S. H. Lamm Comments for SAB Arsenic Teleconference (11/22/2010)

To: Science Advisory Board November 22, 2010
US Environmental Protection Agency
Washington, DC 20460

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Thank you for the opportunity to speak briefly on the data analysis in this report. My name is Steven H. Lamm, MD, DTPH. I am a physician-epidemiologist and have been interested in this issue for over fifteen years. I have published research from southwest Taiwan, from Inner Mongolia, and from the United States. I have submitted multiple reports, letters, and analyses to the EPA and the SAB in these proceedings. I speak as an interested and concerned scientist and for no industrial or advocacy group.

There are others here who will discuss with you the issues of linearity vs non-linearity; single study, weight of evidence, or meta-analysis; and process and procedure. One topic of particular interest to me is the comparison of the analytic results from the ecological studies in SW Taiwan and the US, but I will hold that for another day. While all of these topics are important, I will narrow my attention at present to a more limited question that the SAB has asked of the EPA – *What is the dose-response relationship between bladder and lung cancer and arsenic ingestion based on the data from the SW Taiwan study including the SW regional data as a reference population and in the exposure range relevant to the US population?*

There are two major problems in the EPA analysis that we have addressed –

(1) Use of the southwestern Taiwan population as an additional study village (rather than as a reference population) overwhelms the analysis, making it insensitive to the critical low-exposure village data. 98% of information in the analysis is in that single data point. As EPA's own sensitivity analysis (Table 5-10) showed, its inclusion accounts for up to 88% of the estimated risk. This has increased the risk by up to 8 fold.

(2) The data are "dirty" or confounded, both because of exposure misclassification of villages with high arsenic levels (>500 ug/L) as low-dose villages and because of some additional analytic factor variously proposed as fluorescent or humic substance, artesian water source, or Township 3. These issues have been well discussed in the published literature but are uncited in the Toxicological Review or cast off as "arbitrary." See Brown and Chen (1995), Brown (HERA, Jan 2007), and Lamm et al., particularly (EHP, July 2007). Nonetheless, this geographic heterogeneity is clear and its solution should be a target of arsenic research.

The graphs we submitted last week to the SAB showed that both the low-dose villages with high arsenic levels (> 500 ug/L) and those in Township 3 demonstrate the cancer risk behavior of the high dose villages, not that of the low-exposure villages. The bladder cancer risks in the Township 3 and high exposure villages is about 10 times greater than those in the low exposure villages, and the lung cancer risks are about 5 times greater. It is WRONG to include their data in the analysis of the dose-response in the low-exposure villages, as has been done in the Toxicological Report.

We now submit an analogous graph which shows the specific SMRs for the low-exposure villages by township. Again, the cancer risks in Township 3 do not behave like those in the other townships, all of which behave similarly. The bladder cancer mortality is about 10 times greater in the Township 3 low exposure villages than in the other low exposure villages; the lung cancer mortality is 5 times greater; and the bladder and lung cancer mortality is 6 times greater. The proper data set for the low-exposure villages is that of the other four townships and their 27 bladder and lung cancer deaths.

We propose:

(1) that the EPA discuss the heterogeneity in the underlying data and its source;

(2) that the examination for the dose-response for low-level arsenic exposure be conducted on the data from the ten low-exposure villages outside of Township 3;

(3) that the results of that analysis be included in a meta-analysis of data from similar exposure levels in other studies, including that of northeast Taiwan and of the United States;

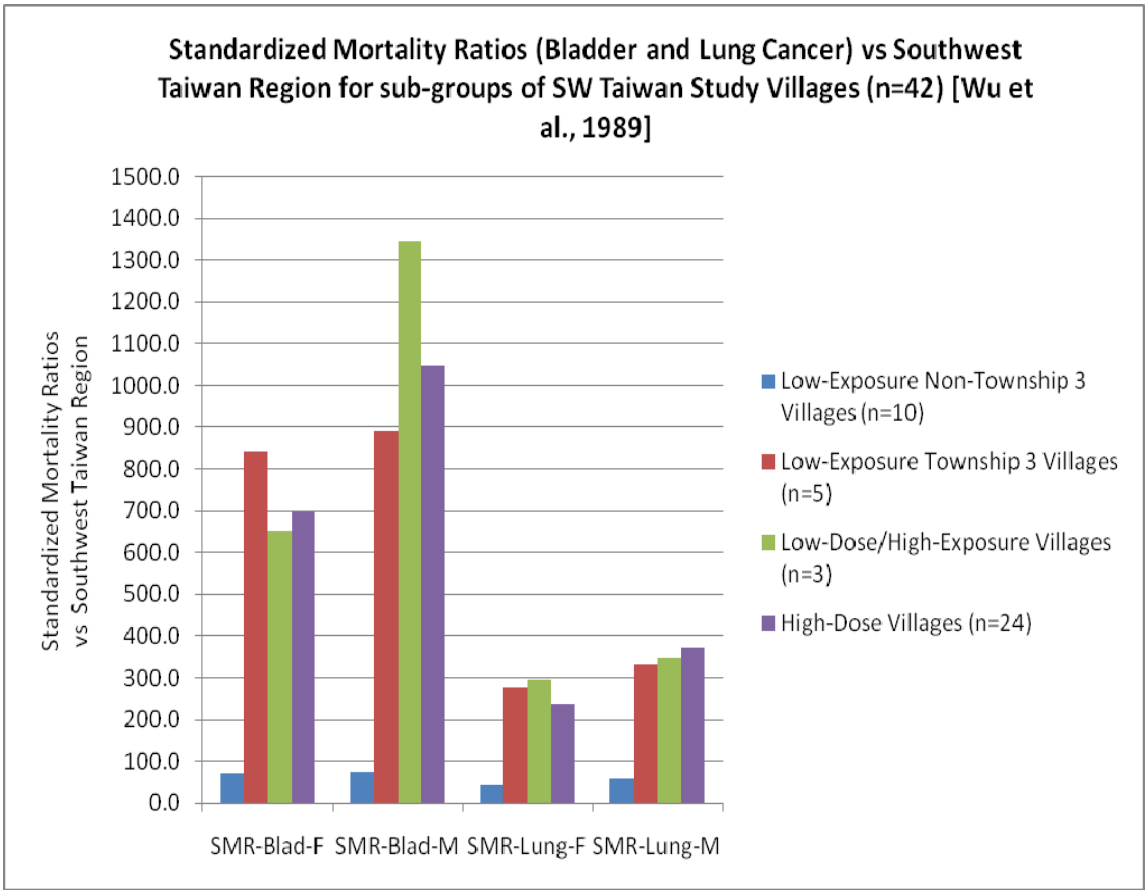
(4) that a "reality check" be conducted to assess the real world likelihood of the validity of the estimate; and

