# **Literature Review Report**

Scientific peer-reviewed open literature covering the publication period of 14 May 2021 to August 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 113898-CA9-4

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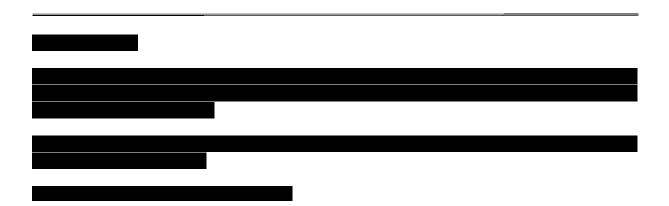


Date of search(es):

08 September 2021

# **Content**

1	Su	mmary	·	5
2	Int	roducti	ion	8
	2.1	Bibli	ographic databases used in the literature search	10
	2.2	Inpu	t parameters used in the literature search	14
	2.3	Keyv	words and search filters used in the literature search	16
	2.4	4 Relevance assessment		19
		2.4.1	Criteria applied for "non-relevance"	19
		2.4.2	Additional criteria for articles on the health and exposure of glyphosate	20
		2.4.3	Categorization of "relevant" articles at full-text level	21
	2.5	Relia	ability assessment	22
3	Sea	arch res	sults	27
			ant (category A) articles after detailed assessment: sorted by data require	` '
•••••	•••••	••••••		31
Table	33:	Releva	ant (category A) articles after detailed assessment: sorted by author(s)	33
			ant but supplementary (category B) articles after detailed assessment: sor	
	•		nt(s)	
			ant but supplementary (category B) articles after detailed assessment: sor	•
	` ′		es of unclear relevance (category C) after detailed assessment: sorted by d	
			es of uncreal relevance (energory e) area declared assessment, sorted by a	
Table	37:	Article	es of unclear relevance (category C) after detailed assessment: sorted by	
autho	r(s)	•••••		63
			es excluded after detailed assessment (i.e. not relevant): sorted by technica author)	
Appe	ndix	1: AG	GG ADVICE on how to present the literature search in the dossier	72
Appe	ndix	<b>2:</b> The	e process of articles selection	73
Appe	ndix	3: OR	RIGINAL SEARCH QUERY – 14 May 2021 – August 2021	74



#### 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.

### 1 Summary

A literature search for glyphosate and its metabolites¹ 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) 1107/2009²", and the Appendix to the EFSA 2092 Guidance Document "Further guidance on performing and presenting the literature search"³, and the EFSA supporting publication from 2019⁴ "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 72) 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 14 May 2021 to August 2021 and is supplementary to the previous searches covering the publication period of January 2010 to 14 May 2021.<sup>6</sup>

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

In total, 543 articles were identified upon removal of duplicates within the current search (14 May 2021 to August 2021) and articles found already in the previous searches (January 2010 to 14 May 2021).

All 543 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 470 of the 543 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 CA9-4 Literature Review Excel File).

For the remaining 73 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, 113898-CA9-2, and 113898-CA9-3 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 23 articles of the remaining 73 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 50 articles of the 73 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>	237	237	n.a.	n.a.	n.a.
Analytical methods a)	43	43	n.a.	n.a.	n.a.
Other non- relevant categories b)	38	38	n.a.	n.a.	n.a.
Ecotoxicology	82	50	32	15	17
E-fate	61	55	6	3	3
Residues	13	4	9	0	9
Toxicology	69	43	26	5	21
Total	543	470	73	23	50

<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.

Page 7 of 76

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	10	5	2
E-fate	0	3	0
Residues	0	9	0
Toxicology	0	15	6
Total	10	32	8

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 73) 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.

#### 2 Introduction

A literature search for glyphosate and its metabolites¹ 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) 1107/2009²", and the Appendix to the EFSA 2092 Guidance Document "Further guidance on performing and presenting the literature search"³, and the EFSA Supporting publication from 2019⁴ "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 72) 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, three additional supplementary literature searches of the glyphosate scientific peer-reviewed open literature were performed in January 2021, May 2021, and September 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). The third search, from September 2021, covers the publication period of 14 May 2021 to August 2021 and is summarized in this Literature Review Report (Document ID: 113898-CA9-4). 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 N-malonyl-AMPA	14 May 2021 – August 2021	Onducted on  08 September 2021
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:	08 September 2021	08 September 2021	08 September 2021	08 September 2021	
Database covers records:	1970-present	1926-present	1973-present	1907-present and more than 180,000 pre-1907	
Date of the latest database update:	04 August 2021	01 September 2021	01 September 2021	07 September 2021	
Language limit:	No	No	No	No	
Document types excluded 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:	D. 1				
	Details are summarized in Chapter 2.2 and 2.3.				
Total number of records retrieved:	287	239	353	272	

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

Data requirement(s) captured in the search	Details of the search(es)			
captarea in the search	5. MEDLINE	6. EMBASE	7. TOXCENTER	
Justification for choosing the source:	Provides literature from every area of medicine.	Provides literature from biomedicinal and pharmaceutical fields, e.g. bioscience, biochemistry, human medicine, forensic science, paediatrics, pharmacy, pharmacology, drug therapy, psychiatry, public health, biomedical engineering, environmental science.	Provides literature on pharmacological, biochemical, physiological, and toxicological effects of drugs and other chemicals.	
Number of records in the database at the time of search:	> 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:	08 September 2021	08 September 2021	08 September 2021	
Database covers records:	1946-present	1974-present	1907-present	
Date of the latest database update:	07 September 2021	07 September 2021	06 September 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:	158	120	353	

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:	08 September 2021	08 September 2021	08 September 2021	08 September 2021
Database covers records:	1969-present	1962-present	1994-present	1974-present
Date of the latest database update:	03 September 2021	24 August 2021	01 September 2021	06 September 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:	Details are summarized in Chapter 2.2 and 2.3.			
Total number of records retrieved:	19	111	129	387

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

Scope of the search	After automatic removal of duplicates within the databases in the current search (14 May 2021-Aug 2021)	After applying search filters <sup>a)</sup> within the current search (14 May 2021-Aug 2021)	After manual removal of duplicates <sup>b)</sup> within the current search (14 May 2021- Aug 2021) and entries found already in the previous searches (Jan 2010 – 14 May 2021) <sup>c)</sup>
14 May 2021 - Aug 2021			
Glyphosate AMPA N-acetyl-AMPA N-acetyl-glyphosate HMPA N-methyl-AMPA N-glyceryl-AMPA N-malonyl-AMPA methylphosphonic acid N-methylglyphosate	1443	1431	543

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, LRR 113898-CA9-2 covers the publication period of 1 July 2020 to 31 December 2020, 113898-CA9-3 covers the publication period of 1 January 2021 to 14 May 2021.

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, 113898-CA9-2, and 113898-CA9-3.

Page 14 of 76

# 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, are provided in **Table 6 - Table 15**.

Table 6: Input parameters – active substance Glyphosate

Substance name	Glyphosate
	Salts: isopropylamine, potassium, ammonium, methylmethanamine
	Saits. Isopropytamine, potassium, ammonum, 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 methyl glycine 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 OR community OR wildlife OR incident 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? 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.
- 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 μg/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 μg/mL or 0.315 mM at 2 hours after oral intake of 2,000 mg/kg bw and 107 μg/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 μg/mL or 1 μM 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 μg/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.

Page 22 of 76

# 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.	

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 / statistica 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.		

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.	red. 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

In vivo studies	
C 11 11 10	
Guideline-specific	
Study in accordance to valid internationally accepted testing guidelines.	
Study performed according to GLP.	
Study completely described and conducted following scientifically acceptable standards.	
Test substance	
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.	
AMPA or other glyphosate metabolite is the tested substance.	
Study	
Test species clearly and completely described.	
Test conditions clearly and completely described.	
Route and mode of administration described.	
Dose levels reported.	
Number of animals used per dose level reported.	
Method of analysis described for analysis test media.	
Validation of the analytical method.	
Analytical verifications of test media.	
Complete reporting of effects observed.	
Statistical methods described.	
Historical control data of the laboratory reported.	
Dose-effect relationship reported.	

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.	2428	n.a.
Total number of articles after removal of duplicates within all databases.	1443	n.a.
Total number of articles after manual removal of duplicates. a)	543	n.a.
Number of articles excluded after rapid assessment (title / abstract).	470	See the Literature Review Excel File.
Total number of full-text documents assessed in detail.	73	n.a.
Number of articles excluded after detailed assessment ( <i>i.e.</i> not relevant).	23	See Table 38
Number of articles not excluded after detailed assessment. b)	50	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 (14 May 2021 – Aug 2021) and entries found already in the previous searches (Jan 2010 – 14 May 2021). 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)	82	n.a.
Number of articles excluded after rapid assessment (title / abstract).	50	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).	15	See Table 38
Number of articles not excluded after detailed assessment. b)	17	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 (14 May 2021 – Aug 2021) and entries found already in the previous searches (Jan 2010 – 14 May 2021). 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.

Page 28 of 76

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

	Number	Justification
Total number of articles after manual removal of duplicates. a)	61	n.a.
Number of articles excluded after rapid assessment (title / abstract).	55	See the Literature Review Excel File.
Total number of full-text documents assessed in detail.	6	n.a.
Number of articles excluded after detailed assessment ( <i>i.e.</i> not relevant).	3	See Table 38
Number of articles not excluded after detailed assessment. b)	3	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 (14 May 2021 – Aug 2021) and entries found already in the previous searches (Jan 2010 – 14 May 2021). 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)	13	n.a.
Number of articles excluded after rapid assessment (title / abstract).	4	See the Literature Review Excel File.
Total number of full-text documents assessed in detail.	9	n.a.
Number of articles excluded after detailed assessment (i.e. not relevant).	0	See Table 38
Number of articles not excluded after detailed assessment b)	9	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 (14 May 2021 – Aug 2021) and entries found already in the previous searches (Jan 2010 – 14 May 2021). 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)	69	n.a.
Number of articles excluded after rapid assessment (title / abstract).	43	See the Literature Review Excel File.
Total number of full-text documents assessed in detail	26	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)	21	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 (14 May 2021 – Aug 2021) and entries found already in the previous searches (Jan 2010 – 14 May 2021). 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 <sup>a)</sup>	43	n.a.
Number of articles excluded after rapid assessment (title / abstract).	43	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 (14 May 2021 – Aug 2021) and entries found already in the previous searches (Jan 2010 – 14 May 2021). 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)	237	n.a.
Number of articles excluded after rapid assessment (title / abstract).	237	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 (14 May 2021 – Aug 2021) and entries found already in the previous searches (Jan 2010 – 14 May 2021). 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)	38	n.a.
Number of articles excluded after rapid assessment (title / abstract).	38	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 (14 May 2021 – Aug 2021) and entries found already in the previous searches (Jan 2010 – 14 May 2021). 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 8.1.5	Diaz-Martín R. D. et al.	2021	Short exposure to glyphosate induces locomotor, craniofacial, and bone disorders in zebrafish (Danio rerio) embryos.	Environmental toxicology and pharmacology, (2021), Vol. 87, Article No. 103700	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 8.2.2, CP 10.2.2	Le Du-Carree J. et al.	2021	Developmental effect of parental or direct chronic exposure to environmental concentration of glyphosate on the larvae of rainbow trout, Oncorhynchus mykiss.	Aquatic toxicology, (2021), Vol. 237, Article No. 105894	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 8.2.2, CP 10.2.2	Le Du-Carree J. et al.	2021	Generational effects of a chronic exposure to a low environmentally relevant concentration of glyphosate on rainbow trout, Oncorhynchus mykiss.	The Science of the total environment, (2021), Vol. 801, Article No. 149462	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 8.2.6.1	Kaeoboon S. et al.	2021	Toxicity response of Chlorella microalgae to glyphosate herbicide exposure based on biomass, pigment contents and photosynthetic efficiency.	Plant Science Today, (2021), Vol. 8, No. 2, pp. 293-300	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 8.2.7	Mendes E. J. et al.	2021	Isolated and combined effects of glyphosate and its by-product aminomethylphosphonic acid on the physiology and water remediation capacity of Salvinia molesta.	Journal of hazardous materials, (2021), Vol. 417, Article No. 125694.	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 8.2.8	Vera M. S. et al.	2021	First evaluation of the periphyton recovery after glyphosate exposure.	Environmental pollution, (2021), Vol. 290, Article No. 117998	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	CP 10.1.3	Goodman R. M. et al.	2021	Influence of Herbicide Exposure and Ranavirus Infection on Growth and Survival of Juvenile Red-Eared Slider Turtles (Trachemys scripta elegans).	Viruses, (2021), Vol. 13, No. 8	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	CP 10.2.1	Fernandez C. et al.	2021	Toxic effects of chlorpyrifos, cypermethrin and glyphosate on the non-target organism Selenastrum capricornutum (Chlorophyta).	Anais da Academia Brasileira de Ciencias, (2021) Vol. 93, Article No. e20200233	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, CP 10.2.2	Houssou A. M. et al.	2021	Acute and Chronic Effects of a Glyphosate and a Cypermethrin-Based Pesticide on a Non-Target Species Eucypris sp. Vavra, 1891 (Crustacea, Ostracoda)	Processes, (2021), Vol. 9, No. 4	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.

KCA 9 Page 32 of 76

Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
10	CP 10.4.2.1	Wee J. et al.	2021	Temperature and Aging Affect Glyphosate Toxicity and Fatty Acid Composition in Allonychiurus kimi (Lee) (Collembola).	Toxics, (2021), Vol. 9, No. 6	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
1	Diaz-Martín R. D. et al.	CA 8.1.5	2021	Short exposure to glyphosate induces locomotor, craniofacial, and bone disorders in zebrafish (Danio rerio) embryos.	Environmental toxicology and pharmacology, (2021), Vol. 87, Article No. 103700	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	Fernandez C. et al.	CP 10.2.1	2021	Toxic effects of chlorpyrifos, cypermethrin and glyphosate on the non-target organism Selenastrum capricornutum (Chlorophyta).	Anais da Academia Brasileira de Ciencias, (2021) Vol. 93, Article No. e20200233	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	Goodman R. M. et al.	CP 10.1.3	2021	Influence of Herbicide Exposure and Ranavirus Infection on Growth and Survival of Juvenile Red-Eared Slider Turtles (Trachemys scripta elegans).	Viruses, (2021), Vol. 13, No. 8	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	Houssou A. M. et al.	CP 10.2.1, CP 10.2.2	2021	Acute and Chronic Effects of a Glyphosate and a Cypermethrin- Based Pesticide on a Non-Target Species Eucypris sp. Vavra, 1891 (Crustacea, Ostracoda)	Processes, (2021), Vol. 9, No. 4	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	Kaeoboon S. et al.	CA 8.2.6.1	2021	Toxicity response of Chlorella microalgae to glyphosate herbicide exposure based on biomass, pigment contents and photosynthetic efficiency.	Plant Science Today, (2021), Vol. 8, No. 2, pp. 293-300	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	Le Du-Carree J. et al.	CA 8.2.2, CP 10.2.2	2021	Developmental effect of parental or direct chronic exposure to environmental concentration of glyphosate on the larvae of rainbow trout, Oncorhynchus mykiss.	Aquatic toxicology, (2021), Vol. 237, Article No. 105894	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	Le Du-Carree J. et al.	CA 8.2.2, CP 10.2.2	2021	Generational effects of a chronic exposure to a low environmentally relevant concentration of glyphosate on rainbow trout, Oncorhynchus mykiss.	The Science of the total environment, (2021), Vol. 801, Article No. 149462	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	Mendes E. J. et al.	CA 8.2.7	2021	Isolated and combined effects of glyphosate and its by-product aminomethylphosphonic acid on the physiology and water remediation capacity of Salvinia molesta.	Journal of hazardous materials, (2021), Vol. 417, Article No. 125694.	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	Vera M. S. et al.	CA 8.2.8	2021	First evaluation of the periphyton recovery after glyphosate exposure.	Environmental pollution, (2021), Vol. 290, Article No. 117998	The article has been classified as relevant by full text - Category A and reliable with restrictions: A detailed summary for this article is provided.

