NIOSH Exposure Assessment (EXA) Program:

Response to EXA Expert Review Panel's Report

November 27, 2018

Table of Contents

Introduction

The NIOSH Exposure Assessment Program (EXAP) is a core and specialty program in the NIOSH Program Portfolio. The NIOSH Program Portfolio is organized into ten Sector Programs that represent industrial sectors and seven health and safety Cross-Sector Programs organized around health outcomes based on the National Occupational Research Agenda (NORA). As a core and specialty program, the mission of the EXAP is to provide national and international leadership in the development and use of effective exposure assessment strategies and tools to prevent work-related illness and injury. Under the NIOSH Strategic Plan, NIOSH's industrial sectors, health and safety cross-sectors, and core and specialty programs develop, organize, and share research and service goals to promote collaboration, avoid duplicative efforts, and maximize impact.

As part of its ongoing program review process, NIOSH used a professional scientific and engineering support contractor to assemble and convene an independent expert panel in 2017 to review the relevance and impact of work conducted in the NIOSH EXAP in the years between 2006 and 2016. The panel consisted of a chair, Dr. Dana Boyd Barr, who in turn recruited the remainder of the independent panel of experts in the content area of exposure assessment, translation science, and program evaluation. NIOSH provided the expert panel with an Exposure Assessment Evidence Package that contained information to demonstrate the relevance and impact of the EXAP's work, with a focus in the areas of methods development and direct-reading methods and sensors. The report described the program's activities, products, and examples of how others have used those products to improve occupational safety and health. EXAP representatives also provided additional detail to the expert panel during an in-person meeting.

Using the information from the evidence package and the in-person meeting, the expert panel developed an Exposure Assessment Review Panel Report. During preparation of the report, the expert panelists provided the panel chair with individual scores for EXAP relevance and impact, rationale for those scores, and recommendations. The panel chair averaged the scores and synthesized the rationale and recommendations into the final report. In the area of relevance, the panel assigned the EXAP a score of 4 out of 5 indicating that "The rationale for the activities completed by the program are justified." In the area of impact, the panel assigned the EXAP a score of 4 out of 5, indicating that "The research program has made some contributions and/or demonstrates great potential to contribute to end outcomes or well-accepted intermediate outcomes." This resulted in a total EXAP score of 8 out of a possible 10.

The expert panel made eleven specific recommendations regarding opportunities to improve the relevance and impact of the EXAP. The following sections provide the NIOSH EXAP responses, which address how the expert panel's recommendations will inform the future directions of the EXAP.

EXA Panel's Summary Recommendations for Future Considerations

Recommendation 1 -- [Modification of NIOSH Methods]

Many of the methods [in the NIOSH Manual of Analytical Methods (NMAM)] are overly prescriptive and inflexible which may result in laboratories modifying them to render them more robust and usable. Although NIOSH is aware that modifications occur to methods in practice, they should be more explicit and make it more widely known that modifications are allowed if the performance metrics of the original method can be achieved. One potential way to achieve this is to include this information which states the minimum performance standards for each method in the chapter "Purpose, Scope and Use of the NMAM."

NIOSH addressing at this time: Yes

Rationale: NIOSH values this feedback. The Institute relies on a performance-based approach for method validation [NIOSH 1995]. The methods are intended to be flexible and are not meant to be prescriptive and unalterable. The use of equivalent, harmonized methods that are fit-for-purpose is acceptable [Ashley 2015]. Modification of NIOSH methods by users such as industrial hygienists and environmental laboratories is permissible as long as acceptable method performance is maintained and demonstrated [Abell and Kennedy 1996].

The NMAM chapters that provide accompanying guidance for the NIOSH methods are excellent resources for explanatory and tutorial material. The NMAM 5th edition chapter on "Purpose, Scope and Use of the NMAM" details the importance of demonstrating and documenting performance. Providing this more explicit information in the NMAM about flexible options and end-user requirements for the modification, documentation, and use of NIOSH methods makes the NIOSH methods more robust and useable.

Recommendation 2 – [Backup Data for NMAM Methods]

Backup data should be publicly available and easily accessible for all adopted methods [in the NMAM]. Recognizing that methods and resulting data need to be 508 compliant, NIOSH could develop a standard template for reporting or recording backup data which would include the common location of all data. Previous backup data could be put in a 508-compliant format by a contractor or NIOSH should clearly indicate that backup data are not available because of non-compliance and those methods should be retired or updated. NIOSH could evaluate NIST and EPA formats for standardizing method to see if elements would be suitable for NIOSH to use.

