

Monsanto[PRIVATE]

FROM (NAME, LOCATION, PHONE): John F. Acquavella, PhD (C2SE) (4-8813)

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SUBJECT: ISEE meeting - epidemiology studies re glyphosate

TO: D. Farmer
J. Cowell
W. Heydens
T. Carrato
D. Goldstein
L. Fisher (Lori, please pass along to Janice Armstrong)
T. Hoogheem
S. Wratten
J. Hjelle

FYI, herein I report on two related papers from the International Society for Environmental Epidemiology (ISEE) meeting this week in Buffalo, New York. Both papers have results for glyphosate (one for non-Hodgkin's lymphoma (NHL) and one for Hodgkin's disease (HD)) that are of interest to us and our scientific outreach activities.

1. "Non-Hodgkin's lymphoma and the pesticide hypothesis: dose response" by Helen McDuffee, Pahwa Punam and colleagues at the Center for Agricultural Medicine at the University of Saskatchewan

We discussed this abstract at our ag epidemiology strategy meeting earlier this year. I learned a bit more about this paper from the author's presentation and from discussions with the author, but I don't yet have enough information to critique this study.

This is a case control study of 517 NHL cases and 1,506 controls funded by Health Canada - the latest in a long line of agricultural epidemiologic studies funded by Health Canada. Epidemiologists from Health Canada have previously published papers where they concluded that pesticides (in the generic sense) are related to various cancers. This latest study addresses individual pesticides in relation to NHL, Hodgkin's disease, and soft tissue sarcoma. [Of historical note, these same cancers were the subject of NCI's Kansas/2,4-D study and, indeed, at least one of Health Canada's epidemiologists have been on the Ag Health Study Advisory Panel since the inception of the Ag Health Study.]

Dr. McDuffee and colleagues identified NHL cases from the various Canadian provincial cancer centers and controls were selected from the general population in proportion to the provincial distribution of the cases. Study subjects were interviewed by mail and phone to ascertain lifetime occupational history and pesticide use. Reported use of a number of pesticides was significantly related to increased

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risk of NHL including mecoprop, malathion, DDT, carbaryl, aldrin, and lindane. When the authors controlled for personal factors including antecedent cancer, family history of cancer, personal history of measles, and allergy desensitization treatments, the only pesticide that was significantly related to NHL was mecoprop (a.k.a. MCPP 2-(4-chloro-2-methylphenoxy) propanoic acid).

Additional analyses found significant relationships for more than 2 days use/year for glyphosate (odds ratio 2.1, 95% CI 1.2-3.7) and mecoprop (odds ratio 2.1, 95% CI 1.2-3.6). The full range of confounding factors was not considered in these analyses, but one presumes that again only mecoprop would remain associated with NHL in a multivariate analysis.

Since the organizers of the ISEE meeting asked me to chair the pesticide session which included this paper, I had the opportunity to spend some time with the author. She struck me as a reasonable person. I was expecting a Canadian of Scottish descent, but Dr. McDuffee is of African descent. She doesn't seem to have any preconceived notions about glyphosate. She agreed to share her paper with me when it is ready for submission for publication. She also agreed to come and present her work to an industry audience (ACPA, us, etc.). I gave her a copy of the Cantox glyphosate review and told her of our ongoing Farm Family Exposure Study (FFES). She was extremely interested in the FFES and asked to be kept informed of the results from this program. We obviously need to establish a relationship with Dr. McDuffee because her research program will be generating findings for the next few years. The FFES would seem to provide a basis for an equitable sharing of information with her.

It remains to be seen how glyphosate is treated in the eventual publication from this study and whether anyone picks up selectively on the (presumably) confounded glyphosate finding that was included in the meeting abstract. Obviously, we need to be as prepared as we can, given limited information. I mention some specific follow-up plans below.

2. "Non-Hodgkin's lymphoma, Hodgkin's disease and pesticide exposure: regional differences" by Pahwa Punam, Helen McDuffee and colleagues at the Center for Agricultural Medicine at the University of Saskatchewan

This study, presented as a poster at the meeting, has the same NHL cases and controls as the previous study and HD cases and controls from across Canada. The point of the analysis was to look for regional differences in the relationships between pesticides and NHL/HD. Most pesticides showed variable findings by province. Of interest to us, the authors reported a significant glyphosate/HD result in British Columbia, but not elsewhere in Canada (see table). [note - As is typical with epidemiologists, only the British Columbia finding was included in the meeting abstract.]

| Province | odds ratio | conf. Interval |
|------------------|------------|----------------|
| Ontario | 0.5 | 0.2-1.9 |
| Quebec | 1.0 | 0.2-5.0 |
| Prairies | 1.6 | 0.9-2.6 |
| British Columbia | 4.0 | 1.4-11.3 |

I spoke with the author and asked her:

- why is there so much variability across provinces for the various pesticides? Wouldn't one expect consistent results if a specific pesticide was carcinogenic?

She didn't have a ready answer. She speculated that the variation might be explained by heavier use or the tendency to use higher exposure application equipment in specific provinces. I pointed out that agricultural glyphosate application would probably not vary that much across the provinces and that the same might be said for most other pesticides. [note - This is one of the problems in agricultural epidemiology: epidemiologists try to explain obviously disparate findings so as to make a causal relationship (rather than systematic error) seem the most plausible explanation.]

The author does not plan to publish this version of her analysis. She plans to go back and do multivariable analyses to see whether the findings for specific pesticides are confounded by findings for other pesticides or the personal factors that Dr. McDuffee considered (e.g. antecedent cancer, allergy desensitization, etc.). She agreed to send me a copy of her poster and to share a manuscript when it is available. I gave her a copy of the Cantox glyphosate review.

This paper is at a much earlier stage than the previous paper. I'm not sure what the results will be once the author has time to do all the analyses she is considering. So, at present, it's probably best to keep in touch with the author, through her senior colleague Dr. McDuffee. In the interim, if we get any inquiries, we can point out that the variation in the findings is inconsistent with a causal relationship with glyphosate.

Follow-up plans

I think our best approach is to develop a collegial relationship with Dr. McDuffee. We can share our findings from the FFES, when available, and ask her to share her findings, when available. Also, I suggest we include Dr. McDuffee in our plans to develop a scientific outreach network in Canada. We've been planning to have a scientific outreach meeting in Canada, so this study provides a good reason to expedite our plans for Canada. This could be important strategically in light of Health Canada's continued investment in agricultural epidemiology and the ongoing networking between Health Canada and the NCI. Dr. McDuffee

would benefit by learning about glyphosate toxicology and exposure assessment.

Donna and I will make plans immediately to arrange a scientific outreach meeting in Canada. I expect that such a meeting could be arranged in October or November. We plan to include several prominent epidemiologists from Canada, along with Len Ritter and Keith Solomon from the University of Guelph. Len is a toxicologist and Keith is an exposure assessor; both know glyphosate well. In addition to our usual scientific outreach agenda, we would ask Dr. McDuffee to present her NHL and HD findings. This would allow her to consider her findings in light of the available glyphosate toxicology/exposure information and to get feedback from the Canadian experts.

Please let me know if you have comments, questions, or other follow-up suggestions.