomeili, M.	2015	Effect of chemical ripeners application on yield, quality and technological ripening of sugarcane (Saccharum officinarum L.)	Iranian Journal of Crop Sciences (2015), Volume 17, Number 1, pp. Pe63-Pe73	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Karmollachaab, A.; Bakhshandeh, A.; Telavat, M. R. M.; Moradi, F.; Shomeili, M.	2015	Sugarcane yield and technological ripening responses to chemical ripeners	Sugar Tech (2016), Volume 18, Number 3, pp. 285-291	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Koakoski, Gessi; Quevedo, Rosmari Mezzalira; Ferreira, Daiane; Oliveira, Thiago Acosta; da Rosa, Joao Gabriel Santos; Abreu, Murilo Sander de; Gusso, Darlan; Marqueze, Alessandra; Kreutz, Luiz Carlos; Giacomini, Ana Cristina Vendrameto; Fagundes, Michele; Barcellos, Leonardo Jose Gil	2014	Agrichemicals chronically inhibit the cortisol response to stress in fish	Chemosphere Vol 112, pag 85 - 91	Not relevant for evaluation of active ingredient as only a formulation was tested.
Kryuchkova, Yelena V.; Burygin, Gennady L.; Gogoleva, Natalia E.; Gogolev, Yuri V.; Chernyshova, Marina P.; Makarov, Oleg E.; Fedorov, Evgenii E.; Turkovskaya, Olga V.	2014	Isolation and characterization of a glyphosate-degrading rhizosphere strain, Enterobacter cloacae K7	Microbiological research Vol 169, pag 99 - 105	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Larsen, Karen; Najle, Roberto; Lifschitz, Adrian; Mate, Maria L.; Lanusse, Carlos; Virkel, Guillermo L.	2014	Effects of Sublethal Exposure to a Glyphosate-Based Herbicide Formulation on Metabolic Activities of Different Xenobiotic-Metabolizing Enzymes in Rats	International journal of toxicology. Vol 33, pag 307-318.	Not relevant for evaluation of active ingredientas only a formulation was tested.
LaVerda, Nancy L.; Goldsmith, David F.; Alavanja, Michael C. R.; Hunting, Katherine L.	2015	Pesticide Exposures and Body Mass Index (BMI) of Pesticide Applicators From the Agricultural Health Study	Journal of toxicology and environmental health. Part A	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Lee, Hung-Chieh; Lu, Po-Nien; Huang, Hui-Lan; Chu, Chien; Li, Hong-Ping; Tsai, Huai-Jen	2014	Zebrafish transgenic line huORFZ is an effective living bioindicator for detecting environmental toxicants	PloS one. Research Support, Non-U.S. Gov't. Vol 9.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Leite, G. H. P.; Alexandre, C.; Crusciol, C.; Siqueira, G. F. de; Silva, M. de A.; A. Silva, M. de	2015	Plant regulators and invertase activity in sugarcane at the beginning of the harvest season	Ciencia Rural (2015), Volume 45, Number 10, pp. 1788-1794	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Leslie, Trent; Baucom, Regina S.	2014	De novo assembly and annotation of the transcriptome of the agricultural weed Ipomoea purpurea uncovers gene expression changes associated with herbicide resistance	G3 (Bethesda, Md.): Research Support, Non-U.S. Gov't. Vol 4, pag 2035–2047.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Mailler, R.; Gasperi, J.; Coquet, Y.; Bulete, A.; Vulliet, E.; Deshayes, S.; Zedek, S.; Mirande-Bret, C.; Eudes, V.; Bressy, A.; Caupos, E.; Moilleron, R.; Chebbo, G.; Rocher, V.	2016	Removal of a wide range of emerging pollutants from wastewater treatment plant discharges by micro-grain activated carbon in fluidized bed as tertiary treatment at large pilot scale	The Science of the total environment. Vol 542, 983–996	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Mandiki, Syaghalirwa N. M.; Gillardin, Virginie; Martens, Koen; Ercken, Dirk; Roeck, Els de; Bie, Tom de; Declerck, Steven A. S.; Meester, Luc de; Brasseur, Catherine; van der Heiden, Edwige; Schippo, Marie-Louise; Kestemont, Patrick	2014	Effect of land use on pollution status and risk of fish endocrine disruption in small farmland ponds	Hydrobiologia. Vol 723, pag 103-120.	No clear link between glyphosate and ED effects. Mixture of pollutants.
Mantovani, Alberto; Fucic, Aleksandra	2014	Puberty dysregulation and increased risk of disease in adult life: possible modes of action	Reproductive toxicology (Elmsford, N.Y.). Vol 44, pag 15-22.	Review- Secondary data.
Mariani, Melisa L.; Romero, Roberto L.; Zalazar, Cristina S.	2015	Modeling of degradation kinetic and toxicity evaluation of herbicides mixtures in water using the UV/H2O2 process	Photochemical & photobiological sciences : Official journal of the European Photochemistry Association and the European Society for Photobiology. Vol 14, pag 608-617.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Mart, Michelle	2015	Pesticides, a love story. America's enduring embrace of dangerous chemicals	Library of Congress. CultureAmerica	Review – Secondary information only.
Marx-Stoelting, P.; Niemann, L.; Ritz, V.; Ulbrich, B.; Gall, A.; Hirsch-Ernst, K. I.; Pfeil, R.; Solecki, R.	2014	Assessment of three approaches for regulatory decision making on pesticides with endocrine disrupting properties	Regulatory toxicology and pharmacology : RTP. Vol 70, pag 590-604.	No new toxicology data. Secondary information only.
Mesnage, R.; Defarge, N.; Spiroux de Vendomois, J.; Seralini, G. E.	2015	Potential toxic effects of glyphosate and its commercial formulations below regulatory limits	Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association. Vol 84, pag 133-153.	No new toxicology data. Secondary information only.
Mesnage, Robin; Arno, Matthew; Costanzo, Manuela; Malatesta, Manuela; Seralini, Gilles-Eric; Antoniou, Michael N.	2015	Transcriptome profile analysis reflects rat liver and kidney damage following chronic ultra-low dose Roundup exposure	Environmental health : a global access science source. Vol 14, pag 70.	Not relevant for evaluation of active ingredientas only a formulation was tested. No ED-linked endpoints.
Meyer, Christopher J.; Norsworthy, Jason K.; Young, Bryan G.; Steckel, Lawrence E.; Bradley, Kevin W.; Johnson, William G.; Loux, Mark M.; Davis, Vince M.; Kruger, Greg R.; Bararpour, Mohammad T.; Ikley, Joseph T.; Spaunhorst, Douglas J.; Butts, Thomas R.	2016	Early-Season Palmer Amaranth and Waterhemp Control from Preemergence Programs Utilizing 4-Hydroxyphenylpyruvate Dioxygenase–Inhibiting and Auxinic Herbicides in Soybean	Weed Technology Vol 30 pag 67 – 75.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Milne, Jeanette	2014	A research roundup of recent papers relevant to wound care	Wounds UK, (June 2014) Vol. 10, No. 2, pp. 116-117	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Moon, Sojung; Lee, Jongbin	2016	Comparison of chemical structures of environmental hormones for cardiac and phototactic effects on daphnia magna	Abstracts, 41st Northeast Regional Meeting of the American Chemical Society, Binghamton, NY, United States	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion. Meeting abstract only.
Myers, J. P.; Antoniou, M. N.; Blumberg, B.; Carroll, L.; Colborn, T.; Everett, L. G.; Hansen, M.; Landrigan, P. J.; Lanphear, B. P.; Mesnage, R.; Vandenberg, L. N.; Vom Saal, F. S.; Welshons, W. V.; Benbrook, C. M.	2016	Concerns over use of glyphosate-based herbicides and risks associated with exposures: a consensus statement	Environmental Health (2016), Volume 15, Number 19	Review - Secondary information.
Nasir, I. A.; Bushra Tabassum; Zahida Qamar; Javed, M. A.; Muhammad Tariq; Farooq, A. M.; Butt, S. J.; Abdul Qayyum; Tayyab Husnain	2014	Herbicide-tolerant sugarcane (Saccharum officinarum L.) plants: an unconventional method of weed removal	Turkish Journal of Biology (2014), Volume 38, Number 4, pp. 439-449	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Navarro, Claudia D. C.; Martinez, Claudia B. R.	2014	Effects of the surfactant polyoxyethylene amine (POEA) on genotoxic, biochemical and physiological parameters of the freshwater teleost Prochilodus lineatus	Comparative biochemistry and physiology. Toxicology & pharmacology : CBP. Vol 165, pag 83-90.	POEA as test substance. No data based on glyphosate as test substance.
Navarro-Martin, L.; Lanctot, C.; Jackman, P.; Park, B. J.; Doe, K.; Pauli, B. D.; Trudeau, V. L.	2014	Effects of glyphosate-based herbicides on survival, development, growth and sex ratios of wood frogs (Lithobates sylvaticus) tadpoles. I: chronic laboratory exposures to VisionMax(R)	Aquatic toxicology (Amsterdam, Netherlands). Vol 154, pag 278-290.	Not relevant for evaluation of active ingredientas only a formulation was tested.
Pan, Shu-Ting; Xue, Danfeng; Li, Zhi-Ling; Zhou, Zhi-Wei; He, Zhi-Xu; Yang, Yinxue; Yang, Tianxin; Qiu, Jia-Xuan; Zhou, Shu-Feng	2016	Computational Identification of the Paralogs and Orthologs of Human Cytochrome P450 Superfamily and the Implication in Drug Discovery	International journal of molecular sciences. Vol 17, No. 7	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Pandey, Aparamita; Rudraiah, Medhamurthy	2015	Analysis of endocrine disruption effect of Roundup® in adrenal gland of male rats	Toxicology Reports. Vol 2, pag 1075–1085.	Not relevant for evaluation of active ingredientas only a formulation was tested.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Perobelli, Juliana Elaine Perobelli, Juliana Elaine	2014	The male peripubertal phase as a developmental window for reproductive toxicology studies	Current Pharmaceutical Design, (1 Jan 2014) Vol. 20, No. 34, pp. 5398-5415	Secondary data.
