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# **Literature Review Report**

Scientific peer-reviewed open literature covering the publication period of January 2021 to 14 May 2021 for the approval of pesticide active substance glyphosate and metabolites

as under Article 8(5) of Regulation (EC) No 1107/2009 (Ref. EFSA Journal 2011; 9(2) 2092)

Report number

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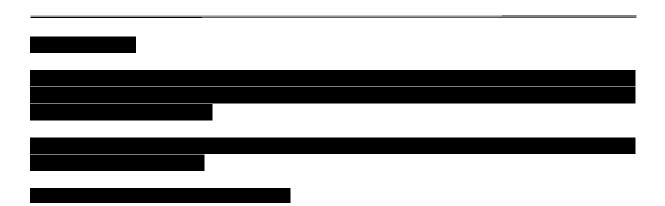
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Date of search(es):

14 May 2021

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#### 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.

All articles used within the glyphosate dossier have been purchased via Copyright Clearance Centre. In some cases, please note that the Copyright Clearance is not overtly visible, and in some instances is part of the article documents. Should the Copyright Clearance proof be required, this can be provided upon request.

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#### 1 Summary

A literature search for glyphosate and its metabolites<sup>1</sup> was conducted according to the requirements stated in the EFSA 2092 Guidance Document (GD) - EFSA Journal 2011;9(2):2092 "Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) 1107/2009<sup>2</sup>", and the Appendix to the EFSA 2092 Guidance Document "Further guidance on performing and presenting the literature search"<sup>3</sup>, and the EFSA supporting publication from 2019<sup>4</sup> "Administrative guidance on submission of dossiers and assessment reports for the peer-review of pesticide active substances".

In addition, a recommendation by the Assessment Group on Glyphosate (AGG)<sup>5</sup> on how to present the literature search in the dossier has been followed. Please refer to **Appendix 1** (page 64) for more details.

This Literature Review Report summarizes the search and evaluation of the glyphosate scientific peer-reviewed open literature covering the publication period of January 2021 to 14 May 2021 and is supplementary to the previous searches covering the publication period of January 2010 to December 2020.<sup>6</sup>

The literature search was conducted accessing 11 bibliographic databases via the service provider STN.

In total, 597 articles were identified upon removal of duplicates within the current search (January 2021 to 14 May 2021) and articles found already in the previous searches (January 2010 to December 2020).

All 597 articles were subsequently assessed for their relevance at title/abstract level ("rapid assessment" according to the procedure and requirements stated in the EFSA 2092 GD).

A total of 523 of the 597 articles were identified as "non-relevant" in the rapid assessment (e.g. publications dealing with chemical synthesis, efficacy, analytical methods or publications which are not related to glyphosate or its metabolites) and excluded from further evaluation. Due to the large quantity of data, and as agreed with the AGG, the list of articles and the justification for their non-relevance is provided in a standalone Literature Review Excel File (Document ID: 113898 CA9-3 Literature Review Excel File).

For the remaining 74 articles, identified as potentially "relevant" or of "unclear relevance" in the rapid assessment, the full-text documents<sup>7</sup> were reviewed in detail ("detailed assessment").

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<sup>&</sup>lt;sup>1</sup> (aminomethyl)phosphonic acid (AMPA), N-acetyl-AMPA, N-acetyl-glyphosate, (hydroxymethyl)phosphonic acid (HMPA), N-methyl-AMPA, N-glyceryl-AMPA, N-malonyl-AMPA, methylphosphonic acid and N-methylglyphosate.

<sup>&</sup>lt;sup>2</sup> European Food Safety Authority, 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. <sup>3</sup> Appendix to EFSA Journal 2011;9(2):2092. Further guidance on performing and presenting the literature search. Available online: https://efsa.onlinelibrary.wiley.com/action/downloadSupplement?doi=10.2903/j.efsa.2011.2092&file=efs22092-sup-0001-Appendix.pdf

<sup>&</sup>lt;sup>4</sup> European Food Safety Authority, 2019. Administrative guidance on submission of dossiers and assessment reports for the peer-review of pesticide active substances. EFSA supporting publication 2019:EN-1612. 49 pp., doi:10.2903/sp.efsa.2019.EN-1612.

<sup>&</sup>lt;sup>5</sup> On 10<sup>th</sup> May 2019, the European Commission appointed four Member States (France, Hungary, the Netherlands and Sweden) to act jointly as 'rapporteurs' for the AIR5 process assessment of glyphosate. This group of Member States is known as the Assessment Group on Glyphosate (AGG).

<sup>&</sup>lt;sup>6</sup> See Literature Review Reports 108689-CA9-1, 113898-CA9-1 and 113898-CA9-2 for more details.

<sup>&</sup>lt;sup>7</sup> All articles used within the glyphosate dossier have been purchased via Copyright Clearance Centre. In some cases, please note that the Copyright Clearance is not overtly visible, and in some instances is part of the article documents. Should the Copyright Clearance proof be required, this can be provided upon request.

A total of 28 articles of the remaining 74 articles were identified as "non-relevant" in the detailed assessment and were excluded from further evaluation. The list of the articles and the justification for their non-relevance is provided in **Table 38** of this Literature Review Report document.

The remaining 46 articles of the 74 articles were identified as "relevant" in the detailed assessment and were classified according to the EFSA 2092 GD (EFSA Journal 2011;9(2):2092, Point 5.4.1).

- Category A Articles which provide data for establishing or refining risk assessment parameters. For all articles of Category A, a reliability assessment was performed as recommended in the EFSA 2092 GD. In addition, summaries were compiled for Category A articles classified as "reliable" or "reliable with restrictions". The list of these Category A & reliable / reliable with restrictions articles can be found in **Table 32** and **Table 33** of this Literature Review Report document.
- Category B Articles relevant to the data requirement but in the opinion of the applicant providing only supplementary information that does not alter existing risk assessment.

  A justification for such decision is provided as recommended in the EFSA 2092 GD. The list of these Category B articles and the justifications can be found in **Table 34** and **Table 35** of this Literature Review Report document.
- Category C Articles for which relevance cannot be clearly determined.

  As recommended in the EFSA 2092 GD, an explanation is provided why the relevance could not be determined. The list of these Category C articles and the explanations can be found in **Table 36** and **Table 37** of this Literature Review Report document.

The full outcome of the literature evaluation is provided in **Table 1**.

**Table 1: Summary of the literature review** 

	Number of	Rapid assessment (title/abstract level)		Detailed assessment (full-text level)	
Section	articles found	non-relevant articles	potentially relevant / unclear relevance	non-relevant articles	relevant articles (Category A+B+C)
Efficacy / Agronomy <sup>a)</sup>	248	248	n.a.	n.a.	n.a.
Analytical methods a)	29	29	n.a.	n.a.	n.a.
Other non- relevant categories b)	54	54	n.a.	n.a.	n.a.
Ecotoxicology	93	61	32	19	13
E-fate	79	74	5	1	4
Residues	18	10	8	3	5
Toxicology	76	47	29	5	24
Total	597	523	74	28	46

<sup>&</sup>lt;sup>a)</sup> Efficacy / Agronomy (e.g. reporting desired effects on organisms to be controlled) and development of analytical methods (artificial measurements) do not provide information useful/required for the environmental or human safety risk assessment.

b) The category "other non-relevant categories" covers a wide range of scientific publications which are not related to glyphosate or its metabolites or are not related to exposure of humans or the environment to glyphosate or its metabolites and thus not relevant for the risk assessments.

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The full outcome of the relevant articles after detailed (full-text) assessment is provided in **Table 2**.

Table 2: Relevant articles by full-text classified according to the EFSA 2092 GD, Point 5.4.1

		Relevant articles by full-tex EFSA 2092 GD, Point 5.4.1		
Section	Category A a Category B b Category C c)			
Ecotoxicology	3	8	2	
E-fate	3	1	0	
Residues	0	5	0	
Toxicology	4	15	5	
Total	10	29	7	

a) Category A: Articles which provide data for establishing or refining risk assessment parameters.

All articles (and their translations) evaluated at full text level (detailed assessment) were submitted to the AGG in a Portable Document Format (PDF).

Please refer to Appendix 2 (page 65) to see the article selection process in detail.

b) Category B: Articles relevant to the data requirement but in the opinion of the applicant providing only supplementary information that does not alter existing risk assessment.

c) Category C: Articles for which relevance cannot be clearly determined.

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#### 2 Introduction

A literature search for glyphosate and its metabolites<sup>1</sup> was conducted according to the requirements stated in the EFSA 2092 Guidance Document - EFSA Journal 2011;9(2):2092 "Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) 1107/2009<sup>2</sup>", and the Appendix to the EFSA 2092 Guidance Document "Further guidance on performing and presenting the literature search", and the EFSA Supporting publication from 2019<sup>4</sup> "Administrative guidance on submission of dossiers and assessment reports for the peer-review of pesticide active substances".

In addition, a recommendation by the Assessment Group on Glyphosate (AGG) on how to present the literature search in the dossier has been followed. Please refer to **Appendix 1** (page 64) for more details.

In June 2020, a Literature Review Report (Document ID: 108689-CA9-1) summarizing results of the search of the glyphosate scientific peer-reviewed open literature published from January 2010 to December 2019 was submitted to the AGG as part of the glyphosate AIR5 dossier. In July 2020 during the dossier completeness check (point 23)<sup>8</sup>, the AGG requested a top-up search for glyphosate open literature covering the publication period of January 2020 to June 2020. In October 2020, a Literature Review Report (Document ID: 113898-CA9-1) summarizing results of this top-up search was submitted to the AGG.

Furthermore, two additional supplementary literature searches of the glyphosate scientific peer-reviewed open literature were performed in January 2021 and in May 2021. The first search, from January 2021, covers the publication period of July 2020 to December 2020 and is summarized in the Literature Review Report Document ID: 113898-CA9-2. The second search, from May 2021, covers the publication period of January 2021 to 14 May 2021 and is summarized in this Literature Review Report (Document ID: 113898-CA9-3). Details for this search are provided below.

The search has been conducted via the online service provider STN (www.stn-international.de) that provides access to a broad range of databases and to published research, journal literature, patents, structures, sequences, properties, and other data.

To offer a comprehensive literature search covering the requirements of the EFSA 2092 GD eleven databases have been used: AGRICOLA, BIOSIS, CABA, HCAPLUS, EMBASE, ESBIOBASE, MEDLINE, TOXCENTER, FSTA, PQSCITECH, and SCISEARCH.

Please refer to **Table 3** for more details on the literature search.

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<sup>&</sup>lt;sup>8</sup> AGG's letter dated 10-July-2020, subject "Glyphosate: Check of completeness of the supplementary dossier for renewal of approval under Commission Implementing Regulation (EU) No 844/2012", section 2: Elements to be submitted in accordance with Article 11(5) of Regulation (EU) No 844/2012, point 23.

Table 3: Overview of the search conducted for glyphosate and its metabolites

Performed for	Covering publication period	<b>Conducted on</b>
Glyphosate AMPA N-acetyl-AMPA N-acetyl-glyphosate HMPA N-methyl-AMPA N-glyceryl-AMPA	January 2021 – 14 May 2021	Conducted on  14 May 2021
N-malonyl-AMPA		
methylphosphonic acid		
N-methylglyphosate		

AMPA = (aminomethyl)phosphonic acid HMPA = (hydroxymethyl)phosphonic acid

A "focused search for grouped data requirements" have been performed (a combination of a substance basic input parameters, keywords and "search filters" defined for the four technical sections – toxicology, residues, environmental fate, and ecotoxicology).

Please refer to Chapter 2.2 and 2.3 (pages 14 and 16) for the input parameters, keywords and search filters used in the literature search.

Regarding details on the bibliographic databases used in the literature search, please refer to Chapter 2.1 (Table 4).

Regarding the number of articles retrieved in the literature search, please refer to Chapter 2.1 (Table 5).

For the relevance and reliability assessment, please refer to Chapter 2.4 and 2.5 (pages 19 and 22).

For the full outcome of the literature search and for the individual technical sections, please refer to **Chapter 3** (page 27).

<sup>&</sup>lt;sup>9</sup> Citation from the EFSA 2092 Guidance Document: If the number of summary records returned by a single concept search\* is extremely large, focused searches for individual or grouped data requirements could be developed. Such searches could combine synonyms for the active substance (one concept) with terms and synonyms for characteristics of the data requirement (second concept).

<sup>\*</sup>NOTE: Single concept search (as defined in the EFSA 2092 GD document) = using the active substance names and its synonyms.

# 2.1 Bibliographic databases used in the literature search

Table 4: Overview of the databases used in the literature search

Data requirement(s)	Details of the search(es)				
captured in the search	1. AGRICOLA	2. BIOSIS	3. CABA	4. HCAPLUS	
Justification for choosing	Provides literature from agriculture	Provides the most comprehensive	Provides literature from agriculture	Provides literature from chemistry	
the source:	and related fields, e.g. biology,	and largest life science literature,	and related sciences, e.g.	and related fields, e.g.	
	biotechnology, botany, ecology	e.g. biosciences, biomedicine etc.	biotechnology, forestry, veterinary	biochemistry, chemical	
	etc.		medicine etc.	engineering etc.	
Number of records in the	> 7.1 million (09/2020)	> 27.8 million (04/2019)	> 9.9 million (09/2020)	> 57.0 million (01/2022)	
database at the time of					
search:					
Database update:	Monthly	Weekly	Weekly	Daily updates bibliographic data;	
				weekly updates indexing data	
Date of the search:	14 May 2021	14 May 2021	14 May 2021	14 May 2021	
Database covers records:	1970-present	1926-present	1973-present	1907-present and more than	
Data of the latest database	CM 2021	12 M - 2021	12.14 - 2021	180,000 pre-1907	
Date of the latest database update:	6 May 2021	12 May 2021	12 May 2021	13 May 2021	
Language limit:	No	No	No	No	
<b>Document types <u>excluded</u></b>	Comments, dissertations,	Comments, dissertations,	Comments, dissertations,	Comments, dissertations,	
that are not "scientific	editorials, meetings reports, news,	editorials, meetings reports, news,	editorials, meetings reports, news,	editorials, meetings reports, news,	
peer-reviewed open	patents, press release	patents, press release	patents, press release	patents, press release	
literature":					
Search strategy:	Details are summarized in Chapter 2.2 and 2.3.				
<b>Total number of records</b>	264	258	467	343	
retrieved:					

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Table 4: Overview of the databases used in the literature search (continued)

Data requirement(s) captured in the search	Details of the search(es)			
captured in the scaren	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:	> 33.5 million (01/2022)	> 34.3 million (08/2018)	> 16.2 million (01/2022)	
Database update:	Six times each week, with an annual reload	Daily	Weekly	
Date of the search:	14 May 2021	14 May 2021	14 May 2021	
Database covers records:	1946-present	1974-present	1907-present	
Date of the latest database update:	13 May 2021	13 May 2021	10 May 2021	
Language limit:	No	No	No	
Document types <u>excluded</u> that are not "scientific peer-reviewed open literature":	Comments, dissertations, editorials, meetings reports, news, patents, press release	Comments, dissertations, editorials, meetings reports, news, patents, press release	Comments, dissertations, editorials, meetings reports, news, patents, press release	
Search strategy:	Details are summarized in Chapter 2.2 and 2.3.			
Total number of records retrieved:	181	127	383	

Table 4: Overview of the databases used in the literature search (continued)

Data requirement(s) captured in the search	Details of the search(es)			
	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 on entire spectrum of biological and biosciences research, e.g. microbiology, biotechnology, ecological & environmental sciences, genetics, plant and crop science, toxicology and many more.	Provides one of the largest multidisciplinary scientific literature covering a broad field of sciences, technology, and biomedicine.
Number of records in the database at the time of search:	> 1.59 million (09/2020)	> 33.6 million (01/2021)	> 9.0 million (01/2021)	> 47.7 million (08/2019)
Database update:	Weekly	Monthly	Weekly	Weekly
Date of the search:	14 May 2021	14 May 2021	14 May 2021	14 May 2021
Database covers records:	1969-present	1962-present	1994-present	1974-present
Date of the latest database update:	14 May 2021	29 Apr 2021	12 May 2021	10 May 2021
Language limit:	No	No	No	No
Document types <u>excluded</u> that are not "scientific peer-reviewed open literature":	Comments, dissertations, editorials, meetings reports, news, patents, press release	Comments, dissertations, editorials, meetings reports, news, patents, press release	Comments, dissertations, editorials, meetings reports, news, patents, press release	Comments, dissertations, editorials, meetings reports, news, patents, press release
Search strategy:	Search strategy: Details are summarized in Chapter 2.2 and 2.3.			
Total number of records retrieved:	30	74	162	354

**Table 5: Total number of articles retrieved** 

Scope of the search	After automatic removal of duplicates within the databases in the current search (Jan 2021 – 14 May 2021)	After applying search filters <sup>a)</sup> within the current search (Jan 2021 – 14 May 2021)	After manual removal of duplicates <sup>b)</sup> within the current search (Jan 2021 – 14 May 2021) and entries found already in the previous searches (Jan 2010 – Dec 2020) <sup>c)</sup>
Jan 2021 – 14 May 2021			
Glyphosate AMPA N-acetyl-AMPA N-acetyl-glyphosate HMPA N-methyl-AMPA N-glyceryl-AMPA N-malonyl-AMPA methylphosphonic acid N-methylglyphosate	1522	1517	597

a) Search filters applied for the four technical sections (residues, environmental fate, toxicology and ecotoxicology). Please refer to Chapter 2.3 for more details (page 16).

Note: LRR 108689-CA9-1 covers the publication period of 1 January 2010 to 31 December 2019, LRR 113898-CA9-1 covers the publication period of 1 January 2020 to 30 June 2020, and LRR 113898-CA9-2 covers the publication period of 1 July 2020 to 31 December 2020.

b) Additional duplicates occurred due to different update frequencies within each database and entries of publications ahead of print.

c) Please refer to the Literature Review Report (LRR) 108689-CA9-1, 113898-CA9-1, and 113898-CA9-2.

are provided in Table 6 - Table 15.

2.2 Input parameters used in the literature search

# The basic input parameters used in the literature search, e.g. IUPAC, chemical name or CAS number,

### Table 6: Input parameters – active substance Glyphosate

Substance name	Glyphosate
	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

### **Table 7: Input parameters – metabolite AMPA**

Substance name	AMPA
IUPAC / CA name	(aminomethyl)phosphonic acid
CAS number(s)	1066-51-9

### Table 8: Input parameters – metabolite N-acetyl glyphosate

Substance name	N-acetyl glyphosate
IUPAC / CA name	N-acetyl-N-(phosphonomethyl)glycine
CAS number(s)	129660-96-4

### Table 9: Input parameters - metabolite N-acetyl AMPA

Substance name	N-acetyl AMPA
IUPAC / CA name	[(acetylamino)methyl]phosphonic acid
CAS number(s)	57637-97-5

### Table 10: Input parameters - metabolite HMPA

Substance name	HMPA	
IUPAC / CA name	(hydroxymethyl)phosphonic acid	
CAS number(s)	2617-47-2	

### Table 11: Input parameters - metabolite N-methyl AMPA

Substance name	N-methyl AMPA	
IUPAC / CA name	[(methylamino)methyl]phosphonic acid	
CAS number(s)	35404-71-8	

## Table 12: Input parameters – metabolite N-glyceryl AMPA

Substance name	N-glyceryl AMPA	
IUPAC / CA name	(2,3-dihydroxypropanoylamino)methylphosphonic acid	
CAS number(s)	No data	

### Table 13: Input parameters – metabolite N-malonyl AMPA

Substance name	N-malonyl AMPA	
IUPAC / CA name	3-oxo-3-(phosphonomethylamino)propanoic acid	
CAS number(s)	no data	

# Table 14: Input parameters – metabolite methylphosphonic acid

Substance name	methylphosphonic acid	
IUPAC / CA name	methylphosphonic acid	
CAS number(s)	993-13-5	

### Table 15: Input parameters – metabolite N-methylglyphosate

Substance name	N-methylglyphosate	
IUPAC / CA name	2-[methyl(phosphonomethyl)amino]acetic acid	
CAS number(s)	24569-83-3	

### 2.3 Keywords and search filters used in the literature search

The approach used for the search was the "focused search for grouped data requirements" which combines the active substance and metabolite basic input parameters, keywords and search filters defined for each technical section. Please refer to **Table 16** for more details on the keywords used and to **Table 17** - **Table 20** for the search filters.