KCA 9 Page 34 of 76

Submission Number	Author(s)	Data requirement (indicated by the corresponding CA / CP data point number)	Year	Title	Source	Justification
10	Wee J. et al.	CP 10.4.2.1	2021	Temperature and Aging Affect Glyphosate Toxicity and Fatty Acid Composition in Allonychiurus kimi (Lee) (Collembola).	Toxics, (2021), Vol. 9, No. 6	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 5.4.1	Nagy K. et al.	2021	Micronucleus Formation Induced by Glyphosate and Glyphosate-Based Herbicides in Human Peripheral White Blood Cells.	Frontiers in public health, (2021) Vol. 9, Article No. 639143	The article has been classified as relevant by full text and downgraded to Category B due to its non-reliability. The article provides information on the genotoxicity profile of glyphosate. Glyphosate a.s. and 3 GBHs were tested. Roundup Mega containing ethoxylated etheralkylamine), Glyfos containing polyethoxylated tallow amine and Fozat containing a wetting agent C12-14-alkyldimethyl betaine. Glyphosate based formulations that contain POEA (polyethoxylated tallow amine) surfactants or surfactants of similar chemical structure (e.g. ethoxylated etheralkylamine), 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 and the fact that the formulations tested contain ethoxylated etheralkylamine (similar chemical structure to POEA), POEA and betaine (not present in the AIR5 glyphosate representative formulation), the article is not considered relevant for use in risk assessment for the formulations as the effects observed cannot be attributed to glyphosate as.  The article nevertheless presents relevance with regard to pure glyphosate.  The study did not fully adhere to OECD 487, including, the purity of glyphosate is missing, no HCD available and no concurrent positive controls. Following AIR2 approval, however, all glyphosate formulations were required to be tested for clastogencity using OECD 487 for re-approval under Article 43, and the quality of reporting in these studies should be compared with the results presented within this paper.
12	CA 5.6, CA 5.7	Cattani D. et al.	2021	Perinatal exposure to a glyphosate-based herbicide causes dysregulation of dynorphins and an increase of neural precursor cells in the brain of adult male rats.	Toxicology, (2021), Vol. 461, Article No. 152922	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 effect of a glyphosate formulation on neurodevelopmental processes associated to long-term brain changes. Only one dose/no dose-response relationship. No HCD reported and no method of analysis.

Data requirement (indicated by the Submission corresponding CA/ Justification Author(s) Year Title Source Number CP data point number) 2021 13 CA 5.7 Bicca Ferreira D. et A subchronic low-dose exposure Environmental science and The article has been classified as relevant by full text - Category B of a glyphosate-based herbicide pollution research and reliable with restrictions for the following reason: The article induces depressive and anxiousinternational, (2021), Vol. 28, provides supplementary information on the effect of a glyphosate like behavior in mice: quercetin formulation on the central nervous system and the therapeutic pp. 67394-67403 therapeutic approach. effect of the flavonoid quercetin. Only one dose/no dose-response relationship. No HCD reported and no method of analysis. CA 5.8 2021 Autism-like Behaviors in Male The article has been classified as relevant by full text and 14 Pu Y. et al. Clinical psychopharmacology Juvenile Offspring after and neuroscience: the official downgraded to Category B due to its non-reliability. The aim of Maternal Glyphosate Exposure. scientific journal of the Korean the study was to investigate whether maternal exposure of pure glyphosate could cause ASD-like behaviours in juvenile offspring. College of Water or 0.098% glyphosate (980 mg/L) was administered as Neuropsychopharmacology, (202), Vol. 19, No. 3, pp. 554drinking water from E5 to P21 (weaning). This level of glyphosate acid in water has a very low pH of approximately 2.3, which may confound the results of the test due to either pH effects on the gastrointestinal tract, or reduced water consumption in the test group causing some degree of dehydration. Male offspring showed ASD-like behavioural abnormalities (i.e., increasing grooming behaviour and social interaction deficit) after maternal exposure of glyphosate. Purity of the active substance missing. Only one dose, no dose-response relationship established, number of animals/group is unclear. Dosing level in water is at least several orders of magnitude higher than worst case human dietary exposures and pH of dose group water is very low. Key parameters of water and food consumption not reported. No record of in-life clinical observations. No HCD reported and no method of analysis. No positive controls employed to verify the validity or accuracy of the method and therefore the relevance to human health assessments is at best tenuous. 15 CA 5.8 Oiu S. et al. 2021 Response of the nuclear Environmental science and The article has been classified as relevant by full text - Category B xenobiotic receptors to alleviate and reliable with restrictions for the following reason: The article pollution research glyphosate-based herbicideinternational, (2021), Vol. 29, provides supplementary information on the effect of Roundup on induced nephrotoxicity in piglet kidneys. The study also investigates the role of kidney pp. 2707-2717 weaned piglets. nuclear xenobiotic receptors. The piglet is not a model validated in the toxicological studies in the EU evaluations, however the information can still be used as supplementary. No dose-effect relationship. No HCD reported and no method of analysis. The article has been classified as relevant by full text and 16 CA 5.8 Sopko B. et al. 2021 Glyphosate Interaction with ACS omega, (2021), Vol. 6, eEF1α1 Indicates Altered downgraded to Category B due to its non-reliability. The paper No. 23, pp. 14848-14857 Protein Synthesis: Evidence for is a review of the literature that provides information on the mode Reduced Spermatogenesis and of action of glyphosate via interaction with eEF1a1 pathway and spermatogeneis and cytostatis effects through a combination of in Cytostatic Effect. silico, in vitro and in vivo information. The aim of the study was to evaluate a previously unknown mechanism to explain a

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Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
17	CA 5.8	Truzzi F. et al.	2021	Comparative Evaluation of the Cytotoxicity of Glyphosate-Based Herbicides and Glycine in	Frontiers in public health, (2021) Vol. 9, Article No. 643898	presumption that glyphosate exposure can negatively affect animals, including humans. Computer modeling suggested a probable interaction between glyphosate and eukaryotic translation elongation factor 1 subunit alpha 1 (eEF1a1), which was said to be confirmed by microcalorimetry, however, details on the calorimetry method are lacking, including concentration(s) of glyphosate interrogated. Only restricted, nondisrupted spermatogenesis was reported in rats after 100 days (i.e. subchronic, not chronic as reported) glyphosate treatments (0.7 and 7 mg/L ad libitum in drinking water). Although the method notes water consumption was monitored, neither water consumption or feed intake were reported. It is important to note, glyphosate is acidic and dose groups drinking water would be a much lower pH than the control group. Only two dose groups were implemented. The results are not consistent with a number of multigenerational rat reproductive studies with doses up to orders of magnitude higher. Cytostatic and antiproliferative effects of glyphosate in GC-1 and SUP-B15 cells were indicated. The meta-analysis of public health data suggested a possible effect of glyphosate use on sperm count, but this is not consistent with reporting in with epidemiology studies or multiple toxicology reproductive studies. Information on purity missing for the pure glyphosate. No HCD. Numerous deficiencies in the in vivo portion and significant underlying assumption in the in silico and meta-analysis.  The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: This article provides supplementary information on the cytotoxicity of
				L929 and Caco2 Cells.		glyphosate but does not alter the risk assessment. No positive control, no metabolic activation. No HCD.
18	CA 5.8.2	Almeida L. L. et al.	2021	Protective effect of melatonin against herbicides-induced hepatotoxicity in rats.	Toxicology Research, (2021), Vol. 10, No. 1, pp. 1-10	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 the ability of melatonine to ameliorate toxic effects of glyphosate on the liver. No information on feed and housing conditions, content of test material not available. Several effects observed are from the mixture of Paraquat with Roundup® (i.e. mixture toxicity). There is only one dose/no dose-response relationship. Finally, there is no HCD reported and no method of analysis.
19	CA 5.9	Boffetta P. et al.	2021	Exposure to glyphosate and risk of non-Hodgkin lymphoma: an updated meta-analysis.	La Medicina del lavoro, (2021), Vol. 112, No. 3, pp. 194-199.	The article has been classified as relevant by full text - Category B and <b>not reliable</b> for the following reason: This is a review article, not primary research on a study population. The meta-analysis approach was standard. However, meta-analysis cannot correct for the validity limitations in the included studies, which precludes

KCA 9 Page 38 of 76

Data requirement (indicated by the Submission corresponding CA/ Justification Author(s) Year Title Source Number CP data point number) calculating a valid assessment of the possible relationship between glyphosate and non-Hodgkin's lymphoma. Limited in several of the included case control studies. Especially limited in Leon et al. (2019) where the exposure assessment was based on crops farmed for 84% of the pooled cohort of 316,270. The indirect methodology made it impossible to discriminate those not exposed to specific pesticides or to know with reasonable certainty those exposed to specific pesticides. In addition, date of first exposure would be unknown for crops originally treated with other pesticides and subsequently treated with glyphosate. In fact, it seems likely that the majority of those judged to have been exposed to most specific pesticides were, in fact, not exposed when there were several pesticides registered for use on specific crops. Cases were more likely to participate than controls in several of the case control studies included in the meta-analysis. There was a substantial amount of second-hand information in several of the case control studies. The meta-analysis was not able to address biases in the included studies, especially recall bias, selection bias, and residual confounding. 20 CA 5.9 He Xiu et al. 2021 The relationship between Environmental research, The article has been classified as relevant by full text - Category B and **not reliable** for the following reason: This is a narrative pesticide exposure during (2021), Vol. 203, Article No. critical neurodevelopment and 111902 review article, not an epidemiologic study. There is no study autism spectrum disorder: A design or study population per se. The two glyphosate epidemiology studies cited in this review involve very unlikely narrative review. exposure scenarios. One study correlated increasing glyphosate use on crops with increases in the general population rate of autism. The second study defined exposure as proximity of the mother's residence on the birth certificate within a 2,000-meter radius of a glyphosate application recorded in the California Pesticide Use Reporting system. Even assuming the mother was home at the address on the birth certificate at the time of application, no one has ever demonstrated glyphosate exposure at appreciable distances from an application. There was no consideration of personal confounding factors in one study and very limited consideration in the other study. The assessment of autism risk from glyphosate exposure is based on two studies with very unlikely exposure scenarios. Therefore, this review does not provide reliable evidence about a possible association between glyphosate and autism. 21 CA 5.9 Lesseur C. et al. 2021 Urinary glyphosate Environmental research, The article has been classified as relevant by full text - Category B and **not reliable** for the following reason: This study was not (2021), Vol. 203, Article No. concentration in pregnant 111811 designed to study glyphosate per se. The authors took advantage of women in relation to length of an ongoing study (TIDES) that had collected a 2nd trimester urine sample from pregnant women to evaluate a possible relationship

Data requirement (indicated by the Submission corresponding CA/ Justification Author(s) Year Title Source Number CP data point number) between glyphosate (and AMPA) in urine and length of gestation gestation. and pre-term birth. Had the study been designed for glyphosate per se, it is unlikely that a single urine sample would have been planned as the basis for the analysis and other potential environmental exposures in urine or blood would have been assessed. The authors took the opportunity to generate some data about glyphosate (and AMPA) and length of gestation from a study that was designed for other purposes. Adapting data from an ongoing study is efficient and it can be informative when the data collection from the ongoing study matches what would have been collected for a high-quality study of the question at hand. In most instances, however, it results in a study that has important limitations. It is debatable whether pregnant women who come to the 4 university hospitals in the TIDES study is an optimum population for the study of glyphosate and length of gestation. Urine concentrations for these women equate to a glyphosate internal dose that is extremely low -0.0008 mg/kg or 0.2% of the European ADI – raising the issue of biological implausibility. Also, taking the analysis at face value requires the strong assumption that a single 2nd trimester urine sample reflects the amount of exposure during the etiologically meaningful time period for affecting length of gestation. The authors did not provide a justification for the adequacy of a single 2nd trimester urine sample. It is also worth noting that there are literally hundreds of chemicals that could have been measured in urine (or blood) to study length of gestation. One normally would not choose to focus on such low levels of glyphosate over other internalized chemicals for the study participants and it can be argued that some of those other exposures would have been important to consider in the analyses. The results of the authors' many analyses differed depending on the specific comparisons being made. Median exposure levels did not differ when outcomes were dichotomized as pre and full term. For the overall population, gestational age was not related to glyphosate values (hazard ratio (HR) 1.08, 95% CI 0.91, 1.29), but there was a weak to moderate association when the analysis was restricted to births that were not medically induced (HR 1.31, 95% CI 1.00, 1.71). The authors noted that 41% of births were medically induced, so presumably the HR for those women was somewhat less than 1.0. Likewise, when length of gestation was dichotomized as pre and full term, the odds ratio (OR) for glyphosate for all births was 1.19 (95% CI 0.86, 1.64) and the OR was 1.54 (95% CI 0.97, 2.57) when restricted to births that were

Data requirement (indicated by the Submission corresponding CA/ Justification Author(s) Year Title Source Number CP data point number) not medically induced. Again, it seems likely that the measure of association was somewhat less than 1.0 for the women who were medically induced. On balance, the results did not show a consistent relationship for glyphosate and length of gestation or pre-term birth and the interpretation of the results for those women who were medically induced is uncertain. The various analyses controlled for relatively few personal factors and no environmental factors. One can only speculate whether the results may have residual confounding. In conclusion, the results have very limited relevance for a glyphosate risk assessment. First, it's unclear whether the urine sampling is a valid representation of the internal dose at a relevant time point for the health outcome under study. Second, the range of internal doses for study participants was so low as to suggest biological implausibility. Third, the findings were based on small numbers and varied across a range of analyses, some showing no association and some showing a weak to moderate association. Lastly, there was limited consideration of confounding factors, both personal and environmental. 22 CA 5.9 Odutola M. K. et 2021 A systematic review and meta-Environmental Research, The article has been classified as relevant by full text - Category B and **not reliable** for the following reason: This is a review article analysis of occupational (2021), Vol. 197, Article No. exposures and risk of follicular 110887 of the literature for numerous exposures, including glyphosate, and lymphoma follicular lymphoma. It is not primary data. The authors used standard meta-analysis routines. However, they had no ability to correct for limitations in the original studies. It seems that the authors had only a superficial knowledge of the details and quality limitations of many of the glyphosate studies because they concluded that the risk of bias was low (viz., systematic error) – other than the small number of cases (viz., random error). Most previous reviewers of glyphosate studies considered the risk of bias to be high for most of the studies. The article has been classified as relevant by full text - Category B 23 CA 5.9 Silver M. K. et al. 2021 Prenatal Exposure to Glyphosate Environmental health and **not reliable** for the following reason: The authors took the and Its Environmental perspectives, (2021), Vol. 129, opportunity to generate some data about glyphosate (and AMPA) Degradate. No. 5, Article No 57011. Aminomethylphosphonic Acid and preterm birth from a cohort (PROTECT) study that was designed for other purposes than glyphosate per se. Adapting data (AMPA), and Preterm Birth: A Nested Case-Control Study in from an ongoing study is efficient and it can be informative when the PROTECT Cohort (Puerto the data collection from the ongoing study matches what would have been collected during a high-quality study of the question at Rico). hand. In most instances, however, the result is studies that have important limitations in study size or necessary information on personal factors and confounders. It is debatable whether pregnant women in the PROTECT cohort, patients at two university hospitals and 5 nearby clinics in northern Puerto Rico, are an

