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State-of-the-Science: The Evolution of Occupational Exposure Limit Derivation and Application

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Introduction

Occupational exposure limits (OELs) are a critical component of the risk assessment and risk management process and their use remains a staple of occupational hygiene practice. There are dozens of organizations and agencies that derive OELs worldwide. Yet while most of these groups describe their administrative procedures as well as the rationale for the derivation of OELs for individual substances, few provide equally complete documentation of the underlying scientific methodology for conducting the quantitative risk assessment employed in OEL development. The paucity of written descriptions of OEL development methodology has resulted in a lack of transparency related to implementation of important scientific principles for OEL development and inconsistent practices for OEL development within and among organizations. The absence of such transparency limits the opportunities for international harmonization of existing values and OEL setting practices among organizations.

Given these and other challenges, the National Institute for Occupational Safety and Health (NIOSH) began 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. Those manuscripts and the key issues they explore comprise this issue of the *Journal of Occupational and Environmental Hygiene*. Utilizing subject matter expertise from researchers and thought leaders in the occupational hygiene profession and affiliated fields of environmental public health, the goal of this effort is to describe the 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 specifically 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

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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 that are actively being incorporated in the OEL process. An essential topic included within the set of complementary and interrelated manuscripts dedicated to this pursuit 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. A brief introduction to each manuscript title in this collection is provided in the following paragraphs.

The initial manuscript, entitled *Historical context and recent advances in exposure-response estimation for deriving occupational exposure limits*[1] describes and contrasts traditional and advanced practices in dose-response modeling from both a toxicological and epidemiological perspective. This issue serves as an appropriate starting topic, since the initial steps in deriving an OEL often address characterization of the adverse effects of a chemical and estimation of the dose-response behavior for such effects. Limitations in traditional methods based on selection of study adverse effect levels have motivated current areas of research for dose-response modeling including biologically-based modeling approaches, and semi-parametric models. The authors describe dose-response modeling for OEL development, as well as provide guidance on when various methods may be appropriately applied. Furthermore, their discussion describes new methods which are being increasingly used for OEL setting, improving on the statistical limitations of the traditional techniques, and making more complete use of growing knowledge of toxic mode of action.

Another manuscript in the series addresses refinements to the dose-response modeling to improve translation to worker health scenarios. The manuscript entitled *Advances in inhalation dosimetry models and methods for occupational risk assessment and exposure limit derivation*[2] provides an overview and practical guide to occupational hygiene professionals concerning the derivation and use of dosimetry concepts in risk assessment and development of OELs for inhaled substances. Dosimetry, the measurement or estimation of internal dose, and dosimetry models and methods can improve the accuracy and reduce the uncertainty of the internal dose estimates at the target tissue, especially through biologically-based and empirically-validated dosimetry models and use of principles based on those models. The primary focus of the manuscript is inhalation dosimetry, for which several practical examples of dose estimation and OEL derivation are provided for inhaled gases and particulates. The authors purport that dosimetry approaches can improve the accuracy and reduce the uncertainty of the internal dose estimates used to derive OELs.

The estimation of the dose-response behavior for adverse effects is only one part of the traditional OEL derivation equation. The dose-response from empirical data often must be extrapolated to estimate an OEL that represents a dose without effects among workers. Such extrapolations are often addressed by accounting for key uncertainties as described in *The scientific basis of uncertainty factors used in setting occupational exposure limits*[3]. In this manuscript the authors present a critical examination of the historical use of uncertainty factors (UFs) in the development of OELs, a practice which dates back more than six decades. The manuscript describes how the use of UFs is predicated on the assumption that a sufficient reduction in exposure from levels at the boundary for the onset of adverse effects will yield an exposure level that is safe for at least the great majority of the exposed population, including vulnerable subgroups. While general principles for UF application are incorporated in most OEL methods, there are differences in the application of the UF approach among groups that conduct occupational risk assessment as well as between occupational and environmental risk assessments. At the core of this manuscript is the message that an understanding of the sources of variability and uncertainty addressed in an OEL are essential to its informed use and interpretation by the risk manager.

