Respiratory Diseases Research Program
Update: September, 2012 to July, 2014

For the NIOSH Board of Scientific Counselors

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Abbreviations Used in Report

ACBS: Asthma Call-Back Survey
ACOEM: American College of Occupational and Environmental Medicine
ACR: American College of Radiology
AHS: Agricultural Health Study
APHA: American Public Health Association
AOEC: Association of Occupational and Environmental Clinics
ATS: American Thoracic Society
BLS: Bureau of Labor Statistics
BRFSS: Behavioral Risk Factor Surveillance System
BSC: Board of Scientific Counselors
Cal/OSHA: California Division of Occupational Safety and Health
CDA: clinical document architecture
CDC: Centers for Disease Control and Prevention
CDPH: California Department of Public Health
CDS: clinical decision support
CFR: code of federal regulations
CIB: current intelligence bulletin
CIR: Chest Image Repository
COPD: chronic obstructive pulmonary disease
CSTE: Council of State and Territorial Epidemiologists
CWP: coal workers' pneumoconiosis
CWHSP: Coal Workers' Health Surveillance Program
DRDS: Division of Respiratory Disease Studies
DSHEFS: Division of Surveillance, Hazard Evaluations, an Field Studies
EHR: electronic health record
ERL: Electronic Radiology Laboratory
ERS: European Respiratory Society
eWoRLD – Work-Related Lung Disease Surveillance System
FTE: fulltime employees
FEV1: forced expiratory volume in 1 second
GAO: Government Accountability Office
GPRA: Government Performance and Results Act
HHE: health hazard evaluation
HL7: Health Level Seven International
HMW: high molecular weight
HRCT: high resolution computed tomography of the chest
ICD-10-CM: International Classification of Diseases, 10th Revision, Clinical Modification
IHE: Integrating the Healthcare Enterprise
I/O: industry and occupation
ILO: International Labour Organization
IOM: Institute of Medicine
IT: information technology
JEM: job-exposure matrix
LMW: low molecular weight

MESA: Multi-Ethnic Study of Atherosclerosis
miRNA – micro-ribonucleic acid
MSHA: Mine Safety and Health Administration
NA: National Academies
NAS: National Academies of Science
NCEH: National Center for Environmental Health
NCHS: National Center for Health Statistics
NCVHS: National Committee on Vital and Health Statistics
NHANES: National Health and Nutrition Examination Survey
NHIS: National Health Interview Survey
NHLBI: National Heart, Lung, and Blood Institute
NIOCCS: NIOSH Industry and Occupation Computerized Coding System
NIOSH: National Institute for Occupational Safety and Health
NORA: National Occupational Research Agenda
NORMS: National Occupational Respiratory Mortality System
OA: occupational asthma
ODH: occupational data for health
OHI: occupational health indicators
ONC: Office of the National Coordinator for Health Information Technology
OPA: ortho-phthalaldehyde
ORD: occupational respiratory disease
OSHA: Occupational Safety and Health Administration
PEL: permissible exposure limit
PHDSC: Public Health Data Standards Consortium
RDRP: Respiratory Diseases Research Program
REL: recommended exposure limit
RNA: ribonucleic acid
SDO: standards development organization
SPFI: spray polyurethane foam insulation
SPIROLA: spirometry longitudinal data analysis software
TDI: toluene diisocyanate
USDOL/DOL: US Department of Labor
VA: Department of Veterans Affairs
VOC: volatile organic compound
WEA: work-exacerbated asthma
WoRLD Surveillance Report: Work-Related Lung Disease Surveillance Report
WRA: work-related asthma
WTC: World Trade Center

Introduction

This report provides an update to the Respiratory Diseases Research Program (RDRP) report submitted to the Board of Scientific Counselors (BSC) in September 2012. That report covered a time interval of about 4.6 years (January 2008 – August 2012). The current report covers work done since that time, a considerably shorter interval of less than 2 years (September 2012 – July 2014).

The current report is one of several prepared by the National Institute for Occupational Safety and Health (NIOSH) for BSC review, in compliance with requirements under the Government Performance and Results Act (GPRA). Under GPRA, NIOSH must identify performance targets and track progress towards those targets over time: http://www.cdc.gov/fmo/topic/Performance/performance_docs/FY2012_CDC_Online_Performance_Appendix.pdf. One of NIOSH's current performance targets is to track the progress of several NIOSH programs that underwent National Academies (NA) reviews during October 2006 to March 2008 in implementing the recommendations of those reviews. RDRP is one such program. RDRP includes all individuals and groups supported by NIOSH to do work that is relevant to occupational respiratory diseases, whether intramural or extramural. RDRP is defined in that manner because this inclusive view is the one most relevant to NIOSH's societal impact in the area. This report is an update to the BSC documenting RDRP's progress in addressing the 5 highest priority NA recommendations to the program.

Selection of priorities and implementation of plans to address them has been an ongoing process since the NA report *Respiratory Diseases Research at NIOSH* was released in 2008: http://www.nap.edu/catalog.php?record_id=12171. That review was very positive. RDRP received a score of 5/5 for relevance and 4/5 for impact. The evaluation committee indicated that had it been able to give a fractional rather than integer score, the score for impact would have been between a 4 and a 5. The committee also made many recommendations for maintaining and improving RDRP. Since 2008, a cross-Institute RDRP steering committee has reviewed the program's strategic goals in detail annually and made adjustments as appropriate. This group has also played an important role in making intramural funding decisions responsive to the strategic goals.

In 2009, RDRP developed an implementation plan in response to the NA review that reflected input from across NIOSH. It listed all the NA recommendations and it identified the highest priorities from among them. These were digital chest imaging, flavorings-related lung disease and occupational respiratory disease (ORD) surveillance: http://www.cdc.gov/niosh/nas/pdfs/RDRP_Implement_for_BSC2.pdf. The BSC reviewed the implementation plan in 2009 and approved it.

In 2011, RDRP was asked to identify highest priority recommendations from the NA review to be tracked for purposes of compliance with GPRA. RDRP selected the 3 existing high priorities, plus 2 more high priority recommendations to address work-related asthma (WRA) and work-related chronic obstructive pulmonary disease (COPD). These 5 priority areas were endorsed by the BSC in 2011.

In 2012, the BSC reviewed RDRP's progress in addressing these 5 priorities. In its review, the BSC assigned scores in 4 areas: relevance sustainability, progress, and potential impact. RDRP's scores ranged between 4.5 and 5, and can be found in the attached 2012 score report in Appendix 6.

The current report is organized around the 5 priorities. Each is described in a separate section, emphasizing the currently-rated areas of progress and impact. Each section is supported by an appendix that contains references and other supporting materials. Unless otherwise specified, the references cited for that section are in its supporting appendix. These are: Appendix 1: Occupational Respiratory Disease Surveillance; Appendix 2: Digital Chest Imaging; Appendix 3: Flavorings-Related Lung Disease; Appendix 4: Work-Related COPD; and Appendix 5: Work-Related Asthma.

Occupational Respiratory Disease Surveillance
(Outputs listed in Appendix 1, unless otherwise specified)

Text from NA Report: "Systems for Surveillance: NIOSH should provide appropriate resources for and engage in high-priority occupational [respiratory] disease surveillance." (p136)

Responsive RDRP Goal: Improve surveillance and workforce screening for work-related respiratory diseases.

Status: In progress

Background: Surveillance is critical for RDRP planning, priority setting, and tracking of progress. See the 2012 report for a more detailed description of background considerations.

External Factors:
Over the past several years, the RDRP surveillance group has prioritized efforts in support of promulgation by the Mine Safety and Health Administration (MSHA) of a new respirable coal mine dust rule. These efforts have contributed to the rule's promulgation and initial implementation was on August 1, 2014. Since October 2010, when MSHA first proposed the rule, Congress has engaged the Government Accountability Office (GAO) to conduct 2 investigations of the rule's scientific basis. RDRP was extensively engaged and expended significant effort on both reviews. GAO's first report, issued in August 2012, found that the evidence used by MSHA to propose lowering the permissible exposure limit (PEL) for respirable coal mine dust did indicate that such a change would reduce miners' risk of disease. Much of this evidence came from NIOSH research. The second GAO investigation, starting in May 2013 and reported in April, 2014, documented that NIOSH surveillance data had helped in motivating MSHA to promulgate its new rule. Also, the (PEL) proposed by MSHA was appropriately based on epidemiological data that allowed evaluation of exposure-response relationships.

RDRP has also devoted much effort to preparing for the expansion of health surveillance services that will be offered to coal miners based on the MSHA rule. NIOSH has the statutory responsibility to manage this health surveillance program. In the past, operators of coal mines were only required to offer health surveillance to underground coal miners. Under the new rule, surveillance will also be offered to surface miners. The rule also expands the surveillance program from only obtaining occupational history and chest radiographs to additionally obtaining a respiratory symptom assessment and spirometry. RDRP must approve health surveillance programs from mines and also approve the medical facilities offering health surveillance testing. RDRP will also manage the flow of information. After the new MSHA rule was announced on May 1, 2014, RDRP worked intensively to revise its regulations found in 42 CFR 37 to allow implementation of the enhanced surveillance. RDRP's Interim Final Rule revising the regulations was published on August 5, 2014.

BSC Evaluation, 2012
The main recommendation from the 2012 report was that RDRP should consider the National Academies' (NA) recommendation to develop an occupational respiratory disease surveillance plan. In response, it should be noted that RDRP is an active component of, and participant in,

the broader NIOSH surveillance program and has actively participated in NIOSH's strategic planning for surveillance. RDRP contributed to the development of NIOSH's original Surveillance Strategic Plan in 2001 (http://www.cdc.gov/niosh/docs/2001-118/). RDRP has continued to actively participate in the cross-Institute Surveillance Program and has contributed to its current goals (http://www.cdc.gov/niosh/programs/surv/goals.html). Additionally, in 2009, RDRP posted a detailed response to this and other NA recommendations in a comprehensive implementation plan (http://www.cdc.gov/niosh/nas/pdfs/RDRP_Implement_for_BSC2.pdf). Identification of ORD surveillance as one of the highest RDRP priorities and a discussion of actions being taken to implement recommendations and advance RDRP surveillance is provided in Section 3 of that document. The BSC also recommended more formal efforts to quantify the impact of RDRP surveillance outputs. This recommendation is also being addressed within the context of broader NIOSH efforts to quantify impact by instituting regular (at least annual) recording of outcomes related to all NIOSH projects by the responsible project officers into an electronic database. This will facilitate retrieval and review of impacts over time.

Implementation of Recommendation

Activity A: Conduct surveillance for work-related respiratory diseases using available data sources, including mortality data, cancer center data, other national data sources or studies, and/or State-based surveillance, with ongoing analysis and dissemination of results.

Background:
RDRP maintains a number of surveillance products, many of which can be accessed via the ORD surveillance home web page at: http://www.cdc.gov/niosh/topics/surveillance/ords/.

Progress made or maintenance efforts since last review:
There has been important progress in this area since the 2012 report. The NIOSH Work-Related Lung Disease (WoRLD) Report is a major source for up-to-date national morbidity, mortality, and hazard surveillance information relevant to occupational respiratory disease (http://www2.cdc.gov/drds/worldreportdata/). The health and hazard surveillance data presented in the report is gleaned from a variety of sources (http://www2a.cdc.gov/drds/WorldReportData/html/SourcesOfData.asp). Since 2008, the report has been converted to electronic format in the Work-Related Lung Disease Surveillance System [eWoRLD], allowing for ongoing updating of its content. The most recent major update was completed in April, 2014. Seventy-five updated tables and figures were added from March 2012 to April, 2014. eWoRLD has had 60,473 visits since 2008, with 23,662 occurring between September 2012 and May 2014.

Another important source of national data documenting burden of occupational respiratory disease is the National Occupational Respiratory Mortality System (NORMS), which enables users to easily obtain national mortality data via queries customized to their information needs (http://webappa.cdc.gov/ords/norms.html). NORMS had 9,143 visits from September 2012 to May 2014. NORMS is typically updated annually, depending on when the most recent annual mortality data becomes available for integration into the system.

RDRP also leverages occupational respiratory disease surveillance information from large national surveys. For example, RDRP has made investments to insert questions about work and work-relatedness of asthma and chronic obstructive pulmonary disease (COPD) into expensive national surveys such as the National Health and Nutrition Examination Survey (NHANES), the National Health Interview Survey (NHIS), and the Behavioral Risk Factor Surveillance System (BRFSS). A new occupational health indicator on work-related asthma (WRA), described below, is an example of this leveraging. Other examples of these activities can be found in Appendix 1, and will be discussed in more detail in the report sections on COPD and WRA.

State-based surveillance has also been an active area of effort (http://www.cdc.gov/niosh/topics/surveillance/ords/StateBasedSurveillance.html). NIOSH currently funds 23 states to conduct population-based "fundamental" surveillance (http://www.cdc.gov/niosh/oep/reports.html#surv). These states report on various occupational health indicators (OHI). Data are available on the Council of State and Territorial Epidemiologists (CSTE) website (http://www.cste.org/group/OHIndicators). Pneumoconiosis hospitalizations, pneumoconiosis mortality, and incidence of malignant mesothelioma are well-established OHI. An important new OHI starting this year, based on data from the BRFSS asthma call-back survey, will be asthma among adults caused or made worse by work. In addition to the states that report on OHI as part of fundamental surveillance, some states are funded to carry out case-based or "expanded" sentinel surveillance. In the area of occupational respiratory diseases, efforts are focused on silicosis (2 states) and/or WRA (5 states). RDRP has provided technical support and subject-matter expertise to assist states in these surveillance activities, as well as in dissemination of information and intervention activities. From 2012 to 2014, RDRP conducted 3 meetings with states conducting enhanced WRA surveillance and silicosis surveillance. In addition, RDRP invites states that are funded for fundamental surveillance, but are interested in surveillance for asthma and silicosis. Typically, 4 to 7 representatives from these states have also participated in the meetings. State-based surveillance has resulted in a number of research publications (Appendix 1). For example, a study using state-based sentinel surveillance data showed that there were gender differences in workplace exposures, occupations, and industries that contributed to WRA. It also documented the agent groups most frequently associated with WRA (White 2014). Another publication documented the burden of isocyanate-induced asthma in Washington State (Reeb-Whitaker 2013).

Impact(s) made since last review (process- or outcome-related):
During the current rating period, eWoRLD and NORMS have played an important role in shaping public policy. For example, MSHA has cited RDRP mortality data documenting 76,000 deaths caused or contributed to by coal workers' pneumoconiosis since 1968 as in important motivator in promulgating the new respirable coal mine dust rule, which became effective on August 1, 2014 (http://www.msha.gov/endblacklung/). Similarly, RDRP surveillance data have been used by proponents and opponents alike of OSHA's proposed silica rule. Thus, the availability of these data continues to have great societal relevance and impact.

RDRP surveillance efforts play an important role in raising awareness about potential emerging issues. For example, after publications documented the occurrence of silicosis among engineered stone countertop workers in other countries, RDRP surveillance investigators based in states and NIOSH posted a NIOSH Science Blog on the topic (http://blogs.cdc.gov/niosh-

science-blog/2014/03/11/countertops/). A physician who read the blog subsequently contacted the authors to report the first recognized case of silicosis in such a worker in the U.S.A. and a case report is in preparation. State participants in surveillance have been motivated to produce numerous pieces of outreach materials, many of them accessible through the NIOSH state-based occupational health surveillance clearinghouse (http://wwwn.cdc.gov/niosh-survapps/statedocs/). States have also been motivated to provide information for the new work-related asthma OHI described above. RDRP assistance with coding and submitting data has facilitated participation in the new OHI by states with NIOSH funding for fundamental or enhanced surveillance. Another example of an effort motivated in part by interactions with RDRP surveillance investigators is OSHA's recently announced National Emphasis Program on occupational exposure to isocyanates (https://www.osha.gov/OshDoc/Directive_pdf/CPL_03-00-017.pdf). Thus, RDRP surveillance has had important, useful, societal impacts.