Data requirement (indicated by the Submission corresponding CA/ Author(s) Year Title Source Justification Number CP data point number) optimum population for the study of glyphosate and pre-term birth. Urine concentrations for these women equate to a glyphosate internal dose that is extremely low – a few percent or less of the European ADI – raising the issue of biological implausibility. Also, taking the analysis at face value requires the strong assumption that one or two 2nd trimester urine sample(s) reflects the amount of exposure during the etiologically meaningful time period for affecting length of gestation. The authors did not provide a justification for the adequacy of a single or two 2nd trimester urine sample(s). It is also worth noting that there are literally hundreds of chemicals that could have been measured in urine (or blood) to study length of gestation. One normally would not choose to focus on such low levels of glyphosate over other possible internalized chemicals for the study participants and it can be argued that some of those other exposures would have been important to consider in the analyses. This was noted as a limitation by the authors. The results of the authors' various analyses differed depending on the specific comparison being made. Analyses based on the visit 3 urine samples showed a weak to moderate relationship between glyphosate and pre-term birth, whereas analyses based on the visit 1 urine sample or the average of the visit 1 and 3 urine samples showed near null odds ratios. On balance, the results did not show a consistent relationship between urinary concentration of glyphosate and pre-term birth. The various analyses controlled for relatively few personal factors and environmental factors. One can only speculate whether the results may have residual confounding. In conclusion, the results of this study have very limited relevance for a glyphosate risk assessment. First, it's unclear whether the urine sampling is a valid representation of the internal dose at a relevant time point for the health outcome under study. Second, the range of internal doses for study participants was so low as to suggest biological implausibility. Third, the findings are based on small numbers of cases and varied across a range of analyses, some showing no association and some showing a weak to moderate association. Lastly, there was limited consideration of confounding 24 CA 5.9 Yokoyama S. et al. 2021 Transient glyphosate Neuropsychopharmacology The article has been classified as relevant by full text - Category B encephalopathy due to a suicide reports, (2021), Vol. 41, No. 3, for the following reason: This is a case report of a man who attempt. pp. 444-447 developed a delayed encephalopathy characterized by confusion seizure activity and decreased perfusion of his left cerebral hemisphere on SPECT 3 days after a suicidal ingestion of formulated glyposate. On intial presentation the patient was asymptomatic, underwent gasric lavage, which is not indicated in

Data requirement (indicated by the Submission corresponding CA/ Justification Author(s) Year Title Source Number CP data point number) an asymptomatic patient, and was admitted to the psychiatric floor. 3 days later he as noted to have a delirium for which he was treated with mirtazipine. This was discontinued when symptoms grew progessively worse. The authors speculate that the cause of the encephalopathy was glyphosate. This is highly unlikely as glyphosate is not neurotoxic, nor does it cause vascular constriction. A unilateral perfusion deficit is very uncommon in a toxin induced encephalopathy. This case is much more consistent with acute alcohol withdrawal, which is a slow onset syndrome that takes 2-3 days to develop, is charcterized by delirium and seizures, reversible vasogenic edema in the hippocampal regions. This presentation is not consistent with glyphosate overdoses and because of the suicidal ingestion should not impact regulatory decisions. 2.5 CA 5.9 Zhang C. Q. et al. 2021 A case of allergic cutaneous Chinese journal of industrial The article has been classified as relevant by full text - Category B vasculitis caused by glyphosate. hygiene and occupational for the following reason: This is a case report of a man who diseases, (2021), Vol. 39, No. developed purpuric skin lesions involving the palms and leukocytoclastic vasculitis after exposure to an agrichemical that 6, pp. 467-468 was reported to be glyphosate. His symptoms improved with steroid therapy, recurred upon reexposure 2 times and resolved with steoid treatment. The article claims that the chemistry involved was glyphosate despite the fact that there was no confirmation of exposure through any definitive identification of the product, urine or blood testing for the presence of glyphosate. Glyphosate is not a sensitizer, nor does it cause immune complex deposition in the vasculature. While the patient was worked up for several diseases associated leukocytoclastic vasculitis, they left out several very prominent infectious etiologies that are much more commonly associated with palmar rashes and vasculitidies. There is no described mechanism in the literature for this constellation of symptoms and no confirmation that the patient was exposed to glyphosate. 26 CA 6.10 Bergero M. et al. 2021 Agrochemical Contamination of Environments, (2021), Vol. 8, The article has been classified as relevant by full text - Category B Honey and Bee Bread Collected No. 7 and reliable with restrictions for the following reason: Monitoring in the Piedmont Region, Italy data from Piedmont (Italy) on pesticides in bee bread and honey (sampling from 4 apiaries). Glyphosate was the most abundant chemical found in bee bread and honey samples, with levels of <10-542 and 10-34 µg/kg, respectively. Analysis of glyphosate in honey was done according to QuPPe M 1.3 method, however no method validation data are provided in the publication. The article has been classified as relevant by full text - Category B 27 CA 6.10 Krogh U. et al. 2021 Performance and mineral status Livestock Science, (2021), of weaning pigs fed diets with Vol. 252, Article No. 104681 and reliable without restrictions: This is an experimental study to different levels of glyphosate investigate effects of glyphosate on performance and mineral status of weaning pigs (weight, feed intake and faeces score; intestine

Data requirement (indicated by the Submission corresponding CA/ Title Justification Author(s) Year Source Number CP data point number) digesta, blood and urine analysis). Pigs were fed with wening diet and tryptophan. containing various concentrations (20 and 200 mg/kg) of glyphosate, at the highest concentration with and without addition of crystalline tryptophan. Neither feed intake, growth rate, serum mineral concentrations nor faeces score were significantly affected by level or source (pure glyphosate salt vs GBH) of the dietary glyphosate. Well described experimental study on the effect of glyphosate on the performance and mineral status of weaning pigs. 28 CA 6.10 Sorensen M. T. et 2021 Feed residues of glyphosate -Animal, (2021), Vol. 15, No. 1 The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: This is a potential consequences for livestock health and literature review report on potential detrimental effects of glyphosate affect livestock gut microbiota and/or mineral status productivity. potentially with derived unfavourable effects on animal health and productivity. Some in vitro growth experiments were conducted with bacteria. Some differences were detected regarding the sensitivity of bacterial growth to glyphosate. The in vitro bacterial growth assays can be considered acceptable. However the new experimental data are limited and provide little additional information to existing studies (also in vivo studies) to this topic. 29 CA 6.3 Edge C. B. et al. 2021 The Persistence of Glyphosate in FORESTS, (2021), Vol. 12, The article has been classified as relevant by full text - Category B Vegetation One Year after No. 5. and reliable with restrictions for the following reason: The study Application describes two experiments conducted in Canada, where glyphosate was applied aerially at rates of 1.35-1.8 kg a.s./ha to forestry areas. Samples of vegetation browsed by deer, moose and bear were collected from sprayed and non-sprayed adjacent blocks (downwind), and analysed for residues of glyphosate and AMPA. Overall, the studies demonstrate that trace levels of glyphosate persist in vegetation for up to one year after application, however, observed concentrations are unlikely to pose risk to wildlife. Analytical work was done at the Agriculture and Food Laboratory at the University of Guelph by means of LC-MS/MS, however no method description and validation data are provided. Analysis on pesticide residues The article has been classified as relevant by full text - Category B 30 CA 6.3 Jin Shan et al. 2021 Journal of Chinese Institute of level in dry tea materials of and reliable with restrictions for the following reason: Monitoring Food Science and Technology, Chenxiang Tieguanyin and the (2021), Vol. 21, pp. 291-29 data from China on pesticides in oolong tea (Chenxiang preliminary studies on the Tieguanyin, 89 raw materials analysed). Glyphosate was detected degradation of pesticide in 13 samples at levels of 0.07-0.79 mg/kg, i.e. below EU and China MRL (2 and 1 mg/kg, respectively). Analytical work was residues. done at the Fujian Inspection and Research Institute for Product Quality by means of LC MS/MS (according to Chinese Standard GB/T 23204-2008), however no method validation data are provided. 31 CA 6.3 2021 AGRICULTURE AND The article has been classified as relevant by full text - Category B Malone M. Seeking justice, eating toxics: overlooked contaminants in HUMAN VALUES, (2021) and reliable with restrictions for the following reason: This is a

Data requirement (indicated by the Submission corresponding CA/ Justification Author(s) Year Title Source Number CP data point number) https://doi.org/10.1007/s10460urban community gardens kind of monitoring study in urban community gardens (UCGs), 021-10236-8 where soil from nine UCGs around Seattle were sampled and analysed for As, Pb, glyphosate and AMPA, and total petroleum hydrocarbons (TPH). Glyphosate and AMPA were found preliminary at two sites. Maximum levels of glyphosate and AMPA were 0.108 and 0.613 mg/kg, respectively, with highest median values of 0.027 and 0.163 mg/kg. Analytical work was done by HRI Laboratories in Iowa by means of LC MS/MS, however no method validation data are provided for soil analyses. The article has been classified as relevant by full text - Category B 32 CA 6.9 Baudry J. et al. 2021 Estimated dietary exposure to Food and Chemical pesticide residues based on Toxicology, (2021), Vol. 153, and reliable without restrictions: This is a dietary risk assessment organic and conventional data in Article No. 112179 study to investigate uptake of reisidues (incl glyphosate) by different population groups, including omnivores, pescoomnivores, pesco-vegetarians, vegetarians and vegans vegetarians, vegetarians and vegans, with further distincion between intake of conventional or organic food source. Highest glyphosate intakes of glyphosate were calculated for vegans consuming conventional food (0.0264 µg/kg bw/day), with highest contributor legume vegetables. The study uses data from the NutriNet-Santé study (consumption survey 2013) and pesticide residue data from Chemisches und Veterinäruntersuchungsamt (CVUA) Stuttgart database. The study shows no risks to all consumer groups from glyphosate residues. Residues of glyphosate in food The article has been classified as relevant by full text - Category B 33 CA 6.9 Vicini J. L. et al. 2021 Comprehensive reviews in and dietary exposure. food science and food safety. and reliable without restrictions: This is a literature review article (2021): Ahead of Print with focus on 1) analytical methods for glyphosate and AMPA, 2) MRL and monitoring data (market surveys) and 3) dieatry risk assessment. It reflects a well written summary of available knowledge and regulatory requirements/assessments. Scientifically solid overall assessment of glyphosate consumer risk from glyphosate and AMPA. Establishment of a HPLC-The article has been classified as relevant by full text - Category B 34 CA 6.9 Wang Y. et al. 2021 Journal of agricultural and food MS/MS Detection Method for chemistry, (2021), Vol. 69, No. and reliable with restrictions for the following reason: The article Glyphosate, Glufosinate-28, pp. 7969-7978 describes 1) development and optimisation of an analycal method for the determation of glyphosate, AMPA and glufosinate-Ammonium, and Aminomethyl Phosphoric Acid in Tea and Its ammonium, 2) monitoring of tea samples (n = 780) from China, Use for Risk Exposure and 3) risk assessment (deterministic and probabilistic) from Assessment. consumption of teas. The results showed that exposure to PMG, GLU and AMPA caused by drinking tea beverages poses no significant risk to human health. Regarding analytical procedures, it is stated that LOQ for Gly and AMPA was 0.3 mg/kg (derived from calibration standards); however the lowest validated concentration was 1.0 mg/kg.

Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
35	CA 7.1.4.1	Akyol N. H. et al.	2021	Comparison of sorption and solute transport behaviour of several herbicides in an alkaline agricultural soil	International Journal of Environmental Analytical Chemistry (2021): Ahead of Print	The article has been classified as relevant by full text and downgraded to Category B due to its non-reliability. The objective of this study was to quantify sorption and solute transport of glyphosate in soil column experiments with an alkaline agricultural soil from Turkey. The adsorption coefficient (Kd) for glyphosate was estimated to be 2.14 L/kg. The soil sampling procedure (e.g. depth and timing), soil storage and pesticide history of the soils are not reported. Soil columns (10-cm long by 2-cm diameter) were smaller than required by the guideline (at least 4 cm and a minimum height of 35 cm). The experiments were conducted in saturated columns with flow from bottom to top at a rate of 0.7 mL/min. Test concentrations were high with 20 to 100 mg/L. Only the column effluent was analysed, soil segments were not analysed. Sample analysis was performed using an UV spectrometer with a detection limit of 0.1 mg/L.
36	CA 7.1.4.3	Giuliano S. et al.	2021	Reducing herbicide use and leaching in agronomically performant maize-based cropping systems: An 8-year study.	The Science of the total environment, (2021), Vol. 788, Article No. 147695	The article has been classified as relevant by full text and downgraded to Category B due to its non-reliability. An 8-year field leaching experiment was carried out at the Domaine de Lamothe - INP PURPAN, Garonne Plain, south-western France (43.506N, 1.237E) from 2011 to 2018. Different cropping systems were compared. Glyphosate and AMPA were detected in less than 50% of the samples and had very low frequencies of leachates with concentration above 1 µg/L (respectively 5% and 0%). No information on the test substance (formulation, purity), the exact application time and the application method is given. Only leachate but no soil samples were analysed. The volume and sampling time of the leachate is not reported. Furthermore, only maximum concentrations of glyphosate and AMPA were reported. It is not reported when (year, season) the maximum concentrations were observed and thus it cannot be connected to glyphosate application or climatic conditions.
37	CA 7.5	Fernandes B. et al.	2020	Levels of glyphosate in vineyard soils and potential adverse effects to the environment.	IOBC/WPRS Bulletin, (2020), No. 154, pp. 129-132	The article has been classified as relevant by full text and downgraded to Category B due to its non-reliability. The levels of glyphosate and AMPA were monitored in two different vineyards from the Douro Demarcated Region (Portugal) over one year from February 2018 to January 2019. The highest concentrations of glyphosate were observed in February (median value of 2.0 mg/kg). The exact location of the vineyards and the weather conditions are not reported. The application method and rate of the glyphosate formulation as well as the formulation type are not described. No information on soil sampling procedure, depth, sample storage and extraction method is provided. The analytical method is not described with sufficient details and was not validated. No individual concentrations are reported, but only

Data requirement (indicated by the Submission corresponding CA/ Justification Author(s) Year Title Source Number CP data point number) median values and they cannot be assigned to a geographic area. 38 CA 8.1.4 2021 The article has been classified as relevant by full text - Category B Lopes A. et al. Evaluation of the genotoxic, Environmental pollution, mutagenic, and histopathological (2021), Vol. 289, Article No. and reliable with restrictions for the following reason: The study hepatic effects of 117911 does not provide an endpoint that can establish, modify or refine polyoxyethylene amine (POEA) the risk assesment parameters for amphibians (it cannot be and glyphosate on integrated into the risk assessment scheme), but its findings can be Dendropsophus minutus used as higher tier supportive information in a broader discussion tadpoles. of the effects of glyphosate on vertebrate wildlife. A quantitative endpoint can be established but based on effects at cellular/mollecular level (genotoxicity and mutagenicity). For the histopathological effects that are relevant for the risk assessment. only a qualitative evaluation was conducted. The study cannot be considered as fully reliable because no analytical verification of the test concentrations in water was conducted. In addition, tested individuals provide from samples from a permanent body of water in Brazil and no record of previous chemical exposure was provided. 39 CA 8.2.8, CP 10.2.3 2021 Effect of herbicides based on FUNDAMENTAL AND The article has been classified as relevant by full text - Category B de Campos Oliveira R. et al. glyphosate on the photosynthesis APPLIED LIMNOLOGY. and reliable with restrictions for the following reason: The study of green macroalgae in tropical (2021), Vol. 195, No. 2, pp. does not provide an endpoint that can establish, modify or refine 85-93 the risk assessment parameters for algae (it cannot be integrated into lotic environments the risk assessment scheme because measured variables and endpoints are not in line with the guidance), but its findings can be used as supportive information in a broader discussion of the effects of glyphosate on aquatic organisms (specifically macroalgae). The species tested are widely distributed and frequently reported as representatives of Chlorophyta in lotic macroalgal communities in Brazil. The study is considered reliable with restrictions because it lacks of analytical verifications of the tested item in the test medium during the exposure phase and because the specimens used for the test come from natural sources and no evidence was provided that they were not previously exposed to pesticides. 40 CA 8.7, CP 10.7 Lorch M. et al. 2021 Repeated annual application of Agriculture, ecosystems & The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: The study glyphosate reduces the environment, (2021), Vol. 319, abundance and alters the does not provide an endpoint that can establish, modify or refine Article No. 107503 community structure of soil the risk assesment parameters (it cannot be integrated into the risk culturable pseudomonads in a assessment scheme), but its findings can be used as higher tier supportive information in a broader discussion of the effects of temperate grassland glyphosate on soil microorganisms. The part of the study conducted in the field is not relevant, because it was conducted in a humid mesophytic meadow of a commercial farm located in Argentina. This is not relatable to the EU risk assessment, because

