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January 13, 2006

Attn: Tom Miller, DFO

Genevieve Matanoski, MD, Chair  
Arsenic Review Panel, Science Advisory Board  
United States Environmental Protection Agency  
1200 Pennsylvania Avenue,  
Washington, DC 20460

Dear Dr. Matanoski,

We submit, herewith attached, a copy of our paper “Arsenic Cancer Risk Factor in SW Taiwan Dataset” which has been published electronically by the journal Environmental Health Perspectives. We believe that it is clearly relevant to the charges and concerns of the Panel.

The panel was asked to consider (Charge C2) whether “the Taiwanese dataset remains the most appropriate choice for estimating cancer risk in humans?” We had previously (9/12/05) answered, “No, if it means the current SW dataset.”, and discussed a number of difficulties or problems with the data. We submitted to you (9/13/05) a graphic analysis demonstrating the lack of homogeneity in the arsenic risk assessment with respect to townships. We have now extended these analyses and present the findings to you from the peer-reviewed published literature.

Our analyses have demonstrated the effect of a strong confounding factor in the SW Taiwan dataset with respect to the data from Townships 0, 3, and 5 as distinguished from those of Townships 2, 4, and 6. Our paper presents a model for the analysis of bladder and lung cancer mortality risk in Townships 2, 4, and 6.\* The use of the 42-village dataset, assuming the validity of our analysis, as the basis for the quantitative risk analysis should be precluded.

With respect to mode of carcinogenic action from exposure to inorganic arsenic (Charge B3), the panel has made the following comments [page 18]:

The primary genotoxic endpoint produced by both inorganic and organic compounds *in vitro* is chromosomal breakage, most likely mediated by DNA strand breaks resulting from cytotoxicity (Kligerman et al., 2003).

Point mutations occur... only at cytotoxic concentrations (Rossman 2003).

And has concluded [page 19] that:

“If arsenic is essential for humans and/or if epidemiological data could be strengthened at the low-dose range to demonstrate either a low-dose benefit or no effect at low dose, then a threshold is certain.”

We recommend that the new analyses be considered in the light of the statement above.

Cordially,

Steven H. Lamm, MD, DTPH

Arnold Engel, MD, MPH  
on behalf of co-authors

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\* More recent most likelihood estimates have been calculated. Those results are in the appendix below and will be placed into the EHP paper in its printed version. - SHL

Appendix (January 13, 2006):

The MLE analytic results are below in tabular and graphic presentation.

**Cancer SMRs for Township Group 2,4,6**

<u>Cancer</u>	<u>UCL</u>	<u>LCL</u>	<u>MLE</u>
Bladder + Lung (M+F)	196	108	147
Bladder (M + F)	144	31	87
Lung (M + F)	227	130	179
Male (Bladder + Lung)	169	81	118
Female (Bladder + Lung)	262	115	178
Bladder (Male)	113	1	60
Bladder (Female)	229	0	105
Lung (Male)	228	84	150
Lung (Female)	358	155	247

