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Sent: Friday, December 30, 2011 8:35 PM
To: NIOSH Docket Office (CDC)
Subject: NIOSH Carcinogen and REL Policy Comments Docket # NIOSH-240
Attachments: NIOSH REL Policy RFI 12 2011.docx

My comments are attached.

Thank you for the opportunity to provide feedback.

Sincerely,

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December 30, 2011

John Howard, Director
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Submitted by e-mail to: nioshdocket@cdc.gov

RE: Docket Number NIOSH-240
Request for Information: Announcement of Carcinogen and Recommended
Exposure Limit (REL) Policy Assessment

Dear Dr. Howard:

Thank you for the opportunity to comment on revisions to the NIOSH Carcinogen and REL Policy. I congratulate you for undertaking this important initiative. NIOSH's role in recommending protective and science-based exposure limits to OSHA is essential to preventing occupational illnesses and diseases from chemical exposures.

To ensure that NIOSH recommendations for workplace exposure limits are timely, consistent, and derived in a transparent manner, scientific guidance should accompany or be included in the Carcinogen and REL Policy. Such guidance is needed since NIOSH's priorities for identifying toxicants for REL development are not obvious (e.g., there are no RELs for established toxicants of concern such as 1-bromopropane and N-methylpyrrolidone), and the scientific basis for many of the existing NIOSH RELs is unclear. The scientific guidance should describe the methodology NIOSH will use to identify and characterize chemical hazards and to derive RELs. OSHA could use the scientific guidance to improve the efficiency of the PEL-setting process. In a report (US GAO 2001), the US General Accounting Office concluded that unlike EPA and some other federal agencies, OSHA had no formal risk assessment guidance. Instead, the report stated, OSHA has primarily described its general risk assessment methods, as well as the rationale for specific models and assumptions selected, in the record of each risk assessment and regulatory action.

To save time and resources, NIOSH should use existing risk assessment guidance developed by US EPA as a template for developing scientific guidance for deriving RELs. In general, the EPA risk assessment guidance is consistent with the methodology NIOSH has used to develop recent RELs for refractory ceramic fibers and titanium dioxide, and with OSHA's methodology for deriving health-based exposure limits for carcinogens, including methylene chloride (OSHA 1997) and for glycol ethers (OSHA 1993). A 2007 California EPA report (prepared for the Occupational Health Branch of the California Department of Public Health) describes how existing EPA and California

EPA risk assessment methods and data, with adjustments to account for occupational exposures, can be used to derive protective occupational exposure limits for chemical substances (OEHHA 2007).

My responses to the questions posed by NIOSH in the Federal Register (76 FR 52664) are detailed below.

(1) *Should there explicitly be a carcinogen policy as opposed to a broader policy on toxicant identification and classification (e.g., carcinogens, reproductive hazards, neurotoxic agents?)*

There should be a broader policy on toxicant identification and classification for several reasons, including the following:

- ◆ A broader toxicant policy is consistent with NIOSH's 1995 REL Policy, and is the only way for NIOSH to be responsive to Section 20(a)(3) of the 1970 OSH Act. On a daily basis, workers are exposed to asthmagens, neurotoxicants, endocrine disruptors, and reproductive and developmental toxicants that have not been adequately identified and do not have protective exposure limits. Limiting the policy to carcinogens will leave workers at high risk for suffering impaired health from exposure to these toxicants.
- ◆ Timely identification of emerging toxicants like endocrine disruptors requires a broader toxicant policy. It allows NIOSH to keep pace with advances in science and with protections afforded to consumers and the general public. For example, it would help to ensure that the REL for a dibutyl phthalate (DBP) is based on developmental and male and female reproductive toxicity, instead of irritation. This is especially important since a pilot biomonitoring study conducted by NIOSH (Hines et al. 2009) showed that DBP levels in some manufacturing workers were 25 times higher than NHANES or general population levels.
- ◆ Some carcinogens, like lead and 1-bromopropane, have multiple toxicities that a carcinogen-only policy would not address. The developmental toxicity of lead and 1-bromopropane for example, of great concern regarding exposure of pregnant workers, would not be identified. In the some cases, as with lead, cancer may not be the most sensitive endpoint, so developing a REL based on cancer would not protect against other important health effects.
- ◆ A broader toxicant policy would help to ensure that NIOSH RELs for carcinogens and non-carcinogens are derived using consistent and transparent scientific methods. Some NIOSH designated carcinogens have numerical RELs, while the RELs for others are "lowest feasible concentrations". Quantitative risk assessment, qualitative assessments of data, and limits of detection were used to derive RELs for some of the carcinogens. For other carcinogens the methods used to derive the RELs are unclear; the RELs are the same as American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), which are based on non-cancer health effects. The method NIOSH uses to derive RELs for reproductive/developmental

toxicants and other toxicants does not appear to be based on quantitative risk assessment, and is also unclear.

