



Detailed and supplemented answers to certain questions asked in Bayer AG's Annual General Meetings 2019 and 2020

Number of scientific studies on the non-carcinogenicity of glyphosate

Annual General Meeting (AGM) 2019: "In your 2018 interim report, you literally state that more than 800 scientific studies and supervisory authorities worldwide confirm that glyphosate and glyphosate-based herbicides are not carcinogenic and that they are safe to use. [...]"

1) Does this statement in the interim report correspond to the truth, in particular with regard to the more than 800 studies which I consider unusually high?"

AGM 2020: "How many scientific studies and confirmations by supervisory authorities worldwide confirm to date (alternatively until December 31, 2019), 'that glyphosate or glyphosate-based herbicides are not carcinogenic and safe, if used as intended' (information at the time of the 2018 interim report: 'more than 800')? How many scientific studies and confirmations by supervisory authorities with this content were added in the fiscal year 2019?"

Regulatory authorities worldwide maintain massive scientific databases in support of their regulatory approvals of glyphosate and glyphosate-based formulations. For example, as of March 7, 2018, the U.S. EPA [database](#) on glyphosate and glyphosate-based formulations contained 4,232 unique studies submitted by Monsanto and other registrants for registration purposes. The U.S. EPA also reviews published literature but does not track those studies in its database. Therefore, the number of studies reviewed is even larger. While registration studies for the (re-)registration of active ingredients and products are submitted to the authorities by the manufacturers, the relevance of studies for assessing the safety and/or carcinogenicity of glyphosate is determined by regulatory authorities according to and in the boundaries of the applicable regulatory legal framework.

Although examination of whether something is safe includes an assessment of whether it is carcinogenic, safety assessments are not limited to carcinogenicity. Safety assessments include a wide variety of additional data, such as whether the substance is a reproductive toxin, a neurotoxin, etc. Regulators examine multiple different endpoints for testing to ensure product safety, and Bayer has therefore conducted testing establishing safety in many areas beyond the fact that glyphosate is not a carcinogen. Further, studies that are considered relevant by regulators include different kind of studies (epidemiology, animal, mechanistic, etc.). For instance, when conducting a carcinogenicity assessment, regulators do not only consider studies that examine a carcinogenic effect in humans and/or animals but also other kinds of studies (e.g., genotoxicity studies).

Given the complexity of such assessments and given that regulators ultimately determine the relevance of the studies for their assessment, it is not possible to determine a definitive number of studies that confirm the non-carcinogenicity of glyphosate and glyphosate-based formulations. Therefore, the approach that we have taken in our annual/quarterly reports and that we have explained in our answers to the questions during the Annual General Meetings is to derive the

relevant number of studies that the U.S. EPA has considered relevant for their safety and carcinogenicity assessment, respectively. Given that the U.S. Roundup™ litigation concerns Roundup™ products/formulations sold in the U.S., we focus on studies considered by the U.S. EPA.

In reviewing the U.S. EPA database linked above, there are some 45 categories of identified studies that relate to human or mammalian health. The relevant categories are as follows:

1. Primary eye irritation in rabbits
2. Primary dermal irritation
3. Dermal sensitization
4. Acute neurotoxicity screen study in rats
5. Subchronic Oral Toxicity: 90-Day Study
6. 21-day dermal-rabbit/rat
7. 90-day dermal-rodent
8. 90-day inhalation-rat
9. Subchronic Neurotoxicity
10. Chronic Toxicity
11. Teratogenicity -- 2 Species
12. 2-generation repro.-rat
13. Dietary: Combined Chronic Toxicity/Oncogenicity Studies
14. Developmental Neurotoxicity
15. Interaction with Gonadal DNA
16. General metabolism
17. Dermal Penetration/Absorption
18. Acute oral toxicity
19. Acute dermal toxicity
20. Acute inhalation toxicity
21. Acute eye irritation
22. Acute dermal irritation
23. Skin sensitization
24. Prenatal developmental toxicity study
25. Reproduction and fertility effects
26. Carcinogenicity
27. Combined chronic toxicity/carcinogenicity
28. Bacterial reverse mutation test
29. In vitro mammalian cell gene mutation test
30. In vitro mammalian chromosome aberration test
31. Mammalian erythrocyte micronucleus test
32. Metabolism and pharmacokinetics
33. Immunotoxicity
34. Inhalation exposure--outdoor
35. Repeated dose 28-day oral toxicity in rodents
36. Androgen Receptor Binding (Rat Prostate)
37. Estrogen Receptor Transcriptional Activation (Human Cell Line HeLa-9903)
38. Hershberger (Rat)

