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**FILED VIA ECF**Honorable Vince Chhabria  
United States District Court, Northern District of CaliforniaRe: *In re Roundup Prods. Liab. Litig.*, No. 3:16-md-02741-VC

To the Honorable Vince Chhabria,

Monsanto submits this letter brief in response to PTO No. 33 regarding the impact of the November 9, 2017 Agricultural Health Study (“2017 AHS study”) on the *Daubert* issue before the Court and what steps should be taken to ensure that the Court can appropriately meet its gatekeeping responsibility to assess the reliability and admissibility of plaintiffs’ experts’ NHL causation testimony in light of this powerful, new contrary evidence.

**I. The Impact of the 2017 AHS Study on the *Daubert* Issue Before the Court**

The significance of the 2017 AHS study on the Court’s *Daubert* inquiry into plaintiffs’ experts’ causation opinions cannot be overstated. As plaintiffs acknowledged in their October 27, 2017 *Daubert* brief, epidemiology is “at the heart of the general causation question” and “unquestionably, epidemiological studies provide the best proof of the general association of a particular substance with particular effects.” Resp. in Opp’n to Monsanto Co.’s *Daubert* & Summ. J. Mot. Based on Failure of Gen. Causation Proof at 19, 20, ECF No. 647 (“Opp. Br.”). While the Court will also be presented with expert testimony regarding rodent carcinogenicity studies and mechanistic studies relating to genotoxicity and oxidative stress, plaintiffs’ experts themselves acknowledge that these types of studies cannot satisfy plaintiffs’ *Daubert* burden of showing through reliable scientific evidence that GBHs can cause NHL in humans. See Monsanto Co.’s Reply Mem. of P. & A. in Supp. of its *Daubert* and Summ. J. Mot. Based on Failure of Gen. Causation Proof at 25 & n.42, 32 & n.54, ECF No. 681 (“Reply Br.”). Where, as here, human epidemiology exists, plaintiffs’ experts must explain how such evidence supports a general causation opinion. See, e.g., *In re Silicone Gel Breast Implants Prod. Liab. Litig.*, 318 F. Supp. 2d 879, 891 (C.D. Cal. 2004) (“Animal studies are not generally admissible where contrary epidemiological evidence in humans exists.”)

Plaintiffs thus devoted the bulk of their *Daubert* Opposition Brief to the argument that the epidemiological data “strongly supports a causal association between [glyphosate based herbicides] and [non-Hodgkin Lymphoma].” Opp. Br. at 22. Even before the publication of the 2017 AHS study, this plaintiff argument failed in the face of their own experts’ opinions that the epidemiological data was “limited” and “not sufficient to show a causal relationship between glyphosate and non-Hodgkin’s lymphoma.” Reply Br. at 7-8 & nn. 9-10. Plaintiffs’ experts contended though that, while they could not exclude the possibility of chance, bias, or confounding in the epidemiologic data, the fact that each of the epidemiological studies (including an earlier 2005 study of the AHS cohort) reported non-statistically significant associations above the null value of 1.0 was enough to get their causation claim before a jury.

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That argument was without merit as a matter of *Daubert* law,<sup>1</sup> and it rested also on the false premise that plaintiffs' experts could selectively ignore unpublished epidemiologic data that had reported negative (< 1.0) associations. But the argument is, in any event, no longer available.

The 2017 AHS study is by far the largest epidemiological study of the potential association between GBHs and NHL. The cohort study was conducted and authored by independent scientists from the National Cancer Institute and National Institutes of Health, with no involvement or funding from Monsanto. With 575 NHL cases, it is more than six times larger than the 2005 AHS study, which plaintiffs' expert Dr. Neugut conceded already was the most powerful study that existed for GBHs and NHL. Dep. of Alfred Neugut 152:22-153:17 (Aug. 7, 2017). It likewise dwarfs the case-control studies upon which plaintiffs' experts seek to rely,<sup>2</sup> notwithstanding those studies' null findings as well in their most recent and comprehensive analyses. Reply Br. at 9-10. The 2017 AHS study conducted a series of epidemiological analyses seeking to identify any hint of an association between GBHs and NHL, examining associations: (1) with increasing exposures to glyphosate measured both by duration and by intensity, (2) using different lag times of exposure to account for the possibility of a cancer latency period before an association might emerge, and (3) for separate subtypes of NHL. The results were uniformly negative, with the vast majority of reported relative risks well below 1.0. Overall, the 2017 AHS study reported that pesticide applicators exposed to GBHs had a roughly 15% *lower risk* of NHL than cohort members without GBH exposure. This finding is not statistically significant and certainly should not be read as suggesting that glyphosate is protective against NHL. But it is devastatingly fatal to any hypothesis that exposure to GBHs increases the risk of NHL. The 2017 AHS study's primary analysis of NHL risk with increasing duration x intensity exposure to GBH is reproduced below (with ascending exposure levels from Q1 to Q4).

