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Expert statement on epidemiological studies which examine the possible correlation between exposure to glyphosate-based herbicides and non-Hodgkin's lymphoma and human fertility disorders in relation to evaluations undertaken by the German Federal Institute for Risk Assessment (BfR) and the European Food Safety Authority (EFSA)

On behalf of GLOBAL 2000, Vienna, and Umweltinstitut, Munich

Bremen, April 17, 2016

Scope of work

- **Evaluating the assessment of epidemiological studies undertaken by the German Federal Institute for Risk Assessment (BfR) and the European Food Safety Agency (EFSA) on the correlation between diseases and glyphosate**

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Evaluating the classification of epidemiological studies by the German Federal Institute for Risk Assessment (BfR) and the European Food Safety Agency (EFSA)

1 Data sources for the evaluation

The analysis is evaluated on the basis of two documents:

A. The so-called Renewal Assessment Report (RAR) on Glyphosate,[1] which was prepared and presented by the German Federal Institute for Risk Assessment (BfR) acting as a Rapporteur Member State (RMS) for the Commission, in cooperation with a similar institution in. The RAR is over 4,000 pages long in its entirety. Volume 3 it's the one with the evaluation of epidemiological studies related to glyphosate. It is unclear the extent to which the BfR or Glyphosate Task Force (GTF) were involved in compiling the Renewal Assessment Report, after the dossier was submitted. The GTF is a consortium including multinational chemical companies, which manufacture glyphosate-based herbicides and submitted the glyphosate "*dossier*" to request its approval in Europe.

B. After involving all EU Member States and incorporating their requested changes, an EFSA document was published in October 2015 [2].

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[1] RMS Germany, Co-RMS Slovakia. Renewal Assessment Report. Glyphosate. Volume 3. Annex B.6.1. Toxicology and metabolism. 18.12.2013. 947 pages. The relevant information for the classification of epidemiological studies are available on pages 518-534, 679-689. (A summary evaluation of the epidemiological studies are available in Volume I of the RAR, p. 63-66 and 80).

[2] EFSA. Final addendum to the Renewal Assessment Report - public version- Risk assessment provided by the rapporteur Member State Germany and co.rapporteur Slovakia for the active substance GLYPHOSATE according to the procedure for the renewal of the inclusion of a second group of active substances in Annex I to Council Directive 91/414/EEC laid down in Commission Regulation (EU) No. 1141/2010. October 2015, 4,322 pages.

2 Classification methods for evaluating epidemiological studies.

The BfR evaluates all publications on toxicological and epidemiological studies using the method Klimisch[3]. This method is a procedure developed to evaluate animal tests data. However, the Klimisch et al. (1997) publication offers no indication that the assessment procedure could be suitable for evaluating epidemiological studies. Nevertheless, just with one exception, all the epidemiological studies that were assigned the Klimisch score 3 ("not reliable").

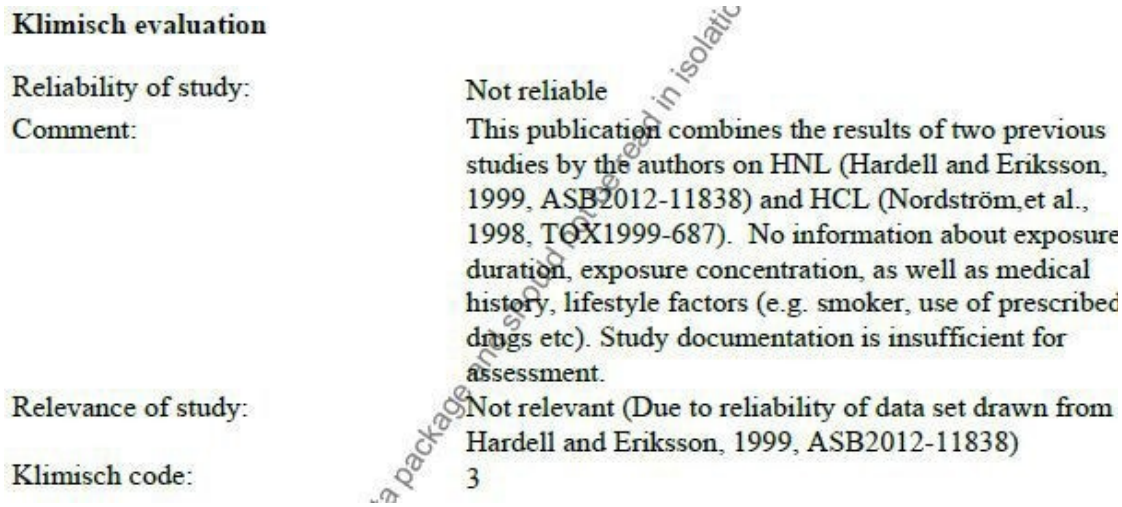
Klimisch and co-authors describe the objective of *reliability* as follows: "*evaluating the inherent quality of a test report or publication relating to preferably standardized methodology and the way that the experimental procedure and results are described to give evidence of the clarity and plausibility of findings*."[4] Klimisch and his co-authors describe category 3 ("not reliable") as follows: "*this includes studies or data from the literature/reports in*

which there are interferences between the measuring system and the test substance or in which organisms/test systems were used which are not relevant in relation to the exposure (e.g. unphysiologic pathways of application) or which were carried out or generated according to a method

igher incidence of a potential risk factor, then this may indicate that this could be a contributory risk factor for the disease.

