検索期間：2021年1月～5月

区分ａに分類された文献とその理由

ヒトに対する毒性

1. Information on the study

Data point:	CA 5.8.3
Report author	Ferramosca A. *et al.*
Report year	2021
Report title	Herbicides glyphosate and glufosinate ammonium negatively affect human sperm mitochondria respiration efficiency.
Document No	Reproductive Toxicology (2021), Vol. 99, pp. 48-55
Guidelines followed in study	None
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under not conducted under GLP/Officially recognised testing facilities. However, all experiments were performed according to principles of good laboratory practice.
Acceptability/Reliability:	Yes (Relevant, Category A acc. EFSA GD 2092, Point 5.4.1) / Reliable with restrictions

2. Assessment and conclusion

Assessment and conclusion by applicant:

Glyphosate was reported to reduce mitochondrial functionality, by decreasing the oxygen consumption rate in the active and in the passive state of mitochondrial respiration. The mitochondrial respiration efficiency was negatively affected only at concentrations of ≥ 100 nM. In the presence of the sex steroid hormone di-hydroxytestosterone (DHT), the negative effect on mitochondria functionality caused by glyphosate was observed from ≥ 0.1 nM. The passive state of mitochondrial respiration was found to be increased, suggesting a stimulus of mitochondrial respiration independent of ADP phosphorylation. In the presence of the mitochondria-targeting flavonoid quercetin, an increase in oxygen consumption rate was observed at concentrations in the range of 0.1 – 10 nM, reaching the highest levels at glyphosate and quercetin concentrations at 10 nM. Glyphosate was concluded to target mitochondria by using a mechanism that is different from that of DHT and quercetin but not described.

The study did not follow any OECD guideline and was not performed under GLP. No information on the test item with regard to purity was given, however, the supplier and batch number were reported. Cytotoxicity tests were not included, but a broad concentration range from 0.1 - 1000 nM was tested to cover the sexual hormones physiologically relevant concentrations (10 nM), triggering endogenously hormone-dependent signalling pathways, and the estimated (nM range) QRC dietary intake. However, it is not clear how these concentrations may be relevant in term of exposure to glyphosate. The authors stated that these concentration are below the NOAEL and acceptable daily intake (ADI) for the glyphosate (50 and 0.5 mg/kg bw per day, respectively). But no calculations have been presented to show whether spermatozoa could be exposed under the normal condition of glyphosate use. Given the novel study type and underlaying assumptions, evaluation of other comparator molecules to which humans are regularly systemically exposed (e.g. in the diet) would provide context to the relevance of these results and credibility to the assay's predictive capacity for effects in humans.

It was not clear from the publication which solvent has been used for which chemical. As solvent controls were included for all solvents used, the weakness was considered to be of minor degree. The criteria for a biological response were not provided.

Overall, the study is sufficiently documented to generally accepted scientific principles. It is considered to be reliable with restriction, but the information provided are not robust enough to impact the risk assessment.

Reliability criteria for *in vitro* toxicology studies

Publication: Ferramosca, 2021: Herbicides glyphosate and glufosinate ammonium negatively affect human sperm mitochondria respiration efficiency.	**Criteria met? Y/N/Uncertain**	**Comments**
Guideline-specific		
Study is in accordance to valid internationally accepted testing guidelines.	N	
Study is performed according to GLP.	N	
Study is completely described and conducted following scientifically acceptable standards.	Y	
Test substance		
Test material (glyphosate) is sufficiently documented and reported (i.e. purity, source, content, storage conditions)	Y	Purity for glyphosate not reported but batch No. given (#45521, Sigma Aldrich)
Only glyphosate acid or one of its salts is the tested substance.	N	Glyphosate alone and in combination with steroid hormones.
AMPA or other glyphosate metabolites is the tested substance.	N	
Study		
Test system is clearly and completely described.	Y	
Test conditions are clearly and completely described.	Y	
Metabolic activation system is clearly and completely described.	N	
Test concentrations is in physiologically acceptable range (< 1 mM).	Y	0.1-1000 nM
Cytotoxicity tests are reported.	N	Concentration range covers both the sexual hormones physiologically relevant concentrations (10 nM), triggering endogenously hormone-dependent signaling pathways, and the estimated (nM range) QRC dietary intake.
Positive and negative controls.	Y	
Complete reporting of effects observed.	Y	
Statistical methods described.	Y	
Historical negative and positive control data reported.	N	Criteria for a biological relevant response not provided.
Dose-effect relationship reported.	Y	
Overall assessment		
Reliable without restrictions	N	
Reliable with restrictions	Y	No information on the test item with regard to purity was given, however, the supplier and batch number were reported. Cytotoxicity tests were not included, but a broad concentration range from 0.1 - 1000 nM was tested. Historical control data were not reported. Results contradict higher tier in vivo multigenerational studies dosed at several orders of magnitude higher, which do not report any adverse outcomes in fecundity or reproductive outcome. No information on whether the tested concentration may reflect physiological exposure to human spermatozoa in vivo following exposure to the accepted regulatory dose levels following

