

From: Bromberg, Kevin L. [REDACTED]
Sent: Tuesday, July 15, 2014 9:58 AM
To: Shallal, Suhair; Carpenter, Thomas
Cc: Zarba, Christopher
Subject: DISCUSSION FOR SAB July 2014 Ammonia.docx - Sorry , previous note was missing two footnotes (full text with footnotes below) - For Charge E Discussion

RfC Derivation for Ammonia:

Dear Chris/Sue:

I was disappointed in the abbreviated discussion of the key study – Holness (1989). I ask that the SAB panel be specifically asked to examine and DISCUSS the KEY ISSUES below when addressing charge Question E on the derivation of the RfC.^[1] These scientists are quite capable of providing valuable advice to EPA, as long as it focuses and tackles the KEY ISSUES:

The Toxicological Review inaccurately references the highest occupational exposure in the Holness et al. (1989) study, a NOAEL of 8.8 mg/m³, as POD for RfC derivation. This NOAEL is based on presentation of data in the study of 58 exposed workers grouped into three exposure categories – high => 12.5 ppm, medium = 6.25 – 12.5 ppm, and low = < 6.25 ppm. However, a review of the actual study shows that the selection of 12.5 ppm does not reflect the “highest occupational exposure” in the Holness et al. study, but rather the lower bound estimate of exposure in the high exposure category of 12 subjects.

The data from Holness should be looked at in its entirety – the data was only broken down into three arbitrary groups to allow for comparison of any differences between lower and higher exposure groups, and when this was done, the authors identifies that THERE WERE NO DIFFERENCES OVER THE ENTIRE RANGE OF THE DATA. Therefore, the selection of a POD based on an arbitrary break point in the data chosen by the authors is not scientifically justified and is arbitrary.^[2]

What is EPA’s procedure for developing NOAELs when the data shows no dose response across the entire range? Is it appropriate to pick the top exposure, when there were 58 subjects, and 12 in the top range – should it be the top 1, the top 3 or the top 12? What has EPA done in the past for NOAELs?

These issues need to be ventilated on Tuesday afternoon fully when charge question E addressing the derivation and scientific validity of the RfC is discussed.

Of course, the other supporting studies, both provided by public commenters (to be provided), and the three supporting studies provided by EPA need to be discussed also. That provides some additional support for an appropriate RfC determination.

I will be returning tomorrow afternoon to hear this discussion and hope that you can ensure a robust consideration of these key issues. I welcome your help on this matter.

[1] Perhaps my concern is premature, and that some of the knowledgeable panelists were reserving the discussion for the discussion of the charge question - but I was concerned by the brief discussion I did hear, and wanted to make sure we didn’t squander this opportunity.

2 EPA’s review offers only that “[i]n the absence of more detailed exposure information, the low-end of the range was considered a reasonable estimate of the NOAEL from the Holness et al. (1989) study.” Is that adequate for an RfC determination?

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