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From: Dempsey, Ruth
Sent: Tuesday, May 02, 2000 2:57 AM
To: Carmines, Edward L.
Cc: Patskan, George J.; Solana, Rick P.; Sanders, Edward
Subject: RE: Ruth's slide.ppt

WOW! How efficient! Thanks for the slide. Just a couple of questions to ensure that I represent the past correctly - (I think I know the answers to some of these, but I just want to be sure!)

- I seem to remember Richard saying that there were some written 'guidelines' for ingredient assessment prior to the most recent version. Although I think these were probably more piecemeal in format - did they actually specify the types of toxicology testing which were performed?

[Carmines, Edward L.] Yes, but they were more suggestive than specific. "Testing Aspects" were listed as:

- Chemistry
- Pyrolysis
- Smoke Chemistry
- In vitro and in vivo Toxicity studies

[Carmines, Edward L.] Under the toxicity test heading there was a list of studies ranging form acutes and gene tox to carcinogenicity and chronic studies.

Was there a minimum battery of tests through which all new ingredients were assessed, or was this also performed on a case by case basis - based on literature / structural analysis?
[Carmines, Edward L.] Testing was judged on a case by case basis and was more driven by our estimates of potential exposure and our knowledge of the toxicity of the material. We didn't use formal structural activity analysis as a tool to make our decisions, but in reality we are always looking at the structure and making toxicological judgements. The most recent testing battery included smoke chemistry, ames, cytotox, and inhalation. We are in the process of adding the micronucleus and lymphoma. Both have been approved, but we haven't actually run an ingredient through them yet.
Am I correct in thinking that most previous was testing basically Ames and Cytotox, the mouse lymphoma and micronucleus tests only being added more recently as our experience with these has evolved?
[Carmines, Edward L.] Yes
Did we do much (if any) inhalation tests for ingredient review in the past?
[Carmines, Edward L.] Inhalation tests as well as skin painting tests have been run in the past but were mostly in response to specific issues or allegations that for ingredient approval. To date we have essentially completed 3 inhalation studies on ingredients.
Did structure-activity analysis also play a significant role in assessment? ***[Carmines, Edward L.]*** Not really. For the most part tox data exits on the GRAS materials and SAR is not necessary
Was the expert panel review a one off review of all the ingredients in use at time X or did we ever ask to review individual ingredients? Was this for the industry list or for PM alone? ***[Carmines, Edward L.]*** The industry expert panel (6 experts) looked at a composite list of all ingredients used by the industry including the maximum use level and made a determination that ingredients were not harmful under the conditions of use.
By the way, it is not my intention to go into great detail on this, I just want to be fully prepared!

Once again - many, many thanks! As you may have gathered - I need as much support as I can get!
[Carmines, Edward L.] Please feel free to call me if you need additional help, I'm on belay
Ed

with kind regards,

Ruth

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