Data requirement (indicated by the Submission corresponding CA/ Justification Author(s) Year Title Source Number CP data point number) the conditions are not representative. The part of the study conducted in the greenhouse is relevant, but it was conducted at only one rate (the same for both pure glyphosate and the GBH). The concentration of glyphosate in the soil was not analyzed. The study is considered as reliable with restrictions because no analytical verifications of the concentration of glyphosate in soil samples were conducted. In addition, the characterization of the soil was not provided (just texture) and the application volume was not reported. CP 10.3.1.4 The article has been classified as relevant by full text - Category B 41 Hernandez J. et al. 2021 Sublethal doses of glyphosate JOURNAL OF INSECT impair olfactory memory CONSERVATION, (2021). and reliable with restrictions for the following reason: The study retention, but not learning in the Vol. 25, No. 4, pp. 683-694 does not provide an endpoint that can establish, modify or refine honey bee (Apis mellifera the risk assesment parameters for bees (it cannot be integrated into scutellata) the risk assessment scheme), but its findings can be used as supportive information (olfactory learning and memory) in a broader discussion on the sub-lethal effects of glyphosate on bees. The study is considered as reliable with restrictions because it is uncertain whether the bees have been previously exposed to pesticides, because no analytical verifications of the stock solution were conducted and because the test temperature (20°C) is low for honey bees (should have been ca. 33°C). In addition, only 2 concentration (0.375 and 1.5 µg/bee) were tested (under both acute and repeated exposure conditions). 42 CP 10.5 The article has been classified as relevant by full text - Category B Jezierska-Tvs S. et 2021 Microbiological Nitrogen AGRICULTURE-BASEL. and **not reliable** for the following reason: The study does not Transformations in Soil Treated (2021), Vol. 11, No. 8. with Pesticides and Their Impact provide an endpoint that can establish, modify or refine the risk on Soil Greenhouse Gas assesment parameters for soil microorganisms (it cannot be integrated into the risk assessment scheme), but its findings can be Emissions used as higher tier supportive information in a broader discussion of the effects of glyphosate on soil nitrogen transformation (nitrification) under realistic field conditions. The study is considered as not reliable because the record of the previous exposure to other chemicals in the field where the soil samples were taken is not reported and no analytical verifications of the concentration of glyphosate in soil samples were conducted. It is therefore not possible to link univocally the glyphosate application with the observed effects in soil nitrification. In addition, the incubation conditions of the soil were not reported. Furthermore, the test item was poorly described. Precipitations regime between

application and soil sampling was not described.

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
35	Akyol N. H. et al.	CA 7.1.4.1	2021	Comparison of sorption and solute transport behaviour of several herbicides in an alkaline agricultural soil	International Journal of Environmental Analytical Chemistry (2021): Ahead of Print	The article has been classified as relevant by full text and downgraded to Category B due to its non-reliability. The objective of this study was to quantify sorption and solute transport of glyphosate in soil column experiments with an alkaline agricultural soil from Turkey. The adsorption coefficient (Kd) for glyphosate was estimated to be 2.14 L/kg. The soil sampling procedure (e.g. depth and timing), soil storage and pesticide history of the soils are not reported. Soil columns (10-cm long by 2-cm diameter) were smaller than required by the guideline (at least 4 cm and a minimum height of 35 cm). The experiments were conducted in saturated columns with flow from bottom to top at a rate of 0.7 mL/min. Test concentrations were high with 20 to 100 mg/L. Only the column effluent was analysed, soil segments were not analysed. Sample analysis was performed using an UV spectrometer with a detection limit of 0.1 mg/L.
18	Almeida L. L. et al.	CA 5.8.2	2021	Protective effect of melatonin against herbicides-induced hepatotoxicity in rats.	Toxicology Research, (2021), Vol. 10, No. 1, pp. 1-10	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 the ability of melatonine to ameliorate toxic effects of glyphosate on the liver. No information on feed and housing conditions, content of test material not available. Several effects observed are from the mixture of Paraquat with Roundup® (i.e. mixture toxicity). There is only one dose/no dose-response relationship. Finally, there is no HCD reported and no method of analysis.
32	Baudry J. et al.	CA 6.9	2021	Estimated dietary exposure to pesticide residues based on organic and conventional data in omnivores, pesco-vegetarians, vegetarians and vegans	Food and Chemical Toxicology, (2021), Vol. 153, Article No. 112179	The article has been classified as relevant by full text - Category B and reliable without restrictions: This is a dietary risk assessment study to investigate uptake of reisidues (incl glyphosate) by different population groups, including omnivores, pescovegetarians, vegetarians and vegans, with further distincion between intake of conventional or organic food source. Highest glyphosate intakes of glyphosate were calculated for vegans consuming conventional food (0.0264 µg/kg bw/day), with highest contributor legume vegetables. The study uses data from the NutriNet-Santé study (consumption survey 2013) and pesticide residue data from Chemisches und Veterinäruntersuchungsamt (CVUA) Stuttgart database. The study shows no risks to all consumer groups from glyphosate residues.
26	Bergero M. et al.	CA 6.10	2021	Agrochemical Contamination of Honey and Bee Bread Collected in the Piedmont Region, Italy	Environments, (2021), Vol. 8, No. 7	The article has been classified as relevant by full text - Category B and reliable with restrictions for the following reason: Monitoring data from Piedmont (Italy) on pesticides in bee bread and honey (sampling from 4 apiaries). Glyphosate was the most abundant

chemical found in bee bread and honey samples, with levels of <10-542 and 10-34 μg/kg, respectively. Analysis of glyphosate in honey was done according to QuPPe M 1.3 method, however no method validation data are provided in the publication. 13 CA 5.7 2021 A subchronic low-dose exposure Environmental science and The article has been classified as relevant by full text - Category B Bicca Ferreira pollution research international. of a glyphosate-based herbicide and reliable with restrictions for the following reason: The article D. et al. induces depressive and anxious-(2021), Vol. 28, pp. 67394provides supplementary information on the effect of a glyphosate like behavior in mice: quercetin formulation on the central nervous system and the therapeutic effect of the flavonoid quercetin. Only one dose/no dose-response therapeutic approach. relationship. No HCD reported and no method of analysis. 19 Boffetta P. et CA 5.9 2021 Exposure to glyphosate and risk La Medicina del lavoro, (2021). The article has been classified as relevant by full text - Category B of non-Hodgkin lymphoma: an Vol. 112, No. 3, pp. 194-199. and **not reliable** for the following reason: This is a review article, updated meta-analysis. not primary research on a study population. The meta-analysis approach was standard. However, meta-analysis cannot correct for the validity limitations in the included studies, which precludes calculating a valid assessment of the possible relationship between glyphosate and non-Hodgkin's lymphoma. Limited in several of the included case control studies. Especially limited in Leon et al. (2019) where the exposure assessment was based on crops farmed for 84% of the pooled cohort of 316,270. The indirect methodology made it impossible to discriminate those not exposed to specific pesticides or to know with reasonable certainty those exposed to specific pesticides. In addition, date of first exposure would be unknown for crops originally treated with other pesticides and subsequently treated with glyphosate. In fact, it seems likely that the majority of those judged to have been exposed to most specific pesticides were, in fact, not exposed when there were several pesticides registered for use on specific crops. Cases were more likely to participate than controls in several of the case control studies included in the meta-analysis. There was a substantial amount of second-hand information in several of the case control studies. The meta-analysis was not able to address biases in the included studies, especially recall bias, selection bias, and residual confounding. 12 Cattani D. et CA 5.6, CA 5.7 2021 Perinatal exposure to a Toxicology, (2021), Vol. 461, The article has been classified as relevant by full text - Category B glyphosate-based herbicide Article No. 152922 and reliable with restrictions for the following reason: The article causes dysregulation of provides supplementary information on the effect of a glyphosate dynorphins and an increase of formulation on neurodevelopmental processes associated to longneural precursor cells in the term brain changes. Only one dose/no dose-response relationship.

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(2021), Vol. 195, No. 2, pp. 85-

brain of adult male rats.

photosynthesis of green

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Effect of herbicides based on

macroalgae in tropical lotic

de Campos Oliveira R. et

al.

39

CA 8.2.8, CP 10.2.3

2021

No HCD reported and no method of analysis.

The article has been classified as relevant by full text - Category B

and reliable with restrictions for the following reason: The study

does not provide an endpoint that can establish, modify or refine

endpoints are not in line with the guidance), but its findings can be used as supportive information in a broader discussion of the

the risk assessment parameters for algae (it cannot be integrated into the risk assessment scheme because measured variables and

effects of glyphosate on aquatic organisms (specifically macroalgae). The species tested are widely distributed and frequently reported as representatives of Chlorophyta in lotic macroalgal communities in Brazil. The study is considered reliable with restrictions because it lacks of analytical verifications of the tested item in the test medium during the exposure phase and because the specimens used for the test come from natural sources and no evidence was provided that they were not previously exposed to pesticides. The article has been classified as relevant by full text - Category B 29 Edge C. B. et CA 6.3 2021 The Persistence of Glyphosate FORESTS, (2021), Vol. 12, in Vegetation One Year after No. 5. and reliable with restrictions for the following reason: The study Application describes two experiments conducted in Canada, where glyphosate was applied aerially at rates of 1.35-1.8 kg a.s./ha to forestry areas. Samples of vegetation browsed by deer, moose and bear were collected from sprayed and non-sprayed adjacent blocks (down-wind), and analysed for residues of glyphosate and AMPA. Overall, the studies demonstrate that trace levels of glyphosate persist in vegetation for up to one year after application, however, observed concentrations are unlikely to pose risk to wildlife. Analytical work was done at the Agriculture and Food Laboratory at the University of Guelph by means of LC-MS/MS, however no method description and validation data are provided. 37 CA 7.5 2020 Levels of glyphosate in vineyard IOBC/WPRS Bulletin, (2020), The article has been classified as relevant by full text and Fernandes B. soils and potential adverse downgraded to Category B due to its non-reliability. The levels of et al. No. 154, pp. 129-132 effects to the environment. glyphosate and AMPA were monitored in two different vineyards from the Douro Demarcated Region (Portugal) over one year from February 2018 to January 2019. The highest concentrations of glyphosate were observed in February (median value of 2.0 mg/kg). The exact location of the vineyards and the weather conditions are not reported. The application method and rate of the glyphosate formulation as well as the formulation type are not described. No information on soil sampling procedure, depth, sample storage and extraction method is provided. The analytical method is not described with sufficient details and was not validated. No individual concentrations are reported, but only median values and they cannot be assigned to a geographic area. 36 Giuliano S. et CA 7.1.4.3 2021 Reducing herbicide use and The Science of the total The article has been classified as relevant by full text and leaching in agronomically environment, (2021), Vol. 788, downgraded to Category B due to its non-reliability. An 8-year performant maize-based Article No. 147695 field leaching experiment was carried out at the Domaine de cropping systems: An 8-year Lamothe - INP PURPAN, Garonne Plain, south-western France study. (43.506N, 1.237E) from 2011 to 2018. Different cropping systems were compared. Glyphosate and AMPA were detected in less than 50% of the samples and had very low frequencies of leachates with concentration above 1 μg/L (respectively 5% and 0%). No information on the test substance (formulation, purity), the exact application time and the application method is given. Only leachate but no soil samples were analysed. The volume and sampling time of the leachate is not reported. Furthermore, only maximum concentrations of glyphosate and AMPA were reported.

It is not reported when (year, season) the maximum concentrations were observed and thus it cannot be connected to glyphosate application or climatic conditions. The article has been classified as relevant by full text - Category B 20 He Xiu et al. CA 5.9 2021 The relationship between Environmental research. and **not reliable** for the following reason: This is a narrative pesticide exposure during (2021), Vol. 203, Article No. review article, not an epidemiologic study. There is no study critical neurodevelopment and 111902 autism spectrum disorder: A design or study population per se. The two glyphosate narrative review. epidemiology studies cited in this review involve very unlikely exposure scenarios. One study correlated increasing glyphosate use on crops with increases in the general population rate of autism. The second study defined exposure as proximity of the mother's residence on the birth certificate within a 2,000-meter radius of a glyphosate application recorded in the California Pesticide Use Reporting system. Even assuming the mother was home at the address on the birth certificate at the time of application, no one has ever demonstrated glyphosate exposure at appreciable distances from an application. There was no consideration of personal confounding factors in one study and very limited consideration in the other study. The assessment of autism risk from glyphosate exposure is based on two studies with very unlikely exposure scenarios. Therefore, this review does not provide reliable evidence about a possible association between glyphosate and autism. 41 CP 10.3.1.4 2021 Sublethal doses of glyphosate JOURNAL OF INSECT The article has been classified as relevant by full text - Category B Hernandez J. et al. impair olfactory memory CONSERVATION, (2021), and reliable with restrictions for the following reason: The study retention, but not learning in the Vol. 25, No. 4, pp. 683-694 does not provide an endpoint that can establish, modify or refine honey bee (Apis mellifera the risk assesment parameters for bees (it cannot be integrated into scutellata) the risk assessment scheme), but its findings can be used as supportive information (olfactory learning and memory) in a broader discussion on the sub-lethal effects of glyphosate on bees. The study is considered as reliable with restrictions because it is uncertain whether the bees have been previously exposed to pesticides, because no analytical verifications of the stock solution were conducted and because the test temperature (20°C) is low for honey bees (should have been ca. 33°C). In addition, only 2 concentration (0.375 and 1.5 µg/bee) were tested (under both acute and repeated exposure conditions). 42 Jezierska-Tys CP 10.5 2021 Microbiological Nitrogen AGRICULTURE-BASEL, The article has been classified as relevant by full text - Category B and **not reliable** for the following reason: The study does not S. et al. Transformations in Soil Treated (2021), Vol. 11, No. 8. provide an endpoint that can establish, modify or refine the risk with Pesticides and Their assesment parameters for soil microorganisms (it cannot be Impact on Soil Greenhouse Gas Emissions integrated into the risk assessment scheme), but its findings can be used as higher tier supportive information in a broader discussion of the effects of glyphosate on soil nitrogen transformation (nitrification) under realistic field conditions. The study is considered as not reliable because the record of the previous exposure to other chemicals in the field where the soil samples were taken is not reported and no analytical verifications of the concentration of glyphosate in soil samples were conducted. It is

