Message

From: [redacted]
Sent: 4/19/1999 8:49:08 AM
To: LARRY D KIER; WILLIAM F HEYDENS; [redacted] DONNA R FARMER
CC: STEPHEN J WRATTEN; [redacted]
Subject: Re: Meeting Minutes 2/25

Donna,

Thanks for this, it accurately reflects the situation.

Please take note of the following update:

I received from prof. Parry the signed secrecy agreement.

As a response I sent him a letter of authorisation and all relevant reports and publications re mutagenicity of glyphosate, its formulations and the surfactants for which we have mutagenicity testing data.
The list was based on the foulder that was composed for Gabriele and the German monograph on Glyphosate:

Glyphosate formulations
Roundup:
- Ames test, Monsanto report ML-91-440
- Mouse micronucleus test, Monsanto report ML-91-434/437
- Comet test on Rana tadpoles, Clements et al., Environmental and Molecular Mutagenesis, 29, 277(1997)
- Drosophila SLRL, Kale et al., Environmental and Molecular Mutagenesis, 25, 148(1995)
- SCE, Vigfusson and Vyse, Mutation Research, 79, 53(1980)

Direct:
- Ames test, Monsanto report ML-91-442
- Mouse micronucleus test, Monsanto report ML-91-436/439

Rodeo:
- Ames test, Monsanto report ML-91-441
- Mouse micronucleus test, Monsanto report ML-91-435/438

Glifos:
- Ames test, BioAgri report G1.1-050/96
- Mouse micronucleus test, BioAgri report G1.2-060/96

Active ingredient (glyphosate):
- Ames test, rec-assay, HGPRT test, UDS test, in-vivo cytogenetics, Li and Long, Fundamental and Applied Toxicology, 10, 537(1988)
- In vitro cytogenetics in human lymphocytes, NOTOX report 141918
- Ames test, Jensen, Scantox report 12323 (1991)
- Mouse lymphoma test, Jensen, Scantox report 12325 (1991)
- Mouse micronucleus test, Jensen, Scantox report 12324 (1991)
- Mouse dominant lethal test, Monsanto report IR-79-014

Surfactants:
Polyethoxylated tallowamine (MON 0818):
- Ames test, Monsanto report ML-89-461
- Mouse micronucleus test, Monsanto report ML-89-463

C8-C10 alkyl sulphate IPA salt (MON 8080):
- Ames test, Monsanto report ML-80-294

Dodigen 4022:
- Ames test, Hoechst report 92.0336
- In-vitro cytogenetics, Hoechst report 92.0337

Tween 20:
- Mouse lymphoma test, Abstract P46, Environmental and Molecular Mutagenesis, 3(3), 320(1981)

Tween 80:
- Mouse micronucleus test, Jenssen and Ramel, Mutation Research, 75,191(1980)

Via separate mail I sent him the composition of all the formulations tested and data on the chemistry of the surfactants (not too detailed).

So, in principle he will start his review this week.

Once the review is ready it will be a good idea to have Larry visit Jim Parry for an overall discussion.

Regards, [redacted]

_____ Reply Separator _____

Subject: Meeting Minutes 2/25
Author: DONNA R FARMER [redacted]5
Date: 4/17/99 7:25 AM

Please find the meeting minutes and actions from our 2/25 meeting below.

We need to discuss where we are on each of these topics as well as well as finalize a letter of comment to the German Addendum. Steve has provided some valuable comments in a recent message, I will draft a letter and provide for discussion.

Bill - what is the drop dead date you need these comments?

Cam where are we in getting this meeting set up?

Donna

1) Update on the German Addendum

Steve Wratten joined us for this discussion. We understand that the Germans current position on the effects observed in the various studies with the formulatons as described in the open literature do not indicate a mutagenic response but rather a cytotoxic response associated with the surfactant(s). Glyphosate, it's salts, the G3 and G4 formulations (with the Dodigen surfactant) and Rodeo are free and clear.

For those formulations/surfactants that can be tested up to the limit levels per OECD guidelines and produce no toxicity such as the Dodigen (the major surfactant in MON 52276) they would be viewed favorably.

Roundup (with MON 0818), Roundup Ultra, the etheramine-based formulations and other formulations either do not meet this standard or the possiblity that they will is low.

It will be up to each country to decide which formulations it does and doesn't want and they could use this for that purpose.

It was felt that this position should not be a regulatory endpoint, it is not defensible and that once the German Addendum is made public comments and a response should be prepared for the ECCO Meetings preferably before 17th May (Mammalian Tox Meeting). Note that the Conclusion meetings are not until the 18th October - Donna will coordinate this response when a copy of the German Addendum is received.

2) Testing program - what do we test? formulations..surfactants? When is data needed? Discussion is dependant upon info from agenda item # 1

No further mutagenicity testing is needed for MON 52276.

Steps have been taken to acquire the cocoamine surfactant used in MON 35012/Roundup 2000 sold in Denmark for testing in the microames and micromicronucleus assays. In addition based on the concern for cytotoxicity it was recommended to also to run this surfactant thru the NRU assay (this assay addresses cytotoxicity and has a good correlation with the oral LD50). - Donna will coordinate and monitor these tests

Management supports the investigation of MON 35050 toxicity to the liver and kidneys to address the findings in the Peluso study. Therfore it was recommended to move forward with a study... evaluating liver and kidney histology, serum enzymes as well as glutathionine levels following high-dose, i.p. exposures of the test material. - [redacted] will draft and circulate a protocol

Donna will followup with [redacted] to get the details/and clarification behind his statement below (in green) as to what is expected, on what materials and by when. "We will need to demonstrate clearly negative Mutagenic (and cytogenic?) results for all the formulations we sell in Europe. These will certainly be required by end 2000 but public pressure may require us to do them earlier."

3) "Detergent-like molecule" testing program? Is this still something we need to do? When do we start? Discussion is dependent info from agenda item #1

In light of the position taken by the German government this investigation maybe even more important than before and could possibly be conducted by
Dr. Parry?
Dr. Williams?
Donna will arrange for further meetings to discuss/design this program

4) Global experts

Review Dr. Parry's analyis - what is our next step? Dr. Parry concluded on his evaluation of the four articles that glyphosate is capable of producing genotoxicity both in vivo and in vitro by a mechanism based upon the production of oxidative damage.

The data that Dr. Parry evaluated is limited and is not consistant with other better conducted studies. In order to move Dr. Parry from his position we will need to provide him with the additional information as well as asking him to critically evalute the quality of all the data including the open literature studies.

As a followup [redacted] will contact Dr. Parry, discuss with him the existance of additional data and ask him to evaluate the full package. [redacted] will also explore his interest (if we can turn his opinion around) in being a spokesperson for us for these type of issues.

Larry as well as others will be available to discuss the data with Parry as needed by e-mail, phone or in person or all the above.

Dr. Williams - discuss the outcome of the Cantox meeting

The panel concluded that glyphosate and Roundup were not mutagenic. That in the evaluation of these types of studies criteria should be set... up front in the evaluation process as to what makes an acceptable study and what does not - this is to be included in the manuscript as well as a weight of evidence approach.

5) Lioi followup

An analysis of what was tested in the Lioi studies was deemed important. Therefore it was recommended that Monsanto EU or Italy contact Lioi and try to get a sample of what they used in their study

as well as getting a sample from the company that Lioi did. Donna will contact [redacted] to ask him to make the requests.