Future plans:
RDRP will continue to work to improve the data available for planning, priority setting, tracking progress in the prevention of occupational respiratory diseases, and communicating this information to those who would benefit from it. An important strategy will be to continue leveraging existing data and systems for occupational respiratory disease surveillance by working with other Federal agencies, parts of CDC, state and local government, etc. State-based surveillance will continue to be very important. RDRP will participate in the secondary review of grant applications submitted by states in response to NIOSH's recent U60 Cooperative Agreement grant announcement to support state-based surveillance. RDRP will work in partnership with states that are funded to provide enhanced occupational respiratory disease surveillance. RDRP will also work in partnership, as possible, with states that are funded to conduct fundamental surveillance, for example to maintain the new OHI for asthma caused or made worse by work. We will use a range of informative data sources to maintain and update surveillance products, such as eWoRLD and NORMS, and to publish peer-reviewed research. We will also continue to be opportunistic, seeking innovative approaches to surveillance, such as by using electronic health records (described in Activity B below).

Activity B: Develop, demonstrate, and disseminate innovative approaches to surveillance for work-related respiratory diseases, including use of information from the healthcare system such as information in electronic health records (EHRs).

Background:
Innovative approaches are needed to improve surveillance for work-related respiratory diseases. Electronic health records provide an important potential opportunity to improve surveillance for work-related disease and injury and to improve quality of care for work-related conditions. Much effort has focused on creating the foundations to realize this potential. See the 2012 report for additional background information.

Progress made or maintenance efforts since last review:
From 2012 to present, great progress has been made in establishing stakeholder and partner policy support, in preparing technical building blocks, and in remaining engaged with the Office of the National Coordinator for Health Information Technology (ONC), the part of HHS that has oversight of electronic health records. RDRP personnel play a key role in the cross-Institute

working group focused on this issue, and participate in many EHR-related activities outside of NIOSH to assure that occupational issues are considered and addressed in the evolving standards for EHRs. Significant personnel time has been dedicated to this effort. A Health and Occupation Informatics Analyst coordinates EHR activities and serves as Project Officer on "Electronic Health Records: Role in prevention and surveillance of occupational illness and injury," which became an official NIOSH project in FY12 (10/1/2011). In addition, a contracted Systems Analyst with informatics expertise is 80% time on the effort, as is a contractor providing administrative support. A number of investigators from across several NIOSH divisions contribute time totaling two full-time equivalents (FTE) to EHR work.

There have been a number of key activities and accomplishments. One was the development of an "information model" that outlines and relates all of the key occupational information that would be of clear health and surveillance value in an EHR. In preparing this model, value sets were defined and approved by healthcare IT code-management systems. Another was development and preliminary testing of a prototype intelligent dropdown for real-time capture and coding of industry and occupation. Through a contract with an investigator at the University of Utah, feasibility was demonstrated for patient entry of industry and occupation to be coded, stored, and used in EHRs. In another activity, NIOSH assisted a Massachusetts community health center that had captured patients' occupation in EHRs during registration to code the information, in part using the NIOSH industry and occupation (I/O) computerized coding system (NIOCCS). NIOSH also provided population health analyses of the data, linking I/O information with demographic information to guide the improvement of patient education materials and care provider training. Work on a Health Level-7 (HL7) committee has provided a "functional profile" and associated glossary for handling information in EHRs that interact with occupational public health programs and the terminology associated with the profile that can be used by system developers. Work with the Public Health Data Consortium led to development of a draft standard data sharing template to facilitate consistent formatting of work information within documents that are shared electronically between systems and which was "product-tested" in an "Interoperability Showcase" as part of the Public Health Informatics Conference, as noted in the impact section below. Three NORA intramural projects were funded to evaluate feasibility, develop clinical decision support modules, and incorporate work information in base HL7 standards for data sharing and EHR system functionality. The EHR group engaged in dialog at the national level through testimony, comment, and presentations. The EHR group also held a workshop on privacy and security issues raised by the inclusion of work information in EHRs. The workshop, held on June 19-20, 2013, included a diverse group of intramural and extramural experts and stakeholders that identified issues and proposed potential solutions.

Impact(s) made since last review (process- or outcome-related):
In 2014, the ONC posted a proposed rule: *Voluntary 2015 Edition Electronic Health Record (EHR) Certification Criteria; Interoperability Updates and Regulatory Improvements* (https://www.federalregister.gov/articles/2014/02/26/2014-03959/voluntary-2015-edition-electronic-health-record-ehr-certification-criteria-interoperability-updates). Because of the work done by NIOSH, ONC acknowledged the efforts of NIOSH and other stakeholders and noted that it is considering adding capabilities for handing I/O data to its 2017 certification requirements for EHRs:

> "The National Institute for Occupational Safety and Health (NIOSH) and other stakeholders are working to develop and support standards and tools for the collection, storage, and exchange of I/O information. It has developed a relational information model of work information (including I/O) for EHR technology and is in the process of translating it into the HL7 [Health Level-7; international standards for transfer of clinical and administrative data between hospital information systems] reference information model format. NIOSH is also working with HL7 [the term HL7 also refers to an international standard setting organization] to reflect functionality for work information in EHR technology and is collaborating with other stakeholders to ensure that I/O information is incorporated into interoperability standards, such as standards to support case reporting to public health. A reusable CDA [clinical document architecture] template of Occupational Data for Health (ODH) is part of the social history section within the published Healthy Weight (HW) trial implementation profile, which has been tested at the 2014 Integrating the Healthcare Enterprise Connectathon. In addition, prototype occupation-related CDS [clinical decision support] knowledge bases for primary care providers are in development."

Thus, RDRP has contributed to a cross-Institute effort to further include occupational health information in electronic health records that could be used to not only improve individual care with clinical decision support knowledge generated by NIOSH and partners, but also to improve our ability to obtain morbidity and mortality surveillance data from healthcare systems. Of particular importance has been the development of materials for adoption into standards that facilitate interoperability (electronically sharing data such that it is fit for use in the receiving system), such as an HL7 "functional profile" that outlines functions or operations that EHRs should perform to meet the needs of public health and a glossary of occupational terms that includes terms such as "current occupation," "occupational history," and "exposure."

Future Plans: RDRP is continuing to play a major role in contributing to NIOSH work on the real-time capture and coding of industry and occupation information in clinical settings with a contract for analyzing the coding language, algorithms, and logic needed, as well as devising and testing strategies for capturing input from patients. Another key activity is the pilot testing of clinical decision support based on the interface of work and health, which will provide a roadmap for ongoing NIOSH efforts to share knowledge in this form. The ODH template was incorporated in the Healthy Weight profile, which is for use in reporting BMI data to public health, which will help us in encouraging the template's use by others. The glossary of occupational terms will be voted on by HL7 as part of a complete glossary of terms for the EHR Functional Model. Proceedings from the privacy and security workshop will be prepared for publication. A communications plan will be prepared, which includes the posting of a NIOSH Topic Page for ongoing dissemination of products and information to our partners and the public. A newly funded project proposal includes incorporating International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) external cause codes and the ODH template into fundamental standards for sharing health data electronically and standards for EHR system operations.

<u>Activity C (new to 2014 Report)</u>: Collect and disseminate surveillance information by carrying out NIOSH's unique responsibilities to conduct Health Hazard Evaluations and to provide coal miners with a national program of health surveillance.

<u>Background</u>:
NIOSH has the unique ability to conduct HHEs based on the Occupational Safety and Health Act of 1970. Although the Health Hazard Evaluation (HHE) Program was reviewed separately by the BSC, it is appropriate to mention HHEs as a relevant RDRP surveillance activity here. RDRP is an active participant in the HHE program and respiratory-related HHEs have played a critical role in recognizing sentinel outbreaks of emerging occupational respiratory diseases. These HHEs have also played an important role in motivating subsequent responses to these emerging issues

NIOSH also has a unique responsibility to provide a national program of health surveillance to coal miners. The Coal Workers' Health Surveillance Program (CWHSP), an RDRP responsibility, was first authorized by language in the Federal Coal Mine Health and Safety Act of 1969. That language was carried forward into the current Federal Mine Safety and Health Act of 1977. As noted earlier in the surveillance section, surveillance was previously based on chest radiography and offered only to active underground coal miners. The surveillance program has had major impact by creating public recognition of respiratory disease caused by coal mine dust as a continuing problem and in motivating MSHA to promulgate a new respirable coal mine dust rule. As of August 1, 2014, new MSHA and NIOSH regulations are expanding the surveillance program to include surface miners and expanding the surveillance testing offered to also include spirometry.

<u>Progress</u>:
Over the period evaluated, 25 respiratory disease-related HHE reports have been posted on the NIOSH website (Appendix 1). Evaluations focused on chemical hazards in 13 of these reports. A range of chemical hazards were evaluated such as chlorine, hydrogen sulfide, phosphine, solvents and hazardous drugs. Three of these HHEs addressing chemical hazards were related to food flavorings such as diacetyl and 2,3-pentanedione. Other issues addressed included hazards related to preserving pet food ingredients with phosphine gas, use of oil- and glycol-based smoke simulants to train fire fighters, emissions from small arms used on a military firing range, and concerns about beryllium contamination in an office complex. Nine of the HHEs primarily addressed infectious hazards, with six of those focused on tuberculosis. One addressed potential exposures in a medical examiner's office, one potential zoonotic disease exposures in people working with marine mammals, and one the emerging issue of coccidioidomycosis (in this case, among prison employees in a part of California where the disease is endemic). Two HHEs focused on indoor environmental quality issues and one HHE focused on allergen exposures among poultry breading workers.

Other products are also derived from work on HHEs. For example, a NIOSH Alert on Indoor Dampness and Mold is based in a large part on HHE experience and provides up-to-date guidance for dealing with this issue (see the update on WRA on page 63 for more information). A report in the Morbidity and Mortality Weekly Report describes a cluster of obliterative bronchiolitis cases in a facility that produces flavored and unflavored coffee and is the site of an

ongoing HHE investigation. A published research paper documented that excess spirometric restriction can occur in flavorings-exposed workers. Additionally, we have worked to improve our ability to provide HHEs. For example, we recently obtained government IT security (Certification and Accreditation) approvals for using a modular, internet-based questionnaire that will make it possible for us to more easily administer health surveys via the internet during HHEs. Finally, RDRP will also participate in, and benefit from, the actions detailed in the recent HHE Program report to the BSC.

Over the period evaluated, there were 4 peer-reviewed publications based on CWHSP data (see Appendix 1). These confirmed the validity of previous observations that the prevalence of coal workers' pneumoconiosis (CWP) had declined over several decades, reaching a low in the mid to late 1990s, but had increased since. It was also documented that coal miners in regions with high frequency of CWP also had higher frequency of abnormal lung function, as measured by spirometry. Also, abnormal spirometry was about 3 times more common than chest radiographic abnormalities suggestive of CWP. Peer reviewed publications identified working in small mines as a risk factor for respiratory disease caused by coal mine dust. We have used CWHSP data to provide information about CWP morbidity for dissemination in eWoRLD and have maintained a CWHSP data query system, allowing users to make customized queries of the data (http://webapp.cdc.gov/ords/cwhsp-database.html). As will be detailed in the section on digital radiography, 2013 was CWHSP's first year for full implementation of using of digital chest radiography to provide surveillance services. This is a major advance that will facilitate provision of services going forward.

Impact:
HHEs have great impact on the individual workplaces where evaluations are provided, which can use the results to make their own improvements. HHEs also have broader impacts. For example, sentinel identification of flavorings-related lung disease has since motivated work by many to better understand and prevent this important problem, as discussed in the section devoted to flavorings.

Operation of the CWHSP has led to important impacts during the rating period. As noted in this activity's "External Factors" above, RDRP responded to numerous requests for information from the GAO about CWHSP information as part of GAO's investigation of MSHA's respirable coal mine dust rule. MSHA and GAO have both noted that CWHSP data helped to motivate promulgation by MSHA of that rule. In fact, MSHA chose to announce the rule at the NIOSH-Morgantown facility to honor the contributions of the CWHSP team. Promulgation of new regulations by MSHA and NIOSH will extend health surveillance from only underground coal miners to underground and surface miners. It will also provide miners not only with periodic chest radiographs, but also with periodic spirometry. This will enhance the ability of the surveillance program to detect respiratory disease caused by coal mine dust in all coal miners. It will also enable us to identify miners at risk for developing chronic obstructive pulmonary disease (COPD), a known complication of coal mine dust exposure.

Future Plans:
We will complete ongoing HHEs. For example, an HHE in progress for which preliminary results have been reported in an abstract is evaluating a cluster of pulmonary lymphoproliferative

disease in workers exposed to an unusual type of metalworking fluid. Another is following up on the cluster of obliterative bronchiolitis in coffee manufacturing workers that was recently reported in the MMWR. We will also continue to solicit new HHEs and prioritize our efforts as was discussed in the HHE Program's report. With regard to the Coal Workers' Health Surveillance Program, we will work to implement the expanded surveillance that was mandated under the new respirable coal mine dust regulations. This will be a major effort that will involve receiving and approving surveillance plans from mines that did not previously have such plans; approving medical facilities to provide spirometry testing; establishing a coordinated spirometry program that receives data, reports results to individual miners, and conducts quality assurance; and analyzing and reporting data in aggregate for public health surveillance purposes.

Digital Chest Imaging
(Outputs listed in Appendix 2, unless otherwise specified)

Text from NA Report: "The committee recommends that the effectiveness of digital radiography in CWP surveillance should be an important continuing research priority, which will extend to all interstitial lung diseases." (p135)

Responsive RDRP Goal: Perform studies and develop updated recommendations for chest imaging of pneumoconiosis that allow implementation of digital imaging for classification of chest radiographs using the International Labour Organization classification system. Transition NIOSH's mandated surveillance activities, including the B Reader certification program, to use of digital chest imaging.

Status: In progress

Background: Due to the widespread adoption of digital radiography in US clinical settings, it is critical that occupational health surveillance for respiratory disease also transition to using digital radiography. See the 2012 report for a more detailed description of background considerations.

External Factors: Just as most medical facilities now use digital radiography exclusively, most physicians (particularly radiologists) are most comfortable working with digital radiographic images. Thus, there is a need to transition physician training and competency testing in use of the International Labour Organization (ILO) classification system to modern digital format. The RDRP program that provides this training and testing to physicians in the U.S.A. is the B Reader certification program. Because ILO classification of chest radiographic images is not typically used in routine clinical care, its use is not generally taught to U.S. physicians nor is competency in its use evaluated in physicians or others except by the B Reader Certification program. Thus, updating physician training and testing into digital format has been another area of RDRP focus over the rating period. See the 2012 report for additional discussion of external factors.

BSC Evaluation, 2012
The BSC evaluation in 2012 was very supportive of RDRP efforts in this area. We thank the BSC for its support.

Implementation of Recommendation

Activities A & B: Perform studies and develop updated recommendations

Background:
By the time of our last report to the BSC in 2012, RDRP had completed sufficient research to support promulgation of new regulations using digital chest radiography. Thus, our primary focus during the current rating period has been more on implementation than on research. Still, there are some significant accomplishments to report.

Progress made or maintenance efforts since last review:

In 2011, with RDRP's assistance, ILO issued guidelines enabling classification of digital chest radiographs. The guidelines provided for comparison of examinees' images to digitized standard images that were displayed side by side on diagnostic medical monitors. During the current rating period, RDRP completed a study validating the use of the new ILO digitized standard images for classification of small pneumoconiotic opacities. It was found that when digital chest radiographs are obtained and displayed appropriately, results of pneumoconiosis classifications using the 2011 ILO digitized standards are comparable to older film-based ILO classifications and to classifications performed using earlier research standards. (Halldin et al 2014, Appendix 2).