39. Female Pubertal (Rat)
40. Male Pubertal (Rat)
41. Steroidogenesis (Human Cell Line- H295R)
42. Uterotrophic (Rat)
43. Androgen Receptor Binding (Rat Prostate)
44. Aromatase (Human Recombinant)
45. Estrogen Receptor Binding.

As of March 2018, there were more than 1,700 studies in these categories, of which more than 800 specifically examine the active ingredient glyphosate or Bayer's glyphosate-based formulations; the others relate to formulations produced by other registrants. With regard to cancer studies specifically, EPA's 2017 [Evaluation of Carcinogenic Potential of glyphosate](#) considered 121 studies that the agency deemed relevant to its analysis, including 63 cancer endpoints in 23 epidemiology studies¹ examining real world use of glyphosate-based formulations; 14 long-term cancer studies in rodents; and 84 genotoxicity studies submitted by Monsanto, other manufacturers or available in the open literature. All of the studies are identified in the EPA report. The EPA report also identified 63 genotoxicity studies of glyphosate-based formulations. Because EPA concluded that glyphosate is not likely to be carcinogenic, it did not proceed to consider biomonitoring and dermal absorption studies for purposes of assessing carcinogenic risk, but EPA did consider those studies as well in its broader safety assessment.

In the fiscal year 2019, three registration studies were added by Bayer. As for the number of confirmations by supervisory authorities, we refer to the overview provided in the answer to the question regarding the number of reviews by regulatory authorities on the safety of glyphosate below.

¹ Note that the 2017 OPP Report states that EPA considered 63 epidemiological studies. This appears though to be based on counting separate epidemiology endpoints as separate studies.

Amount of provisions

AGM 2019: "What amount of provisions were set up throughout the Group in the 2018 annual financial statements for product-related lawsuits by plaintiffs who came into contact with products containing glyphosate manufactured by Monsanto?"

AGM 2020: "What amount of provisions were set up across the Group in the 2019 annual financial statements for product-related lawsuits from plaintiffs who came into contact with products containing glyphosate manufactured by Monsanto?"

In the 2018 consolidated financial statements as of December 31, 2018, global provisions for product-related lawsuits by plaintiffs who came into contact with products containing glyphosate manufactured by Monsanto amounted to €359 million. This amount pertains to anticipated defense costs for this series of litigations. The addition to provisions in 2018 that impacted EBITDA amounted to €241 million.

In the 2019 consolidated financial statements as of December 31, 2019, global provisions for product-related lawsuits by plaintiffs who came into contact with products containing glyphosate manufactured by Monsanto amounted to €404 million. This amount pertains to anticipated defense costs for this series of litigations. The addition to provisions in 2019 that impacted EBITDA amounted to €145 million.

Number of reviews by regulatory authorities on the safety of glyphosate

AGM 2020: "How many 'scientifically sound evaluations by regulatory authorities and other scientific institutions' confirm to date that glyphosate has been safe in use for 40 years when properly used in accordance with the label?"

Glyphosate-based herbicides are approved for use in approximately 150 countries. Countries and regions have varying requirements for pesticide registration including the time periods covered by such approvals. In addition, there can be differences between the review of data on the active substance (i.e., glyphosate) on the one hand and the review of data on products/formulations on the other hand. For instance, in the European Union, the approval process entails two steps: first, an assessment and possible approval of the active substance at EU level by the European Commission (after an assessment of a complete dossier of studies by EU Member States and the European Food Safety Authority (EFSA), addressing the comprehensive data requirements set at EU level) and then an assessment and authorization of the final products by the EU Member States.