The methods for developing dose-response estimates are evolving to more fully incorporate new types of health impact and toxicity data. This reflects the need to ensure that risk assessment tools keep pace and take advantage of developments in basic physiological sciences. In the manuscript entitled *Systems biology and biomarkers of early effects for occupational exposure limit setting*[4], the authors emphasize incorporating a systems biology approach using biomarkers of effect with computational toxicology tools to enable more accurate and timely assessments of chemical exposures. The authors describe biomarkers of effect as an important element of the systems biology approach reflecting alterations at the cellular level that are in many cases considered to be preclinical in nature. Further, this manuscript addresses systems biology, biomarkers of effect, and computational toxicology approaches and their relevance to OEL setting. The implications of such approaches are also described, including decreased uncertainty in OELs through improved understanding of biological responses at lower levels of chemical exposure, and increased ability to establish OELs for chemicals lacking a traditional battery of toxicity testing.

One of the more complex areas addressed in the application of uncertainty factors in traditional OEL approaches is the goal to more fully characterize human variability in sensitivity to chemicals. The manuscript entitled *The Utility of genetic and epigenetic information in occupational health risk assessment and standard setting*[5] delves into a new realm of considerations for risk assessment and management paradigms. Although genetic and epigenetic data have not been widely used in risk assessment and ultimately, standard setting, it is possible to envision such uses. This manuscript addresses the utility of genetic and epigenetic information in risk assessments and describes a framework to organize thinking about such uses. Its authors present a framework for hazard and risk characterization, and describe how genetic and epigenetic data can be used as endpoints in hazard identification, as indicators of exposure, as effect modifiers in exposure assessment and dose-response modeling, as descriptors of mode of action, and to characterize toxicity pathways.

The initial manuscripts in the collection provide a foundation for extending traditional OEL derivation techniques to accommodate developments in biology understanding and mathematical tools. However, some toxicological effects present unique challenges to the OEL process. Sensitization is an example of a particularly challenging health endpoint. In the manuscript, entitled *Setting occupational exposure limits for chemical allergens - Understanding the challenges*[6], Dotson et al. discuss the biological principles involved in the allergic response to highlight how the evolving science of toxicology and risk assessment techniques is enhancing the ability to address the complexities of allergy for developing health-based OELs. In particular, the authors present the current approaches and considerations, as well as future research needs, for conducting occupational risk assessments for low molecular weight chemical respiratory allergens. To date, OELs that explicitly account for protection from respiratory sensitization have been established for only a limited number of chemicals, predominately based on robust epidemiology data sets.

Because the use of OELs is such a standard approach for the practicing occupational hygiene professional, it is fitting that the collection includes developments in OEL interpretation and application. One of the manuscripts covering this theme is dedicated to the topic of interpretation of OELs in the context of exposure assessment. *Occupational risk probability and interpretation of traditional occupational exposure limits: Enhanced information for the occupational risk manager*[7] highlights the basis for key ingredients in an occupational exposure assessment, focusing on important sources of variability and uncertainty that can be useful for characterizing occupational risk in terms of risk probability rather than a binary decision of "acceptable risk or unacceptable risk." Among the key points is the realization that exposure estimates and hazard characterization are impacted by both variability and uncertainty – a well-developed risk characterization reflects and communicates these considerations. And perhaps of greatest relevance is the authors' conclusion that occupational hygienists have a variety of tools available to incorporate concepts of risk probability. Active use of these tools leads to a more robust occupational health program by initiating exposure sampling campaigns, medical surveillance programs or use of personal protective equipment.