Table 16: Keywords used for the active substance glyphosate and its metabolites

Gly1: Glyphosate and AMPA	glyphosat? OR glifosat? OR glyfosat? 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 OR aminomethyl phosphonic OR aminomethylphosphonic OR 1066-51-9	
Gly2: N-acetyl glyphosate and N-acetyl AMPA	2 acetyl phosphonomethyl amino acetic acid OR n acetyl glyphosate OR n acetylglyphosate OR n acetyl n phosphonomethyl glycine OR 129660-96-4 OR n acetyl ampa OR acetylamino methyl phosphonic acid OR acetylaminomethyl phosphonic acid OR 57637-97-5	
Gly 3: HMPA	2617-47-2 OR hydroxymethanephosphonic acid OR hydroxymethyl phosphonate OR hydroxymethylphosphonate OR hydroxymethyl phosphonic acid OR hydroxymethylphosphonic acid OR methanehydroxyphosphonic acid OR phosphonic acid(1w)hydroxymethyl OR phosphonomethanol	
Gly 4: N-methyl AMPA	35404-71-8 OR methylamino methyl phosphonic acid OR methylaminomethyl phosphonic acid OR methylaminomethylphosphonic acid OR n methyl ampa OR nsc 244826 OR phosphonic acid methylamino methyl OR phosphonic acid p methylamino methyl	
Gly 4: N-glyceryl AMPA	2 3 dihydroxy 1 oxopropyl aminomethyl phosphonic acid OR 2 3 dihydroxy 1 oxopropyl aminomethylphosphonic acid OR n glyceryl ampa	
Gly 4: N-malonyl AMPA	3 oxo 3 phosphonomethyl amino propanoic acid OR 3 oxo 3 phosphonomethyl aminopropanoic acid OR n malonyl ampa	
Gly 4: methylphosphonic acid	993-13-5 OR dihydrogen methylphosphonate OR methanephosphonic acid OR methyl phosphonic acid OR methylphosphonic acid OR nsc 119358 OR phosphonic acid methyl OR phosphonic acid p methyl	
Gly 5: N-methylglyphosate (NMG)	24569-83-3 OR 2 methyl phosphonomethyl amino acetic acid OR 2 methyl phosphonomethyl aminoacetic acid OR acetic acid 2 n methyl n phosphonatomethyl amino OR glycine n methyl n phosphonomethyl OR glyphosate n methyl OR methyl glyphosate OR methyl phosphonomethyl amino acetic acid OR methyl phosphonomethyl aminoacetic acid OR n methyl n phosphonomethyl glycine OR n methylglyphosate OR n phosphonomethyl n methylglycine OR n phosphonomethyl n methylglycine	

(1w) = proximity operator (this order, up to 1 word between) AND / OR / NOT = boolean search operators

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<sup>? =</sup> any character(s)

<sup>&</sup>lt;sup>10</sup> Citation from the EFSA 2092 GD: *If the number of summary records returned by a single concept search\* is extremely large, focused searches for individual or grouped data requirements could be developed. Such searches could combine synonyms for the active substance (one concept) with terms and synonyms for characteristics of the data requirement (second concept).* 

<sup>\*</sup>NOTE: Single concept search (as defined in the EFSA 2092 GD document) = using the active substance names and its synonyms.

#### Table 17: Search filters related to the technical section toxicology

#### **Toxicology**

[Gly1] OR [Gly2] OR [Gly3] OR [Gly4] OR [Gly5] AND the following search filters

tox? OR hazard? OR adverse OR health OR NOAEL OR NOEL OR LOAEL OR LOEL OR BMD? OR in vivo OR in vitro OR invivo OR invitro OR mode of action OR skin? OR eye? OR irrit? OR sensi? OR allerg? OR rat OR rats OR dog? OR rabbit? OR guinea pig? OR mouse OR mice OR metabolism OR metabolite? OR metabolic OR distribution OR adsorption OR excretion OR elimination OR kinetic OR cytochrome OR enzym? OR gen? OR muta? OR chromos? OR clastogen? OR DNA OR carcino? OR cancer? OR tumor? OR tumour? OR oncog? OR oncol? OR malign? OR immun? OR neur? OR endocrin? OR hormon? OR gonad? OR disrupt? OR reproduct? OR development? OR malform? OR anomal? OR fertil? OR foet? OR fet? OR matern? OR pregnan? OR embryo? OR epidem? OR medical? OR poison? OR exposure OR operator? OR bystander? OR resident? OR worker? OR occupat? biomonitoring OR human exposure OR microbiome OR oxidative stress OR apoptosis OR necrosis OR cytotoxicity OR Polyoxyethyleneamine OR POEA OR surfactant OR risk assessment?

#### Table 18: Search filters related to the technical section residues

#### Residues

[Gly1] OR [Gly2] OR [Gly3] OR [Gly4] OR [Gly5] AND the following search filters

uptake OR translocation OR rumen OR storage stability OR storage OR stability OR metabolic OR metabolism OR breakdown OR nature of residues OR residue? OR magnitude of residues OR process? OR effects of processing OR dessicant OR preharvest OR preemerg? OR ?resistant? OR ?toleran? OR transgenic OR hydroly? OR rotation? OR succeed? OR plant? OR crop? OR feed? OR animal? OR livestock? OR hen OR cattle OR ruminant? OR goat? OR cow? OR pig? OR dietary OR assessment OR risk assessment OR consum? OR exposure

Table 19: Search filters related to the technical section environmental fate

#### **Environmental fate**

[Gly1] OR [Gly2] OR [Gly3] OR [Gly4] OR [Gly5] AND the following search filters

soil OR water OR sediment OR degradat? OR photo? OR soil residues OR soil accumulat? OR soil contaminat? OR mobility OR sorption OR column leaching OR aged residue OR leach? OR lysimeter OR groundwater OR contaminat? OR microb? OR exudation OR rhizosphere OR dissipation OR saturated zone OR hydrolysis OR drift OR run-off OR runoff OR drainage OR volat? OR atmosphere OR long-range transport OR short-range transport OR transport OR micronutrient OR phosphate OR iron OR manganese OR half-life OR half-lives OR half-lives OR DT50 OR kinetics OR off-site movement OR removal OR drinking water OR water treatment processes OR atmospheric deposition OR tile-drains OR surface water OR monitoring data OR disinfectant OR ozone OR tillage OR infiltration OR hard surface OR rainwater OR rain water OR chelat? OR complex? OR mineralization OR persistence OR ligand

Table 20: Search filters related to the technical section ecotoxicology

#### **Ecotoxicology**

[Gly1] OR [Gly2] OR [Gly3] OR [Gly4] OR [Gly5] AND the following search filters

tox? OR ecotox? OR ?toxic OR ?toxicity OR hazard OR adverse OR endocrine disrupt? OR bioaccumulate? OR biomagnifi? OR bioconcentration OR poison OR effect OR indirect effect? OR direct effect? OR biodivers? OR protection goals OR eco? OR impact OR population OR community OR wildlife OR incident OR wildlife OR incident OR pest OR bird? OR acute OR chronic OR longterm OR mallard OR duck OR quail OR bobwhite OR Anas? OR Colinus? OR wild OR dietary OR aquatic OR fish OR daphni? OR alg? OR chiron? OR sediment dwell? OR benthic OR lemna OR marin? OR estuarine OR crusta? OR gastropod? OR insect OR mollusc OR reptile OR amphib? OR plant AND submerge? OR emerge? OR bee? OR apis OR apidae OR bumble? OR colony OR hive OR pollinator OR solitary OR alg? OR aquatic OR freshwater OR vertebrat? OR mammal? OR rat OR mouse OR mice OR rabbit OR hare OR protection OR model? OR vole OR pest OR arthropod? OR beneficials OR typhlodromus OR aphidius OR parasitoid OR predator OR chrysoperla OR Orius OR spider OR worm? OR ?worm OR Eisenia OR soil OR collembol? OR macro organism OR folsomia OR springtail OR decompos? OR micro organisms OR microorganisms OR microbial OR carbon OR nitrogen OR plant? OR vegetative vigo? OR seedling OR germination OR monocot? OR dicot? OR sewage OR activated sludge OR biodegrad? OR bioaccumulation? OR amphib? OR reptile? OR aquatic plant OR beneficial

### 2.4 Relevance assessment

After removal of duplicates, the remaining articles were assessed for their relevance. First, at "title / abstract level" (so-called "rapid assessment") and second, at "full-text level" (so called "detailed assessment").

Articles that were identified as "non-relevant" in the rapid assessment were excluded from further evaluation and a justification for their non-relevance was provided.

For articles that were not excluded in the rapid assessment (potentially relevant articles and articles of an unclear relevance) a detailed relevance assessment of a full-text document was performed.

Articles that were identified as "non-relevant" in the detailed assessment were excluded from further evaluation and a justification for their non-relevance was provided.

For both assessments (rapid and detailed) the same criteria for non-relevance were applied (see **Chapter 2.4.1** and **2.4.2**).

#### 2.4.1 Criteria applied for "non-relevance"

Articles identified as "non-relevant" in the rapid and detailed assessments belong to one of the following categories and were excluded from further evaluation. A justification for their non-relevance was provided.

- Publications related to efficacy (resistance related articles, new uses of control of pest / crops) or to agricultural / biological research (crop science, breeding, fertilization, tillage, fundamental plant physiology / micro- / molecular biology).
- Publications dealing with analytical methods / development.
- Publications describing new methods of synthesis (discovery / developments) or other aspects of basic (organic / inorganic) chemistry.
- Patents.
- Wastewater treatment.
- Abstracts referring to a conference contribution that does not contain sufficient data / information for regulatory risk assessment.
- Publications focusing on genetically modified organisms / transgenic crops; no data directly relevant to glyphosate evaluation (e.g. crop compositional analysis, gene flow, protein characterization).
- Publications where glyphosate or a relevant metabolite were not the focus of the publication.
- Secondary information including scientific and regulatory reviews<sup>11</sup>.
- Articles dealing with political / socio / economic analysis.
- Observations caused by mixture of compounds / potentially causal factors and thus not attributable to a substance of concern (e.g. mixture toxicity).
- Study design, test system, species tested, exposure routes etc. that are not relevant for the European regulatory purposes.
- Findings not related to ecotoxicology, toxicology, residues, and environmental fate.
- Publications not dealing with EU representative uses / conditions (e.g. field locations, soil properties, non-EU monitoring etc.).

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<sup>&</sup>lt;sup>11</sup> Reviews have been partly evaluated on full text level as well – case by case decision.

• Publications dealing with a Roundup<sup>12</sup> formulation / other glyphosate formulations that is <u>not</u> the representative formulation for the AIR5 dossier and thus not relevant to the EU glyphosate renewal.

Glyphosate and metabolites - Literature Review Report

- Publications dealing with general pesticide exposures (not glyphosate specific).
- Publications generating endpoints that are not relatable to the EU level regulatory risk assessment (e.g. findings based on enzyme, cellular and molecular level etc.).
- Opinion articles where no new data is provided that can be used for the EU regulatory risk assessment.

#### 2.4.2 Additional criteria for articles on the health and exposure of glyphosate

The scientific literature on the health effects of glyphosate can be subdivided in two main parts:

- Articles containing data on glyphosate acid and salts and on the reference glyphosate formulation MON 52276, and
- Articles only containing data on glyphosate formulations and/or co-formulants that have a composition different from that of the reference formulation MON 52276.

In the case of articles only relating to glyphosate formulations *in vitro* testing with the exception of cell/tissue systems <sup>13</sup> that are likely to come in direct contact with formulations and glyphosate formulations containing other active ingredients are excluded. The reason for the exclusion of *in vitro* testing of formulations to assess health effects as a result of systemic exposure is the presence of surfactants which produce cell toxicity based on the destabilization of the cell membrane and the mitochondrial membrane thus masking the specific toxicity of glyphosate. The toxicity of the coformulants in combination with glyphosate is dependent on the concentration and the nature of the coformulants and can be addressed on a case-by-case basis during the evaluation of formulations on an adhoc basis through Zonal and Member State formulation registrations.

In the relevance of glyphosate data, those articles have been considered as not relevant (and reliable) for the assessment for systemic toxicity when only *in vitro* results are presented with glyphosate concentrations above 1 mM. This is because it is physiologically not possible to attain such concentrations in standard regulatory *in vivo* testing due to the limited oral bioavailability (approx. 20%), very low dermal absorption, and rapid systemic elimination of glyphosate in *in vivo* test systems. It thus makes no sense to include such data in the risk assessment of glyphosate. Exceptions can be made in the event of direct contact with formulations resulting in localized effects, but then there is the contribution of the toxicity of the co-formulants which can be better addressed in the evaluation of formulations on an ad-hoc basis through Zonal and Member State formulation registrations.

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<sup>&</sup>lt;sup>12</sup> Roundup is a brand that contains multiple glyphosate-based herbicides, that contain different co-formulants. Of most importance to the toxicity profile associated with a particular product is whether that product contains a surfactant polyethoxylated tallow amine (also polyoxyethyleneamine, POEA) which is not permitted for use in the EU. As the performance / efficacy of herbicidal formulations is dependant on the surfactant system / co-formulants, the findings in articles dealing with POEA based Roundup formulations cannot be related to the representative formulation MON 52276 which is quaternary-ammonium based (and not POEA based).

<sup>&</sup>lt;sup>13</sup> Glyphosate-based herbicides (GBH) contain surfactants that destabilize the cell membrane and the mitochondrial membrane and thus produce a toxicity that is not representative for glyphosate (see Levine S. L. et al, *Cell Biol. Toxicol. (2007) 23:385-400*). This has been clearly demonstrated in the scientific literature and also in some papers reviewed for this submission where *in vitro* glyphosate toxicity is compared against that of GBH and surfactants.

The limit of 1 mM has been based on the single dose oral pharmacokinetic data of a formulation containing 71.7% w/w glyphosate where an oral dose of 1,430 mg/kg bw in the rat gives plasma levels of 38.1  $\mu$ g/mL or 0.225 mM after 2 hours. When extrapolated linearly (which is possible for glyphosate because it is not subject to hepatic metabolism) this gives plasma levels of 53.3  $\mu$ g/mL or 0.315 mM at 2 hours after oral intake of 2,000 mg/kg bw and 107  $\mu$ g/mL or 0.630 mM at 2 hours after oral intake of 4,000 mg/kg bw. A systemic concentration of glyphosate of 1 mM would then represent an oral dose of more than 6,000 mg/kg bw which is completely unreasonable for repeat dose experimental *in vivo* testing under today's OECD test guidelines. The ADI for glyphosate of 0.5 mg/kg bw/day corresponds with a daily systemic concentration of 0.17  $\mu$ g/mL or 1  $\mu$ M when a 60 kg person with 36 L extracellular fluid is considered with a glyphosate oral bioavailability of 20%. The daily systemic dose of glyphosate on the day of application (i.e. highest exposure day), based on the geometric mean of 3.2  $\mu$ g/L in urine, of glyphosate applicators in the US is approx. 0.0001 mg/kg bw/day (Acquavella, 2004<sup>14</sup>) which is 1000 times less than the systemic dose (0.1 mg/kg bw) corresponding with the ADI oral dose of 0.5 mg/kg bw with 20% oral bioavailability.

Many articles that have been considered relevant for the risk assessment of glyphosate and have been assessed for reliability on full text basis, contain experimental data as well on glyphosate as such as on formulations (different from MON 52276) and co-formulants. In such cases, only the toxicology data pertinent to glyphosate and to the reference formulation (if that can be clearly stated by the author of the article) are summarized and discussed. In the case of articles on exposure monitoring and epidemiology, exposure to glyphosate formulations are considered.

### 2.4.3 Categorization of "relevant" articles at full-text level

Articles that were not excluded in the detailed assessment (see Chapter 2.4.1 and 2.4.2) were categorized as recommended in the EFSA 2092 GD - EFSA Journal 2011;9(2):2092, Point 5.4.1.

- Category A Studies that provide data for establishing or refining risk assessment parameters. These studies should be summarised in detail following the subsequent steps of the OECD Guidance documents (OECD, 2005; 2006) and should be considered for reliability.
- Category B Studies that are relevant to the data requirement, but in the opinion of the applicant provide only supplementary information that does not alter existing risk assessment parameters. A justification for such a decision should be provided.
- Category C Studies for which relevance cannot be clearly determined. For each of these studies the applicants should provide an explanation of why the relevance of such studies could not be definitively determined.

The list of Category A articles can be found in **Table 32** and **Table 33**. The list of Category B articles and the justifications can be found in **Table 34** and **Table 35**. The list of Category C articles and the explanations can be found in **Table 36** and **Table 37**.

All articles (and their translations) evaluated at full text level (detailed assessment) were submitted to the AGG in a Portable Document Format (PDF).

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<sup>&</sup>lt;sup>14</sup> Acquavella J. F. et al. (2004), Environmental Health Perspectives, 112(3), 321-326.

# 2.5 Reliability assessment

For articles, which were identified, in the detailed assessment, as relevant articles of Category A (see **Chapter 2.4.3**) a reliability assessment was performed. The reliability criteria for each technical section are summarized in **Table 21** - **Table 23**.

For relevant articles of Category A that were classified either as reliable (without restrictions) or reliable with restrictions, summaries were compiled.

Articles of Category A which were classified as non-reliable were downgraded to articles of Category B and justification for such a decision was provided.

Table 21: Reliability criteria for ecotoxicology, environmental fate and residues

Applied for	Reliability criteria
Ecotoxicology, Environmental Fate, Residues	For guideline-compliant studies (GLP studies): OECD, OPPTS, ISO, and others. The validity/quality criteria listed in the corresponding guidelines are met.
Ecotoxicology, Environmental Fate, Residues	(No) previous exposure to other chemicals is documented (where relevant).
Ecotoxicology	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.
Environmental Fate, Residues	The test substance is dissolved in water or non-toxic solvent.
Ecotoxicology, Environmental Fate, Residues	Test item is sufficiently documented, and reported (i.e. purity, source, content, storage conditions).
Ecotoxicology	For tests including vertebrates, compliance of the batches used in toxicity studies compared to the technical specification.
Ecotoxicology	Species used in the experiment are 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.
Ecotoxicology	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.
Ecotoxicology, Environmental Fate, Residues	Only glyphosate or its metabolites is the test substance (excluding mixture), and information on application of the test substance is described.
Ecotoxicology, Environmental Fate, Residues	The endpoint measured can be considered a consequence of glyphosate (or a glyphosate metabolite).
Ecotoxicology, Environmental Fate, Residues	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.
Ecotoxicology, Environmental Fate, Residues	Analytical verifications performed in test media (concentration) / collected samples, stability of the test substance in test medium should be documented.

Applied for	Reliability criteria	
Ecotoxicology	The test has been performed in several dose levels (at least 3) including a positive / negative control where relevant.	
Ecotoxicology	Suitable exposure throughout the whole exposure period was demonstrated and reported.	
Ecotoxicology	A clear concentration response relationship is reported – in studies where the dose response test design is employed.	
Ecotoxicology	A sufficient number of animals per group to facilitate statistical analysis reported: mortality in control groups reported, observations/findings in positive/negative control clearly reported (where relevant).	
Ecotoxicology, Environmental Fate, Residues	Assessment of the statistical power of the assay is possible with reported data.	
Ecotoxicology, Environmental Fate, Residues	Statistical methodology is reported (e.g., checking the plots and confidence intervals).	
Ecotoxicology	Description of the observations (including time-points), examinations, and analyses performed, with (where relevant) dissections being well documented.	
Ecotoxicology	For terrestrial ecotoxicological 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.	
Ecotoxicology, Environmental Fate, Residues	Field locations relevant / comparable to European conditions.	
Ecotoxicology, Environmental Fate, Residues	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).	
Ecotoxicology, Environmental Fate	Other soils where information on characterization by the parameters: pH, texture, CEC, organic carbon, bulk density, water holding capacity, microbial biomass.	
Ecotoxicology, Environmental Fate, Residues	For tests including agricultural soils, they should not have been treated with test substance or similar substances for a minimum of 1 year.	
Ecotoxicology, Environmental Fate	For soil samples, sampling from A-horizon, top 20 cm layers; soils freshly from field preferred (storage max 3 months at 4 +/- 2°C).	
Ecotoxicology, Environmental Fate, Residues	Data on precipitation is recorded.	
Environmental Fate	The temperature was in the range between 20-25°C and the moisture was reported.	
Environmental Fate	The presence of glyphosate identified in samples were collected from European groundwater, soil, surface waters, sediments or air.	
Ecotoxicology	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.	
Ecotoxicology	For bee studies, temperature of the study should be appropriate to species.	
	For lab aquatic studies:	
Ecotoxicology	The source and / or composition of the media used should be described.	
67	The temperature of the water should be appropriate to the species being tested and generally fall within the 15-25°C.	

Applied for	Reliability criteria
Ecotoxicology, Residues	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).
Ecotoxicology, Environmental Fate, Residues	Analytical results present residues measurements which can be correlated with the existing residues definition of glyphosate, and where relevant its metabolites.
Ecotoxicology, Environmental Fate, Residues	Analytical methods are clearly described; and adequate statement of specificity and sensitivity of the analytical methods is included.
Ecotoxicology	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 is reported.
Environmental Fate	Radiolabel characterization: purity, specific activity, location of label is reported.
Environmental Fate	If degradation kinetics are included: data tables / model description / statistical parameters for kinetic fit to be provided.
Environmental Fate, Residues	Monitoring data: description of matrix analysed, and analytical methods to be fully described.
Environmental Fate	Clear description of application rate and relevance to approved uses.

**Overall assessment:** Reliable / Reliable with restrictions / Not reliable

Table 22: Reliability criteria for toxicology – epidemiology and exposure studies

Reliability criteria – toxicology		
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 / Not reliable

Table 23: Reliability criteria for toxicology – <u>in vitro</u> and <u>in vivo</u> studies

Reliability criteria – toxicology and metabolism		
<i>In vitro</i> studies	<i>In vivo</i> 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 or other glyphosate metabolite is the tested substance.	AMPA or other glyphosate metabolite 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 (< 1 mM).	Dose levels reported.	
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 restriction	ns / Not valiable	

Overall assessment: Reliable / Reliable with restrictions / Not reliable

#### 3 Search results

The full outcome of the literature search and evaluation is provided below.

