National Institute for Occupational Safety and Health

NIOSH **Comments to OSHA**

Comments of the National Institute for Occupational Safety and Health on the Occupational Safety and Health Administration Request for Information Chemical Management and Permissible Exposure Limits (PELs)

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Centers for Disease Control and Prevention
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The National Institute for Occupational Safety and Health (NIOSH) has reviewed the Occupational Safety and Health Administration (OSHA) Request for Information (RFI) *Chemical Management and Permissible Exposure Limits (PELs); Proposed Rule* published in the *Federal Register* (FR) on October 10, 2014 [79 FR 61384]. NIOSH supports the effort of OSHA to explore alternative approaches to Permissible Exposure Limit (PEL) development and to launch a national dialogue on preventing occupational illness through improved approaches to managing exposures to hazardous chemicals. A common goal of NIOSH and OSHA is to reduce or eliminate exposures to hazardous chemicals in the workplace. NIOSH offers the following responses and comments to OSHA.

I. Responses to OSHA questions

Question IV.A.1: OSHA seeks input on the risk assessment process described above. When is a model-based analysis necessary or appropriate to determine significance of risk and to select a new or revised PEL? When should simpler approaches be employed? Are there specific approaches OSHA should consider using when a model-based analysis is not required? To the extent possible, please provide detailed explanation and examples of situations when a model-based risk analysis is or is not necessary to determine significance of risk and to develop a new standard.

Response: NIOSH supports using model-based risk assessment when a quantitative estimate of risk is needed and available data support a quantitative analysis. Quantitative risk assessment is especially useful for estimating risks well outside the range of the data. Statistical modeling enables risk assessors to estimate risks at exposures of interest when no data were collected in that exposure range. However, model-based risk estimation is not needed in some cases. For example: 1) when the goal is to identify the hazard rather than quantify risk; and 2) when exposure concentrations of interest are within or slightly below the observable range of the data.

Question IV.A.2: If there is no OSHA PEL for a particular substance used in your facility, does your company/firm develop and/or use internal occupational exposure limits (OELs)? If so, what is the basis and process for establishing the OEL? Do you use an authoritative source, or do you conduct a risk assessment? If so, what sources and risk assessment approaches are applied? What criteria do facilities/firms consider when deciding which authoritative source to use? For example, is rigorous scientific peer review of the OEL an important factor? Is transparency of how the OEL was developed important?

Response: NIOSH develops Recommended Exposure Limits (RELs) for chemical exposures in the workplace. Quantitative risk assessment is often conducted to develop RELs. A transparent, consistent process that documents clearly the strengths and weaknesses of evidence ensures the scientific quality and integrity of NIOSH guidance. The process conducted to evaluate the evidence in the quantitative risk assessment uses the principles and practices of systematic review.

NIOSH identifies priority chemicals for REL development by evaluating several factors:

- Emerging hazards: newly recognized occupational hazards identified in NIOSH research or field work or by other organizations.
- High exposure chemicals: chemicals with widespread occupational exposure (e.g., high production volume, high estimate of occupational exposures).
- High toxicity chemicals: chemicals with documented severe adverse health effects or with new data that raise concern about severe adverse health effects.
- Formal nominations or requests to NIOSH from stakeholders (e.g., organized labor groups, industry, nongovernmental organizations) for a NIOSH assessment of a specific occupational hazard.
- Requests from other government agencies (e.g., OSHA, the Mine Safety and Health Administration (MSHA), or the U.S. Environmental Protection Agency (EPA)).
- Need for an updated NIOSH assessment based on new technologies, advances in risk assessment methods, improvements in monitoring and analytical methods, or new data.

Completion of a NIOSH quantitative risk assessment includes these steps:

1) identify a priority hazard and its associated adverse health effects

2) perform a sufficiently broad literature search, the results of which are screened to remove irrelevant literature

3) conduct a comprehensive review of studies of all health effects of interest, exposure information, and information about uses, controls, and hazard communication. Epidemiologic studies, animal bioassays, mode-of-action studies, metabolic studies, genetic studies, and *in vitro* studies may be evaluated. The goal of the literature review is to identify good quality, well-conducted studies of exposure and response that consider relevant information about mode of action and represent the most sensitive health effect of interest. Identifying the most sensitive adverse health endpoint is important, because protecting against that endpoint is frequently assumed to protect against all other adverse health effects.

4) select relevant study or studies. When selecting the best studies for risk modeling, these factors are considered:

- Design and conduct of the study
- Route of exposure
- Adequate characterization of exposure and response
- Extent and severity of adverse health effect
- Species, sex, endpoint in the most sensitive data set
- Species, sex, endpoints that correspond to other endpoints of interest
- Confounding factors and biases

The goal is to assess all relevant studies that attempt to characterize the exposure-response relationship of health hazards. Evaluation may lead to selection of a single well-conducted study or a collection of studies of variable quality that may be included in a meta-analysis. The potential mode of action and strength of evidence supporting the proposed mode of action are considered at this point, because they may affect selection of the risk assessment modeling strategy.

5) characterize strengths and weaknesses of the studies, including summarizing issues of study design, adequacy of the exposure-response characterization, and appropriateness of the health endpoints. Identification of biases, mode of action considerations, and dosimetry issues are also outlined.

6) select the modeling approach or analysis method and run the models. Sensitivity analyses that consider alternative data sets, exposure metrics, and/or mode of action hypotheses are conducted on a case-by-case basis. The extrapolation method, use of uncertainty factors, and the assumptions are clearly described. Scientific expertise is applied and alternative hypotheses are explored through sensitivity analyses, where possible.