Another effort has been to develop a web-based Chest Image Repository (CIR). The CIR will provide important infrastructure by providing well-validated images that can be used in future research, quality assurance, teaching, and certification testing efforts. It has been established through a contract with the Electronic Radiology Laboratory (ERL) at Washington University in St. Louis, MO. CIR is collecting, anonymizing, and storing digital images of pneumoconiosis submitted by donors throughout the world. In addition to plain chest radiographic images, CIR also includes chest CT scans and occupational and clinical histories. Ultimately, the digital chest images will represent a range of abnormalities and will be well characterized for presence and severity of abnormalities using the ILO classification system. An important milestone was achieved this year, when all the necessary IT Security requirements were met and the CIR was given the authority to begin acquiring images. As of this report, the CIR has enrolled 26 submitters, 15 of them international. Images from 171 subjects have been reviewed and accepted into the CIR. Images from 57 more subjects are currently under review.

RDRP also provided assistance to the Department of Labor's Office of Workers Compensation programs in promulgating regulations based on NIOSH guidance to enable use of ILO classifications performed using digital chest radiographs as evidence in Black Lung Compensation cases.

Impact(s) made since last review (process- or outcome-related):
RDRP research is at the foundation of efforts to implement digital radiography in the Coal Workers' Health Surveillance Program (see Activity C, below). In addition, the DOL Office of Workers' Compensation Programs published its final rule enabling use of ILO classifications performed using digital chest images as evidence in Black Lung Compensation proceedings in the *Federal Register* on April 17, 2014. The rule acknowledges NIOSH's role (http://webapps.dol.gov/FederalRegister/HtmlDisplay.aspx?DocId=27500&AgencyId=13, Appendix 2).

Future Plans:
The CIR will be an important source of images for research to develop and validate an updated, fully modernized ILO classification system. The most-recently updated ILO classification system uses digitized versions of film radiographs as standard comparison films, which have a different appearance than modern, digitally-acquired and processed images. Thus, NIOSH is partnering with ILO to more fully modernize the classification system by moving to modern, digitally-acquired, standard films. We also anticipate pursuing educational research to document effectiveness of teaching materials and the performance of the NIOSH certification examination

in documenting ILO classification skills. A longer-term goal, to be pursued in the more distant future, will be to use validated repository images in an effort to develop computer-assisted ILO classification.

Activity C: Transition NIOSH's mandated surveillance activities, including the B Reader certification program, to use of digital chest imaging.

Background:
RDRP completed rulemaking early in the rating period that updated the regulations found in 42 CFR part 37 and enabled using digital chest radiographs in the CWHSP. These regulations require NIOSH to certify medical facilities providing digital chest images for the program and specify how images should be acquired, displayed and classified. A major effort during the rated period has been the implementation of digital chest imaging in the surveillance program. An important barrier to implementation has been the U.S. federal government information technology (IT) security requirements that exceed those typically used by medical facilities when they exchange radiographic images in electronic format. Thus, developing electronic infrastructure that was usable by participating medical facilities, but also compliant with federal government IT security requirements was an important challenge.

Progress made or maintenance efforts since last review:
RDRP has made great progress in implementing use of digital chest imaging in the CWHSP. We prepared in advance of the new regulations by acquiring the necessary hardware and software to operate a digital program. Our contractor developed a cloud-based approach for facilities to securely submit encrypted digital chest images to the program via the internet that was able to receive federal IT security clearance. In addition, we received clearance for administrative and physical controls, allowing the CWHSP's B Readers to securely log into the CWHSP image management system located on the CDC network, view chest radiographic images, perform ILO classifications, and submit results. Finally, because many of these B Readers did not have access to the necessary hardware and software to perform classifications of digital images according to NIOSH recommendations, we provided the necessary hardware and software to the B Readers along with technical support.

It was also important to engage medical facilities who performed chest radiography for the surveillance program and encourage them to become digital providers. This involved an application and certification process, and required the facilities to be approved to submit images to RDRP over the cloud-based system described earlier. RDRP informed medical facilities about the opportunity to become digital providers and assisted them with the certification process. RDRP also assisted them with technological issues as necessary.

Progress has also been made in converting the B Reader Certification program to a modern digital format. As an interim step, a high quality, digitized version of the self-study syllabus for learning about ILO classification has been prepared in Digital Imaging and Communications (DICOM) format. It is available for download at no cost from the NIOSH website (http://www.cdc.gov/niosh/topics/chestradiography/breader-study-syllabus.html). Also available for download at no cost is the NIOSH BViewer© software. This software was developed by NIOSH for performing ILO classification of chest radiographs

(http://www.cdc.gov/niosh/topics/chestradiography/digital-images.html). A version of BViewer© has been adapted for administering digitized versions of the B Reader certification and recertification examinations. The examinations have been beta tested and have recently received IT security approval for use. As a result, those taking the B Reader examinations will soon have the option of taking them either in the older, film-based format, or in the new, electronic format. To support this activity, RDRP recently remodeled a laboratory in the Morgantown facility and equipped it with workstations where the electronic examination can be administered.

RDRP is also working to develop an entirely new teaching syllabus, certification examination, and recertification examination for the B Reader Certification program based solely on modern, digitally-acquired chest radiographic images. RDRP posted a contract opportunity for assistance in this effort (Appendix 2). The American College of Radiology (ACR) successfully competed for the contract, *Development of Updated Program to Train and Certify Physicians as Competent to Use the International Labour Office Classification of Radiographs of Pneumoconioses in Digital Format*. Under the contract, ACR is working with RDRP to identify and prioritize important specific competencies needed by B Readers. It will then develop a training program that includes educational content in digital format to achieve the necessary competencies. Companion testing materials for initial certification and recertification ("B Reader examinations") will also be developed. These will be in digital format and engineered to reliably document whether a test taker has the necessary knowledge and ability to accurately classify chest images using the ILO system. Recommendations will also be provided for monitoring the performance of the examinations and improving them over time.

Impact(s) made since last review (process- or outcome-related):
Since the CWHSP first offered the option for using digital chest radiographs late in 2012, they have rapidly been accepted and used. As of August 2014, 52 of the 89 medical facilities approved to submit miners' chest radiographs to the surveillance program were approved to offer digital chest imaging (http://www2a.cdc.gov/drds/cwhsp/xrayfacilitysearch.html). In 2013, the first full year that digital chest images could be accepted, 2,986 out of 4,151, or approximately 72% of images submitted to the CWHSP, were digital. The rapid adoption of digital chest imaging will benefit RDRP in many ways. For example, digital images can be reviewed by multiple B Readers at the same time, speeding up the process of obtaining multiple, independent classifications required by regulations. Also, digital images are more easily stored and retrieved.

Efforts to migrate B Reader training and certification examinations to electronic format are still in their early stages. However, we anticipate that the impact of full modernization efforts will be to make training and competency testing in ILO classification of chest radiographs more accessible, both domestically and internationally. A particularly important anticipated impact will be to certify younger physicians whose entire careers have been in the current digital era. An important impact of the long history of the B Reader Certification Program is that OSHA specified in its proposed silica rule, published in 2013, that silica-exposed individuals should have periodic health surveillance including chest radiography and that chest images should be classified by NIOSH-certified B Readers.

Future Plans:

RDRP will encourage use of digital chest imaging in the CWHSP and continue to enroll clinical providers of digital chest imaging. The recent expansion of coal workers' health surveillance to surface coal miners will more than double the population eligible for surveillance, so we anticipate that more providers will wish to participate in the program. We expect our work with ACR to develop a new electronic format teaching and testing program for ILO classification will take about 4 years to complete. In the meantime, we will make our "digitized" electronic format examination available. OSHA's efforts to promulgate new silica regulations may increase demand for B Readers to classify chest radiographs, since the proposed regulations specify health surveillance including chest radiographs classified by B Readers. If there is increased demand for training by physicians, having electronic format teaching and testing materials available will help us to effectively meet that demand.

Flavorings-Related Lung Disease / Obliterative Bronchiolitis
(Outputs listed in Appendix 3, unless otherwise specified)

Text from NA Report: "In the flavoring industry, the RDRP response to the identification of diacetyl-induced bronchiolitis obliterans has led to surveillance efforts in multiple locations in an effort to detect and prevent disease. The evaluation committee agrees that continued surveillance, prevention of exposures, and mechanistic research to better understand this disease should continue to be a high priority for the RDRP." (p134)

Responsive RDRP Goal: Prevent and reduce flavorings-induced obstructive lung disease, including obliterative bronchiolitis.

Status: In progress

Background: Since the 2012 report, we have continued to learn more about the spectrum of disease potentially caused by flavorings. Also, other work-related causes of obliterative bronchiolitis have been recognized. Over the rating period, NIOSH has continued to vigorously pursue a range of multidisciplinary efforts to address this issue and to develop prevention recommendations.

External Factors: Similar to those detailed in the 2012 report.

BSC Evaluation, 2012: The 2012 BSC review asked if guiding principles could be identified from this course of inquiry that could be used in other settings, especially exposure prevention. Another recommendation was that specific, proven engineering controls be added to the NIOSH Flavorings website.

Guiding principles for prevention have been identified and extended to other venues beyond microwave popcorn manufacturing, including flavorings manufacturers, coffee roasters, snack-food preparation workers and line cooks. These will be presented in detail in the pending NIOSH Criteria Document on diacetyl and 2,3-pendandione. Preventive interventions come from the entire hierarchy of controls, including elimination, substitution, engineering controls, administrative controls, personal protective equipment, worker screening and surveillance, and worker training. From the standpoint of substitution, an important lesson has been that substitution can only reliably be protective if the substituted agent is known to be safer than the original one. For example, switching from diacetyl to 2,3-pentanedione (and potentially other vicinal alkyl diketones) only substitutes one hazard for another. From the standpoint of engineering controls, the use of closed transfer procedures is the preferred control technique. However, when closed transfer is not in place or feasible, RDRP research has documented that relatively low cost exhaust hoods can provide a reasonably effective approach to controlling evaporative emissions from mixing tanks used to produce flavorings and flavored foods (Hirst 2014, Appendix 3). This information has been added to an "exposure control" webpage on the NIOSH flavorings website (http://www.cdc.gov/niosh/topics/flavorings/control.html). Also, the pending NIOSH Criteria Document will include a section devoted to engineering controls. From the standpoint of worker screening and surveillance, an important lesson is that frequent screening with spirometry is needed for a rapidly progressive condition such as flavorings-

induced lung disease. This is because secondary prevention can only be effective if the worker is removed from exposure before significant disease progression has occurred. This issue is addressed in recent American Thoracic Society (ATS) recommendations on longitudinal spirometry (Redlich 2014, Appendix 4). An additional, important lesson from flavorings-induced lung disease and obliterative bronchiolitis identified in returning veterans of the conflicts in Iraq and Afghanistan is that current medical tests have limited sensitivity for diagnosis of obliterative bronchiolitis. Thus, it is important to be attentive to workers' symptoms and have a high clinical index of suspicion, especially in high risk settings (Kreiss 2013, Appendix 3).

Implementation of Recommendation

Activity A: Conduct surveillance, epidemiological studies, and field studies to identify the full range of food production industries at risk for flavorings-related lung disease.

Progress made or maintenance efforts since last review:
This activity has been critical to identifying and addressing the issue of flavorings-related lung disease. As already noted, flavorings were originally identified as a respiratory hazard through a technical assistance request. Observations from field investigations have motivated and informed laboratory investigations and efforts to develop authoritative recommendations. Since 2012, field work associated with HHEs and technical assistance requests has led to recognition of a broader spectrum of disease associated with flavorings exposure than classic obliterative bronchiolitis. For example, in one flavoring manufacturing plant, 30% of workers had spirometric abnormalities with a restrictive pattern, and excessive mean annualized decline in spirometry measurements was associated with being a production worker with higher potential for flavorings exposure (Kreiss 2014, Appendix 3).

Over the rating period, one NIOSH engineering control study and 3 HHEs have been completed (Appendix 3; for a full list of completed HHEs over time, see http://www.cdc.gov/niosh/topics/flavorings/additional.html). Several additional HHEs are also in progress, including an HHE conducted at a coffee processing plant that has been the subject of an MMWR report (Huff 2013, Appendix 3). In addition, we are in the midst of a NORA-funded research project which will conduct field work in Missouri on the sentinel microwave popcorn cohort, with a 13-year follow up of abnormal pulmonary functions and imaging studies, and a special emphasis on those who had restrictive pattern of spirometry abnormalities. We will also conduct similar testing of the flavoring manufacturing production workers with the excess of restrictive pattern abnormalities. In addition, an epidemiological investigation is being implemented to clarify the nature of and risk factors for restrictive lung disease associated with flavorings exposure. Partners involved in this investigation include investigators from the University of Cincinnati and the California Department of Public Health.

Over the rating period, 7 peer reviewed manuscripts and 2 reviews have been published in this area (Appendix 3). The two reviews (Kreiss 2013, Kreiss 2014, Appendix 3) and one of the peer-reviewed papers (Cullinan 2013, Appendix 3) address recognition of obliterative bronchiolitis in 2 newly-recognized settings, returning military veterans and fiberglass workers. One publication documents airborne levels of flavorings-related chemicals in nine food production facilities and one flavor manufacturer (Curwin 2014, Appendix 3). Another documents an engineering control

providing exhaust ventilation for mixing tanks used to produce flavorings or flavored foods (Hirst 2014, Appendix 3). Several publications touched on adverse health effects in flavorings-exposed people. One identified a 4-fold excess in COPD-associated mortality over 12 years of follow up of the sentinel microwave popcorn worker cohort (Halldin 2013, Appendix 3). Another documented a high prevalence of spirometric restriction in workers at one flavoring manufacturing plant (Kreiss 2014, Appendix 3).

Impact(s) made since last review (process- or outcome-related):
HHEs have provided guidance to workplaces on steps they can take to protect workers. HHEs have also advanced approaches to exposure assessment, allowing innovative methods such as sample collection in vacuum canisters and exposure assessment based on chemical derivatization to be evaluated in the field. RDRP field evaluations have also motivated basic research by NIOSH and others, such as the National Institute of Environmental Health Sciences (NIEHS), National Toxicology Program (NTP). Because of RDRP's experience in addressing obliterative bronchiolitis in flavorings-exposed workers, RDRP was invited by the Department of Defense and the Veterans Administration to participate in a workshop to address the issue of respiratory disease in returning veterans of the conflicts in Iraq and Afghanistan.

Dissemination of RDRP field studies, beginning with the sentinel study in 2000, has captured the attention of the mainstream media and the general public. This is reflected in a Google search of the term "diacetyl lung disease," which currently yields about 33,200 results. Many of these are directly linked to NIOSH, since a Google search of the term "NIOSH diacetyl lung disease" yields 6,340 results. Industry has also recognized the hazard and generated their own guidance (http://www.femaflavor.org/workplace-safety). Recognition of work-related hazards has also informed concerns about flavoring exposures from flavored e-cigarettes.

Future plans:
RDRP will complete the HHEs already in progress and respond to new requests as appropriate. We will continue to pursue the previously-described investigations to better characterize restrictive spirometric impairment in flavorings-exposed workers.

Activity B: Conduct basic toxicology research, including inhalation toxicology studies, to better characterize the toxic potential and mechanisms of toxicity of diacetyl and other potentially toxic artificial flavorings.