Publication: Ferramosca, 2021: Herbicides glyphosate and glufosinate ammonium negatively affect human sperm mitochondria respiration efficiency.	**Criteria met? Y/N/Uncertain**	**Comments**
		glyphosate use as herbicide.
Not reliable	N	

1. Information on the study

Data point:	CA 5.9.4
Report author	Shrestha S. *et al.*
Report year	2020
Report title	Pesticide use and incident Parkinson's disease in a cohort of farmers and their spouses.
Document No	Environmental Research (2020), Vol. 191, Article No. 110186 https://doi.org/10.1016/j.envres.2020.110186
Guidelines followed in study	None
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	Not applicable
Acceptability/Reliability:	Yes (Relevance Category A)/Reliable without restrictions

2. Assessment and conclusion

Assessment and conclusion by applicant:

Glyphosate was not associated with PD in analyses based on ever use or in analyses based on IWLDs of use. Given that there is no plausible mechanism for glyphosate causing PD and that glyphosate systemic dose has been found to be minimal for applicators and spouses (Acquavella et al. 2004), those results are considered to be a valid.

References

Acquavella JF, Alexander BH, Mandel JS, et al. Glyphosate biomonitoring for farmers and their families: Results from the farm family exposure study. Environ. Health Perspect. 2004; 112:321-326.

Reliability criteria for epidemiology studies

Publication: Shrestha S. et al., 2020, Pesticide use and incident Parkinson's disease in a cohort of farmers and their spouses.	**Criteria met? Y/N/?**	**Comments**
Guideline-specific		
Study is in accordance to valid internationally accepted testing guidelines/practices.	n/a	Not applicable
Study is completely described and conducted following scientifically acceptable standards.	Yes	
Test substance		
Exposure to formulations with only glyphosate as a.i.	Yes	
Exposure to formulations with glyphosate combined with other a.i.	No	
Exposure to various formulations of pesticides.	Yes	50 pesticides total
Study		
Study design – epidemiological method followed.	Yes	
Description of population is investigated.	Yes	
Description of exposure circumstances.	Yes	
Description of results.	Yes	
Have confounding factors been considered.	Yes	
Statistical analysis.	Yes	
Overall assessment		

Publication: Shrestha S. et al., 2020, Pesticide use and incident Parkinson's disease in a cohort of farmers and their spouses.	**Criteria met? Y/N/?**	**Comments**
Reliable without restrictions	Yes	The finding of no association between glyphosate and Parkinson's disease risk in this study is considered to be valid. The results fit with what is known about glyphosate toxicology and exposure potential.
Reliable with restrictions	No	
Reliability not assignable	No	
Not reliable	No	

1. Information on the study

Data point:	CA 5.9.4
Report author	Werder E. J. *et al.*
Report year	2020
Report title	Herbicide, fumigant, and fungicide use and breast cancer risk among farmers' wives.
Document No	Environmental Epidemiology (2020), Vol. 4, No. 3, Art. No. e097
Guidelines followed in study	None
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	Not applicable
Acceptability/Reliability:	Yes (Relevance Category A)/Reliable without restrictions

2. Assessment and conclusion

Assessment and conclusion by applicant:

This study was undertaken based on the assumption that the properties of pesticides – on the endocrine disruption and estrogenic activity scales – are such that an increase in breast cancer risk is possible from direct use of specific pesticides by female AHS spouses or from presumed indirect exposure related to their husbands' use of specific pesticides. The presumed biologic properties of pesticides underlying the study's hypotheses do not apply to glyphosate, at systemic doses from direct or indirect exposure (10^{-4} mg/kg direct, 10^{-5} mg/kg indirect – see Acquavella et al. 2004). The results of the study did not find clear associations between pesticide use and breast cancer risk and results for glyphosate were consistent across the various analyses in indicating no association with breast cancer.

We conclude that this study provides evidence that glyphosate is not related to breast cancer risk.

References

Acquavella JF, Alexander BH, Mandel JS, et al. Glyphosate biomonitoring for farmers and their families: Results from the farm family exposure study. Environ. Health Perspect. 2004; 112:321-326.

Reliability criteria for epidemiology studies

Publication: Werder E. J. et al., 2020, Herbicide, fumigant, and fungicide use and breast cancer risk among farmers' wives.	**Criteria met? Y/N/?**	**Comments**
Guideline-specific		
Study is in accordance to valid internationally accepted testing guidelines/practices.	n/a	Not applicable
Study is completely described and conducted following scientifically acceptable standards.	Yes	
Test substance		
Exposure to formulations with only glyphosate as a.i.	Yes	
Exposure to formulations with glyphosate combined with other a.i.	Uncertain	
Exposure to various formulations of pesticides.	Yes	26 pesticides
Study		

Study design – epidemiological method followed.	Yes	
Description of population is investigated.	Yes	
Description of exposure circumstances.	Uncertain	No description of how farm spouses applied pesticides.
Description of results.	Yes	
Have confounding factors been considered.	Yes	
Statistical analysis.	Yes	Good.
Overall assessment		
Reliable without restrictions	Yes	This study did not show a relationship between glyphosate and breast cancer. That result is consistent with glyphosate's exposure and toxicological properties.
Reliable with restrictions	No	
Reliability not assignable	No	
Not reliable	No	