Publication by Hardell and co-authors (2002)

In evaluating the Hardell et al (2002) publication, the BfR Renewal Assessment Report offers the following summary:[7]



Klimisch evaluation	
Reliability of study:	Not reliable
Comment:	This publication combines the results of two previous studies by the authors on HNL (Hardell and Eriksson, 1999, ASB2012-11838) and HCL (Nordström,et al., 1998, TOX1999-687). No information about exposure duration, exposure concentration, as well as medical history, lifestyle factors (e.g. smoker, use of prescribed drugs etc). Study documentation is insufficient for assessment.
Relevance of study:	Not relevant (Due to reliability of data set drawn from Hardell and Eriksson, 1999, ASB2012-11838)
Klimisch code:	3

If the BfR's criticisms were true, then the Hardell and co-author publication would really be unusable because key requirements of epidemiological studies would not have been fulfilled.

An examination of the publication, however, leads to a different assessment. The following paragraph is found on page 2 of the Hardell and Eriksson[8] publication of 1999:

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[7] RAR Glyphosate Volume 3, p. 524

[8] Hardell L, Eriksson M. A case-control study of Non-Hodgkin Lymphoma and Exposure to Pesticides. Cancer 1999; 85:1353-1360.

Assessment of Exposure

An 18-page questionnaire was mailed to the study subjects or to the next of kin for deceased individuals with an enclosed letter informing them that participation was voluntary. A complete working history was requested as well as information about exposure to different chemicals. For example, regarding the use of pesticides, subjects were asked for use within different occupations, such as forestry, farming, gardening, etc.; wet contact if not handling the sprayer; brand names of the different pesticides; and so on. In-depth knowledge of concentrations of active ingredients usually was lacking. Information also was assessed on years of exposure and cumulative exposure in days. Also, smoking habits, previous diseases, and certain food habits were assessed, the results of which will be presented in another paper.

Prof. Hardell was requested to submit a copy of the questionnaire used in the study. It was immediately made available and then translated into German by the German parliament's translation service upon request of the Bündnis90/Grüne parliamentary party (see appendix).

To be on the safe side, the second publication, whose data was included in the Hardell et al. publication (2002), was also examined. This publication[9] includes the following paragraph on page 2049 on determining the risk factors:

[9] Nordström M, Hardell L, Magnuson A, Hagberg H, Rask-Andersen A. Occupational exposures, animal exposure and smoking as risk factors for hairy cell leukaemia evaluated in a case-control study. Brit J Cancer 1998: 77:2048-2052.

A complete working history and information about various exposures and leisure time activities were obtained from an extensive questionnaire mailed to the participants. Two written reminders were sent to those who did not return the first questionnaire.

. To obtain an as uniform assessment of exposures as possible, all persons were carefully questioned if data was missing in the questionnaire. These supplementary questions were made over the phone by a trained interviewer, using written instructions. The total numbers of days of exposure to various agents were estimated. A minimum exposure of 1 working day (8 h) and an induction period of at least 1 year were used in the coding of exposures to chemicals. Some exposures (e.g. organic solvents) that may occur both in leisure time activities and occupationally were calculated together in the coding process. All interviews and all coding were made blinded with respect to the persons case or control status. The aim of the study was not disclosed to the subjects, and the questions dealt with a broad range of exposures, without focusing on any one in particular.

As the Nordström et al. (1998) study uses the same questionnaire as the Hardell and Eriksson (1999) study, previous diseases amongst the study participants were recorded in a similar way.

Comparing the publications with the BfR evaluation demonstrates without a doubt **that all the data claimed by the BfR to be missing had actually been ascertained according to scientific epidemiological methodology**.

Other epidemiological studies were treated by the BfR in the same way.

Publication by De Roos and co-authors (2003) A publication by De Roos and co-authors[10], dating to 2003, summarised the data from three previous studies[11,12,13] undertaken by the National Cancer Institute in the USA.