Given the number and diversity of requirements, it is not possible to summarize them here and determine the number of 'scientifically sound' evaluations of glyphosate. In addition, some countries/regions, like Europe and the U.S., require periodic re-reviews in addition to ad hoc reviews that occur whenever registrants request new uses. In Europe glyphosate has undergone two re-reviews under the current requirements and a third review is currently ongoing as part of the renewal process for an approval of glyphosate beyond 2022. In the U.S., there have been numerous safety assessments, including two full re-reviews since the original registration in 1974.

Given the aforesaid difficulties in determining the number of 'scientifically sound' evaluations by authorities, the approach that we have taken below is to indicate the authorities which have (re-) examined the safety of glyphosate after the publication of the IARC (International Agency for the Research on Cancer) monograph 112 in March 2015. Assessments which have been conducted after that date are critical in that the outcome of the assessment of glyphosate by IARC lead to concerns regarding the safety of glyphosate and formed the basis for plaintiff law firms in the U.S. to file lawsuits alleging personal injuries resulting from exposure to glyphosate-based herbicides, including non-Hodgkin lymphoma and multiple myeloma. The first case in the U.S. Roundup™ litigation, as referred to in Bayer's annual report, was filed in the fall of 2015, i.e., after the publication of the IARC monograph. Since the publication of the assessment by IARC in 2015, a number of leading health regulators have reexamined the safety of glyphosate. Their assessments are the most comprehensive and scientifically sound evaluations available. These health authorities include:

- [German Bundesamt für Risikobewertung \(BfR\)](#) in 2015: assessment as Rapporteur Member State for the renewal of the approval of glyphosate in the European Union
- [European Food Safety Authority \(EFSA\)](#) in 2015: peer-review of the assessment by BfR. In September of 2017, after comprehensive review of endocrine data set on glyphosate, EFSA [published](#) its conclusion that glyphosate does not have oestrogen, androgen, thyroid and steroidogenesis (EATS)-mediated endocrine disrupting properties.

- [European Chemicals Agency](#) in 2017
- [U.S. EPA Interim Registration Review Decision](#) in 2020, preceding [draft risk assessments](#) for glyphosate as part of the registration review in 2017. In 2017, U.S. EPA published its [Evaluation of Carcinogenic Potential of glyphosate](#). In September 2015, a [third review](#) was done by the Cancer Assessment Review Committee (CARC). In June of 2015, U.S. EPA completed their [endocrine disruption weight of evidence assessment](#) on glyphosate.
- [Health Canada Pest Management Regulatory Agency \(PMRA\)](#) in 2017, followed by a review of some of the data, after receipt of several notices of objection, by scientists who had not been involved in the 2017 assessment. In 2019, as an outcome of the review, the validity of the 2017 assessment was [confirmed](#).
- [Brazil National Health Surveillance Agency](#) in 2019
- [Australian Pesticides and Veterinary Medicines Authority](#) in 2016
- [Environmental Protection Agency of New Zealand](#) in 2016
- [Korean National Institute of Agricultural Sciences in 2017](#)
- [Food Safety Commission of Japan](#) in 2016
- [Joint FAO/WHO Meeting on Pesticide Residues](#) in 2016 (Joint Meeting of the Food and Agriculture Organization of the United Nations (FAO) Panel of Experts on Pesticide Residues in Food and the Environment and the World Health Organization (WHO) Core Assessment Group on Pesticide Residues (JMPR)).

Costs of carrying out the studies

AGM 2019: "Approximately how high were the costs (in euros or USD) of Bayer or Monsanto in connection with the more than 800 studies in total?"

AGM 2020: "Approximately how high were the costs of Bayer and / or Monsanto in connection with the more than 800 studies in total in EUR and / or in dollars?"

Since some of the more than 800 glyphosate studies that relate to human or mammalian health were conducted by other registrants, we don't have access to their cost information. Additionally, a significant number of the 629 studies conducted by Monsanto were done long ago (see answer to following question below) and cost information is not available. As a result, the company cannot calculate the cost of the more than 800 studies.

Given the wide range of different registration studies, in the following we have provided an overview of ballpark prices (in USD) for some types of toxicity base registration studies. Study design of these studies are base study designs, based on OECD guidelines, <https://www.oecd.org/env/ehs/pesticides-biocides/pesticides-testing-assessment.htm>.

