

EXHIBIT 93

Message

From: WRATTEN, STEPHEN J [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=119523]
Sent: 6/16/2003 10:44:29 PM
To: FARMER, DONNA R [AG/1000] [REDACTED]; [REDACTED]@syngenta.com'
[REDACTED]@syngenta.com]; [REDACTED]@syngenta.com' [REDACTED]@syngenta.com]; GRAHAM, WILLIAM
[AG/8050] [REDACTED]; [REDACTED]@cheminova.dk' [REDACTED]@cheminova.dk]; MARTENS, MARK A
[AG/5040] [REDACTED]
CC: [REDACTED]@cheminova.dk' [REDACTED]@cheminova.dk]
Subject: RE: JMPR Comments

Dear Colleagues

My comments on the sub acute and sub chronic overviews are mostly book-keeping matters as follows:

1. The bibliography does not contain the references for the 21-day dermal exposures, and I had understood that they were to be omitted. Assuming that is the case, the discussion of dermal effects should be deleted and they should not appear in the summary tables.
2. Similarly, the bibliography does not contain the Monsanto Stout (1983) 4-week dietary rat study, but instead contains the 1989 Reyna one month rat pilot (ML-88-272).
3. The Gorburdahun studies are dated 1989 (28-day) and 1990 (52 week) not 1998.
4. The Perry, Atkinson, Strutt, Henderson, and Hudson 13-week rat oral study is dated 1991 in the Bibliography but is dated 1989 in the summary documents. Same for the Perry, Atkinson, Strutt, Hudson, and Jones 13-week mouse oral study. Which is the correct final report date date for these two studies?
5. I have supplied Donna with the ID codes for each study, and I believe these should be entered into Table 1 and Table 2. in the reference column.
6. Finally, and most significantly, what is to be said about the 50 mg/kg/day NOEL in the Atkinson 4-week rat study? The follow on 13-week study by Perry achieved a NOEL of 300 m/k/d, so presumably the shorter study with the lower finding is considered an outlier. I am not familiar with the nephrocalcinosis, but it seems odd that it was not even mentioned in the follow-on study summary (Perry). Is this a reversible effect that could be present at 4 weeks and not at 13 weeks? I presume it was looked for in the later longer-duration study, having seen it earlier. Should the Perry 13-week rat study summary not address specifically that nephrocalcinosis, although present in the 4 week study, was clearly absent at 13-weeks. Should the Higher tier summary that goes across sub-acute and sub-chronic mention this finding and point out that it only shows up in one out of 5 studies, many of which involved higher dosing levels, so this effect is considered spurious and is dismissed from further consideration?

Overall, the ADI piece looks appropriate. The manner in which the dose levels in Brooker 2-gen rat study are translated into mg/kg/day has already been discussed. I believe the 132 - 48 m/k/d should be converted to something else, which was 79 / 87 m/k/d for males and females in the EU. While these latter figures are in the neighborhood of 100 m/k/d, they are clearly measurably lower than 100. Therefore, this will have to be discussed in the text. I can agree to either (1) say that 100 m/k/d represents a nice round median NOAEL figure considering all the data or (2) instead, adopt the 80 m/k/d from the Brooker study as a reference point for an ADI of 0.8.

Steve

-----Original Message-----

From: FARMER, DONNA R [AG/1000]
Sent: Monday, June 16, 2003 11:58 AM
To: [REDACTED]@syngenta.com'; WRATTEN, STEPHEN J [AG/1000];
[REDACTED]@syngenta.com; GRAHAM, WILLIAM [AG/8050]; [REDACTED]@cheminova.dk;
MARTENS, MARK A [AG/5040]
Cc: [REDACTED]@cheminova.dk
Subject: RE: JMPR Comments

Please find attached the subacute/subchronic section and a concept for approaching the ADI.

It is quite remarkable as one looks across all the studies that not much is going on with glyphosate.

We see some clinical signs, decreased body weights, minor changes in clinical chemistry parameters and the histological findings that stand out are the salivary gland alterations and the high-dose male mice liver findings.

Donna

-----Original Message-----

From: [REDACTED]@syngenta.com [mailto:[REDACTED]@syngenta.com]
Sent: Monday, June 16, 2003 5:40 AM
To: [REDACTED]@monsanto.com; [REDACTED]@syngenta.com;
[REDACTED]@monsanto.com; [REDACTED]@monsanto.com;
[REDACTED]@cheminova.dk; [REDACTED]@monsanto.com
Cc: [REDACTED]@cheminova.dk
Subject: RE: JMPR Comments

Stephen et al,

Thanks for your comments, I've annotated your message below. I have attached revised drafts of the sections I have prepared, I consider these complete now, apart from addressing point 4 in your note (to which I seek input from the Monsanto team).

See/speak to you tomorrow.

Best wishes

Ros

-----Original Message-----

From: WRATTEN, STEPHEN J [AG/1000]
[mailto:[REDACTED]]
Sent: 13 June 2003 17:52
To: Costello Jean CHBS; Sheldon Ros GBAP; GRAHAM, WILLIAM [AG/8050];
FARMER, DONNA R [AG/1000]; Kristian Lystbaek (E-mail); MARTENS, MARK A
[AG/5040]
Cc: 'Mette K. Jensen'
Subject: JMPR Comments

Dear Colleagues

So far, I have been able to read through the summary files for ADME, Genetox, Repro/dev, and Chronic. I have seen plenty of comments on formatting, and will not address that further. It seems to me from following the conversation that there is reasonable agreement of what we wish to achieve and advocate, and we are ironing out the locations and wording that will best promote those ends.