Progress made or maintenance issues since last review:
There has been great progress in this area over the rating period. Four peer-reviewed publications have addressed the pathophysiology of flavorings-induced toxicity. One of these makes the novel observation that after diacetyl exposure, apoptosis can be observed in olfactory nerves as well as in the respiratory epithelium (Hubbs 2012, Appendix 3). Another documents dysregulated substance P production in sensory nerves after diacetyl exposure (Goravanahally 2014, Appendix 3). Another demonstrates the potential for immunologic sensitization to diacetyl and diacetyl substitutes (Anderson 2013, Appendix 3). Another investigated the effect of experimental flavorings exposures on airway reactivity (Zaccone 2013, Appendix 3). Research recently published in abstract form identifies aggregates of ubiquitin, a molecule involved in the biological response to damaged protein, as a potential biomarker of toxicity. These data provide

insights into the mechanisms of cell damage caused by diacetyl and related alpha dicarbonyl compounds and inform the accurate modeling of flavorings damage within the airways. In addition, preliminary investigations of powdered flavoring toxicity have been conducted, including development of analytical techniques to assess flavoring composition of powders. Based on these preliminary studies, efforts are underway to obtain powders meeting investigators' specifications for use in further research.

Impact(s) made since last review (process- or outcome-oriented):
Basic toxicology research has profoundly impacted the recognition of diacetyl and related alpha dicarbonyl compounds as respiratory hazards. It has greatly informed efforts to prevent flavorings-associated lung disease. NIOSH work has also motivated others to undertake basic research. For example, NIEHS/NTP is actively working in this area. Another group working with RDRP is based at Duke University. This collaboration has driven studies that may lead to development of biomarkers of workplace exposure, such as amphiregulin (AREG) shedding and Clara cell secretory protein.

Future plans:
More remains to be learned. For example, more information is needed on the fundamental mechanisms of toxicity that would allow better prediction of whether a flavoring chemical represents an inhalational hazard. Ongoing laboratory toxicology studies will further elucidate pathogenic mechanism(s) for the respiratory toxicity of alpha-dicarbonyl flavorings and attempt to identify structure-activity relationships. This information will provide a foundation for developing rapid screening tests to better identify hazardous flavoring chemicals. In addition, respiratory toxicology studies to assess the toxicity of powdered flavorings will continue.

Activity C: Develop protective recommendations for use of artificial flavorings in work settings; and provide regulators with data and risk assessments they will need for worker protection over the long term.

Progress made or maintenance efforts since last review:
There has been excellent progress in this area. A cross-Institute, multidisciplinary team was assembled that conducted a thorough scientific review of diacetyl and 2,3-pentanedione toxicity, the basis for hazard identification. In addition, a risk assessment using data derived from workplace investigations (HHEs) and laboratory-based toxicology studies was developed. The draft criteria document was posted for public comment, discussed at a public meeting, and underwent peer review (http://www.cdc.gov/niosh/docket/archive/docket245.html). Over the rating period, the team has been working to address public comments, which were voluminous. Also, revisions were made to incorporate new data from the National Toxicology Program into the animal risk assessment chapter; and to add a section providing classifications of chemicals consistent with OSHA's recently promulgated Hazard Communication Standard, which is aligned with the Globally Harmonized System of Classification and Labeling of Chemicals. The revised sections were posted for public comment from December, 2013 until February, 2014 (http://www.cdc.gov/niosh/docket/archive/docket245A.html). We anticipate that additional revisions, reviews, and clearances will be completed during calendar year 2014 and that publication of the final document will occur around the end of the year.

Impact(s) made since last review (process- or outcome-related):
The final Criteria Document will contain comprehensive, authoritative recommendations for preventing respiratory disease caused by diacetyl and 2,3-pendanedione. Although the document's recommended exposure limits (REL) will likely receive the most attention, it will provide comprehensive preventive recommendations from across the entire hierarchy of controls. It will provide clear guidelines that will need to be considered by workplaces where these flavoring chemicals are used. In addition, publication will be consistent with NIOSH's responsibility to inform OSHA about chemical hazards and appropriate preventive interventions. Availability of formal NIOSH guidance may assist OSHA in its efforts to enforce requirements for safe working conditions in workplaces where flavoring chemicals are used.

Future plans:
Complete publication of the Criteria Document, as described above. Disseminate the Criteria Document and its recommendations to those who can use the information by a range of traditional and modern pathways of information dissemination.

Chronic Obstructive Pulmonary Disease (COPD)
(COPD surveillance outputs listed in Appendix 1; other outputs listed in Appendix 4, unless otherwise specified)

Text from NA Report: "In terms of chronic obstructive pulmonary disease (COPD), understanding the contribution of occupational exposures is difficult. To understand this issue, the evaluation committee strongly recommends that, for planning preventive strategies, the RDRP continue to support population-based studies of associations between occupational exposures and COPD to better define groups of workers at greatest risk." (p134)

Responsive RDRP Goal: Prevent and reduce work-related COPD.

Status: In progress

Background: About 15 million people in the U.S. have COPD, which includes emphysema and chronic bronchitis. In 2011, COPD caused 143,382 deaths in the U.S. and was the 3rd leading cause of death for all ages. Many people know that COPD is caused by cigarette smoking. About 75–85% of COPD cases can be attributed to smoking. Fewer people are aware that work-related exposures are also an important cause of COPD. Based on a comprehensive review of the literature, the American Thoracic Society has estimated that about 15% of COPD cases can be attributed to work. Among adults that never smoked, 31–40% of COPD cases can be attributed to work. Thus, work-related COPD remains a major health issue.

External Factors: No changes in external factors since 2012.

BSC Review, 2012:
In its 2012 review, the BSC recommended that NIOSH identify high risk populations, develop prevalence data for smoking status by industry, and increase emphasis on conducting longitudinal studies on high risk populations. From the standpoint of spirometry, BSC recommended work to develop spirometry reference standards for specific ethnic and racial minorities common in the US population. It was also recommended to consider developing metrics to evaluate the impact of the spirometry poster "Get Valid Spirometry Results EVERY Time" on clinical practice. The BSC review was supportive of efforts to integrate health protection and health promotion in COPD prevention efforts, but questioned how NIOSH determined which groups of workers should be targeted for study. The next several paragraphs will discuss program efforts responsive to these recommendations.

Identify high risk populations and develop prevalence data for smoking status by industry: In 2014, RDRP updated information about the burden of COPD by industry (http://www2a.cdc.gov/drds/WorldReportData/SectionDetails.asp?ArchiveID=1&SectionTitleID=10) and about smoking and tobacco use by industry (http://www2a.cdc.gov/drds/WorldReportData/SectionDetails.asp?ArchiveID=1&SectionTitleID=17) in eWoRLD. Additional updated surveillance information has been generated and reported in the COPD-related surveillance publications listed in Appendix 1. Also, more work on the US population burden and prevalence of COPD, and the associations with work in specific industries

and occupations is in progress using the NHANES 2007-2012, a representative sample of the US population. NIOSH was instrumental in designing the NHANES 2007-2012 questionnaire, in the collection of occupational data in the NHANES 2007-2012 sample, and in coding the industry and occupational information that was collected, using the standard US coding system for industry and occupation. This information enables RDRP and other researchers to investigate work-related COPD in the U.S.A. on the population level.

Increase emphasis on conducting longitudinal studies on high risk populations: We appreciate the BSC's recommendation to emphasize longitudinal studies. It is very challenging and expensive to conduct longitudinal cohort studies, including spirometry and other forms of respiratory health assessment, in specific occupational groups. However, MSHA's new respirable coal mine dust rule and NIOSH's expansion of coal workers' health surveillance (described in the surveillance update, beginning on page 7) will provide us with a significant new opportunity. It is particularly relevant, because coal miners are known to be at risk for work-related COPD. Another group undergoing careful, ongoing longitudinal monitoring is the cohort of World Trade Center (WTC) response workers, with 9 of the publications listed in Appendix 4 based on follow-up evaluation of the WTC cohort.

Develop spirometry reference standards for specific ethnic and racial minorities common in the US population. Consider developing metrics to evaluate the impact of the spirometry poster "Get Valid Spirometry Results EVERY Time" on clinical practice: There will soon be a release of NHANES spirometry data through 2012. RDRP has played a major role in assisting NHANES in performing spirometry, and we are aware of at least one investigator who is planning to use that data to develop spirometric reference standards for Asian-Americans, a group not specifically addressed by the previous NHANES-based prediction equation. The poster has had important intermediate outcomes. Fifteen spirometer manufacturers are committed to sending a copy with every spirometer that they ship and 90,000 posters have been disseminated. It is now available in six languages. Also, RDRP has a commitment from one pharmaceutical company to work with us to assess the impact of the poster on clinical trial data quality.

Integrated health protection and health promotion for COPD: With regard to combined health protection and health promotion, also known as "Total Worker Health™", previous efforts focused on collaboration with a large construction company using SPIROLA as part of their worksite wellness program to assist in preventing respiratory disease. We have also worked with a municipal fire department. Although this work was facilitated by the existence of partners interested in the effort, the industry focus is appropriate, given the respiratory hazards that construction workers and firefighters are exposed to and the relatively high prevalence tobacco use as a risk factor among workers in the construction industry. Another new major focus of effort during the rating period have been efforts to create the foundation for a body of work demonstrating the usefulness of Total Worker Health™ in the metal and nonmetal mining industry. This industry focus is also appropriate, for reasons paralleling those described for construction.

Implementation of Recommendation

<u>Activity A</u>: Conduct surveillance and epidemiological studies to assess the extent, severity, and burden of work-related COPD and identify industries and occupations associated with COPD

<u>Progress made or maintenance efforts since last review</u>:
During the rated period of September, 2012- July, 2014, there were 28 research studies published or in press related to this area ("COPD surveillance," Appendix 1 and Appendix 4). Also, a substantial body of research has been initiated and is in progress.

Collaborative efforts continue with large national studies. A major RDRP effort has been to participate with other parts of CDC in NHANES 2007-2012. RDRP provided administrative and technical support for the collection and analysis of spirometry data for the survey. RDRP also provided the spirometers and other necessary equipment, technician training, and quality control. RDRP efforts on this collaboration included review of spirometry data quality for each examination period (approximately 3,800 exams/year), site visits to mobile examination centers (6/year), technician training courses (2/year), maintaining file storage for back-up data, and spirometry equipment maintenance. RDRP also reviewed 2007–2010 spirometry data for public release to enable other investigators to use the information to pursue research.

To make the NHANES data useful for evaluation of work-related disease, RDRP proposed that survey items about occupation and industry be included in the 2007–2012 NHANES. This proposal was accepted and the data has been collected. RDRP recently completed a data sharing agreement with CDC's National Center for Health Statistics (NCHS) to obtain more detailed information from NHANES 2007–2012 about longest-held occupation and industry. This will allow RDRP to use a job-exposure matrix (JEM) to create a set of NHANES variables representing known occupational exposure risk factors for COPD. A similar JEM was used during the rating period to evaluate data from the Multiethnic Study of Atherosclerosis (MESA) study. RDRP will use these data to further explore the impact of work-related risk factors for COPD. NHANES-related publications during the rating period (Appendix 1) include one documenting that use of post-bronchodilator spirometry results, instead of pre-bronchodilator, reduces the apparent prevalence of COPD by about one third (Tilert 2013, Appendix 1); and another documenting that the prevalence of airways obstruction in U.S. adults aged 40-79 decreased between 1988-1994 and 2007-2010 from 16.6% to 14.5% (Doney 2014, Appendix 1).

Five papers were published based on National Health Interview Survey (NHIS) data (Appendix 1). One of these made the very interesting observation that among working adults, women had lower prevalence of smoking than men, yet women who smoked were more likely than men to experience adverse health outcomes (Syamlal 2014, Appendix 1).

Studies focused on relationships between specific work settings and COPD (or reduced lung function) are listed in Appendix 4. They were carried out by a diverse group of RDRP-funded intramural and extramural investigators and addressed a wide variety of settings. A study in coal miners documented air trapping and small airways dysfunction in those with accelerated FEV_1 losses (Stansbury 2013, Appendix 4). Another study was a 37-year, mortality follow up of the National Study of CWP (Graber 2014, Appendix 4). It found significant and positive exposure-response relationships between coal mine dust exposure and mortality from pneumoconiosis and

COPD. Mortality due to COPD was modified by smoking status, such that the effect was strongest among never smokers. Another study used g-estimation, a method to adjust for healthy worker effect, to analyze data from a cohort of autoworkers exposed to metalworking fluids. The analysis suggested that limiting exposure could have saved many years of life lost due to COPD (Picciotto 2014, Appendix 4). Other studies documented relationships between levels of high sensitivity C-reactive protein and lung function in firefighters (Gaughan 2014, Appendix 4) and between endotoxin exposure and impaired lung function or death in cotton and silk textile workers (Lai 2014, Appendix 4). Four studies evaluated basic mechanisms of airways inflammation caused by organic dusts (Appendix 4). Eleven studies addressed the still-evolving issue of chronic lung disease from World Trade Center dust exposure (Appendix 4).

Impact(s) made since last review (process- or outcome-related):
A major impact of NIOSH efforts occurred this year with the finalization of the new MSHA respirable coal mine dust rule. The risk assessment used by MSHA included COPD as an adverse health outcome in setting exposure limits. The final rule mandates that coal miners be provided with health screening that includes baseline and periodic symptoms assessment and spirometry for secondary prevention of COPD. This is a major expansion, since the previous rule required screening based only on chest radiography to assess for Coal Workers' Pneumoconiosis. RDRP has already put into place an Interim Final Rule providing regulations to guide the implementation of this new national program of health surveillance. Another major impact was the publication in 2013 of OSHA's proposed silica rule. It also uses a risk assessment that includes COPD as an adverse health outcome in setting exposure limits, and mandates baseline and periodic spirometry for secondary prevention of COPD in silica-exposed workers.

Future plans:
RDRP will continue to seek out and analyze informative data to better document risk factors for work-related COPD that are potential targets for intervention. We will analyze current NHANES data to document occupational and other risk factors for COPD and to determine prevalence of COPD, and abnormal spirometry in the current U.S. population. RDRP will also examine the reliability of occupational exposure assessment with the JEM for COPD. RDRP will conduct further analyses of MESA data, which will allow the evaluation of emphysema documented by high resolution computed tomography (HRCT) of the chest as an outcome in relation to occupational exposure. Additionally, we will establish the national program of health screening and surveillance for coal miners, including symptoms assessment and spirometry, as required under the new MSHA respirable coal mine dust rule.

Activity B: Improve tools such as longitudinal spirometry and respiratory questionnaires and use for early detection and prevention of occupationally-related COPD

Progress made or maintenance efforts since last review:
RDRP has engaged in a number of activities to improve occupational spirometry and apply results to the prevention of COPD. NIOSH has the authority to approve training programs for spirometry technicians. Thus, RDRP has maintained and improved a spirometry course certification program that provides technician training materials and approves training courses (http://www.cdc.gov/niosh/topics/spirometry/training.html). Thirteen of 30 course sponsors have been audited during the rating period (http://www.cdc.gov/niosh/topics/spirometry/sponsor-

renewal-dates.html). On average, over 2,500 professionals complete training in NIOSH-approved spirometry courses each year. NIOSH has also conducted research, using various databases of periodic spirometry monitoring to develop methods for obtaining periodic spirometry data, analyzing it, and using the information for prevention.

Six publications addressed this area during the rating period (Appendix 4). One provides an excellent overview of the sensitivity and specificity of various approaches to evaluating longitudinal spirometry data, taking into account the quality of spirometry monitoring programs (Hnizdo 2012). An official American Thoracic Society (ATS) document provides technical standards for spirometry in the occupational setting, including recommendations for longitudinal spirometry that draw upon NIOSH research (Redlich 2014). Another publication documents that rate of decline in forced expiratory volume in 1 second (FEV1) is associated with increased risk of mortality, even if the FEV1 is still in the normal range (Baughman 2012). Another indication of the importance of preserving lung function is the documentation of an inverse association between lung function and depressive symptoms, even in "healthy" adults (Ochs-Balcom 2013). Another publication identified a sedentary lifestyle as being associated with decreased lung function, indicating sedentary lifestyle as a potential target for intervention (Campbell Jenkins 2014).