検索期間：2021年1月～5月

区分ａに分類された文献とその理由

生活環境動植物及び家畜に対する毒性

1. Information on the study

Data point:	CP 10.2.1
Report author	Gustinasari K. *et al.*
Report year	2021
Report title	Acute toxicity and morphology alterations of glyphosate-based herbicides to *Daphnia magna* and *Cyclops vicinus*
Document No	Toxicological Research, 2021, 37, 197-207
Guidelines followed in study	None
Deviations from current test guideline	• No guideline was used / followed
GLP/Officially recognised testing facilities	• No, not conducted under GLP/Officially recognised testing facilities (no indication)
Acceptability/Reliability:	Yes (Relevant, Category A acc. EFSA GD 2092, Point 5.4.1) / Reliable with restrictions

2. Assessment and conclusion

Assessment and conclusion by applicant:

The study provides regulatory relevant endpoints, specifically the LC_{50} for *D. magna* and *C. vicinus* after 48-hours exposure. However, the study cannot be deemed fully reliable due to the following aspects: First, the exposure concentrations were not analytically verified. Furthermore, previous exposure of *C. vicinus* to contaminants cannot be excluded as they were collected from a river with unknown contamination history. In addition, the exposure medium was not specified (possibly distilled water, but the phrasing is ambiguous) and important info on the culturing conditions is missing (i.e. temperature, etc.). Life-stage and size of the organisms at test start were not documented. Finally, for the morphological alterations, the control values were not reported.

ECOTOXICOLOGY: Reliability criteria for the detailed assessment of full-text documents

Criteria	Criteria met? Yes / No / Uncertain	Comment / Justification
Key criteria		
1. For guideline-compliant studies (GLP studies): OECD, OPPTS, ISO, and others. The validity/quality criteria listed in the corresponding guidelines are met.	No	Non-guideline study
2. No previous exposure to other chemicals is documented (where relevant).	Yes (*D. magna*) and No (*C. vicinus*)	*D. magna* were obtained from a culture, *C. vicinus* were sampled from a river
3. For aquatic studies, the test substance is dissolved in water or where a carrier is required, it is appropriate (non-toxic) and a carrier control / positive control is considered in the test design.	Yes	Test item dissolved in distilled water, no solvent used
4. Glyphosate or its metabolite (test item) are sufficiently documented and reported (i.e. purity, source, content etc.).	Yes	Source and content reported
5. For tests including vertebrates, there is a compliance of the batches used in toxicity studies compared to the technical specification.	No	Invertebrate study

6. 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 etc.	No	Reported: Source, feeding, aeration Not reported: Culturing conditions (incl. type of medium, O_2-content, temperature, pH, conductivity), life-stage or size of test organisms
7. The validity criteria from relevant test guidelines can be extrapolated across different species but not necessarily across different test designs. If different, then the nature of the difference and impact should ideally be discussed.	No	Non-guideline study
8. Only glyphosate or its metabolite is the test substance (excluding mixture with other substances), and information on application of the test substance is described.	Yes	Test with glyphosate formulation SUMIN ATUT 360 SL
9. The endpoint measured can be considered a consequence of glyphosate (or a glyphosate metabolite).	Yes	
10. Study design / test system is well described, including when relevant: concentration in exposure media (dose rates, volume applied, etc.), dilution/mixture of test item (solvent, vehicle) where relevant.	Uncertain	Doses are reported but constitution of exposure medium not clear, no dilution scheme provided
11. Analytical verifications are performed in test media (concentration) / collected samples, stability of the test substance in test medium should be documented.	No	Concentrations were not analytically verified
12. An endpoint can be derived. Findings do deliver a regulatory endpoint, and/or is useful as supporting information.	Yes	Endpoints reported: LC_{50} (12, 24 and 48-h) and NOEC (but not correctly determined)
13. The test has been tested in several dose levels (at least 3) including a positive/negative control where relevant.	Yes	5 treatment levels and a negative control
14. Suitable exposure throughout the whole exposure period was demonstrated and reported.	No	Exposure concentrations were not analytically verified.
15. A clear concentration response relationship is reported – in studies where the dose response test design is employed.	Yes	
16. A sufficient number of animals per group was included to facilitate statistical analysis: mortality in control groups reported, observations/findings in positive/negative control clearly reported (where relevant).	Yes	3 replicates of 10 organisms per treatment group and control; control data reported
17. Assessment of the statistical power of the assay is possible with reported data.	Yes	Mean and standard error provided; no raw data
18. If statistical methodology was applied for findings reported, then the data analysis applied should be clearly documented (e.g., checking the plots and confidence intervals).	Yes	Statistical analysis sufficiently described
19. Description of the observations (including time-points), examinations, and analyses performed, with (where relevant) dissections being well documented.	Yes	
20. For terrestrial ecotox studies in the lab or the field, the substrates used should be adequately described e.g. nature of substrate i.e. species of leaf or soil type.	-	Not applicable, aquatic study