I have been particularly focused on items that may inadvertently lead reviewers toward a determination that the overall controlling NOEL would be lower than approximately 100 mg/kg/d. I have the following observations and comments in that regard.

1. There needs to be better consistency on the salivary gland position. It cannot be presented as a relevant toxic (adverse?) effect in some places and later in others be concluded as a non-adverse adaptive response to feeding of acidic material. It seems to me preferable to consistently promote and provide the non-adverse conclusion (briefly - one sentence) where ever the effect is discussed, even in the study-specific summaries, thereby laying the basis for a more through discussion spanning across different studies at a higher tier, aimed to put the matter to rest. While I concede that salivary effect may determine a "NOEL" (but not a NOAEL), the fewer times it is presented in this manner the better.

Ros added: Agree, I think the main discussion should sit in the chronic section and have already returned comments on this section. I believe we can use the Syngenta 1 (sal gland changes seen) and 2 year (no sal gland effects) studies to argue it is an adaptive effect. Also, it is seen in the rat only.

2. I believe there needs to be a harsher dismissal of the spurious literature articles. This is especially evident in the genotox table. If we are going to list some of the "positive" genotoxicity studies in the summary table, this should only be presented to open the door for a solid (scientifically based, of course) dismissal. I acknowledge that there are some suggestive comments already included about why the result may be incorrect; but I prefer a killing blow. As an example, on the Axelrad study (very loosely called a neurotoxicity study) I would support simply stating that the complete premise of the work is far-fetched adventuring into a theoretical world of "what-ifs", so that the results from such a research project are completely uninterpretable for regulatory purposes, and should not be considered further in this evaluation.

Ros comment: Edited genotox section, extra comment on the "positive" refs have been added to the table or table footnote. The discussion section has not been edited further.
Neurotox Axelrad ref. I had already edited this and have added one more sentence.

3. In reference to the Monsanto rabbit teratology study, I cannot agree to include the statement "In the rabbit, doses of 150 mg/kg and above were associated with dose-related maternal toxicity". For 12 years, US EPA has based its 2 mg/kg/day US ADI on a conclusion that the 175 mg/kg/day represents both a maternal and developmental NOAEL in this study. The US is the biggest glyphosate market in the world, and all 3 companies involved enjoy sales that are supported by this position. Monsanto has repeatedly stated and supported that 175 mg/kg/day conclusion, both in the US and in other world areas, and we cannot now be a party to submitting a document that effectively says this conclusion has been incorrect. I need to see consistency between the table and texts around this issue so that the Monsanto rabbit teratology NOAEL is consistently presented as 175 mg/kg/day. The above sentence should read: "In the rabbit, doses above 175 mg/kg were associated with dose-related maternal toxicity". I accept that the findings from the other company's rabbit studies may indicate numbers that are lower, and that a conclusion encompassing all studies may suggest that the true NOAEL may be something around 100 mg/kg/day, but the stand alone Monsanto study still must be presented as has 175 as a NOAEL.

Ros comment: Agree.

4. In the study specific summary for the Reyna repro study (2.3.1.3-m) there is a reference to the kidney tubular issue in an earlier study. Jean (I believe) questioned this. The study referenced is the earlier Schroeder/Hogan study (2.e.1.4-m) where the kidney effects were seen, so there is nothing omitted from submission in this regard. For some reason, the kidney issue is not now part of the 2.e.1.4-m study summary, but I believe it should be discussed there, so that the basis for the statements made in the summary of follow-on (2.3.1.3-m) study are more apparent.

Ros comment: I agree with the points you raise and had already queried this with Mark. The paragraph in 2e13m raises queries so I suggest edit to this or reference to the other study (I hadn't appreciated the "other study" was in fact 2.e.1.4-m because, as you say, no mention is made of the kidney effect. Can I ask one of the MSO team edit this (or both) study summary(ies) as you wish the data to be represented.

5. In the Brooker (2.e.1.2-c) repro study, I do not like the way the dose is stated in mg/kg/day in both the study-specific summary and in the higher level overview. First is inconsistent with the "m/f" format the other studies employ. More importantly, the "132 - 48" describes a time-dependent dose range. Since this is likely to be considered the prevailing parental NOAEL, I do not wish for the reviewer to see an option to choose the lowest 48 mg/kg/day as the value to take forward. In the EU evaluation of this Brooker study, the German reviewer re-expressed this result as 79 mg/kg/day males and 87 mg/kg/day females. I propose we adopt the same consistent approach. The benefit: this 79/87 dose level is much closer to our target of 100 mg/kg/day.

Ros comment: Agree, since the initial round of draft reviews, the dose received was been calculated from the original report and has been added to the study summary.

6. I would like to find a way not to state in regards to the chronic rat study set that the NOEL is 30 mg/kg/day. This is an open invitation to conclude overall that this figure represents an overall prevailing ADI setting reference point. Can we avoid this statement, and speak only of the NOAEL? Or can we conclude that the alkaline phosphatase findings at levels of 110 - 130% of control with no other pathology are simply adaptive changes that do not constitute relevant effects? However it is handled, it will help move toward our desired result if we do not present a 30 m/k/d reference point.

Ros comment: Agree, as I commented last week, I feel we should distance ourselves from quoting this study NOEL.

7. There are some study ID errors in the ADME study(s) overview - it appears that perhaps an earlier version of the bibliography list was used. Probably each author should double check these vs the bibliography sent by me 22-May (which says "23-May-2003" in the lower left footer if printed). This is the final assignment of study ID codes.

I look forward to our 17-Jun conversation.

Steve Wratten