NIOSH addressing at this time: Yes

Rationale: We concur that it is important to make backup data publically available. Each of the NMAM 5th edition methods has a backup data report to document the validity of the method. The currently 508-compliant reports can be accessed in the NMAM Backup Data Documentation section of the NMAM web page. The NMAM team is working to make all backup data documentation 508 compliant to enable their posting for public viewing.

The NMAM team has worked to provide common formats for documenting and presenting backup data behind NIOSH methods. These formats will be helpful to methods developers and their use will improve the ability of the NMAM team to make the backup data electronically available in a 508-compliant form.

Recommendation 3 – [Updating NMAM Methods]

To maintain a high relevance, NIOSH should update [NMAM] methods to platforms that are available in most laboratories (e.g., ICP-MS for elemental analysis) and maintain a set of robust validation parameters and backup data that are published with each analytical method in a standard format. Approaches to updating methods could be to first update those methods that are used most often or those that require the fewest changes.

NIOSH addressing at this time: Yes

Rationale: NIOSH appreciates this comment and we are committed to providing relevant and reliable methods that support the range of accuracy, cost, time, and technology needs of the occupational health community. The NMAM team routinely receives input from internal NIOSH users and external users, including from NIOSH tracking of internet activity on the NMAM webpage. In planning the transition from the NMAM 4th edition to the NMAM 5th edition, that tracking information was used to support prioritization decisions for the updating of methods.

NMAM content is periodically updated and users are encouraged to visit the NMAM website for the most current listing of methods and guidance chapters. Examples of recently published methodologies of high relevance for available and newly available platforms are the canister method for volatile organic compounds, which involves gas chromatography and mass spectrometry; the chapter on sampling and characterization of bioaerosols, which addresses a variety of methods for sampling and characterization of culturable and non-culturable bioaerosols; and the chapter on analysis of carbon nanotubes and nanofibers on mixed cellulose ester filters by transmission electron microscopy. Other methods that are currently being updated and expanded are the methods for chemical analysis, including newer, higher resolution methods involving liquid chromatography mass spectrometry.

Recommendation 4 – [NMAM Validation Parameters]

NIOSH discusses method metrics, validation and error in multiple introductory chapters (i.e., PS, ME, UA) in the NMAM. To be more concise, validation parameters should be listed alone in a separate chapter with clear definitions of required and optional metrics for each method/matrix combination. Minimum validation parameters should include extraction recovery (where applicable), limit of detection, limit of quantification, precision, accuracy and bias.

NIOSH addressing at this time: Yes

Rationale: We concur that addressing method metrics in a central location, in addition to within the method-specific locations, would increase user awareness of issues and examples for all sources of error and of steps to validate and improve the sampling and analytical methods.

To that end, the NMAM team is building on the information currently available in the NMAM resource document entitled Guidelines for Air Sampling and Analytical Development and Evaluation to create such a summary. The existing guidelines address issues of methods metrics, validation, and error for air sampling. The NMAM team is also developing criteria for validation of wipe sampling analyses.

Recommendation 5 – [Other Sources for Validated Methods]

The German Research Foundation's (Deutsche Forschungsgemeinschaft or DFG) develops compendiums similar to NMAM for German occupational and environmental health using a panel of experts that volunteer to develop

or “prove” proposed methods, largely because these methods are of keen interest to them as well. NIOSH may want to consider a similar approach as it is cost-effective, provides performance-based standards allowing method modifications as needed (e.g., if a laboratory doesn’t have tandem mass spectrometry, they may adapt to single stage mass spectrometry as long as the performance standards are met) and the validation or back-up data are standardized and provided by experts in the field instead of one single contract laboratory. NIOSH should also consider National Institute of Standards and Technology (NIST) strategies for standard reference material (SRM) validation or the Environmental Protection Agency’s (EPA’s) validation of analytical methods which are often carried out in the very labs that will eventually be required to perform the assay to ensure regulatory compliance.