Table 24: Summary of the literature search – all technical sections

	Number	Justification
Total number of articles retrieved from the search.	2643	n.a.
Total number of articles after removal of duplicates within all databases.	1522	n.a.
Total number of articles after manual removal of duplicates. a)	597	n.a.
Number of articles excluded after rapid assessment (title / abstract).	523	See the Literature Review Excel File.
Total number of full-text documents assessed in detail.	74	n.a.
Number of articles excluded after detailed assessment ( <i>i.e.</i> not relevant).	28	See Table 38
Number of articles not excluded after detailed assessment. b)	46	See Table 32-Table 37
Number of summaries presented in the dossier. c)	10	See Table 32, Table 33

a) After removal of duplicates within the current search (Jan 2021 – 14 May 2021) and entries found already in the previous searches (Jan 2010 – Dec 2020). Additional duplicates occurred due to different update frequencies within each database and entries of publications ahead of print.

Table 25: Results of the article selection process for ecotoxicology

	Number	Justification
Total number of articles after manual removal of duplicates. a)	93	n.a.
Number of articles excluded after rapid assessment (title / abstract).	61	See the Literature Review Excel File.
Total number of full-text documents assessed in detail.	32	n.a.
Number of articles excluded after detailed assessment ( <i>i.e.</i> not relevant).	19	See Table 38
Number of articles not excluded after detailed assessment. b)	13	See Table 32-Table 37
Number of summaries presented in the dossier. c)	3	See Table 32, Table 33

a) After removal of duplicates within the current search (Jan 2021 – 14 May 2021) and entries found already in the previous searches (Jan 2010 – Dec 2020). Additional duplicates occurred due to different update frequencies within each database and entries of publications ahead of print.

b) All relevant articles by full-text belonging to the relevance Category A, B, C (acc. to the EFSA Journal 2011;9(2):2092, Point 5.4.1). For details, please refer to Chapter 2.4.3.

c) Summaries were compiled for relevant articles of Category A and classified either as reliable or reliable with restrictions.

b) All relevant articles by full-text belonging to the relevance Category A, B, C (acc. to the EFSA Journal 2011;9(2):2092, Point 5.4.1). For details, please refer to Chapter 2.4.3.

c) Summaries were compiled for relevant articles of Category A and classified either as reliable or reliable with restrictions.

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Table 26: Results of the article selection process for environmental fate

	Number	Justification
Total number of articles after manual removal of duplicates. a)	79	n.a.
Number of articles excluded after rapid assessment (title / abstract).	74	See the Literature Review Excel File.
Total number of full-text documents assessed in detail.	5	n.a.
Number of articles excluded after detailed assessment ( <i>i.e.</i> not relevant).	1	See Table 38
Number of articles not excluded after detailed assessment. b)	4	See Table 32-Table 37
Number of summaries presented in the dossier. c)	3	See Table 32, Table 33

a) After removal of duplicates within the current search (Jan 2021 – 14 May 2021) and entries found already in the previous searches (Jan 2010 – Dec 2020). Additional duplicates occurred due to different update frequencies within each database and entries of publications ahead of print.

Table 27: Results of the article selection process for residues

	Number	Justification
Total number of articles after manual removal of duplicates. a)	18	n.a.
Number of articles excluded after rapid assessment (title / abstract).	10	See the Literature Review Excel File.
Total number of full-text documents assessed in detail.	8	n.a.
Number of articles excluded after detailed assessment (i.e. not relevant).	3	See Table 38
Number of articles not excluded after detailed assessment b)	5	See Table 32-Table 37
Number of summaries presented in the dossier c)	0	See Table 32, Table 33

a) After removal of duplicates within the current search (Jan 2021 – 14 May 2021) and entries found already in the previous searches (Jan 2010 – Dec 2020). Additional duplicates occurred due to different update frequencies within each database and entries of publications ahead of print.

b) All relevant articles by full-text belonging to the relevance Category A, B, C (acc. to the EFSA Journal 2011;9(2):2092, Point 5.4.1). For details, please refer to Chapter 2.4.3.

c) Summaries were compiled for relevant articles of Category A and classified either as reliable or reliable with restrictions.

b) All relevant articles by full-text belonging to the relevance Category A, B, C (acc. to the EFSA Journal 2011;9(2):2092, Point 5.4.1). For details, please refer to Chapter 2.4.3.

c) Summaries were compiled for relevant articles of Category A and classified either as reliable or reliable with restrictions.

Table 28: Results of the article selection process for toxicology

	Number	Justification
Total number of articles after manual removal of duplicates a)	76	n.a.
Number of articles excluded after rapid assessment (title / abstract).	47	See the Literature Review Excel File.
Total number of full-text documents assessed in detail	29	n.a.
Number of articles excluded after detailed assessment ( <i>i.e.</i> not relevant).	5	See Table 38
Number of articles not excluded after detailed assessment b)	24	See Table 32-Table 37
Number of summaries presented in the dossier c)	4	See Table 32, Table 33

a) After removal of duplicates within the current search (Jan 2021 – 14 May 2021) and entries found already in the previous searches (Jan 2010 – Dec 2020). Additional duplicates occurred due to different update frequencies within each database and entries of publications ahead of print.

Table 29: Results of the article selection process for analytical methods

	Number	Justification
Total number of articles after manual removal of duplicates a)	29	n.a.
Number of articles excluded after rapid assessment (title / abstract).	29	See the Literature Review Excel File.
Total number of full-text documents assessed in detail.	n.a.	n.a.
Number of articles excluded after detailed assessment ( <i>i.e.</i> not relevant).	n.a.	n.a.
Number of articles not excluded after detailed assessment b)	n.a.	n.a.
Number of summaries presented in the dossier c)	n.a.	n.a.

a) After removal of duplicates within the current search (Jan 2021 – 14 May 2021) and entries found already in the previous searches (Jan 2010 – Dec 2020). Additional duplicates occurred due to different update frequencies within each database and entries of publications ahead of print.

Table 30: Results of the article selection process for efficacy / agronomy

	Number	Justification
Total number of articles after manual removal of duplicates. a)	248	n.a.
Number of articles excluded after rapid assessment (title / abstract).	248	See the Literature Review Excel File.
Total number of full-text documents assessed in detail.	n.a.	n.a.
Number of articles excluded after detailed assessment ( <i>i.e.</i> not relevant).	n.a.	n.a.
Number of articles not excluded after detailed assessment. b)	n.a.	n.a.
Number of summaries presented in the dossier. c)	n.a.	n.a.

<sup>&</sup>lt;sup>a)</sup> After removal of duplicates within the current search (Jan 2021 – 14 May 2021) and entries found already in the previous searches (Jan 2010 – Dec 2020). Additional duplicates occurred due to different update frequencies within each database and entries of publications ahead of print.

b) All relevant articles by full-text belonging to the relevance Category A, B, C (acc. to the EFSA Journal 2011;9(2):2092, Point 5.4.1). For details, please refer to Chapter 2.4.3.

c) Summaries were compiled for relevant articles of Category A and classified either as reliable or reliable with restrictions.

b) All relevant articles by full-text belonging to the relevance Category A, B, C (acc. to the EFSA Journal 2011;9(2):2092, Point 5.4.1). For details, please refer to Chapter 2.4.3.

c) Summaries were compiled for relevant articles of Category A and classified either as reliable or reliable with restrictions.

b) All relevant articles by full-text belonging to the relevance Category A, B, C (acc. to the EFSA Journal 2011;9(2):2092, Point 5.4.1). For details, please refer to Chapter 2.4.3.

c) Summaries were compiled for relevant articles of Category A and classified either as reliable or reliable with restrictions.

Table 31: Results of the article selection process for "other non-relevant categories"

	Number	Justification
Total number of articles after manual removal of duplicates. a)	54	n.a.
Number of articles excluded after rapid assessment (title / abstract).	54	See the Literature Review Excel File.
Total number of full-text documents assessed in detail.	n.a.	n.a.
Number of articles excluded after detailed assessment ( <i>i.e.</i> not relevant).	n.a.	n.a.
Number of articles not excluded after detailed assessment. b)	n.a.	n.a.
Number of summaries presented in the dossier. c)	n.a.	n.a.

<sup>&</sup>lt;sup>a)</sup> After removal of duplicates within the current search (Jan 2021 – 14 May 2021) and entries found already in the previous searches (Jan 2010 – Dec 2020). Additional duplicates occurred due to different update frequencies within each database and entries of publications ahead of print.

b) All relevant articles by full-text belonging to the relevance Category A, B, C (acc. to the EFSA Journal 2011;9(2):2092, Point 5.4.1). For details, please refer to Chapter 2.4.3.

c) Summaries were compiled for relevant articles of Category A and classified either as reliable or reliable with restrictions.

Table 32: Relevant (category A) articles after detailed assessment: sorted by data requirement(s)

Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
1	CA 5.6	Gorga A. et al.	2021	Low Doses of Glyphosate/Roundup Alter Blood-Testis Barrier Integrity in Juvenile Rats.	Frontiers in endocrinology, (2021), Vol. 12, Article No. 615678	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
2	CA 5.6	Refaie A. A. et al.	2020	Hematological, biochemical, antioxidant and histopathological alterations in kidneys of wistar rat pups exposed to glyphosate herbicide during lactation period.	Current Topics in Pharmacology, (2020), Vol. 24, pp. 69-76	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
3	CA 5.6	Zhao L. et al.	2021	Glyphosate exposure attenuates testosterone synthesis via NR1D1 inhibition of StAR expression in mouse Leydig cells.	The Science of the total environment, (2021), Vol. 785, Article No. 147323	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
4	CA 5.9	Ferreira C. et al.	2021	Urine biomonitoring of glyphosate in children: Exposure and risk assessment.	Environmental research, (2021), Vol. 198, Article No. 111294	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
5	CA 7.3.1	Holtomo O. et al.	2021	Insight of UV-vis spectra and atmospheric implication for the reaction of OH radical towards glyphosate herbicide and its hydrates	RSC Advances (2021), Vol. 11, No. 27, pp. 16404-16418	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
6	CA 7.5	Geissen V. et al.	2021	Cocktails of pesticide residues in conventional and organic farming systems in Europe - Legacy of the past and turning point for the future.	Environmental pollution, (2021), Vol. 278, Article No. 116827	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
7	CA 7.5	Piel S. et al.	2021	Understanding the origins of herbicides metabolites in an agricultural watershed through their spatial and seasonal variations.	Journal of environmental science and health. Part. B, Pesticides, food contaminants, and agricultural wastes, (2021), Vol. 56, No. 4, pp. 313-332	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
8	CA 8.2.6.1, CA 8.2.7	Tajnaiova L. et al.	2020	Determination of the Ecotoxicity of Herbicides Roundup® Classic Pro and Garlon New in Aquatic and Terrestrial Environments	Plants (2020), Vol. 9, No. 9	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
9	CP 10.2.1	Gustinasari K. et al.	2021	Acute toxicity and morphology alterations of glyphosate-based herbicides to Daphnia magna and Cyclops vicinus.	Toxicological research, (2021), Vol. 37, No. 2, pp. 197-207	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
10	CP 10.3.1	Luo Q-H. et al.	2021	Effects of a commercially formulated glyphosate solutions at recommended concentrations on honeybee (Apis mellifera L.) behaviours.	Scientific reports, (2021), Vol. 11, No. 1, Article No. 2115	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.

Table 33: Relevant (category A) articles after detailed assessment: sorted by author(s)

Submission Number	Author(s)	Data requirement (indicated by the corresponding CA / CP data point number)	Year	Title	Source	Justification
4	Ferreira C. et al.	CA 5.9	2021	Urine biomonitoring of glyphosate in children: Exposure and risk assessment.	Environmental research, (2021), Vol. 198, Article No. 111294	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
6	Geissen V. et al.	CA 7.5	2021	Cocktails of pesticide residues in conventional and organic farming systems in Europe - Legacy of the past and turning point for the future.	Environmental pollution, (2021), Vol. 278, Article No. 116827	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
1	Gorga A. et al.	CA 5.6	2021	Low Doses of Glyphosate/Roundup Alter Blood-Testis Barrier Integrity in Juvenile Rats.	Frontiers in endocrinology, (2021), Vol. 12, Article No. 615678	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
9	Gustinasari K. et al.	CP 10.2.1	2021	Acute toxicity and morphology alterations of glyphosate-based herbicides to Daphnia magna and Cyclops vicinus.	Toxicological research, (2021), Vol. 37, No. 2, pp. 197-207	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
5	Holtomo O. et al.	CA 7.3.1	2021	Insight of UV-vis spectra and atmospheric implication for the reaction of OH radical towards glyphosate herbicide and its hydrates	RSC Advances (2021), Vol. 11, No. 27, pp. 16404-16418	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
10	Luo Q-H. et al.	CP 10.3.1	2021	Effects of a commercially formulated glyphosate solutions at recommended concentrations on honeybee (Apis mellifera L.) behaviours.	Scientific reports, (2021), Vol. 11, No. 1, Article No. 2115	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
7	Piel S. et al.	CA 7.5	2021	Understanding the origins of herbicides metabolites in an agricultural watershed through their spatial and seasonal variations.	Journal of environmental science and health. Part. B, Pesticides, food contaminants, and agricultural wastes, (2021), Vol. 56, No. 4, pp. 313-332	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
2	Refaie A. A. et al.	CA 5.6	2020	Hematological, biochemical, antioxidant and histopathological alterations in kidneys of wistar rat pups exposed to glyphosate herbicide during lactation period.	Current Topics in Pharmacology, (2020), Vol. 24, pp. 69-76	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
8	Tajnaiova L. et al.	CA 8.2.6.1, CA 8.2.7	2020	Determination of the Ecotoxicity of Herbicides Roundup® Classic Pro and Garlon New in Aquatic and Terrestrial Environments	Plants (2020), Vol. 9, No. 9	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.
3	Zhao L. et al.	CA 5.6	2021	Glyphosate exposure attenuates testosterone synthesis via NR1D1 inhibition of StAR expression in mouse Leydig cells.	The Science of the total environment, (2021), Vol. 785, Article No. 147323	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.

Table 34: Relevant but supplementary (category B) articles after detailed assessment: sorted by data requirement(s)

Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
11	CA 5.4	Celik D. A. et al.	2021	DNA damages of widely used pesticides; a comet assay report for chlorothalonil and glyphosate potassium salt.	Fresenius Environmental Bulletin, (2021), Vol. 30, No. 4 A, pp. 4170-4176	The article has been classified as relevant by full text - Category B and <b>not reliable</b> for the following reason: The article provides supplementary information on genotoxicity of glyphosate potassium salt demonstrating DNA damage in a comet assay. However, the DNA damage at the mid and high dose is significantly lower than observed at the low dose. No details on the donors, no cytotoxicity assay, no metabolic activation system, no mention of other parameters evaluated in the Comet Assay (ie: hedgehogs, tail length, or tail moment). Only %tail DNA was measured. Furthermore, no positive control and no HCD provided.
12	CA 5.4	Congur G.	2021	Monitoring of glyphosate-DNA interaction and synergistic genotoxic effect of glyphosate and 2,4-dichlorophenoxyacetic acid using an electrochemical biosensor.	Environmental pollution, (2021), Vol. 271, Article No. 116360	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: The article provides a new in vitro method using electrochemical biosensor to monitor DNA interaction of glyphosate and demonstrates a negative effect onto double stranded DNA. The article is relevant but supplementary for the glyphosate a.s. treatment, however not relevant for the glyphosate formulation tested as it contains ether amine ethoxylate (similar to POEA). No dose-effect relationship, no positive control, no HCD. No statistical method presented. The purity of purchased glyphosate was also not provided.
13	CA 5.4	Wozniak E. et al.	2021	Glyphosate and AMPA Induce Alterations in Expression of Genes Involved in Chromatin Architecture in Human Peripheral Blood Mononuclear Cells (In Vitro).	International journal of molecular sciences, (2021), Vol. 22, No. 6	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: The article provides new information on the effect of glyphosate and the metabolite AMPA on expression of genes involved in chromatin architecture in human peripheral blood mononuclear cells (PBMCs). The results provide useful information on epigenetic processes that may be relevant but are difficult to interpret without further guidance. Therefore, the results are not expected to alter the existing risk assessment No HCD, no positive control. No real dose-effect relationship reported. The lack of positive control does not allow assessing the laboratory proficiency.
14	CA 5.6	Mutwedu V. B. et al.	2021	Growth performance and reproductive function impairment of glyphosate-based herbicide in male guinea pig (Cavia porcellus).	Veterinary medicine and science, (2021): Ahead of Print	The article has been classified as relevant by full text - Category B and not reliable for the following reason: The article presents the effects of a glyphosate-based formulation on growth performance and reproductive function impairment in male guinea pigs, which is not the typical animal model of choice for this type of investigation. This study provides interesting information on reproductive functions but the guinea pig is not a model validated for assessing reproductive toxicity in the EU evaluations. Atypical animal model, so historical control data in this species at this lab is paramount to interpret results, and no positive controls to confirm method validity. Findings are confounded by overt general toxicity at high surfactant doses. No necropsy observations of likely gastrointestinal damage resulting from high oral surfactant exposures. No information on the feed, and no method of analysis.

Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
15	CA 5.6	Upadhyay J. et al.	2020	Teratogenic effect of chlorpyrifos and glyphosate on pregnant rats: biochemical and morphological evaluations.	Journal of Pharmaceutical Research International, (2020), Vol. 32, No. 23, Article No. JPRI.61413	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: The article provides information on teratogenic effects of glyphosate-based formulation Topper 77 (Crystal Crop Protection Pvt. Ltd India) which is nowhere close to the glyphosate representative EU formulation for AIR5. According to the webpage (https://www.crystalcropprotection.com/internationalsales/detail/Topper) it contains 71% of glyphosate and it is a SG-formulation. The representative glyphosate formulation for the AIR5 is a SL formulation and contains 360 g a.s./L. Due to formulation tested, the article is classified as relevant but supplementary. No information on purity, content and storage conditions of the test material. One dose level/no dose-effect relationship, no HCD reported.
16	CA 5.7	Luna S. et al.	2021	Glyphosate exposure induces synaptic impairment in hippocampal neurons and cognitive deficits in developing rats.	Archives of toxicology, (2021): Ahead of Print	The article has been classified as relevant by full text and downgraded to Category B due to its non-reliability.  In vitro test: Extremely high and irrelevant supraphysiological doses. No metabolic activation system and cytotoxicity assay. No HCD, no positive control.  In vivo test: No information on body weight and age of animals, no information on diet, no HCD. Route of administration was by s.c. injection in the neck. This route of administration is not relevant and does not represent the normal ADME processes with low absorption and rapid elimination.
17	CA 5.8	Fan X. et al.	2021	Identification of lncRNA expression profiles and analysis of ceRNA in the hippocampus of perinatal glyphosate-exposed mice.	International journal of developmental neuroscience: the official journal of the International Society for Developmental Neuroscience, (2021): Ahead of Print	The article has been classified as relevant by full text - Category B and <b>not</b> reliable for the following reason: The article analyses the role of long noncoding RNAs in the mechanisms of glyphosate neurotoxicity in neuronal development through a perinatal glyphosate exposure (PGE) mouse model. The results provide supplementary information on lncRNA and potential relationship with neurotoxicity. There is no information on the test material (purity, source, content). Test conditions are not clearly and completely described. Only one dose level was reported / no dose-response relationship. No "received dose calculation" possible without information on water consumption. Furthermore, no HCD reported.
18	CA 5.8	Mesnage R. et al.	2021	Urinary excretion of herbicide co-formulants after oral exposure to roundup MON 52276 in rats.	Environmental research, (2021), Vol. 197, Article No. 111103	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: Useful information about the urinary excretion of herbicide co-formulants after exposure to a glyphosate formulation in rats. It is only related to surfactant absorption/excretion which is then formulation specific. No toxicological effect. Housing and environmental conditions not described. No information on diet. No confirmation of received dose.
19	CA 5.8	Mesnage R. et al.	2021	Use of Shotgun Metagenomics and Metabolomics to Evaluate the Impact of Glyphosate or Roundup MON 52276 on the Gut Microbiota and Serum	Environmental health perspectives, (2021), Vol. 129, No. 1, Article No. 17005	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: Potential effects to gut microbiota and serum metabolome are not part of the EU risk assessments. Suitable scientific approaches to assess effects are not specified, thus relevance of the effects remained unclear. However, this paper presents novel data with the use of multi-omics approaches evaluating the impact of glyphosate on the gut

Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
				Metabolome of Sprague- Dawley Rats.		microbiota and serum metabolome of rats. This study may not be useful directly for risk assessment, but could help from a mode of action point of view. Diet, housing and environmental conditions not described, no HCD.
20	CA 5.8	Nozdrenko D. et al.	2021	Analysis of biomechanical parameters of muscle soleus contraction and blood biochemical parameters in rat with chronic glyphosate intoxication and therapeutic use of C60 fullerene.	International Journal of Molecular Sciences, (2021), Vol. 22, No. 9, Article No. 4977	The article has been classified as relevant by full text - Category B and <b>not reliable</b> for the following reason: The article presents an analysis of biomechanical and blood biochemical parameters in rat with chronic glyphosate intoxication and the use of C60 fullerene as effective nanotherapeutics in the treatment of glyphosate-based herbicide poisoning. This study provides useful information but does not alter the existing risk assessment. No information on the test material. Diet, housing and environmental conditions not described. Only one dose/no dose-effect relationship. No HCD.
21	CA 5.8	Pandher U. et al.	2021	Pulmonary inflammatory response from co-exposure to LPS and glyphosate.	Environmental toxicology and pharmacology, (2021) Vol. 86, Article No. 103651	The article has been classified as relevant by full text - Category B and <b>not</b> reliable for the following reason: The article presents an evaluation of the pulmonary inflammatory response from co-exposure to LPS and glyphosate. This study provides useful information concerning to mode of action but does not alter the existing risk assessment. Purity of glyphosate not stated. Diet, housing and environmental conditions not described. One dose/no dose-effect relationship, no HCD.
22	CA 5.8.2	Hashim A. R. et al.	2021	Ameliorative effect of N- acetylcysteine against glyphosate-induced hepatotoxicity in adult male albino rats: histopathological, biochemical, and molecular studies.	Environmental science and pollution research international, (2021): Ahead of Print	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: The article provides supplementary information on the ability of N-acetylcysteine to ameliorate toxic effects of glyphosate on the liver if administered prior to glyphosate exposure. Only one dose/no dose-response relationship, no HCD reported.
23	CA 5.9	Kabat G. C. et al.	2021	On recent meta-analyses of exposure to glyphosate and risk of non-Hodgkin's lymphoma in humans.	Cancer causes & control, (2021), Vol. 32, No. 4, pp. 409-414	The article has been classified as relevant by full text - Category B and <b>not reliable</b> for the following reason: The purpose of this meta-analysis seems to be to critique the Zhang et al. meta-analysis (Exposure to glyphosatebased herbicides and risk for non-Hodgkin lymphoma: a metaanalysis and supporting evidence. Mutat Res (2019) 781:186–206) and to provide a commentary on meta-analyses that combine results from observational studies of pesticides with different designs and different levels of analytic sophistication. The publication does not provide any primary data or improvement of the underlying studies' limitations and therefore is not informative with respect to possible glyphosate/NHL risk per se. The authors' points about the selective nature of the Zhang et al. (2019) meta-analysis seem valid as do the points about the unaddressed systematic errors in the case-control studies included in previous glyphosate meta-analyses. Not reliable about glyphosate risk per se due to the limitations of the studies included in the meta-analysis. Provides valid criticisms about the Zhang et al. (2019) meta-analysis and generally about meta-analyses of pesticide epidemiology studies.

Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
24	CA 5.9	Kimura T. et al.	2021	Lessons for the clinical nephrologist: acute kidney injury by a glyphosate- surfactant herbicide.	Journal of nephrology, (2021): Ahead of Print	The article / case report has been classified as relevant by full text - Category B for the following reason: This is a case report about an elderly patient who ingested a large volume of formulated glyphosate and presented with renal failure which improved with dialysis, which the patient was ultimately able to discontinue. They physicians obtained a kidney biopsy which showed vacuolization of the proximal tubules of the kidney which they suggest was related to the ingestion. Acute renal failure has been widely described in the literature following large ingestions of formulated glyphosate, however, most patients do not get kidney biopsies. This paper suggests that the associated renal failure is due to proximal tubular injury, which is not unexpected in these circumstances. Since this was a large intentional ingestion, it does not apply to agricultural use or practice.
25	CA 5.9	Kunapareddy T., Kalisetty S.	2021	Glyphosate poisoning - a case report.	Journal of postgraduate medicine, (2021), Vol. 67, No. 1, pp. 36-38	The article / case report has been classified as relevant by full text - Category B for the following reason: This is a case report of a patient who intentionally ingested a large amount of formulated glyphosate in a suicide attempt and developed multiorgan failure requiring intensive supportive care and ultimate recovery. Cases such as these have been widely described in the literature and outcomes such as these are not unexpected. The reassuring part of this case is that despite the suicide attempt, the patient survived.
26	CA 6.10	Billenkamp F. et al.	2021	No hints at glyphosate-induced ruminal dysbiosis in cows.	NPJ biofilms and microbiomes, (2021), Vol. 7, No. 1, Article No. 30	The article has been classified as relevant by full text - Category B and reliable without restrictions for the following reason: This is an experimental study to investigate potential detrimental effects of glyphosate on the cattle ruminental microbiome. Cows were fed with feedstuffs with strong differences in dietary fiber and concentrate feed proportion (CFP), either with or without glyphosate residues from pre-harvest treatment. The study is well conducted and analysed. The results show that glyphosate does not have adverse effects on the cattle ruminental microbiome, as it was previously suggested by in vitro studies. While the publication does not correspond to any specific EU data requirement it nevertheless includes interesting data indicating that the residues of glyphosate in cattle feed do not impact cattle ruminental microbiome. The study is reliable with regard to methodology, analysis and statistical evaluation. Further details to animal feedstuff (exposure) provided in: Schnabel, K. et al. Effects of glyphosate residues and different concentrate feed proportions on performance, energy metabolism and health characteristics in lactating dairy cows. Arch. Anim. Nutr. 71, 413 – 427 (2017).
27	CA 6.10	Heymann A. et al.	2021	Effects of glyphosate residues and different concentrate feed proportions in dairy cow rations on hepatic gene expression, liver histology and biochemical blood parameters.	PloS one, (2021), Vol. 16, No. 2, Article No. e0246679	The article has been classified as relevant by full text - Category B and reliable without restrictions for the following reason: This is an experimental study to investigate effects of glyphosate on the cattle hepatotoxic effects (61 lactating German Holstein cows). Cows were fed with feedstuffs with strong differences concentrate feed proportion (CFP), either with or without addition of glyphosate. The results show that glyphosate has no adverse effects on the liver of dairy cows (GLY-responsive gene expression/liver-related blood parameters). The study is reliable with regard to methodology, analysis and

Data requirement Submission Author(s) Year Title Source Justification Number (indicated by the corresponding CA / CP data point number) statistical evaluation. Further details to animal feedstuff (exposure) provided in: Schnabel, K. et al. Effects of glyphosate residues and different concentrate feed proportions on performance, energy metabolism and health characteristics in lactating dairy cows. Arch. Anim. Nutr. 71, 413 – 427 (2017). 28 CA 6.10 Kolakowski 2021 Analysis of Microbiological Journal of food protection, The article has been classified as relevant by full text - Category B and reliable and Chemical Hazards in (2021): Ahead of Print without restrictions for the following reason: Monitoring data from Canada on B. M. et al. pesticides in edible insects (crickets, silkworm, 47 samples). Glyphosate was Edible Insects Available to Canadian Consumers. detected in 36 samples (0.0064-0.15 mg/kg), AMPA was detected in 9 samples (0.007-0.45 mg/kg). Origin of residues unclear. At this timepoint this paper is not relevant for EU because no MRLs are set on insect derived food products. The study is reliable with regard to monitoring data. 29 CA 6.5 Tittlemier S. 2020 Fate of glyphosate in wheat Cereal Chemistry, (2020). The article has been classified as relevant by full text - Category B and reliable during milling and bread with restrictions for the following reason: Processing study of wheat from A. et al. Vol. 98, No. 1, pp. 100production. Focus Issue: Grain 108 Canada; only glyphosate was detected, no residues of AMPA. On average, in and grain-based food safety. the pearling process 50% of glyphosate resided in the outer 17% of the kernels, while in the milling process 81% of glyphosate in the wheat was associated with the bran, shorts, and feeds milling fractions. No changes in glyphosate concentration (corrected for moisture content) were observed during the preparation of dough, fermented dough, and bread. No endpoint is derived, this study is considered supportive for processing of wheat, however no clear processing factors can be derived. Restrictions include absence of validation data in different processed wheat matrices. For the analytical method it is referred to another publication (Tittlemier et al., 2017, Evaluation of a commercially available enzyme-linked immunosorbent assay and a liquid chromatography-tandem mass spectrometric method for the analysis of glyphosate in wheat, oats, barley, malt, and lentils. Cereal Chemistry, 94, 1028-The article has been classified as relevant by full text - Category B and reliable 30 CA 6.9 de Souza 2021 Exposure assessment of Journal fur glyphosate residues in sov-Ferreira A. Verbraucherschutz und without restrictions for the following reason: Glyphosate and AMPA residues were found in Brazilian infant formulas produced with soy extract and/or based infant formulas from the Lebensmittelsicherheit: P. et al. Brazilian market. protein. The residue levels found in the analysed samples are not relevant to the Journal of consumer protection and food safety. representative EU uses supported in the AIR5 dossier. Based on the monitoring data, a risk assessment has been conducted for infants (0-5 months and 6-11 (2021), Vol. 16, No. 1, pp. months age). The study might support the provided risk assessments to show 45-50 absence of consumer risk due to GLY/AMPA residues. The study is reliable with regard to monitoring data. The article has been classified as relevant by full text and **downgraded to** 31 CA 7.5 Kaszkowiak European Journal of 2021 The concentration of K. et al. glyphosate in the tap water in Biological Research, Category B due to its non-reliability. The concentration of glyphosate was Greater Poland Region. (2021), Vol. 11, No. 1, pp. measured in 66 randomly collected drinking water samples from separate 57-64 Water Treatment Plants in Poland. Own data was generated. The concentration of glyphosate in the tested samples did not exceed 0.33 µg/L. The sampling procedure and timing as well as sample volume and storage time prior to analysis are not reported. Furthermore, the analytical method was not described

Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
						in detail and not validated. The article does not provide numerical concentrations for glyphosate but only the maximum detected concentration. Individual results are only presented graphically and cannot be assigned to a sampling location.
32	CA 8.2.1	Liao Yi-yu et al.	2020	Study on Acute and Chronic Toxicity of Glyphosate to Zebrafish	Guangzhou Huagong, (2020) Vol. 48, No. 21, pp. 66-68	The article has been classified as relevant by full text and downgraded to Category B due to its non-reliability. The study reports on endpoints potentially relevant for the aquatic risk assessment (96-hours LC50). However, the study was inadequately reported and can therefore not be deemed reliable based on the following aspects: The test item was not identified (just the source), the exposure concentrations were not reported; only the number of levels (5). Exposure concentrations were not analytically verified. Results per treatment level were not reported, only the calculated LC50 values. Mortality data for the control group were not reported either. In addition, information on the life stage and source of the organisms as well as on important water parameters like pH and dissolved oxygen content is missing. It is impossible to assess whether there was a clear dose-response relationship or whether other factors could have influenced the survival and fitness of the test organisms. The reported results can therefore not be used in a context of a regulatory risk assessment.
33	CA 8.2.1, CP 10.2.1	Shiry N. et al.	2020	A bioassay on tissue cholinesterase activity of Rutilus kutum (Kamensky, 1901) exposed to some common pesticides in Iran.	Veterinary research forum: an international quarterly journal, (2020), Vol. 11, No. 4, pp. 325- 331	The article has been classified as relevant by full text and downgraded to Category B due to its non-reliability. While the study reports on regulatory relevant endpoints for the acute toxicity to fish, the reporting is lacking essential information to ascertain the reliability of the derived endpoints. The identity of the test item (whether the active substance or a formulated product) was not clearly reported, purity of the test item was not provided. The application of the test item is not specified, it is unclear whether a solvent carrier was used. Exposure concentrations were not analytically verified. Composition of the test medium was not reported, neither were the environmental conditions during the test. Furthermore, there is barely any information on the control group, no results are reported for the control and it is unclear if the control group consisted of the same number of individuals as the treatment groups. While LC50 and LOEC values are reported, there is no information on the data distribution, goodness of fit or standard error. Raw data are not reported, hence it is impossible to assess the reliability of the reported endpoints. Overall, the study has do be deemed not reliable due to missing essential information in the report.
34	CA 8.2.5.2	Bringer A. et al.	2021	Toxicity and risk assessment of six widely used pesticides on embryo-larval development of the Pacific oyster, Crassostrea gigas.	The Science of the total environment, (2021), Vol. 779, Article No. 146343	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: The test design allows for the derivation of NOECs, but for the most sensitive endpoint (Abnormal D-larvae (%)), the NOEC was below the lowest tested concentration, therefore no regulatory relevant endpoint can be determined. However, the study provides supplementary information on the sub-lethal effects of glyphosate on oyster larvae (specifically Crassotrea gigas) and could be useful as part of a broader

Source Submission Data requirement Author(s) Year Title Justification Number (indicated by the corresponding CA / CP data point number) discussion Exposure concentrations were not analytically verified (stock solutions only). For the most sensitive endpoint (larvae malformations), significant effects were determined at the lowest tested concentration, therefore no NOEC could be determined. Purity of the test item was not provided. 35 CA 8.2.7. Yu H. et al. 2021 Effects of microplastics and Environmental pollution, The article has been classified as relevant by full text - Category B and **not** (2021), Vol. 279, Article **reliable** for the following reason: The study reports on effects of microplastics glyphosate on growth rate, No. 116900 and glyphosate on growth rate, morphological plasticity, photosynthesis, and morphological plasticity, photosynthesis, and oxidative oxidative stress in the aquatic species Salvinia cucullata. Of all reported stress in the aquatic species endpoints, only plant growth variables (relative growth rate (RGR), average Salvinia cucullata. specific leaf growth rate (ASLG), and yellow-leaf percentage (YLP)) are not on a molecular or cellular level and could be of potential relevance for an EUlevel risk assessment for aquatic plants. It should be noted that currently no standardized test guideline for the testing of chemicals with Salvinia cucullata exists. Furthermore, no regulatory relevant endpoints were calculated (e.g. ECx) and the resuls were not presented in a way that would allow conducting such calculations retroactively. However, it can be inferred from the study that the NOEC for relative growth rate would be 25 mg glyphosate/L and this could therefore serve as supporting information in a regulatory context. While the study reports on endpoints with potential relevance to the regulatory risk assessment of aquatic plants, specifically growth rate, the study can not be deemed reliable due to issues with the test design as well as reporting of the data. The most significant aspects are listed in the following: The test plants were collected from a not specified natural habitat and previous contact with contaminants that could affect the outcome of the test can not be ruled out. The application of the test item is not described and it is unclear whether a solvent carrier was used. If so, a solvent control would have to be included to dismiss possible toxic effects of the carrier. Exposure concentrations were not analytically verified. The test duration was 7 days without renewal of the test substance, the actual exposure concentrations could vary significantly from the nominal concentrations. Composition of the test medium was not reported. Furthermore, the results on growth rate are only reported in the form of a bar graph. Exact values can not be derived from the graph and statistical power can not be assessed. As no raw data are reported, statistical calculations can not be conducted retroactively. It has to be concluded that the study is not reliable for regulatory risk assessment purposes. The article has been classified as relevant by full text - Category B and reliable 36 CA 8.6.2 Jiang L. et 2021 Earthworm casts restrained the Chemosphere, (2021), Vol 279, Article No. 130571 with restrictions for the following reason: The study primarily assesses the al. accumulation and phytotoxicity of soil glyphosate to cowpea effects of earthworm casts on the accumulation and phytotoxicity of soil bound (Vigna unguiculata (L.) Walp.) glyphosate to cowpea plants (Vigna unguiculata). However, the study also plants. reports on the effects of glyphosate alone applied to soil at 12.15 m/kg on on root and shoot length of Vigna unguiculata (in a sort of a seedling growth test). Altough the test is not conducted according to any guidance, its results can be used as part of a broader discussion on the effects of glyphosate on non-target

Source Submission Data requirement Author(s) Year Title Justification Number (indicated by the corresponding CA / CP data point number) terrestrial plants. While the study reports on parameters with potential relevance to the regulatory risk assessment of terrestrial plants, specifically shoot and root weight and shoot and root length of Vigna unguiculata, the study can not be deemed fully reliable due to the following issues. The soil sample was collected from a not specified sampling spot at Danzhou National Agricultural Science and Technology Park. Previous contact with contaminants that could affect the outcome of the test can not be ruled out. In addition, not all relevant soil parameters are reported on, information on cation exchange capacity, bulk density, water retention and microbial biomass is missing from the report. The application of the test item is not described and it is unclear whether a solvent carrier was used. Furthermore, exposure concentrations were not analytically verified. While analytical methods were reported in the material and methods section of the report, no analytical results pertaining to the plant growth experiment are reported. The test duration was 5 weeks, the actual exposure concentrations could vary significantly from the nominal concentrations. The results for the plant growth parameters (weight and length) are only reported in the form of a bar graph, which does not allow for derivation of exact values. Statistical differences between the treatment groups are marked in the graphic, however the underlying statistical methods are not reported. As no raw data are reported, statistical calculations can not be conducted retroactively. CP 10.2.1 Akinbadewa Agraarteadus, (2020), Vol. The article has been classified as relevant by full text - Category B and reliable 37 2020 Sublethal effect of glyphosate A. O. et al. [N-(phosphonomethyl)glycine] 31, No. 2, pp. 122-130 with restrictions for the following reason: No regulatory relevant endpoints are on growth performance and provided, but the findings of the work could serve to support acute effects of biochemical activities in some glyphosate on fish (specifically Clarias gariepinus) as part of a broader organs of Clarias gariepinus discussion. Chronic effects were calculated at 70 days, which is not an agreed (Burchell, 1822) fingerlings. time frame for a test with fish juveniles, and therefore they are not useful for the RA (in fact, at 28 days no mortality at any tested rate was detected). No guideline was followed. Concentrations of the test item in the exposure medium were not analytically verified and the test was conducted under static (96-hour acute test) or semi-static (70 days chronic test) conditions. The accuracy of the exposure concentrations is therefore unclear. Furthermore, endpoints relevant for the risk assessment, such as ECx values, were not calculated. For the long-term exposure test only 2 treatment levels were tested at an aleatory time frame (70 days), therefore ECx values can not be calculated and conclusions should be considered with caution. The test item was not sufficiently described. 38 CP 10.2.2 Sanudi F. et 2021 Effects of Glyphosate The article has been classified as relevant by full text - Category B and **not** Indian Journal of Animal Herbicide on Physiological Research, (2021) Vol. 55, reliable for the following reason: The study reports on chronic effects of Parameters of Koi Carp, No. 3, pp. 266-270 glyphosate exposure to Koi carp (Cyprinus Carpio), incl. oxygen consumption Cyprinus Carpio (Linnaeus, rate, ammonia-nitrogen excretion rate, oxygen:nitrogen ratio and food 1758) Fingerlings. consumption, over a duration of 28 days. The aforementioned parameters are not currently included in the context of an EU-level risk assessment. No ECx or

Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
						NOEC values were reported (only a LOEC of 3.3. mg/L can be established). Therefore, the study can only be used as supplementary information. While the study reports on potentially relevant endpoints for the chronic toxicity to fish, the studies presents with a number of weaknesses due to which the study has to be deemd "not-reliable". The most significant issues are listed in the following: The application of the test item is not specified, it is unclear whether a solvent carrier was used. Exposure concentrations were not analytically verified and since the test design was semi-static (medium exchange every 24h), the actual exposure concentrations could vary significantly from the nominal concentrations. Composition of the test medium was not reported, neither were the environmental conditions during the test. Furthermore, the exact number of organisms per treatment level and replicates per treatment level are not reported. Statistical methods were applied but not described, and since raw data are not reported it is impossible to assess the statistical power retroactively. Lastly, while there were effects on all assessed parameters compared to the control group, not all parameters responded in a clear dose dependent fashion.
39	CP 10.6	Strandberg B. et al.	2021	Effects of glyphosate spraydrift on plant flowering.	Environmental pollution, (2021), Vol. 280, Article No. 116953	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: The study reports on spray-drift exposure of non-target plants to the glyphosate formulation Roundup Bio; 360 g a.i./L using tractor-mounted spray-drift reducing nozzles and effects on plant cover and flowering. While spray drift exposure is of relevance for the non-target plants (off-field) risk assessment, the effects assessed in this study (flowering and plant cover) are not currently taken into account in the context of an EU-level risk assessment. However, the study could be used in the context of a broader discussion regarding mitigation measures for the reduction of spray-drift exposure to non-target plants. The study reports on spray-drift exposure of non-target plants to the glyphosate formulation Roundup Bio; 360 g a.i./L using tractor-mounted spray-drift reducing nozzles and effects on plant cover and flowering. The study was deemed reliable with restrictions based on the following aspects: The tank solution contained a dye marker, sodium fluorescein, along with the glyphosate formulation. While the authors state that the substance has previously been used in tracer experiments, some including biological effects of pesticides, they also state that no publications on the effect of foliar application of sodium fluorescein on plants have been identified. Possible effects of the dye marker on the test plants can therefore not be excluded with certainty. Furthermore the results for estimated glyphosate spray drift deposition in relation to distance to edge of field and spray track are only reported in graphical form, which does not allow for derivation of exact values. The same goes for the effects on flowering in relation to glyphosate exposure. No raw data are reported.