To develop NIOSH recommendations, including RELs, NIOSH may consider data from different sources. For example, a quantitative risk assessment may be based on epidemiologic data, animal data, and mechanistic data. NIOSH considers and evaluates each data set separately and then synthesizes results from the evidence sources for the final recommendation. In NIOSH criteria documents and other policy documents, the basis of the REL is explained, the data and evidence are documented, and the drafts undergo peer review and public comment.

Peer reviewers are chosen for their technical and scientific expertise and freedom from conflicts of interest. They assess the technical quality of the document and make recommendations for improvement or identify areas where scientific uncertainties should be addressed. The NIOSH responses to peer review comments are made publicly available on the NIOSH web site.

Members of the public are invited to comment on NIOSH documents regardless of expertise or recognized interest. Often, a public meeting is held to provide an opportunity for the public to orally present their comments on the draft document, and to ask NIOSH scientists about the proposed NIOSH recommendations. NIOSH considers the public comments in developing the final document and provides written responses on the NIOSH web site.

As further acknowledgement and consideration of advances in toxicology and risk assessment, NIOSH led an effort to develop a collection of manuscripts on relevant topics addressing the state-of-the-science of occupational exposure limits (OELs). In total, 10 manuscripts have been developed and accepted for publication in a peer-reviewed dedicated issue of the *Journal of Occupational and Environmental Hygiene*. The special issue reflects an effort to identify and characterize leading issues pertaining to OELs and their development through research which culminated in a collection of manuscripts focused on each key issue. Utilizing subject matter expertise from researchers and leaders in the occupational hygiene profession and affiliated fields of environmental public health, the goal of this effort was to describe issues related to education and communication of science principles and to understand how they can be incorporated into (and thereby impact) the practices of OEL development and interpretation. Focusing on the state-of-the-science in the fields of exposure science, occupational hygiene, risk assessment, and toxicology, this effort sought to provide a clear description of how advances in these research areas can contribute to the practice of OEL setting–by reviewing the methods used for most OELs that are currently available as well as new methods being incorporated in the OEL process. An essential topic in the set of complementary and interrelated manuscripts is the consideration and interpretation of OELs in the context of evolving risk management practices. The manuscripts are intended to serve as a current critical review of occupational risk assessment methods that will enable occupational hygiene professionals to have a clear understanding of the science methods incorporated in the OELs they develop or use. NIOSH will provide OSHA with the collection of manuscripts for the Agency's review and consideration.

Question IV.A.3: OSHA is considering greater reliance on peer-reviewed toxicological evaluations by other Federal agencies, such as NIOSH, EPA, ATSDR, NIEHS and NTP for hazard identification and dose-response analysis in the observed range. What advantages and disadvantages would result from this approach and could it be used in support of the PEL update process?

Response: NIOSH supports an approach that uses reviews and analyses by other authoritative bodies. The draft NIOSH Carcinogen Policy proposes to accept carcinogen classifications of the U.S. National Toxicology Program (NTP), EPA, or the International Agency for Research on Cancer (IARC) [NIOSH 2013]. NIOSH proposes that this approach avoids duplication of government resources and reduces potential confusion about multiple government analyses of the same chemical in similar exposure scenarios.

Question IV.A.4: OSHA is considering using the Point of Departure (POD) (e.g., BMD, LOAEL, NOAEL), commonly employed by other authoritative organizations for carrying out noncancer risk assessments as a suitable descriptor of the Low End Toxicity Exposure (LETE) level that represents a significant risk of harm. Is this an appropriate application of the POD by OSHA? Are there other exposure values that OSHA should consider for its LETE?

Response: NIOSH supports use of the Point of Departure (POD) concept as a descriptor to represent significant risk of harm. However, NIOSH is concerned that introducing the new terminology, "Low End Toxicity Exposure" (LETE) is confusing when describing a concept that already exists in the field (POD). In addition, the term "low end toxicity exposure" could be misconstrued to mean "low toxicity" which is not the intent. As OSHA noted in the RFI (pages 61392–61393), the Agency for Toxic Substances and Disease Registry (ATSDR) determines a low toxicity value, the "minimal risk level" (MRL). However, ATSDR defines MRL as:

> An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse non-cancer health effects over a specified duration of exposure.

This is different than the LETE concept. LETE corresponds to fatal or severe health effects of concern in rulemaking, at the "low end" (presumably around 5%–10% incidence) of the dose-response. Confusion of these concepts could give a false sense of safety when exposures are at the "low end." In addition, the LETE corresponds to a much higher concentration than what is later identified as corresponding to a significant risk at, for example, a 1/1000 risk level for carcinogens.

An advantage of POD terminology is that it is neutral about the severity of the toxicity. It is simply a "point of departure." For traditional benchmark dose risk assessment, this value is represented by the benchmark dose and is generally within or just below the observable data, increasing confidence in the direct applicability of the finding.

Question IV.A.5: Several methodologies have been utilized to adjust critical study exposures to a worker equivalent under representative occupational exposure conditions including standard ventilation rates, allometric scaling, and toxicokinetic modeling. What are reasonable and acceptable methods to determine worker equivalent exposure concentrations, especially from studies in animals or other experimental systems?

