Miller, Diane M. (CDC/NIOSH/EID)

From:
Sent: Thursday, April 30, 2009 3:34 PM
To: NIOSH Docket Office (CDC)
Cc: Niemeier, Richard W. (CDC/NIOSH/EID)
Subject: NIOSH Docket Number 144
Attachments: Review of NIOSH Hexavalent Chromium Criteria Document Update.doc

Enclosed please find my review of the NIOSH Hexavalent Chromium Criteria Document Update.
<<Review of NIOSH Hexavalent Chromium Criteria Document Update.doc>>

Review of NIOSH Hexavalent Chromium Criteria Document Update

I have carefully reviewed the NIOSH Hexavalent Chromium Criteria Document Update with particular consideration of whether the conclusions and recommendations in the document are scientifically reasonable, appropriately protective, and transparently documented. Overall, I am quite satisfied on all counts. The document is quite well written and appears to be relatively error free. The review of the scientific evidence for the health effects of Cr(VI) is thorough and balanced. The derivation of the REL is adequately supported and clearly described, and I agree with the NIOSH recommendations for protection of workers. Specific comments are provided below.

1. The summary of the risk assessment in Section 7.4.3 needs to be expanded. There are a number of important considerations that are to some extent discussed elsewhere in the document but need to be presented together here in order to provide an appropriate perspective on the REL. These considerations should also be briefly summarized in the introduction, where the REL is first mentioned:

- In the studies on which the REL is based, the average exposures were on the order of 50 micrograms per cubic meter, more that 100-fold higher than the REL. There is strong evidence that at the relatively high concentrations observed in the workplace studies Cr(VI) exposure would be associated with oxidative stress and genotoxicity. However, there are a number of factors that suggest the cellular effects of Cr (VI) are highly dose-dependent, such that carcinogenic potencies observed in these studies would overestimate, perhaps significantly, the potency at the REL.

- The REL is based on studies where the exposure was to soluble forms of Cr(VI). However, there is evidence from animal studies that less soluble Cr(VI) compounds may be more potent than the soluble forms. Therefore the risks at the REL may be higher in different workplace exposures.

- NIOSH estimates that lifetime occupational exposure at the REL would be associated with an increased risk of roughly 1/1000, which is a level of risk consistent with those for other carcinogens in recent OSHA rules. However, until recently OSHA's stated intent was to limit worker risks to 1/10,000, which is more consistent with the lifetime risk for noncancer fatalities in the workplace. Moreover, OSHA's acceptance of 1/1000 risk is driven to a large extent by the regulatory requirement that OSHA balance costs and benefits.

Given the above considerations as a whole, I am comfortable with the REL. However, I am not comfortable with the implication that 1/1000 risk can be justified as a generally reasonable level of protection for the worker. For example, I would be very uncomfortable with a REL for vinyl chloride that was associated with 1/1000 risk, because I believe that the carcinogenic potency of vinyl chloride can be estimated very accurately. In the case of Cr(VI) I am comfortable with the REL because, as I described in the first bullet above, I believe the carcinogenic potency at the REL is greatly over-estimated. My concern is that the criteria document should clearly describe the considerations that factor into the selection of the REL, and should not set a precedent for general acceptance of a 1/1000 lifetime cancer risk increase in workers.

2. I found it difficult to put the epidemiological studies into context because there was often an inadequate characterization of the workplace exposure concentrations. For example, on page 42 of the document I was able to estimate an average exposure concentration of around 43 micrograms per cubic meter for Gibb's Baltimore study only because the average length of employment was given as about 3.3/3.7 years (for whites/non-whites) and the mean cumulative exposure was given as 0.13 and 0.18 micrograms per cubic meter - years. It wasn't until I reached appendix B (NIOSH post-

hearing comments to OSHA) that I was able to verify my estimate (p. B4). Since the effects of Cr(VI) are highly concentration dependent, the mean and range of exposures should be provided for all studies. If exposure concentrations were not measured, this should be stated.

3. It could not find an adequate discussion of the implications of measuring total Cr(VI) exposure rather than inhalable or respirable. My understanding is that all of the standard methods referred to in the document are for total inhaled Cr(VI). The implications of this are that for insoluble Cr(VI) compounds, larger-sized particles that would be deposited in the nasopharynx and swept into the GI tract would be included in the estimate of lung cancer incidence along with the smaller particles that actually reach the lung. This would tend to, in part, offset the fact that the less soluble forms may be more potent than the soluble forms on which the REL is based. Apparently, although it is not clear, DECOS would have preferred using Cr(VI) in inhalable dust (p.95). Was there a rationale for this?

4. Minor comments:

p. 34, line 192: "urinary Cr(VI) levels" should be "urinary Cr levels"

p. p. 37, lines 272-273: This sentence is confusing. 8-OHdG excretion in urine could not possibly be induced by Cr(VI) exposure *in vitro*. It appears that Gao is not an *in vitro* study.

p.73, line 57: Liu et el. 1997 a or b?

p. 74, line 72: "Tsapakos 1983a" should be "Tsapakos and Wetterhahn 1983"

p. 93, lines 134-137. I found this sentence confusing. Does it mean that, if there is a threshold, it is likely to be below 16/29 micrograms per cubic meter?

5. Opinion regarding Action Levels: I agree with the new NIOSH policy to provide general exposure assessment recommendations instead of specific action levels. I believe action levels are better determined on a workplace-specific basis, considering the variability of exposures, monitoring methods, etc., in order to assure protection of the worker at the level of the REL.