20.1. Field locations are relevant/comparable to European conditions. Soils do not completely match the OECD criteria but are from Europe or to some extent representative for the European Agriculture.	-	Not applicable, aquatic study
20.2. Characterization of soil: texture (sandy loam, silty loam, loam, loamy sand), pH (5.5-8.0), cation exchange capacity, organic carbon (0.5-2-5%), bulk density, water retention, microbial biomass (~1% of organic carbon).	-	Not applicable, aquatic study
20.3. Other soils where information on characterization by the parameters: pH, texture, CEC, organic carbon, bulk density, water holding capacity, microbial biomass.	-	Not applicable, aquatic study
20.4. For tests including agricultural soils, they should not have been treated with test substance or similar substances for a minimum of 1 year.	-	Not applicable, aquatic study
20.5. For soil samples, sampling from A-horizon, top 20 cm layers; soils freshly from field preferred (storage max 3 months at 4 +/- 2°C).	-	Not applicable, aquatic study
20.6. Data on precipitation is recorded.	-	Not applicable, aquatic study
21. For lab terrestrial studies, the temperature was appropriate to the species being tested and generally should fall within the range between 20-25°C and soil moisture / relative humidity was reported.	-	Not applicable, aquatic study
22. For bee studies, temperature of the study should be appropriate to species.	-	Not applicable, aquatic study
23. For lab aquatic studies: 23.1. The source and / or composition of the media used should be described.	No	No information on test medium
23.2. The temperature of the water should be appropriate to the species being tested and generally fall within the 15-25ºC.	Yes	Temperature roughly between 21-22 °C at the end of the test, not reported for acclimation period
24. The residue data can be linked to a clearly described GAP table appropriate in the context of the renewal of approval of glyphosate (crop, application method, doses, intervals, PHI).	No	
25. Analytical results present residues measurements which can be correlated with the existing residues definition of glyphosate, and where relevant its metabolites.	No	No residue measurements
26. Analytical methods are clearly described and adequate statement of specificity and sensitivity of the analytical methods is included.	No	No analytical methods reported
27. Assessment of the ECX for the width of the confidence interval around the median value; and the certainty on the level of protection offered by the median ECX.	Uncertain	Underlying equation of the probit curve was reported but no confidence intervals for the LC_{50} or raw data to calculate confidence intervals retroactively

Overall assessment		
Reliable without restrictions	No	

Reliable with restrictions	Yes	The study provides regulatory relevant endpoints, specifically the LC_{50} for *D. magna* and *C. vicinus* after 48-hours exposure. However, the study cannot be deemed fully reliable due to the following aspects: First of, the exposure concentrations were not analytically verified. Furthermore, previous exposure of *C. vicinus* to contaminants cannot be excluded as they were collected from a river with unknown contamination history. In addition, the exposure medium was not specified (possibly distilled water, but the phrasing is ambiguous) and important info on the culturing conditions is missing. Life-stage and size of the organisms at test start were not documented. For the morphological alterations, the control values were not reported
Not reliable	No	

1. Information on the study

Data point:	CP 10.3.1
Report author	Luo Q.H. *et al.*
Report year	2021
Report title	Effects of a commercially formulated glyphosate solutions at recommended concentrations on honeybee (*Apis mellifera* L.) behaviours
Document No	Scientific Reports, 2021, 11, 2115
Guidelines followed in study	None
Deviations from current test guideline	• No guideline was used / followed
GLP/Officially recognised testing facilities	• No, not conducted under GLP/Officially recognised testing facilities (no indication)
Acceptability/Reliability:	Yes (Relevant, Category A acc. EFSA GD 2092, Point 5.4.1) / Reliable with restrictions

2. Assessment and conclusion

Assessment and conclusion by applicant:

The study reports on possibly relevant endpoints for the acute bee risk assessment, specifically a 48-hour oral LD_{50} value, as well as behavioural assessments on bees after glyphosate exposure. However, the study has to be deemed reliable with restrictions based on the following aspects: The colonies used for this study were obtained from an apiary about which no further information was provided. This pertains especially to possible pre-existent contaminant exposure of the colonies as well as health aspects regarding bee specific illnesses and treatments. As stated in OECD Guideline 213 (Honeybees, Acute Oral Toxicity Test), "… bees treated with chemical substances, such as antibiotics, anti-varroa, etc., should not be used for toxicity test for four weeks from the time of the end of the last treatment". This aspect cannot be adequately assessed as information on the bee colonies health or possible contaminant contact points is missing from the study report. The reported temperature during the test was 30 ± 1°C, which is outside the temperature range of 25 ± 2 °C recommended in OECD 213. The study report states an observation timeframe of 48 hours, however exact time-points of observation are not reported. Test concentrations were not analytically verified. Lastly, the LD_{50} value was reported without confidence intervals. The certainty on the level of protection offered by the median LD_{50} value can hence not be assessed. Based on the above mentioned aspects, the reliability of the study is restricted.