Response: When more chemical-specific information is available, such as when differential metabolic rates between humans and experimental animals have been measured, the extrapolation from animal data to humans is usually more reliable. If sufficient chemical-specific information in animals and humans exists to conduct toxicokinetic modeling or biologically-based risk assessment, those methods are preferred for extrapolating exposure-response information from animal bioassays to humans. However, data are often insufficient to conduct toxicokinetic modeling or biologically-based risk assessment. In those cases, techniques such as allometric scaling could be used for estimating risks to workers.

Question IV.A.6: OSHA is considering a Margin of Exposure approach that compares the LETE with the Lowest Technologically Feasible Exposure (LTFE) as a decision tool for low dose extrapolation. Is this a reasonable means of determining if further low dose extrapolation methods are needed to meet agency significant risk findings? What other approaches should be considered?

Response: The best use of risk assessment is to fit the risk assessment technique to the question under consideration. Extensive statistical modeling and low-dose extrapolation have no advantage if the available regulatory options do not require such information. The margin of exposure approach comparing a POD value such as LETE with a LTFE is a good example of an approach that would not require extensive modeling. The margin of exposure approach is a sound one for assessing regulatory options and determining if additional low-dose extrapolation and exposure-response modeling are needed.

Question IV.A.7: Can the uncertainty factor methodology for extrapolating below the observed range for non-cancer effects be successfully adapted by OSHA to streamline its risk assessment process for the purpose of setting updated PELs? Why or why not? Are there advantages and disadvantages to applying extrapolation factor distributions rather than single uncertainty factor values? Please explain your reasoning.

Response: NIOSH has applied uncertainty factors to a POD to develop or support RELs. However, NIOSH does not consider them to be an extrapolation method. Rather, they represent factors such as inter-species or inter-individual variation. Application of these factors provides additional confidence that the resulting REL is protective. However, this application of uncertainty factors is not a quantitative extrapolation and NIOSH does not associate the resulting REL with a quantitative estimate of risk.

It is important to note that commonly used uncertainty factors may not be sufficiently large when viewed individually to account for the true variation in a particular value (such as inter-individual variability). However, since uncertainty factors are usually applied as a set to account for several sources of uncertainty and variability, a person exposed to the chemical of interest would rarely be at the extreme end of every applied uncertainty factor, and thus outside the overall range covered by the set of uncertainty factors.

Regarding the application of distributions of uncertainty factors, some support exists in the literature for such a probabilistic approach. However, NIOSH does not see value in assigning a distribution to the uncertainty factors because it adds unnecessary complexity to the risk assessment without providing additional insight into the actual risk. When data about variation in the population of interest can replace an uncertainty factor, those sources should be considered (even if the information is represented as a distribution).

Question IV.A.8: Are QSAR, read-across, and trend analysis acceptable methods for developing risk assessments for a category of chemicals with similar structural alerts (chemical groupings known to be associated with a particular type of toxic effect, e.g., mutagenicity) or other toxicologically relevant physiochemical attributes? Why or why not? Are there other suitable approaches?

Quantitative Structure-Activity Relationship (QSAR), read-across, and trend analysis *may* be acceptable methods for developing risk assessments for a category of chemicals. However, the acceptability depends on the: 1) methods for selection of chemical members for the categories; 2) quality of validation of the QSAR for a particular chemical; and 3) toxic effects being evaluated. The methods can assess several closely-related chemicals at once, when toxicologic data exist only for one or a few members of the group—a strong advantage because workers are exposed to far more chemicals than have been evaluated toxicologically. However, these types of analyses can add uncertainty to the risk assessment. Ideally, the chemicals within a class have toxicity and potency differences that can be reliably predicted through QSAR, read-across, or trend analysis. In the absence of specific toxicologic data on the chemical of interest, this assumption may be reasonable. However, when new data are available for individual members of a chemical class, the underlying assumptions and resulting decisions about toxicity should be updated.

Question IV.A.9: How should OSHA utilize the new molecular-based toxicity data, high throughput and computer-based computational approaches being generated on many workplace chemicals and the updated NRC risk-based decision making framework to inform future Agency risk assessments?

Response: NIOSH notes that many technical risk assessment and statistical issues must be addressed before molecular-based toxicity and high throughput data can be used for quantitative risk assessment. However, these approaches have shown promise for elucidating modes of action and informing risk assessment decisions [EPA 2014]. NIOSH anticipates that these methods will be validated against traditional toxicology endpoints and that use of these data sources for quantitative risk assessment will increase.

The 2009 National Research Council (NRC) risk-based decision making framework (OSHA Exhibit #24) has useful elements for fitting the risk assessment strategy to the problem. OSHA has proposed using the POD in a margin of exposure approach for determination of significant risk at feasible workplace exposure concentrations in lieu of extensive statistical modeling. NIOSH concurs that this approach is an appropriate example of fitting the risk assessment to the problem as described in the NRC report.

Question IV.B.1: OSHA described how it obtains information necessary to conduct its industry profiles. Are there additional or better sources of information on the industries where exposures are likely, the numbers of workers and current exposure levels that OSHA could use?

Response: Page 61397 lists information sources that OSHA may use to develop technological feasibility analyses. NIOSH notes that the Current Population Survey conducted by the U.S. Census Bureau (http://www.census.gov/cps/) is an additional source that provides current estimates of the number of employees in a given industry. The U.S. Bureau of Labor Statistics Quarterly Census of Employment and Wages is a useful source of the number of establishments in a given industry. Commercial databases (e.g., Dun & Bradstreet) are another source of employment information.