therefore not possible to link univocally the glyphosate application with the observed effects in soil nitrification. In addition, the incubation conditions of the soil were not reported. Furthermore. the test item was poorly described. Precipitations regime between application and soil sampling was not described. 30 CA 6.3 2021 Journal of Chinese Institute of The article has been classified as relevant by full text - Category B Jin Shan et al. Analysis on pesticide residues level in dry tea materials of Food Science and Technology, and reliable with restrictions for the following reason: Monitoring Chenxiang Tieguanyin and the (2021), Vol. 21, pp. 291-29 data from China on pesticides in oolong tea (Chenxiang preliminary studies on the Tieguanyin, 89 raw materials analysed). Glyphosate was detected degradation of pesticide in 13 samples at levels of 0.07-0.79 mg/kg, i.e. below EU and residues. China MRL (2 and 1 mg/kg, respectively). Analytical work was done at the Fujian Inspection and Research Institute for Product Quality by means of LC MS/MS (according to Chinese Standard GB/T 23204-2008), however no method validation data are provided. The article has been classified as relevant by full text - Category B 27 Krogh U. et al. CA 6.10 2021 Performance and mineral status Livestock Science, (2021), Vol. 252, Article No. 104681 and reliable without restrictions: This is an experimental study to of weaning pigs fed diets with investigate effects of glyphosate on performance and mineral different levels of glyphosate status of weaning pigs (weight, feed intake and faeces score; and tryptophan. intestine digesta, blood and urine analysis). Pigs were fed with wening diet containing various concentrations (20 and 200 mg/kg) of glyphosate, at the highest concentration with and without addition of crystalline tryptophan. Neither feed intake, growth rate, serum mineral concentrations nor faeces score were significantly affected by level or source (pure glyphosate salt vs GBH) of the dietary glyphosate. Well described experimental study on the effect of glyphosate on the performance and mineral status of weaning pigs. 21 Lesseur C. et CA 5.9 2021 Urinary glyphosate Environmental research. The article has been classified as relevant by full text - Category B concentration in pregnant (2021), Vol. 203, Article No. and **not reliable** for the following reason: This study was not women in relation to length of 111811 designed to study glyphosate per se. The authors took advantage of an ongoing study (TIDES) that had collected a 2nd trimester gestation. urine sample from pregnant women to evaluate a possible relationship between glyphosate (and AMPA) in urine and length of gestation and pre-term birth. Had the study been designed for glyphosate per se, it is unlikely that a single urine sample would have been planned as the basis for the analysis and other potential environmental exposures in urine or blood would have been assessed. The authors took the opportunity to generate some data about glyphosate (and AMPA) and length of gestation from a study that was designed for other purposes. Adapting data from an ongoing study is efficient and it can be informative when the data collection from the ongoing study matches what would have been collected for a high-quality study of the question at hand. In most instances, however, it results in a study that has important limitations. It is debatable whether pregnant women who come to the 4 university hospitals in the TIDES study is an optimum population for the study of glyphosate and length of gestation. Urine

concentrations for these women equate to a glyphosate internal dose that is extremely low – 0.0008 mg/kg or 0.2% of the European ADI – raising the issue of biological implausibility. Also, taking the analysis at face value requires the strong assumption that a single 2nd trimester urine sample reflects the amount of exposure during the etiologically meaningful time period for affecting length of gestation. The authors did not provide a justification for the adequacy of a single 2nd trimester urine sample. It is also worth noting that there are literally hundreds of chemicals that could have been measured in urine (or blood) to study length of gestation. One normally would not choose to focus on such low levels of glyphosate over other internalized chemicals for the study participants and it can be argued that some of those other exposures would have been important to consider in the analyses. The results of the authors' many analyses differed depending on the specific comparisons being made. Median exposure levels did not differ when outcomes were dichotomized as pre and full term. For the overall population, gestational age was not related to glyphosate values (hazard ratio (HR) 1.08, 95% CI 0.91, 1.29), but there was a weak to moderate association when the analysis was restricted to births that were not medically induced (HR 1.31, 95% CI 1.00, 1.71). The authors noted that 41% of births were medically induced, so presumably the HR for those women was somewhat less than 1.0. Likewise, when length of gestation was dichotomized as pre and full term, the odds ratio (OR) for glyphosate for all births was 1.19 (95% CI 0.86, 1.64) and the OR was 1.54 (95% CI 0.97, 2.57) when restricted to births that were not medically induced. Again, it seems likely that the measure of association was somewhat less than 1.0 for the women who were medically induced. On balance, the results did not show a consistent relationship for glyphosate and length of gestation or pre-term birth and the interpretation of the results for those women who were medically induced is uncertain. The various analyses controlled for relatively few personal factors and no environmental factors. One can only speculate whether the results may have residual confounding. In conclusion, the results have very limited relevance for a glyphosate risk assessment. First, it's unclear whether the urine sampling is a valid representation of the internal dose at a relevant time point for the health outcome under study. Second, the range of internal doses for study participants was so low as to suggest biological implausibility. Third, the findings were based on small numbers and varied across a range of analyses, some showing no association and some showing a weak to moderate association. Lastly, there was limited consideration of confounding factors, both personal and environmental.

38 2021 Lopes A. et al. CA 8.1.4 Evaluation of the genotoxic, Environmental pollution, The article has been classified as relevant by full text - Category B (2021), Vol. 289, Article No. and reliable with restrictions for the following reason: The study mutagenic, and histopathological hepatic effects 117911 does not provide an endpoint that can establish, modify or refine of polyoxyethylene amine the risk assesment parameters for amphibians (it cannot be (POEA) and glyphosate on integrated into the risk assessment scheme), but its findings can be Dendropsophus minutus used as higher tier supportive information in a broader discussion of the effects of glyphosate on vertebrate wildlife. A quantitative tadpoles. endpoint can be established but based on effects at cellular/mollecular level (genotoxicity and mutagenicity). For the histopathological effects that are relevant for the risk assessment, only a qualitative evaluation was conducted. The study cannot be considered as fully reliable because no analytical verification of the test concentrations in water was conducted. In addition, tested individuals provide from samples from a permanent body of water in Brazil and no record of previous chemical exposure was provided. CA 8.7, CP 10.7 The article has been classified as relevant by full text - Category B 40 Lorch M. et al. 2021 Repeated annual application of Agriculture, ecosystems & glyphosate reduces the environment, (2021), Vol. 319, and reliable with restrictions for the following reason: The study abundance and alters the Article No. 107503 does not provide an endpoint that can establish, modify or refine community structure of soil the risk assessment parameters (it cannot be integrated into the risk culturable pseudomonads in a assessment scheme), but its findings can be used as higher tier temperate grassland supportive information in a broader discussion of the effects of glyphosate on soil microorganisms. The part of the study conducted in the field is not relevant, because it was conducted in a humid mesophytic meadow of a commercial farm located in Argentina. This is not relatable to the EU risk assessment, because the conditions are not representative. The part of the study conducted in the greenhouse is relevant, but it was conducted at only one rate (the same for both pure glyphosate and the GBH). The concentration of glyphosate in the soil was not analyzed. The study is considered as reliable with restrictions because no analytical verifications of the concentration of glyphosate in soil samples were conducted. In addition, the characterization of the soil was not provided (just texture) and the application volume was not reported. 31 Malone M. CA 6.3 2021 Seeking justice, eating toxics: AGRICULTURE AND The article has been classified as relevant by full text - Category B overlooked contaminants in HUMAN VALUES, (2021) and reliable with restrictions for the following reason: This is a urban community gardens https://doi.org/10.1007/s10460kind of monitoring study in urban community gardens (UCGs), 021-10236-8 where soil from nine UCGs around Seattle were sampled and analysed for As, Pb, glyphosate and AMPA, and total petroleum hydrocarbons (TPH). Glyphosate and AMPA were found preliminary at two sites. Maximum levels of glyphosate and AMPA were 0.108 and 0.613 mg/kg, respectively, with highest median values of 0.027 and 0.163 mg/kg. Analytical work was done by HRI Laboratories in Iowa by means of LC MS/MS, however no method validation data are provided for soil analyses. 11 CA 5.4.1 2021 Frontiers in public health, The article has been classified as relevant by full text and Nagy K. et al. Micronucleus Formation Induced by Glyphosate and (2021) Vol. 9, Article No. downgraded to Category B due to its non-reliability. The Glyphosate-Based Herbicides in 639143 article provides information on the genotoxicity profile of

Clinical psychopharmacology

and neuroscience: the official

Neuropsychopharmacology,

College of

scientific journal of the Korean

Human Peripheral White Blood glyphosate. Glyphosate a.s. and 3 GBHs were tested. Roundup Mega containing ethoxylated etheralkylamine), Glyfos containing Cells. polyethoxylated tallow amine and Fozat containing a wetting agent C12-14-alkyldimethyl betaine. Glyphosate based formulations that contain POEA (polyethoxylated tallow amine) surfactants or surfactants of similar chemical structure (e.g. ethoxylated etheralkylamine), 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 and the fact that the formulations tested contain ethoxylated etheralkylamine (similar chemical structure to POEA), POEA and betaine (not present in the AIR5 glyphosate representative formulation), the article is not considered relevant for use in risk assessment for the formulations as the effects observed cannot be attributed to glyphosate a.s. The article nevertheless presents relevance with regard to pure glyphosate. The study did not fully adhere to OECD 487, including, the purity of glyphosate is missing, no HCD available and no concurrent positive controls. Following AIR2 approval, however, all glyphosate formulations were required to be tested for clastogencity using OECD 487 for re-approval under Article 43, and the quality of reporting in these studies should be compared with the results presented within this paper. 22 Odutola M. K. CA 5.9 2021 A systematic review and meta-Environmental Research, The article has been classified as relevant by full text - Category B analysis of occupational (2021), Vol. 197, Article No. and **not reliable** for the following reason: This is a review article et al. exposures and risk of follicular 110887 of the literature for numerous exposures, including glyphosate, and follicular lymphoma. It is not primary data. The authors used lymphoma standard meta-analysis routines. However, they had no ability to correct for limitations in the original studies. It seems that the authors had only a superficial knowledge of the details and quality limitations of many of the glyphosate studies because they concluded that the risk of bias was low (viz., systematic error) – other than the small number of cases (viz., random error). Most previous reviewers of glyphosate studies considered the risk of

Pu Y. et al.

14

CA 5.8

2021

Autism-like Behaviors in Male

Maternal Glyphosate Exposure.

Juvenile Offspring after

bias to be high for most of the studies.

The article has been classified as relevant by full text and

downgraded to Category B due to its non-reliability. The aim

of the study was to investigate whether maternal exposure of pure

glyphosate could cause ASD-like behaviours in juvenile offspring.

Water or 0.098% glyphosate (980 mg/L) was administered as drinking water from E5 to P21 (weaning). This level of glyphosate

(202), Vol. 19, No. 3, pp. 554acid in water has a very low pH of approximately 2.3, which may confound the results of the test due to either pH effects on the gastrointestinal tract, or reduced water consumption in the test group causing some degree of dehydration. Male offspring showed ASD-like behavioural abnormalities (i.e., increasing grooming behaviour and social interaction deficit) after maternal exposure of glyphosate. Purity of the active substance missing. Only one dose, no dose-response relationship established, number of animals/group is unclear. Dosing level in water is at least several orders of magnitude higher than worst case human dietary exposures and pH of dose group water is very low. Key parameters of water and food consumption not reported. No record of in-life clinical observations. No HCD reported and no method of analysis. No positive controls employed to verify the validity or accuracy of the method and therefore the relevance to human health assessments is at best tenuous. Oiu S. et al. CA 5.8 The article has been classified as relevant by full text - Category B 15 2021 Response of the nuclear Environmental science and xenobiotic receptors to alleviate pollution research international. and reliable with restrictions for the following reason: The article glyphosate-based herbicide-(2021), Vol. 29, pp. 2707-2717 provides supplementary information on the effect of Roundup on induced nephrotoxicity in piglet kidneys. The study also investigates the role of kidney weaned piglets. nuclear xenobiotic receptors. The piglet is not a model validated in the toxicological studies in the EU evaluations, however the information can still be used as supplementary. No dose-effect relationship. No HCD reported and no method of analysis. 23 Silver M. K. et CA 5.9 2021 Prenatal Exposure to Glyphosate Environmental health The article has been classified as relevant by full text - Category B and **not reliable** for the following reason: The authors took the and Its Environmental perspectives, (2021), Vol. 129, Degradate. No. 5, Article No 57011. opportunity to generate some data about glyphosate (and AMPA) Aminomethylphosphonic Acid and preterm birth from a cohort (PROTECT) study that was (AMPA), and Preterm Birth: A designed for other purposes than glyphosate per se. Adapting data Nested Case-Control Study in from an ongoing study is efficient and it can be informative when the PROTECT Cohort (Puerto the data collection from the ongoing study matches what would have been collected during a high-quality study of the question at Rico). hand. In most instances, however, the result is studies that have important limitations in study size or necessary information on personal factors and confounders. It is debatable whether pregnant women in the PROTECT cohort, patients at two university hospitals and 5 nearby clinics in northern Puerto Rico, are an optimum population for the study of glyphosate and preterm birth. Urine concentrations for these women equate to a glyphosate internal dose that is extremely low – a few percent or less of the European ADI – raising the issue of biological implausibility. Also, taking the analysis at face value requires the strong assumption that one or two 2nd trimester urine sample(s) reflects the amount of exposure during the etiologically meaningful time period for affecting length of gestation. The authors did not provide a justification for the adequacy of a single or two 2nd trimester urine sample(s). It is also worth noting that there are literally hundreds of chemicals that could have been measured in urine (or blood) to study length of gestation. One

normally would not choose to focus on such low levels of glyphosate over other possible internalized chemicals for the study participants and it can be argued that some of those other exposures would have been important to consider in the analyses. This was noted as a limitation by the authors. The results of the authors' various analyses differed depending on the specific comparison being made. Analyses based on the visit 3 urine samples showed a weak to moderate relationship between glyphosate and pre-term birth, whereas analyses based on the visit 1 urine sample or the average of the visit 1 and 3 urine samples showed near null odds ratios. On balance, the results did not show a consistent relationship between urinary concentration of glyphosate and pre-term birth. The various analyses controlled for relatively few personal factors and environmental factors. One can only speculate whether the results may have residual confounding. In conclusion, the results of this study have very limited relevance for a glyphosate risk assessment. First, it's unclear whether the urine sampling is a valid representation of the internal dose at a relevant time point for the health outcome under study. Second, the range of internal doses for study participants was so low as to suggest biological implausibility. Third, the findings are based on small numbers of cases and varied across a range of analyses, some showing no association and some showing a weak to moderate association. Lastly, there was limited consideration of confounding factors. 16 Sopko B. et al. CA 5.8 2021 Glyphosate Interaction with ACS omega, (2021), Vol. 6, The article has been classified as relevant by full text and eEF1a1 Indicates Altered No. 23, pp. 14848-14857 downgraded to Category B due to its non-reliability. The Protein Synthesis: Evidence for paper is a review of the literature that provides information on the Reduced Spermatogenesis and mode of action of glyphosate via interaction with eEF1α1 pathway Cytostatic Effect. and spermatogeneis and cytostatis effects through a combination of in silico, in vitro and in vivo information. The aim of the study was to evaluate a previously unknown mechanism to explain a presumption that glyphosate exposure can negatively affect animals, including humans. Computer modeling suggested a probable interaction between glyphosate and eukaryotic translation elongation factor 1 subunit alpha 1 (eEF1a1), which was said to be confirmed by microcalorimetry, however, details on the calorimetry method are lacking, including concentration(s) of glyphosate interrogated. Only restricted, nondisrupted spermatogenesis was reported in rats after 100 days (i.e. subchronic, not chronic as reported) glyphosate treatments (0.7 and 7 mg/L ad libitum in drinking water). Although the method notes water consumption was monitored, neither water consumption or feed intake were reported. It is important to note, glyphosate is acidic and dose groups drinking water would be a much lower pH than the control group. Only two dose groups were implemented. The results are not consistent with a number of multigenerational rat reproductive studies with doses up to orders of magnitude higher. Cytostatic and antiproliferative effects of