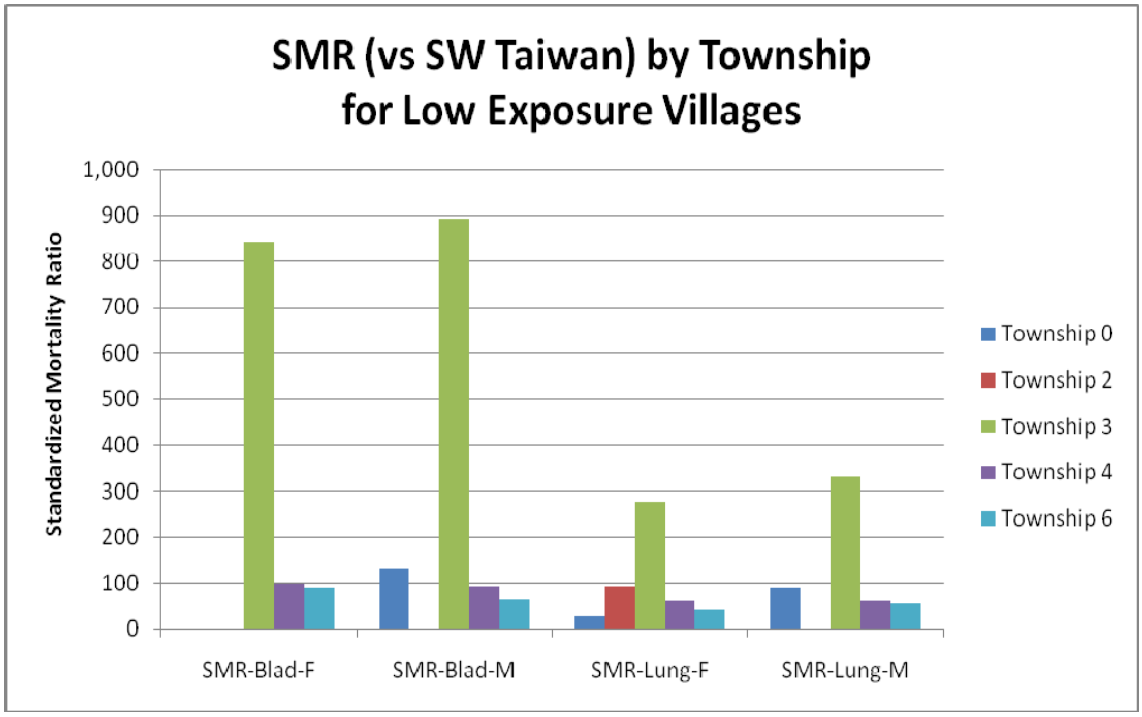
(5) that a research goal should be the ascertaining of the reasons for the geographic heterogeneity in cancer risk in the southwest Taiwan study.

I hope that the panelists will have an opportunity to review those figures as well as the letter from Prof. Wilson prior to concluding their deliberations.

Thank you,

Steven H. Lamm, MD
Jun Lu, PhD
Shayan Robbins, BA


Standardized Mortality Ratios (Bladder and Lung Cancer) vs Southwest Taiwan Region for sub-groups of SW Taiwan Study Villages (n=42) [Wu et al., 1989]
Standardized Mortality Ratios vs Southwest Taiwan Region
1500.0
1400.0
1300.0
1200.0
1100.0
1000.0
900.0
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
SMR-Blad-F
SMR-Blad-M
SMR-Lung-F
SMR-Lung-M
Low-Exposure Non-Township 3 Villages (n=10)
Low-Exposure Township 3 Villages (n=5)
Low-Dose/High-Exposure Villages (n=3)
High-Dose Villages (n=24)


SMR (vs SW Taiwan) by Township for Low Exposure Villages
Standardized Mortality Ratio
1,000
900
800
700
600
500
400
300
200
100
0
SMR-Blad-F
SMR-Blad-M
SMR-Lung-F
SMR-Lung-M
Township 0
Township 2
Township 3
Township 4
Township 6