Question IV.B.2: In cases where there is no exposure information available, to what degree should OSHA rely on modeling results to develop exposure profiles and feasible control strategies? Please explain why or why not.

Response: If no exposure information is available or can be reasonably obtained for a given work process, modeling can fill empirical knowledge gaps. One approach uses Computational Fluid Dynamics (CFD) for estimating exposure, when the required information for building a model is available. The most important information pieces, known as boundary conditions, are geometry, ventilation, and source characteristics. Note that contaminant source location and contaminant source strength data tie the CFD model to the specific workplace scenario in the absence of exposure data. Parametric analysis is an important capability of CFD that can be used to understand the range of possible exposures and the sensitivity of the model to changes or errors in model inputs. In parametric analysis, a range of an input variable is used to create a range of results, so that worker exposure variability can be addressed by using exposure determinant variability. The source variable is often difficult to specify as a CFD boundary condition, and parametric analysis would be an important method for creating a range of reasonable results rather than a single estimate. In general, building a CFD model of a real work process is resource-intensive and proportionate to the accuracy needed. A combination of measurements and modeling has been widely adopted in many engineering disciplines, including environmental engineering [Tu et al. 2008].

Question IV.B.3: What partnerships should OSHA seek to obtain information required to most efficiently construct models of work environments? More specifically, how should OSHA select facility layouts to model that are representative of typical work environments in a

particular industry? Note that the considerations should include variables such as work area dimensions, production volumes and ventilation rates in order to develop models for both large and small scale operations.

Response: CFD and other simulation techniques, such as multi-physics modeling, have become integral to manufacturing processes in many industries [Johnson et al. 2003; Computing Community Consortium 2014]. An opportunity could exist in partnering with companies that are already modeling their processes: information collected by the company could be used for exposure estimation. For example, a NIOSH simulation of exposures during painting of a military aircraft used computer-aided design (CAD) information provided by engineers at the facility, who used it for an unrelated engineering simulation of a design component [NIOSH 2011a]. If companies do not have well-packaged, available information, partnerships are still crucial for collecting information needed to build accurate models, and to obtain access to facilities for measurement of dimensions, ventilation, and material quantities used.

Question IV.B.4: Should OSHA use only models that have been validated? If so, what criteria for model validation should be employed?

Response: NIOSH recommends that OSHA use only models that have been validated. Validation can be internal or external, and a model should be subjected to at least one form of validation. Internal validation refers to error checking techniques such as evaluating a solution for independence from the effects of grid and time-step size and number of iterations. External validation is comparison with results generated by other means, such as experiments or analytical solutions to classical flows. It may be helpful to adopt validation standards set by another agency, such as the American Institute of Aeronautics and Astronautics [AIAA 1998]. The user of the model, in this case OSHA, knows their reliability requirements and can develop validation criteria salient to work environments and understandable to objective third parties. For example, contaminant concentration within an area of interest is a highly sensitive solution variable that can be used as a validation metric, while modelers in more traditional applications of fluid dynamics might not include this variable in their protocol.

The following criteria should be employed for CFD model validation: 1) compare the CFD modeling results with available experimental data to check if the phenomenon is represented with sufficient accuracy; 2) perform sensitivity analyses and parametric studies to evaluate uncertainty from insufficient understanding of physical processes; 3) conduct simulations using different models, geometries, and initial/boundary conditions to assess the adequacy and sensibility of model results.

Question IV.B.5: What exposure models are you aware of that can be useful for predicting workplace exposures and help OSHA create exposure profiles and in what circumstances?

Response: Exposure models range from simple to complex. CFD models involve the complex pattern of change in variables over space and time, whereas the simplest exposure model estimates a single concentration value that represents the whole workspace. This concentration is calculated from volumetric air exchange and contaminant generation rates. Monte Carlo methods can create a distribution of exposure outcomes for a given distribution of model inputs. Dedicated CFD software packages and add-ons to general model building software are commercially available. Shareware codes are also available such as those from the National

Institute of Standards and Technology (NIST). Information on the NIST codes can be found at [http://www.nist.gov/el/fire_protection/buildings/fire-modeling-programs.cfm] and [http://www.bfrl.nist.gov/IAQanalysis/CONTAM/].

Question IV.B.6: Should OSHA consider CFD models primarily for indoor operations, outdoor operations, or both? What limitations exist with these two different types of models?

Response: NIOSH recommends that CFD models should be used primarily for indoor operations. Worker exposure concentrations will be more variable in outdoor environments than indoor workspaces because of airflow (wind), turbulence, and thermal gradients, so the sensitivity of the model to a range of possible environmental scenarios would be particularly important for outdoor applications. The large domain usually needed for outdoor operations can lead to larger grid size and reduced accuracy of the model.

As noted in the RFI (page 61400), NIOSH has used CFD models in mine safety research. CFD models predicted hazardous carbon monoxide (CO) and soot particle concentrations from a source of fire (e.g., spontaneous combustion of coal, burning of conveyor belt) in underground coal mines, under specific ventilation airflow conditions [Yuan and Smith 2012; Yuan et al. 2014]. These models were developed by solving the equations for gas flow, heat and mass transfer, and chemical reactions in a mine fire incident. Specific boundary conditions were applied to the CFD model to simulate different mine fire conditions. The models were subsequently validated against large-scale experimental results or field data collected during a mine fire event. NIOSH also used CFD models to predict the development of oxygen depletion when nitrogen injection was applied to eliminate explosive atmospheres that may form in sealed areas of underground coal mines [Yuan and Smith 2014]. The purpose was to quantify the hazard from potential fires in underground mines. CFD modeling is helpful for designing better ventilation and fire protection systems. The accuracy of our CFD modeling is based on the available field data to validate the CFD model and on the current computing power.

