

Message

From: GARNETT, RICHARD P [AG/] [/O=MONSANTO/OU=EA-5040-01/CN=RECIPIENTS/CN=107838]
Sent: 7/9/2004 3:37:26 PM
To: HEALY, CHARLES E [AG/1000] [/O=MONSANTO/OU=NA-1000-01/cn=Recipients/cn=297008]
Subject: RE: MON 59117 GI tract study

Fair comment!

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

From: HEALY, CHARLES E [AG/1000]
Sent: 09 July 2004 17:33
To: GARNETT, RICHARD P [AG/]
Subject: RE: MON 59117 GI tract study

Richard,

I don't know that I would go so far as to say that the results were positive, but I would say that they were a) not entirely surprising and b) certainly not adverse.

Chuck

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

From: GARNETT, RICHARD P [AG/]
Sent: Friday, July 09, 2004 1:29 AM
To: HEALY, CHARLES E [AG/1000]
Subject: RE: MON 59117 GI tract study

Chuck,

Thanks. So it looks like the study results are very positive even though there was more GI absorption than expected.

Regards
Richard

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

From: HEALY, CHARLES E [AG/1000]
Sent: 08 July 2004 22:37
To: GARNETT, RICHARD P [AG/]
Subject: RE: MON 59117 GI tract study

Richard:

At 24 hrs there was still some material in the body, but this would not represent a toxicological concern inasmuch as we have longer term studies for MON 59117 with repeated exposures at higher levels with no adverse toxicological consequences. Eventually (if we had gone longer), the test material would have been totally eliminated.

This was a GLP study, so it could be included in future dossiers.

Please let me know if there are further questions.

Kind regards,

Chuck

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

From: GARNETT, RICHARD P [AG/]
Sent: Thursday, July 08, 2004 6:52 AM
To: HEALY, CHARLES E [AG/1000]
Cc: FARMER, DONNA R [AG/1000]; WRATTEN, STEPHEN J [AG/1000]
Subject: RE: MON 59117 GI tract study

Chuck,
Thank you and sorry for the late reply.

To check my non-toxicologist's understanding of the summary ... Over half of the dose was absorbed but does "rapidly eliminated" mean everything was accounted for in 24 hours. Whilst I'm reassured that you conclude there are no reportable findings, do we know the tox. implications? Was the study to GLP and therefore should be included in future dossiers for products containing MON 59117?

Regards
richard

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

From: HEALY, CHARLES E [AG/1000]
Sent: 04 June 2004 20:23
To: GARNETT, RICHARD P [AG/]
Cc: WRATTEN, STEPHEN J [AG/1000]; FARMER, DONNA R [AG/1000]
Subject: RE: MON 59117 GI tract study

Richard:

This work was completed last year. The full report can be viewed in Documentum. Below is a copy of the summary page of the report. Basically what we demonstrated was that the material is absorbed through the GI tract as shown. Nothing I am aware of that needs to be reported. We were hoping that we could demonstrate that the material was not absorbed as a means to obviate the need to perform toxicity testing with similar inert ingredients. Obviously that hope was not realized. Please let me know if you need more information.

IV. SUMMARY

Two groups of female Sprague-Dawley Crl:CD(SD)IGS BR rats, six animals per group, were administered 14C-MON 59117 orally by gavage as a diet slurry (five parts of deionized water to one part diet). The dose levels were 1 and 10 mg/kg. Each group consisted of three animals with both a bile duct cannula and a portal vein cannula and three animals with no cannulae. All animals were fasted overnight and then allowed approximately 2 1/2 hours to eat prior to dose administration. The actual dose administered was quantified by weighing the dosing syringe before and after delivery of the dose.

Following dosing, the animals were placed in individual metabolism cages where urine, feces, and, where applicable, bile were periodically collected through 48 hours post-dosing. Following each collection, the metabolism cages were rinsed with water, which was retained. At 1, 2, and 4 hours after dosing, a blood sample was collected from each animal. At approximately 48 hours postdosing, the animals were euthanized and the gastrointestinal (GI) tract removed. The contents of the GI tract were separated from the tissue and retained. All carcasses were retained. The metabolism cages were washed with methanol, which was retained. At the request of the Sponsor's Representative, only urine, bile, cage rinse, and cage wash samples were analyzed for total 14C using liquid scintillation techniques.

MON 59117 equivalents were apparently rapidly absorbed and eliminated as evidenced by the appearance of radioactivity in the urine and in the bile. Absorption was at least 56% of dose at dosages of 1 and 10 mg/kg. Approximately 17-27% of the dose was eliminated in the urine and

approximately 31-36% of the dose was found in the bile.

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

From: WRATTEN, STEPHEN J [AG/1000]
Sent: Tuesday, June 01, 2004 4:52 PM
To: HEALY, CHARLES E [AG/1000]
Subject: FW: MON 59117 GI tract study

Chuck

Weren't you involved in this? My recollection was that we had hoped to show little or no uptake, and th einitial data essentially refuted that concept and we quit.

Can you inform Richard?

Steve

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

From: GARNETT, RICHARD P [AG/]
Sent: Friday, May 28, 2004 5:37 AM
To: FARMER, DONNA R [AG/1000]; WRATTEN, STEPHEN J [AG/1000]
Subject: MON 59117 GI tract study

Was this study completed and did it show anything which we might need to report concerning our MON 78294 formulation which contains this surfactant?

Regards Richard