(2) *What evidence should form the basis for determining that substances are carcinogens? How should these criteria correspond to nomenclature and categorization (e.g., known, reasonably anticipated, etc.)?*

Evidence consistent with that used by the National Toxicology Program (NTP) and the International Agency for Research on Cancer (IARC) should be used to determine that substances are carcinogenic. This means that evidence will be derived from:

- ◆ Cancer studies in humans
- ◆ Cancer studies in experimental animals
- ◆ Mechanistic and other relevant data

These criteria should correspond to the following nomenclature and categorization used by IARC. The IARC methodology integrates the human and non-human evidence streams into multiple categories related to human cancer, and uses mechanistic and relevant information, if warranted, to upgrade the evidence and to assign a substance to a higher evidence category. The multiple categories of evidence make maximum use of the available cancer data and help to facilitate risk communication and risk management activities. It also maximizes the use of mechanistic and other relevant data, which will become a significant part of the cancer dataset as the results of *in vitro* toxicology studies become more established and available in the future.

- ◆ Group 1 *Carcinogenic* to humans
- ◆ Group 2A *Probably carcinogenic* to humans
- ◆ Group 2B *Possibly carcinogenic* to humans
- ◆ Group 3 *Not classifiable* as to its carcinogenicity to humans
- ◆ Group 4 *Probably not carcinogenic* to humans

(3) *Should 1 in 1,000 working lifetime risk (for persons occupationally exposed) be the target level for a recommended exposure limit (REL) for carcinogens or should lower targets be considered?*

A 1 in 1,000 working lifetime risk should not be the target level for a REL for carcinogens. Lower targets should be considered for many reasons, including the following:

- ◆ A 1/1000 lifetime cancer risk is an unacceptably high risk, particularly since workers often are exposed to multiple carcinogens simultaneously during their working lifetimes, and some environmental agencies set targets of 1/100,000 to 1/1,000,000 lifetime cancer risks for non-occupational exposures to the same chemicals.

- ◆ NIOSH's charge, in part, is to "describe exposure levels at which no employee will suffer impaired health or functional capacities or diminished life expectancy as a result of his (or her) work experiences". The working lifetime cancer risk that is an appropriate target for RELs should be based on reasonable and maximal protections against workers developing occupational cancer. It should not be based on the 1/1000 lifetime cancer risk that OSHA has established as being "significant" in response to the 1980 Benzene Decision. In lieu of setting a policy that a specific working lifetime cancer risk will be the target level for RELs, NIOSH can derive and propose to OSHA, different RELs that correspond to a range of lifetime cancer risks (e.g., 1/100,000, 1/20,000, etc.).
- ◆ Lower targets would comply with the Supreme Court's 1980 Benzene Decision. Although OSHA has adopted a one in a thousand lifetime cancer risk as "significant" based on the Benzene Decision, it actually represents the uppermost end of a million-fold range that was suggested by the Court. The Court stated that a one in a billion risk of incurring health damage may not be considered significant but a one in a thousand risk would be considered significant. Consistent with that statement, OSHA could have adopted as "significant", targets similar to those set by environmental agencies of one in a million or one in a hundred thousand lifetime cancer risks, or targets substantially below one in a thousand.
- ◆ OSHA's experience of setting a target of one in a thousand for lifetime cancer risks for health-based exposure limits emphasizes the need to set lower targets for RELs. The PELs for recently regulated carcinogens have unacceptably high working lifetime cancer risks as shown by the following examples.
 - Hexavalent chromium = 10-45/1000
 - Asbestos = 6.7/1000
 - Methylene chloride = 3.6/1000
 - Benzene = 10/1000
 - Cadmium = 3-15/1000

(4) *In establishing NIOSH RELs, how should the phrase "to the extent feasible" (defined in the 1995 NIOSH Recommended Exposure Limit Policy) be interpreted and applied?*

"To the extent feasible" should be interpreted as meaning that to the extent data and /or resources permit, NIOSH will derive RELs for non-carcinogens (or non-threshold toxicants) based on No Observed Adverse Effect Levels or NOAELs, and will project the residual risks or hazard index at other exposure levels if the RELs are not based on NOAELs. In the revised policy, NIOSH RELs should be health-based, only. NIOSH RELs should not be based on feasibility.