Question IV.B.8: To what extent and in what circumstances should OSHA argue that feasibility for a regulatory alternative can be established by proving that the feasibility of reducing the highest exposures to the level proposed by that regulatory alternative?

Response: For "like" industries and processes, information on the feasibility for controlling exposures determined in one industry can probably be transferred to a similar industry/process. For other industries and processes using the same chemical, it is uncertain whether the transfer of exposure control technology has any utility without understanding the quantity of chemical used, and information on the processes and tasks.

Question IV.B.10: What are the appropriate criteria that OSHA should use to assess whether control strategies implemented in a process from one industry are applicable to a process from another industry (e.g., similarity of chemicals, type, extent and duration of exposures, similar uses)?

Response: The examples provided (similarity of chemicals, type, extent and duration of exposures, similar uses) are all appropriate criteria for assessing the transferability of control strategies across industries.

Question IV.B.11: Regardless of the industries involved, are there criteria that OSHA should use to show that control strategies implemented in a process from one operation are applicable to a process from another operation? Please explain.

Response: The examples provided in question IV.B.10 are all appropriate criteria that OSHA should use. However, the transfer of "exposure control" strategies found to be acceptable in one industry to a different industry or process will be questionable without confirmation of its effectiveness based on exposure measurement data.

Question IV.C.1: Should OSHA consider greater use of process oriented regulations, such as regulations on abrasive blasting, welding, or degreasing, as an approach to health standards? Should such an approach be combined with a control banding approach?

Response to first question only: NIOSH notes that one benefit of this approach would be an improved definition of the exposed population. For example, the number of welders in a particular industry may be small, but the aggregated number of welders across all industries is a substantial exposed population. A "process oriented" regulation also acknowledges that application and worker exposure to the chemical across many industry sectors can vary considerably. The protection of workers can often be best accomplished by supplementing the PEL with specific risk management requirements such as application of engineering controls (e.g., local ventilation) to limit exposures when performing specific job tasks.

Question IV.C.3: To what extend* (sic) *and in what circumstances can OSHA argue that feasibility for a regulatory alternative can be established by the enforcement of a lower PEL (e. g., the 1989 PEL) by an individual state or states?

Response: NIOSH notes that the Hazardous Waste Operations and Emergency Response standards (29 CFR 1910.120/1926.65) instruct employers to observe published exposure limits where PELs are not available. The experience of employers regulated by these standards may be an additional source of information for OSHA.

Question V.A.1: How might publicly available information on the properties and toxicity of HPV chemicals be utilized by employers to identify chemical hazards and protect workers from these hazards?

Response: The summaries of screening data published under the EPA High Production Volume (HPV) program provide screening level toxicity information on subject chemicals and closely related "supporting" chemicals. These data provide information that can be used for hazard identification and preliminary assessment of risk. When data are scarce, these summaries may help employers choose chemical alternatives.

Quantitative and qualitative data on HPV chemicals, particularly results of mammalian toxicologic studies, can be used to estimate a range of appropriate exposure limits using hazard banding techniques. Publicly available toxicity data on HPV chemicals allows: 1) regulatory and research agencies to prioritize chemicals for the development of authoritative exposure limits; and 2) employers to identify chemicals that may be harmful at concentrations routinely found in the workplace that should be eliminated or substituted.

Question V.A.2: How might the information on the properties and toxicity of chemicals generated by CompTox, ToxCast, and/or Tox21 be utilized by employers to identify chemical hazards and protect workers from these hazards? OSHA is also interested to hear from commenters who may currently make use of these data in their worker protection programs.

Response: Information available through databases such as CompTox, ToxCast, and Tox21 are currently useful in hazard identification and alternative assessment. Methods are under development to use results for full quantitative risk assessment.

Question V.A.3: Are QSAR, read-across, and trend analysis useful and acceptable methods for developing hazard information utilizing multiple data sets for a specific group of chemicals?

Response: NIOSH has applied toxicity data from one compound to estimate toxicity from another compound. For example, recommendations for metal salts were applied to the entire class of compounds (e.g., all hexavalent chromium compounds). This application is possible because of a good understanding of the mode of action for hexavalent chromium (the most active component of many hexavalent chromium compounds). Although the toxicity of individual compounds may vary due to solubility, metabolism, or other factors, it is reasonable to estimate toxicity for this class of compounds based on robust data from a single compound. NIOSH has less experience with applying these methods to organic compounds, although NIOSH used diacetyl as a model compound to estimate the toxicity of 2,3-pentanedione, a closely related di-α-ketone, for development of a draft REL [NIOSH 2011b]. NIOSH has not directly used QSAR methods for REL development and is exploring use with other information to estimate risks to workers.

Question V.A.4: Are there other acceptable methods that can be used to develop hazard information for multiple chemicals within a group?

Response: NIOSH is not able to recommend other acceptable methods to develop hazard information for multiple chemicals within a group at this time. When applying toxicity information developed for one chemical to multiple chemicals, it is important to report clearly the basis for the relationship between chemicals and to describe the presumed similarity in toxic response.