The BfR evaluated the publication as follows:

Klimisch evaluation

Reliability of study:	Not reliable
Comment:	No useful information about exposure duration, exposure concentration, as well as medical history, lifestyle factors (e.g. smoker, use of prescribed drugs etc were reported. Specific lymphomas are not identified (NHL captures all types of lymphoma other than Hodgkin's lymphoma). Documentation is insufficient to associate exposures with specific NHL diseases.
Relevance of study:	Not relevant (No report of identifying various types of lymphoma under the NHL umbrella; no definite association between specific NHL diseases and glyphosate can be made)
Klimisch code:	3

In order to explain the facts, the data of pesticide use of the participants are given in the publication by De Roos et al. (2003) and the data on smoking and diseases are given in the publications of the three different studies examined, quoted as the data source for the De Roos et al. (2003).

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[10] De Roos AJ, Zahm SH, Cantor KP, Weisenburger DD, Holmes FF, Burmeister LF, Blair A. Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men. Occup Environ Med 2003; 60:e11.

[11] Zahm SH, Weisenburger DD, Babbitt PA et al. A case-control study of non-Hodgkin's lymphoma and the herbicide 2,4-dichlorphenoxyacetic acid (2,4-D) in eastern Nebraska. Epidemiology 1990; 1:349-356.

[12] Hoar SK, Blair A, Holmes FF et al. Agricultural herbicide use and risk of lymphoma and soft-tissue sarcoma. JAMA 1986; 256:1141-1147

[13] Cantor KP, Blair A, Everett G et al. Pesticides and other agricultural risk factors for non-Hodgkin's lymphoma among men in Ilowa dna Minnesota. Cancer Res 1992; 52:2447-2455.

Investigating pesticide use (De Roos et al., 2003), p. 2.

Interviews

Interviews were conducted with the subjects or their next of kin if the subjects were dead or incapacitated. In each study, detailed questions were asked about the use of agricultural pesticides as well as other known or suspected risk factors for NHL. In Nebraska, information was obtained through questioning about the use of any pesticide, followed by prompting for selected specific pesticides, with details on the total number of years of use and average number of days per year. In Iowa and Minnesota, use was assessed by a direct question about a selected list of specific pesticides. Pesticide users were also asked the first and last year each pesticide was used. In Kansas, use of pesticides was assessed by an open ended question without prompting for specific pesticides, and duration of use and days per year were obtained for groups of pesticides (herbicides, insecticides, and fungicides), but not for each pesticide individually.

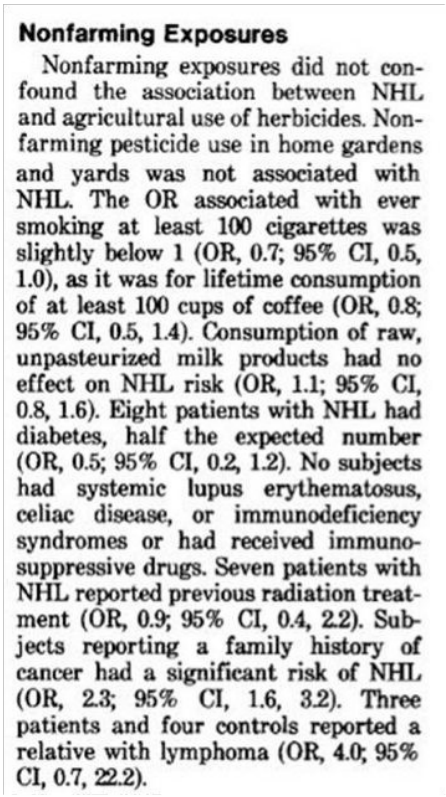
Smoking and previous diseases in the publication by Zahm et al., 1990 (p. 352)

None of the other factors covered in the interviews, including family history of cancer, prior radiation treatment, other aspects of the medical history, tobacco consumption, or use of hair coloring products, was responsible for the observed 2,4-D associations.

Smoking and previous diseases in the publication by Cantor et al, 1986 (p. 2447).

We asked about sociodemographic characteristics, medical history, smoking habit, occupational history, residential history, familial history of cancer, and other known and suspected risk factors.

Smoking and previous diseases in the publication by Hoar et al 1986, (p. 1145).



Nonfarming Exposures

Nonfarming exposures did not confound the association between NHL and agricultural use of herbicides. Nonfarming pesticide use in home gardens and yards was not associated with NHL. The OR associated with ever smoking at least 100 cigarettes was slightly below 1 (OR, 0.7; 95% CI, 0.5, 1.0), as it was for lifetime consumption of at least 100 cups of coffee (OR, 0.8; 95% CI, 0.5, 1.4). Consumption of raw, unpasteurized milk products had no effect on NHL risk (OR, 1.1; 95% CI, 0.8, 1.6). Eight patients with NHL had diabetes, half the expected number (OR, 0.5; 95% CI, 0.2, 1.2). No subjects had systemic lupus erythematosus, celiac disease, or immunodeficiency syndromes or had received immunosuppressive drugs. Seven patients with NHL reported previous radiation treatment (OR, 0.9; 95% CI, 0.4, 2.2). Subjects reporting a family history of cancer had a significant risk of NHL (OR, 2.3; 95% CI, 1.6, 3.2). Three patients and four controls reported a relative with lymphoma (OR, 4.0; 95% CI, 0.7, 22.2).

