How can EU authorities say that glyphosate is not genotoxic?

Dr. Helmut Burtscher Schaden
Umweltchemiker
GLOBAL 2000 (Friends of the Earth Austria)
helmut.burtscher@global2000.at
Neustiftgasse 36, A-1070 Wien

26 November 2021
Table of contents

Summary

1. Background

2. The secret studies of the manufacturers
   2.1 The disclosure of secret manufacturer studies
   2.2 The evaluation criteria
   2.3 The subject of the assessment

3. Results
   3.1 The assessment of AGG is based on flawed studies
   3.2 Less sensitive test methods were preferred
   3.3 The “new” studies provide little that is new

4. Annex

Abbreviations

EFSA   European Food Safety Agency
IARC   International Agency for the Research on Cancer
RAR    Renewal Assessment Report for the renewal of a pesticide registration
dRAR   Daft Renewal Assessment Report
AGG    Assessment Group on Glyphosate (Authorities which drafted the 2021 dRAR, namely: ANSES for France, Nebih for Hungary, Ctgb for the Netherlands and KEMI for Sweden)
GRG    Glyphosate Renewal Group (a consortium of companies applying for the renewal of the approval in the EU)
Summary

Is glyphosate genotoxic? The answer depends on where you look.

Just as the EU was approving glyphosate in 2015, the World Health Organization’s International Agency for Research on Cancer (IARC) published its monograph on what the publicly available scientific literature says about the popular pesticide. IARC’s authoritative review concluded that there is “strong evidence” that exposure to glyphosate is genotoxic, meaning it can damage DNA.

The European Food Safety Authority (EFSA) held firm however to its judgement that glyphosate is not genotoxic, citing unpublished studies which glyphosate manufacturers had shared with EU authorities as the basis.

Now it appears that the EU is repeating the same mistake -- overlooking serious shortcomings in the latest scientific dossier from glyphosate manufacturers, and brushing aside all evidence that glyphosate is genotoxic.

The question whether this trust in the manufacturers’ studies is justified from a scientific point of view is thus becoming quite explosive. Two internationally renowned experts in genetic toxicology, who, at the request of the NGO SumOfUs, for the first time carried out an independent review based on the original study reports found clear answers:

- Regarding the scientific quality and compliance with test guidelines, the scientists assessed 18 of 35 manufacturer studies relevant according to the authorities' assessment as "not reliable", 15 others as "party reliable" and only two as reliable.

- In addition to methodological deficiencies, the cancer researchers also criticize the selection of tests. All test systems that were used were older than 30 years. The most frequently used in vivo model (with mice), the so called micronucleus assay with bone marrow cells, detects only 5-6 out of 10 carcinogens.

- One of the scientists’ main criticisms was that none of the studies submitted by the industry concerned the induction of DNA damage in the liver (and in other
inner organs), while results of published studies with adequate methods indicated that the herbicide causes DNA damage in this organ in mice.

- These studies are not fit to be used to prove that glyphosate is not genotoxic. Nor could these studies or their consistently negative results be used to dismiss all the genotoxicity evidence from the published scientific literature as erroneous or non relevant to exposure.

The issue of genotoxicity is central to the decision of whether glyphosate will be approved again in the EU. Genotoxicity is the underlying molecular mechanism for the development of cancer, heritable mutations and reproductive damage. However, if a pesticide active ingredient proves to be carcinogenic, mutagenic or toxic to reproduction, it must not be approved under the EU Pesticides Regulation. The European Chemicals Agency (ECHA) and the European Food Safety Agency (EFSA) have the final say in this matter.

1. Background

Glyphosate is authorised for use in the Europe Union until December 2022. In the current glyphosate re-approval process, the verdict of EU authorities on whether glyphosate is genotoxic (DNA-damaging) or not, expected in mid-2022, is of central importance. This applies both to the health risks posed by the weedkiller and to the legal requirements for approval. That’s because genotoxicity is the underlying molecular mechanism for the development of cancer, heritable mutations, and reproductive harm. If a pesticide active substance is considered to be probably carcinogenic, mutagenic or toxic to reproduction, then it must not be authorized under the EU Pesticide Regulation¹.