Table 35: Relevant but supplementary (category B) articles after detailed assessment: sorted by author(s)

Submission Number	Author(s)	Data requirement (indicated by the corresponding CA / CP data point number)	Year	Title	Source	Justification
37	Akinbadewa A. O. et al.	CP 10.2.1	2020	Sublethal effect of glyphosate [N-(phosphonomethyl)glycine] on growth performance and biochemical activities in some organs of Clarias gariepinus (Burchell, 1822) fingerlings.	Agraarteadus, (2020), Vol. 31, No. 2, pp. 122-130	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: No regulatory relevant endpoints are provided, but the findings of the work could serve to support acute effects of glyphosate on fish (specifically Clarias gariepinus) as part of a broader discussion. Chronic effects were calculated at 70 days, which is not an agreed time frame for a test with fish juveniles, and therefore they are not useful for the RA (in fact, at 28 days no mortality at any tested rate was detected). No guideline was followed. Concentrations of the test item in the exposure medium were not analytically verified and the test was conducted under static (96-hour acute test) or semi-static (70 days chronic test) conditions. The accuracy of the exposure concentrations is therefore unclear. Furthermore, endpoints relevant for the risk assessment, such as ECx values, were not calculated. For the long-term exposure test only 2 treatment levels were tested at an aleatory time frame (70 days), therefore ECx values can not be calculated and conclusions should be considered with caution. The test item was not sufficiently described.
26	Billenkamp F. et al.	CA 6.10	2021	No hints at glyphosate-induced ruminal dysbiosis in cows.	NPJ biofilms and microbiomes, (2021), Vol. 7, No. 1, Article No. 30	The article has been classified as relevant by full text - Category B and reliable without restrictions for the following reason: This is an experimental study to investigate potential detrimental effects of glyphosate on the cattle ruminental microbiome. Cows were fed with feedstuffs with strong differences in dietary fiber and concentrate feed proportion (CFP), either with or without glyphosate residues from pre-harvest treatment. The study is well conducted and analysed. The results show that glyphosate does not have adverse effects on the cattle ruminental microbiome, as it was previously suggested by in vitro studies. While the publication does not correspond to any specific EU data requirement it nevertheless includes interesting data indicating that the residues of glyphosate in cattle feed do not impact cattle ruminental microbiome. The study is reliable with regard to methodology, analysis and statistical evaluation. Further details to animal feedstuff (exposure) provided in: Schnabel, K. et al. Effects of glyphosate residues and different concentrate feed proportions on performance, energy metabolism and health characteristics in lactating dairy cows. Arch. Anim. Nutr. 71, 413 – 427 (2017).
34	Bringer A. et al.	CA 8.2.5.2	2021	Toxicity and risk assessment of six widely used pesticides on embryo-larval development of the Pacific oyster, Crassostrea gigas.	The Science of the total environment, (2021), Vol. 779, Article No. 146343	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: The test design allows for the derivation of NOECs, but for the most sensitive endpoint (Abnormal D-larvae (%)), the NOEC was below the lowest tested concentration, therefore no regulatory relevant endpoint can be determined. However, the study provides supplementary information on the sub-lethal effects of glyphosate on oyster larvae (specifically Crassotrea gigas) and could be useful as part of a broader discussion Exposure concentrations were not analytically verified (stock

Data requirement Submission Author(s) Year Title Source Justification Number (indicated by the corresponding CA / CP data point number) solutions only). For the most sensitive endpoint (larvae malformations), significant effects were determined at the lowest tested concentration, therefore no NOEC could be determined. Purity of the test item was not provided. The article has been classified as relevant by full text - Category B and **not** 11 Celik D. A. et CA 5.4 2021 DNA damages of widely used Fresenius Environmental pesticides; a comet assay Bulletin, (2021), Vol. 30, **reliable** for the following reason: The article provides supplementary report for chlorothalonil and information on genotoxicity of glyphosate potassium salt demonstrating DNA No. 4 A, pp. 4170-4176 damage in a comet assay. However, the DNA damage at the mid and high dose glyphosate potassium salt. is significantly lower than observed at the low dose. No details on the donors, no cytotoxicity assay, no metabolic activation system, no mention of other parameters evaluated in the Comet Assay (ie: hedgehogs, tail length, or tail moment). Only %tail DNA was measured. Furthermore, no positive control and no HCD provided. The article has been classified as relevant by full text - Category B and reliable 12 Congur G. CA 5.4 2021 Monitoring of glyphosate-Environmental pollution. DNA interaction and (2021), Vol. 271, Article with restrictions for the following reason: The article provides a new in vitro synergistic genotoxic effect of No. 116360 method using electrochemical biosensor to monitor DNA interaction of glyphosate and 2,4glyphosate and demonstrates a negative effect onto double stranded DNA. The dichlorophenoxyacetic acid article is relevant but supplementary for the glyphosate a.s. treatment, however using an electrochemical not relevant for the glyphosate formulation tested as it contains ether amine biosensor. ethoxylate (similar to POEA). No dose-effect relationship, no positive control, no HCD. No statistical method presented. The purity of purchased glyphosate was also not provided. The article has been classified as relevant by full text - Category B and reliable 30 de Souza CA 6.9 2021 Exposure assessment of Journal fur glyphosate residues in soy-Verbraucherschutz und without restrictions for the following reason: Glyphosate and AMPA residues Ferreira A. P. were found in Brazilian infant formulas produced with soy extract and/or et al. based infant formulas from the Lebensmittelsicherheit: Brazilian market. Journal of consumer protein. The residue levels found in the analysed samples are not relevant to protection and food safety. the representative EU uses supported in the AIR5 dossier. Based on the (2021), Vol. 16, No. 1, pp. monitoring data, a risk assessment has been conducted for infants (0-5 months 45-50 and 6-11 months age). The study might support the provided risk assessments to show absence of consumer risk due to GLY/AMPA residues. The study is reliable with regard to monitoring data. The article has been classified as relevant by full text - Category B and **not** 17 Fan X. et al. CA 5.8 2021 Identification of lncRNA International journal of reliable for the following reason: The article analyses the role of long expression profiles and developmental analysis of ceRNA in the neuroscience: the official noncoding RNAs in the mechanisms of glyphosate neurotoxicity in neuronal hippocampus of perinatal iournalof the International development through a perinatal glyphosate exposure (PGE) mouse model. glyphosate-exposed mice. Society for Developmental The results provide supplementary information on lncRNA and potential relationship with neurotoxicity. There is no information on the test material Neuroscience, (2021): (purity, source, content). Test conditions are not clearly and completely Ahead of Print described. Only one dose level was reported / no dose-response relationship. No "received dose calculation" possible without information on water consumption. Furthermore, no HCD reported

Submission Number	Author(s)	Data requirement (indicated by the corresponding CA / CP data point number)	Year	Title	Source	Justification
22	Hashim A. R. et al.	CA 5.8.2	2021	Ameliorative effect of N- acetylcysteine against glyphosate-induced hepatotoxicity in adult male albino rats: histopathological, biochemical, and molecular studies.	Environmental science and pollution research international, (2021): Ahead of Print	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: The article provides supplementary information on the ability of N-acetylcysteine to ameliorate toxic effects of glyphosate on the liver if administered prior to glyphosate exposure. Only one dose/no dose-response relationship, no HCD reported.
27	Heymann A. et al.	CA 6.10	2021	Effects of glyphosate residues and different concentrate feed proportions in dairy cow rations on hepatic gene expression, liver histology and biochemical blood parameters.	PloS one, (2021), Vol. 16, No. 2, Article No. e0246679	The article has been classified as relevant by full text - Category B and reliable without restrictions for the following reason: This is an experimental study to investigate effects of glyphosate on the cattle hepatotoxic effects (61 lactating German Holstein cows). Cows were fed with feedstuffs with strong differences concentrate feed proportion (CFP), either with or without addition of glyphosate. The results show that glyphosate has no adverse effects on the liver of dairy cows (GLY-responsive gene expression/liver-related blood parameters). The study is reliable with regard to methodology, analysis and statistical evaluation. Further details to animal feedstuff (exposure) provided in: Schnabel, K. et al. Effects of glyphosate residues and different concentrate feed proportions on performance, energy metabolism and health characteristics in lactating dairy cows. Arch. Anim. Nutr. 71, 413 – 427 (2017).
36	Jiang L. et al.	CA 8.6.2	2021	Earthworm casts restrained the accumulation and phytotoxicity of soil glyphosate to cowpea (Vigna unguiculata (L.) Walp.) plants.	Chemosphere, (2021), Vol. 279, Article No. 130571	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: The study primarily assesses the effects of earthworm casts on the accumulation and phytotoxicity of soil bound glyphosate to cowpea plants (Vigna unguiculata). However, the study also reports on the effects of glyphosate alone applied to soil at 12.15 m/kg on on root and shoot length of Vigna unguiculata (in a sort of a seedling growth test). Altough the test is not conducted according to any guidance, its results can be used as part of a broader discussion on the effects of glyphosate on non-target terrestrial plants. While the study reports on parameters with potential relevance to the regulatory risk assessment of terrestrial plants, specifically shoot and root weight and shoot and root length of Vigna unguiculata, the study can not be deemed fully reliable due to the following issues. The soil sample was collected from a not specified sampling spot at Danzhou National Agricultural Science and Technology Park. Previous contact with contaminants that could affect the outcome of the test can not be ruled out. In addition, not all relevant soil parameters are reported on, information on cation exchange capacity, bulk density, water retention and microbial biomass is missing from the report. The application of the test item is not described and it is unclear whether a solvent carrier was used. Furthermore, exposure concentrations were not analytically verified. While analytical methods were reported in the material and methods section of the report, no analytical results pertaining to the plant growth experiment are reported. The test duration was 5 weeks, the actual exposure concentrations could vary significantly from the nominal concentrations. The results for the plant growth parameters (weight and length)

Submission Author(s) Data requirement Year Title Source Justification Number (indicated by the corresponding CA / CP data point number) are only reported in the form of a bar graph, which does not allow for derivation of exact values. Statistical differences between the treatment groups are marked in the graphic, however the underlying statistical methods are not reported. As no raw data are reported, statistical calculations can not be conducted retroactively. 23 CA 5.9 2021 The article has been classified as relevant by full text - Category B and not Kabat G. C. et On recent meta-analyses of Cancer causes & control, exposure to glyphosate and (2021), Vol. 32, No. 4, pp. **reliable** for the following reason: The purpose of this meta-analysis seems to risk of non-Hodgkin's 409-414 be to critique the Zhang et al. meta-analysis (Exposure to glyphosatebased herbicides and risk for non-Hodgkin lymphoma: a metaanalysis and supporting lymphoma in humans. evidence. Mutat Res (2019) 781:186-206) and to provide a commentary on meta-analyses that combine results from observational studies of pesticides with different designs and different levels of analytic sophistication. The publication does not provide any primary data or improvement of the underlying studies' limitations and therefore is not informative with respect to possible glyphosate/NHL risk per se. The authors' points about the selective nature of the Zhang et al. (2019) meta-analysis seem valid as do the points about the unaddressed systematic errors in the case-control studies included in previous glyphosate meta-analyses. Not reliable about glyphosate risk per se due to the limitations of the studies included in the meta-analysis. Provides valid criticisms about the Zhang et al. (2019) meta-analysis and generally about meta-analyses of pesticide epidemiology studies. 31 CA 7.5 2021 European Journal of The article has been classified as relevant by full text and **downgraded to** Kaszkowiak The concentration of K. et al. glyphosate in the tap water in Biological Research, Category B due to its non-reliability. The concentration of glyphosate was Greater Poland Region. (2021), Vol. 11, No. 1, pp. measured in 66 randomly collected drinking water samples from separate 57-64 Water Treatment Plants in Poland. Own data was generated. The concentration of glyphosate in the tested samples did not exceed 0.33 μg/L. The sampling procedure and timing as well as sample volume and storage time prior to analysis are not reported. Furthermore, the analytical method was not described in detail and not validated. The article does not provide numerical concentrations for glyphosate but only the maximum detected concentration. Individual results are only presented graphically and cannot be assigned to a sampling location. 24 Kimura T. et CA 5.9 2021 Lessons for the clinical Journal of nephrology, The article / case report has been classified as relevant by full text - Category B (2021): Ahead of Print for the following reason: This is a case report about an elderly patient who nephrologist: acute kidney injury by a glyphosateingested a large volume of formulated glyphosate and presented with renal surfactant herbicide. failure which improved with dialysis, which the patient was ultimately able to discontinue. They physicians obtained a kidney biopsy which showed vacuolization of the proximal tubules of the kidney which they suggest was related to the ingestion. Acute renal failure has been widely described in the literature following large ingestions of formulated glyphosate, however, most patients do not get kidney biopsies. This paper suggests that the associated renal failure is due to proximal tubular injury, which is not unexpected in these

Submission Number	Author(s)	Data requirement (indicated by the corresponding CA / CP data point number)	Year	Title	Source	Justification
						circumstances. Since this was a large intentional ingestion, it does not apply to agricultural use or practice.
28	Kolakowski B. M. et al.	CA 6.10	2021	Analysis of Microbiological and Chemical Hazards in Edible Insects Available to Canadian Consumers.	Journal of food protection, (2021): Ahead of Print	The article has been classified as relevant by full text - Category B and reliable without restrictions for the following reason: Monitoring data from Canada on pesticides in edible insects (crickets, silkworm, 47 samples). Glyphosate was detected in 36 samples (0.0064-0.15 mg/kg), AMPA was detected in 9 samples (0.007-0.45 mg/kg). Origin of residues unclear. At this timepoint this paper is not relevant for EU because no MRLs are set on insect derived food products. The study is reliable with regard to monitoring data.
25	Kunapareddy T., Kalisetty S.	CA 5.9	2021	Glyphosate poisoning - a case report.	Journal of postgraduate medicine, (2021), Vol. 67, No. 1, pp. 36-38	The article / case report has been classified as relevant by full text - Category B for the following reason: This is a case report of a patient who intentionally ingested a large amount of formulated glyphosate in a suicide attempt and developed multiorgan failure requiring intensive supportive care and ultimate recovery. Cases such as these have been widely described in the literature and outcomes such as these are not unexpected. The reassuring part of this case is that despite the suicide attempt, the patient survived.
32	Liao Yi-yu et al.	CA 8.2.1	2020	Study on Acute and Chronic Toxicity of Glyphosate to Zebrafish.	Guangzhou Huagong, (2020) Vol. 48, No. 21, pp. 66-68	The article has been classified as relevant by full text and downgraded to Category B due to its non-reliability. The study reports on endpoints potentially relevant for the aquatic risk assessment (96-hours LC50). However, the study was inadequately reported and can therefore not be deemed reliable based on the following aspects: The test item was not identified (just the source), the exposure concentrations were not reported; only the number of levels (5). Exposure concentrations were not analytically verified. Results per treatment level were not reported, only the calculated LC50 values. Mortality data for the control group were not reported either. In addition, information on the life stage and source of the organisms as well as on important water parameters like pH and dissolved oxygen content is missing. It is impossible to assess whether there was a clear dose-response relationship or whether other factors could have influenced the survival and fitness of the test organisms. The reported results can therefore not be used in a context of a regulatory risk assessment.
16	Luna S. et al.	CA 5.7	2021	Glyphosate exposure induces synaptic impairment in hippocampal neurons and cognitive deficits in developing rats.	Archives of toxicology, (2021): Ahead of Print	The article has been classified as relevant by full text and downgraded to Category B due to its non-reliability.  In vitro test: Extremely high and irrelevant supraphysiological doses. No metabolic activation system and cytotoxicity assay. No HCD, no positive control.  In vivo test: No information on body weight and age of animals, no information on diet, no HCD. Route of administration was by s.c. injection in the neck. This route of administration is not relevant and does not represent the normal ADME processes with low absorption and rapid elimination.

Submission Number	Author(s)	Data requirement (indicated by the corresponding CA / CP data point number)	Year	Title	Source	Justification
18	Mesnage R. et al.	CA 5.8	2021	Urinary excretion of herbicide co-formulants after oral exposure to roundup MON 52276 in rats.	Environmental research, (2021), Vol. 197, Article No. 111103	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: Useful information about the urinary excretion of herbicide co-formulants after exposure to a glyphosate formulation in rats. It is only related to surfactant absorption/excretion which is then formulation specific. No toxicological effect. Housing and environmental conditions not described. No information on diet. No confirmation of received dose.
19	Mesnage R. et al.	CA 5.8	2021	Use of Shotgun Metagenomics and Metabolomics to Evaluate the Impact of Glyphosate or Roundup MON 52276 on the Gut Microbiota and Serum Metabolome of Sprague- Dawley Rats.	Environmental health perspectives, (2021), Vol. 129, No. 1, Article No. 17005	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: Potential effects to gut microbiota and serum metabolome are not part of the EU risk assessments. Suitable scientific approaches to assess effects are not specified, thus relevance of the effects remained unclear. However, this paper presents novel data with the use of multi-omics approaches evaluating the impact of glyphosate on the gut microbiota and serum metabolome of rats. This study may not be useful directly for risk assessment, but could help from a mode of action point of view. Diet, housing and environmental conditions not described, no HCD.
14	Mutwedu V. B. et al.	CA 5.6	2021	Growth performance and reproductive function impairment of glyphosate-based herbicide in male guinea pig (Cavia porcellus).	Veterinary medicine and science, (2021): Ahead of Print	The article has been classified as relevant by full text - Category B and <b>not reliable</b> for the following reason: The article presents the effects of a glyphosate-based formulation on growth performance and reproductive function impairment in male guinea pigs, which is not the typical animal model of choice for this type of investigation. This study provides interesting information on reproductive functions but the guinea pig is not a model validated for assessing reproductive toxicity in the EU evaluations. Atypical animal model, so historical control data in this species at this lab is paramount to interpret results, and no positive controls to confirm method validity. Findings are confounded by overt general toxicity at high surfactant doses. No necropsy observations of likely gastrointestinal damage resulting from high oral surfactant exposures. No information on the feed, and no method of analysis.
20	Nozdrenko D. et al.	CA 5.8	2021	Analysis of biomechanical parameters of muscle soleus contraction and blood biochemical parameters in rat with chronic glyphosate intoxication and therapeutic use of C60 fullerene.	International Journal of Molecular Sciences, (2021), Vol. 22, No. 9, Article No. 4977	The article has been classified as relevant by full text - Category B and <b>not reliable</b> for the following reason: The article presents an analysis of biomechanical and blood biochemical parameters in rat with chronic glyphosate intoxication and the use of C60 fullerene as effective nanotherapeutics in the treatment of glyphosate-based herbicide poisoning. This study provides useful information but does not alter the existing risk assessment. No information on the test material. Diet, housing and environmental conditions not described. Only one dose/no dose-effect relationship. No HCD.

Submission Number	Author(s)	Data requirement (indicated by the corresponding CA / CP data point number)	Year	Title	Source	Justification
21	Pandher U. et al.	CA 5.8	2021	Pulmonary inflammatory response from co-exposure to LPS and glyphosate.	Environmental toxicology and pharmacology, (2021) Vol. 86, Article No. 103651	The article has been classified as relevant by full text - Category B and <b>not reliable</b> for the following reason: The article presents an evaluation of the pulmonary inflammatory response from co-exposure to LPS and glyphosate. This study provides useful information concerning to mode of action but does not alter the existing risk assessment. Purity of glyphosate not stated. Diet, housing and environmental conditions not described. One dose/no dose-effect relationship, no HCD.
38	Sanudi F. et al.	CP 10.2.2	2021	Effects of Glyphosate Herbicide on Physiological Parameters of Koi Carp, Cyprinus Carpio (Linnaeus, 1758) Fingerlings.	Indian Journal of Animal Research, (2021) Vol. 55, No. 3, pp. 266-270	The article has been classified as relevant by full text - Category B and <b>not reliable</b> for the following reason: The study reports on chronic effects of glyphosate exposure to Koi carp (Cyprinus Carpio), incl. oxygen consumption rate, ammonia-nitrogen excretion rate, oxygen:nitrogen ratio and food consumption, over a duration of 28 days. The aforementioned parameters are not currently included in the context of an EU-level risk assessment. No ECx or NOEC values were reported (only a LOEC of 3.3. mg/L can be established). Therefore, the study can only be used as supplementary information. While the study reports on potentially relevant endpoints for the chronic toxicity to fish, the studies presents with a number of weaknesses due to which the study has to be deemd "not-reliable". The most significant issues are listed in the following: The application of the test item is not specified, it is unclear whether a solvent carrier was used. Exposure concentrations were not analytically verified and since the test design was semi-static (medium exchange every 24h), the actual exposure concentrations could vary significantly from the nominal concentrations. Composition of the test medium was not reported, neither were the environmental conditions during the test. Furthermore, the exact number of organisms per treatment level and replicates per treatment level are not reported. Statistical methods were applied but not described, and since raw data are not reported it is impossible to assess the statistical power retroactively. Lastly, while there were effects on all assessed parameters compared to the control group, not all parameters responded in a clear dose dependent fashion.
33	Shiry N. et al.	CA 8.2.1, CP 10.2.1	2020	A bioassay on tissue cholinesterase activity of Rutilus kutum (Kamensky, 1901) exposed to some common pesticides in Iran.	Veterinary research forum: an international quarterly journal, (2020), Vol. 11, No. 4, pp. 325- 331	The article has been classified as relevant by full text and downgraded to Category B due to its non-reliability. While the study reports on regulatory relevant endpoints for the acute toxicity to fish, the reporting is lacking essential information to ascertain the reliability of the derived endpoints. The identity of the test item (whether the active substance or a formulated product) was not clearly reported, purity of the test item was not provided. The application of the test item is not specified, it is unclear whether a solvent carrier was used. Exposure concentrations were not analytically verified. Composition of the test medium was not reported, neither were the environmental conditions during the test. Furthermore, there is barely any information on the control group, no results are reported for the control and it is unclear if the control group consisted of the same number of individuals as the treatment groups. While LC50 and LOEC values are reported, there is no