NIOSH addressing at this time: No

Rationale: NIOSH appreciates this insightful comment regarding opportunities to go beyond our existing strategies and collaborations to streamline processes to get important methods more quickly validated. NIOSH concurs on the value of fostering and increasing collaborations with strategic methods development partners to streamline the adaption and validation of methods. However, a key challenge for NIOSH is that the fundamental validation scheme that currently underpins user confidence in the NMAM methods requires a degree of rigor that is challenging to achieve on a volunteer basis. The NIST SRM round robin series requests that participating experts in the field each use their own methods to validate the concentration of the SRM. This conflicts with the NIOSH approach, which requires that validation of NMAM methods be done under specific conditions laid out in the NMAM method. Any user-defined set of alternative conditions would require rigor in ensuring that the altered method could be reproduced by qualified experts.

As noted in our response to Recommendation 1 (see page 3), NIOSH already provides flexibility to end users who may have legitimate changes to the methods. NIOSH is aware that making these changes requires efforts by the end user, including collaborations with others, to verify that the methods they employ are capable of meeting the user’s analytical requirements. Such collaborations provide opportunities to illustrate the flexibility or optimization of methods for individual settings. Such demonstrations and collaborations also encourage other individual and organizational users to publish their validation results and experiences.

Recommendation 6 – [Prioritization of Exposure Assessment Research]

Prioritization of research with a limited budget should involve a strategic process that is need-and burden-driven. NIOSH should ensure objective, transparent and strategic prioritization of research efforts in the EXA program.

NIOSH addressing at this time: Yes

Rationale: NIOSH concurs on the importance of prioritization of our exposure assessment research activities. That prioritization is currently occurring as an integral part of the NIOSH Strategic Plan using the Burden, Need, and Impact (BNI) method. In this priority-setting process, burden is a foundational factor that considers risks from exposure to hazards; occurrence of injuries, illnesses, and deaths due to work-related factors; and impacts on economic factors and well-being. Need considers the extent to which NIOSH is the most appropriate organization to conduct the research. Factors such as intellectual capital, statutory authority, mission relevance, and financial capital are some of the considerations. Impact is a factor that is being assessed in terms of the potential that the proposed work will be successful in the adoption of policy, interventions, technologies, or solutions to occupational health problems in a timely and cost-effective manner. At each intersection between a work sector and a health concern in the NIOSH Strategic Plan, needed research and research-to-practice

activities are identified and research is being proposed. All of NIOSH research is guided by BNI in a transparent process through the NIOSH Strategic Plan.

Recommendation 7 – [Sharing of Best Practices]

NIOSH has several means of developing and publicizing "Best Practices" including the development of Recommended Exposure Limits (RELs) and the NIOSH Criteria Documents, as well as Research to Practice program and the Training and Education branch. Health Hazard Evaluation reports (HHE) could also be "mined" for best practice recommendations and/or HHEs could be a venue for testing exposure assessment strategies, instruments and methods. Both intramural and extramural research funding, particularly those that involve partnerships with employers or associations, could incorporate a goal of developing a best practices industry standard across many categories of exposure assessment. In addition to developing its own expanded set of best practices, NIOSH could be more proactive in working with the Occupational Safety and Health Administration (OSHA) to assist in translating non-regulatory (RELs) developed by NIOSH into regulatory Permissible Exposure Limits (PELs).

NIOSH addressing at this time: Yes

Rationale: NIOSH appreciates this insightful comment regarding opportunities to increase our use of resources such as the NIOSH Health Hazard Evaluations (HHEs) to identify the need for new methods, evaluate new methods, and to identify and share best practices. Similarly, NIOSH appreciates the recommendation to be more proactive in working with OSHA to assist in translating our non-regulatory RELs to regulatory PELs. A notable NIOSH activity for the development and sharing of best practices was the NIOSH publication on Criteria for a Recommended Standard: Occupational Exposure to Diacetyl and 2, 3-Pentandione. OSHA shares information about that guidance on their safety and health topic page on Flavorings-Related Lung Disease. Another notable activity to improve the availability of sound guidance for limiting occupational exposures is the ongoing NIOSH work to develop a current intelligence bulletin on the NIOSH Occupational Exposure Banding Process: Guidance for the Evaluation of Chemical Hazards. Occupational exposure banding is a process of quickly assigning chemicals into specific categories or bands that are assigned based on a chemical's potency and the negative health outcomes associated with exposure to the chemical. The output of this process is an occupational exposure band, which corresponds to a range of exposure concentrations that is expected to be protective to worker health. This is an example of work that requires integration across the broad spectrum of NIOSH programs. In addition to the application of methods from the NIOSH EXAP, the NIOSH occupational exposure banding process uses available, but often limited, toxicological data to determine a potential range of chemical exposure levels that can be used as targets for exposure controls to reduce risk among workers. In the Federal Register Notice presenting its hazard communication final rule, OSHA has noted the work by NIOSH in this area and pointed to "control banding as a guidance approach to recommending control measures for chemical exposures which would be readily available to small and medium-sized employers with chemicals in their workplaces to provide them with workplace-specific control recommendations."