In 2015, there was disagreement on this issue between the European Food Safety Authority (EFSA) on the one hand, and the WHO’s international cancer research agency (IARC) on the other: although around three-quarters of all published genotoxicity studies reported DNA-damaging effects of glyphosate (see below. Fig. 1), EFSA relied

instead on the manufacturers' genotoxicity studies, which had reported no adverse effects. Consequently, EFSA declared glyphosate as "not genotoxic."

The dossier, which manufacturers submitted to EU authorities included 46 studies that investigated the genotoxicity of the herbicidal active substance glyphosate in bacteria, mammalian cells or in animal experiments in different experimental settings. These studies were conducted either by the glyphosate manufacturers themselves or on their behalf by external contract laboratories.

However, since these studies were kept under lock and key as "trade secrets" and "intellectual property," they were not included in the cancer assessment of glyphosate by the WHO cancer research agency. This is because the agency only evaluated publicly available and therefore verifiable studies. In these, it identified "strong evidence of genotoxicity" for glyphosate.

*Fig. 1: Independent studies from the scientific literature (left) and the studies of the glyphosate manufacturers (right) came to opposite conclusions regarding the genotoxicity of glyphosate*

*Source: Renewal Assessment Report (RAR) from the 2015 glyphosate evaluation*

Studies from the scientific literature          Studies by glyphosate manufacturers

- not genotoxic
- inconclusive
- genotoxic

n=72                                     n=46

The fact that the EU authorities consistently excluded from their assessment as "not reliable" those studies in which the experts of the WHO cancer research agency had identified evidence of the DNA-damaging potential of glyphosate, raised questions and provoked criticism. The outrage was correspondingly great when a plagiarism report\(^2\) in

---

September 2017 found that the entire argumentation with which the agency had justified the exclusion of published studies (see Fig. 2) had been copied word for word from Monsanto’s application for approval.

Fig. 2: This facsimile shows the 46-page subsection on published genotoxicity studies in the 2015 Renewal Assessment Report of glyphosate (RAR 2015). The competent authority had copied almost the entire text (highlighted in red) verbatim from Monsanto’s application for approval, concealing the true origin of the text, as evidenced by a plagiarism report.

Despite these unresolved contradictions and outcries from the scientific community, EU authorities recommended the re-approval of glyphosate in November 2015. However, this was met with resistance from some member states. A two-year political stalemate in the EU ensued, ending in December 2017 with an extension of glyphosate’s approval by five years instead of 15.

2. The secret studies of the manufacturers

The fact that the manufacturers’ studies all reported the absence of genotoxicity, while the vast majority of independent studies reached different conclusions, fuelled the desire for an independent review of the reliability and scientific quality of the industry studies. This was made possible years later by a March 2019 European Court of Justice ruling\(^3\) that declared EFSA’s secrecy of manufacturer studies unlawful.

---

2.1 The disclosure of secret manufacturer studies

In August 2019, the non-profit organisation SumOfUs requested EFSA for access to all manufacturer genotoxicity studies submitted in the past glyphosate approval process. At the end of 2019, SumOfUs received from EFSA 53 manufacturer studies from the previous approval process (2012 to 2015). These consisted of 41 studies on the pure active substance glyphosate and 13 additional studies on formulations and co-formulants of weed killers containing glyphosate.

The NGO requested two renowned experts in genetic toxicology, Siegfried Knasmüller and Armen Nersesyan to systematically analyze the 53 studies for their scientific quality. The results were published by SumOfUs on July 3, 2021 and widely reported in the media: In their analysis, the scientists criticised substantial methodological deficiencies in the conduct of the studies and the use of insufficiently sensitive test methods. The conclusion of the EU authorities that glyphosate is not genotoxic cannot be derived from the available manufacturer studies, the scientists said.

In order to evaluate the studies of the current approval procedure, Armen Nersesyan made a second request via the applicant’s website (https://www.glyphosate.eu/) to obtain the genotoxicity studies of the manufacturers submitted for the current approval procedure that had not already been submitted for the previous approval procedure.

