Message

From: Schlosser, Paul [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=121CF759D94E4F08AFDE0CEB646E711B-SCHLOSSER, PAUL]
Sent: 8/6/2021 8:09:57 PM
To: White, Paul [White.Paul@epa.gov]; Thayer, Kris [thayer.kris@epa.gov]; Morozov, Viktor [Morozov.Viktor@epa.gov]
CC: Kapraun, Dustin [Kapraun.Dustin@epa.gov]
Subject: RE: Model of fate of chloroprene oxidation products

Ex. 5 Deliberative Process (DP)

From: White, Paul <White.Paul@epa.gov>
Sent: Friday, August 6, 2021 3:19 PM
To: Schlosser, Paul <Schlosser.Paul@epa.gov>; Thayer, Kris <thayer.kris@epa.gov>; Morozov, Viktor <Morozov.Viktor@epa.gov>
Cc: Kapraun, Dustin <Kapraun.Dustin@epa.gov>
Subject: RE: Model of fate of chloroprene oxidation products

Have to agree, Paul. The mouse and rat curves look quite different and we certainly don't expect them to line up.

Paul

From: Schlosser, Paul <Schlosser.Paul@epa.gov>
Sent: Friday, August 6, 2021 2:29 PM
To: White, Paul <White.Paul@epa.gov>; Thayer, Kris <thayer.kris@epa.gov>; Morozov, Viktor <Morozov.Viktor@epa.gov>
Cc: Kapraun, Dustin <Kapraun.Dustin@epa.gov>
Subject: RE: Model of fate of chloroprene oxidation products

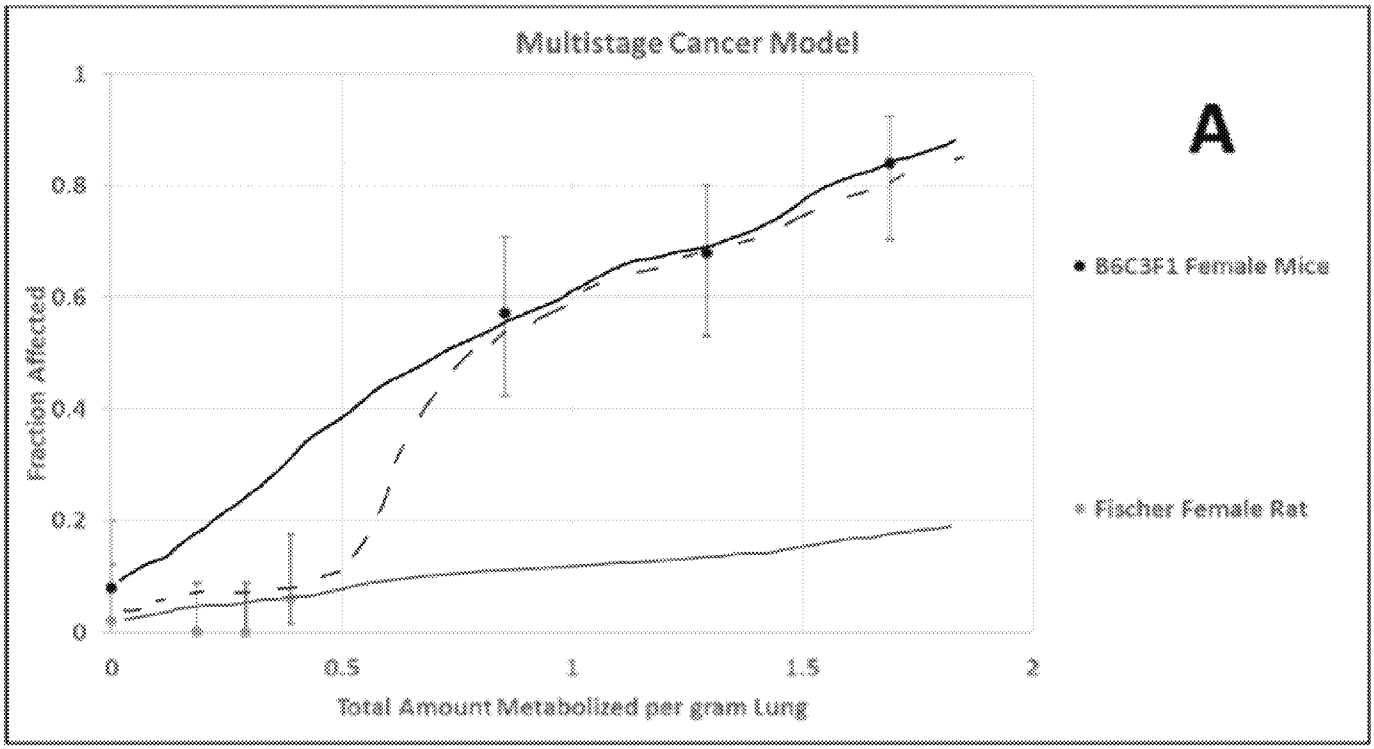
Including Dustin...