Cancer Site - NHL	GBH Use	No. with NHL	RR (95% CI)
	None	135	1.0 (reference)
	Q1	113	0.83 (0.59 to 1.18)
	Q2	104	0.83 (0.61 to 1.12)
	Q3	112	0.88 (0.65 to 1.19)
	Q4	111	0.87 (0.64 to 1.2)

2017 AHS study at 5. Plaintiffs' experts cannot proffer a general causation opinion that does not address this powerfully negative epidemiological evidence. *See In re Zolofit (Sertraline Hydrochloride) Prod. Liab. Litig.*, No. 12-md-2342, 2015 WL 7776911, at \*9 (E.D. Pa. Dec. 2,

<sup>1</sup> *See, e.g., Nelson v. Tenn. Gas Pipeline Co.*, 243 F.3d 244, 253 (6th Cir. 2001) (“[b]efore any inferences are drawn about causation, the possibility of other reasons for the association must be examined, including chance, biases ... , and confounding causes”)

<sup>2</sup> The most powerful of the published case control studies (McDuffie 2001) includes data for only 51 GBH-exposed NHL cases. Moreover, as plaintiffs' experts concede, case-control studies generally are viewed as less reliable than cohort studies because they are more susceptible to recall and selection biases. Reply Br. at 17.

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2015) (excluding testimony of expert who failed to account for more recent epidemiologic findings contrary to his causation opinion).

At the November 9, 2017 CMC, plaintiffs' counsel suggested that their experts had addressed the 2017 AHS study through their consideration of an earlier 2013 unpublished analysis of the AHS cohort. That suggestion is incorrect on numerous grounds. First, only one of plaintiffs' six causation experts, Dr. Ritz, offered any analysis of the 2013 study, with plaintiffs' other epidemiologist, Dr. Neugut, refusing even to read the study because it was unpublished. Indeed, in their *Daubert* opposition brief at pages 34-38, plaintiffs focused their attack on the 2013 study on the fact that it had not been published, a criticism that is completely mooted by the peer-reviewed publication of the 2017 AHS study in the *Journal of the National Cancer Institute*, one of the most prestigious and impactful journals on cancer in the world. Plaintiffs likewise relied on the unpublished status of the 2013 study in seeking to continue to rely on prior meta-analyses of the glyphosate epidemiology that did not include this new data, thus ignoring the fact that inclusion of the new evidence reduced the meta-analysis relative risk to a completely null 1.0.<sup>3</sup>

Plaintiffs' argument also ignores the numerous substantive differences between the 2013 and 2017 studies. While the 2013 analysis likewise was powerfully negative, it was based on an earlier review of the cohort's health status, at which time there were only about half of the number of NHL cases included in the 2017 study. Further, because the 2013 analysis was part of a draft paper that was looking at potential NHL associations for some 15-20 other pesticides as well, it did not include the many detailed analyses of GBHs and NHL included in the 2017 AHS study. Finally, the 2017 AHS study included a number of "sensitivity analyses" that specifically addressed and refuted hypothesized methodological concerns that had been proffered by Dr. Ritz in an attempt to explain away the 2013 findings. Simply put, plaintiffs' experts have offered no testimony or expert methodology that could account for the 2017 AHS study results.

## **II. Steps Necessary to Ensure that the Court Can Meet its Gatekeeping Responsibility in Light of the 2017 AHS Study**

As the discussion above makes clear, the 2017 AHS study is not just one additional piece of scientific evidence; it is the most powerful scientific evidence that now exists regarding GBH exposure and NHL, and it is directly contrary to plaintiffs' experts' general causation opinions. Accordingly, it is vital that the Court has the fullest opportunity to explore plaintiffs' experts' causation opinions in light of the 2017 AHS study at the *Daubert* hearing and that Monsanto has discovery of those opinions in advance of the *Daubert* hearing to adequately cross-examine plaintiffs' experts on whatever methodology they put forth to try to explain away the study's findings. *See Glastetter v. Novartis Pharm. Corp.*, 107 F. Supp. 2d 1015, 1024-25 & n.5 (E.D. Mo. 2000) (finding that "[c]ross-examination of plaintiffs' expert witnesses in this case [at *Daubert* hearing] is particularly instructive" and "demonstrate[d] the unreliability" of the experts' conclusions), *aff'd*, 252 F.3d 986 (8th Cir. 2001).

