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**From:** Cagen, Stuart SZ SCC  
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**Bcc:**  
**Received Date:** 2001-01-23 15:27:26 GMT  
**Subject:** RE: Benzene

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Rob:

Thanks for the reply. More questions:

1) are the investigators on their own for the exposure assessment ? Jeff and I know that guys like Jerry Lynch and others were valuable to the UAB study.

2) is someone lined up for the dose response modeling ? The butadiene folks used Bob Sielken.

Thanks

Stuart

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

**From:** arschna [SMTP:arschna@erenj.com]  
**Sent:** Tuesday, January 23, 2001 9:00 AM  
**To:** 'Cagen, Stuart SZ SCC'  
**Cc:** Harrison, M.C. (Myron); Caldwell, Daniel J.; Russo, L.B. (Lynn); 'Beatty, Patrick (Chevron)'; 'R. Jeffrey Lewis'  
**Subject:** RE: Benzene

Stuart - a fundamental aim of the three studies on benzene in China is for use in risk assessment. As you're well aware, for epidemiology studies to be useful in dose response assessment (rather than simply hazard ID), quantitative estimates of exposure, as in the UAB/SBR study, are necessary. This permits calculation of slope factors, etc. This is a feature of all three epidemiology studies being proposed in Shanghai, and exposure estimating may even be more precise than the UAB studies, since they will be done on individuals (with access to workplace records), rather than broader worker groups as in the SBR study. Slope factors are only appropriate for clear, positive findings, however. For negative studies, adequate power must be present, so that the epidemiology studies can be used as "consistency checks" in risk assessment. This is also a feature of all three studies.

However, benzene risk assessment is a bit more complicated. Before regulators move away from linear, no threshold assumptions, mechanistic information is necessary. With benzene, it is difficult, because there is no good animal model. Shanghai is one of the few places which has both the technological sophistication and degree of exposure necessary to develop

reliable mechanistic insights on benzene-induced leukemia and related blood disorders. The data should prove to be most valuable in understanding whether precursor conditions are necessary, whether gross chromosomal alterations are necessary, a precursor, or a byproduct of exposure, etc. etc. This mechanistic emphasis, in my mind, is probably the most valuable aspect of the study, because there is no reason to move away from the pliofilm-derived risk estimates without mechanistic insights that suggest benzene's carcinogenicity is not the simple result of a one hit/adduct/cancer mechanism.

I hope this helps. There are, of course, other good reasons for moving forward with the studies related to product stewardship which I did not mention.

Rob

On 01.19.2001 10:51 AM, Cagen, Stuart SZ SCC  
[SMTP:SC724012@MSXSCC.SHELL.COM] wrote:

> Jeff/Rob:

>

> This has probably already been discussed but please humor me - as a new  
> comer to benzene - so I can have some closure.

>

> The issue may have been previously developed or may be discussed next  
week

> at the benzene consortium meeting but I would like to know how the study  
can

> be optimized for benzene risk assessment purposes. What I have in mind  
is

> to emulate the risk assessment success that we anticipate as a result of  
the

> UAB butadiene study. The concept is that a combination of a robust epi

> study and a world class exposure assessment can lead to a ready to use

> regulatory (EPA) risk assessment. I realize there are special additional

> attractions to the benzene China study, but I don't necessarily have the

> confidence in the exposure assessment leading to a useable risk  
assessment

> for this study as I did for the UAB BD study.

>

> Is the question comprehensible ? Can either of you answer this or  
reassure

> me in other ways ?

>

> Thanks

>

> Stuart

>

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