Question V.A.8: Should OSHA pursue efforts to obtain data from ECHA that companies are required to provide under REACH?

Response: Yes. Data provided to REACH can be a rich source of information on hazards to workers. Obtaining the original data would be helpful in assessing risks.

Question V.B.1: To what extent do you currently consider elimination and substitution for controlling exposures to chemical hazards?

Response: The NIOSH Prevention through Design National Initiative promotes elimination and substitution as effective solutions to hazard control. A recent and potentially useful addition to the "informed substitution" process described in the RFI is the three-level "functional substitution" model [Tickner et al. 2015]. The first level, Chemical Function, results in a "drop-in" (i.e., simple) chemical replacement with a safer chemical. The second level, End Use Function, changes a product or process to achieve the same function that the chemical provided (e.g., replacing degreasing by halogenated solvents with water-based and ultrasonic cleaning). The third level, Function as Service, seeks a complete re-thinking of the end product or service to eliminate the chemical (e.g., replacing paper receipts containing bisphenol A (BPA) with e-receipts). At each level, the hazard is "designed out"—the goal of Prevention through Design. In addition to substitution frameworks discussed in the RFI, the National Academy of Sciences (NAS) recently completed a study of various methods of alternatives assessment, and proposed a unified framework to use the best from each system, and include improvements in existing methods judged to be deficient. NIOSH recommends consideration of the results and recommendations of the NAS report [NAS 2014].

Other possible approaches include requiring a summary of functional substitution options considered and/or adopted, and the use of Occupational Exposure Banding (OEB) to evaluate substitute candidates.

Question V.B.4: What information and support do businesses need to identify and transition to safer alternatives? What are the most effective means to provide this information and support?

Response: Businesses, especially smaller businesses, may benefit from a central web page of organized links to alternatives databases. One source where many of these databases are provided is the Toxics Use Reduction Institute (TURI) at the University of Massachusetts Lowell (see http://www.turi.org/Our_Work/Research/Alternatives_Assessment/Databases), which studies the uses of chemicals of concern, and the availability of safer, technically feasible, and affordable alternatives. Another example is the Pharos database offered by the Healthy Building Network (see http://www.healthybuilding.net/content/pharos-v3). The Pharos Project is a database for identifying health hazards associated with building products, and focuses on increasing awareness about issues of human health and well-being associated with the building industry. The Pharos Project "encourages manufacturers to disclose all ingredients in building products; helps architects, designers and building owners avoid using products that contain harmful chemicals; and creates incentives for product redesign and modification to reduce the impacts of hazardous materials use throughout the lifecycle of building products."

Question V.B.8: How could OSHA use the information generated under HazCom 2012 to pursue means of managing and controlling chemical exposures in an approach other than substance-by-substance regulation?

Response: The HazCom 2012 standard requires that the hazards of chemicals be characterized; this requirement facilitates grouping or banding of chemicals according to their toxicity and potential to cause adverse health effects. The HazCom 2012 requirement can also identify lack of health and safety data. Data generated by the hazard characterization process will enable OSHA to prioritize chemicals of greatest concern, and identify chemicals that require additional consideration of toxicity and potential adverse health effects. NIOSH agrees with OSHA that the hazard characterization driven by the HazCom 2012 standard will provide a consistent process with objective criteria for assessing chemicals and assigning the appropriate hazard phrase(s) according to the Globally Harmonized System for Classification and Labeling of Chemicals (GHS) conventions. The hazard phrase can then be used as a basic information piece for assigning chemicals to categories in a hazard banding process.

Question V.B.9: How could such an approach satisfy legal requirements to reduce significant risk of material impairment and for technological and economic feasibility?

Response: Control Banding (CB) tools could be used as a basis for satisfying legal requirements given appropriate evidence of their validity. CB tools can be used to select appropriate exposure control measures based on hazard information for the chemical. It is critical first to characterize any uncertainties associated with the exposure assessment models and hazard rankings, and with linkage of the hazard assessment to the control bands. Initial research studies to assess CB tools have shown "reasonably good" agreement with predicted exposure ranges using occupational exposure limits [Tischer et al. 2003] as well some cases where "under-control" and "over-control" were indicated [Jones and Nicas 2006]. When COSHH (Control of Substances Hazardous to Health) Essentials was evaluated using German (BAuA) field studies from the period 1991–2001, using nearly 1,000 personal measurements in 18 industrial applications [Tischer et al. 2003], the scheme was considered successful from a precautionary viewpoint because measured values were rarely higher than the predicted exposure ranges. However, up to 98% of actual results in certain situations were lower than the model's predicted exposure range. Jones and Nicas [2006] evaluated both the COSHH Essentials and the International Labour Organization's International Chemical Control Toolkit. Specifically, Jones and Nicas [2006] analyzed the margin of safety afforded by the systems and, for each hazard band, defined the minimal margin as the ratio of the minimum airborne concentration that produced the toxicologic endpoint of interest in experimental animals to the maximum concentration in workplace air permitted by the exposure band. The authors concluded that although these systems predict exposures comparable with current occupational exposure limits, the minimal margins are better indicators of health protection. The results of these evaluation studies suggest that the CB tools provide guidance which indicates good agreement with corresponding occupational exposure limits; where exceptions were noted, CB tools generally indicated more protective controls.