He received eleven studies, never before independently reviewed. These eleven “new” studies did not include any studies on the pure active substance glyphosate, but only studies dealing with metabolites (Intermediates formed during the metabolism of glyphosate) or glyphosate-containing formulations (substance mixtures). Nonetheless,

---

4 Prof. Siegfried Knasmüller was head of the Environmental Toxicology Group at the Institute of Cancer Research, Medical University of Vienna. He published 255 articles in peer-reviewed journals (Scopus) as well as four text books on genetic toxicology. He has a Hirsch-index of 52, and was cited > 9,000 times. Currently, SK is editor of the journal “Mutation Research – Genetic Toxicology” and co-editor of the journal “Food and Chemical Toxicology”.

5 Dr. Armen Nersesyan studied biophysics at Yerevan State University and at the Institute of Normal and Pathological Physiology, Moscow (USSR). He also studied animal science at the University of Utrecht (the Netherlands) and molecular epidemiology at the NCI, Bethesda (US) and the IARC (France). Since 2003 he worked at the Institute of Cancer Research of Medical University of Vienna till his retirement in 2018. He published 144 articles in peer-reviewed journals and has a Hirsch-index of 32, he was cited > 2,000 times.

6 We refer to these as "new" studies, as they were not the subject of the previous approval procedure. However, the completion date of the majority of these "new" studies is between 2004 and 2007.
the scientists also evaluated the scientific quality and reliability of these studies for completeness.

2.2 The evaluation criteria

The 53 "old" and the 11 "new" studies were scrutinized by the two scientists on the basis of the original study reports and the raw data contained therein to determine whether they were conducted in accordance with the OECD test guidelines\textsuperscript{7} applicable to the selected test system as well as other international guidelines.

Results were considered “reliable” if the study was conducted in accordance with the applicable OECD guideline. They were classified as "partly reliable" if the study in question had minor deviations from the applicable OECD test guideline in force at the time of publication of the RAR. A "minor" deviation is one that would not be expected to strongly affect the accuracy of a result obtained in a particular test system. A classification as "not reliable" was made if the study in question showed substantial deviations from the OECD test guideline valid at the time of publication of the RAR (a deviation is classified as "substantial" if it can lead to a significant impairment of the sensitivity and/or accuracy of the test system).

2.3 The subject of the assessment

On September 23, 2021, the European Food Safety Authority (EFSA) published the preliminary assessment report, the so-called Draft Renewal Assessment Report\textsuperscript{8} (dRAR) on glyphosate. In it, a total of 59\textsuperscript{9} genotoxicity studies involving the pesticide active substance glyphosate are listed in chapter B.6.4 Genotoxicity. 19 of these studies were excluded from the evaluation by the competent authorities acting as Rapporteur member states called Assessment Group on Glyphosate\textsuperscript{10} (AGG), as

---

\textsuperscript{7} In order to ensure that studies are conducted and interpreted correctly, the legally defined data requirements for the approval of plant protection product active substances specify binding test guidelines - in particular OECD test guidelines - according to which the relevant studies must be conducted with the active substances or products.

\textsuperscript{8} https://www.efsa.europa.eu/en/topics/topic/glyphosate

\textsuperscript{9} The number of 59 studies is derived from the 60 studies listed, of which one study was listed twice (however, this study was removed from the evaluation as unacceptable).

\textsuperscript{10} The Assessment Group on Glyphosate (AGG) is composed of the four Member States France, Hungary, the Netherlands and Sweden, who act jointly as rapporteurs for the evaluation of glyphosate with a view to renewal of the authorization.
unacceptable (most of them, namely 18, had already been classified as unacceptable in the previous approval procedure in 2015). Of the remaining 40 genotox studies relevant to the ongoing EU genotoxicity assessment of glyphosate, three studies were not shared by EFSA with SumOfUs\textsuperscript{11}, although these studies had been submitted by Monsanto in the previous approval process. These studies were therefore not available for evaluation by the two scientists, nor were the two "new" studies that were indicated as "ongoing".

Thus, Knasmüller and Nersesyan were able to review 35 genotoxicity studies relevant for the current approval procedure with regard to compliance with the relevant test guidelines on the basis of the original study reports. For the remaining five studies for which original reports were not available - these were, in addition to the two "new" genotoxicity studies mentioned above- three old studies from the 1980s and 1990s, two of which had been assessed by BfR as "not acceptable" in 2015 - a detailed review was not possible. A rough assessment of their significance, however, can be made based on the descriptions of the selected test systems contained in the dRAR.