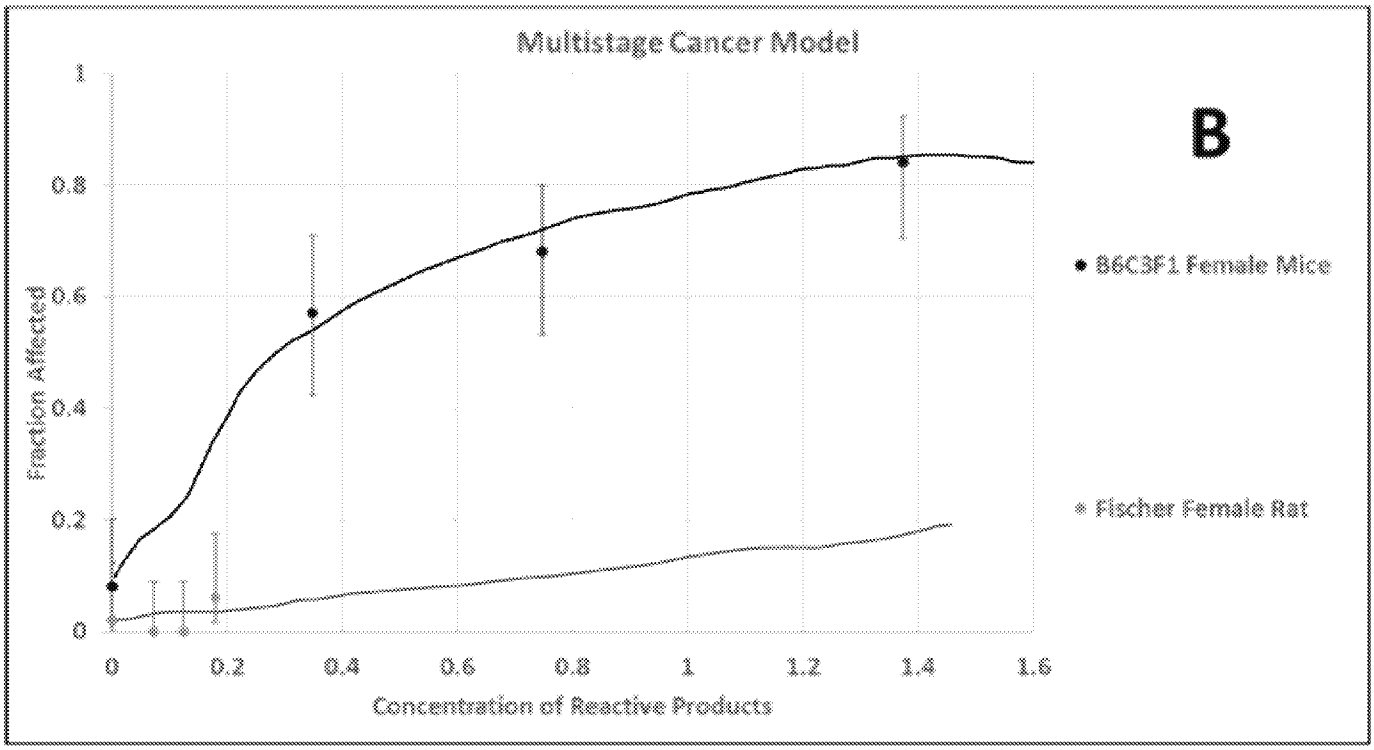
Ex. 5 Deliberative Process (DP)