Assessment and conclusion by RMS:

ECOTOXICOLOGY: Reliability criteria for the detailed assessment of full-text documents

Criteria	Criteria met? Yes / No / Uncertain	Comment / Justification
Key criteria		
1. For guideline-compliant studies (GLP studies): OECD, OPPTS, ISO, and others. The validity/quality criteria listed in the corresponding guidelines are met.	No	Non-guideline study

2. No previous exposure to other chemicals is documented (where relevant).	No	Bees were acquired from a forest apiary, previous contact of the colony with contaminants is unknown
3. For aquatic studies, the test substance is dissolved in water or where a carrier is required, it is appropriate (non-toxic) and a carrier control / positive control is considered in the test design.	-	No carrier was used, test substance was directly dissolved in sucrose solution
4. Glyphosate or its metabolite (test item) are sufficiently documented and reported (i.e. purity, source, content etc.).	Uncertain	Content reported, Source and purity not reported
5. For tests including vertebrates, there is a compliance of the batches used in toxicity studies compared to the technical specification.	-	Non-vertebrate study
6. 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 etc.	Yes	Source, life-stage and haltering conditions reported
7. The validity criteria from relevant test guidelines can be extrapolated across different species but not necessarily across different test designs. If different, then the nature of the difference and impact should ideally be discussed.	No	Non-guideline study
8. Only glyphosate or its metabolite is the test substance (excluding mixture with other substances), and information on application of the test substance is described.	Yes	Roundup formulation; 356 g/L
9. The endpoint measured can be considered a consequence of glyphosate (or a glyphosate metabolite).	Yes	
10. Study design / test system is well described, including when relevant: concentration in exposure media (dose rates, volume applied, etc.), dilution/mixture of test item (solvent, vehicle) where relevant.	Yes	
11. Analytical verifications are performed in test media (concentration) / collected samples, stability of the test substance in test medium should be documented.	No	Concentrations were not analytically verified
12. An endpoint can be derived. Findings do deliver a regulatory endpoint, and/or is useful as supporting information.	Yes	An oral LD_{50} (48-hours) is reported
13. The test has been tested in several dose levels (at least 3) including a positive/negative control where relevant.	Yes	3 treatment levels and a negative control were tested
14. Suitable exposure throughout the whole exposure period was demonstrated and reported.	No	Exposure concentrations were not analytically verified
15. A clear concentration response relationship is reported – in studies where the dose response test design is employed.	Yes	Increased mortality with increased test item concentration was observed
16. A sufficient number of animals per group was included to facilitate statistical analysis: mortality in control groups reported, observations/findings in positive/negative control clearly reported (where relevant).	Yes	70 individuals per treatment group per experiment, experiment was repeated 6 times in total

17. Assessment of the statistical power of the assay is possible with reported data.	Yes	Mean and standard error as well as curve equation are reported but no raw data
18. If statistical methodology was applied for findings reported, then the data analysis applied should be clearly documented (e.g., checking the plots and confidence intervals).	Yes	Statistical methods were described incl. level of power
19. Description of the observations (including time-points), examinations, and analyses performed, with (where relevant) dissections being well documented.	Uncertain	Mortality was observed over 48-hours but exact time-points of observations not mentioned
20. For terrestrial ecotox studies in the lab or the field, the substrates used should be adequately described e.g. nature of substrate i.e. species of leaf or soil type.	-	Not applicable, Bee study
20.1. Field locations are relevant/comparable to European conditions. Soils do not completely match the OECD criteria but are from Europe or to some extent representative for the European Agriculture.	-	Not applicable, Bee study
20.2. Characterization of soil: texture (sandy loam, silty loam, loam, loamy sand), pH (5.5-8.0), cation exchange capacity, organic carbon (0.5-2-5%), bulk density, water retention, microbial biomass (~1% of organic carbon).	-	Not applicable, Bee study
20.3. Other soils where information on characterization by the parameters: pH, texture, CEC, organic carbon, bulk density, water holding capacity, microbial biomass.	-	Not applicable, Bee study
20.4. For tests including agricultural soils, they should not have been treated with test substance or similar substances for a minimum of 1 year.	-	Not applicable, Bee study
20.5. For soil samples, sampling from A-horizon, top 20 cm layers; soils freshly from field preferred (storage max 3 months at 4 +/- 2°C).	-	Not applicable, Bee study
20.6. Data on precipitation is recorded.	-	Not applicable, Bee study
21. For lab terrestrial studies, the temperature was appropriate to the species being tested and generally should fall within the range between 20-25°C and soil moisture / relative humidity was reported.	No	According to OECD 213 (Honeybees, Acute Oral Toxicity Test) the temperature should be 25 ± 2 °C; the reported temperature was 30 ± 1 °C
22. For bee studies, temperature of the study should be appropriate to species.	No	See above
23. For lab aquatic studies: 23.1. The source and / or composition of the media used should be described.	-	Not applicable, Bee study
23.2. The temperature of the water should be appropriate to the species being tested and generally fall within the 15-25ºC.	-	Not applicable, Bee study
24. The residue data can be linked to a clearly described GAP table appropriate in the context of the renewal of approval of glyphosate (crop, application method, doses, intervals, PHI).	No	
25. Analytical results present residues measurements which can be correlated with the existing residues definition of glyphosate, and where relevant its metabolites.	No	No residue measurements

26. Analytical methods are clearly described and adequate statement of specificity and sensitivity of the analytical methods is included.	No	No analytical measurements conducted
27. Assessment of the ECX for the width of the confidence interval around the median value; and the certainty on the level of protection offered by the median ECX.	No	LC_{50} reported but not the corresponding confidence interval; no raw data to re-calculate retroactively