Pradedova, E. V.; Nimaeva, O. D.; Karpova, A. B.; Salyaev, R. K.	2015	The effect of herbicides on hydrogen peroxide generation in isolated vacuoles of red beet root (Beta vulgaris L.)	Journal of Stress Physiology & Biochemistry (2015), Volume 11, Number 4, pp. 100-112, 24	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Queiroz, A. R. S.; Vidal, R. A.	2014	The development of dichlorophenoxyacetate herbicide tolerant crops: literature review. O desenvolvimento de culturas tolerantes ao herbicida diclorofenoxiacetato: revisao de literatura	Planta Daninha (2014), Volume 32, Number 3, pp. 649-654, 28	Review article - Secondary data.
Raadt, Wanda M. de; Wijnen, Petal A.; Bast, Aalt; Drent, Marjolein Wijnen, Petal A.; Bekers, Otto Bast, Aalt; Drent, Marjolein	2015	Acute eosinophilic pneumonia associated with glyphosate surfactant exposure	Sarcoidosis Vasculitis and Diffuse Lung Diseases, (2015) Vol. 32, No. 2, pp. 172-175	Not relevant for evaluation of active ingredient as data refer to a formulation. Poisoning with glyphosate surfactant.
Ren-Yi, Gui; Lei, Xu; Yi, Kuang; III-Ming, Chung; Jian-Chun, Qin; Li, Liu; Sheng-Xiang, Yang; Li-Chun, Zhao	2015	Chaetominine, (+)-alantrypinone, questin, isorhodoptilometrin, and 4-hydroxybenzaldehyde produced by the endophytic fungus Aspergillus sp. YL-6 inhibit wheat (Triticum aestivum) and radish (*Raphanus sativus*) germination	Journal of Plant Interactions Vol 10, pag 87–92	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Rondon-Barragan, I. S.; Marin-Mendez, G. A.; Chacon, R. A.; Naranjo, L.; Eslava-Mocha, P. R.	2014	The effects of Roundup® and Cosmoflux® 411F on the immune response of white cachama (Piaractus brachypomus) challenged with Aeromonas hydrophila. Efectos del Roundup® y Cosmoflux® 411F sobre la respuesta inmune frente al desafio con Aeromonas hydrophila e	Orinoquia (2014), Volume 18, Number 2, pp. 38-51	Not relevant for evaluation of active ingredient as only a formulation was tested.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Samsel, A.; Seneff, S.	2015	Glyphosate, pathways to modern diseases IV: Cancer and related pathologies	JBPC (Journal of Biological Physics and Chemistry). Vol 15, pag 121-159.	Review article - Secondary data.
Scognamiglio, Viviana; Antonacci, Amina; Patrolecco, Luisa; Lambreva, Maya D.; Litescu, Simona C.; Ghuge, Sandip A.; Rea, Giuseppina	2016	Analytical tools monitoring endocrine disrupting chemicals	TrAC, Trends in Analytical Chemistry, (2016) Vol. 80, pp. 555-567	Secondary data.
Sealey, L. A.; Hughes, B. W.; Sriskanda, A. N.; Guest, J. R.; Gibson, A. D.; Johnson-Williams, L.; Pace, D. G.; Bagasra, O.	2016	Environmental factors in the development of autism spectrum disorders	Environment international. Vol 88, pag 288-298.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Sellers, Brent A.; Lancaster, Sarah R.; Langeland, Kenneth A.	2014	Herbicides for Postemergence Control of Mile-a-Minute (Mikania micrantha)	Invasive Plant Science and Management. Vol 7, pag 303-309.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Seneff, Stephanie; Swanson, Nancy; Li, Chen	2015	Aluminum and Glyphosate Can Synergistically Induce Pineal Gland Pathology Connection to Gut Dysbiosis and Neurological Disease	AS (Agricultural Sciences). Vol 6, pag 42-70.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Seralini, G.-E.	2015	Why glyphosate is not the issue with Roundup	JBPC (Journal of Biological Physics and Chemistry). Vol 15, No. 3, pag 111-119.	Review article – Secondary data only.
Seralini, Gilles-Eric; Clair, Emilie; Mesnage, Robin; Gress, Steeve; Defarge, Nicolas; Malatesta, Manuela; Hennequin, Didier; Vendomois, Joel Spiroux de	2014	Republished study: long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize	Environmental Sciences Europe, (2014) Vol. 26, No. 1, pp. 1-17	Article retracted. Not considered reliable any more.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Séralini, Gilles-Eric; Clair, Emilie; Mesnage, Robin; Gress, Steeve; Defarge, Nicolas; Malatesta, Manuela; Hennequin, Didier; Spiroux de Vendômois, Joël	2014	Retraction notice to "Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize" [Food Chem. Toxicol. 50 (2012) 4221–4231]	Food and Chemical Toxicology Vol 63, pag 244	Retraction notice referring to the article from Seralini et al. (2014) "Republished study: long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize".
Shaw, Gary M.; Yang, Wei; Roberts, Eric; Kegley, Susan E.; Padula, Amy; English, Paul B.; Carmichael, Suzan L.	2014	Early pregnancy agricultural pesticide exposures and risk of gastroschisis among offspring in the San Joaquin Valley of California	Birth defects research. Part A, Clinical and molecular teratology. Vol 100, pag 686-694.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Shu Jun; Zhou JunHong; Cheng XiangRong; Yu MuKui; Zhang Lei; Shu, J.; Zhou, J. H.; Cheng, X. R.; Yu, M. K.; Zhang, L.	2015	Effect of glyphosate with two surfactants on physiological and biochemical characteristics of Miscanthus floridulus	Forest Research, Beijing (2015), Volume 28, Number 5, pp. 725-730	Not relevant for evaluation of active ingredient as only a formulation was tested
Soltani, N.; Shropshire, C.; Sikkema, P. H.	2015	Effect of biostimulants added to postemergence herbicides in corn, oats and winter wheat	Agricultural Sciences (2015), Volume 6, Number 5, pp. 527-534	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Stahlman, P. W.	2016	Herbicide resistance in kochia: from single to multiple resistance	Indian Journal of Weed Science (2016), Volume 48, Number 2, pp. 117-121	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Stewart, Michael; Olsen, Greg; Hickey, Christopher W.; Ferreira, Bianca; Jelic, Aleksandra; Petrovic, Mira; Barcelo, Damia	2014	A survey of emerging contaminants in the estuarine receiving environment around Auckland, New Zealand	The Science of the total environment. Vol 468-469, pag 202-210.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Stokes, M. E.; McCourt, P.	2014	Towards personalized agriculture: what chemical genomics can bring to plant biotechnology	Frontiers in Plant Science (2014), Volume 5, Number July, 344	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Swanson, N. L.; Leu, A.; Abrahamson, J.; Wallet, B.	2014	Genetically engineered crops, glyphosate and the deterioration of health in the United States of America	Journal of Organic Systems (2014), Volume 9, Number 2, pp. 6-37	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Travaglia, Claudia; Masciarelli, Oscar; Fortuna, Julieta; Marchetti, Gisela; Cardozo, Paula; Lucero, Martín; Zorza, Edgardo; Luna, Virginia; Reinoso, Herminda	2015	Towards sustainable maize production Glyphosate detoxification by Azospirillum sp. and Pseudomonas sp	Crop Protection Vol 77, pag 102–109.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Varayoud, Jorgelina; Durando, Milena; Ramos, Jorge G.; Milesi, Maria M.; Ingaramo, Paola I.; Munoz-de-Toro, Monica; Luque, Enrique H.	2016	Effects of a glyphosate-based herbicide on the uterus of adult ovariectomized rats	Environ Toxicol. 2016 Jul 27	Not relevant for evaluation of active ingredient as only a formulation was tested
Viana, R. S.; Figueiredo, P. A. M.; Lisboa, L. A. M.; Assumpcao, A. C. N. D.; Sa, M. E.; May, A.	2015	Application of chemical growth regulators on the technological quality of sweet sorghum cv. Biomatrix 535. Aplicacao de fitorreguladores quimicos na qualidade tecnologica do sorgo sacarino cv. Biomatrix 535	Revista Brasileira de Milho e Sorgo (2015), Volume 14, Number 3, pp. 326-334	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Vieira, Carlos Eduardo Delfino; Costa, Patricia Gomes; Lunardelli, Bruna; Oliveira, Luciana Fernandes de; Cabrera, Liziara da Costa; Risso, Wagner Ezequiel; Primel, Ednei Gilberto; Meletti, Paulo Cesar; Fillmann, Gilberto; Martinez, Claudia Bueno dos Reis	2016	Multiple biomarker responses in Prochilodus lineatus subjected to short-term in situ exposure to streams from agricultural areas in Southern Brazil	The Science of the total environment. Vol 542, pag 44-56.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Volterrani, M.; Grossi, N.; Gaetani, M.; Caturegli, L.; Nikolopoulou, A. E.; Lulli, F.; Magni, S.	2015	The effect of increasing application rates of nine plant growth regulators on the turf and stolon characteristics of pot-grown 'patriot' hybrid bermudagrass	HortTechnology (2015), Volume 25, Number 3, pp. 397-404	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Wagner, Norman; Veith, Michael; Lotters, Stefan; Viertel, Bruno	2016	Population and life-stage-specific effects of two herbicide formulations on the aquatic development of European common frogs (Rana temporaria)	Environmental toxicology and chemistry 2016 Jun 13.	Not relevant for evaluation of active ingredient as only a formulation was tested

