German Federal Institute for Risk Assessment

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Animal study on glyphosate and cancer: Detailed analysis required

In a study on rats, a team of researchers, with significant involvement from the Ramazzini Institute in Bologna, Italy, investigated whether relatively low long-term doses of the active substance glyphosate in plant protection products may promote the development of cancer in rodents. The scientists conclude that this is the case (Panzacchi et al., Carcinogenic effects of long-term exposure from prenatal life to glyphosate and glyphosate-based herbicides in Sprague-Dawley rats, *Environmental Health* (2025) 24:36, https://doi.org/10.1186/s12940-025-01187-2).

The German Federal Institute for Risk Assessment (BfR) has reviewed the study in an initial analysis, particularly with regard to whether it calls into question the previous assessment of glyphosate with respect to its carcinogenic potential.

The BfR concludes that, due to its design, the study is only very limited in its comparability with the many long-term studies on glyphosate that are already available. Therefore it does not refute their findings. The results published by Panzacchi et al. (2025) require detailed analysis. To this end, the raw data must be made available and the historical control data must be evaluated appropriately.

In the opinion of the BfR, the study does not justify a change in the assessment of the active substance glyphosate. The report on the current assessment of glyphosate by the European Food Safety Authority (published in the EFSA Journal 2023; 21(7): 8164) was prepared by the Member States France, Hungary, the Netherlands and Sweden. In the interest of a harmonised consideration of the study by Panzacchi et al. (2025), the BfR therefore welcomes an analysis of the study at EU level.

The publication by Panzacchi et al. (2025) is a description of a long-term study of rats exposed to the active substance glyphosate (purity: 99%, presumably not entirely corresponding to the technical active substance used in plant protection products) and two plant protection products (PPP) containing glyphosate.

The study is part of a larger research programme launched by the Italian Ramazzini Institute in 2019. The aim of the recently published study was to investigate the carcinogenic potential of the active substance glyphosate and two PPPs containing glyphosate after long-term administration to rats in doses that are intended to at least approximate real human exposure.

The study design can be described as follows:

- Glyphosate was administered in doses of 0.5 mg/kg body weight (kg) per day (equal to the current Acceptable Daily Intake – ADI in the EU), 5 mg/kg BW/d and 50 mg/kg BW/d via drinking water from the sixth day of pregnancy to pregnant female rats (F0 generation). The concentrations of the PPPs were adjusted to achieve roughly comparable glyphosate doses.
- After the birth of the offspring (F1 generation), the maternal animals were treated until the end of lactation (usually day 21), then removed from the study and apparently not further examined.
- Following a random procedure that was described only in part, 51 male and 51 female rats per test substance (glyphosate or PSM) and dose were selected from the F1 offspring and then treated via drinking water for a maximum of 104 weeks (approx. 2 years). A control group of equal size was recruited from 51 male and 51 female F1 animals, which, like their mothers, received untreated drinking water.
- In this experimental design, sequential exposure of the F1 animals via different pathways and at all stages of development can be assumed: *in utero*, postnatally via milk (a route of exposure that is rather negligible according to the information available here), and above all via drinking water.
- At the end of the experiment, the animals still alive at that time were killed and dissected and a large number of their organs were examined histopathologically, primarily for neoplastic changes (tumours). Immunohistochemical methods were also used. It can be assumed, although not explicitly stated, that the same procedures were followed for animals that died before the end of the study or were killed prematurely due to poor health.
- During the experiment, the animals were apparently observed regularly for clinical signs of toxicity, weighed at unspecified intervals, and their feed intake was apparently also determined.

According to Panzacchi et al. (2025), treatment with glyphosate and the two PPPs containing glyphosate had no effect on the animals' condition, mortality, feed intake or body weight development, but numerous tumours were found. These tumours originated in a wide variety of organs and organ systems. The evaluations focus heavily on leukaemia and lymphoma. A small number (1–2) of neoplasms were observed in the groups treated with glyphosate. Since the incidence in the control group was always 0, there was a statistically significant increase for some of the leukaemic diseases – and even more so when they were combined. However, this can hardly be described as dose-dependent, which overall tends to argue against a link to the treatment. On the other hand, there are indications of dose dependence in lymphoblastic leukaemia and myeloma for the two PPPs. Furthermore,

indications of a leukaemic effect arise from the time of occurrence of these neoplasms, i.e. their first detection in animals that had died in the meantime.

Additionally, benign as well as malignant skin tumours were observed rarely in the treated group, but not in the control group. Here, too, there is no clear dose-response relationship. The same applies to tumours of the thyroid, pancreas and bone tissue.

There are some significant discrepancies between the study design and the guideline-compliant studies required in the approval process for PPP active substances. A large number of such guideline-compliant studies have been carried out for the active substance glyphosate. These discrepancies make it difficult to interpret the results and compare the studies.

- Administration via drinking water: This approach is possible but is only carried out in justified cases (as there is generally no realistic route of exposure for humans). To the BfR's knowledge, with one exception, all available long-term studies with glyphosate have been conducted with administration in food. It is unknown whether administration in drinking water has an effect on bioavailability and thus on internal (systemic) exposure.
- Conducting a long-term study on animals that were already exposed *in utero* and then during lactation: This kind of study design was discussed decades ago but did not gain widespread acceptance. Comparability with regulatory long-term studies is therefore limited.
- In the current study, no blood and urine tests were performed that could provide information on the health status of the animals and possible chronic toxicity. There are no reports of non-neoplastic findings.
- Dose selection: Compared to almost all other long-term studies with glyphosate, very low doses were tested. The studies available to the BfR included doses of approximately 1000 mg/kg bw per day. The effects described by Panzacchi et al. (2025) were not observed at the high doses used in the earlier long-term studies. The use of higher, comparable doses would have been useful.
- Historical control data: Reference No. 31 does not contain any historical control data from the Ramazzini Institute. The handling of historical control data from the National Toxicology Programme (NTP, reference 30) is questionable, at least insofar as only average frequencies are reported, but not the variability between studies. For example, the incidence of leukaemia in male NTP control groups is up to 6% (in female Harlan SD rats up to 4%). This puts the findings of Panzacchi et al. (2025) (max. 1.96% leukaemia in the glyphosate-treated dose groups M/F) into perspective and calls for a more appropriate statistical analysis.
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Further information on glyphosate

In 2022, the European Chemicals Agency (ECHA) conducted a risk assessment of glyphosate. It concluded that glyphosate does not meet the scientific criteria for hazard classification as a carcinogenic, mutagenic or reprotoxic substance: https://echa.europa.eu/hot-topics/glyphosate

As part of the EU re-evaluation of the active substance glyphosate completed in 2023 in accordance with Regulation (EC) No. 1107/2009, all assessment authorities of the EU Member States involved in the procedure and the European Food Safety Authority (EFSA) concluded that there is no established link between exposure to glyphosate and an increased risk of cancer: https://www.bfr.bund.de/cm/349/glyphosate-efsa-information-on-re-evaluation-as-a-plant-protection-active-substance-published.pdf https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2023.8164).

About the BfR

The German Federal Institute for Risk Assessment (BfR) is a scientifically independent public health institute within the portfolio of the German Federal Ministry of Agriculture, Food and Regional Identity (BMLEH). The BfR advises the Federal Government and the States ('Laender') on questions related to food, feed, chemical and product safety. The BfR conducts independent research on topics that are closely linked to its assessment tasks.

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