Message

From: GARNETT, RICHARD P [AG/5040] [/O=MONSANTO/OU=EA-5040-01/CN=RECIPIENTS/CN=107838]
Sent: 2/10/2003 8:43:00 AM
To: BROECKAERT, FABRICE [AG/5040] [/O=MONSANTO/OU=EA-5040-01/CN=RECIPIENTS/CN=591489]
CC: VAN BELLINGHEN, CHANTAL [AG/5040] [/O=MONSANTO/OU=EA-5040-01/CN=RECIPIENTS/CN=82265]
Subject: RE: dermal absorption

Fabrice,
Agree with your argument, and that the mixing and loading component of the models is small, but I'm not totally convinced. My point is that since it is widely accepted that higher concentrations (eg undiluted product) show a lower % absorption than low concentrations (eg spray solutions) then there is the opportunity to differentiate between the two.

There are 3 studies which used undiluted formulated product (none of them in vivo:

Wester	in vitro	=/< 0.4%
Franz	in vitro	0.063% (c25-50% of absorbed glyphosate was found in the dermis)
Maibach	in vitro	1.8% (low accountability)

Where diluted material was also tested (Wester and Franz) the absorption was several times greater. So then the question is whether you can dismiss Maibach. In a "precautionary" approach you would not, however given the low accountability and the fact it is very close the absorption of the same formulation in a diluted form in other studies, I think there is an argument for dismissing it.

In the end I agree it makes little difference to the outcome of the model, but we need to take what we can get.

Should we also start referring to the Wester 96 paper which showed 1.4% absorption of a 1% solution of MON 2139, which was reduced by cotton "overalls"?

regards richard

-----Original Message-----
From: BROECKAERT, FABRICE [AG/5040]
Sent: 07 February 2003 16:56
To: GARNETT, RICHARD P [AG/5040]
Cc: VAN BELLINGHEN, CHANTAL [AG/5040]
Subject: RE: dermal absorption

Richard,

~ 98% of the absorbed dose originates from field application and so the impact will be negligeable. The work of Wester showed 2.2 +/- 1.5% *in vivo* with the concentrated formulation and a max of 2.2 +/- 0.5% *in vitro* with the spray dilution. I suppose that's the reason why a derm pen value of < 3% was selected. We should remember that Wester excluded the presence of glyphosate in the skin due to the absence of partition of glyphosate with the stratum corneum. By contrast, in the Franz study, a large amount of glyphosate was detected in the epidermis (0.5-5%). And as we know now, 5-20% of the dose of glyphosate could be stored in the skin.

I think we should be really happy if the regulators allow us to use the 3% derm pen values.

Regards, Fabrice

-----Original Message-----
From: GARNETT, RICHARD P [AG/5040]
Sent: Friday, February 07, 2003 3:29 PM
To: BROECKAERT, FABRICE [AG/5040]; VAN BELLINGHEN, CHANTAL [AG/5040]
Subject: dermal absorption

Chantal, Fabrice,
The Listing of end points gives <3% for dermal absorption. However, this is a generalised end point to cover all situations (for MON 2139 and similar formulations).

Pilliod v. Monsanto
EX. 0025
Case No: RG17862702

It is recognised in the section 2.4 of the Guidance Document that dermal absorption is inversely proportional to concentration (area dose) of the material applied, and therefore that studies should be done with undiluted material and at a spray concentration. Following this logic we should also carry out our risk assessment using data on undiluted product (*in vitro* max. is 0.4 % from the Wester study, excluding Maibach due to the low recovery) for the mixing/loading part of the operator exposure model and on diluted product for the spraying part (the 3% value). Does this have any significant impact on the outcome of the modelling?

This then raises the question which started me thinking. In the review recently completed for MON 78294 for France, the table shows Wester *in vivo* studies were done with undiluted and 1:29 dilution Roundup. The comparison of studies done previously (and my memory) shows that the 1:29 dilution was applied at two different amounts/unit area, but that it was not applied undiluted. Could you check please. If this is true it gives a reason to use the 0.4% for absorption of undiluted material based on the fact that the Franz *in vivo* data on undiluted product were much lower, and Maibach can be dismissed due to low recovery?

Am I barking up the wrong tree?

thanks and regards
Richard