### 3. Results

#### 3.1 The assessment of AGG is based on flawed studies

Chapter B.6.4 Genotoxicity of the 2021 dRAR cites a total of 40 manufacturers’ genotoxicity studies investigating the isolated active substance glyphosate that are considered relevant\textsuperscript{12} by the AGG. These 40 studies will be of crucial importance for the upcoming assessment of the genotoxicity of glyphosate by the European Chemical Agency (ECHA) and the European Food Safety Authority (EFSA).

\textsuperscript{11} Two of these studies had been rejected as unacceptable by the BfR in 2015, but were re-evaluated as "supportive" by the AGG. The third study had been assessed as acceptable by BfR. As it is not clear to us why these studies were not submitted to SumOfUs by EFSA, we have written to EFSA asking for clarification.

\textsuperscript{12} These studies were classified by the AGG as either "acceptable", "acceptable with restrictions", or "supportive". In contrast, 19 other manufacturer studies were rejected by the AGG as "not acceptable".
However, Knasmüller and Nersesyan, after reviewing the original study reports disclosed by EFSA, came to the conclusion that at least 18 of these studies must be determined as "not reliable", 15 others as "partly reliable" and only two as "reliable". Original study reports were not available from five studies because they had not been disclosed by EFSA (see Section 2.3).

Unlike the two experts in genetic toxicology, the AGG had rated 13 of these studies as "reliable" and 27 as "reliable with restrictions" (19) or "supportive" (8).

*Fig.3: More than half of those studies that EU authorities considered relevant to the approval process were of unacceptable scientific quality, according to independent experts in genetic toxicology. Only two studies were in full compliance with the applicable test guidelines (left diagram). The right diagram shows the draft assessment by the EU-authorities.*
The contrast with the assessment by Germany's Federal Institute for Risk Assessment (BfR) acting as Rapporteur Member State in 2015 is even greater (source: RAR 2015).

**Fig. 4:** Of the 40 "relevant" manufacturer genotoxicity studies from the current approval procedure of glyphosate, 38 studies were already available to the BfR in the previous approval process (exception are two new studies from 2021). Of these, BfR had classified 33 studies as "acceptable", three studies as "acceptable with restrictions" and two studies as "not acceptable". The latter were upgraded by the AGG as "supportive".

### Assessment by BfR (RAR 2015)

![Pie chart showing distribution of assessments by BfR (RAR 2015)]

### Tab. 1: Assessments of the 40 manufacturer genotoxicity studies "relevant" to the current approval process in the 2021 dRAR, the 2015 RAR, and the Knasmüller & Nersesyan analysis.

<table>
<thead>
<tr>
<th>Classification</th>
<th>2021 dRAR</th>
<th>2015 RAR</th>
<th>Knasmüller &amp; Nersesyan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptable / reliable</td>
<td>13</td>
<td>33</td>
<td>2</td>
</tr>
<tr>
<td>Acceptable with restrictions / supplementary</td>
<td>27</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>Not acceptable / not reliable</td>
<td>0</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>Assessment not possible</td>
<td>0</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

An overview of the studies listed in the 2021 dRAR and their assessments by Knasmüller and Nersesyan, as well as their current classification by AGG in the 2021 dRAR and their previous classification by BfR in the 2015 RAR can be found in Annex at the end of this document.
3.2 Less sensitive test methods were preferred

In addition to the methodological failures, the cancer researchers also criticise the choice of test methods. In the manufacturer studies, mainly old and insensitive test systems were used, some of which are now known to produce a high rate of false negative results. Available modern, OECD-standardized test systems that provide more reliable results, on the other hand, were not used. The 40 "relevant" genotoxicity studies used seven different test systems.

The most frequently used tests were bacterial tests, so-called Ames tests, which have been used since the mid-1970s to test whether a test substance produces mutations in bacteria. 16 of the 40 "relevant" genotoxicity tests (40 percent) are such bacterial tests commissioned between 1978 and 2014. This is despite the fact that the question of the genotoxicity of glyphosate in bacteria has long been scientifically clarified: glyphosate is not genotoxic in bacteria. This was also stated by the IARC when it classified glyphosate as genotoxic in 2015. Independent published scientific studies have described DNA-damaging effects of glyphosate in a variety of different test systems, but not in bacterial tests.

