Annex 1 to the GDCh/SEC Open Letter of XXX to the European Commission "To keep alive advanced non-selective Herbicide Technologies in Europe"

"Glyphosate is probably carcinogenic to humans (Group 2A)" ??

Not without reason, Monsanto during the past decades has earned a reputation of a bad kind of capitalist acting worldwide and everybody showed understanding when Greenpeace attacked Monsanto vehemently in 2005 already[1].
But does this justify the condemnation of the best researched herbicide ever because this would likely hurt Monsanto? Have therefore farmers all over Europe to be punished by banning Glyphosate which was lauded a once in a century herbicide still in 2008?

We have

- carefully analysed the IARC (**I**nternational **A**gency for **R**esearch on **C**ancer) statements in their Monograph 112 of 2015[2]. In this Monograph IARC claims that Glyphosate be probably carcinogenic to humans Group 2A.
- carefully analysed IARC´s own Statutes (Preamble)[3,3a,3b].
- identified relevant facts insufficiently recognized in Monograph 112 or not considered at all.
- highlighted the numerous statements of scientist independent of Monsanto and of regulatory agencies which came to much more differentiated conclusions about glyphosate[4-19]

Glyphosat ≠ Glyphosate-based formulation

The **A**gricultural **H**ealth **S**tudy (AHS), the main base of Conclusion 6.1 "There is limited evidence in humans for the carcinogenicity of glyphosate"[2] (page 398) has been inaugurated in 1993 as great US national project. Every participant had to specify from a list of 22 different pesticides in a 21 pages questionnaire those products they had contact with how, when and how frequently, with one pesticide only or with several pesticides at the same time over a period of several years!![2] (page 331, left column, Cohort Studies). De Roos el al. in the abstracts of their study[20] explain that according to the AHS questionnaire each and every product to be mixed or used containing a glyphosate component was to be termed glyphosate. Sorahan[21] calls these products simply "a range of Roundup® branded products". Other publications in the AHS emphasize in the same sense that in reality only glyphosate-based proprietary formulations e.g. from manufacturers Monsanto, Syngenta, Cheminova and many others, but definitely never the active ingredient alone had been used. At least in the initial phase of the AHS also Syngenta´s Touchdown®, competitive proprietary formulation to Monsanto´s Roundup® had been used by the farmers. It´s a fact but not surprising that Monograph 112 only mentions briefly the alarming analysis of Sorensen et al. "Rapid lethal intoxination caused by the herbicide glyphosate-trimesium (Touchdown)"[22]. This incident would have shown that not only glyphosate ≠ glyphosate

formulation but even glyphosate ≠ glyphosate. Of course, trimesium glyphosate thereafter has been immediately withdrawn in the middle of the AHS.

In order to generate commercially available, storable glyphosate products for agriculture, the various different active ingredients of what is termed glyphosate in the AHS (in[2] page 321: glyphosate-isopropylamine salt,- mono-ammonium salt, -diammonium salt, -sodium and trimesium salt and also glyphosate acid) must first be transformed in water-based formulations containing emulsifiers, preservatives, defoamers, p_H-stabilizers etc. and in particular adjuvants i.e. surfactants which are essential to make the wax-coated plant leaf surface wettable and permeable. Without such transformation in a formulation the active ingredients cannot be absorbed by the plant, are just chemicals not even freely available on market and therefore could not have come in contact with people at all. The powerful surfactants of choice in the US to do this job are still today tallowamine-ethoxylates (POEA, **P**oly**o**xy**e**thylene**a**mines) which are available after few chemical reactions almost at disposal costs from the tallow piles of the American slaughterhouses. In Europe, POEA are banned since 2016 for health reasons. Since many years groups of scientists independent of Monsanto have discovered and published that there are many significantly weaker physiological effects of glyphosate or even non-existing on the one hand and of glyphosate-based formulations or Roundup® on the other hand[4-17]. Even the Monograph 112 itself concedes under Toxicokinetic data (page 364) e.g. at Gasnier et al. and Larsen et al.: „The Working Group noted that it was not clear whether the effects were caused by glyphosate alone or by adjuvants contained in the formulation.“ Furthermore, Monograph 112 mentions numerous examples of significantly different physiological effects of glyphosate and of glyphosate-based formulations in animals under Non-human mammals in vivo as well as in vitro tests but equally in Humans in vitro experiments. The latter ones are found under 4.2.2 „Receptor-mediated mechanisms“ in the sub-groups „Sex-hormone pathway disruption“, under 4.2.3„Oxidative stress, inflammation and immunomodulation“ and under 4.2.4 „Cell proliferation and death“.
It would have been appropriate from a scientific point of view if Monograph 112 had clearly stated that there are numerous cases of evidence of significantly different reactions in animal in vivo as well as in human in vitro experiments between glyphosate and glyphosate-based formulations containing POEA and other proprietary components.