The HazCom 2012 standard, through incorporation of the GHS criteria for the classification and labeling of chemicals, improves upon the original hazard communication standard. NIOSH recognizes the utility of this standard for hazard characterization as a starting point for health hazard banding and OEB of chemicals. Furthermore, the GHS conventions adopted by the HazCom 2012 provide more consistent and uniform hazard phrases and pictograms for safety data sheets as well as labeling to prevent miscommunication of potential hazards and to facilitate hazard recognition and awareness.

Question V.B.10: Please describe your experience in using health hazard and/or control banding to address exposures to chemicals in the workplace.

Response: NIOSH recognizes the importance of authoritative OELs and has recently published several important RELs, including the first authoritative recommendation for carbon nanotubes. However, NIOSH also recognizes that chemicals are introduced at a rate that outpaces OEL development. While NIOSH develops new OELs and updates existing OELs, guidance is needed for the thousands of chemicals that lack exposure limits. The recently proposed NIOSH OEB process will be useful for those chemicals. As noted in OSHA Exhibit #127 and the RFI (page 61415), the proposed OEB process classifies chemicals into one of five bands and "*includes a three-tiered evaluation system based on the availability of toxicological data to define a range of concentrations for controlling chemical exposures.*" Users begin the OEB process by performing a Tier 1 evaluation that relies on hazard codes and categories from the GHS. Tier 2 involves review of authoritative summaries of chemical toxicity, while Tier 3 requires toxicologic expertise and assessment of the scientific literature. These evaluations are data intensive, requiring users to go through a detailed process, health endpoint by health endpoint. Additional expertise is necessary to understand the criteria of each health endpoint, and professional judgment is required to select the appropriate band.

Various CB tools are available including COSHH Essentials (inhalation), Stoffenmanager tool (inhalation and dermal), Einfaches Massnahmenkonzept Gefahrstoffe (EMKG) "Easy-to-use *workplace* control scheme for hazardous substances" (German CB tool) (inhalation), International Chemical Control Toolkit (ICCT), and RISKOFDERM (Dermal). NIOSH experience suggests that the CB tools are much easier to use than other complicated tools such as computational fluid dynamics (CFD). Even so, training and expertise is recommended to ensure the user reaches the appropriate control guidance solution. For example, such training would enable the user to distinguish between a "fine dust" and "extremely dusty products" when entering case-specific information into the Stoffenmanager tool (and the developer includes some explanation to facilitate this type of training). Also, a user must be familiar with terminologies such as the types of respirators.

In CB tools, the hazard banding is decided based on risk- or hazard-, or R- or H-phrases. Although a user can obtain R- or H- phrases from various sources (e.g., Safety Data Sheets (SDS), European Chemicals Agency (ECHA) database), the definitions of R- or H-phrases are unclear. For example, the difference between R23 (Toxic by inhalation) and R26 (Very toxic by inhalation) is not clear. This issue can be a shortcoming for use of CB tools.

NIOSH researched the COSHH Essentials tool for chemicals with OELs and found that the tool provided reasonable results for liquids (acetone, ethyl benzene, methyl ethyl ketone, toluene, xylene, and isopropanol); however, the tool underestimated some tasks [Lee et al. 2009, 2011]. NIOSH has also used the COSHH Essentials tool, Stoffenmanager tool, and RISKOFDERM for a chemical with no OEL to assist decision-making for selection of control strategies. Confidence in the recommended control strategies was based on actual exposure measurements.

For a CB model to be used in a health standard, confidence must exist in the:

1) hazard phrases assigned to the chemical

2) assignation of the phrases to health hazard bands

3) exposure assessment model

4) methodology for combining hazard bands and exposure assessment in a risk assessment

5) linkage of the risk assessment to a particular control strategy.

A thorough treatment and assessment of the state-of-the-science of CB methodology is detailed by NIOSH [2009] (OSHA Exhibit #135). The potential utility and limitations of CB models are described in greater detail, including the need for training, consistent terminology, and validation to ensure the effectiveness for the models.

Question V.B.11: Are additional studies available that have examined the effectiveness of health hazard and control banding strategies in protecting workers?

Response: Additional studies have investigated the effectiveness of CB tools: Lee et al. [2009] and Tischer et al. [2003, 2009]. In addition, chapter 10 of the NIOSH [2009] state-of-the-science review of CB methodology (OSHA Exhibit #135), provides recommendations to facilitate CB implementation in the United States. The recommendations for improving awareness and standardization of concepts include: 1) to "coordinate terminology to ensure a singular CB vocabulary is established, adopted, understood, and communicated..."; and 2) to "adopt the GHS to work toward ensuring standardized hazard statements are available on U.S. chemical labels and MSDSs to promote widespread CB applications." Both recommendations were met by promulgation of the OSHA HazCom 2012 standard. NIOSH also recommended "NIOSH and OSHA cooperation in focusing on CB utility for special emphasis areas, such as hazard communication and guidance for small businesses. The State OSHA plans, fitting within the OSHA Alliance, may provide mechanisms to implement CB strategies and demonstration projects for control-focused solutions and guidance." NIOSH suggests that OSHA consider all the NIOSH document's recommendations.

As an additional resource for CB research and studies, Zalk [2010] provided a thorough description of CB approaches for a variety of occupational chemicals, including engineered nanomaterials.

Question V.B.12: How can OSHA most effectively use the concepts of health hazard and control banding in developing health standards?