The phrase should not be interpreted to mean that NIOSH should derive RELS based on feasibility. NIOSH's charge, as indicated above, is to provide health-based recommendations to OSHA. OSHA addresses feasibility as a component of the PEL-development process. NIOSH activities, if any, related to feasibility of exposure limits should be conducted separately from the development of health-based RELs.

The statement in the 1995 REL Policy regarding the development of RELs based on "what can be achieved by engineering controls and measured by analytical techniques" is outdated and should not be applied to the revised NIOSH REL policy. With the advent of green chemistry and development of safer chemical alternatives, the emphasis has shifted from controlling chemical hazards using engineering controls to eliminating hazardous chemicals. As a result, "feasibility" in terms of achieving exposure limits is assessed differently than it was in 1995. A consideration of available safer alternatives should be an essential component of any exposure limit feasibility determination. Assessments of feasibility related to analytical measurements have also changed due to significant advances in analytical chemistry.

(5) (a) *In the absence of data, what uncertainties or assumptions are appropriate for use in the development of RELs? (b) What is the utility of a standard "action level" (i.e., an exposure limit set below the REL typically used to trigger risk management actions) and how should it be set? (c) How should NIOSH address worker exposure to complex mixtures?*

(a) **The uncertainties and assumptions used by EPA and California EPA and described in their respective risk assessment guidelines are appropriate to use in developing RELs. Adjustments for occupational exposures can be made, if needed.**

For example, in developing RELs for carcinogens, in the absence of definitive data to the contrary, a no-threshold mechanism is assumed. For non-carcinogens, in the absence of human data, animal data are used and an uncertainty factor of 10 is applied based on the assumption that humans are more sensitive than experimental animals. The assumptions regarding developmental effects that OSHA used in the glycol ethers risk assessment are also appropriate to use in developing RELs (OSHA 1993).

(b) **Action levels can capture short-term exposures that may be harmful, and that may not be apparent in an 8-hour TWA measurement. This can be especially important for exposures to developmental toxicants and other toxicants where short, high exposures are of concern.**

Action levels are also useful because they can capture task-related exposures and don't require monitoring over an 8-hour period, which can be resource and time prohibitive. The recent air monitoring of formaldehyde exposures in hair salons which showed overexposure to the formaldehyde Action Level is an example of the utility of Action Levels. An integrated assessment, which includes the physical and chemical properties, the potential adverse health effects, and the potential for exposure of a substance, could be used to set Action Levels.

(c) **To develop RELs for complex chemical mixtures, NIOSH should consult with other agencies such as EPA and the European Union that are determining how to address health risks from multiple chemicals and other exposures.**

The EPA report, *Concepts, Methods, and Data Sources for Cumulative Health Risk Assessment of Multiple Chemicals, Exposures and Effects: A Resource Document* (2008) has information on technical approaches for assessing human health risks associated with multiple chemicals, exposures, and effects.

A European Union Workshop on the State of the Art Report on Mixture Toxicity held in June 2010 was convened to discuss a report from contractors on mixture toxicity and to provide feedback to the EU Commission on what could/should be done to address mixture toxicity. One of the ten conclusions of the Chair was that the EU had sufficient information to develop technical guidelines for the assessment of mixture toxicity, which could be applied across the different pieces of EU legislation.

References

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Occupational Safety and Health Administration (OSHA). 1993. Occupational exposure to 2-methoxyethanol, 2-ethoxyethanol and their acetates (glycol ethers). *Federal Register* 54:15526-15632.

Office of Environmental Health Hazard Assessment (OEHHA). 2007. Occupational health hazard risk assessment project for California: Identification of chemicals of concern, possible risk assessment methods, and examples of health protective occupational air concentrations.

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Hines et al., *Ann. Occup. Hyg.*, Vol. 53 2009

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