Table 6
Literature excluded by rapid assessment

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Wang, Ru-ping; Wang, Jun; Sun, Chang-qing; Ru, Shao-guo	2014	Research progress of estrogenic/anti-androgenic activity induced by organophosphorus pesticides	Haiyang Kexue (2014), 38(12), 128-135	Review article without new experimental data from glyphosate or products with glyphosate.
YU, Cheng-Yu; HE, Bei-Ru	2014	Evaluation of Male-Sterility Induction Effect of Various Amino Acid Biosynthesis Inhibiting-Herbicides on Rapeseed (Brassica napus)	Acta Agronomica Sinica Vol 40, pag 264.	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.
Zhang YinXia; Te-chato, S.; Zhang, Y. X.; Sompong Te-chato	2015	Optimization of certain parameters for transformation of indica rice Hom Kra Dang Ngah variety via agrobacterium-mediated transformation	Kasetsart Journal, Natural Science (2015), Volume 49, Number 5, pp. 676-686,	Endpoint addressed not suitable to address the data gap regarding potential endocrine activity set in the EFSA Conclusion.

APPENDIX 3 REFERENCES EXCLUDED AFTER DETAILED ASSESSMENT.

Table 6 contain the bibliographic references for the literature excluded after detailed assessment.

Table 7
Literature excluded from further consideration after detailed assessment for relevance

Author(s)	Year	Title	Source	Reason(s) for exclusion
Armiliato, Neide; Ammar, Dib; Nezzi, Luciane; Straliotto, Marcos; Muller, Yara M. R.; Nazari, Evelise M.	2014	Changes in ultrastructure and expression of steroidogenic factor-1 in ovaries of zebrafish Danio rerio exposed to glyphosate	Journal of toxicology and environmental health. Part A, Vol 77 N° 7, pag 405–414	Paper is based on finding of a commercialized product containing glyphosate and not on the active substance. The specifications, and the co-formulants of that product cannot be verified or extrapolated to the one used in the EU.
Omran, Nahla Elsayed; Salama, Wesam Mohamed	2016	The endocrine disruptor effect of the herbicides atrazine and glyphosate on Biomphalaria alexandrina	Toxicology and industrial health. Vol 32, N° 4, pag 656–665.	Paper is based on finding of a commercialized product containing glyphosate and not on the active substance. The specifications, and the co-formulants of that product cannot be verified or extrapolated to the one used in the EU.

APPENDIX 4 REFERENCES CONSIDERED RELEVANT FOR TIER II SUMMARIES

Articles included for Tier II summaries, see Appendix 1.

A4.1 Brennan, J., *et al.*, 2016: Development of a recombinant human ovarian (BG1) cell line containing estrogen receptor alpha and beta for improved detection of estrogenic/antiestrogenic chemicals.

A4.2 Dai, P., *et al*, 2016: Effect of glyphosate on reproductive organs in male rat.

A4.3 Defarges, N., Takacs, E., Lozano, V.L., Mesnage, R., Spiroux de Vendomois, J., Seralini, G.E., Szekacs, A. (2016); Co-formulants in glyphosate-based herbicides disrupt aromatase activity in human cells below toxic levels.

A4.4 Lanctot, C., *et al*, 2014: Effects of glyphosate-based herbicides on survival, development, growth and sex ratios of wood frog (*Lithobates sylvaticus*) tadpoles. II: agriculturally relevant exposures.

A4.5 Uren, T., et al, 2014: Effects of glyphosate and its formulation, roundup, on reproduction in zebrafish (*Danio rerio*) - Results from a fish full life cycle study with the fathead minnow

APPENDIX 5 REFERENCES EXCLUDED AFTER DETAILED ASSESSMENT

Articles excluded after detailed assessment at full text level, see Appendix 3.