The second most frequently used test was the bone marrow micronucleus test. Used in nine studies, this test system accounts for 23 percent of the relevant manufacturer studies, according to the AGG assessment. This test system also dates from the early 1970s and is known for its low sensitivity. Knasmüller and Nersesyan point to validation studies showing that between 40 and 50 percent of the genotoxic carcinogens tested are not indicated in this micronucleus test.

The two cancer researchers also criticize manufacturer studies for testing genotoxicity exclusively in bone marrow, even though independent studies from the scientific literature have demonstrated genotoxic effects in inner organs other than the bone marrow, particularly the liver. The fact that the manufacturers do not use test systems capable of detecting genotoxicity in those organs where published studies have already demonstrated DNA damage from glyphosate is therefore a major point of criticism by the two cancer researchers.

---

13 The 40 genotoxicity studies are composed of 16 ames tests, 9 micronucleus assays with polychromatic erythrocytes of rodents, 4 gene mutations in mammalian cells in vitro (Hprt test), 3 dominant lethal assay, 2 chromosomal aberration test in rodents in vivo, 1 micronucleus assays in human peripheral lymphocytes, and 1 rec-assay.
3.3 The “new” studies provide little that is new

The eleven "new" studies deal exclusively with metabolites and formulations of glyphosate and are therefore not relevant for the assessment of the genotoxicity of the active substance. The two other new studies, which were indicated on the applicant’s website as “ongoing” are two in vitro studies with the active substance glyphosate (one HPRT test and one micronucleus small nuclear test with peripheral lymphocytes). But here, too, the clients (Bayer) opted for test setups, in which no new findings are to be expected.

Nevertheless, analysis of the original study reports by Knasmüller and Nersesyan revealed deficiencies in the conduct of these "new" studies. Only two of the eleven studies could be classified as "reliable", six were only "partially reliable" and three were classified by the scientists as "not reliable".

![Fig. 5: Of leven "new" manufacturer genotoxicity studies on metabolites and formulations, Knasmüller and Nersesyan classified three studies as "not reliable," six as "partially reliable," and two as "reliable"](image-url)
4. Annex

* GRG = Glyphosate Renewal Group, ** AGG = Assessment Group on Glyphosate
*** 1 = acceptable (reliable); 2 = acceptable (reliable) with restrictions; 2.5 = supplementary; 3 = not acceptable (not reliable)

