

Message

From: HEYDENS, WILLIAM F [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=230737]
Sent: 4/2/2002 12:45:18 PM
To: HEALY, CHARLES E [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=297008]
Subject: RE: TNO dermal penetration studies: new issues and topics for the conf call of Tuesday, 2 April (8 A.M STL time)

Chuck,

Thanks. I would like to sit in but will probably not do so due to time considerations. My primary concern is with the glyphosate in terms of the potential for this work to blow Roundup risk evaluations (getting a much higher dermal penetration than we've ever seen before).

Bill

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

From: HEALY, CHARLES E [AG/1000]
Sent: Monday, April 01, 2002 3:42 PM
To: HEYDENS, WILLIAM F [AG/1000]
Subject: FW: TNO dermal penetration studies: new issues and topics for the conf call of Tuesday, 2 April (8 A.M STL time)

Bill,

As a follow-up to Fabrice's message below, we are having a conference call with Brussels Tuesday morning (Apr 2) at 8 a.m. in A2215N. I don't know if you want to sit in or even have time to or just would like an update afterwards. In any case, just wanted to make you aware of the call. Joel, Donna, Abby, Christophe, Ruth, Steve, and I will all be on the call with Fabrice and Mark.

Chuck

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

From: GUSTIN, CHRISTOPHE [AG/1000]
Sent: Friday, March 29, 2002 9:29 AM
To: HEALY, CHARLES E [AG/1000]
Subject: RE: TNO dermal penetration studies: new issues and topics for the conf call of Tuesday, 2 April (8 A.M STL time)

Chuck,

I will send you a copy of Fabrice fax. Could you circulate it to Abby, Joel, Donna and Steve Wratten please. Did Cam find us a room for Tuesday (8:10:30)?

Thanks,
Christophe

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

From: BROECKAERT, FABRICE [AG/5040]
Sent: Friday, March 29, 2002 7:58 AM
To: GUSTIN, CHRISTOPHE [AG/1000]; LI, ABBY A [AG/1000]; HEALY, CHARLES E [AG/1000]; MARTENS, MARK A [AG/5040]; KRONENBERG, JOEL M [AG/1000]
Cc: HEYDENS, WILLIAM F [AG/1000]; FARMER, DONNA R [AG/1000]; MCKENNA, RUTH M [AG/1000]
Subject: TNO dermal penetration studies: new issues and topics for the conf call of Tuesday, 2 April (8 A.M STL time)
Importance: High

Dear all,

As today we received preliminary surprising results on *in vitro* dermal penetration of propachlor and glyphosate through rat skin, it is imperative that we work closely together and communicate well on the conduct, the practical difficulties and the results associated with these studies. Christophe, could you please circulate the fax I will send to you this morning ?

Please find herewith a summary of issues (with data) we have to discuss during our conf call of next Tuesday:

Propachlor:

- Our attempt to demonstrate that the dermal penetration of propachlor through human skin is lower than with rat

skin failed. Indeed,

* concentrate formulation: % penetration with human skin = % penetration with *rat skin*

* spray dilution: % penetration *human skin* > % dermal penetration *rat skin* ($p < 0.05$) (see attached table)

- Microautoradiographies clearly show stores of propachlor in the epidermis of human skin

Triallate:

- The UK's PSD wants to take into consideration the stores of triallate in skin tissues for the derivation of the dermal penetration factor (% dermal penetration + stores = 0.22% + 26.9% = 27.1%) (see attached table)

- Our attempt to show that triallate is stored in the stratum corneum by micro-autoradiography failed due to experimental problems

Glyphosate:

- The EU rapporteur for glyphosate used a dermal penetration factor of 3% based on several published *in vitro/in vivo* dermal penetration studies

- We launched human and rat *in vitro* dermal penetration studies with MON 35012 with and without surfactant

- Preliminary results with rat skin are not acceptable (see fax); due to very bad reproductibility that TNO cannot explain, they proposed to repeat the study in parallel with the human skin study. However, we can already conclude that:

* for the concentrate MON 35012, the % *in vitro* dermal penetration of glyphosate through rat skin is between 5 and 10%

* for the spray dilution of MON 35012, the % *in vitro* dermal penetration of glyphosate through rat skin will be around 2%

* The dermal penetration of glyphosate itself in the absence of surfactant is lower than 1.5%.

In the light of these results, should we continue to place *in vitro* dermal penetration studies at TNO ?

Propachlor: can we use rat dermal penetration results for the risk assessment ?

Triallate:

- pharmacokinetics modelling

- tape-stripping

Glyphosate:

- Reproductibility by repeating the study ?

- Results with human skin ?

<< File: TNO_Dermal_Penetration.doc >>

Regards, Fabrice