The role of occupational hygienists continues to grow and OELs as well as other tools in the field are being stretched by the need to advance considerations to non-traditional risk questions. One area of growth is highlighted in the manuscript entitled *Aggregate exposure and cumulative risk assessment – Integrating occupational and non-occupational risk factors*[8]. The manuscript reflects a broadening of the scope of applied risk assessment thinking for the development of OELs. It acknowledges that OELs and other risk management tools need to incorporate consideration of complex exposures to chemicals and other stressors by multiple pathways and exposure routes, combined exposures to multiple stressors (e.g., chemical and non-chemical), and the possibility that such cumulative exposures may modify the toxic effects observed. The authors note that tools and models used in related fields of environmental public health provide a path forward for occupational risk assessment; such techniques can be adopted and modified for occupational scenarios. At the core of this manuscript is exploration of themes to ensure that occupational risk assessments account for the complexity of the workplace exposure environment – including multiple routes of exposure (aggregate risk) and exposures to multiple stressors (cumulative risk).

A third issue in the application of OELs relates to identifying OELs, evaluating OEL alternatives, and making informed choices as a savvy consumer of risk assessment information. The final manuscript in the collection provides a condensed and carefully-considered description of *International perspectives and global harmonization of OEL practices*[9]. Throughout, its authors seek to derive understanding of efforts to encourage coordination among OEL-setting organizations and processes, amidst a historically-confusing landscape of OELs reflecting significant overlap in coverage among organizations for many chemicals, while other important chemicals have no OELs at all. Ultimately, the authors conclude that the basis for differences in OELs for the same chemical reflects a mix of risk policy and risk assessment methodology differences. Consequently, a systematic framework for documentation and selection of OELs can aid the occupational risk manager – and encourage the most effective use of current OEL resources.

While the list of topics for OELs covered in this issue of the *Journal of Occupational and Environmental Hygiene* is in no way exhaustive, it does represent some of the most relevant, promising, and readily-applicable scientific advances which can be integrated into risk assessment and management of occupational hazards. The purpose of this collection of manuscripts is to inform the practitioner, to stimulate the researcher, and to provide a basis for more protective and scientifically-sound guidance and policy.

References

1. Wheeler M, Park RM, Bailer AJ, Whittaker C. Historical context and recent advances in exposure-response estimation for deriving occupational exposure limits. J. Occup. Envion. Hyg. 2015 this issue:
2. Kuempel ED, Sweeney LM, Morris JB, Jarabek AM. Advances in inhalation dosimetry models and methods for occupational risk assessment and exposure limit derivation. J. Occup. Envion. Hyg. 2015 this issue:
3. Dankovic DA, Naumann BD, Maier A, Dourson ML, Levy LS. The scientific basis of uncertainty factors used in setting occupational exposure limits. J. Occup. Envion. Hyg. 2015 this issue:
4. DeBord DG, Burgoon L, Edwards SW, Haber LT, Kanitz MH, Kuempel E, Thomas RS, Yucesoy B. Systems biology and biomarkers of early effects for occupational exposure limit setting. J. Occup. Envion. Hyg. 2015 this issue:
5. Schulte PA, Sofge CW, Curran CP. The Utility of genetic and epigenetic information in occupational health risk assessment and standard setting. J. Occup. Envion. Hyg. 2015 this issue:
6. Dotson GS, Maier A, Siegel PD, Anderson SE, Green BJ, Stefaniak AB, Codispoti CD, Kimber I. Setting occupational exposure limits for chemical allergens - Understanding the challenges. J. Occup. Envion. Hyg. 2015 this issue:
7. Waters M, McKernan L, Maier A, Jayjock M, Brosseau L, Schaeffer V. Occupational risk probability and interpretation of traditional occupational exposure limits: Enhanced information for the occupational risk manager. J. Occup. Envion. Hyg. 2015 this issue:
8. Lentz TJ, Dotson GS, Williams PRD, Maier MA, Gadagbui B, Pandalai SP, Lamba A, Hearl F, Mumtaz M. Aggregate exposure and cumulative risk assessment – Integrating occupational and non-occupational risk factors. J. Occup. Envion. Hyg. 2015 this issue:
9. Deveau M, Chen C-P, Johanson G, Krewski D, Maier MA, Niven KJ, Ripple S, Schulte PA, Silk J, Urbanus JH, Zalk DM, Niemeier R. International perspectives and global harmonization of OEL practices. J. Occup. Envion. Hyg. 2015 this issue: