GLOBAL 2000's response to ECHA regarding the agency's glyphosate assessment

We appreciate that ECHA took the time to address[1] the six questions raised at the end of our response[2] dated 21 August 2017, even though the agency stated in its 8 August communication that it would not engage in any public discussion "at this critical decision-making stage".

We challenge the Standing Committee on Plants Animals Food and Feed (SCoPAFF) to objectively evaluate the carcinogenicity data on glyphosate in the light of the precautionary approach put forth in Regulation (EC) 1107/2009, which states:

"The precautionary principle should be applied and this **Regulation should ensure that industry demonstrates that substances** or products produced or placed on the market **do not have any harmful effect** on human or animal health or any unacceptable effects on the environment."

Statistically increased incidences of the same tumour type in three different studies (dose-dependent in two cases and supported by historical control data in two cases) emphatically fail to constitute a 'demonstration' that glyphosate does not have any harmful effect on human health. On the contrary, they constitute a demonstration that glyphosate poses a serious health hazard.

We also challenge the statements made in the Opinion issued by the Risk Assessment Committee (RAC), and reproduced by ECHA in its letter dated 01 September 2017, in response to the six questions we asked in our communication of 21 August 2017.

1. ECHA states that a "tendency" was noted for increased incidences of malignant lymphomas in male mice in the high dose groups in four of five available studies. This statement is inaccurate. There were statistically significant increases in two of these studies and – if a one-sided test was used – in a third study. The term

1 https://echa.europa.eu/documents/10162/22931011/echa_global_2000_2.pdf/9619650d-519f-0b4d-333c-9a9b721e5312

2 http://www.pan-germany.org/download/Global2000-Response-to-ECHA_20170821_FIN.pdf

"tendency" is used for non-significant increases – which could be applied to the increases seen in the lower dose groups of at least two studies. Scientifically invalid reference is made to "global" historical control data in order to state that these incidences were mostly within the "available control incidence". The truth is that the significant increase in two studies was supported by historical control data (where it was even outside the range of the control incidence) and for the other studies no valid historical control data were available.

2. Neither in RAC's Opinion nor in the CLH report were "non-neoplastic lymph node lesions" discussed in detail. Therefore the claim that "elevated tumour incidences (meaning malignant lymphoma) were not supported by parallel increases in non-neoplastic lymph node lesions" has no transparent basis – or perhaps no basis at all.

3. In question 5 of our communication dated 21 August 2017, we re-emphasized that 2 of the 3 mouse studies that were valid with regard to malignant lymphoma showed a statistically significant increase at doses not exceeding the Maximum Tolerated Dose. We also re-emphasized that in the third study the presumed excessive toxicity (as measured by a pronounced reduction of body weight gain) was associated with a similar reduction in food intake, due to a lack of palatability resulting from the high glyphosate concentration in the test diet. ECHA never addressed these points, in spite of its claim that the "the issue has been extensively considered" in their previous response.

4. Concerning the epidemiological evidence, ECHA and its RAC refer to the Agricultural Health Study (AHS) as "the only prospective cohort study available". However, this study had a follow-up time of only 6.7 years. This time period is considered too short with regard to non-Hodgkin lymphoma.[3] Therefore, it is wrong to pitch the – up to now – negative outcome for non-Hodgkin lymphoma in the AHS study against the statistically significant positive findings in several case-control studies, including a meta-analysis. These positive findings are even recognized by ECHA.

While we are convinced that the existing evidence warrants a category 1B classification (in line with IARC's assessment of a different database) we challenge EFSA, ECHA and ScoPAFF to explain why they did not at least consider a category 2 classification, which,

3 This was indirectly acknowledged even by Tim Bowmer, Chairman of the RAC at the conference "Glyphosate: Harmless Tool or Sneaky Poison?" held in Brussels on 10 May 2017. Bowmer stated that it would be key to follow that study and to find out how it had developed since the last time it was reported. "For me that is the key study that could change the paradigm here", Bowmer said.

according to Regulation (EC) 1272/2008 is based on limited evidence of carcinogenicity.

Remember that "limited evidence" according to this regulation (item 3.6.2.2.3) is characterized as follows: the data suggest a carcinogenic effect but are limited for making a definitive evaluation because, e.g. (a) the evidence of carcinogenicity is restricted to a single experiment; (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the studies; and (c) the agent increases the incidence only of benign neoplasms or lesions of uncertain neoplastic potential.

Even when leaving out all other existing evidence, the criteria for a category 1B classification are clearly fulfilled, because a significant increase in malignant lymphoma was demonstrated for male mice in three independent studies, supported by valid historical control data and dose-dependence in two studies. ECHA states in its own Guidance "Effects seen only in one sex in a test species may be less convincing than effects seen in both sexes... **However, there is no requirement for a mechanistic understanding of tumour induction in order to use these findings to support classification**" (ECHA Guidance 2015, p. 377-378, emphasis added).

Concluding that no classification of glyphosate is warranted is a travesty of science.

Sincerely

Helmut Burtscher for Global 2000, Peter Clausing, and Claire Robinson

Vienna, 14 September 2017