Submission Author(s) Data requirement Year Title Source Justification Number (indicated by the corresponding CA / CP data point number) information on the data distribution, goodness of fit or standard error. Raw data are not reported, hence it is impossible to assess the reliability of the reported endpoints. Overall, the study has do be deemed not reliable due to missing essential information in the report. 39 Strandberg B. CP 10.6 2021 Effects of glyphosate spray-Environmental pollution, The article has been classified as relevant by full text - Category B and reliable (2021), Vol. 280, Article with restrictions for the following reason: The study reports on spray-drift et al. drift on plant flowering. No. 116953 exposure of non-target plants to the glyphosate formulation Roundup Bio; 360 g a.i./L using tractor-mounted spray-drift reducing nozzles and effects on plant cover and flowering. While spray drift exposure is of relevance for the nontarget plants (off-field) risk assessment, the effects assessed in this study (flowering and plant cover) are not currently taken into account in the context of an EU-level risk assessment. However, the study could be used in the context of a broader discussion regarding mitigation measures for the reduction of spray-drift exposure to non-target plants. The study reports on spray-drift exposure of non-target plants to the glyphosate formulation Roundup Bio; 360 g a.i./L using tractor-mounted spray-drift reducing nozzles and effects on plant cover and flowering. The study was deemed reliable with restrictions based on the following aspects: The tank solution contained a dye marker, sodium fluorescein, along with the glyphosate formulation. While the authors state that the substance has previously been used in tracer experiments, some including biological effects of pesticides, they also state that no publications on the effect of foliar application of sodium fluorescein on plants have been identified. Possible effects of the dye marker on the test plants can therefore not be excluded with certainty. Furthermore the results for estimated glyphosate spray drift deposition in relation to distance to edge of field and spray track are only reported in graphical form, which does not allow for derivation of exact values. The same goes for the effects on flowering in relation to glyphosate exposure. No raw data are reported. 29 2020 The article has been classified as relevant by full text - Category B and reliable Tittlemier S. CA 6.5 Fate of glyphosate in wheat Cereal Chemistry, (2020). during milling and bread Vol. 98, No. 1, pp. 100with restrictions for the following reason: Processing study of wheat from A. et al. production. Focus Issue: Grain 108 Canada; only glyphosate was detected, no residues of AMPA. On average, in and grain-based food safety. the pearling process 50% of glyphosate resided in the outer 17% of the kernels, while in the milling process 81% of glyphosate in the wheat was associated with the bran, shorts, and feeds milling fractions. No changes in glyphosate concentration (corrected for moisture content) were observed during the preparation of dough, fermented dough, and bread. No endpoint is derived, this study is considered supportive for processing of wheat, however no clear processing factors can be derived. Restrictions include absence of validation data in different processed wheat matrices. For the analytical method it is referred to another publication (Tittlemier et al., 2017, Evaluation of a commercially available enzyme-linked immunosorbent assay and a liquid chromatography-tandem mass spectrometric method for the analysis of

Submission Number	Author(s)	Data requirement (indicated by the corresponding CA / CP data point number)	Year	Title	Source	Justification
						glyphosate in wheat, oats, barley, malt, and lentils. Cereal Chemistry, 94, 1028-1036).
15	Upadhyay J. et al.	CA 5.6	2020	Teratogenic effect of chlorpyrifos and glyphosate on pregnant rats: biochemical and morphological evaluations.	Journal of Pharmaceutical Research International, (2020), Vol. 32, No. 23, Article No. JPRI.61413	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: The article provides information on teratogenic effects of glyphosate-based formulation Topper 77 (Crystal Crop Protection Pvt. Ltd India) which is nowhere close to the glyphosate representative EU formulation for AIR5. According to the webpage (https://www.crystalcropprotection.com/internationalsales/detail/Topper) it contains 71% of glyphosate and it is a SG-formulation. The representative glyphosate formulation for the AIR5 is a SL formulation and contains 360 g a.s./L. Due to formulation tested, the article is classified as relevant but supplementary. No information on purity, content and storage conditions of the test material. One dose level/no dose-effect relationship, no HCD reported.
13	Wozniak E. et al.	CA 5.4	2021	Glyphosate and AMPA Induce Alterations in Expression of Genes Involved in Chromatin Architecture in Human Peripheral Blood Mononuclear Cells (In Vitro).	International journal of molecular sciences, (2021), Vol. 22, No. 6	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: The article provides new information on the effect of glyphosate and the metabolite AMPA on expression of genes involved in chromatin architecture in human peripheral blood mononuclear cells (PBMCs). The results provide useful information on epigenetic processes that may be relevant but are difficult to interpret without further guidance. Therefore, the results are not expected to alter the existing risk assessment No HCD, no positive control. No real dose-effect relationship reported. The lack of positive control does not allow assessing the laboratory proficiency.
35	Yu H. et al.	CA 8.2.7.	2021	Effects of microplastics and glyphosate on growth rate, morphological plasticity, photosynthesis, and oxidative stress in the aquatic species Salvinia cucullata.	Environmental pollution, (2021), Vol. 279, Article No. 116900	The article has been classified as relevant by full text - Category B and <b>not</b> reliable for the following reason: The study reports on effects of microplastics and glyphosate on growth rate, morphological plasticity, photosynthesis, and oxidative stress in the aquatic species Salvinia cucullata. Of all reported endpoints, only plant growth variables (relative growth rate (RGR), average specific leaf growth rate (ASLG), and yellow-leaf percentage (YLP)) are not on a molecular or cellular level and could be of potential relevance for an EU-level risk assessment for aquatic plants. It should be noted that currently no standardized test guideline for the testing of chemicals with Salvinia cucullata exists. Furthermore, no regulatory relevant endpoints were calculated (e.g. ECx) and the resuls were not presented in a way that would allow conducting such calculations retroactively. However, it can be inferred from the study that the NOEC for relative growth rate would be 25 mg glyphosate/L and this could therefore serve as supporting information in a regulatory context. While the study reports on endpoints with potential relevance to the regulatory risk assessment of aquatic plants, specifically growth rate, the study can not be deemed reliable due to issues with the test design as well as reporting of the data. The most significant aspects are listed in the following: The test plants were collected from a not specified natural habitat and previous contact with contaminants that could affect the outcome of the test can not be ruled out. The application of the test item is not described and it is unclear whether a solvent

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Submission Number	Author(s)	Data requirement (indicated by the corresponding CA / CP data point number)	Year	Title	Source	Justification
						carrier was used. If so, a solvent control would have to be included to dismiss possible toxic effects of the carrier. Exposure concentrations were not analytically verified. The test duration was 7 days without renewal of the test substance, the actual exposure concentrations could vary significantly from the nominal concentrations. Composition of the test medium was not reported. Furthermore, the results on growth rate are only reported in the form of a bar graph. Exact values can not be derived from the graph and statistical power can not be assessed. As no raw data are reported, statistical calculations can not be conducted retroactively. It has to be concluded that the study is not reliable for regulatory risk assessment purposes.

Table 36: Articles of unclear relevance (category C) after detailed assessment: sorted by data requirement(s)

Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
40	CA 5.8	Zhang L. et al.	2021	Involvement of mitochondrial fission in renal tubular pyroptosis in mice exposed to high and environmental levels of glyphosate combined with hard water.	Environmental pollution, (2021), Vol. 283, Article No. 117082	The relevance of this article is unclear (Category C) for the following reason: Although this publication provides information about involvement of mitochondrial fission in renal tubular pyroptosis in mice exposed to glyphosate combined with hard water, it is uncertain without further guidance, how these data can be related to the EU level regulatory risk assessment and how to interpret the data within the context of a renewal.
41	CA 5.8.2	Hu J. et al.	2021	Low-dose exposure of glyphosate-based herbicides disrupt the urine metabolome and its interaction with gut microbiota.	Scientific reports, (2021), Vol. 11, No. 1, Article No. 3265	The relevance of this article is unclear (Category C) for the following reason: Potential effects to gut microbes are not part of the EU risk assessments. Suitable scientific approaches to assess effects are not specified, thus relevance of the effects remained unclear.
42	CA 5.9	Franke A. A. et al.	2021	Pilot study on the urinary excretion of the glyphosate metabolite aminomethylphosphonic acid and breast cancer risk: The Multiethnic Cohort study.	Environmental pollution, (2021), Vol. 277, Article No. 116848	The relevance of this article is unclear (Category C) for the following reason: Exposure was presumably to AMPA, from uncertain sources. The population ivestigated were mostly post-menopausal women who were participants in the Hawaii biospecimen subcohort of the Multi-ethnic Cohort.
43	CA 5.9	Lesseur C. et al.	2021	Maternal urinary levels of glyphosate during pregnancy and anogenital distance in newborns in a US multicenter pregnancy cohort.	Environmental pollution, (2021), Vol. 280, Article No. 117002	The relevance of this article is unclear (Category C) for the following reason: First, it is unclear why the second trimester urine sample was selected for the analysis and whether it is representative of glyphosate and AMPA exposure during the etiologically relevant time period for affecting AGD. Second, it seems that chemicals and pesticides other than glyphosate were measured in urine (and blood) samples. Potential confounding from non-glyphosate exposures was not considered. Third, for female infants, there was a discrepancy between the results for the continuous and categorical analyses. In the former there were no significant results, while there were significant results in the categorical analyses. In general, dichotomizing at the median for highly positively skewed exposure variables does not create a clear exposure distinction between the groups being compared – both groups include primarily those with exposure values near the median. The discrepancy between the continuous and categorical analyses could be explained by those with the very highest exposure values having AGD similar to those with exposure values in the lower exposure group. It is obviously more informative to arrange comparison for groups that differ appreciably in the amount of exposure. Note also that there were no significant AGD findings for male infants. Lastly, the glyphosate and AMPA values are so low as to be of questionable biological plausibility given recent regulatory toxicology reviews for glyphosate and AMPA.

Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
44	CA 5.9	Meloni F. et al.	2021	Occupational exposure to glyphosate and risk of lymphoma:results of an Italian multicenter case-control study.	Environmental health: a global access science source, (2021), Vol. 20, No. 1, Article No. 49	The relevance of this article is unclear (Category C) for the following reason: This study is a very low quality case control study for evaluating glyphosate. The exposure to various formulations of pesticides was not described clearly, but likely exposure to multiple pesticides for those with relevant occupations (i.e. mixture toxicity). The authors only controlled for age, gender, study centre, and education. There was no control for exposures other than glyphosate.
45	CA 8.4	Anshu et al.	2020	Individual and combined toxic effects of herbicides on growth parameters and fecundity of Eisenia fetida	International Journal of Current Microbiology and Applied Sciences, (2020), Vol. 9, No. 12, pp. 1997-2005	The relevance of this article is unclear (Category C) for the following reason: No regulatory relevant endpoints are provided. In addition, results at 30, 60 and 90 days were provided, when the accepted time frame is 28 days (mortality and growth) and 56 days (reproduction) for Eisenia fetida. Earthworms were exposed to the test item all along the study period (90 days), while the agreed regulatory exposure period is of only 28 days (earthworms should have been removed after that). Therefore, the conclusions of the study are not comparable to any accepted regulatory endpoint. Thus its relevance remains unclear.
46	CP 10.4.2	Kozak V. M. et al.	2020	Influence of herbicides, insecticides and fungicides on food consumption and body weight of Rossiulus kessleri (Diplopoda, Julidae).	Biosystems Diversity, (2020), Vol. 28, No. 3, pp. 272-280	The relevance of this article is unclear (Category C) for the following reason: The study assesses the effects of a glyphosate formulation (Roundup, 450 g/L, IPA salt) on body weight, food consumption and production of feces of Russilus kessleri, a millipede (Diplopoda, Julidae), over a duration of 20 days. No endpoints relevant to the risk assessment were reported, as no reproduction effects were investigated. While soil-dwelling organisms are relevant for the EU level risk assessment, the species Russilus kessleri is not commonly used as a representative species for soil organisms. Furthermore, the described test system is not in accordance with the standardized test systems for soil organisms, as no soil was included in the test system, only dried litter. In addition, the test organisms were collected in the wild from a not specified source ("near an airport"), so previous contaminant exposure can not be ruled out.

Table 37: Articles of unclear relevance (category C) after detailed assessment: sorted by author(s)

Submission	Author(s)	Data requirement	Year	Title	Source	Justification
Number	Author(s)	(indicated by the corresponding CA / CP data point number)	Teal	Title	Source	
45	Anshu et al.	CA 8.4	2020	Individual and combined toxic effects of herbicides on growth parameters and fecundity of Eisenia fetida	International Journal of Current Microbiology and Applied Sciences, (2020), Vol. 9, No. 12, pp. 1997- 2005	The relevance of this article is unclear (Category C) for the following reason: No regulatory relevant endpoints are provided. In addition, results at 30, 60 and 90 days were provided, when the accepted time frame is 28 days (mortality and growth) and 56 days (reproduction) for Eisenia fetida. Earthworms were exposed to the test item all along the study period (90 days), while the agreed regulatory exposure period is of only 28 days (earthworms should have been removed after that). Therefore, the conclusions of the study are not comparable to any accepted regulatory endpoint. Thus its relevance remains unclear.
42	Franke A. A. et al.	CA 5.9	2021	Pilot study on the urinary excretion of the glyphosate metabolite aminomethylphosphonic acid and breast cancer risk: The Multiethnic Cohort study.	Environmental pollution, (2021), Vol. 277, Article No. 116848	The relevance of this article is unclear (Category C) for the following reason: Exposure was presumably to AMPA, from uncertain sources. The population ivestigated were mostly post-menopausal women who were participants in the Hawaii biospecimen subcohort of the Multi-ethnic Cohort.
41	Hu J. et al.	CA 5.8.2	2021	Low-dose exposure of glyphosate-based herbicides disrupt the urine metabolome and its interaction with gut microbiota.	Scientific reports, (2021), Vol. 11, No. 1, Article No. 3265	The relevance of this article is unclear (Category C) for the following reason: Potential effects to gut microbes are not part of the EU risk assessments. Suitable scientific approaches to assess effects are not specified, thus relevance of the effects remained unclear.
46	Kozak V. M. et al.	CP 10.4.2	2020	Influence of herbicides, insecticides and fungicides on food consumption and body weight of Rossiulus kessleri (Diplopoda, Julidae).	Biosystems Diversity, (2020), Vol. 28, No. 3, pp. 272-280	The relevance of this article is unclear (Category C) for the following reason: The study assesses the effects of a glyphosate formulation (Roundup, 450 g/L, IPA salt) on body weight, food consumption and production of feces of Russilus kessleri, a millipede (Diplopoda, Julidae), over a duration of 20 days. No endpoints relevant to the risk assessment were reported, as no reproduction effects were investigated. While soil-dwelling organisms are relevant for the EU level risk assessment, the species Russilus kessleri is not commonly used as a representative species for soil organisms. Furthermore, the described test system is not in accordance with the standardized test systems for soil organisms, as no soil was included in the test system, only dried litter. In addition, the test organisms were collected in the wild from a not specified source ("near an airport"), so previous contaminant exposure can not be ruled out.
43	Lesseur C. et al.	CA 5.9	2021	Maternal urinary levels of glyphosate during pregnancy and anogenital distance in newborns in a US multicenter pregnancy cohort.	Environmental pollution, (2021), Vol. 280, Article No. 117002	The relevance of this article is unclear (Category C) for the following reason: First, it is unclear why the second trimester urine sample was selected for the analysis and whether it is representative of glyphosate and AMPA exposure during the etiologically relevant time period for affecting AGD. Second, it seems that chemicals and pesticides other than glyphosate were measured in urine (and blood) samples. Potential confounding from non-glyphosate exposures was not considered. Third, for female infants, there was a discrepancy between the results for the continuous and categorical analyses. In the former there were no

Submission Number	Author(s)	Data requirement (indicated by the corresponding CA / CP data point number)	Year	Title	Source	Justification
						significant results, while there were significant results in the categorical analyses. In general, dichotomizing at the median for highly positively skewed exposure variables does not create a clear exposure distinction between the groups being compared – both groups include primarily those with exposure values near the median. The discrepancy between the continuous and categorical analyses could be explained by those with the very highest exposure values having AGD similar to those with exposure values in the lower exposure group. It is obviously more informative to arrange comparison for groups that differ appreciably in the amount of exposure. Note also that there were no significant AGD findings for male infants. Lastly, the glyphosate and AMPA values are so low as to be of questionable biological plausibility given recent regulatory toxicology reviews for glyphosate and AMPA.
44	Meloni F. et al.	CA 5.9	2021	Occupational exposure to glyphosate and risk of lymphoma:results of an Italian multicenter casecontrol study.	Environmental health: a global access science source, (2021), Vol. 20, No. 1, Article No. 49	The relevance of this article is unclear (Category C) for the following reason: This study is a very low quality case control study for evaluating glyphosate. The exposure to various formulations of pesticides was not described clearly, but likely exposure to multiple pesticides for those with relevant occupations (i.e. mixture toxicity). The authors only controlled for age, gender, study centre, and education. There was no control for exposures other than glyphosate.
40	Zhang L. et al.	CA 5.8	2021	Involvement of mitochondrial fission in renal tubular pyroptosis in mice exposed to high and environmental levels of glyphosate combined with hard water.	Environmental pollution, (2021), Vol. 283, Article No. 117082	The relevance of this article is unclear (Category C) for the following reason: Although this publication provides information about involvement of mitochondrial fission in renal tubular pyroptosis in mice exposed to glyphosate combined with hard water, it is uncertain without further guidance, how these data can be related to the EU level regulatory risk assessment and how to interpret the data within the context of a renewal.

Table 38: Articles excluded after detailed assessment (i.e. not relevant): sorted by technical section (and by author)

Submission Number	Technical section	Author(s)	Year	Title	Source	Reason for not including publication in dossier (based on relevance criteria)
47	Ecotoxicology	Canosa I. S. et al.	2021	In vitro Interference of a Glyphosate Commercial Formulation with the Stimulation of Ovarian Maturation by Progesterone, in the Estuarine Crab Neohelice granulata.	Bulletin of environmental contamination and toxicology, (2021), Vol. 106, No. 4, pp. 583-588	The article has been classified as not relevant by full text for the following reason: Roundup Ultramax is not the representative formulation for the glyphosate EU renewal. In addition it contains etheralkylamine ethoxylate (https://www.raiffeisen.com/agrar_sdb/111/ebb9b8dd2b70ad89b50c16a5dc67ec50?variante=), which does have a similar structure to POEA. Glyphosate based formulations that contain POEA (polyethoxylated tallow amine) surfactants or surfactants of similar chemical structure, are generally more toxic than the active substance itself. In addition, the composition of formulations is an important consideration when comparing the endpoints achieved in public literature with those achieved in regulatory studies conducted with either the technical material or studies conducted with the representative formulation MON 52276. Co-formulants may ameliorate or enhance potential effects on test organisms. For example, POEA based surfactants (not permitted for use in Europe) or surfactants with similar structure, may lead to enhanced sensitivity. For this reason, the findings in the paper cannot be related to the representative formulation, and are therefore not relevant to the regulatory risk assessment for the glyphosate EU renewal.
48	Ecotoxicology	Castelli L. et al.	2021	Impact of Chronic Exposure to Sublethal Doses of Glyphosate on Honey Bee Immunity, Gut Microbiota and Infection by Pathogens.	Microorganisms, (2021), Vol. 9, No. 4	The article has been classified as not relevant by full text for the following reason: This study evaluates the effects of non-lethal doses of glyphosate (0.1 µg/bee/d) on gut microbiota, immune response and lifespan of honeybees (Apis mellifera hybrids). These findings are largely based on cellular/molecular level and cannot be related to the risk assessment. The data on the bees lifespan cannot be expressed in the form of an endpoint relevant to the risk assessment as only one treatment concentration was tested. Overall, it can be concluded that the generated outcomes are not relatable to the EU level risk assessment.
49	Ecotoxicology	Cruz Souza C. E. et al.	2021	Physiological and morphoanatomical effects of glyphosate in Eugenia uniflora, a Brazilian plant species native to the Atlantic Forest biome.	Environmental science and pollution research international, (2021), Vol. 28, No. 17, pp. 21334-21346	The article has been classified as not relevant by full text for the following reason: Roundup Ultra is not the representative formulation for the glyphosate EU renewal. The surfactant system in the formulated product used in this study was not specified by the author. It is therefore not possible to confirm whether the product used contained POEA surfactant / surfactants of similar chemical structure. Glyphosate based formulations that contain POEA surfactants / surfactants of similar chemical structure, are generally more toxic than the active substance itself. In addition, the composition of formulations is an important consideration when comparing the endpoints achieved in public literature with those achieved in regulatory studies conducted with either the technical material or studies conducted with the representative formulation MON 52276. Co-formulants may ameliorate or enhance potential effects on test organisms. For example, POEA based surfactants (not permitted for use in Europe) / surfactants with similar structure, may lead to enhanced sensitivity. For this reason and the fact that it is unclear whether the formulated product contained POEA / surfactants of similar chemical structure, the article is not considered relevant for use in risk assessment. In addition, it seems that Roundup Ultra is a WG formulation (http://www.roundup.com.br/produtos-da-familia-roundup). The representative formulation for the glyphosate EU renewal is a SL formulation.
50	Ecotoxicology	Davico C. E. et al.	2021	Reproductive toxicity of Roundup WG (R) herbicide: impairments in	Environmental Science and Pollution Research International, (2021), Vol. 28, No. 12	The article has been classified as not relevant by full text for the following reason: Roundup WG is not the representative formulation for the glyphosate EU renewal. The representative formulation for the glyphosate EU renewal is MON 52276, which has a nominal glyphosate acid equivalent (a.e.) content of 360 g/L, formulated using glyphosate isopropyl-ammonium

Submission Number	Technical section	Author(s)	Year	Title	Source	Reason for not including publication in dossier (based on relevance criteria)
				ovarian follicles of model organism Danio rerio.		salt and a quaternary-ammonium based surfactant. In addition, MON 52276 is a SC formulation whereas Roundup tested in this study is a WG formulation. In addition, the composition of formulations is an important consideration when comparing the endpoints achieved in public literature with those achieved in regulatory studies conducted with either the technical material or studies conducted with the representative formulation MON 52276. Co-formulants may ameliorate or enhance potential effects on test organisms. As co-formulants were not identified in this paper, the findings in the paper cannot be related to the representative formulation, and are therefore not relevant to the regulatory risk assessment for the glyphosate EU renewal.
51	Ecotoxicology	Díaz-Martín R. D. et al.	2021	Changes in microtubule stability in zebrafish (Danio rerio) embryos after glyphosate exposure.	Heliyon, (2021), Vol. 7, No. 1, Article No. E06027	The article has been classified as not relevant by full text for the following reason: This study evaluates the effects of glyphosate on microtubule stability in zebrafish embryos (Danio rerio). These findings are based on molecular/cellular level effects and cannot be related to the risk assessment. Overall, it can be concluded that the generated outcomes are not relatable to the EU level risk assessment.
52	Ecotoxicology	Galon L. et al.	2020	Damage to lemon tree caused by simulated drift of herbicides.	Revista de Ciencias Agroveterinarias, (2020), Vol. 19, No. 3, pp. 319-328	The article has been classified as not relevant by full text for the following reason: Effects on local (non-European) species under tropical/ subtropical environmental- resp. agricultural conditions. Effects observed in this greenhouse study conducted in Brazil are not easily transferrable to European conditions, not relevant for the risk assessment. In addition Roundup Original tested in this study is not the representative formulation for the glyphosate EU renewal (the representative formulation is MON 52276). Moreover, it contains POEA surfactants that is not permitted for use in formulated herbicidal products in the EU. Therefore, the findings of this paper are not relevant to the regulatory risk assessment for the glyphosate EU renewal.
53	Ecotoxicology	Glinski D. A. et al.	2021	Route of exposure influences pesticide body burden and the hepatic metabolome in post-metamorphic leopard frogs.	The Science of the total environment, (2021), Vol. 779, Article No. 146358	The article has been classified as not relevant by full text for the following reason: This study evaluates the effects of glyphosate exposure on the hepatic metabolome of post-metamorphic southern leopard frogs (L. sphenocephala). These findings are based on molecular/cellular level effects and cannot be related to the risk assessment. The parameter body burden was not assessed for glyphosate. Overall, it can be concluded that the generated outcomes are not relatable to the EU level risk assessment.
54	Ecotoxicology	Korkmaz V. et al.	2021	The bioremediation of glyphosate in soil media by some newly isolated bacteria: The COD, TOC removal efficiency and mortality assessment for Daphnia magna.	Environmental Technology & Innovation, (2021), Vol. 22, Article No. 101535.	The article has been classified as not relevant by full text for the following reason: It is not possible to confirm the identity of the glyphosate based herbicide used in the study as only "Glyphosate, 480 gr of active material" is mentioned. The surfactant system in the formulated product used in this study was also not specified by the authors. The composition of formulations is an important consideration when comparing the endpoints achieved in public literature with those achieved in regulatory studies conducted with either the technical material or studies conducted with the representative formulation MON 52276. Co-formulants may ameliorate or enhance potential effects on test organisms. Given this uncertainty over what was tested in this study, the paper is not considered relevant to the glyphosate EU renewal.