A5.1 Armiliato, N., et al, 2014: Changes in ultrastructure and expression of steroidogenic factor-1 in ovaries of zebrafish Danio rerio exposed to glyphosate

A5.1 Omran, N; Salama, W., 2016: The endocrine disruptor effect of the herbicides atrazine and glyphosate on Biomphalaria alexandrina

APPENDIX 6

ORIGINAL SEARCH QUERY – COMPLETE STN SEARCH TO BE INCLUDED. RAW DATA

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Connecting via Winsock to STN at stnk.fiz-karlsruhe.de on port 23


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 NEWS 84 Jan 12  STN Express 8.6 Now Available
 NEWS 85 Jan 12  PatentPak Now available to STN Express 8.6
                 and STN on the Web customers
 NEWS 86 Jan 12  CAplus Family of Files Updated with New Data to
                 Support PatentPak in STN
 NEWS 87 Feb 10  Emtree in Classic STN Updated for 2016 with
                 Additional Thesaurus Fields and Expanded Terminology
 NEWS 88 Mar 24  CHEMLIST Content Expanded with the Addition of
                 Information from Vermont
 NEWS 89 Apr 27  Data Quality Improved in CNFULL and FRFULL
 NEWS 90 Jun 16  Latest New STN Release Now Available
 NEWS 91 Jun 27  May 2016 Update to Emtree in STN Provides Expanded
                 Terminology for Biomedical and Pharmacological
                 Searchers
 NEWS 92 Jul 15  Non-conventional Patent Families for Chinese
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L1   QUE GLYPHOSAT#

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            (GLYPHOMAX OR GLYPHOMAXES)
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          ROUNDUP
            (ROUNDUP OR ROUNDUPS)
L5    QUE GLYFOS OR GLYPHODIN OR GLYPHOMAX OR PHORSAT OR ROUNDUP

=> que MON 2139 or MON2139 or MON 3539 or MON3539 or MON 6000 or MON6000

          MON
            (MON OR MONS)
          MON 2139
            (MON(W)2139)
          MON
            (MON OR MONS)
          MON 3539
            (MON(W)3539)
          MON
            (MON OR MONS)
          MON 6000
            (MON(W)6000)
L6    QUE MON 2139 OR MON2139 OR MON 3539 OR MON3539 OR MON 6000 OR MON6000

=> que NSC 151063 or NSC151063

          NSC
            (NSC OR NSCS)
          NSC 151063
            (NSC(W)151063)
L7    QUE NSC 151063 OR NSC151063

=> que 1071-83-6 or 40465-66-5 or 38641-94-0 or 70393-85-0 or 81591-81-3

          1071-83-6
            (1071(W)83(W)6)
          40465-66-5
            (40465(W)66(W)5)
          38641-94-0
            (38641(W)94(W)0)
          70393-85-0
            (70393(W)85(W)0)
          81591-81-3
            (81591(W)81(W)3)
L8    QUE 1071-83-6 OR 40465-66-5 OR 38641-94-0 OR 70393-85-0 OR 81591-81-3

=> que 1071-83-6/rn,crn

'RN' IS NOT A VALID FIELD CODE
'CRN' IS NOT A VALID FIELD CODE
L9    QUE 1071-83-6/RN,CRN

=> que Hormon?

L10   QUE HORMON?

=> que Endocrine(10a)(system? or disrupt? or mode of action?)
```

```
          ENDOCRINE
            (ENDOCRINE OR ENDOCRINES)
          MODE
            (MODE OR MODES)
          OF
            (OF OR OFS)
          MODE OF ACTION?
            (MODE(W)OF(W)ACTION?)
L11   QUE ENDOCRINE(10A)(SYSTEM? OR DISRUPT? OR MODE OF ACTION?)

=> que Thyroid?(10a)(effect? or pathway? or inhibit?)

L12   QUE THYROID?(10A)(EFFECT? OR PATHWAY? OR INHIBIT?)

=> que Androgen?(10a)(system? or disrupt? or mode of action?)

          MODE
            (MODE OR MODES)
          OF
            (OF OR OFS)
          MODE OF ACTION?
            (MODE(W)OF(W)ACTION?)
L13   QUE ANDROGEN?(10A)(SYSTEM? OR DISRUPT? OR MODE OF ACTION?)

=> que Estrogen?(10a)(effect? or pathway? or inhibit?)

L14   QUE ESTROGEN?(10A)(EFFECT? OR PATHWAY? OR INHIBIT?)

=> que Steroido?

L15   QUE STEROIDO?

=> que Aromatase?(10a)(effect? or pathway? or inhibit?)

L16   QUE AROMATASE?(10A)(EFFECT? OR PATHWAY? OR INHIBIT?)

=> que Cytochrome P450(10a)(effects? or pathway? or inhibit?)

          CYTOCHROME
            (CYTOCHROME OR CYTOCHROMES)
          CYTOCHROME P450
            (CYTOCHROME(W)P450)
L17   QUE CYTOCHROME P450(10A)(EFFECTS? OR PATHWAY? OR INHIBIT?)

=> que Intersex?(10a)(effect? or symptom?)

L18   QUE INTERSEX?(10A)(EFFECT? OR SYMPTOM?)

=> que hormon? or endocrin? or thyroid? or androgen? or estrogen? or
steroido? or aromatase or cytochrome(w)(p450 or p 450) or intersex?

          AROMATASE
            (AROMATASE OR AROMATASES)
          CYTOCHROME
            (CYTOCHROME OR CYTOCHROMES)
          P 450
            (P(W)450)
L19   QUE HORMON? OR ENDOCRIN? OR THYROID? OR ANDROGEN? OR ESTROGEN? OR
STEROIDO
          ? OR AROMATASE OR CYTOCHROME(W)(P450 OR P 450) OR INTERSEX?
```

```
=> que py>2013

'2013' NOT A VALID FIELD CODE
L20  QUE PY>2013

=> que p/dt

'DT' IS NOT A VALID FIELD CODE
L21  QUE P/DT

=> d his

     (FILE 'HOME' ENTERED AT 14:18:32 ON 10 OCT 2016)
CHARGED TO COST=FIZ 15206 ROSA CRIOLLO KNOELL CONSU

     FILE 'STNGUIDE' ENTERED AT 14:18:37 ON 10 OCT 2016
CHARGED TO COST=FIZ 15206 ROSA CRIOLLO KNOELL CONSU
L1              QUE GLYPHOSAT#
L2              QUE N(W)(PHOSPHONOMETHYL(W)GLYCINE OR PHOSPHOMETHYLGLYCINE)
OR
L3              QUE 2(W)(PHOSPHONOMETHYL(W)AMINO OR
PHOSPHONOMETHYLAMINO)(W)ACE
L4              QUE CARBOXYMETHYLAMINO METHYLPHOSPHONIC ACID OR
CARBOXYMETHYLAM
L5              QUE GLYFOS OR GLYPHODIN OR GLYPHOMAX OR PHORSAT OR ROUNDUP
L6              QUE MON 2139 OR MON2139 OR MON 3539 OR MON3539 OR MON 6000
OR M
L7              QUE NSC 151063 OR NSC151063
L8              QUE 1071-83-6 OR 40465-66-5 OR 38641-94-0 OR 70393-85-0 OR
8159
L9              QUE 1071-83-6/RN,CRN
L10             QUE HORMON?
L11             QUE ENDOCRINE(10A)(SYSTEM? OR DISRUPT? OR MODE OF ACTION?)
L12             QUE THYROID?(10A)(EFFECT? OR PATHWAY? OR INHIBIT?)
L13             QUE ANDROGEN?(10A)(SYSTEM? OR DISRUPT? OR MODE OF ACTION?)
L14             QUE ESTROGEN?(10A)(EFFECT? OR PATHWAY? OR INHIBIT?)
L15             QUE STEROIDO?
L16             QUE AROMATASE?(10A)(EFFECT? OR PATHWAY? OR INHIBIT?)
L17             QUE CYTOCHROME P450(10A)(EFFECTS? OR PATHWAY? OR INHIBIT?)
L18             QUE INTERSEX?(10A)(EFFECT? OR SYMPTOM?)
L19             QUE HORMON? OR ENDOCRIN? OR THYROID? OR ANDROGEN? OR
ESTROGEN?
L20             QUE PY>2013
L21             QUE P/DT

=> fil toxcenter hcaplus MEDLINE BIOSIS EMBASE CABA AGRICOLA
COST IN EUROS                                        SINCE FILE      TOTAL
                                                          ENTRY    SESSION
FULL ESTIMATED COST                                        0,18       0,73

FILE 'TOXCENTER' ENTERED AT 14:19:31 ON 10 OCT 2016
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Please see "HELP USAGETERMS" for details.

