# Disappearance of Elevated Risk of Lung Cancer in Workers Exposed to Chromium [Cr(VI)] at Levels Slightly Above Proposed OSHA PEL (After Splitting Multi-Plant Study into Separate Components)

**Reported Lung Cancer Odds Ratios in Combined Four-Plant Study[†]**

| Mean Exposure to Cr(VI)* | OR | 95% CI |
|---|---|---|
| Low (< 1.2 $ug/m^3$) | Ref | -- |
| Intermediate (1.2 - <5.8 $ug/m^3$) | 4.9 | 1.5 - 16.0 |
| High (≥ 5.8 $ug/m^3$) | 20.2 | 6.2 - 65.4 |

**Reported Lung Cancer Odds Ratio in German Component of the Four-Plant Study[‡]**

| Mean Exposure to Cr(VI)* | OR | 95% CI |
|---|---|---|
| Low and Intermediate (<5.8 $ug/m^3$) | Ref | -- |
| High (≥ 5.8 $ug/m^3$) | 6.9 | 2.6 – 18.2 |

*Mean Exposure to Cr(VI) derived by dividing cumulative urinary chromium exposure by 0.77 (conversion factor for air concentration), and then dividing by 45 years (OSHA's working life assumption).

[†]Adapted from Table 17 in: Final report: Collaborative cohort mortality study of four chromate production facilities, 1958-1998. Submitted by Applied Epidemiology, Inc. to the Industrial Health Foundation, September 27, 2002; Docket H054A, Exhibit 48-1-2.

[‡]Adapted from Birk T, Mundt KA, Dell LD, et al: Lung cancer mortality in the German chromate industry, 1958-1998. *J Occup Environ Med* (in press) Docket H054A, Exhibit 48-4.

# Hexavalent chromium study's conclusions unjustified (HRG Publication #1755)

**This Letter to the Editor appeared in the October 10, 2005 issue of the Journal of Occupational and Environmental Medicine**

To the Editor: Luippold et al [1] assert that their study of hexavalent chromium, a known lung carcinogen, demonstrates an "absence of an elevated lung cancer risk" in workplaces in which hexavalent chromium exposures had been reduced by changes in production processes. Their data do not support this conclusion for the following three reasons.

First, the impact of the well known selection bias known as the "healthy worker effect" on the results of lifetable analyses is readily apparent in this study. The magnitude of this bias can be assessed by the proximity of the standardized mortality ratio (SMR) for "all cause" mortality to 1.00. In the Luippold study, the SMR for all causes combined is 0.59 (95% confidence interval _ 0.39–0.85), as it is for deaths from heart disease, the largest subcategory. This powerful bias would mask anything but a very large increase in lung cancer risk.

Second, the length of follow-up in this study is too short to permit meaningful conclusions. Not a single worker in Plant 2 had been followed for more than 18 years (the average length of follow-up was 10 years), and 40% of the Plant 1 population had been followed for fewer than 10 years. Because, as the authors themselves state, "the average latency for lung cancer may be longer than 20 years," this study would be extremely unlikely to detect a real increased risk of lung cancer.

Finally, this study is very small, with a total of 27 observed deaths from all causes. Given that the expected number of lung cancer deaths is a paltry 3.75, the chromium exposure would have to more than double the risk of lung cancer, and nine lung cancer deaths would have had to have been observed before the SMR would have reached a level of statistical significance based on the Poisson distribution (SMR 2.4; P _ 0.05). But even in the Gibb study, the most robust study of hexavalent chromium carcinogenicity, the SMR in the highest exposure group, in which exposures were approximately 15 times greater than the present study, was only 2.24 (95% confidence interval: 1.60–3.03). [2] Because the Luippold study could not have detected an increase in lung cancer even at the highest exposure level in the Gibb study, it is obviously statistically underpowered to detect any increase in cancer at lower exposure levels.

In summary, the conclusions promoted by the authors of this study are not supported by their data. The Occupational Safety and Health Administration currently is promulgating a new hexavalent chromium exposure standard. [3] Several industry groups [4] cited the Luippold study in their comments opposing the OSHA proposal, although it provides essentially no useful information in understanding the lung cancer risk associated with hexavalent chromium exposure.

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**References**

1. Luippold RS, Mundt KA, Dell LD, Birk T. Low level hexavalent chromium exposure and rate of morality among US chromate production employees. J Occup Enviorn Med. 2005;47:381-385.

2. Gibb HJ, Lees PSJ, Pinsky PF, Rooney BC. Lung cancer among workers in chromium chemical production. Am J

Ind Med. 2000;38:115-126.