An important developmental activity during the rating period was the establishment of a group at the NIOSH-Spokane facility that will focus on developing and demonstrating integrated health protection / health promotion (Total Worker Health™) interventions in the metal and nonmetal mining industry. This industry is associated with exposures to respiratory hazards, and extraction workers have relatively high smoking prevalence. Over the last year, RDRP has hired 3 doctoral-level staff who will have a strong focus on this effort. In addition, a health technician has been hired, who will play an important role in collecting health data in workplaces to inform the Total Worker Health™ efforts.

Another prevention-related activity was the drafting of a NIOSH Current Intelligence Bulletin (CIB) *Promoting Health and Preventing Disease and Injury through Workplace Tobacco Policies*. The content of this CIB addresses use of tobacco products among workers, secondhand exposures in workplaces, occupational health and safety concerns relating to tobacco product use and secondhand exposures, and available interventions to eliminate or reduce these hazards. The CIB concludes with updated NIOSH recommendations relating to tobacco product use in places of work and tobacco product use by workers. The draft CIB was posted for public comment in August (http://www.gpo.gov/fdsys/pkg/FR-2014-08-15/pdf/2014-19384.pdf). It has also been distributed to peer reviewers for their comments.

Impact(s) made since last review (process- or outcome-oriented):
A popular product noted in the last report was a poster intended for display in spirometry laboratories as a handy reference for the spirometry technician. This poster illustrates spirometry problems and how to rectify them. Fifteen spirometer manufacturers are committed to sending one of these posters with every spirometer they ship and 90,000 posters have already been disseminated. Currently, it is available in six languages (English, Spanish, Portuguese, Indonesian, Chinese, and Turkish), with plans for five more translations (Arabic, French, Italian, Russian, and Thai): http://www.cdc.gov/niosh/docs/2011-135/. A reference guide for clinicians

who interpret spirometry was developed in 2012. This guide discusses how to recognize and attain good quality spirometry and the impact of poor quality spirometry on test results and interpretation: http://www.cdc.gov/niosh/docs/2012-116/pdfs/2012-116.pdf . At least 13,000 copies of the guide have been disseminated. The guide is being translated into Spanish. RDRP has further been approached by ATS to collaborate with them to include several RDRP products, including a spirometry manual, the poster, and the reference guide for clinicians, in the ATS library. This will result in further dissemination of these products.

RDRP's spirometry materials available on the NIOSH website remain quite popular. Monthly averages for downloads over the 12 months from July 2013 to July 2014 are: posters – 200; reference guide for clinicians – 115; spirometry training guide – 150; NHANES reference calculator page hits (calculates percent predicted values for spirometry) – 3,400.

Spirometry Longitudinal Data Analysis (SPIROLA) Software has been maintained on the NIOSH website to help surveillance programs evaluate longitudinal data and to monitor the quality of their data: http://www.cdc.gov/niosh/topics/spirometry/spirola.html. The most recent update of SPIROLA (3.0.2), in March 2014, improved overall usability, decreased data loading times, added filtering options so the user could easily identify individuals with intervention plans and added an Asian-American reference equation correction factor. The current version was downloaded 118 times by non-CDC users between April and July, 2014. Engaged partners are currently using SPIROLA to demonstrate use of accelerated pulmonary function decline to target secondary prevention by minimizing occupational risks (hazardous exposures) and addressing non-occupational causes (smoking, weight gain, sedentary lifestyle). NIOSH is currently engaged in developing a web-based version of SPIROLA which will allow for increased accessibility for users and enhanced features to evaluate workplace and lifestyle interventions' effectiveness on lung function decline. As previously noted, the ATS technical statement on spirometry in the workplace reflects acceptance and dissemination of the approach to evaluation of longitudinal spirometry used by SPIROLA into clinical circles.

Future plans:
Maintain high quality spirometry training courses through site visits and re-certification. Provide additional training materials, including a spirometry training video. Translate spirometry poster into additional languages, as noted above. Continue to work with partners in the construction industry and firefighting to demonstrate usefulness of longitudinal spirometry in COPD prevention through a combination of targeted health protection for occupational causes and health promotion for non-occupational causes. Expand the "Total Worker Health™" effort to stakeholders in metal and nonmetal mining. Continue to maintain and improve longitudinal spirometry software (SPIROLA) as a tool available for evaluating populations over time, in desktop and future web-based versions. Evaluate peer review comments and public comments on the draft NIOSH Current Intelligence Bulletin *Promoting Health and Preventing Disease and Injury through Workplace Tobacco Policies* and use those comments to develop a responsive final CIB.

Work-Related Asthma
(Asthma surveillance outputs listed in Appendix 1; other outputs listed in Appendix 5, unless otherwise specified)

Text from NA Report: "Because the contribution of occupational exposures to the burden of adult asthma is high, work in pursuit of the four WRA subgoals can have a potentially large impact on improved occupational safety and health among the U.S. workforce." (p134)

Responsive RDRP Goal: Prevent and reduce the full range of work-related asthma (WRA), including work-exacerbated asthma; occupational asthma; and irritant-induced asthma

Status: In progress

Background: Detailed background information was presented in the 2012 report. However, a few items are worth repeating. WRA is the most frequently diagnosed occupational respiratory disorder in many industrialized countries, including in the U.S.A. WRA can be divided into two broad categories: 1) new-onset asthma that is caused by exposures at work; or 2) work-exacerbated asthma (WEA) that is not caused by work, but is worsened by exposures at work. New-onset asthma can be divided into occupational asthma (OA), typically caused after a latent period by sensitizing workplace asthmagens, and irritant-induced asthma (sometimes called "reactive airways dysfunction syndrome").

External Factors: These are discussed in the 2012 report to the BSC.

BSC Evaluation, 2012:
In 2012, BSC reviewers noted that "current WRA research efforts at NIOSH represent an exemplary partnership between extramural research, state-based surveillance, and NIOSH's intramural research and surveillance program activities." Reviewers noted the limited resources available for work-related asthma surveillance and prevention activities, and the importance of prioritizing efforts. It was recommended to consider emphasizing partnerships with health care provider groups for work-related asthma recognition and clinical care. It was also recommended to consider work in the area of medical screening programs and to consider developing a long-term strategic research plan addressing indoor air quality.

To address the resource constraints noted by the BSC, RDRP looks for opportunities to obtain useful surveillance data by working with others, thus leveraging its investments to amplify outcomes and impacts. Excellent examples are engaging with BRFSS and the Asthma Call-Back Survey, and working with States. RDRP has pursued several efforts that involve connections with health care providers and the health care system. An important initiative with great potential for impacting on asthma recognition by clinicians and provision of care is a newly-funded intramural National Occupational Research Agenda (NORA) project to develop clinical decision support capabilities in electronic health records. This project includes development of a module for assessment and management of asthma in adults that will prompt clinicians to collect and consider occupational information, making it more likely that work place factors will be considered and evaluated. Through a partnership with NCHS's National Ambulatory Care Survey, RDRP has been able to incorporate questions about assessment and management of adult

asthma in relationship to work into the survey. Inserting the questions involved only a small investment, relative to the cost of the survey as a whole, and thus represents another example of leveraging. These data will be available in 2014 for analysis, and will provide useful information about the current state of clinical care for WRA.

RDRP has also worked to address WRA specifically in the healthcare industry. In response to input from CSTE that indicated the importance of the issue, RDRP worked with the NIOSH Healthcare and Social Assistance Sector Program to assemble a workgroup of intramural and extramural experts to address occupational safety and health issues related to use of disinfectants. This dynamic group has drafted a report identifying what is known and what needs to be learned about this issue. The group is currently in the process of pursuing publication in a peer-reviewed journal. RDRP has also collaborated with the Milwaukee Veterans Administration Medical Center to conduct a study evaluating the prevalence of respiratory symptoms and asthma among medical center employees. This medical center was previously studied about 10 years ago, and so the current study will allow RDRP to evaluate both cross-sectional and longitudinal data.

RDRP appreciates the BSC recommendation to consider work in the area of medical screening programs. Related publications during the rating period documented the usefulness of hand symptoms in predicting latex allergy (Wang 2012, Appendix 5), the clinical significance of noneosinophilic inflammation detected by sputum analysis (Lemiere 2014, Appendix 5), evaluated inflammation demonstrated by nasal lavage in occupants of a water damaged building (Akpinar-Elci 2013, Appendix 5), and used serial peak flow monitoring in an investigation of a damp building (White 2013, Appendix 5). An animal study documented the potential usefulness of detecting isocyanate-protein conjugates with an anti-isocyanate monoclonal antibody as a biomarker of exposure (Nayak 2014, Appendix 5). Also, RDRP has continued to maintain the "Prevention of Occupational Asthma" website, which provides an easily accessible library of the world literature documenting the effectiveness of interventions to prevent WRA, including primary and secondary interventions (http://www.cdc.gov/niosh/topics/asthma/OccAsthmaPrevention-Query1.html). This website has been quite popular and was visited an average of 410 times per month in 2013.

RDRP also appreciates the BSC's interest in indoor air quality. As noted in the 2008 National Academies Review *Respiratory Diseases Research at NIOSH*, indoor air quality involves far more than just respiratory disease:

> "While the indoor environmental quality work of the RDRP is judged to be relevant to occupational health and safety in the general sense, it is not always clearly related to WRA. The EC recommends that the RDRP reexamine whether its indoor air-quality-related research is sufficiently relevant to work-aggravated asthma. Moreover, the RDRP should reevaluate the relative commitment of resources to indoor air-quality investigations, as the health effects are often not airway in nature (that is, systemic or neurologic complaints)" [*Respiratory Diseases Research at NIOSH: Reviews of Research Programs of the National Institute for Occupational Safety and Health*, page 51 (http://www.nap.edu/catalog.php?record_id=12171)].

In response to this guidance from the National Academies, RDRP's 2009 Implementation Plan (which was presented to and approved by the BSC) specified a strategic focus on areas that were clearly related to WRA: indoor dampness and mold; and use of consumer products indoors with

the potential to cause and exacerbate asthma, such as cleaning agents (http://www.cdc.gov/niosh/nas/pdfs/RDRP_Implement_for_BSC2.pdf). We have continued our emphasis on indoor dampness and mold, cleaning agents and disinfectants, and have recently added novel work evaluating emissions from office equipment, such as printers using nano-enabled toners, to our portfolio of work.

Implementation of Recommendation:

Activity A: **Assess the extent, severity, burden, and risk factors for WRA and approaches to prevention across a broad range of industries and occupations**

Progress made or maintenance efforts since last review:
RDRP has leveraged several large studies to carry out this work. RDRP investigators have partnered with CDC's National Center for Environmental Health (NCEH) to add questions about WRA to the BRFSS Asthma Call-back Survey (ACBS) which collects information from adults who report an asthma diagnosis. The value of ACBS is enhanced by NIOSH sponsorship of an Industry and Occupation Module in the BRFSS for the survey years 2013-2016. In 2013, 20 states participated in the BRFSS Industry and Occupation Module and, in 2014, 24 states are participating. When several years of BRFSS data are available for states administering both the ACBS and the Module [n= 19 and 20, for 2013 and 2014], we can analyze the data to better understand WRA prevalence patterns.

ACBS has been extremely informative. During the rated period, 6 publications have documented findings from the study. Individuals with work-related asthma have more days with asthma symptoms, and those with more days of asthma symptoms are less likely to work or be able to carry out their usual activities (Knoeller 2013, Appendix 1). They also have worse metrics for quality of life (Knoeller 2013, Appendix 1). Individuals with WRA are less likely to be currently employed for wages and more likely to be unable to work than those with non-work-related asthma (White 2013, Appendix 1). Similarly to previous studies, ACBS data showed that health care workers have higher prevalence of current asthma, and those with current asthma have higher proportions of asthma attacks than non–health care workers (White 2013, Appendix 1). Analysis of ACBS data also allowed for estimation of the annual incidence of health professional diagnosed new-onset occupational asthma. The proportion of incident asthma identified by respondents or diagnosed by professionals as work-related was 18.2%. The proportion diagnosed by professionals was considerably less, 4.7% (Mazurek 2013, Appendix 1). A study based on 2006–2009 ACBS data showed the estimated annual average influenza vaccination coverage was 48.5% in those with WRA and 42.8% in adults with non-WRA. This was higher than the general U.S. adult population of similar age during the 2006–2007 season (39.9%), but less than the Healthy People 2010 target of 60% (Mazurek 2014, Appendix 1).

As noted in the section on COPD, RDRP collaborated with NCHS to leverage occupational respiratory disease-related information from the NHANES study during the years 2007-2012. RDRP provided administrative and technical support for NHANES to conduct spirometry, and was able to add questions regarding work to allow for the development of a job exposure matrix (JEM) to assess risks for WRA. Work is currently underway on that effort. RDRP has partnered with other parts of NIOSH and with CDC's National Center for Health Statistics (NCHS) to add

questions about WRA to an occupational health supplement to the National Health Interview Survey (NHIS). Two publications used this data source during the rating period. One documented that adults with health-professional diagnosed WRA were more likely to work outdoors, have frequent exposure to second hand smoke, and more likely to have frequent workplace exposure to vapors, gas, dust, or fumes than adults with asthma not diagnosed as work-related (White 2014, Appendix 1). Another documented that 37% of working adults with current asthma developed it while employed. Occupations most often identified as held at time of asthma onset were office and administrative support, sales and related, and management (Knoeller 2013, Appendix 1). RDRP has also entered into partnership with NCHS to include questions relevant to WRA in the National Ambulatory Medical Care Survey. Data collection is in progress. This will provide information on physician compliance with NIH guidelines on diagnosis and management that are relevant to WRA when caring for adults with asthma. In addition, much state-based surveillance has focused on WRA, as was noted in the surveillance section.

Impact(s) made since last review (process- or outcome-related):
RDRP engagement and support has helped to motivate action by others. The leveraging of large national surveys to address WRA can be seen as a type of intermediate outcome. In another intermediate outcome, the Council of State and Territorial Epidemiologists (CSTE) will soon be reporting a new occupational health indicator (OHI) that is based on data from the BRFSS ACBS: asthma among adults caused or made worse by work (http://www.cste.org/group/OHIndicators). Another example of an effort by others motivated in part by RDRP work is OSHA's recently announced National Emphasis Program on occupational exposure to isocyanates (https://www.osha.gov/OshDoc/Directive_pdf/CPL_03-00-017.pdf).

Future Plans:
RDRP will continue to leverage its resources by collaborating with large national surveys. It will analyze additional data from the ACBS and NHIS-Occupational Health Supplement. Data from the National Ambulatory Medical Care Survey will be analyzed to better understand quality of care of adults with asthma. The 2007-2012 NHANES is providing information about usual occupation, industry, asthma status, and objective measurement of spirometry and exhaled nitric oxide (a marker of airways inflammation in asthma). This, together with the exposure-related variables that are being generated using a JEM, will provide an excellent opportunity to evaluate burden and severity of asthma in the context of occupational risk factors. RDRP will also continue to work with State partners to pursue State-based surveillance, including implementation of the new Occupational Health Indicator of asthma among adults caused or made worse by work.

Activity B: Identify, document, and characterize emerging causes of WRA, including novel host factors, novel occupational exposures, and irritant inhalation exposures encountered during natural or man-made disasters

Progress made or maintenance of efforts since last review:
There are numerous examples of progress. For example, studies are evaluating WRA in healthcare workers and evaluating relationships to exposures such as cleaning agents, disinfectants and other known asthmagens in healthcare. These have involved development of

novel methods for assessing exposures such as volatile organic compounds (VOCs) and quaternary ammonium compounds, and in reconstructing exposures using JEMs. They are being pursued in partnership with the Service Employees International Union and the Veterans Administration. An intramural-extramural workgroup was assembled to address hazards associated with surface disinfectants used in healthcare, and has drafted a document identifying key knowledge gaps. Several publications during the rating period have addressed measurement of volatiles in healthcare settings, primarily cleaning agents and disinfectants (Bello 2012, LeBouf 2014, Appendix 5). Laboratory work suggested that triclosan, an antimicrobial product found in soaps, detergents, etc, can act as an adjuvant for sensitization to high molecular weight agents (Anderson 2013, Appendix 5).