FILE COVERS 1907 TO 3 Oct 2016 (20161003/ED)

MEDLINE content in TOXCENTER was updated on January 25, 2015 to
```

reflect the 2015 MEDLINE reload.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE 'HCAPLUS' ENTERED AT 14:19:31 ON 10 OCT 2016
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FILE COVERS 1907 - 10 Oct 2016 VOL 165 ISS 17
FILE LAST UPDATED: 9 Oct 2016 (20161009/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2015
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2015

HCAplus includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2016.

HCAplus now includes the comprehensive Cooperative Patent Classification (CPC). See HELP CPC for details.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy

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FILE 'MEDLINE' ENTERED AT 14:19:31 ON 10 OCT 2016

FILE LAST UPDATED: 9 Oct 2016 (20161009/UP). FILE COVERS 1946 TO DATE.

MEDLINE(R) is a registered trademark of the U.S. National Library of Medicine (NLM).

The 2016 MEDLINE reload was completed on January 23, 2016. The 2016 MeSH thesaurus is available as a source of terminology for your searches.

This file contains CAS Registry Numbers for easy and accurate substance identification.

See HELP RANGE before carrying out any RANGE search.

FILE 'BIOSIS' ENTERED AT 14:19:31 ON 10 OCT 2016

FILE COVERS 1926 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT

```
FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 5 October 2016 (20161005/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926
through 1968.  These records have been re-indexed to match current
BIOSIS indexing.

FILE 'EMBASE' ENTERED AT 14:19:31 ON 10 OCT 2016
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 FILE COVERS: Embase-originated material 1947 to 7 Oct 2016 (20161007/ED)
              Unique MEDLINE content 1948 to present
              Emtree thesaurus last updated September 2016

This file contains CAS Registry Numbers for easy and accurate
substance identification.

The content in Embase Alert (EMBAL) is strictly complementary
to that in Embase (EMBASE).  EMBAL contains, at any given time,
approximately 100,000 novel records not yet available in Embase.
Search both databases for the most timely and comprehensive
results.

FILE 'CABA' ENTERED AT 14:19:31 ON 10 OCT 2016
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FILE LAST UPDATED: 5 OCT 2016       <20161005/UP>
FILE COVERS 1973 TO DATE

<<< SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE IN
    THE BASIC INDEX (/BI), ABSTRACT (/AB), AND TITLE (/TI) FIELDS  >>>

FILE 'AGRICOLA' ENTERED AT 14:19:31 ON 10 OCT 2016
Compiled and distributed by the National Agricutural Library
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All rights reserved. (2016)

FILE LAST UPDATED: 5 OCT 2016       <20161005/UP>
FILE COVERS 1970 TO DATE

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE IN THE BASIC
    INDEX (/BI), ABSTRACT (/AB), AND TITLE (/TI) FIELDS <<<
CHARGED TO COST=FIZ 15206 ROSA CRIOLLO KNOELL CONSU

=> s l1-8 and l19 and l20 not p/dt
FILE 'TOXCENTER'
          8151 GLYPHOSAT#
       1163409 N
           916 PHOSPHONOMETHYL
         62938 GLYCINE
          1196 GLYCINES
         63763 GLYCINE
                 (GLYCINE OR GLYCINES)
            10 PHOSPHOMETHYLGLYCINE
           478 N(W)(PHOSPHONOMETHYL(W)GLYCINE OR PHOSPHOMETHYLGLYCINE)
           133 PHOSPHONOMETHYLGLYCINE
             1 PHOSPHONOMETHYLGLYCINES
           133 PHOSPHONOMETHYLGLYCINE
                 (PHOSPHONOMETHYLGLYCINE OR PHOSPHONOMETHYLGLYCINES)
```

```
       4148529 2
           916 PHOSPHONOMETHYL
        482420 AMINO
            22 AMINOS
        482431 AMINO
                 (AMINO OR AMINOS)
             8 PHOSPHONOMETHYLAMINO
        100609 ACETIC
             1 ACETICS
        100610 ACETIC
                 (ACETIC OR ACETICS)
       1786557 ACID
        415788 ACIDS
       1954902 ACID
                 (ACID OR ACIDS)
             4 2(W)(PHOSPHONOMETHYL(W)AMINO OR
PHOSPHONOMETHYLAMINO)(W)ACETIC(W
               )ACID
             1 PHOSPHONOMETHYLIMINOACETIC
       1786557 ACID
        415788 ACIDS
       1954902 ACID
                 (ACID OR ACIDS)
             0 PHOSPHONOMETHYLIMINOACETIC ACID
                 (PHOSPHONOMETHYLIMINOACETIC(W)ACID)
            48 CARBOXYMETHYLAMINO
           831 METHYLPHOSPHONIC
       1786557 ACID
        415788 ACIDS
       1954902 ACID
                 (ACID OR ACIDS)
             0 CARBOXYMETHYLAMINO METHYLPHOSPHONIC ACID
                 (CARBOXYMETHYLAMINO(W)METHYLPHOSPHONIC(W)ACID)
             0 CARBOXYMETHYLAMINOMETHANEPHOSP
             7 GLYFOS
             1 GLYPHODIN
             3 GLYPHOMAX
             0 PHORSAT
          1567 ROUNDUP
             2 ROUNDUPS
          1568 ROUNDUP
                 (ROUNDUP OR ROUNDUPS)
          3930 MON
            43 MONS
          3968 MON
                 (MON OR MONS)
           145 2139
            11 MON 2139
                 (MON(W)2139)
             0 MON2139
          3930 MON
            43 MONS
          3968 MON
                 (MON OR MONS)
            53 3539
             0 MON 3539
                 (MON(W)3539)
             0 MON3539
          3930 MON
            43 MONS
          3968 MON
```

```
                (MON OR MONS)
          9547 6000
             0 MON 6000
                (MON(W)6000)
             0 MON6000
          7991 NSC
          1382 NSCS
          8750 NSC
                (NSC OR NSCS)
             0 151063
             0 NSC 151063
                (NSC(W)151063)
             0 NSC151063
          9360 1071-83-6
            71 40465-66-5
          1875 38641-94-0
            31 70393-85-0
           187 81591-81-3
        294492 HORMON?
        322963 ENDOCRIN?
         80068 THYROID?
         43167 ANDROGEN?
        111329 ESTROGEN?
          5942 OESTROGEN?
        113627 ESTROGEN?
                (ESTROGEN? OR OESTROGEN?)
          9295 STEROIDO?
         10924 AROMATASE
            50 AROMATASES
         10939 AROMATASE
                (AROMATASE OR AROMATASES)
        162984 CYTOCHROME
         14319 CYTOCHROMES
        166047 CYTOCHROME
                (CYTOCHROME OR CYTOCHROMES)
         50736 P450
       1569409 P
        117091 450
         87792 P 450
                (P(W)450)
        107761 CYTOCHROME(W)(P450 OR P 450)
           956 INTERSEX?
       1373438 PY>2013
       1250273 P/DT
L22          72 (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8) AND L19 AND
L20
                NOT P/DT

FILE 'HCAPLUS'
         13285 GLYPHOSAT#
       4507912 N
          2502 PHOSPHONOMETHYL
        276655 GLYCINE
          5770 GLYCINES
        278527 GLYCINE
                (GLYCINE OR GLYCINES)
            14 PHOSPHOMETHYLGLYCINE
             1 PHOSPHOMETHYLGLYCINES
            15 PHOSPHOMETHYLGLYCINE
                (PHOSPHOMETHYLGLYCINE OR PHOSPHOMETHYLGLYCINES)
           663 N(W)(PHOSPHONOMETHYL(W)GLYCINE OR PHOSPHOMETHYLGLYCINE)
```