glyphosate in GC-1 and SUP-B15 cells were indicated. The metaanalysis of public health data suggested a possible effect of glyphosate use on sperm count, but this is not consistent with reporting in with epidemiology studies or multiple toxicology reproductive studies. Information on purity missing for the pure glyphosate. No HCD. Numerous deficiencies in the in vivo portion and significant underlying assumption in the in silico and meta-analysis. 28 Sorensen M. CA 6.10 2021 Feed residues of glyphosate -Animal, (2021), Vol. 15, No. 1 The article has been classified as relevant by full text - Category B T. et al. potential consequences for and reliable with restrictions for the following reason: This is a livestock health and literature review report on potential detrimental effects of productivity. glyphosate affect livestock gut microbiota and/or mineral status potentially with derived unfavourable effects on animal health and productivity. Some in vitro growth experiments were conducted with bacteria. Some differences were detected regarding the sensitivity of bacterial growth to glyphosate. The in vitro bacterial growth assays can be considered acceptable. However the new experimental data are limited and provide little additional information to existing studies (also in vivo studies) to this topic. The article has been classified as relevant by full text - Category B 17 Truzzi F. et al. CA 5.8 2021 Comparative Evaluation of the Frontiers in public health, Cytotoxicity of Glyphosate-(2021) Vol. 9, Article No. and reliable with restrictions for the following reason: This article Based Herbicides and Glycine 643898 provides supplementary information on the cytotoxicity of in L929 and Caco2 Cells. glyphosate but does not alter the risk assessment. No positive control, no metabolic activation. No HCD. 2021 Residues of glyphosate in food The article has been classified as relevant by full text - Category B 33 Vicini J. L. et CA 6.9 Comprehensive reviews in food and dietary exposure. science and food safety, (2021): and reliable without restrictions: This is a literature review article Ahead of Print with focus on 1) analytical methods for glyphosate and AMPA, 2) MRL and monitoring data (market surveys) and 3) dieatry risk assessment. It reflects a well written summary of available knowledge and regulatory requirements/assessments. Scientifically solid overall assessment of glyphosate consumer risk from glyphosate and AMPA. 34 Wang Y. et al. CA 6.9 2021 Establishment of a HPLC-Journal of agricultural and food The article has been classified as relevant by full text - Category B MS/MS Detection Method for chemistry, (2021), Vol. 69, No. and reliable with restrictions for the following reason: The article Glyphosate, Glufosinate-28, pp. 7969-7978 describes 1) development and optimisation of an analycal method Ammonium, and Aminomethyl for the determation of glyphosate, AMPA and glufosinate-Phosphoric Acid in Tea and Its ammonium, 2) monitoring of tea samples (n = 780) from China, Use for Risk Exposure and 3) risk assessment (deterministic and probabilistic) from Assessment. consumption of teas. The results showed that exposure to PMG, GLU and AMPA caused by drinking tea beverages poses no significant risk to human health. Regarding analytical procedures, it is stated that LOQ for Gly and AMPA was 0.3 mg/kg (derived from calibration standards); however the lowest validated concentration was 1.0 mg/kg. The article has been classified as relevant by full text - Category B 24 Yokoyama S. CA 5.9 2021 Transient glyphosate Neuropsychopharmacology encephalopathy due to a suicide reports, (2021), Vol. 41, No. 3, for the following reason: This is a case report of a man who et al. attempt. pp. 444-447 developed a delayed encephalopathy characterized by confusion seizure activity and decreased perfusion of his left cerebral

hemisphere on SPECT 3 days after a suicidal ingestion of formulated glyposate. On intial presentation the patient was asymptomatic, underwent gasric lavage, which is not indicated in an asymptomatic patient, and was admitted to the psychiatric floor. 3 days later he as noted to have a delirium for which he was treated with mirtazipine. This was discontinued when symptoms grew progessively worse. The authors speculate that the cause of the encephalopathy was glyphosate. This is highly unlikely as glyphosate is not neurotoxic, nor does it cause vascular constriction. A unilateral perfusion deficit is very uncommon in a toxin induced encephalopathy. This case is much more consistent with acute alcohol withdrawal, which is a slow onset syndrome that takes 2-3 days to develop, is charcterized by delirium and seizures, reversible vasogenic edema in the hippocampal regions. This presentation is not consistent with glyphosate overdoses and because of the suicidal ingestion should not impact regulatory decisions. 25 Zhang C. Q. et CA 5.9 2021 A case of allergic cutaneous Chinese journal of industrial The article has been classified as relevant by full text - Category B al. hygiene and occupational for the following reason: This is a case report of a man who vasculitis caused by glyphosate. diseases, (2021), Vol. 39, No. developed purpuric skin lesions involving the palms and 6, pp. 467-468 leukocytoclastic vasculitis after exposure to an agrichemical that was reported to be glyphosate. His symptoms improved with steroid therapy, recurred upon reexposure 2 times and resolved with steoid treatment. The article claims that the chemistry

involved was glyphosate despite the fact that there was no confirmation of exposure through any definitive identification of the product, urine or blood testing for the presence of glyphosate. Glyphosate is not a sensitizer, nor does it cause immune complex deposition in the vasculature. While the patient was worked up for several diseases associated leukocytoclastic vasculitis, they left out several very prominent infectious etiologies that are much more commonly associated with palmar rashes and vasculitidies. There is no described mechanism in the literature for this constellation of symptoms and no confirmation that the patient

was exposed to glyphosate.

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
43	CA 5.6	Kafshgiri Kaboli S. et al.	2021	Glyphosate effects on the female reproductive systems: a systematic review.	Reviews on environmental health, (2021): Ahead of print	The relevance of this article is unclear (Category C) for the following reason: The paper is a review of the literature that provides information on the effect of glyphosate formulations on the female reproductive system. The review does not provide all the necessary information, especially on the test material used, but refers to the original studies / there are no information on the formulation used and if they are similar to the representative formulation in EU / formulation accepted in EU.
44	CA 5.8	Maddalon A. et al.	2021	Glyphosate-based herbicides: Evidence of immune- endocrine alteration.	Toxicology, (2021), Vol. 459, Article No. 152851	The relevance of this article is unclear (Category C) for the following reason: This paper is a review of published epidemiological studies and studies performed in vitro and in vivo in animals, the possible association between glyphosate based herbicides and immune-endocrine alterations. Overall, the authors could not conclude on the immune-endocrine alteration reported in the analysed publications and stated that further studies are required. No information was provided on the criteria used to select the publications and to conclude on their reliability. Most of the experiments were performed with glyphosate formulations and only few of them with pure glyphosate. However, the details on the test items used are not available for all the studies included in this review - some trade names are provided but not for all the studies. Moreover, the co-formulant POEA, is mentioned and likely to be included in some of the formulations. Lack of criteria in the selection of the reviewed publications and/or the high heterogeneity in the reported results and/or no firm conclusion on whether the observed effects could be unequivocally associated to exposure to glyphosate and/or glyphosate herbicides.
45	CA 5.8	Milesi M. M. et al.	2021	Glyphosate Herbicide: Reproductive Outcomes and Multigenerational Effects.	Frontiers in endocrinology, (2021), Vol. 12, Article No. 672532	The relevance of this article is unclear (Category C) for the following reason: This paper is a review of the literature that provides information on the effects of glyphosate and glyphosate based formulations on reproductive health and endocrine functions. Overall, there is an absence of criteria for selecting the publications and their relevance/acceptability. Analyses of the selected publications highlighted the importance and need of further evaluating the toxicology of glyphosate and its formulations to the reproductive performance. Most of the experiments were performed with glyphosate formulations and only few of them with pure glyphosate. However, the details on the test items used are not available for all the studies included in this review - some trade names are provided but not for all the studies. Moreover, the co-formulant POEA, is mentioned and likely to be included in some of the formulations. Lack of criteria in the selection of the reviewed publications and/or the high heterogeneity in the reported results and/or no firm conclusion on whether the observed effects could be unequivocally associated to exposure to glyphosate and/or glyphosate herbicides.

Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
46	CA 5.8	Mohammadi K. et al.	2021	A systematic review and meta-analysis of the impacts of glyphosate on the reproductive hormones.	Environmental science and pollution research international, (2021) doi: 10.1007/s11356-021-16145-x	The relevance of this article is unclear (Category C) for the following reason: The paper is a review of the literature and meta-analysis that provides information on the effect of glyphosate on the reproductive hormones. Among the initial 279 records identified, 54 articles were retrieved for full-text evaluation, and then only eight studies were eligible for this systematic review and meta-analysis. There are some experiences performed with pure glyphosate, however the details on the test items used are not available for all the studies included in this review. Overall, the outcome of this review based on the qualified studies could suggest a possible effect of glyphosate and/or glyphosate based herbicides on the health reproductive system due to a tendency in decreasing testosterone and follicle-stimulating hormone (FLH). However, as indicated by the authors this review may be affected by a series of limitations among which the high heterogeneity within the hormonal measurements and the small sample size of the final eligible studies for this review. Lack of criteria in the selection of the reviewed publications and/or the high heterogeneity in the reported results and/or no firm conclusion on whether the observed effects could be unequivocally associated to exposure to glyphosate and/or glyphosate herbicides.
47	CA 5.8	Rossetti M. F. et al.	2021	Epigenetic Changes Associated With Exposure to Glyphosate-Based Herbicides in Mammals.	Frontiers in endocrinology, (2021), Vol. 12, Article No. 671991	The relevance of this article is unclear (Category C) for the following reason: This paper is a review of the literature that provides information on epigenetic changes associated with exposure to glyphosate and glyphosate formulations. However, the details on the test items used are not available for all the studies included in this review.
48	CA 5.8	Weisenburger D. D. et al.	2021	A Review and Update with Perspective of Evidence that the Herbicide Glyphosate (Roundup) is a Cause of Non- Hodgkin Lymphoma.	Clinical lymphoma, myeloma & leukemia, (2021), Vol. 21, No. 9, pp. 621-630	The relevance of this article is unclear (Category C) for the following reason: This paper is a review of the literature that provides information on exposure to glyphosate formulations and non-hodgkin lymphoma. However, the details on the formulation used are not available for all the studies included in this review.
49	CA 8.2.5, CP 10.2.2	Song Y. et al.	2020	protective effects of melatonin on survival, immune response, digestive enzymes activities and intestinal microbiota diversity in Chinese mitten crab (Eriocheir sinensis) exposed to glyphosate	Comparative biochemistry and physiology: CBP (2020), Vol. 238, Article No. 108845	The relevance of this article is unclear (Category C) for the following reason: The only information from this study that is relevant for the risk assessment is the effect of glyphosate on survival rate. The rest of the investigated parameters are all based on findings at cellular/mollecular level and therefore not relevant. Glyphosate has been tested at only one concentration (48.945 mg/L) and this concentrations was calculated as the 96 h LC50 value in a previous study. Mortality in this study at that concentration is lower than 50%, but still the relevance of the findings of this study for the risk assessment is not clear. In addition, the test item was not identified (not clear whether it is active substance or a product -and which kind of formulation.)
50	CA 8.4.1, CP 10.4.1	Zaller J. G. et al.	2021	Effects of glyphosate-based herbicides and their active ingredients on earthworms, water infiltration and glyphosate leaching are influenced by soil properties	Environmental Sciences Europe, (2021) Vol. 33, No. 1, Article No. 51	The relevance of this article is unclear (Category C) for the following reason: This is a greenhouse experiment where established weed populations of common amaranth (Amaranthus retroflexus) were sprayed with three glyphosate-based herbicides GBHs (Roundup LB Plus, Roundup PowerFlex, Touchdown Quattro) and their corresponding Als (salts of glyphosate isopropylammonium, potassium, diammonium) to examine their effects on the activity and physiological biomarkers of the earthworm species Lumbriculus terrestris. The route of exposure

KCA 9 Page 62 of 76

Submission Number	Data requirement (indicated by the corresponding CA / CP data point number)	Author(s)	Year	Title	Source	Justification
						to earthworms (herbicides were sprayed to the plants and not to the soil) is not in line with the EU process and therefore, no relatable endpoint can be established as not direct effects were assessed. Moreover, some of the studied variables are based on a cellular or molecular level and the only information that could be integrated in the EU evaluation is related to the variation in the density and activity of the earthworms 4 weeks after weed control applications. In addition, final conclusions were expressed in terms of GBH or AI and not for every single treatment. Nevertheless, weeds were treated at recommended dosages just as they would be applied to kill weeds before sowing, so the study somehow mimics what really happens to earthworms living in the soil when exposed to glyphosate residues after the weeds in a field are treated before sowing the crop. The soil is natural and glyphosate concentrations in soil and leachate were measured, so the real exposure to earthworms 26 days after GBH/AI applications is known.

Table 37: Articles of unclear relevance (category C) 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
43	Kafshgiri Kaboli S. et al.	CA 5.6	2021	Glyphosate effects on the female reproductive systems: a systematic review.	Reviews on environmental health, (2021): Ahead of print	The relevance of this article is unclear (Category C) for the following reason: The paper is a review of the literature that provides information on the effect of glyphosate formulations on the female reproductive system. The review does not provide all the necessary information, especially on the test material used, but refers to the original studies / there are no information on the formulation used and if they are similar to the representative formulation in EU / formulation accepted in EU.
44	Maddalon A. et al.	CA 5.8	2021	Glyphosate-based herbicides: Evidence of immune- endocrine alteration.	Toxicology, (2021), Vol. 459, Article No. 152851	The relevance of this article is unclear (Category C) for the following reason: This paper is a review of published epidemiological studies and studies performed in vitro and in vivo in animals, the possible association between glyphosate based herbicides and immune-endocrine alterations. Overall, the authors could not conclude on the immune-endocrine alteration reported in the analysed publications and stated that further studies are required. No information was provided on the criteria used to select the publications and to conclude on their reliability. Most of the experiments were performed with glyphosate formulations and only few of them with pure glyphosate. However, the details on the test items used are not available for all the studies included in this review - some trade names are provided but not for all the studies. Moreover, the co-formulant POEA, is mentioned and likely to be included in some of the formulations. Lack of criteria in the selection of the reviewed publications and/or the high heterogeneity in the reported results and/or no firm conclusion on whether the observed effects could be unequivocally associated to exposure to glyphosate and/or glyphosate herbicides.
45	Milesi M. M. et al.	CA 5.8	2021	Glyphosate Herbicide: Reproductive Outcomes and Multigenerational Effects.	Frontiers in endocrinology, (2021), Vol. 12, Article No. 672532	The relevance of this article is unclear (Category C) for the following reason: This paper is a review of the literature that provides information on the effects of glyphosate and glyphosate based formulations on reproductive health and endocrine functions. Overall, there is an absence of criteria for selecting the publications and their relevance/acceptability. Analyses of the selected publications highlighted the importance and need of further evaluating the toxicology of glyphosate and its formulations to the reproductive performance. Most of the experiments were performed with glyphosate formulations and only few of them with pure glyphosate. However, the details on the test items used are not available for all the studies included in this review - some trade names are provided but not for all the studies. Moreover, the co-formulant POEA, is mentioned and likely to be included in some of the formulations. Lack of criteria in the selection of the reviewed publications and/or the high heterogeneity in the reported results and/or no firm conclusion on whether the observed effects could be unequivocally associated to exposure to glyphosate and/or glyphosate herbicides.