This proves that all the information claimed by the BfR to be missing had actually been investigated in full in accordance with current scientific methodology.

Publication by Eriksson and co-authors (2008)

Eriksson et al. (2008)[14] questioned a total of 910 patients with non-Hodgkin's lymphoma, as well as a control group of 1,016 patients. The large number of patients allowed them to differentiate between various subgroups of non-Hodgkin's lymphoma during their analysis. The overall result indicated a

[14] Eriksson M, Hardell L, Carlberg M, Akerman M. Pesticide exposure as risk factor for non-Hodgkin's lymphoma including histpathological subgroup analysis. Int J Cancer 2008; 123:1657-1663.

doubling of the risk of disease after exposure to glyphosate, with a significant rise in the risk of disease for longer periods of exposure (where exposure exceeded 10 days, additional risk rose by 136%).

BfR evaluation of the study by Eriksson and co-authors (2008)

Klimisch evaluation

Reliability of study:	Not reliable
Comment:	Multiple avenues for bias were introduced in study design, execution and data processing. No information about exposure duration, used glyphosate products and application rates. Other factors (i.e. smoking habits, medication etc.) were assessed but not included in the evaluation.
Relevance of study:	Relevant with reservation
Klimisch code:	3

Description of the evaluation of exposures and other factors in the Eriksson and co-authors study (2008), page 1658.

Assessment of exposure

All subjects who accepted to participate received a comprehensive questionnaire, which was sent out shortly after the subjects had been telephone interviewed by the other research group we had collaboration with as stated earlier. Their interview, however, did not focus on work environment or chemical exposure, but rather dealt with other life style factors and diseases. Our questionnaire included a total work history with in depth questions regarding exposure to pesticides, organic solvents and several other chemicals. For all pesticides not only numbers of years and numbers of days per year, but also approximate length of exposure per day were questioned. Since most work with pesticides was performed in an individualized manner, no job-exposure matrix was judged to be applicable. Furthermore, the questionnaire also included questions on *e.g.*, smoking habits, medications, leisure time activities and proximity from home to certain industrial installations, but data on these factors are not included in this article.

Specially trained interviewers scrutinized the answers and collected additional exposure information by phone if important data were lacking, incomplete or unclear. These interviewers were blinded with regard to case/control status. All exposures during the same calendar year as the diagnosis and the year before were disregarded in the cases. Correspondingly, the year of enrolment and the year before were disregarded for the controls. As in our previous lymphoma studies we used a minimum criterion of one full day exposure to be categorized as exposed.[8,18]

This shows again that all the information claimed by the BfR to be missing had actually been investigated in full in accordance with current scientific methodology.

The BfR only evaluated positively one epidemiological study on the potential correlation between the use of herbicides and glyphosate.

This was a publication, which drew data from the Agricultural Health Study by De Roos AJ et al. (2005)[15]. There is no discernable qualitative difference between this study and all the studies noted above which were negatively evaluated by the BfR. The authors include leading epidemiologists at the National Cancer Institute in the USA, as in the other studies, which were dismissed. The medical journal is a top international scientific publication, along with other publications, which the BfR dismisses as “not reliable”.

Studies negatively evaluated by the BfR

A series of other epidemiological studies were lumped together by the BfR and branded unusable for evaluating the potential dangers to health posed by glyphosate-based herbicides on the basis that the increased risk of disease demonstrated by the authors of these publications was not statistically significant (Pahwa et al., 2012[16]; McDuffie et al., 2001[17]; Lee et al., 2004[18]). The grounds for deciding that other studies, whose results where also not statistically significant, were worthy of extensive evaluation is not clear.

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[15] De Roos AJ, Blair A, Rusiecki JA et al. Cancer incidence among glyphosate-exposed pesticide applicators in the Agricutural Health Study. Environ Health Perspect 2005; 113:49-54.

[16] Pahwa P, Karunanayake CP, Dosman JA et al. Multiple myeloma and exposure to pesticides: A Canadian case-control study. J Agromed 2012; 17:40-50.

[17] McDuffie HH, Pahwa P, McLaughlin JR et al. Non-Hodgkin's lymphoma and specific pesticides exposure in men: Cross-Canada Study of Pesticides and Health. Cancer Epidemiol Biomarkers Prev 2001; 10:1155-1163.

