

Author's response to reviews

Title: Selected science: A case study of an industry campaign to undermine an OSHA hexavalent chromium standard

Authors:

David Michaels (eo hdmm@gwumc.edu)
Celeste Monforton (eo hcnm@gwumc.edu)
Peter Lurie (plurie@citizen.org)

Version: 4 **Date:** 8 February 2006

Author's response to reviews: see over

Point-by-point response to Editor's comments and summary of changes:

It is of paramount importance that your manuscript is in strict accordance with our instructions for authors, cf. the pre-acceptance checklist at <http://www.biomedcentral.com/info/edgr-preacceptcheck.asp> The revised manuscript needs to be in accordance with the instructions before it is being considered further.

-We have reviewed the pre-acceptance checklist carefully and tried to comply with all of the instructions.

The abstract must follow EH instructions.

-Our article, and thus our abstract, does not follow the traditional “background, methods, results, conclusion” format. We note that some of the articles published in EH journal do not follow this typical format. (E.g., O’Neill, Richards, et al.: 2005, 4:21; Broughton: 2005, 4:6; Vogel JM: 2005, 4:2.) We hope the editors will consider publishing our abstract without these mandatory four sections.

Pages in references need to be the full number (i.e., 213-218, not 213-8). Refs 4, 10, 34, 43-49, 53-59, 62 and 63 are not formatted correctly.

-All page numbers in references now include the full number (i.e., 213-218, not 213-8).

-Ref 4 and Ref 10 have been corrected to conform to the formatting instructions.

-The other references mentioned (now renumbered) are atypical sources (i.e., not journal articles or books) and using the on-line resources recommended by the editor, we have not been able to identify a reference style for these types of sources. We are happy to format them in any way (and as promptly as possible) as soon as we receive guidance.

Please add the issue number for reference 8.

-The issue number (i.e., issue 6, plain text, not bold) has been added to reference #8.

There needs to be a space between ref 12 and ref 13.

-A space was added between reference 12 and 13.

There may still be a problem with refs 18 and 19, and we will need to ask BMC about possible revision when the paper is accepted.

-Ref 18 now has 18869 after the term “Federal Register,” indicating the correct page number.

-Ref 19 now has a link to a PDF version of the document.

-We will continue to wait for further instructions from the editors or BMC on the proper formatting of Ref 18 and Ref 19.

Refs 30-32 should be formatted according to the instructions for additional files and not listed as refs.

-Ref 24, Ref 25, Ref 30, Ref 31 and Ref 56 have been deleted. They are additional files and have been formatted in the document accordingly. The remaining references have been renumbered appropriately.

There needs to be a space between ref 33 and 34.

-A space was added between references 33 and 34.

Please go through the entire ref list and reformat according to EH instructions at <http://www.ehjournal.net/info/instructions/>

-We have reviewed all the on-line resources provided at <http://www.ehjournal.net/info/instructions/>, but we do not see a reference style that fits the nontraditional sources used in our article (e.g., a letter sent from a trade association to a federal agency and now available through OSHA's on-line docket (through an http:address.) If appropriate, we will use the "Web links and URLs" style. These documents do not have formal titles, however, and we did not want to format them using this style, if that is not the appropriate BMC style. We are happy to format them in any way as soon as we receive the necessary guidance.

Table 1 should be two separate tables so that it will fit on the portrait format, please adjust text references accordingly.

-We have created two separate tables to display this information and adjusted the text references accordingly. We also re-titled the tables.

Page 10 - "[W]hile we have not had any..." If this is a quote, it should be in quotes, not with the bracket on the W.

-We've corrected this to read "while we have not had any..."

Response to Comments provided by Sverre Langard:

In Nordic countries the TLVs were reduced to about 1/5 of the current US TLV level already in the 1980s. Those reductions were based on scientific evidence present already 25 years ago. It is puzzling that some Western countries have not lowered their extremely high TLVs for CrVI exposure.

Our paper makes a similar point: that strong scientific evidence supporting the lowering of the standard for occupational exposure to CR(VI) has been available for many years. The paper addresses activities of the chromium industry undertaken over the last ten years to prevent a strengthening of the US OSHA standard.

There are obvious mistakes like on p. 6, where the authors refer to a meeting in 1996 and further saying that " - - the industry commissioned new studies - - that questioned the health effects of low levels of exposure to CrVI (26-29)" where ref. 26 is from 1994.

--We have deleted reference 26 from the manuscript, renumbered the references accordingly, and modified the sentence.