Response: The NIOSH OEB framework and tool under development are being subjected to multiple rounds of internal and external validity testing. The completion of this validated framework and tool could assist OSHA in assessing chemical hazards, prioritizing them, and determining a priority order for potential regulation or guidance. OSHA could also consider a novel approach of recommending OEBs in conjunction with a comprehensive safety management system. With regard to the latter, it is suggested that OSHA consider the research and scientific literature on safety and health management systems as they continue to evolve and merit further exploration and validation. This approach could complement the current health-based standard approach. Also, as indicated in the previous response, OSHA is advised to consider the recommendations and guidance provided in (OSHA Exhibit #135), *Qualitative Risk Characterization and Management of Occupational Hazards: Control Banding (CB)* [NIOSH 2009].

Question V.B.13: How might OSHA use voluntary guidance approaches to assist businesses (particularly small businesses) with implementing the principles of hazard banding in their chemical safety plans? Could the GHS chemical classifications be the starting point for a useful voluntary hazard banding scheme? What types of information, tools, or other resources could OSHA provide that would be most effective to assist businesses, unions, and other safety and health stakeholders with operationalizing hazard banding principles in the workplace?

Response: A health hazard banding approach for assessing and managing chemicals in the workplace has greater potential for effectiveness since the adaptation of the GHS in the HazCom

2012 standard. OSHA might consider providing guidance, especially to small- and medium-sized businesses, for performing hazard banding and OEB assessments for chemicals with no or out-of-date OELs. The NIOSH OEB framework and tool could provide a useful resource for OSHA to adapt and promote. OSHA might also develop its own hazard banding guidance in the form of an OSHA e-Tool.

Question V.B.15: OSHA requests comment on whether and how task based exposure control approaches might be effectively used as a regulatory strategy for health standards.

Response: The Center for Construction Research and Training (CPWR) Task-Based Exposure Assessment Model (T-BEAM) for construction "uses tasks (or specialized skills) as the central organizing principle for data collection, because trade-specific skills form the thread of continuity in the career of a construction worker" [Susi et al. 2000]. This focus on trade-specific tasks could be used by OSHA to develop a framework for task-based control approaches. For example, welding and grinding are common tasks across a variety of industries, and task-based controls should be effective in limiting exposures to acceptable levels in a variety of settings.

The NIOSH Workplace Solutions series of documents addresses issues of task-based exposure control approaches (available at http://www.cdc.gov/niosh/pubs/workplace_date_desc_nopubnumbers.html). These guidance documents offer easy-to-understand, easy-to-access, and easy-to-use recommendations that translate the results of NIOSH research into occupational safety and health practice.

The CPWR also provides resources to address task-based hazards in its Construction Solutions database (available at http://www.cpwrconstructionsolutions.org/). The database contains nearly 200 tasks, searchable also by line of work and hazard, and is designed for owners, contractors, and workers to provide guidance and solutions with practical control measures to reduce or eliminate hazards.

II. Comments about the text

Page 61384, first sentence of the Summary states that "*OSHA is reviewing its overall approach to managing chemical exposures in the workplace…*". However, the issue of how to apply PELs to extended, irregular, and atypical work schedules is not addressed. In addition, the issue of mixed exposures is only briefly addressed. While these complex issues will likely require considerable study to resolve, NIOSH suggests that OSHA take this opportunity to initiate the process of addressing these issues in the framework of the RFI.

Page 61385, list of acronyms: "REL Recommended Exposure Level" should be "REL Recommended Exposure Limit."

Page 61396, middle column: delete the "a" in "Tox 21 has already screened over a 1000 compounds…"

Page 61398, "*a. Computational Fluid Dynamics Modeling to Predict Workplace Exposures*", third, fourth, and fifth sentences, suggested revision:

"…systems of partial differential equations that describe conservation of energy, mass, and momentum. The solutions to these equation systems describe how a fluid will move through the specified area, or geometry, as a function of time. For some physical phenomena, such as the laminar flow…can be solved using analytical mathematics."

Page 61399, first paragraph under Question IV. B.3, suggested revision in bold: "Grid cell size refers to the division of space according to nodes, and time step refers to ~~the value attributed to the time variable to numerically solve the equations~~ **the size of the time interval for which the equations are solved sequentially,** with reference to the nodes. Another method for model evaluation is the comparison between the solutions of different models to the same problem in that a similarity of findings across multiple CFD models would provide greater confidence in the results. Arguably, the best performance evaluation is the comparison of model results to those of a field experiment, **a laboratory mock-up, or an experimental scaled model of** that ~~simulates on different scales the actual~~ work environment."

Page 61399, the "*Low Cost*" paragraph could include that CFD simulations are generally less expensive than building multiple prototypes to test various conditions.

Page 61399, suggest replacing the first sentence of the "*Speed*" paragraph with "Once a CFD simulation is built over several days or weeks, the solutions to a new set of source or ventilation conditions can be obtained within one or several days."

Page 61399, suggest replacing the word "realistic" in the heading "*Ability to simulate realistic conditions*" with "a variety of." The most realistic test will always be sampling of the actual situation of interest. The paragraph beginning with "*The Agency also realizes that even if an appropriate mathematical model…*" could include sentences such as: "Low-cost, speed, and high accuracy are not always achievable together. More accurate models are more computationally expensive."

Pages 61414–61415, the paragraph under "*4. Occupational Exposure Banding*", second sentence: "…the moist toxic chemicals" should be "…the most toxic chemicals."

Page 61420, first complete paragraph: "Recommended Exposure Levels (RELs)" should be "Recommended Exposure Limits (RELs)."

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