[18] Lee WJ, Cantor KP, Berzofsky JA et al. Non-Hodgkin's lymphoma among asthmatics exposed to pesticides. Int J Cancer 2004; 111:298-302.

3.1 Epidemiological studies on the correlation between the incidence of non-Hodgkin's lymphoma and glyphosate, which were not evaluated by the BfR

In its Renewal Assessment Report the BfR neglected to evaluate four epidemiology studies. These include two studies published prior to 2000 (Brown et al, 1993; Cantor et al., 1992)[19,20] and two other published more recently Cocco et al, 2013; Orsi et al., 2009)[21,22]. The reason given by the BfR for not considering the studies published prior to 2000 was that such studies had already been dealt with in an earlier Assessment Report. Although formally correct, this argument ignores the fact that it is essential to analyse the entire body of scientific publications if a complete assessment of the possible impact of a pesticide on health is to be made.

Ignoring the publications by Orsi et al. (2009) and Cocco et al. (2013) is completely inexplicable.

3.2 Epidemiological studies on the correlation between human fertility disorders and glyphosate

The BfR Renewal Assessment Report includes assessments of several publications, which suggest that herbicides containing the active ingredient glyphosate could have a serious impact on human fertility.

Study by Savitz and co-authors (1997)

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[19] Brown LM, Burmeister LF, Everett GD et al. Pesticide exposure and multiple myeloma in Iowa men. Cancer Causes Control 1993; 4:153-156.

[20] Cantor KP, Blair A, Everett G et al. 1992; Cancer Res 1992; 52:2447-2455.

[21] Cocco P, Satta G, Dubois S et al. Lymphoma risk and occupational exposure to pesticides: results of the Epilymph study. Occup Environ Med 2013; 70:91-98.

[22] Orsi L, Delabre L, Monnereau A et al. Occupational exposure to pesticides and lymphoid neoplasms among men: results of a French case-control study.Occup Environ Med 2009; 66:291-298.

Savitz et al. (1997)[23] examined the possibility of adverse effects on pregnancies resulting from paternal exposure to pesticides as part of an Ontario Farm Family Health Study. They analysed the course of 3,984 pregnancies in 1,898 couples. They discovered that spontaneous abortions occurred more frequently when the father had mixed or used pesticides to kill weeds on farms. Miscarriages occurred more frequently after the use of various pesticides (significant increase in risk for herbicides in total of +40%, Thiocarbamate +90%, for insecticides in total +60%, for Carbarly +110%. For glyphosate there was a non-significant increase in risk of +40%.) Preterm births occurred more frequently after the use of various pesticides (significant total increase in risk after use of herbicides on the farm of +110%, after using Triazines +220%, Atrazine +390%, and after 2.4-DB +250%. For glyphosate there was a non-significant increase in risk of +140%.)

BfR assessment of the publication by Savitz and co-authors (1997)

Klimisch evaluation

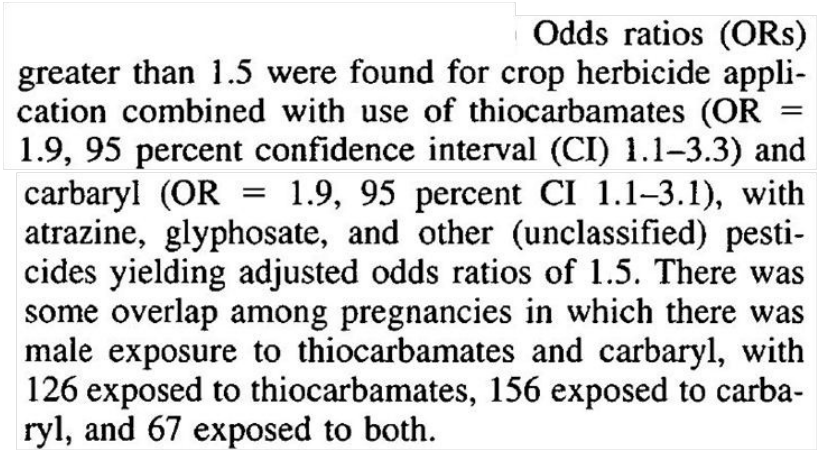
Reliability of study:	Not Reliable
Comment:	No information about exposure duration, used glyphosate products and application rates. No information, if the subjects used more than one pesticide. Due to study design and evaluation methods, study results are not reliable.
Relevance of study:	Not Relevant (Study design is not suitable for assessment of glyphosate exposure).
Klimisch code:	3

Since the questioning was performed by the Ontario Farm Family Health Study, an exact assessment of how the questions were actually asked was only possible by analysing the questionnaire itself. The questionnaire is included in the PhD thesis by TE Arbuckle, submitted to the University of North Carolina at Chapel Hill in 1994. As attempts to gain access to this work had not been successful at the time, it was necessary to rely on other

[23] Savitz DA, Arbuckle T, Kaczor D et al. Male pesticide exposure and pregnancy outcome. Am J Epidemiol 1997; 146:1025-1036.

publications produced as part of the Ontario Farm Family Health Study. These include the publication by Arbuckle et al (2001; see below), which describes the survey methodology and level of detail. The BfR claims that it was unclear whether a single person had used more than one type of pesticide were disproved by the Savitz publication: the results section (p. 1028) give several indicators that the analyses had considered the use of several pesticides.