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<sup>3</sup> Reply Br. at 10. This meta-relative risk would be even lower if it incorporated instead the 2017 AHS study, which would have even greater weight than the 2013 study in a meta-analysis and reports an updated AHS relative risk that is even lower than that reported in the 2013 study.

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Each of the plaintiffs' six retained expert witnesses purports to opine about the glyphosate epidemiology so as to be able to reach an overall opinion on general causation. While Monsanto believes that three of those experts are not qualified to opine regarding epidemiology and has moved to exclude such opinions on those grounds, *see* Monsanto Co.'s Notice of Mot. & *Daubert* & Summ. J. Mot. Based on Failure of Gen. Causation Proof at 11 n.16, ECF No. 545, each of the six experts' general causation opinions cannot now properly be evaluated and tested through cross-examination without further discovery on how those experts account for the 2017 AHS study findings. *See Mitchell v. Ford Motor Co.*, 318 F. App'x. 821, 825 (11th Cir. 2009) (striking expert testimony where expert failed to supplement his report with new scientific bases for his opinion prior to *Daubert* hearing, preventing opposing party from fully deposing expert).

The Court's resolution of Monsanto's *Daubert* challenge of plaintiffs' experts' general causation opinions is centrally important to hundreds of cases pending in the MDL and likely will shape the course as well of thousands of additional cases pending in state courts in California, Delaware, and Missouri. The Court previously recognized the importance of securing a full scientific record for this challenge, granting plaintiffs' request to continue a previously-scheduled *Daubert* hearing to allow for discovery and supplemental expert reports regarding a single kidney tissue from one of 200 test mice in one of the 14 animal carcinogenicity studies here at issue. The 2017 AHS study is of dramatically greater significance to the general causation question, and it is directly relevant to the opinions proffered by every one of plaintiffs' experts. Monsanto is unaware of any other ongoing study of GBHs and NHL that would have any similar impact on the state of the science in the near future.

While Monsanto appreciates the Court's desire to hold with the current schedule and is eager as well to hold plaintiffs to their *Daubert* burden at the evidentiary hearing, Monsanto and the Court will be severely prejudiced if any of plaintiffs' experts are allowed to offer general causation opinions without prior disclosure and discovery regarding the 2017 AHS Study. Because plaintiffs have proffered all of their experts as opining on the epidemiological evidence and general causation, each of those six experts will need to supplement their expert reports and be made available for supplemental depositions (limited to the impact of the 2017 AHS study). Monsanto believes such discovery could be conducted in relatively short order, with only minimal delay in the current schedule as follows:

- December 1, 2017: Deadline for plaintiffs' experts' supplemental reports addressing 2017 AHS study
- December 15, 2017: Deadline for Monsanto's experts' supplemental reports addressing 2017 AHS study
- January 12, 2018: Deadline for supplemental depositions of plaintiffs' experts (3 hour limit per deposition)
- January 26, 2018: Deadline for supplemental depositions of Monsanto's experts (3 hour limit per deposition)
- February 5, 2018: Monsanto's supplemental *Daubert* brief (15 page limit)

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- February 15, 2018: Plaintiffs' supplemental *Daubert* opposition brief (15 page limit)
- February 22, 2018: Monsanto's supplemental *Daubert* reply brief (10 page limit)
- March \_\_-\_\_ 2018: *Daubert* evidentiary hearing

Because plaintiffs are proffering expert epidemiology and general causation opinions from each of their six expert witnesses, Monsanto does not believe that the alternative proposed by the Court of limiting supplemental disclosures and deposition to only two plaintiff experts is feasible. Monsanto notes, however, that plaintiffs have only designated two experts with primary expertise in epidemiology (Dr. Neugut and Dr. Ritz). If plaintiffs agree to limit their other four expert witnesses solely to subsidiary scientific opinions regarding animal toxicology and mechanistic data, Monsanto believes that the Court's proposal might be possible on the following schedule, with further briefing deferred until after the *Daubert* hearing:

- November 17, 2017: Deadline for supplemental reports addressing 2017 AHS study by two of plaintiffs' experts
- November 22, 2017: Deadline for supplemental reports addressing 2017 AHS study by two of Monsanto's experts
- December 1, 2017: Deadline for supplemental depositions of plaintiffs' two experts (3 hour limit per deposition)
- December 8, 2017: Deadline for supplemental depositions of Monsanto's two experts (3 hour limit per deposition)

Monsanto is available for oral argument on December 20, 2017 if the *Daubert* hearing remains scheduled for the prior week.

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Respectfully submitted,

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