<table>
<thead>
<tr>
<th>Study Identification</th>
<th>Study Title</th>
<th>Test System</th>
<th>Conclusions in the DRAR 2021 by manufacturers (GRG*) and EU-authorities (AGG**)</th>
<th>Classification***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knasmüller and Nersesyan Report</td>
<td>Glyphosate: Reverse Mutation Assay 'Ames Test' using Salmonella typhimurium and Escherichia coli</td>
<td>AmesTest</td>
<td>Conclusion GRG: Valid, Category 2a Conclusion AGG: The study is considered to be acceptable.</td>
<td>2 1 1</td>
</tr>
<tr>
<td>Study number 21 B.6.4.1.1.</td>
<td>Reverse Mutation Assay using Bacteria (Salmonella typhimurium) with Glyphosate tech.</td>
<td>AmesTest</td>
<td>Conclusion GRG: Valid, Category 2a Conclusion AGG: The study is considered to be acceptable.</td>
<td>2 1 1</td>
</tr>
<tr>
<td>Study number 4 B.6.4.1.3.</td>
<td>Mutagenicity study of Glyphosate TC in the Salmonella typhimurium Reverse Mutation Assay (in vitro)</td>
<td>AmesTest</td>
<td>Conclusion GRG: Valid, Category 2a Conclusion AGG: [..] As some deviations regarding the historical controls (see above) were identified, the study is considered acceptable but with restrictions.</td>
<td>1 2 1</td>
</tr>
<tr>
<td>Study number 19 B.6.4.1.4.</td>
<td>Salmonella typhimurium and Escherichia coli Reverse Mutation Assay with Solution of Glyphosate TC spiked with Glyphosate</td>
<td>AmesTest</td>
<td>Conclusion GRG: Valid, Category 2a Conclusion AGG: The study is considered to be acceptable.</td>
<td>3 1 1</td>
</tr>
<tr>
<td>Study number</td>
<td>B.6.4.1 .5.</td>
<td>Procedure</td>
<td>AmesTest Conclusion GRG: Valid, Category 2a Conclusion AGG: The study is considered to be acceptable.</td>
<td></td>
</tr>
<tr>
<td>-------------</td>
<td>------------</td>
<td>-----------</td>
<td>--------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Study number 3</td>
<td>B.6.4.1 .6.</td>
<td>Reverse Mutation Assay using bacteria (Salmonella typhimurium) with Glyphosate TC</td>
<td>Conclusion GRG: Valid, Category 2a Conclusion AGG: [..] As some deviations regarding the historical controls were identified (see above), the study is considered acceptable but with restrictions.</td>
<td></td>
</tr>
<tr>
<td>Study number 18</td>
<td>B.6.4.1 .7.</td>
<td>Mutagenicity study of Glyphosate TC in the Salmonella typhimurium Reverse Mutation Assay (in vitro)</td>
<td>Conclusion GRG: Valid, Category 2a Conclusion AGG: The study is considered to be acceptable.</td>
<td></td>
</tr>
<tr>
<td>Study number 15</td>
<td>B.6.4.1 .9.</td>
<td>Glyphosate technical - Salmonella typhimurium and Escherichia coli Reverse Mutation Assay</td>
<td>Conclusion GRG: Valid, Category 2a Conclusion AGG: The study is considered to be acceptable.</td>
<td></td>
</tr>
<tr>
<td>Study number 16</td>
<td>B.6.4.1 .10.</td>
<td>Salmonella typhimurium and Escherichia coli Reverse mutation assay with Glyphosate technical (NUP-05068)</td>
<td>Conclusion GRG: Valid, Category 2a Conclusion AGG: The study is considered to be acceptable.</td>
<td></td>
</tr>
<tr>
<td>Study number 17</td>
<td>B.6.4.1 .11.</td>
<td>Salmonella thphimurium and Escherichia coli reverse mutation assay with Glyphosate technical (NUP-05067)</td>
<td>Conclusion GRG: Valid, Category 2a Conclusion AGG: The study is considered to be acceptable</td>
<td></td>
</tr>
</tbody>
</table>
| Study number | B.6.4.1   | Glyphosate Acid: An Evaluation of Mutagenic Potential Using S. typhimurium and E. coli | Conclusion GRG: Valid, Category 2a  
Conclusion AGG: The study is considered acceptable but with restrictions (reliable with restrictions) due to the deviations noted above. | 2 | 2 | 1 |
|--------------|----------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------------|---------|---------|---------|
| Study number 20 | B.6.4.1   | Technical glyphosate: Reverse mutation assay "Ames test" using Salmonella typhimurium and Escherichia coli | Conclusion GRG: Valid, Category 2a  
Conclusion AGG: The study is considered acceptable but with restrictions (reliable with restrictions) due to the deviations noted above. | 2 | 2 | 1 |
| Study number 1 | B.6.4.1   | HR-001: Reverse Mutation Test                                                      | Conclusion GRG: Valid, Category 2a  