Proof of the recording of multiple exposures by Savitz et al.; p. 1028



Odds ratios (ORs) greater than 1.5 were found for crop herbicide application combined with use of thiocarbamates (OR = 1.9, 95 percent confidence interval (CI) 1.1–3.3) and carbaryl (OR = 1.9, 95 percent CI 1.1–3.1), with atrazine, glyphosate, and other (unclassified) pesticides yielding adjusted odds ratios of 1.5. There was some overlap among pregnancies in which there was male exposure to thiocarbamates and carbaryl, with 126 exposed to thiocarbamates, 156 exposed to carbaryl, and 67 exposed to both.

BfR's criticism that the length of exposure was not recorded is completely inappropriate because the question (exposure during the 3 months prior to conception) does not ask about the length of exposure to pesticides, but rather whether there was any exposure during the critical 3-month period. Claims of a failure to record multiple exposures are disproved in the text in the results section (see above).

Study by Arbuckle and co-authors (2001)

Arbuckle et al. (2001)[24] examined the extent to which exposure to glyphosate prior to conception might increase the risk of spontaneous abortion. 2,110

[24] Arbuckle TE, Lin Z, Mery LS. An exploratory analysis of the effect of pesticide exposure on the risk of spontaneous abortion in an Ontario farm population. Environ Health Perspect 2001; 109:851-857.

women living on a farm with a total of 3,936 births served as the study population within the framework of the Ontario Farm Family Health Study. The key result of the study is that women exposed prior to conception had a significantly increased likelihood (70%) of spontaneous abortion during the 12th and 19th weeks of pregnancy.

BfR assessment of the study by Arbuckle and co-authors

Klimisch evaluation	
Reliability of study:	Not reliable
Comment:	No information about exposure duration, used glyphosate products and application rates. No information, if the subjects used more than one pesticide.
Relevance of study:	Not relevant (Study design is not suitable for assessment of glyphosate exposure).
Klimisch code:	3

Three highly relevant confounding factors were not considered in the OFFHS questionnaire: history of previous spontaneous abortion(s), maternal age and smoking.

Additional remarks: *Three extremely important influential factors were not considered in the Ontario Farm Family Health questionnaire: previous spontaneous abortions, the age of the mother, smoking.*

Investigation by Arbuckle et al (2001), p. 851

We pooled pesticide exposure information from the farm operator (the person responsible for the day-to-day operations of the farm, if different from the husband or wife), husband, and wife to construct a history of monthly agricultural and residential pesticide use. For each pesticide reported, we identified the active ingredients and uses using a database of registered pesticide products in Canada. Where possible, we categorized the active ingredients into chemical families. We divided all pesticides reported into four major classes of use: herbicides, insecticides, fungicides, and miscellaneous others (including those that could not be classified). We identified the active ingredients and chemical families that were most frequently used on the farms in the study, as well as those most likely to have adverse reproductive effects according to the literature. This categorization produced 17 pesticide unit variables that we examined in this study

We merged reproductive and pesticide exposure history data to create pesticide unit variables for months preceding and during each pregnancy. Exposure to pesticides was analyzed for two windows: preconception, the 4-month period from 3 months before conception to the calendar month of conception (consistent with potential sperm-mediated effects); and postconception, the 3-month period from the first calendar month after conception to the end of the first trimester (consistent with a fetotoxic effect). Exposures that occurred after a pregnancy loss but within the period of interest (i.e., first trimester) were not considered in assessing exposure status. We also created pregnancy-specific variables for all other time-related factors (parental age, smoking, farm activities, and alcohol and caffeine intake).

All the data, which the BfR claimed were missing are actually contained in the study but are handled in a differentiated manner.

Only a quick glance at the publication is needed to be clear that figure 1 (below) indicates the age of the mother, otherwise it would have been impossible to differentiate according to maternal age (≤34, >34).

Figure 1 of the publication by Arbuckle et al (2001), p. 855.