3. Occupational Safety and Health Administration, US Department of Labor. Occupational Exposure to Hexavalent Chromium. 69 Federal Register, October 4, 2004, 59306-474.

4. The Society of the Plastics Industry, Inc. Post-hearing comments, (Docket H054A Exhibit #47-24-1), April 20, 2005; Collier Shannon Scott on behalf of the Specialty Steel Industry, Exhibit #47-27-1, April 20, 2005; Surface Finishing Industry Council, comments prepared by The Policy Group, (Exhibit #47-35-1), April 20, 2005.

concentration (Ex. 35–156). Nasal septum atrophy, a condition that can progress to ulceration and perforation, was observed less frequently among workers with 8-hour mean exposure concentrations less than 2 μg/m³ and those with peak exposures less than 20 μg/m³ than among workers exposed to higher concentrations. It is not clear whether workers who had nasal septum atrophy at these exposure levels eventually developed ulcerations or perforations. Although Lindberg and Hedenstierna's results suggest increasing risk of nasal septum damage with increasing exposure concentrations, there are considerable uncertainties associated with the cross-sectional study design and the possible contribution of hand-to-nose transfer of Cr(VI) to the observed nasal effects.

*C. Significance of Risk and Risk Reduction*

The Supreme Court's benzene decision of 1980 states that "before he can promulgate any permanent health or safety standard, the Secretary [of Labor] is required to make a threshold finding that a place of employment is unsafe—in the sense that significant risks are present and can be eliminated or lessened by a change in practices" (*IUD* v. *API,* 448 U.S. at 642). The Court broadly describes the range of risks OSHA might determine to be significant:

> It is the Agency's responsibility to determine in the first instance what it considers to be a "significant" risk. Some risks are plainly acceptable and others are plainly unacceptable. If, for example, the odds are one in a billion that a person will die from cancer by taking a drink of chlorinated water, the risk clearly could not be considered significant. On the other hand, if the odds are one in a thousand that regular inhalation of gasoline vapors that are 2 percent benzene will be fatal, a reasonable person might well consider the risk significant and take the appropriate steps to decrease or eliminate it. (*IUD* v. *API,*448 U.S. at 655).

The Court further stated, "The requirement that a 'significant' risk be identified is not a mathematical straitjacket * * *. Although the Agency has no duty to calculate the exact probability of harm, it does have an obligation to find that a significant risk is present before it can characterize a place of employment as 'unsafe' and proceed to promulgate a regulation." (*IUD* v. *API,*448 U.S. at 655).

Table VIII–1 presents the estimated excess risk of lung cancer associated with various levels of Cr(VI) exposure allowed under the current rule, based on OSHA's risk assessment and assuming either 20 years' or 45 years' occupational exposure to Cr(VI) as indicated. The purpose of the OSH Act, as stated in Section 6(b), is to ensure "that no employee will suffer material impairment of health or functional capacity even if such employee has regular exposure to the hazard * * * for the period of his working life." 29 U.S.C. 655(b)(5). Taking a 45-year working life from age 20 to age 65, as OSHA has done in significant risk determinations for previous standards, the Agency preliminarily finds an excess lung cancer risk of approximately 100 to 350 per 1000 workers exposed at the current PEL of 52 μg/m³ Cr(VI). This risk is clearly significant, falling well above the level of risk the Supreme Court indicated a reasonable person might consider acceptable. Even assuming only a 20-year working life, the excess risk of about 50 to 200 per 1000 workers is still clearly significant. The proposed PEL of 1 μg/m³ Cr(VI) is expected to reduce these risks substantially, to below 10 excess lung cancers per 1000 workers. However, even at the proposed PEL, the risk posed to workers with a lifetime of regular exposure is still clearly significant.

**Table VIII–1.—Expected Excess Lung Cancer Deaths Per 1000 Workers**

| | *Cr(VI) concentratin, μg/m³* | *20-year exposure* | *45-year exposure* |
|---|---|---|---|
| Current PEL | 52 | 43–198 | 101–351 |
| | 20 | 17–83 | 41–164 |
| | 10 | 9–43 | 21–86 |
| | 5.0 | 4.3–22 | 10–45 |
| | 2.5 | 2.1–11 | 5.3–23 |
| Proposed PEL | 1.0 | 0.85–4.4 | 2.1–9.1 |
| | 0.5 | 0.43–2.2 | 1.1–4.6 |
| | 0.25 | 0.21–1.1 | 0.53–2.3 |