Overall assessment		
Reliable without restrictions	No	
Reliable with restrictions	Yes	The study reports on possibly relevant endpoints for the acute bee risk assessment, specifically a 48-hour oral LD_{50} value, as well as behavioural assessments on bees after glyphosate exposure. However, the study has to be deemed reliable with restrictions based on the following aspects: The colonies used for this study were obtained from an apiary about which no further information was provided. This pertains especially to possible pre-existent contaminant exposure of the colonies as well as health aspects regarding bee specific illnesses and treatments. As stated in OECD Guideline 213 (Honeybees, Acute Oral Toxicity Test), "… bees treated with chemical substances, such as antibiotics, anti-varroa, etc., should not be used for toxicity test for four weeks from the time of the end of the last treatment". This aspect cannot be adequately assessed as information on the bee colonies health or possible contaminant contact points is missing from the study report. The reported temperature during the test was 30 ± 1 °C, which is outside the temperature range of 25 ± 2 °C recommended in OECD 213. The study reports states an observation timeframe of 48 hours, however exact time-points of observation are not reported. Test concentrations were not analytically verified. Lastly, the LD_{50} value was reported without confidence intervals. The certainty on the level of protection offered by the median LD_{50} value can hence not be assessed. Based on the above mentioned aspects, the reliability of the study is restricted.
Not reliable	No	

1. Information on the study

Data point:	CA 8.2.6.1 and CA 8.2.7
Report author	Tajnaiová L. *et al.*
Report year	2020
Report title	Determination of the Ecotoxicity of Herbicides Roundup® Classic Pro and Garlon New in Aquatic and Terrestrial Environments
Document No	Plants, 2020, 9, 1203
Guidelines followed in study	No OECD guideline mentioned. Modified EN ISO 8692, EN ISO 20079 and EN ISO 23753-1
Deviations from current test guideline	• No OECD guideline was used / followed
GLP/Officially recognised testing facilities	• No, not conducted under GLP/Officially recognised testing facilities (no indication)
Acceptability/Reliability:	Yes (Relevant, Category A acc. EFSA GD 2092, Point 5.4.1) / Reliable with restrictions

2. Assessment and conclusion

Assessment and conclusion by applicant:

The study reports on endpoints with possible relevance to the EU-level risk assessment for aquatic organisms, specifically freshwater algae (*Desmodesmus subspicatus*) and aquatic plants (*Lemna minor*) for the glyphosate metabolite AMPA. For *D. subspicatus*, a regulatory relevant endpoint is reported (IC_{50} for inhibition of growth rate, usually described as ErC_{50}). For the *Lemna* test, no regulatory relevant endpoint was reported but the assessed parameters (growth rate, front area and chlorophyll content) could potentially serve as supporting information in a weight of evidence approach.
As the tests differed both in design as in the reported endpoints, assessments of reliability should be looked at separately.

Test with *D. subspicatus*: The report states that the test was conducted according to ISO 8692 with not further specified modifications. Furthermore, it is reported, that the test fulfilled the validity criteria laid down by OECD test guideline for freshwater algae. There are however important information missing from the report. Specifically, no data of the negative control are presented not even in the supplementary material. No raw data are provided so, the validity criteria could not be checked. Furthermore, the IC_{50} value was calculated without confidence intervals and no parameters to judge the fit of the curve used for calculating the IC_{50} are presented. The certainty of the level of protection can therefore not be fully assessed.

Test with *L. minor*: While relevant parameters were assessed (such as growth rate and front area), no regulatory relevant endpoints, such as ECx values, were calculated. No justifications are provided. Furthermore, control data are only presented for the parameters front area and chlorophyll content, and only in a graphical format. Due to the lack of raw data, no regulatory relevant endpoints can be calculated retroactively.

For both tests: The purity of the test material was not reported. Furthermore, exposure concentrations were not analytically verified. Especially for the *Lemna* test, which lasted 7 days without renewal of the test substance, actual exposure concentrations could vary significantly from the nominal concentrations.

Based on the above mentioned issues for both tests, the study can only be deemed reliable with restrictions.

ECOTOXICOLOGY: Reliability criteria for the detailed assessment of full-text documents