```
          627 PHOSPHONOMETHYLGLYCINE
           37 PHOSPHONOMETHYLGLYCINES
          628 PHOSPHONOMETHYLGLYCINE
                (PHOSPHONOMETHYLGLYCINE OR PHOSPHONOMETHYLGLYCINES)
     14072878 2
         2502 PHOSPHONOMETHYL
      1644510 AMINO
           82 AMINOS
      1644555 AMINO
                (AMINO OR AMINOS)
           45 PHOSPHONOMETHYLAMINO
       448886 ACETIC
           23 ACETICS
       448895 ACETIC
                (ACETIC OR ACETICS)
      6846559 ACID
      2221238 ACIDS
      7520284 ACID
                (ACID OR ACIDS)
            5 2(W)(PHOSPHONOMETHYL(W)AMINO OR
PHOSPHONOMETHYLAMINO)(W)ACETIC(W
              )ACID
            2 PHOSPHONOMETHYLIMINOACETIC
      6846559 ACID
      2221238 ACIDS
      7520284 ACID
                (ACID OR ACIDS)
            1 PHOSPHONOMETHYLIMINOACETIC ACID
                (PHOSPHONOMETHYLIMINOACETIC(W)ACID)
          356 CARBOXYMETHYLAMINO
         2199 METHYLPHOSPHONIC
      6846559 ACID
      2221238 ACIDS
      7520284 ACID
                (ACID OR ACIDS)
            0 CARBOXYMETHYLAMINO METHYLPHOSPHONIC ACID
                (CARBOXYMETHYLAMINO(W)METHYLPHOSPHONIC(W)ACID)
            0 CARBOXYMETHYLAMINOMETHANEPHOSP
            9 GLYFOS
            1 GLYPHODIN
            9 GLYPHOMAX
            0 PHORSAT
         2267 ROUNDUP
            4 ROUNDUPS
         2269 ROUNDUP
                (ROUNDUP OR ROUNDUPS)
         4632 MON
          295 MONS
         4910 MON
                (MON OR MONS)
          599 2139
           11 MON 2139
                (MON(W)2139)
            1 MON2139
         4632 MON
          295 MONS
         4910 MON
                (MON OR MONS)
          222 3539
            3 MON 3539
                (MON(W)3539)
```

```
            1 MON3539
         4632 MON
          295 MONS
         4910 MON
                (MON OR MONS)
        44519 6000
            0 MON 6000
                (MON(W)6000)
            0 MON6000
         7485 NSC
         3422 NSCS
         9493 NSC
                (NSC OR NSCS)
            1 151063
            0 NSC 151063
                (NSC(W)151063)
            0 NSC151063
        15103 1071-83-6
          270 40465-66-5
         2901 38641-94-0
           59 70393-85-0
          523 81591-81-3
       593877 HORMON?
       121771 ENDOCRIN?
       131330 THYROID?
        73519 ANDROGEN?
       161891 ESTROGEN?
         1517 OESTROGEN?
       161937 ESTROGEN?
                (ESTROGEN? OR OESTROGEN?)
        19515 STEROIDO?
        13653 AROMATASE
          113 AROMATASES
        13672 AROMATASE
                (AROMATASE OR AROMATASES)
       211924 CYTOCHROME
        19752 CYTOCHROMES
       215170 CYTOCHROME
                (CYTOCHROME OR CYTOCHROMES)
        39343 P450
      4036651 P
       280448 450
        91989 P 450
                (P(W)450)
        94051 CYTOCHROME(W)(P450 OR P 450)
         1026 INTERSEX?
      6150522 PY>2013
     11600250 P/DT
L23         43 (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8) AND L19 AND
L20
               NOT P/DT

FILE 'MEDLINE'
         2248 GLYPHOSAT#
      1684416 N
          560 PHOSPHONOMETHYL
        70079 GLYCINE
         1597 GLYCINES
        70997 GLYCINE
                (GLYCINE OR GLYCINES)
            2 PHOSPHOMETHYLGLYCINE
```

```
          158 N(W)(PHOSPHONOMETHYL(W)GLYCINE OR PHOSPHOMETHYLGLYCINE)
           37 PHOSPHONOMETHYLGLYCINE
      6497573 2
          560 PHOSPHONOMETHYL
       938828 AMINO
           15 AMINOS
       938839 AMINO
                (AMINO OR AMINOS)
            4 PHOSPHONOMETHYLAMINO
        42012 ACETIC
      2227705 ACID
       748617 ACIDS
      2526639 ACID
                (ACID OR ACIDS)
            3 2(W)(PHOSPHONOMETHYL(W)AMINO OR
PHOSPHONOMETHYLAMINO)(W)ACETIC(W
              )ACID
            1 PHOSPHONOMETHYLIMINOACETIC
      2227705 ACID
       748617 ACIDS
      2526639 ACID
                (ACID OR ACIDS)
            1 PHOSPHONOMETHYLIMINOACETIC ACID
                (PHOSPHONOMETHYLIMINOACETIC(W)ACID)
           39 CARBOXYMETHYLAMINO
          433 METHYLPHOSPHONIC
      2227705 ACID
       748617 ACIDS
      2526639 ACID
                (ACID OR ACIDS)
            0 CARBOXYMETHYLAMINO METHYLPHOSPHONIC ACID
                (CARBOXYMETHYLAMINO(W)METHYLPHOSPHONIC(W)ACID)
            0 CARBOXYMETHYLAMINOMETHANEPHOSP
            1 GLYFOS
            0 GLYPHODIN
            0 GLYPHOMAX
            0 PHORSAT
          983 ROUNDUP
            6 ROUNDUPS
          989 ROUNDUP
                (ROUNDUP OR ROUNDUPS)
         1517 MON
          270 MONS
         1775 MON
                (MON OR MONS)
          200 2139
            1 MON 2139
                (MON(W)2139)
            0 MON2139
         1517 MON
          270 MONS
         1775 MON
                (MON OR MONS)
           99 3539
            0 MON 3539
                (MON(W)3539)
            0 MON3539
         1517 MON
          270 MONS
         1775 MON
                (MON OR MONS)
```

```
          8548 6000
             0 MON 6000
                 (MON(W)6000)
             0 MON6000
          6451 NSC
          2915 NSCS
          7955 NSC
                 (NSC OR NSCS)
             0 151063
             0 NSC 151063
                 (NSC(W)151063)
             0 NSC151063
          1462 1071-83-6
             0 40465-66-5
             0 38641-94-0
             0 70393-85-0
             0 81591-81-3
        674628 HORMON?
        141392 ENDOCRIN?
        195050 THYROID?
         82509 ANDROGEN?
        169288 ESTROGEN?
         21030 OESTROGEN?
        178660 ESTROGEN?
                 (ESTROGEN? OR OESTROGEN?)
         17460 STEROIDO?
         14036 AROMATASE
            84 AROMATASES
         14055 AROMATASE
                 (AROMATASE OR AROMATASES)
        144216 CYTOCHROME
         30129 CYTOCHROMES
        151080 CYTOCHROME
                 (CYTOCHROME OR CYTOCHROMES)
         40763 P450
       2619616 P
         94011 450
         65097 P 450
                 (P(W)450)
         77600 CYTOCHROME(W)(P450 OR P 450)
          2607 INTERSEX?
       3085473 PY>2013
             0 P/DT
L24          28 (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8) AND L19 AND
L20
                NOT P/DT

FILE 'BIOSIS'
          8101 GLYPHOSAT#
       1738994 N
          1240 PHOSPHONOMETHYL
        109855 GLYCINE
          4082 GLYCINES
        112331 GLYCINE
                 (GLYCINE OR GLYCINES)
             6 PHOSPHOMETHYLGLYCINE
           795 N(W)(PHOSPHONOMETHYL(W)GLYCINE OR PHOSPHOMETHYLGLYCINE)
           131 PHOSPHONOMETHYLGLYCINE
       6167791 2
          1240 PHOSPHONOMETHYL
        791039 AMINO
```