Submission Number	Technical section	Author(s)	Year	Title	Source	Reason for not including publication in dossier (based on relevance criteria)
55	Ecotoxicology	Lacava M. et al.	2021	pest-specific effects of glyphosate on functional response of a wolf spider.	Chemosphere, (2021), Vol. 262, Article No. 127785	The article has been classified as not relevant by full text for the following reason: It is not possible to confirm the identity of the test item used in the study as only 'Roundup' is mentioned. Roundup is a brand that contains multiple glyphosate-based herbicides, that contain different co-formulants. Of most importance to the toxicity profile associated with a particular product is whether that product contained POEA based surfactants (not permitted for use in Europe) or surfactants with similar structure. The surfactant system in the formulated product used in this study was also not specifed by the author. Given this uncertainty over what was tested in this study, the paper is not considered relevant to the glyphosate EU renewal.
56	Ecotoxicology	Martinez- Garcia L. B. et al.	2021	Litter quality drives nitrogen release, and agricultural management (organic vs. conventional) drives carbon loss during litter decomposition in agro-ecosystems.	SOIL BIOLOGY & BIOCHEMISTRY, (2021), Vol. 153, Article No. 108115	The article has been classified as not relevant by full text for the following reason: It is not possible to confirm the identity of the test item used in the study as only 'Roundup' is mentioned. Roundup is a brand that contains multiple glyphosate-based herbicides, that contain different co-formulants. Of most importance to the toxicity profile associated with a particular product is whether that product contained POEA based surfactants (not permitted for use in Europe) or surfactants with similar structure. The surfactant system in the formulated product used in this study was also not specifed by the author. Given this uncertainty over what was tested in this study, the paper is not considered relevant to the glyphosate EU renewal.
57	Ecotoxicology	Owagboriaye F. et al.	2021	Impacts of a glyphosate-based herbicide on the gut microbiome of three earthworm species (Alma millsoni, Eudrilus eugeniae and Libyodrilus violaceus): A pilot study.	Toxicology reports, (2021), Vol. 8, pp. 753-758	The article has been classified as not relevant by full text for the following reason: This study investigated the impact of a glyphosate formulation (Roundup Alphée; 7.20 g/L) on the gut microbial communities of three earthworm species (Alma millsoni, Eudrilus eugeniae and Libyodrilus violaceus). The findings are based on molecular/cellular level effects and cannot be related to the risk assessment. In addition, the publication is not dealing with EU representative conditions as the tested species and soils used are native to Africa. Overall, it can be concluded that the generated outcomes are not relatable to the EU level risk assessment.
58	Ecotoxicology	Parlapiano I. et al.	2021	Effects of commercial formulations of glyphosate on marine crustaceans and implications for risk assessment under temperature changes.	Ecotoxicology and environmental safety, (2021), Vol. 213, Article No. 112068	The article has been classified as not relevant by full text for the following reason: None of the glyphosate formulations tested is the representative formulation for the glyphosate EU renewal. The representative formulation for the glyphosate EU renewal is MON 52276, which has a nominal glyphosate acid equivalent (a.e.) content of 360 g/L, formulated using glyphosate isopropyl-ammonium salt and a quaternary-ammonium based surfactant. Moreover, it is unclear whether the formulations tested contained POEA or not. In the discussion part of this paper, the author states that "Formulations vary between different brands and between different countries. These are cocktails of chemicals composed by glyphosate as active principle (36-48%), water, salts, and co-formulants such as polyoxyethylene tallow amine (POEA). Formulations with POEA are relatively toxic compared to other formulations (Mesnage et al., 2013; Mesnage and Antoniou, 2018)." This statement adds uncertainty concerning the relevance of the findings in the paper to the EU renewal of glyphosate.  In addition, the composition of formulations is an important consideration when comparing the endpoints achieved in public literature with those achieved in regulatory studies conducted with either the technical material or studies conducted with the representative formulation MON 52276. Co-formulants may ameliorate or enhance potential effects on test organisms. For example, POEA based surfactants (not permitted for use in Europe) or surfactants with similar structure, may lead to enhanced sensitivity.

Submission Number	Technical section	Author(s)	Year	Title	Source	Reason for not including publication in dossier (based on relevance criteria)
Number	section					For this reason and the uncertainties associated with the product tested (surfactant system not specified, may contain POEA -> POEA based surfactants are not to be used in agrochemical products in the EU), the article is not considered relevant for use in risk assessment.
59	Ecotoxicology	Portinho J. L. et al.	2021	Resting egg banks can facilitate recovery of zooplankton communities after short exposure to glyphosate.	Ecotoxicology, (2021), Vol. 30, No. 3, pp. 492- 501	The article has been classified as not relevant by full text for the following reason: The study does report on short-term viability and recovery of zooplankton communities after exposure to glyphosate. However, the study design, test system and species tested (study conducted in Brazil with native, wild sampled organisms) are not relevant for the European regulatory purposes. The study design does not resemble any test currently used in a regulatory context and no regulatory relevant endpoints can be derived from this study.
60	Ecotoxicology	Rodriguez- Miguel A. et al.	2021	Exposure to sublethal concentrations of the glyphosate-based herbicide Faena® increases sensitivity in the progeny of the American cladoceran Daphnia exilis (Herrick, 1895).	Environmental science and pollution research international, (2021): Ahead of Print	The article has been classified as not relevant by full text for the following reason: The glyphosate formulation tested is the representative formulation for the glyphosate EU renewal. The representative formulation for the glyphosate EU renewal is MON 52276, which has a nominal glyphosate acid equivalent (a.e.) content of 360 g/L, formulated using glyphosate isopropyl-ammonium salt and a quaternary-ammonium based surfactant. Moreover, it is unclear whether the formulation tested contained POEA or not. In the introduction of this paper, the author states that "Polyoxyethylene tallow amine (POEA) is a common surfactant included in glyphosate-based herbicides; it is assumed to be the main responsible for the toxicity of the commercial products in some aquatic organisms (Perkins et al. 2000; Thompson et al. 2004)." This statement adds uncertainty concerning the relevance of the findings in the paper to the EU renewal of glyphosate.  In addition, the composition of formulations is an important consideration when comparing the endpoints achieved in public literature with those achieved in regulatory studies conducted with either the technical material or studies conducted with the representative formulation MON 52276. Co-formulants may ameliorate or enhance potential effects on test organisms. For example, POEA based surfactants (not permitted for use in Europe) or surfactants with similar structure, may lead to enhanced sensitivity.  For this reason and the uncertainties associated with the product tested (surfactant system not specified, may contain POEA -> POEA based surfactants are not to be used in agrochemical products in the EU), the article is not considered relevant for use in risk assessment.
61	Ecotoxicology	Sanchez Albanil J. A. et al.	2021	Glyphosate-based herbicides affect behavioural patterns of the livebearer Jenynsia multidentata.	Environmental science and pollution research international, (2021): Ahead of Print	The article has been classified as not relevant by full text for the following reason: None of the glyphosate formulations tested is the representative formulation for the glyphosate EU renewal. The representative formulation for the glyphosate EU renewal is MON 52276, which has a nominal glyphosate acid equivalent (a.e.) content of 360 g/L, formulated using glyphosate isopropyl-ammonium salt and a quaternary-ammonium based surfactant. Moreover, Roundup Original (RO) and Roundup Transorb (RT) contain POEA (stated by the authors in the Materials and methods part of the paper "RO is a liquid formulation composed of glyphosate isopropylamine salt (IPA) (480 g/L), glyphosate acid equivalent (360 g/L GlyAE) and surfactant MON 0818, the Monsanto code for the POEA designation. RT is also a liquid made from glyphosate isopropylamine salt (IPA), but at 648 g/L, glyphosate acid equivalent, at 480 g/L GlyAE, and POEA.). The 3rd formulation tested was Roundup RWG which is a granular formulation. The representative formulation for the glyphosate EU renewal is a soluble concentrate (SL)  The composition of formulations is an important consideration when comparing the endpoints achieved in public literature with those achieved in regulatory studies conducted with either the technical material or studies conducted with the representative formulation MON 52276. Co-formulants may ameliorate or enhance potential effects on test organisms. For example,

Submission Number	Technical section	Author(s)	Year	Title	Source	Reason for not including publication in dossier (based on relevance criteria)
						POEA based surfactants (not permitted for use in Europe) or surfactants with similar structure, may lead to enhanced sensitivity. For this reason and the fact that POEA based surfactants are not to be used in agrochemical products in the EU, the article is not considered relevant for use in risk assessment.
62	Ecotoxicology	Straw E. A. et al.	2021	Roundup causes high levels of mortality following contact exposure in bumble bees.	JOURNAL OF APPLIED ECOLOGY, (2021): Ahead of Print	The article has been classified as not relevant by full text for the following reason: The products used in the study are not related to the representative formulation for the glyphosate EU renewal. 'Roundup No glyphosate' contains 'acetic acid' only. 'Weedol' is a mixture of glyphosate and pyraflufen-ethyl and 'Roundup Ready-To-Use' is a mixture of glyphosate and pelargonic acid (effects observed cannot be attributed to the substance of concern, i.e. mixture toxicity). The surfactant system used in 'Roundup ProActive is alkyl polysaccharide + nitronyl based, whereas the surfactant used in the representative formulation (MON 52276) for the glyphosate EU renewal is quaternary-ammonium based. The composition of formulations is an important consideration when comparing the endpoints achieved in public literature with those achieved in regulatory studies conducted with either the technical material or studies conducted with the representative formulation MON 52276. Co-formulants may ameliorate or enhance potential effects on test organisms. As the performance / efficacy of herbicidal formulations is dependant on the surfactant system / co-formulants, the findings in the paper cannot be related to the representative formulation, and are therefore not relevant to the regulatory risk assessment for the glyphosate EU renewal.  Further points for clarification:  The authors acknowledge in the paper that tier methodology is not designed to replicate field realistic exposure (spraying conditions or label recommended application rates), it is instead designed to assess the lethality (hazard) the herbicide products pose to bumble bees.  The results from this study are not surprising considering that the bees were confined and directly sprayed with high volumes of the formulations and in some instances at application rates that greatly exceeded registered rates.  It cannot be concluded from this study that there will be unacceptable risk to bees from applications of lawn and garden and agricultural Roundupâ formulations when
63	Ecotoxicology	Sylwestrzak Z. et al.	2021	Ecotoxicological Studies on the Effect of Roundup(®) (Glyphosate Formulation) on Marine Benthic	International journal of environmental research and public health, (2021), Vol. 18, No. 3	The article has been classified as not relevant by full text for the following reason: It is not possible to confirm the identity of the test item used in the study as only 'Roundup' is mentioned. Roundup is a brand that contains multiple glyphosate-based herbicides, that contain different co-formulants. Of most importance to the toxicity profile associated with a particular product is whether that product contained POEA based surfactants (not permitted for use in Europe) or surfactants with similar structure. POEA surfactant was discussed on

Submission Number	Technical section	Author(s)	Year	Title	Source	Reason for not including publication in dossier (based on relevance criteria)
				Microalgae.		multiple occasions in the paper. These statements add uncertainty concerning the relevance of the findings in the paper to the EU renewal of glyphosate. Given this uncertainty over what was tested in this study, the paper is not considered relevant to the glyphosate EU renewal.
64	Ecotoxicology	Szabo R. et al.	2020	Toxicity test of individual and combined toxic effects of glyphosate herbicide and heavy metals on chicken embryos.	AGROFOR International Journal, (2020), Vol. 5, No. 3, pp. 64-71	The article has been classified as not relevant by full text for the following reason: Glialka Star is not the representative formulation for the glyphosate EU renewal. In addition it contains etheralkylamine ethoxylate (https://www.gazdabolt.hu/gyomirto-szer/1710-glialka-star-1-l.html; under "Dokumentok"), which does have a similar structure to POEA. Glyphosate based formulations that contain POEA (polyethoxylated tallow amine) surfactants or surfactants of similar chemical structure, are generally more toxic than the active substance itself. In addition, the composition of formulations is an important consideration when comparing the endpoints achieved in public literature with those achieved in regulatory studies conducted with either the technical material or studies conducted with the representative formulation MON 52276. Co-formulants may ameliorate or enhance potential effects on test organisms. For example, POEA based surfactants (not permitted for use in Europe) or surfactants with similar structure, may lead to enhanced sensitivity. For this reason, the findings in the paper cannot be related to the representative formulation, and are therefore not relevant to the regulatory risk assessment for the glyphosate EU renewal.
65	Ecotoxicology	Zeng H. et al.	2021	Physiological and metagenomic strategies uncover the rhizosphere bacterial microbiome succession underlying three common environmental stresses in cassava.	Journal of hazardous materials, (2021), Vol. 411, Article No. 125143	The article has been classified as not relevant by full text for the following reason: The study reports on dynamics of rhizosphere bacterial microbiome of cassava under glyphosate exposure. The reported results are entirely on a molecular or cellular level and are hence not relatable to the EU level risk assessment. Cassava plant growth is also reported, but only graphically and it is not the scope of the publication. The study is therefore considered non-relevant.
66	Fate and behaviour in the environment	Hartmann A. et al.	2021	Risk of groundwater contamination widely underestimated because of fast flow into aquifers.	Proceedings of the National Academy of Sciences of the United States of America, (2021), Vol. 118, No. 20, Article No. e2024492118	The article has been classified as not relevant by full text for the following reason: A continental-scale model to quantify the risk of groundwater contamination with glyphosate and other compounds in the carbonate rock regions of Europe, North Africa and the Middle East was developed. The consistency of the model for glyphosate was evaluated with US data. The article does not report any measured data. The model results were qualitatively compared with referenced literature data for US, Switzerland and Ireland.
67	Residues in or on treated products, food and feed	Cebotari V., Buzu I.	2020	Conformity of rapi, peas and maize flowers, concerning pesticide residues for organic beekeeping.	Scientific Papers, Series D. Animal Science, (2020), Vol. 63, No. 1, pp. 415-421	The article has been classified as not relevant by full text for the following reason: Monitoring of flowers of rape, pea and maize flowers for residues of glyphosate in Moldova (1 sampling site per crop, 5 replicate samples per crop). Glyphosate was detected in all samples. The study is not reliable: No description of the analytical procedure and no analytical validation data. In addition, the publication cannot be used to derive an endpoint. Furthermore, since the dataset is far too small to be considered representative of a country or region and since the agricultural practice at the sampling sites is not reported, the data are not usable or supportive for regulatory evaluations.
68	Residues in or on treated products, food and feed	Taghizadeh S. F. et al.	2021	Residues levels of pesticides in walnuts of Iran and associated health risks.	Human and Ecological Risk Assessment, (2021), Vol. 27, No. 1	The article has been classified as not relevant by full text for the following reason: Monitoring data from Iran on pesticides in walnuts (sampling from 5 sites). Glyphosate was detected in samples from 4 sites (no information provided on sample size, residue range in mg/kg). The study is not reliable and thus not relevant: It is unclear what was analysed: "Green husk and

Submission Number	Technical section	Author(s)	Year	Title	Source	Reason for not including publication in dossier (based on relevance criteria)
						hard shells of walnuts were separated and then homogenized". Analytical method used was GC/MS. Extraction with acetonitrile. No information on how glyphosate is used in nut orchards. Sample size and residue levels not provided in tabular form. Unclear statistics which cannot be reproduced.
69	Residues in or on treated products, food and feed	Tiurina D. G. et al.	2021	Glyphosate in diets for poultry.	Ptitsevodstvo, (2021), No. 3, pp. 27-30	The article has been classified as not relevant by full text for the following reason: Very limited information on glyphosate in poultry feed. One in-vitro experiment with baceria (Bacillus megaterium) incubation on glyphosate containing medium, only very limited description. The study is not reliable and thus not relevant: Poorly described study with some poultry feed monitoring data and an irrelevant in-vitro assay on bacterial degradation of glyphosate. The exact nature/composition of the analysed samples is not given. There is no information to assess the accuracy of the residue determination.
70	Toxicology and metabolism	Cardoso M. F. C. et al.	2021	Cardiovascular damage associated with subchronic exposure to the glyphosate herbicide in Wistar rats.	Toxicology and industrial health, (2021), Vol. 37, pp. 210-218	The article has been classified as not relevant by full text for the following reason: The publication is dealing with a glyphosate formulation Roundup Original. It is known that this formulation contains POEA. The representative formulation for the glyphosate AIR5 does not contain POEA. POEA is banned in the EU. Thus the paper is not relevant to the EU glyphosate renewal. In addition, the publication does not provide any relevant information to be used in the risk assessment. There are no HCD to understand the relevance of the observed increase of fatty streaks. The conclusion of glyphosate atherogenic potential is not supported either by other correlated histopathology findings and/or appropriated biomarker of atherogenic risk.
71	Toxicology and metabolism	Panza S. B. et al.	2021	Perinatal exposure to low doses of glyphosate-based herbicide combined with a high-fat diet in adulthood causes changes in the jejunums of mice.	Life sciences, (2021), Vol. 275, Article No. 119350	The article has been classified as not relevant by full text for the following reason: The publication is dealing with a glyphosate formulation Roundup Original. It is known that this formulation contains POEA. The representative formulation for the glyphosate AIR5 does not contain POEA. POEA is banned in the EU. Thus the paper is not relevant to the EU glyphosate renewal.
72	Toxicology and metabolism	Romano R. M. et al.	2021	Could Glyphosate and Glyphosate- Based Herbicides Be Associated With Increased Thyroid Diseases Worldwide?	Frontiers in endocrinology, (2021), Vol. 12, Article No. 627167	The article has been classified as not relevant by full text for the following reason: This article is a review of other publications. No study developed for glyphosate in this documents. This article is not relevant for risk assessment and does not bring any new information to the renewal dossier.
73	Toxicology and metabolism	Stewart B. W. et al.	2021	Enhanced communication of IARC Monograph findings to better achieve public health outcomes.	CARCINOGENESIS, (2021), Vol. 42, No. 2, pp. 159-168	The article has been classified as not relevant by full text for the following reason: The article is a summary of keywords to be used to improve communication to reach public health outcomes. No study developed for glyphosate in this documents. This article is not relevant for risk assessment and does not bring any new information to the renewal dossier.
74	Toxicology and metabolism	Wang R. et al.	2021	Renal tubular injury induced by glyphosate combined with hard water: the role of cytosolic phospholipase A2.	Annals of translational medicine, (2021), Vol. 9, No. 2, Article No. 130	The article has been classified as not relevant by full text for the following reason: This publication suggests renal tubulary injury induced by glyphosate based formulation containing POEA surfactant combined with hard water. However, these data were obtained at excessively high doses of POEA surfactant, which are not relevant the EU level regulatory review. The lack of substantial body weight loss and potentially mortality at these exceedingly high POEA oral exposures for 90-days are not consistent with data published in the US EPA assessment

Submission Number	Technical section	Author(s)	Year	Title	Source	Reason for not including publication in dossier (based on relevance criteria)
						for this POEA surfactant, with a NOAEL of 33 mg/kg bw/day and 39 mg/kg bw/day in males/females, respectively, and LOAEL of 99 mg/kg bw/day and 123 mg/kg bw/day in males/females, respectively (US EPA, 2009. Alkyl amine polyalkoxylates Human Health Risk Assessment, pages 58 and 59 of 94). Therefore, any findings are likely a consequence of overt toxicity to the gastrointestinal tract of treated animals. Furthermore, key study details on feed and water consumption are lacking, and as such the results are difficult to place in context relative to these key indicators of animal health.

