Gorst, Janet

From: Russell French, Sarah (SK) <SKRussellFrench@dow.com>
Sent: Friday, 1 April 2011 2:04 PM
To: Gorst, Janet
Subject: RE: A1042 and A1046 [Sec: UNCLASSIFIED]
Attachments: Role of Animal Feeding Trials (EFSA, Food Chem Tox 2008).pdf

Dear Janet,

Firstly I would like to clarify that currently a 90-day rat feeding study is not an EU requirement. Please find attached to this email a review published by EFSA of the value of animal feeding studies, in which the EFSA indicated that in general these studies do not add to the safety assessment and should only be conducted for traits that have an intentionally modified nutrient composition (e.g., a modified fatty acid profile). The EFSA summary review indicates that for simple input traits such as AAD-1 and AAD-12 a 90-day rat feeding study would not improve the quality of the risk assessment.
Presently, Dow AgroSciences LLC has no 90-day rat feeding study to submit to any regulatory agency (Including the EU) for either product.

Regards,
Sarah

Dow AgroSciences
Science for growth

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From: Gorst, Janet [mailto:Janet.Gorst@foodstandards.gov.au]
Sent: Thursday, 31 March 2011 10:52 AM
To: Russell French, Sarah (SK)
Subject: A1042 and A1046 [Sec: UNCLASSIFIED]

Dear Sarah

I just wanted to check something with you regarding both A1042 (corn line DAS-40278-9) and A1046 (soybean line DAS-68416-4).

In neither of the application dossiers for these two applications did Dow include a 90-day feeding study . Given that in both cases, it was concluded the GM food derived from each line was compositionally equivalent to conventional varieties, FSANZ does not require a 90-day feeding study. BUT if such a study has been done FSANZ does need to see the study.

I note that for both applications Dow has made submissions 'to the appropriate agencies for food, feed and/or environmental approvals' in a number of countries including the EU. A submission for a food approval to the EU would automatically have to include a 90-day feeding study since this is an absolute requirement in the EU for a GM food. I just wanted to check whether a food approval for either DAS-40278-9 or DAS-68416-4 had been made to the EU and if so would request that Dow forward the 90-day feeding study to FSANZ.

Kind regards
Janet

Dr Janet Gorst
Senior Scientist, Risk Assessment - Chemical Safety

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6/1/11

Food Standards Australia New Zealand
Dr Janet Gorst
Senior Scientist, Risk Assessment – Chemical Safety
PO Box 7186
Canberra BC ACT 2610

Dear Dr Janet Gorst,

As per my letter dated 30/11/10, please find attached the two final audited versions of the Nature of Residue and Magnitude of Residue studies for 2,4-D on DAS-68416-4 soybeans (see below).

Graper, L.K., Balcer, J.L., Smith, K.P. and Hogan, P.S., 2010, *A Nature of the Residue Study with [14C]-2,4-D DMA Applied to AAD-12 Soybeans.* Dow AgroSciences Study ID 090051.

Culligan, J.F., 2010, *Magnitude of the Residue of 2,4-D in/on Herbicide Tolerant Soybeans Containing the Aryloxyalkanoate Dioxygenase-12 (AAD-12) Gene.* Dow AgroSciences Study ID 090053

Please note both hard and electronic versions of the reports are attached.

Regards,

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Gorst, Janet

From: Gorst, Janet
Sent: Monday, 18 April 2011 4:26 PM
To: 'Clare Chandler'
Subject: RE: A1042, 2nd Assessment Report [Sec: UNCLASSIFIED]

Classification: UNCLASSIFIED

Thank you very much Clare for your response; and yes, it was useful to read the ESR comments. I appreciate that sometimes, when you are closely involved with something, you can't see the wood for the trees and everything looks crystal clear and obvious to you while a pair of fresh eyes can see ambiguities. Thanks to ESR for the fresh eyes.