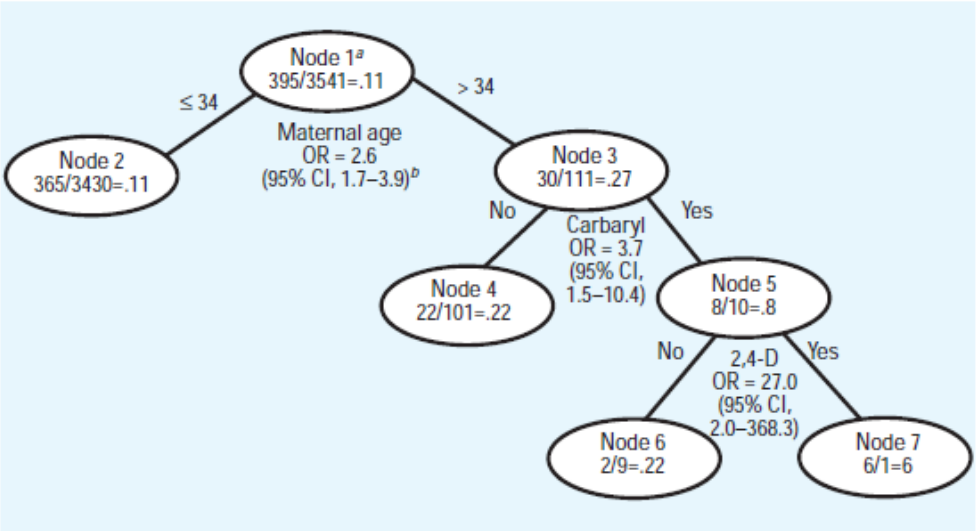


Figure 1. Classification and Regression Tree analysis of crude spontaneous abortion risk (< 20 weeks' gestation)—preconception exposure to pesticide active ingredients and other risk factors.

[a]In the nodes, the numerators represent the number of cases; the denominators are the number of non-cases. [b]Left branch of node used as referent group.

Publication by Garry and co-authors (2002)

Garry et al. (2002)[25] carried out a study of 1,070 farmers with a licence to apply pesticides in the Red River Valley in Minnesota, USA. Of the group, 851 farmers were married or living in a marriage-type partnership. 851 women living together with pesticide users took part in a telephone interview held at a chronological interval after telephone interviews with their male partners. This resulted in a total of 695 interviews with families. Of these 695 interviews, for 536 of the births there had been paternal use of pesticides. The specific outcome for glyphosate use demonstrated a 260% increase in the risk of children developing ADHS (hyperactivity) where the father had used glyphosate at the time of conception.

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[25] Garry VF, Harkins ME Eriksson LL et al. Birth defects, season of conception, and sex of childen born to pesticide applicators living in the Red River Valley of Minnesota, USA. Environ Health Perspect 2002; 110 (suppl. 3):441-449.

Klimisch evaluation	
Reliability of study:	Not reliable
Comment:	Epidemiological study with some methodological / reporting deficiencies (selection of study subjects, no information about exposure duration, exposure concentration, pesticide use frequency).
Relevance of study:	Not relevant because of methodological deficiencies.
Klimisch code:	3

The BfR entirely failed to recognise that the question of whether pesticide use at the time of conception could lead to disruptions in embryonic development, was not related to the duration of the use or concentration of the pesticide, but rather to the time of use.

The selection of study participants (as described above) is entirely in line with the design of a scientific study to examine such a question. There is absolutely no recognisable distortion caused by the choice of study participant.

4 Epidemiological studies in the EFSA report

After gathering feedback from all EU states, on 19th of November 2015 the EFSA uploaded the final version of the Renewal Assessment Report[26] and published it online. This version marks all the changes to the earlier RAR version[27] in colour. The paragraphs on epidemiological studies are found on pages 1040-1058 (carcinogenicity), and pages 1186-1188 and 1207-1216 (human reproduction).

Where these pages include statements about individual publications, we find the same formulations used as in the BfR's Renewal Assessment Report, i.e.

[26] see footnote 2.

[27] see footnote 1.

they adhere to the claims that the studies are “not reliable” because relevant data, e.g. exposure to glyphosate, smoking behaviour and previous diseases, was not recorded.

By 28th of September 2015 at the very latest, the date of the public hearing of the German parliamentary committee on food and agriculture, it must had been clear to the BfR that there was absolutely no basis for any of these claims. This had been proven both in a detailed statement to this parliamentary committee proceeding[28], and later in an open letter to Vytenis Andriukaitis, EU Commissioner for Health & Safety, written by 94 scientific experts from 25 countries[29].

For the first time the EFSA report includes a reference to the Schinasi and Leon meta-analysis[30] on page 78, and in identical form on page 1043:

- Schinasi and Leon (2014, ASB2014-4819) published the results of epidemiologic research on the relationship between non-Hodgkin lymphoma (NHL) and occupational exposure to pesticides. Phenoxy herbicides, carbamate insecticides, organophosphorus insecticides and lindane were positively associated with NHL. However, no association between NHL an glyphosate was reported.

