

Message

From: FARMER, DONNA R [Redacted]
Sent: 12/1/2010 6:53:51 PM
To: Amy Williams [Redacted]
Subject: second half and additional articles
Attachments: Glyphosate Dev Repro Review rest.docx; mladinic_2009.pdf; prasad_2009.pdf; cavalcante_2008.pdf; conners_2004.pdf; holeckova_2006.pdf; piesova_2005.pdf; bolognesi_2009.pdf; pazymino_2007.pdf

Amy,

See attached.

Donna

From: Amy Williams [Redacted]
Sent: Wednesday, December 01, 2010 10:38 AM
To: FARMER, DONNA R [Redacted]
Cc: John DeSesso; SALTMIRAS, DAVID A [Redacted]
Subject: RE: First half - second reply

Donna and David,

We've received the disk with the Knapp studies and will work on verifying/revising the related text in the manuscript. Can you let us know when to expect comments back on the second half of the paper? Thanks so much.

Best regards,

Amy Lavin Williams, PhD, DABT

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[Redacted]

Redacted

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From: FARMER, DONNA R [AG/1000] **Redacted**

Sent: Tuesday, November 23, 2010 4:35 PM

To: Amy Williams

Cc: John DeSesso; SALTMIRAS, DAVID A **Redacted**

Subject: RE: First half - second reply

Amy,

See responses below.

Have a few other things to send will do tomorrow.

Need to go get my daughter from a retreat.

Donna

From: Amy Williams **Redacted**

Sent: Tuesday, November 23, 2010 9:51 AM

To: FARMER, DONNA R **Redacted**

Cc: John DeSesso; SALTMIRAS, DAVID A **Redacted**

Subject: RE: First half - second reply

Donna,

When can we expect comments on the rest of the document? I'm trying to get the document finalized and out the door as quickly as possible. Along those lines, I have a few more questions to ask:

- In the abstract, we listed 2 mg/kg/d as the RfD based on what was proposed in the glyphosate RED. In the revisions, someone changed that to 1.75 mg/kg/d. I realize this is based on a dose of 175 mg/kg/d in a developmental study with an uncertainty of 100, but the RED did not propose an RfD of 1.75 mg/kg/d; it listed the RfD as 2 mg/kg/d. In the IRIS database, the RfD is listed as 0.1 mg/kg/d. What value do you believe we should use? I need to be able to back the number up with a citation as well.

See attachment

For many years the only dataset that was available for glyphosate was Monsanto'stoday there are a number of other full data sets.

The original Monsanto set of studies that supported glyphosate used high doses of ~ 30 mg/kg/day. These studies were reviewed by the WHO in 1986
<http://www.inchem.org/documents/jmpr/jmpmono/v86pr08.htm>

They concluded that there were no effects related to treatment and set the ADI at 0.3 mg/kg/day. In the US, IRIS reviewed the same studies and came to a different conclusion on the 3 gen rat repro study and concluded the effects at the high-dose were related to treatment and in 1990 they set the ADI at 0.10 mg/kg/day based on that study. <http://www.epa.gov/iris/subst/0057.htm> The effects observed in that first study were not reproduced in the second repro study by Monsanto nor in any other repro study by any other manufacturing at much higher doses.

Glyphosate was re-registered in 1993. Monsanto conducted several new studies for that re-registration to meet the guidelines in place at that time and the two key studies were the 2-gen rat repro and the rat chronic study with high doses of 20,000 ppm.