<u>The criteria for hazard-classification applied in Monograph 112 are questionable from a scientific perspective; the respective IARC-Statutes pre-determine the results</u>

The definition of cancer hazards according to the IARC Statutes reads: “A cancer hazard is an agent that is capable of causing cancer under some circumstances”[23] and ”The IARC Monographs identify carcinogenic hazards i.e. those agents having the potential to cause cancer under some circumstances“[24]. Very obviously, “under some circumstances” invites the phantasy on the part of the research scientists in terms of methods and/or doses to be used in the studies in order to produce positive results. The Briefing Notes from the IARC Director instruct the Council members that the same

understanding shall also apply in their hazard classification job. This is not only an option, it is rather requested by IARC-Statue: „The Monograph evaluations group agents according to the strength of evidence, not their potency" [25]. Thus, for IARC´s grouping/classification of hazards it is irrelevant how dangerous actually an agent is but rather how convincingly an evidence of hazard can be presented, under which circumstances ever!

We have to accept this as a principle of proceeding but it prevents openness to the results. Results are pre-determined. The existence of a hazard is a done deal. Three examples may highlight our objections:

1. The publication of N. Benachour and G. E. Séralini: "Glyphosate formulations induce apoptosis and necrosis in human umbilical, embryonic and placental cells", Chem Res Toxicol., 22(1):97-105; 2008. The comment of the official Agence Francaise de Sécurité Sanitaire des Aliments of march 26, 2009[26] is a devastating assessment of the study starting from inappropriate cell-materials used, to study methods and the results of the study. Interestingly, the study also emphasized the strong impact of POEA present in the formulation.
2. The strongly disputed publication of Paganelli et al: "Glyphosate-based herbicides produce teratogenic effects on vertebrates by impairing retinoic acid signalling" Chem Res Toxicol, 23(10):1586-95 (2010). Such effects were observed after injection of glyphosate and glyphosate-based formulations into embryos of chickens and frogs. In the EU Standing Committee meeting of 22-23 November 2010 the Rapporteur Member State, Germany, was requested to comment: "The studies had been performed under highly artificial conditions, extremely different from what can be expected in agricultural circumstances and it is hardly possible to predict adverse effects on mammals on this basis."
3. The 2008 Case Control Study of Erikson et al. in Sweden[27]. This study produced remarkably high statistical Odds Ratios and therefore appears as a perfectly convincing evidence of carcinogenicity of glyphosate and other pesticides. However, in contrast to other Studies (e.g. De Roos et al. (2005)[20], or Lee et al. (2007)[28], Andreotti et al. (2009)[29] in which all usual chances of physical contact with the pesticide (pesticide mixing, application method, equipment repairs, equipment cleaning etc., even type of tractor cabin (open, closed, with charcoal filter), frequency of gloves- and cloths changes after contamination/spill and others) have been translated into algorithms for the calculation (Andreotti et al.), the study of Erikson et al. declared in Discussion, page 13: "Use of protective equipment was not asked for which might have been a disadvantage of the study. However, such use would have diluted the exposure and thus bias the result towards unity". This is very difficult to understand but helps to make Odds Ratios look big.

<u>Overall Conclusion</u>

Scientifically correct and factually unassailable the following formulations in 6. Evaluation would have been:

6.1 *There is limited evidence in humans for the carcinogenicity of glyphosate-based formulations containing POEA and other proprietary ingredients and to a lesser degree of the various chemical variants of the active ingredient glyphosate.*
6.2 *There is significant evidence in experimental animals for the carcinogenicity of glyphosate-based formulations containing POEA and other proprietary ingredients and to a lesser degree of the various chemical variants of the active ingredient glyphosate.*
6.3 Overall evaluation: Glyphosate-based herbicides have been shown to present potential hazards. In order to avoid that such potential hazards turn into actual risks to the user it is strongly requested to strictly follow the safety instructions on the product labels and to avoid in particular skin contact and inhalation of sprays.

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