Conclusion AGG: The study is considered acceptable but with restrictions (reliable with restrictions) due to the deviations noted above. | 3 | 2 | 1 |
| Study not submitted by EFSA | B.6.4.1   | Mutagenicity – Salmonella typhimurium reverse mutation assay (Ames test)           | Conclusion GRG: Supportive, Category 2a  
Conclusion AGG: The study is considered to be supportive due to the noted Deviations. | n.d. | 2 | 3 |
| Study number 5 | B.6.4.1   | Mutagenicity test: Ames Salmonella Assay with Glyphosate, batch 206-JaK-25-1       | Conclusion GRG: Supportive, Category 2a  
Conclusion AGG: The study is considered to be supportive due to the noted deviations. | 3 | 2.5 | 1 |
| Study number: 24 | B.6.4.1   | Glyphosate Acid: In Vitro Cytogenetic Assay In Human Lymphocytes                   | Conclusion GRG: Supportive, Category 2a  
Conclusion AGG: The study is considered to be acceptable but with restrictions (reliable with restrictions) due to the noted deviations. | 3 | 2 | 1 |
| Study number: 30 | B.6.4.1 .26. | Technical glyphosate: Chromosome aberration test in CHL cells in vitro | Chromosomal aberration test in mammalian cells in vitro | Conclusion GRG: Valid, Category 2a  
Conclusion AGG: The study is considered acceptable but with restrictions (reliable with restrictions) due to the noted deviations. |
|---|---|---|---|---|
| Study number: 26 | B.6.4.1 .27. | HR-001: In vitro cytogenicity test | Chromosomal aberration test in mammalian cells in vitro | Conclusion GRG: Valid, Category 2a  
Conclusion AGG: The study is considered acceptable but with restrictions (reliable with restrictions) due to the noted deviations. |
| Study number: 29 | B.6.4.1 .28. | Evaluation of the ability of glyphosate to induce chromosome aberrations in cultured peripheral human lymphocytes (with independent repeat) | Chromosomal aberration test in mammalian cells in vitro | Conclusion GRG: Supportive, Category 2a  
Conclusion AGG: The study is considered acceptable but with restrictions (reliable with restrictions) due to the noted deviations. |
| Study number: 32 | B.6.4.1 .30. | Glyphosate Acid: L5178Y TK +/- Mouse Lymphoma Gene Mutation Assay | Gene mutations in mammalian cells in vitro (Hprt test) | Conclusion GRG: Valid, Category 2a  
Conclusion AGG: The study is considered to be acceptable but with restrictions (reliable with restrictions) due to the noted deviations. |
| Study number: 25 | B.6.4.1 .31. | Mutagenicity test: In vitro Mammalian Cell Gene Mutation Test with Glyphosate, batch 206-JaK-25-1 | Gene mutations in mammalian cells in vitro (Hprt test) | Conclusion GRG: Valid, Category 2a  
Conclusion AGG: The study is considered to be acceptable but with restrictions (reliable with restrictions) due to the noted deviations. |
| Study number: 27 | B.6.4.1 .32. | CHO/HGPRT Gene Mutation Assay with Glyphosate | Gene mutations in mammalian cells in vitro (Hprt test) | Conclusion GRG: Valid, Category 2a<br>Conclusion AGG: The study is considered to be acceptable but with restrictions (reliable with restrictions) due to the noted deviations. | 2 | 2 | 1 |
| Study number: 31 | B.6.4.1 .35. | HR-001: DNA Repair Test (Rec-Assay) | Rec-Assay | Conclusion GRG: Supportive, Category 2a<br>Conclusion AGG: The study is considered to be supportive due to the noted deviations. Rec assay is not a standard method for DNA damage and repair. | 3 | 2.5 | 2.5 |
| Study number: 14 | B.6.4.1 .36. | The report of mutagenic study with bacteria for CP 67573 | AmesTest | Conclusion GRG: Supportive, Category 2a<br>Conclusion AGG: The study is considered supportive due to the noted deviations. | 3 | 2.5 | 2.5 |
| Study not submitted by EFSA | B.6.4.1 .40. | Glyphosate: V79 HPRT Gene Mutation Assay | Gene mutations in mammalian cells in vitro (Hprt test) | Conclusion GRG: Yes/yes; Category 1<br>Conclusion AGG: The study is considered to be acceptable. | n.d. | 1 | n.d. |
| Study not submitted by EFSA | B.6.4.1 .41. | Glyphosate: Micronucleus Test in Human Lymphocytes in vitro | Micronucleus assay | Conclusion GRG: Yes/yes, Category 1<br>Conclusion AGG: The study is considered to be acceptable. | n.d. | 1 | n.d. |