Studies addressed WRA in wildland firefighting (Gaughan 2014, Appendix 5) and during restoration work after the flooding associated with Hurricane Katrina (Rando 2012, Rando 2014, Appendix 5). Both of these are emerging issues, in view of the expected impact of global climate change on forest fires and flooding events. One study evaluated formaldehyde exposures during simulated use of a hair straightening product, following up on the "Brazilian Blowout" issue (Stewart 2013, Appendix 5). Ten publications addressed WRA in agriculture and food production (Appendix 5). One of these was based on collaboration with NIEHS's Agricultural Health Study and documented risk factors for exacerbation of asthma in pesticide applicators (Henneberger 2014, Appendix 5). A number of publications documented relationships between exposure to World Trade Center dust and respiratory conditions, including WRA (Appendices 4 and 5). One HHE described relationships between exposures, immune sensitization, and asthma in poultry breading workers, and another HHE examined asthma symptoms among poultry workers after a chlorine gas release (Appendix 1).

A potentially important laboratory study documents the impact of combined exposure to graphene oxide nanoparticles and high molecular weight allergen in an ovalbumin-induced murine model of asthma. Combined exposure attenuated Th2 immune responses, but potentiated airway remodeling and airway hyperreactivity, suggesting the need to anticipate WRA as a potential adverse health outcome of exposure to this type of nanoparticle (Shurin 2014, Appendix 5).

Impact(s) made since last review (process- or outcome-related):
RDRP work has led to increased recognition of hazards associated with a variety of agents. Over the years, RDRP research has informed the Association of Occupational and Environmental Clinics (AOEC) in assigning asthmagen designations to substances included in the AOEC Exposure Code List (http://www.aoecdata.org/Default.aspx). This list is used by 3rd party certification organizations like Green Seal (http://www.greenseal.org/) and EcoLogo (http://site.ul.com/global/eng/pages/offerings/businesses/environment/services/ELmark/index.jsp) in their certification processes for cleaning agents. RDRP work also motivated an authoritative and broad based intramural/extramural workgroup to come together to identify issues in surface disinfection, a useful intermediate outcome. Work funded by RDRP has changed how future disasters, such as flooding or WTC-like events, will be managed in the future.

Future Plans:

RDRP will complete studies of asthma in healthcare workers that evaluate, in particular, impacts of cleaning agents and disinfectants. RDRP will pursue a new study assessing exposures and toxicological properties of emissions from office machines that use nano-enabled toners, an emerging new type of exposure. RDRP will continue to be opportunistic, conducting investigations including HHEs and designed studies, and following up on potential emerging causes of WRA.

Activity C: Evaluate the impact of indoor air quality on WRA and the effectiveness of building remediation in preventing WRA associated with poor indoor air quality

Progress made or maintenance efforts since last review:
Over the rating period, a number of RDRP publications have been in the area of indoor air quality (13 are listed in the section "Indoor Environmental Quality / Dampness / Mold" in Appendix 5 and others, described above with emerging hazards, addressed cleaning agents and disinfectants). Examples include a publication documenting relationships between exposure to microbial agents and respiratory symptoms in a damp building (Cho 2013, Appendix 5). Another publication documented work-related changes in serial peak flows in occupants of an office building with a history of dampness, thus indicating that serial peak flows may be a useful measure to determine WRA in office settings (White 2013, Appendix 5). A publication documented 2 individuals with vocal cord dysfunction that was temporally related to occupancy of water-damaged buildings (Cummings 2013, Appendix 5). Two publications reported laboratory-based studies evaluating respiratory responses to experimental exposure to fungi or fungal constituents and one sought to better characterize fungal allergens. Two focused on exposures and respiratory health effects associated with restoration work in Post-Katrina New Orleans (Rando 2012, Rando 2014, Appendix 5).

In addition, much work continues to be in progress. A manuscript has been drafted documenting dampness and mold-related evaluations performed at several public schools in Maine. Work in these schools also guided the development of a software tool for assessing indoor dampness and mold, the NIOSH Dampness and Mold Assessment Tool. Further development of this tool has been an important focus during the rating period. RDRP partnered with the Philadelphia School District and the staff of the Philadelphia Federation of Teachers Union, and Health and Welfare Fund to pilot using the tool to prioritize buildings for repair and remediation. The scientific basis for the NIOSH Dampness and Mold Assessment Tool is RDRP research documenting that subjective visual assessment and mold odors can provide information about mold problems that correlates well with objective measures. Over 250 evaluations were completed in 190 buildings, with 18,000 rooms/spaces evaluated. Although the demonstration work in Philadelphia is temporarily on hold as the school district works through unrelated issues, much has been accomplished. Based on beta testing and feedback from users the software was improved, for example, by adding improved capabilities for users to generate customized reports and improved capabilities for online help. In addition, a contractor is working to port the program to smartphones using Apple or Android operating systems, adding the additional capability of using the smartphone to take pictures of mold and damage. Pending resolution of issues in Philadelphia, additional beta testers are being identified to complete the software tool's development. After completion, we anticipate making the Windows and smartphone application-based versions of the tool freely available to the public.

Another RDRP dissemination effort was the publication of a NIOSH Alert, "Preventing Occupational Respiratory Disease from Exposures Caused by Dampness in Office Buildings, Schools, and Other Nonindustrial Buildings." This authoritative document provides up-to-date information about hazards, health effects, and state of the art interventions to protect health (http://www.cdc.gov/niosh/docs/2013-102/).

During the rating period, RDRP also revised and updated an Indoor Environmental Quality website (http://www.cdc.gov/niosh/topics/indoorenv/). This dissemination effort brings together a wide range of materials for those with an interest in the topic.

Impact(s) made since last review (process- or outcome-related):
RDRP work in this area has been very influential. This is reflected in a Google search of the terms "NIOSH dampness mold" which generated 122,000 results. The NIOSH Alert has been influential, and is cited in the American Industrial Hygiene Association's "Position Statement on Mold and Dampness in the Build Environment" (https://www.aiha.org/government-affairs/PositionStatements/P-Mold-03-26-13.pdf). The web page where the Alert is found has been visited 13,547 times and the full document has been downloaded 5,319 times through July 2014. In addition to providing information helping the Philadelphia School District evaluate and prioritize buildings for renovations, the NIOSH Dampness and Mold Assessment Tool has generated much interest from other groups and RDRP has received approximately 200 inquiries about its availability from a diverse, international group of requesters. RDRP's web resources have also been highly trafficked. The IEQ home page had a total of 19,142 visits in 2013. The page within the IEQ website devoted to mold had even more visits, a total of 32,080 in 2013.

Future Plans: RDRP will complete its demonstration project of the NIOSH Dampness and Mold Assessment Tool, working with the Philadelphia Public Schools and other partners. Based on feedback from users, the tool will be finalized and made available to the public. RDRP will continue laboratory and field studies evaluating hazards associated with indoor chemical exposures and microbial-derived agents. In this regard, subchronic animal exposure to dry fungal spore aerosols are now in progress to assess both allergy and toxicity endpoints in collaboration with NIEHS/NTP. In addition, RDRP will pursue studies evaluating exposures and potential hazards associated with office machines that use nano-enabled toners.

Activity D: Develop and validate screening tools and demonstrate effectiveness of screening and surveillance for WRA prevention in occupational settings (Previously: "Develop and implement demonstration projects that address the role of screening and surveillance in WRA in occupational settings")

Background:
When workers are potentially exposed to asthmagens, health screening and surveillance can be an important intervention in support of WRA prevention. Early detection of immune sensitization or early, minimal to mild WRA creates an opportunity for secondary prevention by eliminating the worker's hazardous exposures before their WRA progresses to full-blown clinical disease. Detection of these adverse health effects also identifies breakdowns in exposure

controls that, if corrected, can improve primary prevention for similarly exposed co-workers. Thus, work to improve screening tools, demonstrate effectiveness, and disseminate knowledge in this area is relevant and important.

Progress made or maintenance efforts since last review:
As previously noted, several publications during the rating period touched on screening tools. They documented the usefulness of hand symptoms in predicting latex allergy (Wang 2012, Appendix 5), the clinical significance of noneosinophilic inflammation detected by sputum analysis (Lemiere 2014, Appendix 5), documented use of nasal lavage to detect upper airway inflammation in occupants of a water damaged building (Akpinar-Elci 2013, Appendix 5), and demonstrated use of serial peak flow monitoring in an investigation of a damp building (White 2013, Appendix 5). An animal study showed proof of concept for detecting isocyanate-protein conjugates with an anti-isocyanate monoclonal antibody as a biomarker of exposure (Nayak 2014, Appendix 5).

RDRP also continued its work in partnership with the American Chemistry Council and participating facilities to demonstrate a medical monitoring program evaluating workers at all toluene diisocyanate production facilities in the U.S. The project also measures exposures in various jobs and tasks. Working with partners, a medical monitoring protocol was established and deployed for five years. Data collection was completed June 30, 2012. Recent progress involved evaluation of all medical records by an experienced pulmonary physician to independently identify incident cases. Data analysis in collaboration with industry partners is in progress.

Another activity responsive to this goal is maintenance of the "Prevention of Occupational Asthma" website (http://www.cdc.gov/niosh/topics/asthma/occasthmaprevention.html). This involves ongoing review of the world literature to identify studies documenting effective measures to prevent work-related asthma, including secondary prevention. This innovative website provides easy access and supports customized queries on prevention of occupational asthma across the full range of hazards, occupations, and industries.

Impact(s) made since last review (process- or outcome-related):
As a result of the demonstration project in isocyanate production plants, nearly 200 employees have had regular medical monitoring using initial and periodic questionnaires and spirometry since 2007. Another impact of RDRP efforts is dissemination of effective interventions via the "Prevention of Occupational Asthma" website, which was visited an average of 410 times per month in 2013.

Future plans:
RDRP and partners will complete their analysis of data to evaluate the usefulness of the monitoring program in isocyanate production plants and disseminate the results. RDRP will continue to update and maintain the Prevention of Occupational Asthma website as a resource for documentation of effective approaches to asthma prevention. In addition, a new project has been initiated using an animal model to assess the potential of exosomes, which are 50-100 nm vesicles shed from all cell types and found in all body fluids, to be used as biomarkers of WRA. Immunological stimulation of cells causes increases in the number of secreted exosomes and

exosomes have been shown to carry markers such as protein and ribonucleic acid (RNA) that reflect the stimulation. The current study will evaluate whether exosomes from various body fluids in an experimental isocyanate-induced WRA model will carry useful protein and/or microRNA biomarkers.

Activity E: Carry out research and other activities to prevent isocyanate-induced asthma (Previously: "Develop improved tools for detection of allergic sensitization to low molecular weight allergens such as isocyanates or high molecular weight allergens such as mold allergens")

Background:
Isocyanates are reactive, low molecular weight agents that are widely used to produce a range of products, including paints, glues, foams, plastics, and polyurethanes. Isocyanates are one of the most important causes of WRA, which occurs in 5-15% of exposed workers. Thus, prevention of isocyanate-induced asthma is relevant and important.

Progress:
Much progress has been made in this area. One line of investigation has focused on identifying and characterizing sensitizing antigens created when diisocyanates bind to proteins, forming diisocyantate-protein adducts. Research has been conducted to characterize these adducts and raise monoclonal antibodies against them. These monoclonal antibodies are tools that can be used to develop enzyme-linked immunosorbent assays, which, in turn, can be used for biomonitoring and/or determination of protein-binding sites. Thus far, multiple monoclonal antibodies have been produced against 2,4- and 2,6- toluene diisocyanates and methylene diphenyldiisocyanate protein adducts. Monclonal antibody specificity has been assessed and a patent application filed. Adduction sites of diisocyanates on human albumin and hemoglobin have been identified using ultra-high performance liquid chromatography-quadrapole-time of flight mass spectrometry. The potential role of the skin in TDI allergic/asthmatic sensitization has also been demonstrated in a murine immunohistochemical study employing one of the monoclonal antibodies developed in the NIOSH laboratory (Nayak 2014, Appendix 5). Influence of the body's antioxidant thiols on protein adduction has been assessed in collaboration with Yale researchers (Wisnewski 2013, Appendix 5).

Other work demonstrated potential usefulness of micro RNAs (miRNA) as biomarkers. miRNA have been demonstrated to have a regulatory role in the immune system and changes in expression of specific miRNA may be useful in early detection of diisocyanate sensitization (Anderson 2013, Appendix 5). The expression kinetics of several miRNA have been examined following TDI dermal exposure in mice and MiR-210, a specific type of miRNA, has been identified as a promising marker for further study as a biomarker of TDI sensitization.

Two publications by Ceballos et al addressed use of gloves to protect against dermal isocyanate exposure. One found that commonly used latex and nitrile gloves were ineffective barriers against the isocyanates used in a clear-coat formulation, but butyl rubber gloves were protective (Ceballos 2014, Appendix 5). Another found that automotive spray painters often used ineffective latex gloves and were not always aware that dermal exposure to isocyanates could contribute to development of WRA (Ceballos 2014, Appendix 5). Three publications have

evaluated genetic risk factors diisocyante-induced asthma (Bernstein 2013, Yucesoy 2012, Yucesoy 2014, Appendix 5).

RDRP participated in organizing the NIH's Isocyanates and Health Conference, which was held in April 2013 (http://www.niehs.nih.gov/news/newsletter/2013/5/spotlight-isocyanates/). The purpose of this international multidisciplinary conference was to identify and discuss the latest knowledge and important issues on the health effects of isocyanates, including current best evidence about exposure monitoring, environmental controls and clinical management. Conference themes included worker and consumer exposure issues; toxicity testing/animal models/biomarkers; human cancer risk; environmental exposure/monitoring; respiratory epidemiology and disease; occupational health surveillance/management; research to practice/health communication (integrated across each theme). RDRP staff contributed 5 presentations and contributed to the development of the proceedings document, which has been submitted for publication.

Another important activity has been RDRP participation in the Spray Polyurethane Foam Insulation (SPFI) intitiative. In 2009, the EPA established an initiative to investigate and address the hazards associated with the use of SPFI. SPFI is made by the reaction of methylenebis(phenyl isocyanate) with polyols in the presence of catalysts and other additives. A workgroup of Federal partners was established that included EPA, NIOSH, OSHA, the Consumer Products Safety Commission, and NIST. The group interacts with industry groups such as the American Chemistry Council's Center for the Polyurethanes Industry and the Spray Polyurethane Foam Alliance via periodic conference calls and face-to-face meetings. The Federal partners engage the industry groups in the areas such as product stewardship, information dissemination, and safe re-entry and re-occupancy times. RDRP has participated in a comparison of sampling and analytical methods for isocyanates in SPFI application with industry and academic partners. Studies presented in preliminary form by Bello et al. at NIH's Isocyanates and Health Conference found that a method developed by RDRP measured much higher levels of total reactive isocyanate group than the other methods in the comparison. Also, RDRP staff has developed an engineering control for use in SPFI application.

Finally, RDRP has been participating in a cross-Institute effort to produce a NIOSH Criteria Document for toluene diisocyanate (TDI). TDI is a type of diisocyanate that is primarily used in the manufacture of flexible and rigid foams, coatings, elastomers, and adhesives for the furniture and automobile industries. The purpose of the criteria document is to evaluate and analyze the scientific literature concerning potential health effects, toxicology, engineering controls, work practices, personal protective equipment and recommendations pertaining to TDI. A quantitative risk assessment will be performed and an updated recommended exposure limit (REL) for TDI will be established based on the risk assessment. In addition to a proposed REL, the document will contain exposure assessment guidance and sampling and analytical method recommendations, medical surveillance, and hazard guidance. The internal draft of the criteria document is nearing completion. As part of this effort, NIOSH posted a request for information in the *Federal Register* Vol. 78, No. 121 on June 24, 2013 and obtained information in response from the American Chemistry Council Diisocyanates Panel and the Polyurethane Foam Association.