Workers exposed to lower concentrations of Cr(VI) and for shorter periods of time may also have significant excess cancer risk. OSHA's estimates of risk are therefore proportional to concentration for any given exposure duration; for example, workers exposed for 20 years to 10 μg/m³ Cr(VI) have about ten times the risk of workers exposed for 20 years to 1 μg/m³ Cr(VI). The Agency's risk estimates are also roughly proportional to duration for any given exposure concentration, but not exactly proportional due to competing mortality effects. The estimated risk to workers exposed at any fixed concentration for 10 years is about one-half the risk to workers exposed for 20 years; the risk for five years' exposure is about one-fourth the risk for 20 years. For example, about 11 to 55 out of 1000 workers exposed at the current PEL for five years are expected to die from lung cancer as a result of their exposure. Those exposed to 5 μg/m³ Cr(VI) for 5 years have an estimated excess risk of 1–6 lung cancer deaths per 1000 workers. It is thus not only workers exposed for many years at high levels who have significant cancer risk under the current standard; even workers exposed for shorter periods at levels below the current PEL are at substantial risk, and will benefit from implementation of the proposed PEL.

To further demonstrate significant risk, OSHA compares the risk from currently permissible Cr(VI) exposures to risks found across a broad variety of occupations. The Agency has used similar occupational risk comparisons in the significant risk determination for substance-specific standards promulgated since the benzene decision. This approach is supported by evidence in the legislative record that Congress intended the Agency to regulate unacceptably severe occupational hazards, and not "to establish a utopia free from any hazards"(116 Cong. Rec. 37614 (1970), Leg. Hist 480), or to address risks comparable to those that exist in virtually any occupation or workplace. It is also consistent with Section 6(g) of the OSH Act, which states: "In

# Comments on OSHA's Proposed Rule on hexavalent chromium (HRG Publication #1717)

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Docket Office
Docket H054A
Room N-2625
Occupational Safety and Health Administration
U.S. Department of Labor
200 Constitution Ave, NW
Washington, DC 20210

To whom it may concern:

Public Citizen's Health Research Group submits the following comments on the Occupational Safety and Health Administration's (OSHA's) Proposed Rule on hexavalent chromium.[1] This rulemaking would not be taking place at all were it not for a successful lawsuit filed in March 2002 by Public Citizen and the Paper, Allied-Industrial, Chemical and Energy Workers International Union (PACE). We look forward to seeing this rulemaking completed, its content improved in the ways set forth below, and the regulation speedily enacted, lest thousands more workers suffer preventable death from lung cancer due to exposure to hexavalent chromium.

*OSHA's Risk Assessment*

The essential basis for the risk assessment put forth by OSHA is the decision to place heavy and equal emphasis on just two studies: the Gibb[2] and Luippold[3] studies. Both studies find markedly elevated risks of lung cancer among hexavalent chromium-exposed workers and, as discussed below, find dose-response relationships well characterized by linear models. Both followed their subjects for an average of 30 years. However, their results are quite different. The Gibb study generates maximum likelihood estimates of excess lung cancer risk that are three to five times higher than those produced by the Luippold study at equivalent levels of cumulative hexavalent chromium exposure. The confidence intervals for the two studies do not overlap, which OSHA characterizes as "statistical inconsistency."[4] Nonetheless, by using the maximum likelihood estimates from the two studies as the range for its risk assessment, the agency has effectively chosen to weigh the studies equally.

Yet the two studies do not merit equal weighting. As the table below illustrates, in almost every respect the Gibb study is superior to the Luippold study.

| | **Gibb Study** | **Luippold Study** |
|---|---|---|
| Workers | 2,357 | 482 |
| Person-years of follow-up | 70,736 | 14,048 |
| Loss to follow-up | 0% | 10% |
| Lung cancer deaths | 122 | 51 |
| Exposure data collection | Routine | Industrial hygiene surveys |
| Exposure measurements | ~70,000 | >800 |
| Includes low exposures? | Yes | No |
| Smoking assessment | 93% of cohort | 35% of cohort |

The Gibb study has five times more workers and person-years of follow-up, 2.4 times as many lung cancer deaths, much better smoking data and over 80 times as many exposure measurements, and these were more randomly obtained than in the Luippold study.

Moreover, the Luippold study has inconsistent inclusion criteria, excluding certain workers who later worked at other chromate plants, but including an unknown number who worked at another chromate plant, because exposure data were available. Although the Gibb study had many short-term workers, a fact played up repeatedly by the industry, when the industry consultant Exponent reanalyzed the Gibb data to exclude the short-term workers, it found little impact on the dose-response relationship described by the full cohort. The remaining studies cited by OSHA are still weaker, with little or no smoking data, limited follow-up and exposure assessments that are

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