Criteria	Criteria met? Yes / No / Uncertain	Comment / Justification
Key criteria		
1. For guideline-compliant studies (GLP studies): OECD, OPPTS, ISO, and others. The validity/quality criteria listed in the corresponding guidelines are met.	Uncertain	The study states that tests were conducted according to standardized test guidelines with modifications (not specified); EN ISO 8692 (growth inhibition of green algae) and EN ISO 20079 (duckweed growth inhibition test) with modifications. For algae: validity criteria according to OECD guidelines for freshwater algae were met For *Lemna*: no validity criteria mentioned
2. No previous exposure to other chemicals is documented (where relevant).	Yes	Test cultures were obtained from research institutes in Germany and Czech Republic
3. For aquatic studies, the test substance is dissolved in water or where a carrier is required, it is appropriate (non-toxic) and a carrier control / positive control is considered in the test design.	Uncertain	Not reported whether a solvent was used to prepare the test solutions
4. Glyphosate or its metabolite (test item) are sufficiently documented and reported (i.e. purity, source, content etc.).	Uncertain	Source of the test material was reported but no information on purity
5. For tests including vertebrates, there is a compliance of the batches used in toxicity studies compared to the technical specification.	-	Non-vertebrate study
6. 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 etc.	Yes	-
7. The validity criteria from relevant test guidelines can be extrapolated across different species but not necessarily across different test designs. If different, then the nature of the difference and impact should ideally be discussed.	Uncertain	Standardized test guidelines were inferred (see point 1.); validity criteria were met for the freshwater algae assay, for the *Lemna* assay validity was not discussed
8. Only glyphosate or its metabolite is the test substance (excluding mixture with other substances), and information on application of the test substance is described.	Uncertain	Glyphosate metabolite (AMPA) was tested but the preparation of test solutions was not described

9. The endpoint measured can be considered a consequence of glyphosate (or a glyphosate metabolite).	Yes	-
10. Study design / test system is well described, including when relevant: concentration in exposure media (dose rates, volume applied, etc.), dilution/mixture of test item (solvent, vehicle) where relevant.	No	Missing information on preparation of test solutions (no info on use of solvent)
11. Analytical verifications are performed in test media (concentration) / collected samples, stability of the test substance in test medium should be documented.	No	Concentrations were not analytically verified
12. An endpoint can be derived. Findings do deliver a regulatory endpoint, and/or is useful as supporting information.	Yes and No	Algae: Endpoints reported: IC_{50} *Lemna*: no regulatory relevant endpoint reported
13. The test has been tested in several dose levels (at least 3) including a positive/negative control where relevant.	Yes	*Lemna*: 10 levels and a control; 5 levels pH adjusted assay Algae: 15 levels and a control; 5 levels pH adjusted assay 3 replicates for all treatment and control levels
14. Suitable exposure throughout the whole exposure period was demonstrated and reported.	No	Exposure concentrations were not analytically verified.
15. A clear concentration response relationship is reported – in studies where the dose response test design is employed.	Yes	-
16. A sufficient number of animals per group was included to facilitate statistical analysis: mortality in control groups reported, observations/findings in positive/negative control clearly reported (where relevant).	Uncertain	Sufficient number of organisms and treatments was included but control results were not sufficiently reported for all endpoints (only for front area and chlorophyll content for the *Lemna* test)
17. Assessment of the statistical power of the assay is possible with reported data.	Uncertain	No raw data reported, however statistical test results are reported
18. If statistical methodology was applied for findings reported, then the data analysis applied should be clearly documented (e.g., checking the plots and confidence intervals).	Yes	Statistical methods were reported
19. Description of the observations (including time-points), examinations, and analyses performed, with (where relevant) dissections being well documented.	Yes	-
20. For terrestrial ecotox studies in the lab or the field, the substrates used should be adequately described e.g. nature of substrate i.e. species of leaf or soil type.	-	Not applicable, aquatic study
20.1. Field locations are relevant/comparable to European conditions. Soils do not completely match the OECD criteria but are from Europe or to some extent representative for the European Agriculture.	-	Not applicable, aquatic study
20.2. Characterization of soil: texture (sandy loam, silty loam, loam, loamy sand), pH (5.5-8.0), cation exchange capacity, organic carbon (0.5-2-5%), bulk density, water retention, microbial biomass (~1% of organic carbon).	-	Not applicable, aquatic study

20.3. Other soils where information on characterization by the parameters: pH, texture, CEC, organic carbon, bulk density, water holding capacity, microbial biomass.	-	Not applicable, aquatic study
20.4. For tests including agricultural soils, they should not have been treated with test substance or similar substances for a minimum of 1 year.	-	Not applicable, aquatic study
20.5. For soil samples, sampling from A-horizon, top 20 cm layers; soils freshly from field preferred (storage max 3 months at 4 +/- 2°C).	-	Not applicable, aquatic study
20.6. Data on precipitation is recorded.	-	Not applicable, aquatic study
21. For lab terrestrial studies, the temperature was appropriate to the species being tested and generally should fall within the range between 20-25°C and soil moisture / relative humidity was reported.	-	Not applicable, aquatic study
22. For bee studies, temperature of the study should be appropriate to species.	-	Not applicable, aquatic study
23. For lab aquatic studies: 23.1. The source and / or composition of the media used should be described.	Uncertain	Medium type mentioned: Bolds Basel Medium (BBM) and Steinberg medium; composition not mentioned
23.2. The temperature of the water should be appropriate to the species being tested and generally fall within the 15-25ºC.	Yes	Algae: 23 ± 2 ◦C *Lemna*: 24 ± 1 ◦C.
24. The residue data can be linked to a clearly described GAP table appropriate in the context of the renewal of approval of glyphosate (crop, application method, doses, intervals, PHI).	No	-
25. Analytical results present residues measurements which can be correlated with the existing residues definition of glyphosate, and where relevant its metabolites.	No	No residue measurements
26. Analytical methods are clearly described and adequate statement of specificity and sensitivity of the analytical methods is included.	No	No analytical methods reported
27. Assessment of the ECX for the width of the confidence interval around the median value; and the certainty on the level of protection offered by the median ECX.	No	IC_{50} value reported without C.I.
Overall assessment		
Reliable without restrictions	No	