The EPA selected the **lowest NOEL** in the glyphosate toxicology data base to set the ADI which was based on the maternal effects observed in the rabbit teratology study. In the 1993 RED the RfD was 2 mg/kg/day ...this was "rounded up" from 1.75. Lately we have been seeing them use the non-rounded post- FQPA cPAD of "1.75 mg/kg/day" value - <http://www.federalregister.gov/articles/2004/11/10/04-25098/glyphosate-pesticide-tolerance>

The IRIS database and website for glyphosate is completely out of date, in the Revision History section the last entry for tox information was 1990 – they did not revise after the RED!. Note that the cancer classification is a “D”...in 1991 it was concluded to be an “E” – Evidence of non-carcinogenicity in humans. We have repeatedly asked them to update and revise because the discrepancies have been problematic for us – note that the last entry in the revision history it is no longer being assessed by IRIS. The MCL for glyphosate of 700 ppm is based on the IRIS database <http://www.epa.gov/safewater/pdfs/factsheets/soc/glyphosa.pdf> From their “What are the health effects?” they state: “Short-term: EPA has found glyphosate to potentially cause the following health effects when people are exposed to it at levels above the MCL for relatively short periods of time: congestion of the lungs; increased breathing rate.” [We have no idea how they came to this conclusion since the inhalation study for glyphosate was waived.]

Long-term: Glyphosate has the potential to cause the following effects from a lifetime exposure at levels above the MCL: kidney damage, reproductive effects.” The subsequent studies do no support this conclusion at all. We also asked that the MCL be revised based on the new data and they also said no...why because they saw no need as glyphosate is never found in finish drinking water therefore they saw no concern to put resources to the review.

In Canada and Japan...which is based on Monsanto data only the RfD is 0.75 mg/kg/day...same rabbit teratology study different conclusion on high-dose effects.

EU - 0.3 mg/kg/day – based on our first chronic study even though there were multiple submitters

WHO 2004 - 1.0 mg/kg/day multiple submitters based on another companies chronic rat study.

If you use the RED as your reference – the correct value for the RfD is 2 mg/kg/day (as edited is not correct because the RED does not use 1.75 mg/kg/day....understand your confusion)

If you use the post-FQPA cPAD then I would use 1.75 mg/kg/day.

Do not use the IRIS value it is of no value today.

- More discussion was added to the introduction on dermal absorption, including data from Nielsen, 2009. The paper you sent to me earlier this week was Nielson, 2010. I cannot find the data that was added to the introduction in the 2010 paper and I cannot find a Nielsen, 2009 paper. Are the numbers wrong or is there another reference? If the numbers are right and based on the 2010 paper, can someone lead me through the calculations?

David...you added this section , please respond.

- For the study of Reyna, 1990, some doses in mg/kg/d were added to the document corresponding with the ppm amounts administered in the diet. I am not clear on from where those doses are derived. Can someone show me where these values came from?

They were what was published in the William's et al. paper page 127. Below is a table lifted from a Monsanto Summary of that study. I am okay with going with approximate mg/kg/day.

Generation/Sex	Dietary concentration of glyphosate (ppm)		
	2,000	10,000	30,000
F0 Parents: Males	132	666	1,983
Females	160	777	2,322
F1 Parents: Males	140	711	2,230
Females	163	804	2,536

- Can you forward the studies from Knapp (2007, 2008)? We do not have those in-house to verify the data. Plus, we will need to make some revisions since, as noted in the comments, at least some of the text was lifted directly from the report summaries.

David ...where are you on getting these studies to them?

- In the section on genotoxicity, one of the reviewers mentioned a study by Kier and Stegman (1993) in which AMPA was tested. I do not have this study and cannot find it in Pubmed. Can you forward it so it can be added to the paper?

David ..can you send them a copy of this report as well with the others?. The WHO 1997 review of AMPA <http://www.inchem.org/documents/jmpr/jmpmono/v097pr04.htm> and in 2004 ...the the WHO in the glyphosate review...reviewed a few new studies and came to the same conclusion on AMPA

- An additional 7 papers on genotoxicity were recommended to be added to the report. These include Mladinic et al (2009), Prasad et al (2009), Cavalcante et al (2008), Conner and Black (2004), Holeckova (2006), Piesova et al (2005), and Bolognesi et al (2009). Would you like these added, and if so, can you forward these papers for review? Alternatively, we can order them in-house. Let me know.

Will forward in another email.