Submission Number	Author(s)	Data requirement (indicated by the corresponding CA / CP data point number)	Year	Title	Source	Justification
46	Mohammadi K. et al.	CA 5.8	2021	A systematic review and meta-analysis of the impacts of glyphosate on the reproductive hormones.	Environmental science and pollution research international, (2021) doi: 10.1007/s11356-021-16145-x	The relevance of this article is unclear (Category C) for the following reason: The paper is a review of the literature and meta-analysis that provides information on the effect of glyphosate on the reproductive hormones. Among the initial 279 records identified, 54 articles were retrieved for full-text evaluation, and then only eight studies were eligible for this systematic review and meta-analysis. There are some experiences performed with pure glyphosate, however the details on the test items used are not available for all the studies included in this review. Overall, the outcome of this review based on the qualified studies could suggest a possible effect of glyphosate and/or glyphosate based herbicides on the health reproductive system due to a tendency in decreasing testosterone and follicle-stimulating hormone (FLH). However, as indicated by the authors this review may be affected by a series of limitations among which the high heterogeneity within the hormonal measurements and the small sample size of the final eligible studies for this review. Lack of criteria in the selection of the reviewed publications and/or the high heterogeneity in the reported results and/or no firm conclusion on whether the observed effects could be unequivocally associated to exposure to glyphosate and/or glyphosate herbicides.
47	Rossetti M. F. et al.	CA 5.8	2021	Epigenetic Changes Associated With Exposure to Glyphosate-Based Herbicides in Mammals.	Frontiers in endocrinology, (2021), Vol. 12, Article No. 671991	The relevance of this article is unclear (Category C) for the following reason: This paper is a review of the literature that provides information on epigenetic changes associated with exposure to glyphosate and glyphosate formulations. However, the details on the test items used are not available for all the studies included in this review.
49	Song Y. et al.	CA 8.2.5, CP 10.2.2	2020	protective effects of melatonin on survival, immune response, digestive enzymes activities and intestinal microbiota diversity in Chinese mitten crab (Eriocheir sinensis) exposed to glyphosate	Comparative biochemistry and physiology: CBP (2020), Vol. 238, Article No. 108845	The relevance of this article is unclear (Category C) for the following reason: The only information from this study that is relevant for the risk assessment is the effect of glyphosate on survival rate. The rest of the investigated parameters are all based on findings at cellular/mollecular level and therefore not relevant. Glyphosate has been tested at only one concentration (48.945 mg/L) and this concentrations was calculated as the 96 h LC50 value in a previous study. Mortality in this study at that concentration is lower than 50%, but still the relevance of the findings of this study for the risk assessment is not clear. In addition, the test item was not identified (not clear whether it is active substance or a product -and which kind of formulation.)
48	Weisenburger D. D. et al.	CA 5.8	2021	A Review and Update with Perspective of Evidence that the Herbicide Glyphosate (Roundup) is a Cause of Non-Hodgkin Lymphoma.	Clinical lymphoma, myeloma & leukemia, (2021), Vol. 21, No. 9, pp. 621-630	The relevance of this article is unclear (Category C) for the following reason: This paper is a review of the literature that provides information on exposure to glyphosate formulations and non-hodgkin lymphoma. However, the details on the formulation used are not available for all the studies included in this review.
50	Zaller J. G. et al.	CA 8.4.1, CP 10.4.1	2021	Effects of glyphosate-based herbicides and their active ingredients on earthworms, water infiltration and	Environmental Sciences Europe, (2021) Vol. 33, No. 1, Article No. 51	The relevance of this article is unclear (Category C) for the following reason: This is a greenhouse experiment where established weed populations of common amaranth (Amaranthus retroflexus) were sprayed with three glyphosate-based herbicides GBHs (Roundup LB Plus, Roundup PowerFlex, Touchdown Quattro) and their corresponding AIs (salts of glyphosate isopropylammonium, potassium, diammonium) to examine their effects on the activity and physiological

KCA 9 Page 65 of 76

Submission Number	Author(s)	Data requirement (indicated by the corresponding CA / CP data point number)	Year	Title	Source	Justification
				glyphosate leaching are influenced by soil properties		biomarkers of the earthworm species Lumbriculus terrestris. The route of exposure to earthworms (herbicides were sprayed to the plants and not to the soil) is not in line with the EU process and therefore, no relatable endpoint can be established as not direct effects were assessed. Moreover, some of the studied variables are based on a cellular or molecular level and the only information that could be integrated in the EU evaluation is related to the variation in the density and activity of the earthworms 4 weeks after weed control applications. In addition, final conclusions were expressed in terms of GBH or AI and not for every single treatment.  Nevertheless, weeds were treated at recommended dosages just as they would be applied to kill weeds before sowing, so the study somehow mimics what really happens to earthworms living in the soil when exposed to glyphosate residues after the weeds in a field are treated before sowing the crop. The soil is natural and glyphosate concentrations in soil and leachate were measured, so the real exposure to earthworms 26 days after GBH/AI applications is known.

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)
51	Ecotoxicology	Abdelmagid A. D. et al.	2021	Evaluation of Foeniculum vulgare impact on glyphosate hepato-toxicity in Nile tilapia: Biochemical, molecular and histopathological study	Aquaculture Research, (2021): Ahead of Print	The article has been classified as not relevant by full text for the following reason: The findings of this study are only based on cellular and molecular level that cannot be related to the risk assessment. The materials and methods section refers to an ecotoxicological LC50 endpoint, for which no information is provided.
52	Ecotoxicology	Banjare P. et al.	2021	Predictive classification-based QSTR models for toxicity study of diverse pesticides on multiple avian species	Environmental Science and Pollution Research, (2021), Vol. 28, No. 14, pp. 17992-18003	The article has been classified as not relevant by full text for the following reason: This article deals with general pesticide QSAR/QSTR effects models (not glyphosate specific) for birds, where glyphosate or a relevant metabolite are not the focus of the publication.
53	Ecotoxicology	Barbosa da Costa N. et al.	2021	Resistance, resilience, and functional redundancy of freshwater bacterioplankton communities facing a gradient of agricultural stressors in a mesocosm experiment.	Molecular ecology, (2021), Vol. 30, pp. 4771-4788	The article has been classified as not relevant by full text for the following reason: Roundup Super Concentrate contains POEA. This is clearly stated in the article by Muller et al. (2021): Toxicological Effects of Roundup(®) on Drosophila melanogaster Reproduction (Toxics 2021, 9, 161. https://doi.org/10.3390/toxics9070161).  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.
54	Ecotoxicology	Fantón N. et al.	2021	Biomarkers of exposure and effect in the armoured catfish Hoplosternum littorale during a rice production cycle	Environmental pollution, (2021), Vol. 287, Article No. 117356	The article has been classified as not relevant by full text for the following reason: This higher tier field study under the realistic conditions that the armoured catfish Hoplosternum littorale is exposed to a variety of pesticides during a rice production cycle is conducted in a rice field in Argentina. Therefore, this publication is considered not relevant because it does not deal with EU representative conditions. In addition, although metabolite AMPA bioaccumulation in fish liver and muscle was measured, the observed effects are caused by a mixture of compounds (mixture toxicity). No control group was used.
55	Ecotoxicology	Gao X. et al.	2021	Glyphosate exposure disturbs the bacterial endosymbiont community and reduces body weight of the predatory ladybird beetle Harmonia axyridis (Coleoptera: Coccinellidae).	The Science of the total environment, (2021), Vol. 790, Article No. 147847	The article has been classified as not relevant by full text for the following reason: The findings of this study do not generate endpoints that are relatable to the EU level risk assessment. Larvae of the non-target leaf-dwelling predatory ladybird beetle Harmonia axyridis were orally exposed to two different glyphosate concentration in sucrose solution. NTA oral exposure in the lab cannot be integrated into the EU RA scheme. Furthermore, some findings are based on cellular and molecular level that cannot be related to the risk assessment.

Submission Number	Technical section	Author(s)	Year	Title	Source	Reason for not including publication in dossier (based on relevance criteria)
56	Ecotoxicology	Hébert M-P. et al.	2021	Widespread agrochemicals differentially affect zooplankton biomass and community structure.	Ecological applications: a publication of the Ecological Society of America, (2021), Article No. e02423	The article has been classified as not relevant by full text for the following reason: Roundup Super Concentrate contains POEA. This is clearly stated in the article by Muller et al. (2021): Toxicological Effects of Roundup(®) on Drosophila melanogaster Reproduction (Toxics 2021, 9, 161. https://doi.org/10.3390/toxics9070161).  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.
57	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: The study design and the test system are not relevant for the European regulatory purposes. Daphnia magna was exposed to filtrated water taken from soil previously treated with a single concentration of 1000 mg glyphosate/L (not clear whether sprayed onto or mixed in). It is not possible to know which is the real concentration at which D. magna was exposed. In addition, the test item was not identified.
58	Ecotoxicology	Macri I. N. et al.	2021	Evaluating the impact of post- emergence weed control in honeybee colonies located in different agricultural surroundings.	Insects, (2021), Vol. 12, No. 2	The article has been classified as not relevant by full text for the following reason: The publication is dealing with genetically modified crops, which is not relevant for the glyphosate EU renewal. In addition, the experiment was performed with a mixture of 3 commercially formulated herbicides: an atrazine-based herbicide (Gesaprim® Syngenta), a 2,4-D-based herbicide (Voleris® Syngenta) and a glyphosate-based herbicide (Sulfosato Touchdown® Syngenta), thus the effect cannot be attributable to the substance of concern and can be seen as a consequence of the mixture toxicity. Based on the information in the safety data sheet provided on Syngenta's webpage (https://www.syngenta.com.ar/product/crop-protection/herbicida-no-selectivo/sulfosato-touchdown), Sulfosato Touchdown formulation contains polyethoxylated tallow amine (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,

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, 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. Finally, the study was conducted under field conditions in Argentina and therefore, not representative for the EU conditions.
59	Ecotoxicology	Muller K. et al.	2021	Toxicological Effects of Roundup(®) on Drosophila melanogaster Reproduction.	Toxics, (2021), Vol. 9, No. 7	The article has been classified as not relevant by full text for the following reason: None of the formulations tested is the representative formulation for the EU glyphosate renewal. Roundup® Ready to Use is a mixture of pelargonic acid and glyphosate thus the effects observed cannot be attributable to glyphosate only and can be seen as a consequence of the mixture toxicity. Roundup® Super Concentrate contains 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.
60	Ecotoxicology	Sudmoon R. et al.	2021	The effect of glyphosate on genotoxicity in Ipomoea aquatica	Toxicological & Environmental Chemistry, (2021): Ahead of Print.	The article has been classified as not relevant by full text for the following reason: This study investigates the effects of glyphosate on growth rate and genotoxicity of Ipomoea aquatica. The plants were grown in a soil collected from an organic agricultural field in Thailand which was supplemented with glyphosate at 1- to 3-fold the recommended dose. After 30 days, lengths and dry weights of the roots and shoots were found to decrease in a concentration dependent manner. The study aimed to simulate field conditions and the plants were grown in the open field with added organic fertilizers. Therefore, the publication is not dealing with EU representative uses / conditions (e.g. field locations, soil properties, non-EU monitoring etc.) and it is not relevant for the risk assessment. In addition, the concentration of glyphosate in the soil was not analyzed.
61	Ecotoxicology	Torres-Badia M. et al.	2021	Impaired mammalian sperm function and lower phosphorylation signaling caused by the herbicide Roundup® Ultra Plus are due to its surfactant component.	Theriogenology, (2021), Vol. 172, pp. 55-66	The article has been classified as not relevant by full text for the following reason: Pig spermatozoa were incubated in Tyrode's basal medium (TBM) or Tyrode's complete medium (TCM) (1 h at 38.5 C) with several Roundup dilutions or equivalent concentrations of glyphosate or POEA. The study design, the test system and mostly the exposure route are not relevant for the European regulatory purposes regarding ecotoxicology. In addition, most of the findings are based on

Submission	Technical	Author(s)	Year	Title	Source	Reason for not including publication in dossier (based on relevance
Number	section	Author(s)	Tear	THE	Source	criteria)  cellular and molecular level that cannot be related to the risk assessment. In addition, the formulation tested contains POEA (See Materials and Methods - The commercially available Roundup® Ultra Plus contains 36% (w/v) of the active ingredient glyphosate (GLY) and 6% (w/v) of the surfactant, polyoxyethylene amine (POEA).
62	Ecotoxicology	Torres-Moya F. et al.	2020	Study of the effects of glyphosate application on Collembola populations under controlled conditions.	Agronomia Colombiana, (2020), Vol. 38, No. 3, pp. 398-405	The article has been classified as not relevant by full text for the following reason: The objective of this research was to determine the effect of the application of different glyphosate doses on variation in collembolan (springtail) populations, but he study design, the test system and the mode of exposure of this study are not relevant for the European regulatory purposes. In addition, the publication does not deal with EU representative conditions (e.g. soil properties, non-EU monitoring of populations) because part of the soil used for the tests as well as all tested individuals were taken from a field location in Colombia.
63	Ecotoxicology	Wided O. et al.	2021	Protective role of Spirulina platensis against glyphosate induced toxicity in marine mussel Mytilus galloprovincialis	Journal of Environmental Science and Health, Part C: Toxicology and Carcinogenesis, (2021): Ahead of Print	The article has been classified as not relevant by full text for the following reason: The findings of this study are only based on cellular and molecular level that cannot be related to the risk assessment.
64	Ecotoxicology	Yang C. et al.	2021	Reproductive toxicity due to herbicide exposure in freshwater organisms.	Comparative biochemistry and physiology. Toxicology & pharmacology, (2021), Vol. 248, Article No. 109103	The article has been classified as not relevant by full text for the following reason: This review article presents only secondary information dealing with general herbicide exposures (not glyphosate specific), where no new data is provided that can be used for risk assessment.
65	Ecotoxicology	Zheng T. et al.	2022	Alleviative effects of Ginkgo biloba extract on oxidative stress, inflammatory response and immune suppression induced by long-term glyphosate exposure in tilapia (Oreochromis niloticus)	Aquaculture, (2022), Vol. 546, Article No. 737325	The article has been classified as not relevant by full text for the following reason: The findings of this study are only based on cellular and molecular level that cannot be related to the risk assessment.
66	Fate and behaviour in the environment	Barrow N. J.	2021	Some comments on: Phosphate and glyphosate sorption in soils following long-term phosphate applications by Munira et al. (2018)	Geoderma, (2021), Vol. 402, Article No. 115334	The article has been classified as not relevant by full text for the following reason: Ther article is commenting on another article (Phosphate and glyphosate sorption in soils following long-term phosphate applications by Munira et al. (2018)). The comment is related to the influence of phosphate on the adsorption of glyphosate. Another equation for calculating the Kf value in the presence of phosphate is proposed. There is no impact on the results for non-phosphate-amended soil. Furthermore the comment does not give any results but only further recommendations for data evaluation and interpretation.
67	Fate and behaviour in the environment	Sadatsharifi M. et al.	2021	The fate of a hazardous herbicide: a DFT-based ab initio study on glyphosate degradation.	Environmental science. Processes & impacts, (2021), Vol. 23, No. 7, pp. 1018-1028	The article has been classified as not relevant by full text for the following reason: Calculations were performed using density functional theory and post-Hartree-Fock correlated ab initio methods to find the possible mechanisms for the degradation process by small (hydroxyl, peroxyl, and superoxide) radicals. Rate constants (s -1) were calculated from the ab initio results for different elementary steps (transition steps for the reaction of glyphosate anions and radicals). No endpoints for EU risk assessment are generated. Quantum chemical calculations were