Reliable with restrictions	Yes	The study reports on endpoints with possible relevance to the EU-level risk assessment for aquatic organisms, specifically freshwater algae (*Desmodesmus subspicatus*) and aquatic plants (*Lemna minor*) and the glyphosate metabolite AMPA. For *D. subspicatus,* a regulatory relevant endpoint is reported (IC_{50} for inhibition of growth rate, usually described as ErC_{50}). For the lemna test, no regulatory relevant endpoint was reported but the assessed parameters (growth rate, front area and chlorophyll content) could potentially serve as supporting information in a weight of evidence approach. As the tests differed both in design as in the reported endpoints, assessments of reliability should be looked at separately. Test with *D. subspicatus:* The report states that the test was conducted according to ISO 8692 with not further specified modifications. Furthermore, it is reported, that the test fulfilled the validity criteria laid down by OECD test guideline for freshwater algae. There are however important information missing from the report. Specifically, no data of the negative control are presented not even in the supplementary material. Furthermore, the IC_{50} value was calculated without confidence intervals and no parameters to judge the fit of the curve used for calculating the IC_{50} are presented. The certainty of the level of protection can therefore not be fully assessed. Test with *L. minor:* While relevant parameters were assessed (such as growth rate and front area), no regulatory relevant endpoints, such as ECx values, were calculated. No justifications is provided. Furthermore, control data are only presented for the parameters front area and chlorophyll content, and only in a graphical format. Due to the lack of raw data, no regulatory relevant endpoints can be calculated retroactively. For both tests: The purity of the test material was not reported. Furthermore, exposure concentrations were not analytically verified. Especially for the lemna test, which lasted 7 days without renewal of the test substance, actual exposure concentrations could vary significantly from the nominal concentrations. Based on the above listed limitations, the study can only be deemed reliable with restrictions.
Not reliable	No	

検索期間：2021年1月～5月

区分ａに分類された文献とその理由

環境動態

1. Information on the study

Data point:	CA 7.5/XX
Report author	Geissen, V. *et al.*
Report year	2021
Report title	Cocktails of pesticide residues in conventional and organic farming systems in Europe - Legacy of the past and turning point for the future
Document No	Environmental Pollution (2021):278, 116827
Guidelines followed in study	SANTE/11813/2017
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Relevant (Category A acc. to EFSA GD, Point 5.4.1) / Reliable with restrictions

2. Assessment and conclusion

Assessment and conclusion by applicant:

In this study several compounds, including glyphosate and AMPA, were analysed in 340 agricultural topsoil samples from 4 representative EU study sites in Spain, Portugal and the Netherlands. Soil samples were collected between 2015 and 2018 after harvest or before the start of the growing season.

No information on the sampling procedure and storage time of the topsoil samples is provided. This does not allow to assess the representativeness of the soil samples. Furthermore, only maximum and median values are reported and the results cannot be assigned to a respective sampling period. Therefore, the article is considered reliable with restrictions.

1. Information on the study

Data point:	CA 7.3.1/009
Report author	Holtomo O. *et al.*
Report year	2021
Report title	Insight of UV-vis spectra and atmospheric implication for the reaction of •OH radical towards glyphosate herbicide and its hydrates
Document No	RSC Advances (2021), 11(27), 16404-16418
Guidelines followed in study	None
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Relevant (Category A acc. to EFSA GD, Point 5.4.1) / Reliable with restrictions

2. Assessment and conclusion

Assessment and conclusion by applicant:

The aim of the study was the estimation of the atmospheric half-life of glyphosate considering reactions with OH-radical or Cl-atoms. The calculations yielded an atmospheric lifetime of glyphosate of 2.34 hours. The EU agreed method to determine the half-life of an active substance is the Atkinson approach. The calculation in the publication cannot be considered a common method and the endpoint should not supersede the endpoint calculated using the Atkinson method.
The study is considered reliable with restrictions.

1. Information on the study

Data point:	CA 7.5/
Report author	Piel S. *et al.*
Report year	2021
Report title	Understanding the origins of herbicides metabolites in an agricultural watershed through their spatial and seasonal variations
Document No	Journal of environmental science and health. Part. B, Pesticides, food contaminants, and agricultural wastes, Part B (2021), Vol. 56(4), pp. 313-332
Guidelines followed in study	None
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Relevant (Category A acc. to EFSA GD, Point 5.4.1) / Reliable with restrictions

2. Assessment and conclusion

Assessment and conclusion by applicant:

The aim of this study was to understand the spatial and seasonal variations of glyphosate and AMPA and to determine their origins in the Vilaine River watershed, Britany-France.

The sample storage time prior to analysis is not reported. Individual concentrations for glyphosate and AMPA assigned to sampling stations and sampling campaigns is presented graphically. Thus, no exact but narrative concentrations can be given for respective sampling locations and periods.

Therefore, the study is considered reliable with restrictions.