Impact:
Biomonitoring through the use of anti-diisocyanate-monoclonal antibodies may aid in prevention, and the results of adduct mapping using monoclonal antibodies may be useful for early detection and intervention for sensitized workers. Anti-diisocyanate monoclonal antibodies have been disseminated to one academic institution and a chemical company that uses diisocyanates.

As a result of the SPFI Initiative, industry has established a certification program for sprayers to help ensure greater safety during application, and a better and safer product for the occupant.

The publication of a criteria document is anticipated to have great impact. In addition to the independent influence of the document, establishment of an updated REL and other prevention recommendations can potentially facilitate rulemaking by OSHA, leading to additional prevention of WRA.

Future plans:
Anti-diisocyanate monoclonal antibodies will be made available to new partners in academia and industry. Proteomic tools will be applied to mechanistic studies of asthmagenesis and for assessment of potential novel biomarkers. Further miRNA studies will be conducted to assess their role in disease and as early markers of diisocyanate sensitization. Publication of the proceedings document from the Isocyanates and Health Conference will be pursued to completion.

Work will continue on the TDI criteria document. It must pass through a rigorous process of internal and then external (public and peer) review. All review comments will be considered and addressed accordingly before the document is finalized.

Appendix 1

Occupational Respiratory Disease Surveillance
(September, 2012 – July, 2014)

Publications

Work-related asthma

Anderson NJ(1), Fan ZJ, Reeb-Whitaker C, Bonauto DK, Rauser E. Distribution of asthma by occupation: Washington State Behavioral Risk Factor Surveillance System Data, 2006-2009. J Asthma. 2014 Jul 15:1-8. [Epub ahead of print]

Hudson NL, Kasner EJ, Beckman J, Mehler L, Schwartz A, Higgins S, Bonnar-Prado J, Lackovic M, Mulay P, Mitchell Y, Larios L, Walker R, Waltz J, Moraga-McHaley S, Roisman R, Calvert GM. Characteristics and magnitude of acute pesticide-related illnesses and injuries associated with pyrethrin and pyrethroid exposures--11 states, 2000-2008. Am J Ind Med. 2014 Jan;57(1):15-30. doi: 10.1002/ajim.22216. Epub 2013 Jun 20.

Knoeller GE, Mazurek JM, Storey E. Occupation held at the time of asthma symptom development. Am J Ind Med. 2013 Oct;56(10):1165-73. doi: 10.1002/ajim.22203. Epub 2013 Jun 21.

Knoeller GE(1), Mazurek JM, Moorman JE. Asthma symptoms among adults with work-related asthma. J Asthma. 2013 Mar;50(2):166-73. doi: 10.3109/02770903.2012.754029. Epub 2012 Dec 21.

Knoeller GE(1), Mazurek JM, Moorman JE. Health-related quality of life among adults with work-related asthma in the United States. Qual Life Res. 2013 May;22(4):771-80. doi: 10.1007/s11136-012-0206-7. Epub 2012 Jun 4.

Mazurek JM, Knoeller GE, Moorman JE, Storey E. Occupational asthma incidence: findings from the behavioral risk factor surveillance system asthma call-back survey--United States, 2006-2009. J Asthma. 2013 May;50(4):390-4. doi: 10.3109/02770903.2013.769267. Epub 2013 Feb 22.

Mazurek JM, White GE, Moorman JE, Storey E. Influenza vaccination among persons with work-related asthma. Am J Prev Med. 2014 Aug;47(2):203-11. doi: 10.1016/j.amepre.2014.04.007. Epub 2014 Jun 18.

Reeb-Whitaker C, Anderson NJ, Bonauto DK.: Prevention Guidance for Isocyanate-Induced Asthma using Occupational Surveillance Data. J Occ Environ Hygiene. 2013; 10:597-608.

White GE, Mazurek JM, Moorman JE. Work-related asthma and employment status--38 states and District of Columbia, 2006-2009. J Asthma. 2013 Nov;50(9):954-9. doi: 10.3109/02770903.2013.829491. Epub 2013 Aug 21.

White GE, Mazurek JM, Moorman JE. Asthma in health care workers: 2008 and 2010 Behavioral Risk Factor Surveillance System Asthma Call-back Survey. J Occup Environ Med. 2013 Dec;55(12):1463-8. doi: 10.1097/JOM.0000000000000006.

White GE, Seaman C, Filios M, Mazurek J, Flattery J, Harrison RJ, Reilly MJ, Rosenman KD, Lumia ME, Stephens AC, Pechter E, Fitzsimmons K, Davis LK.: Gender Differences in Work-Related Asthma: Surveillance Data from California, Massachusetts, Michigan, and New Jersey, 1993-2008. J Asthma. 2014 Epub ahead of print. http://dx.doi.org/10.3109/02770903.2014.903968.

White GE, Mazurek JM, Storey E. Employed adults with asthma who have frequent workplace exposures. J Asthma. 2014 Jul 16:1-17. [Epub ahead of print]

Chronic Obstructive Pulmonary Disease; and Tobacco Use

Bang KM, Syamlal G, Mazurek JM, Wassell JT. Chronic obstructive pulmonary disease prevalence among nonsmokers by occupation in the United States. J Occup Environ Med. 2013 Sep;55(9):1021-6. doi: 10.1097/JOM.0b013e31829baa97.

Doney B, Hnizdo E, Graziani M, Kullman G, Burchfiel C, Baron S, Fujishiro K, Enright P, Hankinson JL, Stukovsky KH, Martin CJ, Donohue KM, Barr RG. Occupational Risk Factors for COPD Phenotypes in the Multi-Ethnic Study of Atherosclerosis (MESA) Lung Study. COPD. 2014 Aug;11(4):368-80. doi: 10.3109/15412555.2013.813448. Epub 2014 Feb 25.

Doney B, Hnizdo E, Dillon CF, Ryne Paulose-Ram R, Tilert T, Wolz M, Beeckman-Wagner L. Prevalence of airflow obstruction in U.S. adults aged 40–79 years: NHANES data 1988–1994 and 2007–2010. COPD: J Chronic Obstruc Pulm Dis 2014, in press.

Doney B, Hnizdo E, Syamlal G, Kullman G, Burchfiel C, Martin CJ, Mujuru P. Prevalence of Chronic Obstructive Pulmonary Disease among U.S. Working Adults Aged 40-70 Years: National Health Interview Survey Data 2004-2011. J Occup Environ Med 2014, in press.

Mazurek JM, Syamlal G, King BA, Castellan RM. Smokeless tobacco use among working adults - United States, 2005 and 2010. MMWR Morb Mortal Wkly Rep. 2014 Jun 6;63(22):477-82.

Syamlal G, Mazurek JM, Dube SR. Gender Differences in Smoking Among U.S. Working Adults. Am J Prev Med. 2014 Jul 18. pii: S0749-3797(14)00281-5. doi: 10.1016/j.amepre.2014.06.013. [Epub ahead of print]

Tilert T, Dillon C, Paulose-Ram R, Hnizdo E, Doney B. Estimating the U.S. prevalence of chronic obstructive pulmonary disease using pre- and post-bronchodilator spirometry: the National Health and Nutrition Examination Survey (NHANES) 2007-2010. Respir Res. 2013 Oct 9;14:103. doi: 10.1186/1465-9921-14-103.

Yong LC, Luckhaupt SE, Li J, Calvert GM. Quit interest, quit attempt and recent cigarette smoking cessation in the US working population, 2010. Occup Environ Med. 2014 Jun;71(6):405-14. doi: 10.1136/oemed-2013-101852. Epub 2014 Feb 4.

Coal Miners' Surveillance / Coal Workers' Pneumoconiosis

Blackley DJ, Halldin CN, Wang ML, Laney AS. Small mine size is associated with lung function abnormality and pneumoconiosis among underground coal miners in Kentucky, Virginia and West Virginia. Occup Environ Med. 2014 Jul 22. pii: oemed-2014-102224. doi: 10.1136/oemed-2014-102224. [Epub ahead of print]

Laney AS(1), Petsonk EL. Small pneumoconiotic opacities on U.S. coal worker surveillance chest radiographs are not predominantly in the upper lung zones. Am J Ind Med. 2012 Sep;55(9):793-8. doi: 10.1002/ajim.22049. Epub 2012 Apr 19.

Laney AS, Attfield MD. Examination of potential sources of bias in the US Coal Workers' Health Surveillance Program. Am J Public Health. 2014 Jan;104(1):165-70. doi: 10.2105/AJPH.2012.301051. Epub 2013 May 16.

Wang ML, Beeckman-Wagner LA, Wolfe AL, Syamlal G, Petsonk EL. Lung-function impairment among US underground coal miners, 2005 to 2009: geographic patterns and association with coal workers' pneumoconiosis. J Occup Environ Med. 2013 Jul;55(7):846-50. doi: 10.1097/JOM.0b013e31828dc985.

Other Surveillance-Related Publications

Anderson NJ, Bonauto DK, Fan ZJ, Spector JT. Distribution of influenza-like illness (ILI) by occupation in Washington State, September 2009-August 2010. PLoS One. 2012;7(11):e48806. doi: 10.1371/journal.pone.0048806. Epub 2012 Nov 12.

Das R, McNary J, Fitzsimmons K, Dobraca D, Materna B, Cummings K, Mohle-boetani J, Wheeler C, McDowell A, Iossifova Y, Kreiss K.: Occupational Coccidiodomycosis in California. JOEM. 2012; 54(5).

Dang GTT, Barros N, Higgins SA, Langley RL, Lipton D.: Descriptive Review of Asbestosis and Silicosis Hospitalization Trends in North Carolina. 2002-2011. NC Med. 2013; 74:368-375.

Kasner EJ, Keralis JM, Mehler L, Beckman J, Bonnar-Prado J, Lee SJ, Diebolt-Brown B, Mulay P, Lackovic M, Waltz J, Schwartz A, Mitchell Y, Moraga-McHaley S, Roisman R, Gergely R, Calvert GM. Gender differences in acute pesticide-related illnesses and injuries among farmworkers in the United States, 1998-2007. Am J Ind Med. 2012 Jul;55(7):571-83. doi: 10.1002/ajim.22052. Epub 2012 Apr 11.

Kreiss K. Occupational lung disease: from case reports to prevention. Chest. 2013 Jun;143(6):1529-31. doi: 10.1378/chest.12-3001. (editorial, addresses flock workers' lung)

Laney AS, Storey E.: Occupational Disease Surveillance. Chapter for new edition of Current Occupational and Environmental Medicine (In press).

Stanbury M, Rosenman KD.: Occupational Health Disparities: A State Public Health-based Approach. Am J Ind Med. 2014; 57(5):596-604.

Syamlal G, Schleiff PL, Mazurek JM, Doney B, Greskevitch M. Respirator use among U.S. farm operators: evidence from the 2006 Farm and Ranch Safety Survey. J Agromedicine. 2013;18(1):27-38. doi: 10.1080/1059924X.2012.743379.

Weissman DN. Medical surveillance for the emerging occupational and environmental respiratory diseases. Curr Opin Allergy Clin Immunol. 2014 Apr;14(2):119-25. doi: 10.1097/ACI.0000000000000033.

Other products

Respiratory Disease-Related Health Hazard Evaluation Reports

Armstrong JL, Kummings KJ, Boylstein R, Ham J, Blackley D. Evaluation of Exposures and a Potential Hydrogen Sulfide Release Event at an Aircraft Engine Services Facility, West Virginia. Health Hazard Evaluation Report 2014-0042-3216, July, 2014. http://www.cdc.gov/niosh/hhe/reports/pdfs/2014-0042-3216.pdf

Bailey R, Piacitelli C, Martin S, Cox-Ganser J. Evaluation of indoor environmental quality at an accounting office. Health Hazard Evaluation Report 2011-0096-3176, April 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2011-0096-3176.pdf

Bailey RL, Piacitelli CA. Evaluation of respiratory concerns at a cream cheese manufacturing facility. Health Hazard Evaluation Report 2011-0102-3194, September 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2011-0102-3194.pdf

Beaucham C, Tapp L. Evaluation of exposure to chemicals at a polymer additive manufacturing facility. Health Hazard Evaluation Report 2012-0176-3215, June 2014. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0176-3215.pdf

Broadwater K, Page E, Burr G. Evaluation of indoor environmental quality in a natural history building. Health Hazard Evaluation Report 2014-0037-3213, June 2014. http://www.cdc.gov/niosh/hhe/reports/pdfs/2014-0037-3213.pdf

Cummings KJ, Boylstein RJ, Stanton ML, Piacitelli CA. An evaluation of respiratory health at a flavoring manufacturing facility – Kentucky. Health Hazard Evaluation Report 2012-0012-3192, September 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0012-3192.pdf

Cummings KJ, Piacitelli C, Stanton M, Bailey RL. Evaluation of respiratory concerns at a snack food production facility. Health Hazard Evaluation Report 2011-0037-3172, March 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2011-0037-3172.pdf

De Perio MA, Burr GA. Evaluation of Coccidioides Exposures and Coccidioidomycosis Infections among Prison Employees. Health Hazard Evaluation Report 2013-0113-3198, January, 2014. http://www.cdc.gov/niosh/hhe/reports/pdfs/2013-0113-3198.pdf

De Perio MA, Niemeier RT. Evaluation of Exposure to Tuberculosis Among Employees at a Long-term Care Facility. Health Hazard Evaluation Report 2012-0137-3178, revised June 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0137-3178.pdf

Fent KW, Musolin K, Methner M. Evaluation of Chemical Exposures during Fire Fighter Training Exercises Involving Smoke Simulant. Health Hazard Evaluation Report 2012-0028-3190, July 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0028-3190.pdf

Fent KW, Tapp L, Wiegand D. Evaluation of Safety Climate, Health Concerns, and Pharmaceutical Dust Exposures at a Mail Order Pharmacy. Health Hazard Evaluation Report 2012-0044-3199, December 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0044-3199.pdf

Gibbins J, Niemeier RT, De Perio MA, Mueller C. Evaluation of Zoonotic Disease and Exposures in Persons Working with Marine Mammals. Health Hazard Evaluation Report 2011-0105-3173, April 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2011-0105-3173.pdf

King BS, Page E. Evaluation of Potential Employee Exposures at a Medical Examiner's Office. Health Hazard Evaluation Report 2012-0135-3184, June 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0135-3184.pdf

LeBouf RF, McCague AB, Armstrong J, Boylstein R, Bailey RL, Kreiss K. Evaluation of health concerns at a pet food manufacturing facility – Missouri. Health Hazard Evaluation Report 2012-0260-3202, January 2014. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0260-3202.pdf

Martin SB, Lawrence RB, Mead KR. Evaluation of Environmental Controls at a Homeless Shelter Associated with a Tuberculosis Outbreak – Texas. Health Hazard Evaluation Report 2013-0145-3209, May 2014. http://www.cdc.gov/niosh/hhe/reports/pdfs/2013-0145-3209.pdf

Martin SB, Mead KR, Lawrence RB, Beaty M. Evaluation of Environmental Controls at a Homeless Shelter (City Rescue Mission–New Life Inn) Associated with a Tuberculosis Outbreak – Florida. Health Hazard Evaluation Report 2012-0155-3180, July 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0155-3180.pdf

Martin SB, Mead KR, Lawrence RB, Beaty M. Evaluation of Environmental Controls at a Homeless Shelter (Trinity Rescue Mission) Associated with a Tuberculosis Outbreak – Florida. Health Hazard Evaluation Report 2012-0265-3183, July 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0265-3183.pdf