This statement is in direct contrast to the results of the meta-analysis on which Schinasi and Leon reported. In their analysis (see table 5 below) they reach contrary findings, namely that there is a statistically significant increase in the risk of disease of 50% (odds ratio: 1.5). There was even a doubling of the risk of disease for B-cell lymphomas, a sub-form of non-Hodgkin's lymphoma, amongst those coming into contact with glyphosate-based herbicides through their professional work (odds ratio: 2.0). It is absolutely

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[28] Greiser E. Statement of the individual expert Prof. Dr. Eberhard Greiser. German parliament. Committee for food and agriculture. Committee proceeding 18 (10)326-H. ÖA "glyphosate" on 28 September 2015. 27. September 2015.

[29] Portier CJ, Armstrong BK, Baguley BC et al. Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA). J Epidemiol Comm Health. online 3.3.2016 as 10.1136/jech 2015 207005.

[30] Schinasi L, Leon ME. Non-Hodgkin lymphoma and occupational exposure to agricultural pesticides chemical groups and active ingredients: Systematic review and meta-analysis. J Environ Res Public Health 2014; 11:4449-4527.

clear that both references to the results of the meta-analysis by Schinasi and Leon in the EFSA report fail to reflect the actual results.

Schinasi & Leon (2014), page 4513. Table 5.

Table 5. Meta analytic summary estimates of association between herbicides and insecticides with non-Hodgkin lymphoma.

Chemical group or active ingredient	Meta Risk Ratio estimate, 95% CI	I^2	Papers contributing
HERBICIDES			
Amide herbicides			
Amide herbicides	1.3, 0.8–1.9	22.2%	[18,27,34,46]
Alachlor	0.9, 0.6–1.3	43.0%	[30,39]
Aromatic acid herbicides			
Benzoic acid herbicides	1.3, 0.9–1.9	0.0%	[18,27,34,46]
Dicamba	1.4, 1.0-2.1	0.0%	[30,43]
Carbamate/thiocarbamate herbicides			
Carbamate/thiocarbamate herbicides	1.4, 1.1–2.0	0.0%	[18,43,60]
Dinitroanilines			
Dinitroanilines	1.2, 0.8–1.7	0.0%	[27,43]
Trifluralin	0.9, 0.6–1.3	0.0%	[18,30,43,45]
Organophosphorus herbicides			
Glyphosate	1.5, 1.1–2.0	32.7%	[30–33,43,46]
Glyphosate-association with B cell lymphoma	2.0, 1.1–3.6	0.0%	[32,63]

Searching the 4,322 pages of the EFSA report for another appearance of the name Schinasi revealed a reference on page 4,136 indicating that there is a relationship between exposure to glyphosate and B-cell lymphoma, but without any figure being given. Finally, on pages 4,182 and 4,183 of the same report with reference to Schinasi and Leon's recommendation that further studies are necessary, the report concludes that the possibility that glyphosate has an effect on the risk of NHL cannot be completely ruled out, as the latest meta-analysis had demonstrated a minimal affect for NHL and B-cell lymphoma. The IARC monograph on glyphosate[31] only refers to NHL, so the mention of an effect on B-cell lymphoma refers to the meta-analysis undertaken by Schinasi and Leon. In epidemiology a 100% increase in risk is a very large effect. If the BfR and EFSA regard such an increase in risk as only a minimal effect, then this simply demonstrates an almost inexplicable

[31] IARC Monographs 112. Glyphosate, 29.7.2015, Lyon; p. 30, paragraph 2.4. Meta-analyses.

lack of judgement by these two authorities in matters of epidemiology and in estimating the risk of disease.

Summary

"Assessment of the conduct of the German Federal Institute for Risk Assessment and the European Food Safety Authority in evaluating epidemiological studies examining the correlation between exposure to glyphosate and danger to health"

The German Federal Institute for Risk Assessment (BfR) has taken a classification method exclusively developed to evaluate animal studies and used it to undertake a scientific evaluation of epidemiological studies. Both institutions have significantly altered the methods and results of epidemiological studies in order to pretend that relevant data (e.g. exposure to glyphosate, smoking behaviour, previous diseases) was completely lacking. Taking these alleged errors as their basis, they then assessed the studies as "not reliable". This approach is not on a par with a scientifically-based discussion on study design or results, instead it represents a deliberate falsification of study content, presumably with the intention of qualifying the studies as scientifically inferior. Actually, as a result of this approach, scientific publications on scientifically-excellent studies have been incorrectly dismissed.

Bremen/Musweiler

5 April 2016

Greiser E. Statement of the individual expert Prof. Dr. Eberhard Greiser.