Recommendations 8 – [Metrics for Assessing NIOSH Impact]

NIOSH has strived to incorporate impact assessment into the industrial hygiene paradigm which is commendable. These are informative metrics, however, additional metrics could be included during the onset of an activity to record information on impact and relevance as it is being generated. The methods within NMAM are generally unique for exposures that cause occupational risk. However, the real impact is realized when worker protection is measured either as a decrease in work days lost, or fewer fatalities or less money paid out

in workmen's compensation claims. A great need exists to capture and characterize more intermediate data to better demonstrate the ultimate impact of reduced exposure/improved worker health. NIOSH should expend time and energy in developing interpretable and creative metrics that can be integrated into programs or research priorities. More cross-disciplinary integration on developing metrics and assessing impact is needed. Suggested planning and data collection tools include logic models, surveys, and data collection from key informants.

NIOSH addressing at this time: No

Rationale: NIOSH appreciates this comment regarding the significant value of capturing and characterizing intermediate data on intervention effectiveness to better demonstrate the ultimate impact of reduced exposure/improved worker health. While the Institute is proactively taking steps to build its evaluation capacity, for example, by examining ways in which intermediate outcomes may be systematically collected, after careful assessment of EXAP's current resources including the Program's expertise, NIOSH has determined that it will not actively pursue the full implementation of this recommendation at this time. However, should the appropriate opportunity present itself, NIOSH will remain open to pursuing this recommendation in the future.

Recommendation 9 – [Sensor Performance Fundamentals]

For sensors to be used in general industry, a steady focus on fundamentals of sensor technology and well-resourced determination of fundamental sensor performance parameters would be a more appropriate focus. In other words, while the sensor and direct reading technology is impactful, NIOSH impact may be improved by solving fundamental performance issues for sensor technologies that are currently heavily used in multiple industries rather than funding relatively high-risk or one-of-a-kind sensors that may only impact a narrow segment of the working population, exhibiting limited overall impact on worker health.

NIOSH addressing at this time: No

Rationale: NIOSH concurs that having robust criteria, methods, and facilities for sensor performance validation is essential, especially for widely used methods. At the same time, there is a need to push the development and validation of methods for specific hazards such as peracetic acid or opioids for which currently available sensors are lacking or are poorly characterized. Given that NIOSH is both a creator and a user of sensor methods, such as in our Health Hazard Evaluations, emergency responses, and collaborations with other agencies, NIOSH believes that some work on special methods is justified through the BNI priority setting process.

Recommendation 10 – [Impact Recording for SBIR Grants]

The performance and use metrics of the Small Business Innovation Research (SBIR) grants have not been adequately recorded thus prohibiting their proper evaluation of relevance and impact. This seems to be a lost opportunity for NIOSH to capitalize on instrumentation development that could be potentially impactful. NIOSH should implement a better reporting system for SBIR grantees so the full impact of this program can be adequately evaluated.

NIOSH addressing at this time: Yes

Rationale: NIOSH recognizes the reporting limitations noted in Recommendation 10. As the panel noted, the outputs products of an SBIR grant are often not readily available for assessment of their relevance and impact, including through the National Institutes of Health (NIH) online reporting tool (NIH RePORTER). This lack of

information is in large part due to the time needed for grantees to complete products, attain patents, and achieve impacts once grant funding has ended. However, recognizing this "time lag," NIOSH plans to actively explore other options to identify and record SBIR outputs and impact. This may include leveraging previously untapped reporting systems or developing new systematic means to collect this information. More information about how these actions relate to SBIR Phase 1 Grants and SBIR Phase 2 Grants follows.

