From: Cagen, Stuart SZ SCC
Sent: Wednesday, January 24, 2001 3:18 PM
To: Clegg, Patsy M SCC-CHSE-PC; Tsai, Shan SP SHLOIL-SPS
Subject: FW: Benzene

Follow Up Flag: Follow up
Due By: Monday, July 02, 2001 5:00 PM
Flag Status: Flagged
file in china study

-----Original Message-----
From: Beatty, Patrick (PWBE) [SMTP:PWBE@chevron.com]
Sent: Wednesday, January 24, 2001 2:33 PM
To: 'arschna'; 'Cagen, Stuart SZ SCC'
Subject: RE: Benzene

I have spoken to Otto and emphasized to him that his exposure experts need to coordinate with Tom Armstrong to ensure that we have a consistent approach that will not invite criticisms when the studies are reported in the literature. I believe that he is amenable to that.

I agree with Rob that we have adequate technical expertise associated with the current PI's to perform any require dose-response modeling. I would support having external expertise on the Science Advisory Panel to comment on their activities.

Patrick

> -----Original Message-----
> From:arschna [SMTP:arschna@erenj.com]
> Sent: Tuesday, January 23, 2001 9:06 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
> > > >
> > > >
> > >
> > >
>
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