On p. 11 the authors have derived air levels by dividing the urinary levels by an arbitrary conversion factor of 0.77, and from that come up with rate ratios (that they call "odds ratios" of 22 at an annual level of 5.8 µg CrVI/m³, and an RR of 4.9 for estimated levels ranging 1.2-5.8 µg CrVI/m³. Rate ratios for lung cancer at 20+ were certainly seen among workers exposed at mg-levels in the 1950s, 1960s and 1970s, figures two orders of magnitude higher than 5.8 µg CrVI/m³+. To come up with such high rate ratios at these assumed (calculated) exposure levels, there must be something wrong with the applied conversion factor.

The conversion factor used in the analysis was not selected arbitrarily. It is the conversion factor selected by the authors of the original study to allow the combining of urine and air measurements. This is how it is presented on page 52 of the Applied Epidemiology study:

“Our search for an alternative to an empirically derived conversion factor resulted in an exposure equivalent for carcinogenic substances (EKA) published by the Deutsche Forschungsgemeinschaft.¹ This factor was used to convert air data for the U.S. plants to urinary equivalents ... Although the EKA is based on data from at least one of the German plants in the current study, we considered this conversion factor a reasonable alternative because it is the only one available in the literature that pertains to chronic exposure scenarios. This conversion factor (0.77) was slightly smaller than the overall ratio of urine data to air data that we calculated for each plant (0.92 for Uerdingen and 0.85 for Leverkusen). Ultimately we chose to use this published value rather than our own derived value(s) mainly because the agreement, or correlation between the air and

¹ Deutsche Forschungsgemeinschaft. Alkali chromates (Cr(VI)). In: Henschler D, Lehnert G, eds. Biological exposure values for occupational toxicants and carcinogens: critical data evaluation for BAT and EKA values. Weinheim, Germany: VCH Verlagsgesellschaft, 1994; 187-203.

urinary values in our data was very poor, and the estimates we derived were not very different from this published value.”

The odds ratios we present may be considered rate ratios but they were reported in the two studies under discussion as odds ratios, and we wanted to report them exactly as reported in the original study.

The only change we have made is to transform the categories selected by the authors of the original study into those used by US OSHA for risk assessment. OSHA assumes that a worker may have an exposure of 45 years, so we calculate a risk estimate for a population that shares a 45 year lifetime work history at a selected average exposure level. This calculation requires first transforming a cumulative exposure level to an average exposure level; for example, a cumulative exposure level of 450 ug/m^3 , which may have been accumulated over 15 years at an average annual exposure 30 ug/m^3 , is transformed in the OSHA risk assessment model to an average exposure of 10 ug/m^3 a year for 45 years.

While these risk estimates may seem high, we are accurately reporting what was found in the study (see table 18, page 108 of the Applied Epidemiology Study, available at <http://dockets.osha.gov/vg001/V047A/05/55/31.PDF>). Reproduced below is salient portion of the table (changed only to correct an error in the table – the report listed the categories in ug/m^3 , but it is clear that they meant to use ug/L – see, for example, page 68):

Cumulative Exposure	Odds Ratio	95% Confidence Interval
Low (<40 ug/L)	ref	
Intermediate (40 ug/L - 200 ug/L)	4.9	1.5-16.0
High (>200 ug/L)	20.2	6.2-65.4

We did choose not to present smoking adjusted ORs, which were slightly lower, because smoking adjusted ORs were not reported in the comparison study (Birk et al, in press). We have re-titled the tables so that the difference between the two is more easily understood.

Based on strong epi-data from 1950s-1970s there is no logic connection between the author's exposure extrapolations and outcome rate ratios (Table 1) and extrapolation from the dose-response curves that can be derived from many of the high exposure studies in the early period (1950s-1970s).

The ORs reported in this study are higher than the risk estimates in some of the papers to which the reviewer is probably referring. The SMRs in the present study are consistent with those of Gibb (new reference 30) and much of the other literature on occupational exposure to Cr(VI). In comparison with SMRs, based on comparisons with standardized populations, these odds ratios were calculated using logistic regression with the referent being the lowest exposure category. This study has relatively few lung cancers, and it is possible that the low risk of lung cancer in the referent group has driven up the odds ratios in the high and intermediate group. In our paper, we are reporting the results found in the original study.

None of these concerns, however, question the basic findings of this paper: that the original study was hidden from a regulatory agency that was actively asking for such studies, and that the eventual reporting of the study was done in a way in which an important finding, elevated risk at the intermediate exposure level, was obscured.