
From: Breckenridge Charles USGR
Sent: 06 January 2015 19:31
To: Botham Phil GBJH
Cc: Hertl Peter CHBS
Subject: RE: Society of Toxicology Abstracts (2) for Approval
Attachments: Goodman_2014.pdf; Adami_2011.pdf; Mandel_2012.pdf; Acquavella_AHS2006.pdf; PD WOE_Metaanalysis_7_23_14_Submitted.pdf

Phil:

I have copied Peter on this email so that he is aware of a recent development in the potential availability of a qualified epidemiologist (See below).

Smeyne at the SOT: OK I will bring the topic of Smeyne attending the SOT up during the team meeting tomorrow. However, I would rather have Rich work on his microglia counts and the publication rather than go to the SOT

The impact of his presence at the SOT is so small that it would not even be measurable on the Richter scale.

Meta-Analysis Paper: I have been rethinking the response to the editor on the Meta-analysis paper. I want to give us the best chance of having the revision accepted by the European J. of Epidemiology. One of the most time-consuming recommendations by one reviewer was that 2 epidemiologists should independently rank the studies according to a pre-defined quality category

I spoke with Jack Mandel today about ranking the herbicide, fungicide and insecticide publications and perhaps farming, well water consumption and rural living but not cigarette smoking. Jack and Ellen Chang would do this independently) as recommended by the reviewer, and Ellen would be added as a co-author.

Jack will send a proposal and we will get a cost estimate for Ellen's time. (Jack is no longer charging his hours through Exponent). We may have to ask for a time extension from the editor since our response is due by February 3rd.

I have attached a prototype paper (Goodman_2014), where Jack used this approach to establish quality criteria for epidemiology birth defect studies atrazine. The idea of assigning a quality score to epidemiology and toxicology studies was proposed in the Adami 2011 framework paper, which I have also attached.

I do not think we need to do this for paraquat because the Mandel (2012) paper, already provided a critical review of the PQ studies published up to that point in time. However, Ellen Chang has already ranked the PQ studies into 5 tiers, as part of an exercise I asked her to do for the November PQ meeting (See below) - so to some extent we have quality categories already in mind.

- **Tier 1: individual-level exposure and outcome measures, validated exposure assessment, incident (newly diagnosed) clinically confirmed PD, ≥ 5 exposed cases**
 - None
- **Tier 2: individual-level exposure and outcome measures, incident unconfirmed PD, ≥ 5 exposed cases**
 - Kamel et al. 2007 (prospective analysis)
- **Tier 3: individual-level exposure and outcome measures, prevalent (pre-existing) PD, ≥ 5 exposed cases**
 - Hertzman et al. 1994, Liou et al. 1997, Engel et al. 2001, Kamel et al. 2007 (cross-sectional analysis), Elbaz et al. 2009, Tanner et al. 2009, Tanner et al. 2011 (Goldman et al. 2012, Kamel et al. 2014)

- **Tier 4: ecologic (group-level) exposure measures, individual-level outcome measures, ≥ 5 exposed cases**
 - Costello et al. 2009 (Gatto et al. 2009, Ritz et al. 2009, Gatto et al. 2010, Wang et al. 2011, Lee et al. 2012)
- **Tier 5: ecologic exposure and outcome measures *or* < 5 exposed cases**
 - Semchuk et al. 1992, Seidler et al. 1996, Rajput et al. 1997, Hertzman et al. 1990, Howard et al. 1979, Kuopio et al. 1999, Baldi et al. 2003, Dhillon et al. 2008, Firestone et al. 2010, Rugbjerg et al. 2011, Tomenson et al. 2011

Once we have categorical quality scores, we could re-derive the meta-analysis scores (Sielken) to see if there is any impact on our initial evaluation – which was based upon all studies. Jack suggested that we might only do the meta-analysis of the high quality studies. For completeness, I have attached copy of the meta-paper that we submitted in case you want to look over what we did initially.

Bottom Line on the Meta-analysis paper: Would you support a 2015 PQ budget cost – which my guess would likely be approximately 30K to 50K for Ellen Chang and some statistical analysis by Bob to do the task outlined above.

Epidemiologist for Hire: Jack told me that John Acquavella has been bought out into retirement by Amgen. I don't know that he is available but in case you are interested, I would attest to his ability. I estimate that John is in his mid to late 50s so he is already late in his career. I have attached one of his papers where I first got to know him.

Gerald Swain, formerly of Dow, also is of a similar quality and experience.

My personal recommendation, however, is that Syngenta does not need a full time epidemiologist - but rather can make do by acquiring the specialist skillset needed to match a specific problem at hand.

CBB