"Here, our analysis showed that tumor incidence tracks with total metabolized or expected concentration of RP rather than inhaled CP or 1-CEO concentrations. All the bioassay concentrations (12.8, 30 and 80 ppm) are expected to cause much more than 30% depletion of GSH (Figure F3 top panel). Depletion of GSH to 30 % basal levels is predicted to occur at 6.8 ppm and 50% depletion at 15.3 ppm. The middle panel (Figure F3) in the plots for RP and rate of formation of RP show the non-linear relationship between RP and rate of metabolism and the increasing slope of the RP curve at low CP concentrations. Our modeling results capture the non-linear relationship between RP and total rate of metabolism. These results demonstrate the marked increase in the slope of RP as the exposure increases..."

Ex. 5 Deliberative Process (DP)

-Paul





From: White, Paul <White.Paul@epa.gov>
Sent: Friday, August 6, 2021 1:45 PM
To: Schlosser, Paul <Schlosser.Paul@epa.gov>; Thayer, Kris <thayer.kris@epa.gov>; Morozov, Viktor <Morozov.Viktor@epa.gov>
Subject: RE: Model of fate of chloroprene oxidation products

Damn, that request for correction process is still driving our lives...

From: Schlosser, Paul <Schlosser.Paul@epa.gov>
Sent: Friday, August 6, 2021 1:37 PM
To: Bernstein, Amanda <bernstein.amanda@epa.gov>; Brinkerhoff, Chris <Brinkerhoff.Chris@epa.gov>; Choi, Kyoungju <Choi.Kyoungju@epa.gov>; Dzierlenga, Michael <Dzierlenga.Michael@epa.gov>; El-Masri, Hisham <El-Masri.Hisham@epa.gov>; Jarabek, Annie <Jarabek.Annie@epa.gov>; Kapraun, Dustin <Kapraun.Dustin@epa.gov>; Kenyon, Elaina <Kenyon.Elaina@epa.gov>; Lin, Yu-Sheng <Lin.Yu-Sheng@epa.gov>; Morozov, Viktor <Morozov.Viktor@epa.gov>; Phillips, Martin B. <phillips.martinb@epa.gov>; Prasad, Bidya <Prasad.Bidya@epa.gov>; Sasso, Alan <Sasso.Alan@epa.gov>; Simmons, Jane <Simmons.Jane@epa.gov>; Tan, Cecilia <Tan.Cecilia@epa.gov>; White, Paul <White.Paul@epa.gov>; Zurlinden, Todd <zurlinden.todd@epa.gov>
Subject: Model of fate of chloroprene oxidation products

PKWG colleagues,

Ramboll scientists have previously developed a PBPK model for chloroprene in mice, rats, and humans, that has been under review by the EPA. In response to comments from external peer reviewers, Ramboll recently developed a provisional model to describe the fate of the two primary oxidative metabolites of CP, 1-CEO and 2-CEO. I am reading through the document now and it contains a fair level of detail regarding the chemistry, predicted fate of the metabolites.

The document will be sent back to the external panel that first reviewed the PBPK model (along with those revisions), but the panel was not formed with such a detailed chemical model in mind, and only a subset of initial reviewers are available for this follow-up review. We are seeking to add someone with in vitro metabolism expertise who has a chemistry background.

But given that, it would be good to have a couple of other internal EPA reviewers go over the analysis. If you're interested, let me know and I'll send a copy.

Thanks,
-Paul

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Paul M. Schlosser, Ph.D.
CPHEA, U.S. EPA
Ex. 6 Personal Privacy (PP) me)
E: schlosser.paul@epa.gov
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