Cheers
Janet

From: Clare Chandler [mailto:Clare.Chandler@maf.govt.nz]
Sent: Monday, 18 April 2011 1:19 PM
To: Gorst, Janet
Subject: RE: RE: A1042, 2nd Assessment Report [Sec: UNCLASSIFIED]

Hi Janet
Thank you for your reply. We agree that the inclusion of the extra statement would help, so we will put that suggestion into our submission that we send to your tomorrow.

The comments came from ESR, and I have talked with them about your response. I will provide you with their comments in this email, but this will not form part of our submission. We hope this feedback is useful for future summaries prepared by FSANZ:

"The footnotes to the table say: "Statistically significant differences (adj P) between the control and DAS-40278-9 are highlighted in green. Statistically significant overall treatment effects are highlighted in grey". I guess if paired comparisons are statistically different then they are highlighted in green, while an overall treatment effect means at least one significant difference in the pairwise comparisons and is highlighted in grey.

What was puzzling me was two instances that Janet mentioned: where there are no significant differences in green but an overall treatment effect is claimed in grey: moisture and behenic acid. My understanding now is that for these two instances there was a significant difference using the P value, which disappeared with the adjusted P (although if the threshold was $p < 0.05$ then it looks to me as if the moisture differences were not significant even with the unadjusted p).

I think it would have been clearer if the two relevant tables highlighted these specific instances using a third colour and a different explanation, or perhaps no colour at all. But I think we can accept their explanation."

I hope this is helpful

regards

Clare

Clare Chandler | Senior Adviser, Food Science
Science, Information and Risk Directorate | Policy, Science and Economics Branch
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From: Gorst, Janet [mailto:Janet.Gorst@foodstandards.gov.au]
Sent: Friday, 15 April 2011 1:07 p.m.
To: Clare Chandler
Subject: RE: A1042, 2nd Assessment Report [Sec: UNCLASSIFIED]

Hi there Clare

My apologies for the delay in responding to you but I haven't been at my desk very much in the last week. Derek Castles is not involved at all with the project.

When I received the MAF submission for the 1st Assessment Report I read over what had been written by the Risk Assessor in the Safety Assessment and I'm afraid I was a bit mystified about the MAF comments on the Compositional Analysis. It seemed well explained to me that there were 5 treatments in total (a non-GM unsprayed; a GM unsprayed; a GM sprayed with 2,4-D; a GM sprayed with quizalofop; a GM sprayed with both 2,4-D and quizalofop) and that the four GM treatments were each compared with the non-GM unsprayed control. In the cases where there was an overall treatment effect (i.e. where the was a significant difference between all/any of the GM treatments compared with the unsprayed control) there was a discussion about this significance except in the case of Moisture and Behenic acid where, while there was an overall treatment effect, the individual comparisons of the GM treatments with the non-GM control did not show a significant difference as reflected in the adjusted P value.

Would it help, if we added into the last paragraph of Section 6.2 of the Safety Assessment, something along the lines of the following

The significance of an overall treatment effect was estimated using an F-test, while paired contrasts were made between the unsprayed non-GM control and each of the four GM treatments using t-tests. Probability values were adjusted using False Discovery Rate procedures to improve discrimination of true differences (Benjamini and Hochberg 1995).

Apologies again for not getting back to you sooner. Happy to have a phone chat if things are still not clear.

Kind regards
Janet

From: Clare Chandler [mailto:Clare.Chandler@maf.govt.nz]
Sent: Thursday, 14 April 2011 7:28 AM
To: Gorst, Janet
Cc: Castles, Derek
Subject: FW: A1042, 2nd Assessment Report

Hi Janet
Have you had a chance to find out about this? I am copying this to Derek as well, as I see Derek is also involved with this project.

many thanks

regards

Clare

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From: Clare Chandler
Sent: Friday, 8 April 2011 11:22 a.m.
To: 'Gorst, Janet'
Subject: A1042, 2nd Assessment Report

Hi Janet

I note that you are the project manager for A1042. We are reviewing the second assessment report, and have a questions regarding para 8.1.2.5 of the report. It states that the issue raised by MAF is addressed in an amended section 6 of the Safety Assessment (SD1).