Species	Study Type	Ballpark price on base study design (specific design needs or routes of administration will have an impact on study cost)
Rat	28-day	\$180,000
Rat	90-day	\$420,000
Mouse	28-day	\$230,000
Mouse	90-day	\$370,000
Dog	28-day	\$270,000
Dog	90-day	\$430,000
Rat	Acute Neurotoxicity	\$220,000
Rat	Subchronic Neurotoxicity	\$340,000
Rat	DRF Developmental	\$60,000
Rat	Developmental (OECD 414)	\$190,000
Rat	Developmental (OECD 421)	\$190,000
Rat	Developmental/28 Day Combination (OECD 422)	\$280,000
Rabbit	DRF Developmental	\$80,000
Rabbit	Developmental	\$230,000
Rat	2-Gen	\$810,000
Rat	Extended 1-Gen (Cohort 1 only)	\$920,000
Rat	Chronic/Carcinogenicity	\$1,400,000

Mouse	Chronic/Carcinogenicity	\$1,100,000
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In addition to the average costs of the different types of studies, in the following, we have indicated the cost range for a number of studies that have been submitted to the U.S. EPA in 2012 in order for the EPA to be able to assess potential endocrine disrupting properties of glyphosate. The costs for the relevant studies were in the range of around USD 12,000 to around USD 98,000.

The costs of some other studies submitted to the U.S. EPA in the 2012 submission were in the range of or below the values indicated in the table above. For instance, the costs of a Glyphosate Acid: Acute Neurotoxicity Study in Rat was around USD 108,000 and the costs of a Glyphosate Acid: Subchronic Neurotoxicity Study in Rats was around USD 178,000.

In order to give an idea of the total costs that are associated with the development of a molecule, a [study](#) by CropLife published in 2016 found that the total costs associated with bringing a molecule to market have increased over time from an estimated USD 152 million in 1995 to the most recent estimate of USD 286 million from 2010 to 2014. A material part of the cost is related to the registration procedure including the studies to be provided.

However, the common notion that the results of registration studies are less reliable than the results of “independent” studies in the published literature, solely because registration studies are funded by the manufacturer, is false. Apart from the fact that it is obvious that a manufacturer who seeks the approval of an active substance or product needs to show that the substance/formulation meets the regulatory requirements and therefore needs to fund required safety studies, the U.S. EPA has extremely rigorous [requirements](#) for registration studies, and all of the Monsanto studies initiated since the early 1980s were conducted according to [internationally recognized guidelines](#) and the [OECD Principles on Good Laboratory Practice](#) (GLP) which cover the organizational process and the conditions under which laboratory studies are planned, performed, monitored, recorded and reported and which have been developed to promote the quality and validity of test data used for determining the safety of chemicals and chemicals products. The principles of GLP are required to be followed by test facilities carrying out studies to be submitted to national authorities for the purposes of assessment of chemicals and other uses relating to the protection of man and the environment.

Data from the studies carried-out

AGM 2019: "How many of these over 800 studies date a) from before 2010, b) from 2010 to 2013, c) from 2014, d) from 2015, e) from 2016, f) from 2017 and g) from 2018?"

AGM 2020: "How many of these more than 800 studies date a) before 2010, b) from 2010 to 2014, c) from 2014, d) from 2015, e) from 2016, f) from the year 2017 and g) from the year 2018 and h) from the time thereafter until today?"

The U.S. EPA [database](#) to which we have referred above identifies all of the regulatory-required studies relating to glyphosate and Monsanto's glyphosate-based formulations, i.e. the "more than 800", including the dates when they were conducted. These are freely accessible on the EPA website and you can download these there.

Nonetheless, in the overview below, we have bucketed the relevant studies into the date ranges outlined in the question. These study numbers represent studies on glyphosate and Monsanto's glyphosate-based formulations that have been reviewed by the U.S. EPA as evidenced by their inclusion in the EPA bibliography. The most recent studies (2018 to 2020) may not already be included in the EPA bibliography yet and have, in the overview below, been put in one bucket.

Before 2010	561
2010 to 2013	190
2014	24
2015	14
2016	43
2017	23
2018 to 2020	17