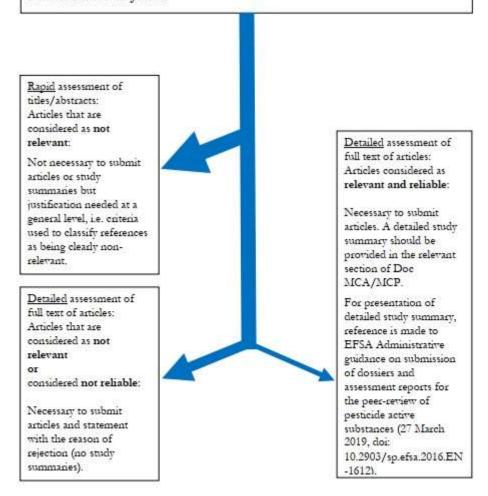
## Appendix 1: AGG ADVICE on how to present the literature search in the dossier

ASSESSMENT GROUP ON GLYPHOSATE (AGG)

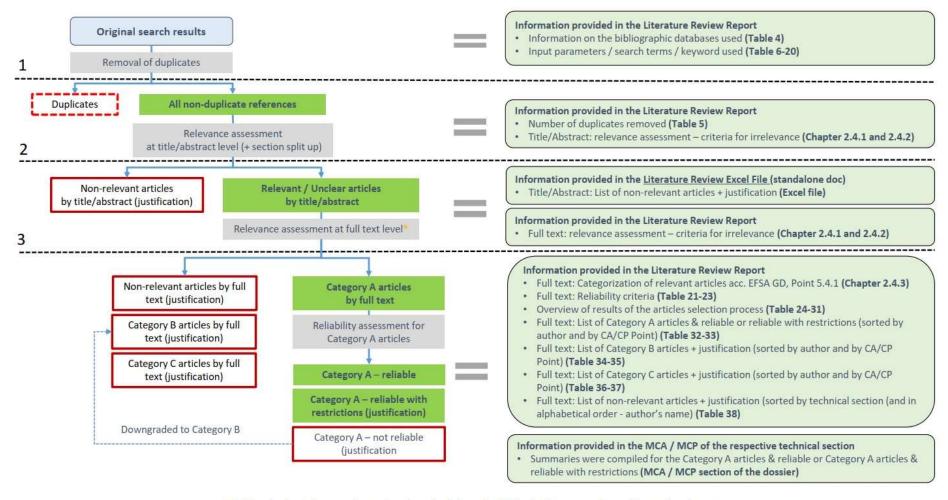
October 2019

## ADVICE TO GTF2: HOW TO PRESENT THE LITERATURE SEARCH IN THE DOSSIER TO BE SUBMITTED JUNE 2020

The literature search should be carried out and presented as recommended in the EFSA Guidance EFSA Journal 2011;9(2):2092) including its recently published Appendix, available at the EFSA Journal.



## **Appendix 2: The process of articles selection**



All articles (and their translations) evaluated at full-text level (detailed assessment) are submitted to the AGG.

## Appendix 3: ORIGINAL SEARCH QUERY - January 2021 – 14 May 2021

Preparing the search queries on STN:

FILE 'STNGUIDE' ENTERED AT 12:26:50 ON 13 MAY 2021

- CHARGED TO COST=113898 L1 QUE SPE=ON ABB=ON PLU=ON GLYPHOSAT? OR GLIFOSAT? OR GLYFOSAT? 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 OR AMINOMETHYL PHOSPHONIC OR AMINOMETHYLPHOSPHONIC SAVE TEMP L1 GLY1/O
- QUE SPE=ON ABB=ON PLU=ON 2 ACETYL PHOSPHONOMETHYL AMINO ACETIC ACID OR N ACETYL GLYPHOSATE OR N ACETYLGLYPHOSATE OR N L2 ACETYL N PHOSPHONOMETHYL GLYCINE OR 129660-96-4 OR N ACETYL AMPA OR ACETYLAMINO METHYL PHOSPHONIC ACID OR ACETYLAMINOMETHYL PHOSPHONIC ACID OR 57637-97-5 SAVE TEMP L2 GLY2/Q
- QUE SPE=ON ABB=ON PLU=ON 2617-47-2 OR HYDROXYMETHANEPHOSPHON IC ACID OR HYDROXYMETHYL PHOSPHONATE OR HYDROXYMETHYL PHOSPHONI L3 C ACID OR METHANEHYDROXYPHOSPHONIC ACID OR PHOSPHONIC ACID(1W)H YDROXYMETHYL OR PHOSPHONOMETHANOL
- QUE SPE=ON ABB=ON PLU=ON HYDROXYMETHYLPHOSPHONATE OR 1.4 HYDROXYMETHYLPHOSPHONIC ACID
- L5
- QUE SPE=ON ABB=ON PLU=ON L3 OR L4 SAVE TEMP L5 GLY3/Q QUE SPE=ON ABB=ON PLU=ON 35404-71-8 OR METHYLAMINO METHYL L6 PHOSPHONIC ACID OR METHYLAMINOMETHYL PHOSPHONIC ACID OR METHYLAMINOMETHYLPHOSPHONIC ACID OR N METHYL AMPA OR NSC
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- L9 ONATE OR METHANEPHOSPHONIC ACID OR METHYL PHOSPHONIC ACID OR METHYLPHOSPHONIC ACID OR NSC 119358 OR PHOSPHONIC ACID METHYL OR PHOSPHONIC ACID P METHYL QUE SPE=ON ABB=ON PLU=ON (L6 OR L7 OR L8 OR L9)
- L10
- L11
- SAVE TEMP L10 GLY4/Q QUE SPE=ON ABB=ON PLU=ON 24569-83-3 OR 2 METHYL PHOSPHONOMET HYL AMINO ACETIC ACID OR 2 METHYL PHOSPHONOMETHYL AMINOACETIC ACID OR ACETIC ACID 2 N METHYL N PHOSPHONATOMETHYL AMINO OR GLYCINE N METHYL N PHOSPHONOMETHYL OR GLYPHOSATE N METHYL OR METHYL GLYPHOSATE

  QUE SPE=ON ABB=ON PLU=ON METHYL PHOSPHONOMETHYL AMINO
- L12 ACETIC ACID OR METHYL PHOSPHONOMETHYL AMINOACETIC ACID OR N METHYL N PHOSPHONOMETHYL GLYCINE OR N METHYLGLYPHOSATE OR N PHOSPHONOMETHYL N METHYL GLYCINE OR N PHOSPHONOMETHYL N METHYLGLYCINE
- L13
- QUE SPE=ON ABB=ON PLU=ON (L11 OR L12)

  SAVE TEMP L13 GLY5/Q

  QUE SPE=ON ABB=ON PLU=ON TOX? OR HAZARD? OR ADVERSE OR
  HEALTH OR NOAEL OR NOEL OR LOAEL OR LOEL OR BMD? OR IN VIVO OR
  IN VITRO OR INVIVO OR INVITRO OR MODE OF ACTION OR SKIN? OR
  EYE? OR IRRIT? OR SENS!? OR ALLERG?

  OUE SPE=ON ADPE-ON BLI-ON BAT OR DATS OR DOG? OR PARDET? OR L14
- QUE SPE=ON ABB=ON PLU=ON RAT OR RATS OR DOG? OR RABBIT? OR GUINEA PIG? OR MOUSE OR MICE OR METABOLISM OR METABOLITE? OR METABOLIC OR DISTRIBUTION OR ADSORPTION OR EXCRETION OR L15
- ELIMINATION OR KINETIC OR CYTOCHROME OR ENZYM?

  QUE SPE=ON ABB=ON PLU=ON GEN? OR MUTA? OR CHROMOS? OR L16 CLASTOGEN? OR DNA OR CARCINO? OR CANCER? OR TUMOR? OR TUMOUR? OR ONCOG? OR ONCOL? OR MALIGN? OR IMMUN? OR NEUR? OR ENDOCRIN?
- OR HORMON? OR GONAD? OR DISRUPT?

  QUE SPE=ON ABB=ON PLU=ON REPRODUCT? OR DEVELOPMENT? OR
  MALFORM? OR ANOMAL? OR FERTIL? OR FOET? OR FET? OR MATERN? OR
  PREGNAN? OR EMBRYO? OR EPIDEM? OR MEDICAL? OR POISON? OR L17 EXPOSURE OR OPERATOR? OR BYSTANDER? OR RESIDENT? OR WORKER? OR
- OUE SPE=ON ABB=ON PLU=ON BIOMONITORING OR HUMAN EXPOSURE OR L18 MICROBIOME OR OXIDATIVE STRESS OR APOPTOSIS OR NECROSIS OR CYTOTOXICITY OR POLYOXYETHYLENEAMINE OR POEA OR SURFACTANT OR
- L19
- CYTOTALCHY OR POLYOXYETHY LENEAMINE OR POEA OR SURFACTANT C RISK ASSESSMENT?

  QUE SPE=ON ABB=ON PLU=ON (L14 OR L15 OR L16 OR L17 OR L18)

  SAVE TEMP L19 TOX/Q

  QUE SPE=ON ABB=ON PLU=ON UPTAKE OR TRANSLOCATION OR RUMEN
  OR STORAGE STABILITY OR STORAGE OR STABILITY OR METABOLIC OR
  METABOLISM OR BREAKDOWN OR NATURE OF RESIDUES OR RESIDUE? OR L20
- METABOLISM OR BREAKDOWN OR NATURE OF RESIDUES OR RESIDUE? OF MAGNITUDE OF RESIDUES OR PROCESS? OR EFFECTS OF PROCESSING QUE SPE=ON ABB=ON PLU=ON DESSICANT OR PREHARVEST OR PREEMERG? OR ?RESISTANT? OR ?TOLERAN? OR TRANSGENIC OR HYDROLY? OR ROTATION? OR SUCCEED? OR PLANT? OR CROP? OR FEED? OR ANIMAL? OR LIVESTOCK? OR HEN OR CATTLE OR RUMINANT? QUE SPE=ON ABB=ON PLU=ON GOAT? OR COW? OR PIG? OR DIETARY OR ASSESSMENT OR RISK ASSESSMENT OR CONSUM? OR EXPOSURE L21
- L22
- QUE SPE=ON ABB=ON PLU=ON (L20 OR L21 OR L22) SAVE TEMP L23 RES/Q L23
- SAVE TEMP L23 RES/Q
  QUE SPE=ON ABB=ON PLU=ON SOIL OR WATER OR SEDIMENT OR
  DEGRADAT? OR PHOTO? OR SOIL RESIDUES OR SOIL ACCUMULAT? OR
  SOIL CONTAMINAT? OR MOBILITY OR SORPTION OR COLUMN LEACHING OR
  AGED RESIDUE OR LEACH? OR LYSIMETER OR GROUNDWATER
  QUE SPE=ON ABB=ON PLU=ON CONTAMINAT? OR MICROB? OR EXUDATION
  OR RHIZOSPHERE OR DISSIPATION OR SATURATED ZONE OR HYDROLYSIS
  OR DRIFT OR RUN-OFF OR RUNOFF OR DRAINAGE OR VOLAT? OR L24
- L25
- ATMOSPHERE OR LONG-RANGE TRANSPORT OR SHORT-RANGE TRANSPORT QUE SPE=ON ABB=ON PLU=ON TRANSPORT OR MICRONUTRIENT OR L26

PHOSPHATE OR IRON OR MANGANESE OR HALF-LIFE OR HALF-LIFE OR HALF-LIVES OR HALF-LIVES OR DT50 OR KINETICS OR OFF-SITE MOVEMENT OR REMOVAL OR DRINKING WATER OR WATER TREATMENT

- QUE SPE=ON ABB=ON PLU=ON ATMOSPHERIC DEPOSITION OR TILE-DRAINS OR SURFACE WATER OR MONITORING DATA OR DISINFECTANT OR 1.27 OZONE OR TILLAGE OR INFILTRATION OR HARD SURFACE OR RAINWATER OR RAIN WATER OR CHELAT? OR COMPLEX? OR MINERALIZATION OR PERSISTENCE OR LIGAND
- QUE SPE=ON ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27) L28
- SAVE TEMP L28 FATE/Q QUE SPE=ON ABB=ON PLU=ON TOX? OR ECOTOX? OR ?TOXIC OR ?TOXICITY OR HAZARD OR ADVERSE OR ENDOCRINE DISRUPT? OR BIOACCUMULATE? OR BIOMAGNIFI? OR BIOCONCENTRATION OR POISON OR EFFECT OR INDIRECT EFFECT? OR DIRECT EFFECT? OR BIODIVERS? OR
- PROTECTION GOALS OR ECO?

  QUE SPE=ON ABB=ON PLU=ON IMPACT OR POPULATION OR COMMUNITY
  OR WILDLIFE OR INCIDENT OR PEST OR BIRD? OR ACUTE OR CHRONIC
  OR LONG-TERM OR MALLARD OR DUCK OR QUAIL OR BOBWHITE OR ANAS? L30 OR COLINUS? OR WILD OR DIETARY OR AQUATIC OR FISH OR DAPHNI? OR ALG? OR CHIRON?
- QUE SPE=ON ABB=ON PLU=ON SEDIMENT DWELL? OR BENTHIC OR LEMNA OR MARIN? OR ESTUARINE OR CRUSTA? OR GASTROPOD? OR INSECT OR MOLLUSC OR REPTILE OR AMPHIB? OR BEE? OR APIS OR L31
- APIDAE OR BUMBLE? OR COLONY OR HIVE OR POLLINATOR
  QUE SPE=ON ABB=ON PLU=ON PLANT AND (SUBMERGE? OR EMERGE?)
  QUE SPE=ON ABB=ON PLU=ON SOLITARY OR ALG? OR AQUATIC OR
  FRESHWATER OR VERTEBRAT? OR MAMMAL? OR RAT OR MOUSE OR MICE OR L32 L33 RABBIT OR HARE OR PROTECTION OR MODEL? OR VOLE OR PEST OR ARTHROPOD? OR BENEFICIALS OR TYPHLODROMUS OR APHIDIUS OR
- PARASITOID QUE SPE=ON ABB=ON PLU=ON PREDATOR OR CHRYSOPERLA OR ORIUS L34 OR SPIDER OR WORM? OR ?WORM OR EISENIA OR SOIL OR COLLEMBOL? OR MACRO ORGANISM OR FOLSOMIA OR SPRINGTAIL OR DECOMPOS? OR MICRO ORGANISMS OR MICROORGANISMS OR MICROBIAL OR CARBON OR
- QUE SPE=ON ABB=ON PLU=ON PLANT? OR VEGETATIVE VIGO? OR L35 SEEDLING OR GERMINATION OR MONOCOT? OR DICOT? OR SEWAGE OR ACTIVATED SLUDGE OR BIODEGRAD? OR BIOACCUMULATION? OR AMPHIB? OR REPTILE? OR AQUATIC PLANT OR BENEFICIAL
- QUE SPE=ON ABB=ON PLU=ON (L29 OR L30 OR L31 OR L32 OR L33 L36 OR L34 OR L35) SAVE TEMP L36 ECO/Q

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 12:37:35 ON 13 MAY 2021

Final search - Update May 2021:

FILE 'MEDLINE' ENTERED AT 11:33:55 ON 14 MAY 2021

CHARGED TO COST=113898

- 4624 S GLY1/Q OR GLY2/Q OR GLY3/Q OR GLY4/Q OR GLY5/Q 183 S L1 AND ED>20210104
- $181~\mathrm{S}$  L2 NOT (COMMENT? OR DISSERTATION OR EDITORIAL OR MEETING? OR SAVE TEMP L3 GLYMEDL/A L3

FILE 'AGRICOLA' ENTERED AT 11:37:05 ON 14 MAY 2021

CHARGED TO COST=113898

- 7599 S GLY1/Q OR GLY2/Q OR GLY3/Q OR GLY4/Q OR GLY5/Q
- 264 S L4 AND ED>20210104
- 264 S L5 NOT (COMMENT? OR DISSERTATION OR EDITORIAL OR MEETING? OR SAVE TEMP L6 GLYAGRI/A

FILE 'BIOSIS' ENTERED AT 11:41:49 ON 14 MAY 2021

- CHARGED TO COST=113898 L7  $\,$  11785 S GLY1/Q OR GLY2/Q OR GLY3/Q OR GLY4/Q OR GLY5/Q
- 277 S L7 AND ED>20210104
- 258 S L8 NOT (COMMENT? OR DISSERTATION OR EDITORIAL OR MEETING? OR SAVE TEMP L9 GLYBIOS/A

FILE 'CABA' ENTERED AT 11:43:47 ON 14 MAY 2021

- CHARGED TO COST=113898 L10 19552 S GLY1/Q OR GLY2/Q OR GLY3/Q OR GLY4/Q OR GLY5/Q
- 467 S L10 AND ED>20210104 467 S L11 NOT (COMMENT? OR DISSERTATION OR EDITORIAL OR MEETING? OR L12 SAVE TEMP L12 GLYCABA/A

FILE 'FSTA' ENTERED AT 11:45:37 ON 14 MAY 2021

CHARGED TO COST=113898

- 582~S~GLY1/Q~OR~GLY2/Q~OR~GLY3/Q~OR~GLY4/Q~OR~GLY5/QL13
- 33 S L13 AND ED=20210104 30 S L14 NOT (COMMENT? OR DISSERTATION OR EDITORIAL OR MEETING? OR L15 SAVE TEMP L15 GLYFSTA/A

FILE 'PQSCITECH' ENTERED AT 11:47:54 ON 14 MAY 2021

CHARGED TO COST=113898

- 5625 S GLY1/Q OR GLY2/Q OR GLY3/Q OR GLY4/Q OR GLY5/Q 104 S L16 AND ED>20210104
- 74~S~L17~NOT~(COMMENT?~OR~DISSERTATION~OR~EDITORIAL~OR~MEETING?~OR~SAVE~TEMP~L18~GLYPQSCI/AL18

FILE 'TOXCENTER' ENTERED AT 11:50:25 ON 14 MAY 2021

CHARGED TO COST=113898

- 17721 S GLY1/Q OR GLY2/Q OR GLY3/Q OR GLY4/Q OR GLY5/Q
- L20
- 573 S L19 AND ED>20210104
  383 S L20 NOT (COMMENT? OR DISSERTATION OR EDITORIAL OR MEETING? OR L21 SAVE TEMP L21 GLYTOXC/A

FILE 'EMBASE' ENTERED AT 11:52:13 ON 14 MAY 2021 CHARGED TO COST=113898

- L22 L23 6164 S GLY1/Q OR GLY2/Q OR GLY3/Q OR GLY4/Q OR GLY5/Q
- 127 S L22 AND ED>20210104 127 S L23 NOT (COMMENT? OR DISSERTATION OR EDITORIAL OR MEETING? OR SAVE TEMP L24 GLYEMBA/A L24

#### FILE 'ESBIOBASE' ENTERED AT 11:54:26 ON 14 MAY 2021

- CHARGED TO COST=113898 L25  $\,$  5381 S GLY1/Q OR GLY2/Q OR GLY3/Q OR GLY4/Q OR GLY5/Q
- L26
- 162 S L25 AND ED=20210104 162 S L26 NOT (COMMENT? OR DISSERTATION OR EDITORIAL OR MEETING? OR SAVE TEMP L27 GLYESBIO/A

### FILE 'HCAPLUS' ENTERED AT 11:56:17 ON 14 MAY 2021

- CHARGED TO COST=113898 L28 30693 S GLY1/Q OR GLY2/Q OR GLY3/Q OR GLY4/Q OR GLY5/Q
- L29 L30
- 729 S L28 AND ED=20210104 343 S L29 NOT (COMMENT? OR DISSERTATION OR EDITORIAL OR MEETING? OR SAVE TEMP L30 GLYHCAP/A

#### FILE 'SCISEARCH' ENTERED AT 11:58:14 ON 14 MAY 2021

- SAVE TEMP L33 GLYSCIS/A

# FILE 'HOME' ENTERED AT 12:00:27 ON 14 MAY 2021 CHARGED TO COST=113898

FILE 'MEDLINE, AGRICOLA, BIOSIS, CABA, FSTA, PQSCITECH, TOXCENTER, EMBASE, ESBIÓBASE, HCAPLUS, SCISEARCH' ENTERED AT 12:03:58 ON 14 MAY 2021 CHARGED TO COST=113898

- 1522 DUP REM L3 L6 L9 L12 L15 L18 L21 L24 L27 L30 L33 (1121 DUPLICAT SAVE L34 GLY202105/A 1237 S L34 AND TOX/Q SAVE TEMP L35 GLYTOX/A 1364 S L34 AND RES/Q L34
- L35
- L36
- SAVE TEMP L36 GLYRES/A 932 S L34 AND FATE/Q L37

- L38
- 932 S L34 AND FATE/Q
  SAVE TEMP L37 GLYFATE/A
  1436 S L34 AND ECO/Q
  SAVE TEMP L38 GLYECO/A
  1517 S L35 OR L36 OR L37 OR L38
  SAVE L39 GLY202105FIN/A L39