```
           24 AMINOS
       791051 AMINO
                (AMINO OR AMINOS)
            3 PHOSPHONOMETHYLAMINO
        77628 ACETIC
      2083589 ACID
       576671 ACIDS
      2321989 ACID
                (ACID OR ACIDS)
            1 2(W)(PHOSPHONOMETHYL(W)AMINO OR
PHOSPHONOMETHYLAMINO)(W)ACETIC(W
                )ACID
            0 PHOSPHONOMETHYLIMINOACETIC
      2083589 ACID
       576671 ACIDS
      2321989 ACID
                (ACID OR ACIDS)
            0 PHOSPHONOMETHYLIMINOACETIC ACID
                (PHOSPHONOMETHYLIMINOACETIC(W)ACID)
           37 CARBOXYMETHYLAMINO
          243 METHYLPHOSPHONIC
      2083589 ACID
       576671 ACIDS
      2321989 ACID
                (ACID OR ACIDS)
            0 CARBOXYMETHYLAMINO METHYLPHOSPHONIC ACID
                (CARBOXYMETHYLAMINO(W)METHYLPHOSPHONIC(W)ACID)
            0 CARBOXYMETHYLAMINOMETHANEPHOSP
            6 GLYFOS
            0 GLYPHODIN
            1 GLYPHOMAX
            0 PHORSAT
         1306 ROUNDUP
           16 ROUNDUPS
         1315 ROUNDUP
                (ROUNDUP OR ROUNDUPS)
         8054 MON
          309 MONS
         8345 MON
                (MON OR MONS)
          274 2139
            4 MON 2139
                (MON(W)2139)
            0 MON2139
         8054 MON
          309 MONS
         8345 MON
                (MON OR MONS)
           90 3539
            0 MON 3539
                (MON(W)3539)
            0 MON3539
         8054 MON
          309 MONS
         8345 MON
                (MON OR MONS)
        12366 6000
            1 MON 6000
                (MON(W)6000)
            0 MON6000
         7301 NSC
```

```
          2643 NSCS
          8602 NSC
                 (NSC OR NSCS)
             0 151063
             0 NSC 151063
                 (NSC(W)151063)
             0 NSC151063
          7017 1071-83-6
             0 40465-66-5
           449 38641-94-0
             4 70393-85-0
            52 81591-81-3
        765060 HORMON?
       2762370 ENDOCRIN?
        168354 THYROID?
         82082 ANDROGEN?
        169916 ESTROGEN?
         13030 OESTROGEN?
        174327 ESTROGEN?
                 (ESTROGEN? OR OESTROGEN?)
         20612 STEROIDO?
         13687 AROMATASE
           101 AROMATASES
         13709 AROMATASE
                 (AROMATASE OR AROMATASES)
        170888 CYTOCHROME
         12272 CYTOCHROMES
        174482 CYTOCHROME
                 (CYTOCHROME OR CYTOCHROMES)
         55222 P450
       2374283 P
         59218 450
         27560 P 450
                 (P(W)450)
         73422 CYTOCHROME(W)(P450 OR P 450)
          3978 INTERSEX?
       2044668 PY>2013
        551645 P/DT
L25         29 (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8) AND L19 AND
L20
               NOT P/DT

FILE 'EMBASE'
          2764 GLYPHOSAT#
       2249968 N
          1040 PHOSPHONOMETHYL
         95785 GLYCINE
          1275 GLYCINES
         96308 GLYCINE
                 (GLYCINE OR GLYCINES)
             3 PHOSPHOMETHYLGLYCINE
           180 N(W)(PHOSPHONOMETHYL(W)GLYCINE OR PHOSPHOMETHYLGLYCINE)
            50 PHOSPHONOMETHYLGLYCINE
       8046929 2
          1040 PHOSPHONOMETHYL
        971938 AMINO
           105 AMINOS
        971966 AMINO
                 (AMINO OR AMINOS)
             9 PHOSPHONOMETHYLAMINO
        125318 ACETIC
```

```
            1 ACETICS
       125318 ACETIC
                (ACETIC OR ACETICS)
      3556007 ACID
       493701 ACIDS
      3644317 ACID
                (ACID OR ACIDS)
            2 2(W)(PHOSPHONOMETHYL(W)AMINO OR
PHOSPHONOMETHYLAMINO)(W)ACETIC(W
              )ACID
            0 PHOSPHONOMETHYLIMINOACETIC
      3556007 ACID
       493701 ACIDS
      3644317 ACID
                (ACID OR ACIDS)
            0 PHOSPHONOMETHYLIMINOACETIC ACID
                (PHOSPHONOMETHYLIMINOACETIC(W)ACID)
           75 CARBOXYMETHYLAMINO
          962 METHYLPHOSPHONIC
      3556007 ACID
       493701 ACIDS
      3644317 ACID
                (ACID OR ACIDS)
            0 CARBOXYMETHYLAMINO METHYLPHOSPHONIC ACID
                (CARBOXYMETHYLAMINO(W)METHYLPHOSPHONIC(W)ACID)
            0 CARBOXYMETHYLAMINOMETHANEPHOSP
            1 GLYFOS
            0 GLYPHODIN
            0 GLYPHOMAX
            0 PHORSAT
          774 ROUNDUP
            3 ROUNDUPS
          777 ROUNDUP
                (ROUNDUP OR ROUNDUPS)
         2491 MON
          460 MONS
         2931 MON
                (MON OR MONS)
          354 2139
            1 MON 2139
                (MON(W)2139)
            0 MON2139
         2491 MON
          460 MONS
         2931 MON
                (MON OR MONS)
          154 3539
            0 MON 3539
                (MON(W)3539)
            0 MON3539
         2491 MON
          460 MONS
         2931 MON
                (MON OR MONS)
        13244 6000
            0 MON 6000
                (MON(W)6000)
            0 MON6000
        10885 NSC
         4020 NSCS
        13015 NSC
```

```
                (NSC OR NSCS)
            0 151063
            0 NSC 151063
                (NSC(W)151063)
            0 NSC151063
         2320 1071-83-6
            0 40465-66-5
            7 38641-94-0
            0 70393-85-0
            0 81591-81-3
       859600 HORMON?
       397409 ENDOCRIN?
       286340 THYROID?
       115554 ANDROGEN?
       250907 ESTROGEN?
        33992 OESTROGEN?
       261594 ESTROGEN?
                (ESTROGEN? OR OESTROGEN?)
        26992 STEROIDO?
        23444 AROMATASE
          103 AROMATASES
        23458 AROMATASE
                (AROMATASE OR AROMATASES)
       197098 CYTOCHROME
        10726 CYTOCHROMES
       198001 CYTOCHROME
                (CYTOCHROME OR CYTOCHROMES)
       102126 P450
      3656168 P
        60945 450
        19455 P 450
                (P(W)450)
       104788 CYTOCHROME(W)(P450 OR P 450)
         3465 INTERSEX?
      3770338 PY>2013
            1 P/DT
L26         36 (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8) AND L19 AND
L20
               NOT P/DT

FILE 'CABA'
        16045 GLYPHOSAT#
       647242 N
          315 PHOSPHONOMETHYL
       113695 GLYCINE
         3452 GLYCINES
       114455 GLYCINE
                (GLYCINE OR GLYCINES)
            5 PHOSPHOMETHYLGLYCINE
          282 N(W)(PHOSPHONOMETHYL(W)GLYCINE OR PHOSPHOMETHYLGLYCINE)
           50 PHOSPHONOMETHYLGLYCINE
      2327274 2
          315 PHOSPHONOMETHYL
       197303 AMINO
           12 AMINOS
       197311 AMINO
                (AMINO OR AMINOS)
            1 PHOSPHONOMETHYLAMINO
        65656 ACETIC
            2 ACETICS
        65657 ACETIC
```