However, we are unable to find any change that explains what a 'treatment effect' is.

Can you let me know if we are missing something?

We are happy with the changes made to section 4.

kind regards

Clare

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Gorst, Janet

From: Russell French, Sarah (SK) <SKRussellFrench@dow.com>
Sent: Tuesday, 24 May 2011 2:28 PM
To: Gorst, Janet
Subject: RE: A1042 [Sec: UNCLASSIFIED]

Hi Janet,

Please find responses to your questions below. Please let me know if this response satisfies your requirements.

Regards,
Sarah

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From: Gorst, Janet [mailto:Janet.Gorst@foodstandards.gov.au]
Sent: Friday, 29 April 2011 11:55 AM
To: Russell French, Sarah (SK)
Subject: A1042 [Sec: UNCLASSIFIED]

Hi Sarah

Following the end of the second consultation period I am now preparing the Approval Report for A1042. You may be interested to hear that there were 58 submissions, many from New Zealand taking the form of a campaign letter.

At the moment I just have three questions raised in the submissions but there may be others as I progress through the various issues raised.

1. In the 2nd Assessment Report I wrote "Applications concerning corn line DAS-40278-9 have been made to the appropriate agencies for food, feed and/or environmental approvals in the United States of America, Canada, Japan, South Korea, Taiwan, Mexico, Argentina and the European Union. These applications are still under consideration. It is likely that dossiers will be submitted to the regulatory authorities of trade partners for import clearance including in Brazil, Colombia and South Africa". Is this information still current? If not could I have an update.

We received FDA approval (US) on 14 April 2011. All other approvals (including USDA) are still pending; many are projected to be approved early 2012. We are planning submissions in Brazil, Columbia, and South Africa.

2. Has Dow publicly released the PCR or ELISA detection methodology for DAS-40278-9 (or when does it plan to do so)? At the moment FSANZ has given CCI status to a) sequence data that would be required to develop a PCR detection method and b) an ELISA detection method (the latter was given CCI status on the grounds that a patent was being filed on the method – so maybe the patent has now been granted?).

PCR: The PCR method was officially submitted to JRC prior to the submission of AAD-1 corn dossier to EFSA. Publication of the method in EURL site after validation and ring trial will take a year or so based on the methods currently in the queue for validation.

ELISA: The patent for the ELISA method has been filed, however, it is still pending for decision. Currently the ELISA kit is available for internal users. We can release once either the patent is granted or the event is deregulated in US or Canada.

3. With regards to the acute oral toxicity study (071128), multifocal erosions/ulcers were observed in the glandular mucosa of one male mouse and there was a dark focus in the cerebrum in one female mouse. I am wondering if Dow has any historical data/references regarding the natural occurrence of stomach erosions/ulcers and dark foci in the cerebrum of CRL:CD1 mice. Dow concludes that the findings in study 071128 were considered to be unassociated with test material administration – evidence to support this conclusion is needed.

An OECD, OPPTS, JMAFF, EEC guideline-compliant acute oral toxicity study with the AAD-1 protein was conducted. The purpose of these studies is to evaluate lethality. Gross pathology in acute studies is evaluated to determine if there are any unusual findings, particularly severe target organ effects in several animals. The results of the study showed no lethality at the limit dose of 2,000 mg/kg AAD-1 protein, which was the highest dose that could be tested. The gross pathology effects observed (glandular mucosa of one male mouse, dark focus in cerebrum in on female mouse) were not considered to be treatment-related. They were only reported in one animal each, and one was attributed to stress (likely a result of oral gavage administration) and the other a spontaneous incidence.