- A bit of text was added to the report for a study by Benachour et al (2007). After some review, I realized that the year given is incorrect. It should be Benachour et al (2009). Earlier this week, you forwarded the 2007 paper. Can you forward the 2009 paper for our review? The text that was added is very limited and needs to be revised. I will also be moving discussion of this study to a more appropriate section of the document.

See attached – the text was only a place holder please revise upon your review.

- The single name 'Pagenelli' was added to the report. I did a search to find that this is reference to a study, Paganelli et al 2010. I assume you would like discussion of this study added to the paper. Can you provide the paper for review?

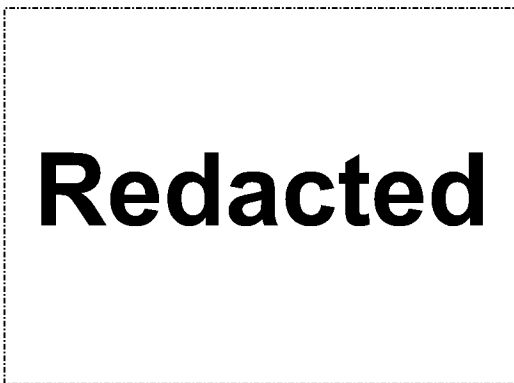
See attached.

Thanks for your assistance.

Best regards,

Amy Lavin Williams, PhD, DABT

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From: FARMER, DONNA R; Redacted
Sent: Friday, November 19, 2010 10:41 AM
To: Amy Williams
Subject: RE: First half - second reply

Amy,

Attached are the external publications listed below – the Romano paper was one that was reviewed by Bill Kelce...so you should already have a copy and an extensive review of that publication.

I thought David had sent you copies of the Knapp and Moxon study reports. I will check with him on those and the Ward studies.

Donna

From: Amy Williams [Redacted]
Sent: Friday, November 19, 2010 8:53 AM
To: FARMER, DONNA R [Redacted] John DeSesso
Subject: RE: First half - second reply

Donna,

You have added significant text to the document with regard to the following references:

- Bo Nielsen et al., 2009
- Ward, 2010
- Moxon, 2000
- Knapp, 2007
- Knapp, 2008
- Benachour et al., 2007
- Romano, 2010

- Gasiner et al., 2009

Unless someone from Monsanto plans to be listed as an author, we need to see these references in order to verify that we are in agreement with the newly added text. As such, could you forward these papers to us? Thanks so much.

Best regards,

Amy Lavin Williams, PhD, DABT

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From: FARMER, DONNA R; Redacted
Sent: Friday, November 19, 2010 8:20 AM
To: John DeSesso
Cc: Amy Williams
Subject: RE: First half - second reply

John,

Can you provide me the specific references? Is it the surfactant studies or the additional references for the gasiner paper.

Thanks,

Donna

From: John DeSesso; [Redacted]
Sent: Thursday, November 18, 2010 3:01 PM
To: FARMER, DONNA R; [Redacted]
Cc: Amy Williams
Subject: RE: First half - second reply

Hi Donna,

Since there will not e authors from Monsanto on the manuscript, can we get copies of the papers that are summarized in the new text? We need to independently verify that our conclusions coincide.

Thanks,

John

From: FARMER, DONNA R; [Redacted]
Sent: Thursday, November 18, 2010 2:50 PM
To: John DeSesso
Subject: First half

John,

Attached is the first 46 pages.

I added a section in genotox from the Gasnier study...see a attached a critique we did that I took that from. Am working on a section for gasiner in the

mechanistic section. Also we cut and pasted in summaries of the POEA surfactant studies. Attached are more detailed summaries – see Knapp. For right now I think we should go with POEA surfactants. I am checking to find out if there are any concerns with using MON 0818 and MON 8109 as well as indicating they are tallow and coco-derived – will get back to you on that as well as sending the remaining pages. Hope to have them done this afternoon if not will send tomorrow.

<<Glyphosate Dev Repro Review Part I.docx>> <<Publication 4 Gasnier 2009.docx>>
<<Knapp studies.docx>>

Regards,

Donna

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