SBIR Phase I Grants: Most SBIR grants are for Phase I research, defined as pilot/feasibility work, proof-of-concept efforts, or prototype development, with a 6 month period of performance that is often extended an additional 6 months with a no-cost time extension. Phase I SBIR grantees provide a final report within 15 months of receiving the initial award, which is often not enough time to see significant outcomes beyond the success or failure of the pilot study to adequately develop results that merit further study (Phase II). The Phase I outputs are different from other research awards. While some SBIR awards generate peer reviewed manuscripts, most do not. Instead, the outputs typically include instrumentation, devices, or technologies and their associated patents or inventions. Any patent or invention generated through Federal funding should be reported by the investigator to iEdison (a clearinghouse for federally funded patent and inventions). NIOSH is working to gain access to iEdison to better identify SBIR outputs.

SBIR Phase II Grants: SBIR Phase II grant applicants must first successfully complete a Phase I project. A successful Phase II application is one of the significant outputs from a Phase I project. Phase II applications are evaluated on the scientific and technical merit of the Phase I work, along with the commercial potential of the proposed Phase II project. The objective of a Phase II award should include the continued research and development efforts initiated during Phase I, with a focus towards product refinement and commercialization. Results from a successful Phase II award should be "pre-commercialization" of a product, often including partnering with a larger entity to assist with production, distribution, and other means to eventually get the technology to market. The grantee's two-year period of performance and reporting requirements are completed well before product commercialization. NIOSH will evaluate the feasibility of contacting SBIR Phase II grantees after their performance period ends to document additional outcomes including instrumentation development and commercialization of products.

Recommendation 11 – [Alternate Methods for Impact Assessment]

NIOSH cited the lack of resources for conducting longitudinal studies or randomized control trials as well as employers' reluctance to participate in health studies as barriers to fully evaluate impacts [of exposure assessment, hazard assessment, risk characterization, and risk management] on occupational health. While impact is challenging to quantify, potential and actual impacts on health can be assessed without these "gold standard" methods. Suggestions for ways to do this include case studies, comparing exposure levels measured with real-time sensors vs old method, commercialization of sensors, and return on investment.

NIOSH addressing at this time: No

Rationale: This recommendation provides an instructive reinforcement to the panel's recommendation 8 regarding the value of improving the manner in which we identify and apply metrics for assessing NIOSH impact. The Institute is dedicated to continuing to demonstrate its impact by examining ways to evaluate its return on investment and place increased emphasis on translational research, to name a few. While the Program may be able to make some progress in this area, after careful assessment of EXAP's current resources including the Program's expertise, NIOSH has determined that it will not actively pursue the full implementation of this recommendation at this time. However, should the appropriate opportunity present itself, NIOSH will remain open pursuing this recommendation in the future.

References

Abell MT, Kennedy ER [1996]. Performance-based methods. Anal Chem 68: 459A.

Andrews RN, et al. [2016]. Interlaboratory evaluation of cellulosic acid-soluble internal air sampling capsules for multi-element analysis. J Occup Environ Hyg 13: 40-47.

Ashley K [2015]. Harmonization of NIOSH sampling and analytical methods with related international voluntary consensus standards. J Occup Environ Hyg 12: D107-D115.

Ashley K, et al. [2012]. Interlaboratory evaluation of trace element determination in workplace air filter samples by inductively coupled plasma mass spectrometry. J Environ Monit 14: 360-367.

Ashley K, O'Connor PF [2016]. Purpose, scope and use of the NIOSH Manual of Analytical Methods; Chapter PS. In NIOSH Manual of Analytical Methods, 5th ed. NIOSH: Cincinnati.

Kennedy ER, et al. [2016]. Development and evaluation of methods; Chapter ME. In NIOSH Manual of Analytical Methods, 5th ed. NIOSH: Cincinnati.

NIOSH [1995]. Guidelines for air sampling and analytical development and evaluation. NIOSH: Cincinnati; DHHS (NIOSH) Publ. No. 95-117.

Oatts TJ, et al. [2012]. Preparation, certification and interlaboratory analysis of workplace air filters spiked with high-fired beryllium oxide. J Environ Monit 14: 391-401.