Message

From: FARMER, DONNA R [FND/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=180070]
Sent: 2/13/2001 7:09:03 PM
To: MARTENS, MARK A [AG/5045] [/O=MONSANTO/OU=EA-5040-01/cn=Recipients/cn=21606]; 'Larry Kier' [redacted]HEYDENS, WILLIAM F [FND/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=230737]
CC: GARNETT, RICHARD P [AG/5040] [/O=MONSANTO/OU=EA-5040-01/cn=Recipients/cn=107838]
Subject: RE: Position on Parry's recommendations

Mark - I have looked at the re-worked mutagenicity responses. They look fine but I do think it is worthwhile to make the point - that in widely accepted studies for evaluating mutagenicity conducted under GLP conditions and according to international regulatory guidelines that glyphosate, it's formulations and surfactants used in those formulations are all negative.

These are robust studies and provide a greater degree of certainty in the results. The numerous other studies were not conducted according to standard guidelines and not under GLP - and that in itself created many of the items of confusion/concern pointed out in the responses. In addition emphasize that several of these studies do not directly evaluate mutagenicity, not widely accepted etc.

Conclusion - the weight of evidence is - no evidence of mutagenicity!

See specific comments on this message below:

-----Original Message-----
From: MARTENS, MARK A [AG/5045]
Sent: Monday, February 12, 2001 8:34 AM
To: 'Larry Kier'; FARMER, DONNA R [FND/1000]; HEYDENS, WILLIAM F [FND/1000]
Cc: GARNETT, RICHARD P [AG/5040]
Subject: Position on Parry's recommendations
Importance: High

Dear all,

Further to our conference call of last week find herewith Parry's recommendations with suggestions for rebuttal, if possible:

In vitro cytogenetics data on glyphosate formulations - agree
The in-vitro CA tests on MON 59117 and MON 58121 can be used. These are surfactants and no glyphosate formulations. We can argue that results from components of mixtures can be used to assess the genotoxicity of the mixtures. The database on glyphosate should be sufficient to dismiss its role in the possible genotoxicity of formulations containing it.

In vitro micronucleus assay with and without antioxidants - why not use the MON 35050 study here as well. I still see no need to do these assays.....but if testing surfactant solutions get discussed then - let's include talk about laundry detergents, hand soap, dishwashing detergents, shampoos as well and not limit it to those used only in AG. People have significantly more exposure surfactant solutins used in those products then they would AG products. I don't know for sure how suppliers would react - but if somebody came to me and said they wanted to test Roundup I know how I would react - with serious concern. We have to really think about doing formulations even if they are not on the market....glyphosate is still in there and could get caught up in some false positive finding .
We can first ague that glyphosate is not genotoxic and that it is highly unlikely that it causes oxidative stress (is not metabolised with consumption of GSH for example), we can then refer to the negative micronucleus tests on glyphosate formulations and the negative in vitro CA test on glyphosate (NOTOX study). As a fall back position we can agree with some testing on either surfactant solutions (would suppliers agree with this?) or with glyphosate formulations which don't exist anymore on the market (e.g. MON 35050).

Oxidative damage in vivo- agree
Can be sufficiently addressed by MON 35050 I.P. study

Micronucleus test with repeated dosing - agree
NTP study should be sufficient to show that such a test is not needed.

COMET assay in liver and kidney of mice - agree. And the example that Larry found with similar results with people following exercise indicates no need to do this.
The MON 35050 I.P. and its coherence with the alkaline elution data of Bolognesi et al. should be sufficient to demonstrate the possibility of oxidative damage produced by the formulation when administered via the I.P. route.

In vitro data on surfactants - same comment as above. We have a large number of mutagenicity studies on our alkyl amines and there is no evidence of mutagenicity. For this class of chemical I see no need for further testing. If he continues to push we may still need to consider that we need to end the relationship.
Presentation of all the genotox data that were produced on MON 58121, MON 59112 and MON 59117 could do but may not be found to be sufficient to cover all currently used surfactants. What other surfactants do we currently use in any great amount but alkyl amines and Dodigen?

The strategy we propose to follow is:
(1) Overview of glyphosate formulations and their chemistry (Richard) ok
(2) Presentation of the new Monsanto data (Mark)ok
(3) Discuss flaws of published data using revised rebuttals (Mark)ok
(4) Discuss recommendations made in Parry's report ok
(5) Discuss way forward on basis of data and clarifications provided. ok
No decisions will be made but possibilities for further collaboration will be explored (whenever) if needed.

Larry,
We plan to call you around 14.00 h UK time to discuss any genetox question. Which no should we dial?

We also have the finalized reports for the hepatotoxicity studies conducted on glyphosate and MON 52276 in preparation for the UDS (that thankfully have not been asked for yet). They show no evidence of liver toxicity - up to 2000 mg/kg oral dose. No biologically relevant clin chem changes or histopath.

Comments are welcome.

Regards, Mark