To: Cagen, Stuart Z SCC <szcagen@Shell.Com>; Clegg, Patsy M SCC-CHSE-PC <pmclegg@Shell.Com>
From: Tsai, Shan SP SHLOIL-SPS </O=SHELL/OU=MSXSOC/CN=RECIPIENTS/CN=ST196949>
Cc:
Bcc:
Received Date: 2001-01-23 21:41:17 GMT
Subject: RE: Benzene

Follow Up Flag: Follow up
Due By: Monday, September 24, 2001 3:00 PM
Flag Status: Flagged
china file - why to do the study

Stuart,

I totally agree with you on the importance of exposure assessment. The magnitutre of exposure assessment for this project is not as great as that of the UAB study, since there are only limited numbers of cases and controls that we need to collect exposure data. However, I will make sure this issue is being properly addressed in the protocol. Quantitative risk assessment should be one of the most important outcomes of this study.

Shan

-----Original Message-----
From: Cagen, Stuart SZ SCC
Sent: Tuesday, January 23, 2001 3:23 PM
To: Clegg, Patsy PM SCC; Tsai, Shan SP SHLOIL-SPS
Subject: FW: Benzene

Patsy/Shan:

Rob has some good answers to my questions but it is still worth challenging some of these points at the meeting on Friday. If we decide to help fund this project we should be included in industry oversight, especially for the risk assessment applications. Shan: please pay special attention to all of those elements that made the UAB study a success. I hope to join you via speakerphone. I hope the technology is decent.

Stuart

-----Original Message-----
From: arschna [SMTP:arschna@erenj.com]
Sent: Tuesday, January 23, 2001 11:06 AM
To: 'Cagen, Stuart SZ SCC'; 'arschna'
Cc: Harrison, M.C. (Myron); Caldwell, Daniel J.; Russo, L.B. (Lynn); 'Beatty, Patrick (Chevron)'; 'R. Jeffrey Lewis'
Subject: RE: Benzene

No - there will be many IH and epi resources involved in exposure assessment. For the disease progression and molecular epi studies, exposure assessment will involve several resources. First, Tom Armstrong, who has much experience in benzene exposure estimating (principal on Canadian IOL study; tecnical advisor to UK Institute of Petroleum and Australian Healthwatch studies) will lead the effort. Tom will rely heavily on resources within the Shanghai CDC, particularly Lu Wei, Zhong Zhou, Lipiang Bao and others. SCDC have access to all worksites in Shanghai, and we have

toured several worksites as a team already. Tom Armstrong and Jerry Lynch are former colleagues and know each others' work quite well.

I am less sure who is involved regarding the NHL/AML case control study. However, Otto Wong, (the PI) lists Lu Wei from SCDC as a contributor, as well as an industrial hygienist from Fudan University. Otto plans on developing a detailed exposure assessment procedure as part of the investigation itself. I am sure that Otto knows the importance of a detailed and accurate exposure assesment procedure.

In addition, there will need to be exposure assessment expertise as part of the Scientific Advisory Committee. Persons like Jerry Lynch, Nurt Esmen, Bob Herrick etc. should be considered.

As for dose resposne modelling, I beleive it is too early to budget for that. We are not sure what the study will show, and therefore whether modelling is appropriate. However, our biostatistician is very adept at modelling and has alot of experience in this area. Since we plan on using him in the study, if modelling is indicated, it can be performed by him. Otto Wong is also a biostatistician, and has previous experience in the area as well. However, a detailed modelling exercise would not be covered, but I suggest we could add that at a later date if it is indicated.

Please come back if this raises more questions!

Rob

On 01.23.2001 10:27 AM, Cagen, Stuart SZ SCC [SMTP:SC724012@MSXSCC.SHELL.COM] wrote:
> 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),
> > quantitiative 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 chormosomal
> > 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
> > >
> > >
> >
> >