Submission Number	Technical section	Author(s)	Year	Title	Source	Reason for not including publication in dossier (based on relevance criteria)
						applied to determined structures and energies of molecular forms (isomers, intermediates, transition states) of glyphosate.
68	Fate and behaviour in the environment	Voutchkova D. D. et al.	2021	Estimating pesticides in public drinking water at the household level in Denmark	GEUS BULLETIN, (2021), Vol. 47, DOI:10.34194/geusb.v47.6090	The article has been classified as not relevant by full text for the following reason: Data on pesticide residues in Danish drinking water was taken from the national database Jupiter (https://eng.geus.dk/products-services-facilities/data-andmaps/national-well-database-jupiter). The highest amount detected was 3.2 µg/L for glyphosate and 1.2 µg/L for AMPA (see supplemental material). No information on location and timing of the detection are reported. The article contains secondary information and does not generate new data. Jupiter database was covered by applicant's evaluation on public monitoring data.
69	Toxicology and metabolism	Barbosa A. et al.	2021	Study of muscle fibers of the extensor digitorium longus and soleus muscles of C57BL/6 females exposed to glyphosate during pregnancy and lactation.	Einstein (Sao Paulo, Brazil), (2021), Vol. 19, Article No. eAO5657	The article has been classified as not relevant by full text for the following reason: The aim of this study was to evaluate the morphology and morphometry of the muscles extensor digitorium longus and soleus of C57BL/6 females, who were exposed to glyphosate during pregnancy and lactation.  Glyphosate group presented lower weight gain during pregnancy and also lower final body weight and naso-anal length; however, the other body parameters evaluated did not present a significant difference in relation to the Control Group. Significant differences were also not observed in the analysis of muscle fibers and connective tissue. Importantly, although weight gain was measured, there were not records of feed intake for each group, which is most likely the main determinant in ascribing cause for the weight differences reported.  The publication is dealing with a glyphosate formulation Roundup Original containing 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.
70	Toxicology and metabolism	de Maria Serra F. et al.	2021	Subchronic exposure to a glyphosate-based herbicide causes dysplasia in the digestive tract of Wistar rats.	Environmental science and pollution research international, (2021), Vol. 28, pp. 61477-61496	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 containing 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.
71	Toxicology and metabolism	Giambo F. et al.	2021	Toxicology and Microbiota: How Do Pesticides Influence Gut Microbiota? A Review	INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH, (2021), Vol. 18, No. 11	The article has been classified as not relevant by full text for the following reason: This paper is a review of the literature on the influence of pesticide exposure on gut microbial. Glyphosate is mentioned in only one paragraph of the article and no information is available on the test item, the experimental conditions and the description of the results.
72	Toxicology and metabolism	Kogevinas M.	2021	Glyphosate Exposure during Pregnancy and Preterm Birth (More Research Is Needed).	Environmental health perspectives, (2021), Vol. 129, No. 5, Article No. 51301	The article has been classified as not relevant by full text for the following reason: This is a commentary on a single published article, not original research. There is no study design or study population per se. There is no information in this commentary to evaluate the appropriateness of a study population. The conclusion of the author is that more research is needed. As such, the commentary does not

KCA 9 Page 71 of 76

Submission Number	Technical section	Author(s)	Year	Title	Source	Reason for not including publication in dossier (based on relevance criteria)
						contribute relevant / reliable information to the assessment of risk from glyphosate use.
73	Toxicology and metabolism	Mesnage R. et al.	2020	Computational modelling provides insight into the effects of glyphosate on the shikimate pathway in the human gut microbiome.	Current research in toxicology, (2020), Vol. 1, pp. 25-33	The article has been classified as not relevant by full text for the following reason: The publication studies the presence and activity of the shikimate pathway by assessing faecal metagenomes from different datasets. There is also the reference to a previous microbiome study to understand the effects of glyphosate/glyphosate formulated product on the gut microbiota at different stages of the rat digestive tract. However, the main part of the article is focussing on the metagenomes and metatranscriptomes and not evaluating the effect on gut microbiota after exposure to glyphosate. Moreover, potential effects to gut microbiota and serum metabolome are not part of the EU risk assessments.

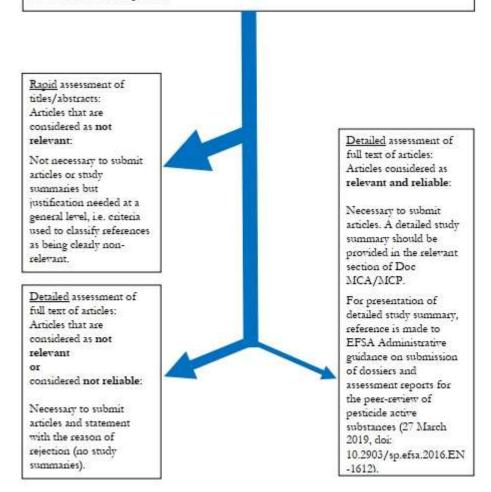
## Appendix 1: AGG ADVICE on how to present the literature search in the dossier

ASSESSMENT GROUP ON GLYPHOSATE (AGG)

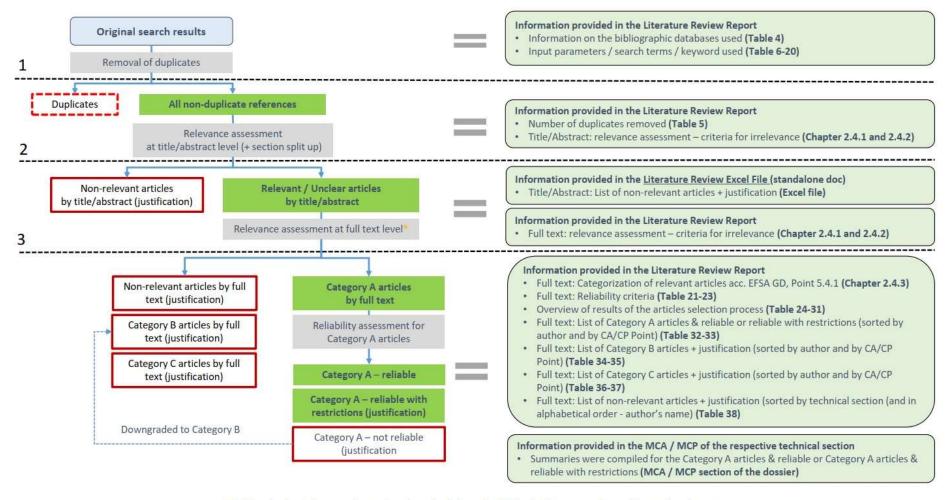
October 2019

# 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 – 14 May 2021 – August 2021

Preparing the search queries on STN:

FILE 'STNGUIDE' ENTERED AT 10:45:08 ON 08 SEP 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
- L2 OUE SPE=ON ABB=ON PLU=ON 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 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 HYDROXYMETHYLPHOSPHONIC ACID QUE SPE=ON ABB=ON PLU=ON L3 OR L4 1.4
- L5
- SAVE TEMP L5 GLY3/Q
- L6 QUE SPE=ON ABB=ON PLU=ON 35404-71-8 OR METHYLAMINO METHYL PHOSPHONIC ACID OR METHYLAMINOMETHYL PHOSPHONIC ACID OR 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 QUE SPE=ON ABB=ON PLU=ON 2 3 DIHYDROXY 1 OXOPROPYL AMINOMETHYL PHOSPHONIC ACID OR 2 3 DIHYDROXY 1 OXOPROPYL AMINOMETHYLPHOS PHONIC ACID OR N GLYCERYL AMPA QUE SPE=ON ABB=ON PLU=ON 3 OXO 3 PHOSPHONOMETHYL AMINO PROBANOLO ACID OR 2 OXO 3 PHOSPHONOMETHYL AMINOR 2 OXO 3 PHOSPHONOMETHYL AMINOR OR 2 OXO 3 PHOSPHONOMETHYL AMINOR 2 OXO 3 PHOSPHONOMETHYL 2 OXO 3 OXO 3 PHOSPHONOMETHYL 3 OXO 3 PHOSPHO
- L7
- L8 PROPANOIC ACID OR 3 OXO 3 PHOSPHONOMETHYL AMINOPROPANOIC ACID OR N MALONYL AMPA
- QUE SPE=ON ABB=ON PLU=ON 993-13-5 OR DIHYDROGEN METHYLPHOSPH ONATE OR METHANEPHOSPHONIC ACID OR METHYL PHOSPHONIC ACID OR L9 METHYLPHOSPHONIC ACID OR NSC 119358 OR PHOSPHONIC ACID METHYL OR PHOSPHONIC ACID P METHYL
- L10 QUE SPE=ON ABB=ON PLU=ON (L6 OR L7 OR L8 OR L9) 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 L11 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 METHYLGLYCINE OR N PHOSPHONOMETHYL N METHYLGLYCINE
- QUE SPE=ON ABB=ON PLU=ON (L11 OR L12) SAVE TEMP L13 GLY5/Q L13
- 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 L14 IN VITRO OR INVIVO OR INVITRO OR MODE OF ACTION OR SKIN? OR EYE? OR IRRIT? OR SENSI? OR ALLERG?
- 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 L15 METABOLIC OR DISTRIBUTION OR ADSORPTION OR EXCRETION OR ELIMINATION OR KINETIC OR CYTOCHROME OR ENZYM?
- ELIMINATION OR KINETIC OR CYTOCHROME OR ENZYM?

  QUE SPE=ON ABB=ON PLU=ON 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?

  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 L16
- L17 EXPOSURE OR OPERATOR? OR BYSTANDER? OR RESIDENT? OR WORKER? OR OCCUPAT?
- L18 OUE SPE=ON ABB=ON PLU=ON BIOMONITORING OR HUMAN EXPOSURE OR MICROBIOME OR OXIDATIVE STRESS OR APOPTOSIS OR NECROSIS OR CYTOTOXICITY OR POLYOXYETHYLENEAMINE OR POEA OR SURFACTANT OR RISK ASSESSMENT?
- QUE SPE=ON ABB=ON PLU=ON (L14 OR L15 OR L16 OR L17 OR L18) SAVE TEMP L19 TOX/Q L19
- QUE SPE=ON ABB=ON PLU=ON UPTAKE OR TRANSLOCATION OR RUMEN OR STORAGE STABILITY OR STORAGE OR STABILITY OR METABOLIC OR L20 METABOLISM OR BREAKDOWN OR NATURE OF RESIDUES OR RESIDUE? OR MAGNITUDE OF RESIDUES OR PROCESS? OR EFFECTS OF PROCESSING
- AGNITUDE 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 OUT SPECON ADDRESSION (2) OR DELY OR LEY OR COMPANY OF THE SPECON ADDRESSION (2) OR DELY OR LEY OR COMPANY OF THE SPECON ADDRESSION (2) OR DELY OR LEY OR COMPANY OF THE SPECON ADDRESSION (2) OR DELY OR LEY OR COMPANY OF THE SPECON ADDRESSION (2) OR DELY OR LEY OR COMPANY OF THE SPECON ADDRESSION (2) OR DELY OR LEY OR COMPANY OF THE SPECON ADDRESSION (2) OR DELY OR LEY OR COMPANY OF THE SPECON ADDRESSION (2) OR DELY OR LEY OR COMPANY OR L21
- 1.22
- QUE SPE=ON ABB=ON PLU=ON (L20 OR L21 OR L22) SAVE TEMP L23 RES/Q L23
- 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 L25 OR DRIFT OR RUN-OFF OR RUNOFF OR DRAINAGE OR VOLAT? OR ATMOSPHERE OR LONG-RANGE TRANSPORT OR SHORT-RANGE TRANSPORT
- QUE SPE=ON ABB=ON PLU=ON TRANSPORT OR MICRONUTRIENT OR PHOSPHATE OR IRON OR MANGANESE OR HALF-LIFE OR HALF-LIFE OR L26 HALF-LIVES OR HALFLIVES OR DT50 OR KINETICS OR OFF-SITE MOVEMENT OR REMOVAL OR DRINKING WATER OR WATER TREATMENT PROCESSES
- QUE SPE=ON ABB=ON PLU=ON ATMOSPHERIC DEPOSITION OR TILE-DRAI NS OR SURFACE WATER OR MONITORING DATA OR DISINFECTANT OR L27 OZONE OR TILLAGE OR INFILTRATION OR HARD SURFACE OR RAINWATER OR RAIN WATER OR CHELAT? OR COMPLEX? OR MINERALIZATION OR
- L28
- OR KAIN 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) SAVE TEMP L28 FATE/Q QUE SPE=ON ABB=ON PLU=ON TOX? OR ECOTOX? OR ?TOXIC OR ?TOXIC TY OR HAZARD OR ADVERSE OR ENDOCRINE DISRUPT? OR BIOACCUMULATE? OR BIOMAGNIFI? OR BIOCONCENTRATION OR POISON OR PUBLICATION OR POISON OR PROPERTY OF BIOACCUMULATE? OR BIOMAGNIFI? OR BIOCONCENTRATION OR POISON OR PUBLICATION OR PUBLICATIO L29 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
- L30 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? 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 L31 LEMINA ON MAINTY ON ESTUARNING ON CAUSTIA, ON GAST INTO OF ON INSECT OR MOLLUSC OR REPTILE OR AMPHIB? OR BEE? OR APIS OR 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
  - 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 NITROGEN
- OUE 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

Final search - Update Sep 2021:

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- 4783 SEA SPE=ON ABB=ON PLU=ON GLY1/O OR GLY2/O OR GLY3/O OR L1 GLY4/Q OR GLY5/Q
- L2
- 158 SEA SPE=ON ABB=ON PLU=ON L1 AND ED>20210513 158 SEA SPE=ON ABB=ON PLU=ON L2 NOT (COMMENT? OR DISSERTATION OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/DT SAVE TEMP L3 GLYMEDL/A

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- 126 SEA SPE=ON ABB=ON PLU=ON L16 AND ED>20210513 111 SEA SPE=ON ABB=ON PLU=ON L17 NOT (COMMENT? OR DISSERTATION OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/DT SAVE TEMP L18 GLYPQSCI/A

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- 121 SEA SPE=ON ABB=ON PLU=ON L22 AND ED>20210513 120 SEA SPE=ON ABB=ON PLU=ON L23 NOT (COMMENT? OR DISSERTATION L24 OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/DT SAVE TEMP L24 GLYEMBA/A

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- GLY4/Q OR GLY5/Q

  129 SEA SPE=ON ABB=ON PLU=ON L25 AND ED>20210513

  129 SEA SPE=ON ABB=ON PLU=ON L26 NOT (COMMENT? OR DISSERTATION OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/DT 1.27 SAVE TEMP L27 GLYESBIO/A

#### FILE 'HCAPLUS' ENTERED AT 11:18:54 ON 08 SEP 2021

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- GLY4/Q OR GLY5/Q
  GLY4/Q OR GLY2/Q OR GLY2/Q OR GLY2/Q OR GLY3/Q OR
  GLY4/Q OR GLY5/Q
  440 SEA SPE=ON ABB=ON PLU=ON L28 AND ED>20210513
  272 SEA SPE=ON ABB=ON PLU=ON L29 NOT (COMMENT? OR DISSERTATION
  OR EDITORIAL OR MEETING? OR NEWS? OR PATENT OR PRESS RELEASE)/DT L30 SAVE TEMP L30 GLYHCAP/A

#### FILE 'SCISEARCH' ENTERED AT 11:20:57 ON 08 SEP 2021

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- 390 SEA SPE=ON ABB=ON PLU=ON GL11/Q OR GL12/Q OR GL13/Q OR GL14/Q OR GL15/Q L33 SAVE TEMP L33 GLYSCIS/A

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ANSWERS '1-158' FROM FILE MEDLINE ANSWERS '159-436' FROM FILE AGRICOLA

ANSWERS '159-436' FROM FILE AGRICOLA ANSWERS '437-632' FROM FILE BIOSIS ANSWERS '633-907' FROM FILE CABA ANSWERS '908-919' FROM FILE FSTA ANSWERS '920-999' FROM FILE PQSCITECH

ANSWERS '1000-1132' FROM FILE TOXCENTER

ANSWERS '1133-1170' FROM FILE EMBASE

ANSWERS '1171-1199' FROM FILE ESBIOBASE ANSWERS '1200-1275' FROM FILE HCAPLUS ANSWERS '1276-1443' FROM FILE SCISEARCH

SAVE L34 GLY202109/A

1162 SEA SPE=ON ABB=ON PLU=ON L34 AND TOX/Q SAVE TEMP L35 GLYTOX/A L35

1285 SEA SPE=ON ABB=ON PLU=ON L34 AND RES/Q L36

869 SEA SPE=ON ABB=ON PLU=ON L34 AND FATE/Q L37 SAVE TEMP L37 GLYFATE/A

1365 SEA SPE=ON ABB=ON PLU=ON L34 AND ECO/O L38

1431 SEA SPE=ON ABB=ON PLU=ON (L35 OR L36 OR L37 OR L38) SAVE L39 GLY202109FIN/A

FILE 'MEDLINE, AGRICOLA, BIOSIS, CABA, FSTA, PQSCITECH, TOXCENTER, EMBASE, ESBIOBASE, HCAPLUS, SCISEARCH' ENTERED AT 12:56:47 ON 08 SEP 2021 CHARGED TO COST=113898 D ALL 1-TOT

#### SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 14:10:05 ON 08 SEP 2021