| Study number: 82 | B.6.4.2 .1. | Glyphosate TGAI: Micronucleus test of glyphosate TGAI in mice. | Micronucleus assays with polychromatemic erythrocytes of rodents | Conclusion GRG: Valid, Category 2a<br>Conclusion AGG: The study is considered to be acceptable. | 3 | 1 | 1 |
| Study number: 53  | B.6.4.2.7. | Glyphosate Technical: Micronucleus Test In The Mouse | Micronucleus assays with polychromatotic erythrocytes of rodents | Conclusion GRG: Valid, Category 2a  
Conclusion AGG: The study is considered to be acceptable but with restrictions (reliable with restrictions) due to the noted deviations. | 2 | 1 | 1 |
| Study not submitted by EFSA | B.6.4.2.8. | A micronucleus study in mice for glifosate técnico | Micronucleus assays with polychromatotic erythrocytes of rodents | Conclusion GRG: Valid, Category 2a  
Conclusion AGG: The study is considered to be acceptable but with restrictions (reliable with restrictions) due to the noted deviations. | n.d. | 2 | 1 |
| Study number: 56  | B.6.4.2.9. | Glyphosate Acid: Mouse Bone Marrow Micronucleus Test | Micronucleus assays with polychromatotic erythrocytes of rodents | Conclusion GRG: Valid, Category 2a  
Conclusion AGG: The study is considered acceptable but with restrictions (reliable with restrictions) due to the noted deviations. | 3 | 2 | 1 |
| Study number | B.6.4.2 .10. | Glyphosate technical: Mutagenicity - Micronucleus Test in Swiss Albino Mice | Micronucleus assays with polychromatic erythrocytes of rodents | Conclusion GRG: Supportive, Category 2a Conclusion AGG: The study is considered acceptable but with restrictions (reliable with restrictions) due to the noted deviations and the t-test used. | 3 | 2 | 1 |
| Study number | B.6.4.2 .12. | Mutagenicity test: Micronucleus test with Glyphosate, batch 206-JaK-25-1. Final report | Micronucleus assays with polychromatic erythrocytes of rodents | Conclusion GRG: Valid, Category 2a Conclusion AGG: The study is considered to be acceptable but with restrictions (reliable with restrictions) due to the noted deviations. | 3 | 2 | 1 |
| Study number | B.6.4.2 .14. | Micronucleus test of Glyphosate TC in Bone Marrow Cells of the CD Rat by oral Administration | Micronucleus assays with polychromatic erythrocytes of rodents | Conclusion GRG: Valid, Category 2a Conclusion AGG: [...] The study is considered acceptable but with restrictions (reliable with restrictions) due to the noted deviations. | 2 | 2 | 1 |
| Study number | B.6.4.2 .15. | Genetic toxicology: in vivo mammalian bone marrow cytogenetic test – Chromosomal analysis | Chromosomal aberration test in rodents in vivo | Conclusion GRG: Supportive, Category 2a Conclusion AGG: The study is considered supportive due to the noted deviations | 3 | 2.5 | 1 |
| Study number | B.6.4.2 .16. | In Vivo Bone Marrow Cytogenetics Study of Glyphosate in Sprague-Dawley Rats | Chromosomal aberration test in rodents in vivo | Conclusion GRG: Supportive, Category 2a Conclusion AGG: The study is considered supportive due to the noted deviations. | 3 | 2.5 | 1 |
| Study number | B.6.4.3 .1. | Dominant lethal test in Wistar rats | Dominant Lethal Assay | Conclusion GRG: Supportive, Category 2a Conclusion AGG: The study is considered supportive due to the noted deviations. | 3 | 2.5 | 1 |
### Mutagenic Testing of Glyphosate

<table>
<thead>
<tr>
<th>Study number</th>
<th>Test Type</th>
<th>Conclusion GRG</th>
<th>Conclusion AGG</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.6.4.3.1.</td>
<td>Mutagenic testing of glyphosate in rats by dominant lethal test</td>
<td>Supportive, Category 3a</td>
<td>The study is considered supportive due to the noted deviations.</td>
</tr>
<tr>
<td>B.6.4.3.2.</td>
<td>Dominant lethal mutagenicity assay with technical Glyphosate in mice</td>
<td>Supportive, Category 2a</td>
<td>The study is considered supportive due to the noted deviations.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>n.d.</th>
<th>2.5</th>
<th>3</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th></th>
<th>3</th>
<th>2.5</th>
<th>1</th>
</tr>
</thead>
</table>

Annex table also available in [Google Spreadsheets here](#).

Cover photo from Shutterstock.

**Contact:**
Dr. Helmut Burtscher Schaden  
GLOBAL 2000 (Friends of the Earth Austria)  
[helmut.burtscher@global2000.at](mailto:helmut.burtscher@global2000.at)