USEPA United States Environmental Protection Agency, *Health Effects Test Guidelines*, OPPTS 870.1100 (Acute Oral Toxicity), EPA712-C-02-190,December 2002. http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series870.htm

OECD Organisation for Economic Co-Operation and Development. *OECD Guideline for the Testing of Chemicals*, Guideline Number 423 (Acute Oral Toxicity – Acute Toxic Class Method), 17 December 2001. http://puck.sourceoecd.org/vl=3702670/cl=13/nw=1/rpsv/ij/oecdjournals/1607310x/v1n4/s25/p1

JMAFF Japan MAFF Acute Oral Toxicity Study, 2002

EC EEC Methods Number B.1 tris Acute Oral Toxicity, 2004

Lui, C. and Crawford, J.M. (2005). The Gastrointestinal Tract. In: *Pathologic Basis of Disease*. Kumar, V., Abbas, A.K., and Fausto, N. (eds), Elsevier Saunders Press, pp819-820.

Leininger, J.R., Jokinen, M.P., Dangler, C. A., and Whiteley, L.O. (1999). Oral Cavity, Esophagus, and Stomach. In *Pathology of the Mouse*. Maronpot, R.R., Boorman, G.A., and Gaul, B.A. (eds), Cache River Press, p34.

Many thanks
Janet

Dr Janet Gorst
Senior Scientist, Risk Assessment - Chemical Safety

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Gorst, Janet

From: Russell French, Sarah (SK) <SKRussellFrench@dow.com>
Sent: Thursday, 26 May 2011 10:47 AM
To: Gorst, Janet
Subject: RE: another question [SEC: UNCLASSIFIED]

Hi Janet,

The cyst that was observed in the cortex of the kidney of one female mouse in the acute oral toxicity study (081037) was a single unilateral cyst. It does not represent a treatment-related effect because both kidneys would be expected to have lesions and in more than one animal for it to be treatment-related (Seely, 1999). For this reason, it was interpreted to be spontaneous. Furthermore, no lethality or effects on body weight or treatment-related gross pathology signs were observed at the limit dose of 2000 mg/kg, as defined by the OECD, OPPTS, JMAFF and EEC test guidelines for conducting acute oral toxicity studies in rodents.

Seely, J.C. (1999). Kidney. In : *Pathology of the Mouse*. Maronpot, R.R., Boorman, G. A., and Gaul, B. W. (eds). Cache River Press, Vienna, USA. pp 207-234.

USEPA United States Environmental Protection Agency, *Health Effects Test Guidelines*, OPPTS 870.1100 (Acute Oral Toxicity), EPA712-C-02-190,December 2002. http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series870.htm

OECD Organisation for Economic Co-Operation and Development. *OECD Guideline for the Testing of Chemicals*, Guideline Number 423 (Acute Oral Toxicity – Acute Toxic Class Method), 17 December 2001. http://puck.sourceoecd.org/vl=3702670/cl=13/nw=1/rpsv/ij/oecdjournals/1607310x/v1n4/s25/p1

JMAFF Japan MAFF Acute Oral Toxicity Study, 2002

EC EEC Methods Number B.1 tris Acute Oral Toxicity, 2004

Regards,
Sarah

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From: Gorst, Janet [mailto:Janet.Gorst@foodstandards.gov.au]
Sent: Monday, 23 May 2011 1:23 PM
To: Russell French, Sarah (SK)
Subject: another question [SEC: UNCLASSIFIED]

Dear Sarah

Along the lines of a question I have asked you about A1042, I'm afraid I need to ask a similar question about A1046.

With regards to the acute oral toxicity study (081037), "a cyst in the cortex of the kidney was observed in one female mouse, which was interpreted to be a spontaneous alteration unassociated with test material administration". Does Dow have any historical evidence or reference to support the interpretation?

Many thanks
Janet

Dr Janet Gorst
Senior Scientist, Risk Assessment - Chemical Safety

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