```
                (ACETIC OR ACETICS)
        913041 ACID
        324997 ACIDS
       1025261 ACID
                (ACID OR ACIDS)
             2 2(W)(PHOSPHONOMETHYL(W)AMINO OR
PHOSPHONOMETHYLAMINO)(W)ACETIC(W
               )ACID
             0 PHOSPHONOMETHYLIMINOACETIC
        913041 ACID
        324997 ACIDS
       1025261 ACID
                (ACID OR ACIDS)
             0 PHOSPHONOMETHYLIMINOACETIC ACID
                (PHOSPHONOMETHYLIMINOACETIC(W)ACID)
             6 CARBOXYMETHYLAMINO
            48 METHYLPHOSPHONIC
        913041 ACID
        324997 ACIDS
       1025261 ACID
                (ACID OR ACIDS)
             0 CARBOXYMETHYLAMINO METHYLPHOSPHONIC ACID
                (CARBOXYMETHYLAMINO(W)METHYLPHOSPHONIC(W)ACID)
             0 CARBOXYMETHYLAMINOMETHANEPHOSP
            14 GLYFOS
             0 GLYPHODIN
             1 GLYPHOMAX
             0 PHORSAT
          2618 ROUNDUP
            13 ROUNDUPS
          2628 ROUNDUP
                (ROUNDUP OR ROUNDUPS)
          1635 MON
            74 MONS
          1705 MON
                (MON OR MONS)
           164 2139
            23 MON 2139
                (MON(W)2139)
             0 MON2139
          1635 MON
            74 MONS
          1705 MON
                (MON OR MONS)
            49 3539
             0 MON 3539
                (MON(W)3539)
             0 MON3539
          1635 MON
            74 MONS
          1705 MON
                (MON OR MONS)
          9342 6000
             0 MON 6000
                (MON(W)6000)
             0 MON6000
           924 NSC
           206 NSCS
          1043 NSC
                (NSC OR NSCS)
             0 151063
```

```
             0 NSC 151063
                 (NSC(W)151063)
             0 NSC151063
         14903 1071-83-6
             0 40465-66-5
         14903 38641-94-0
         14902 70393-85-0
             0 81591-81-3
        277966 HORMON?
         36383 ENDOCRIN?
         19179 THYROID?
         13420 ANDROGEN?
         28348 ESTROGEN?
         28623 OESTROGEN?
         32628 ESTROGEN?
                 (ESTROGEN? OR OESTROGEN?)
          4886 STEROIDO?
          2074 AROMATASE
            73 AROMATASES
          2081 AROMATASE
                 (AROMATASE OR AROMATASES)
         27645 CYTOCHROME
          2549 CYTOCHROMES
         28188 CYTOCHROME
                 (CYTOCHROME OR CYTOCHROMES)
          8972 P450
        985399 P
         30353 450
          9075 P 450
                 (P(W)450)
         11437 CYTOCHROME(W)(P450 OR P 450)
          1473 INTERSEX?
        933234 PY>2013
          9220 P/DT
L27         52 (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8) AND L19 AND
L20
               NOT P/DT

FILE 'AGRICOLA'
          5365 GLYPHOSAT#
        203996 N
           200 PHOSPHONOMETHYL
         30027 GLYCINE
          1800 GLYCINES
         30671 GLYCINE
                 (GLYCINE OR GLYCINES)
             2 PHOSPHOMETHYLGLYCINE
           188 N(W)(PHOSPHONOMETHYL(W)GLYCINE OR PHOSPHOMETHYLGLYCINE)
            27 PHOSPHONOMETHYLGLYCINE
        616582 2
           200 PHOSPHONOMETHYL
        111857 AMINO
             2 AMINOS
        111859 AMINO
                 (AMINO OR AMINOS)
             1 PHOSPHONOMETHYLAMINO
         16786 ACETIC
        340868 ACID
        136591 ACIDS
        397627 ACID
                 (ACID OR ACIDS)
```

```
             1 2(W)(PHOSPHONOMETHYL(W)AMINO OR
PHOSPHONOMETHYLAMINO)(W)ACETIC(W
               )ACID
             0 PHOSPHONOMETHYLIMINOACETIC
        340868 ACID
        136591 ACIDS
        397627 ACID
                 (ACID OR ACIDS)
             0 PHOSPHONOMETHYLIMINOACETIC ACID
                 (PHOSPHONOMETHYLIMINOACETIC(W)ACID)
             5 CARBOXYMETHYLAMINO
            37 METHYLPHOSPHONIC
        340868 ACID
        136591 ACIDS
        397627 ACID
                 (ACID OR ACIDS)
             0 CARBOXYMETHYLAMINO METHYLPHOSPHONIC ACID
                 (CARBOXYMETHYLAMINO(W)METHYLPHOSPHONIC(W)ACID)
             0 CARBOXYMETHYLAMINOMETHANEPHOSP
             1 GLYFOS
             0 GLYPHODIN
             0 GLYPHOMAX
             0 PHORSAT
           940 ROUNDUP
             9 ROUNDUPS
           948 ROUNDUP
                 (ROUNDUP OR ROUNDUPS)
           522 MON
            25 MONS
           547 MON
                 (MON OR MONS)
            55 2139
             1 MON 2139
                 (MON(W)2139)
             0 MON2139
           522 MON
            25 MONS
           547 MON
                 (MON OR MONS)
            22 3539
             1 MON 3539
                 (MON(W)3539)
             0 MON3539
           522 MON
            25 MONS
           547 MON
                 (MON OR MONS)
          1319 6000
             0 MON 6000
                 (MON(W)6000)
             0 MON6000
           385 NSC
           176 NSCS
           486 NSC
                 (NSC OR NSCS)
             0 151063
             0 NSC 151063
                 (NSC(W)151063)
             0 NSC151063
          7790 1071
         21484 83
```

```
        324663 6
             1 1071-83-6
                 (1071(W)83(W)6)
             0 40465
         22263 66
        438364 5
             0 40465-66-5
                 (40465(W)66(W)5)
             0 38641
         23294 94
        438801 0
             0 38641-94-0
                 (38641(W)94(W)0)
             0 70393
         31961 85
        438801 0
             0 70393-85-0
                 (70393(W)85(W)0)
             0 81591
         20965 81
        499240 3
             0 81591-81-3
                 (81591(W)81(W)3)
         55558 HORMON?
         10215 ENDOCRIN?
          5790 THYROID?
          4005 ANDROGEN?
          8926 ESTROGEN?
          1474 OESTROGEN?
          9856 ESTROGEN?
                 (ESTROGEN? OR OESTROGEN?)
          1855 STEROIDO?
           859 AROMATASE
             8 AROMATASES
           860 AROMATASE
                 (AROMATASE OR AROMATASES)
         17388 CYTOCHROME
          1885 CYTOCHROMES
         18026 CYTOCHROME
                 (CYTOCHROME OR CYTOCHROMES)
          4597 P450
        416751 P
         12367 450
          5342 P 450
                 (P(W)450)
          6085 CYTOCHROME(W)(P450 OR P 450)
           691 INTERSEX?
        219217 PY>2013
             4 P/DT
L28          5 (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8) AND L19 AND
L20
               NOT P/DT

TOTAL FOR ALL FILES
L29        265 (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8) AND L19 AND
L20
               NOT P/DT

=> dup rem l29
PROCESSING COMPLETED FOR L29
L30         115 DUP REM L29 (150 DUPLICATES REMOVED)
```

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ANSWERS '1-49' FROM FILE TOXCENTER
ANSWERS '50-57' FROM FILE HCAPLUS
ANSWERS '58-64' FROM FILE MEDLINE
ANSWERS '65-67' FROM FILE BIOSIS
ANSWERS '68-78' FROM FILE EMBASE
ANSWERS '79-114' FROM FILE CABA
ANSWER '115' FROM FILE AGRICOLA
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