Martin SB, Mead KR, Lawrence RB, Beaty M. Evaluation of Environmental Controls at a Homeless Shelter (City Rescue Mission –McDuff Campus) Associated with a Tuberculosis Outbreak – Florida. Health Hazard Evaluation Report 2012-0264-3182, July 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0264-3182.pdf

Martin SB, Mead KR, Lawrence RB, Beaty M. Evaluation of Environmental Controls at a Homeless Shelter (Community Rehabilitation Center) Associated with a Tuberculosis Outbreak

– Florida. Health Hazard Evaluation Report 2012-0263-3181, July 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0263-3181.pdf

McCague AB, Armstrong JL, Cummings KJ, Park JH. Evaluation of Exposures and Health at a Specialty Chemicals Plant, West Virginia. Health Hazard Evaluation Report 2012-0222-3203, February 2014. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0222-3203.pdf

Methner MM, Tapp L, Ramsey J. Evaluation of Metals, Solvents, Formaldehyde, Ventilation, and Ergonomic Risks during the Manufacture of Electrical Cable Accessories. Health Hazard Evaluation Report 2012-0025-3207, May 2014. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0025-3207.pdf

Methner, MM, Gibbins J, Niemeier T. Evaluation of Instructor and Range Officer Exposure to Emissions from Copper-Based Frangible Ammunition at a Military Firing Range. Health Hazard Evaluation Report 2012-0091-3187, July 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2012-0091-3187.pdf

Meza F, Mueller C, King B. Evaluation of Health Effects of a Chlorine Gas Release in a Poultry Processing Plant — Arkansas. Health Hazard Evaluation Report 2011-0128-3166, revised February 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2011-0128-3166.pdf

Page E, Couch J. Evaluation of Employee Health Concern and Suspected Contamination at an Office Complex. Health Hazard Evaluation Report 2010-0061-3206, April 2014. http://www.cdc.gov/niosh/hhe/reports/pdfs/2010-0061-3206.pdf

Page EH, Dowell CH, Mueller CA, Biagini RE. Evaluation of Sensitization and Exposure to Flour Dust, Spices, and Other Ingredients Among Poultry Breading Workers. Health Hazard Evaluation Report 2009-0131-3171, April 2013. http://www.cdc.gov/niosh/hhe/reports/pdfs/2009-0131-3171.pdf

Electronic Health Records – technical products:

Staes C, Edwards H, Duncan J, Peelay J. Report: "*Development of Interface Business Requirements for Patient Entry of Occupational History Information for Electronic Health Records. Summary of findings and recommendations*." University of Utah. A report re: the initial business requirements for patient entry of industry and occupation to be coded, stored, and used in EHRs (September 2013)

Occupational Data for Health (ODH) template published. The template was published by Integrating the Healthcare Enterprise (iHE) as part of the Healthy Weight Draft Standard for Trial Implementation. (September 2013)

Occupational Data for Health (ODH) Information Model initial development; completed for work history thus far. It will be updated to include risks and exposures, among other areas. An information model is a standard IT document for EHR system developers. (July 2013)

Prototype coding dropdown and assisted search tools for industry and occupation developed. (June 2013)

Occupational Data for Health (ODH) template. A template for work information was developed for use in electronic data sharing documents, or CDA (Clinical Document Architecture). The template standardizes the collection and display of work information in the correct format (e.g., industry and occupation for a given job are forever linked), and is available for data sharing documents of this type.

Glossary. Drafted a glossary of common work information terms for use by the primary standards development organization (SDO) in the US, Health Level Seven International (HL7). The glossary provides guidance in defining occupational health -related terms to ensure consistent data collection and use in EHR standards.

Occupational Death, Illness, and Fatality (ODIF) Functional Profile Version 1.1 published by the SDO HL7 and registered with ANSI 3/24/13 – The ODIF was developed as part of the Public Health Functional Profile, of the Electronic Health Record System (EHR-S) Functional Model. (January 2013)

Appendix 2

Digital Chest Imaging
(September, 2012 – July, 2014)

Publications

Halldin CN, Petsonk EL, Laney AS.: Validation of the International Labour Office Digitized Standard Images for Recognition and Classification of Radiographs of Pneumoconiosis. Acad Radiol. 2014; 21:305-311.

Other Products

Federal register notice: National Institute for Occupational Health (NIOSH)-Certified B Readers; Training and Testing. 78 FR 35935, pages 35935 -35936, June 14, 2013. https://www.federalregister.gov/articles/2013/06/14/2013-14147/national-institute-for-occupational-health-niosh-certified-b-readers-training-and-testing

Contract opportunity: Development of Updated Program to Train and Certify Physicians as Competent to Use the International Labour Office International Classification of Radiographs of Pneumoconioses in Digital Format, Solicitation Number: 2013-N-15006. https://www.fbo.gov/index?s=opportunity&mode=form&tab=core&id=2b7f679b2b7443b950d141908d7ef859&_cview=1

Impact of NIOSH work on recent Department of Labor regulations

Excerpt from *Federal Register* April 17, 2014:

Black Lung Benefits Act: Standards for Chest Radiographs;
On June 13, 2013, the Office of Workers' Compensation Programs (OWCP) published a direct final rule (78 FR 35549) and a companion notice of proposed rulemaking (NPRM) (78 FR 35575) to update the existing quality standards for administering and interpreting film-based chest radiographs and to add parallel standards for digital radiographs for claims under the Black Lung Benefits Act (BLBA), 30 U.S.C. 901-944…This final rule completes the process begun by the notice of proposed rulemaking.

As explained in the NPRM, OWCP proposed adding digital radiography standards to the existing standards because digital radiography systems are rapidly replacing traditional analog film-based systems in medical facilities. 78 FR 35576-35577….This final rule fills the technological gap with regulatory quality standards for digital radiographs. As it did when it first promulgated quality standards for film-based chest X-rays, See 78 FR 35576-35577 (summarizing history of X-ray quality standards and Department's authority to adopt them), the Department has based the standards adopted in this final rule largely on those promulgated in 2012 by the Department of Health and Human Services for use in the National Institute for Occupational Safety and Health (NIOSH) Coal Workers' Health Surveillance Program (CWHSP) (the NIOSH rules). See 42 CFR 37.1 et seq.; see also 77 FR 56718-56735 (September 13, 2012) (NIOSH final rule); 77 FR 1360-1385 (January 9, 2012) (NIOSH proposed rule). Under the CWHSP, NIOSH approves medical facilities for participation in monitoring the health of the nation's coal miners through periodic chest X-ray screening. See 42 CFR 37.44-37.45; see also 78 FR 35577 (discussing the CWHSP). Congress designated NIOSH as the Department's statutory advisor for establishing standards for BLBA medical testing. 30 U.S.C. 902(f)(1)(D).

The standards adopted here will ensure that claim adjudications continue to be based on high-quality, uniform radiographs. By adopting quality standards for digitally acquired chest X-rays, the Department intends that interpretations of film and digital X-rays--so long as they are made and interpreted in accordance with the applicable quality standards--will be put on equal footing both for admission into evidence and for the weight accorded them…

Appendix 3

Flavorings-Related Lung Disease / Obliterative Bronchiolitis
(September, 2012 – July, 2014)

Publications

Anderson SE, Franko J, Wells JR, Lukomska E, Meade BJ.: Evaluation of the hypersensitivity potential of alternative butter flavorings. Food Chem Toxicol. 2013; 62:373-381.

Cullinan P, McGavin CR, Kreiss K, Nicholson AG, Maher TM, Howell T, Banks J, Newman Taylor AJ, Chen CH, Tsai PJ, Shih TS, Burge PS. Obliterative bronchiolitis in fibreglass workers: a new occupational disease? Occup Environ Med. 2013 May;70(5):357-9. doi: 10.1136/oemed-2012-101060. Epub 2013 Jan 15.

Cummings KJ, Boylstein RJ, Stanton ML, Piacitelli CA, Edwards NT, LeBouf RF, Kreiss K. Respiratory symptoms and lung function abnormalities related to work at a flavouring manufacturing facility. Occup Environ Med. 2014 Aug;71(8):549-54. doi: 10.1136/oemed-2013-101927. Epub 2014 Jun 2.

Curwin BD, Deddens JA, McKernan LT. Flavoring exposure in food manufacturing. J Expo Sci Environ Epidemiol. 2014 Jul 23. doi: 10.1038/jes.2014.52. [Epub ahead of print]

Goravanahally MP, Hubbs AF, Fedan JS, Kashon ML, Batelli LA, Mercer RR, Goldsmith WT, Jackson MC, Cumpson A, Frazer DG, Dey RD.:Diacetyl increases sensory innervation and substance P production in rat trachea. Tox. Pathol. 2014; 42:582-590.

Halldin CN, Suarthana E, Fedan KB, Lo Y-C, Turabelidze G, Kreiss K. Increased Respiratory Disease Mortality at a Microwave Popcorn Production Facility with Worker Risk of Bronchiolitis Obliterans. PLOS ONE. 2013; 8(2):e57935. http://dx.doi.org/10.1371/journal.pone.0057935.

Hirst DV, Dunn KH, Shulman SA, Hammond DR, Sestito N. Evaluation Of Engineering Controls For The Mixing Of Flavorings Containing Diacetyl And Other Volatile Ingredients. J Occup Environ Hyg. 2014 Mar 20:0. [Epub ahead of print]

Hubbs AF, Cumpston AM, Goldsmith WT, Battelli LA, Kashon ML, Jackson MC, Frazer DG, Fedan JS, Goravanahally MP, Castranova V, Kreiss K, Willard PA, Friend S, Schwegler-Berry D, Fluharty KL, Sriram K. Respiratory and olfactory cytotoxicity of inhaled 2,3-pentanedione in Sprague-Dawley rats. Am J Pathol. 2012 Sep;181(3):829-44. doi: 10.1016/j.ajpath.2012.05.021. Epub 2012 Aug 13.

Huff S, Stocks JM, Saito R, Blihartz P, Levin J, Glazer C, Bailey R, Cummings K, Kreiss K, McCague AB. Obliterative bronchiolitis in workers in a coffee-processing facility - Texas, 2008-2012. MMWR Morb Mortal Wkly Rep. 2013 Apr 26;62(16):305-7.

Kreiss K. Work-related spirometric restriction in flavoring manufacturing workers. Am J Ind Med. 2014 Feb;57(2):129-37. doi: 10.1002/ajim.22282. Epub 2013 Nov 22.

Kreiss K.: Occupational causes of constrictive bronchiolitis. Curr Opin Allergy Clin Immunol 2013; 13:167-172.

Kreiss K.: Experience with emerging lung diseases from the National Institute for Occupational Safety and Health. (Invited paper) Borden Institute, US Army medical Department, Office of the Surgeon General. (in press).

Zaccone EJ, Thompson JA, Ponnoth DS, Cumpston AM, Goldsmith WT, Jackson MC, Kahon ML, Frazer DG, Hubbs AF, Shimko MJ, Fedan JS.: Popcorn flavoring effects on reactivity of rat airways in vivo and in vitro. J. Tox. Environ. Hlth, Part A: Current Issues. 2013; 76:669-689.

Other Products

NIOSH Engineering Report
Garcia A, Hammond DR, Hirst DVL, Curwin D. In-depth survey report. Process evaluation at Kraft Atlantic, Inc. Division of Applied Research and Technology, Engineering and Physical Hazards Branch, EPHB Report No. 322-15a, October, 2012.
http://www.cdc.gov/niosh/surveyreports/pdfs/322-15a.pdf

Health Hazard Evaluation Reports (also listed in Appendix 1, Surveillance)

Bailey RL, Piacitelli CA. Evaluation of respiratory concerns at a cream cheese manufacturing facility. Health Hazard Evaluation Report 2011-0102-3194, September 2013.
http://www.cdc.gov/niosh/hhe/reports/pdfs/2011-0102-3194.pdf

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Appendix 4

Chronic Obstructive Pulmonary Disease
(September, 2012 – July, 2014)

Publications (also, see COPD & tobacco surveillance publications in Appendix 1, which are not repeated here)

General Issues in Work-Related COPD / Various Work Settings

Blanc P, Hnizdo E, Kreiss K, Toren K.: Chronic obstructive airways disease due to occupational exposure. Asthma in the Workplace, 4th edition. Edited by Malo J-L, Chan-Yeung M, Bernstein DI. New York: CRC Press 2013, Print ISBN: 978-1-84214-591-3, eBook ISBN: 978-1-84184-925-6, DOI.

Cummings KJ, McCague AB, Kreiss K. Nonmalignant respiratory disease mortality in styrene-exposed workers. Epidemiology. 2014 Jan;25(1):160-1. doi: 10.1097/EDE.0b013e3182a70b0f. PubMed PMID: 24296936. (letter)

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Graber JM, Stayner LT, Cohen RA, Conroy LM, Attfield MD.: Respiratory disease mortality among US coal miners; results after 37 years of follow-up. Occup Environ Med 2014; 71(1):30-39. Link http://dx.doi.org/10.1136/oemed-2013-101597

Graber JM, Cohen RA, Basanets A, Stayner LT, Kundiev Y, Conroy L, Mukhin VV, Lysenko O, Zvinchuk A, Hryhorczuk DO. Results from a Ukrainian-US collaborative study: prevalence and predictors of respiratory symptoms among Ukrainian coal miners. Am J Ind Med. 2012 Dec;55(12):1099-109. doi: 10.1002/ajim.21997. Epub 2011 Dec 13. PubMed PMID: 22169933.

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Disease Study 2010. Lancet. 2012 Dec 15;380(9859):2095-128. doi: 10.1016/S0140-6736(12)61728-0. Erratum in: Lancet. 2013 Feb 23;381(9867):628. AlMazroa, Mohammad A [added]; Memish, Ziad A [added]. PubMed PMID: 23245604.

Picciotto S, Chevrier J, Balmes J, Eisen EA. Hypothetical interventions to limit metalworking fluid exposures and their effects on COPD mortality: G-estimation within a public health framework. Epidemiology. 2014 May;25(3):436-43. doi: 10.1097/EDE.0000000000000082. PubMed PMID: 24608667.

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Agriculture / Food Production

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World Trade Center

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Cho SJ, Nolan A, Echevarria GC, Kwon S, Naveed B, Schenck E, Tsukiji J, Prezant DJ, Rom WN, Weiden MD. Chitotriosidase is a biomarker for the resistance to World Trade Center lung injury in New York City firefighters. J Clin Immunol. 2013 Aug;33(6):1134-42. doi: 10.1007/s10875-013-9913-2. Epub 2013 Jun 7. PubMed PMID: 23744081; PubMed Central PMCID: PMC3722498.

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Redlich CA, Tarlo SM, Hankinson JL, Townsend MC, Eschenbacher WL, Von Essen SG, Sigsgaard T, Weissman DN; American Thoracic Society Committee on Spirometry in the Occupational Setting. Official American Thoracic Society technical standards: spirometry in the occupational setting. Am J Respir Crit Care Med. 2014 Apr 15;189(8):983-93. doi: 10.1164/rccm.201402-0337ST. PubMed PMID: 24735032.

Other Products

Spirometry longitudinal data analysis (SPIROLA) software, version 3.0.2, update provided on March 28, 2014. This software is an easy-to-use visual and quantitative tool intended to assist the health care provider in monitoring and interpreting computerized longitudinal spirometry data for individuals as well as for a group. It also assists in evaluating the quality of spirometry provided by a spirometry monitoring program: http://www.cdc.gov/niosh/topics/spirometry/spirola-software.html

Poster, "Get Valid spirometry results EVERY Time." This poster provides concise information on how to identify and correct technical and equipment errors encountered during spirometry testing, using the most current standard professional practice guidelines. Graphic examples and descriptive text enable the user to easily identify common testing problems. Since the original poster was produced in 2011, a number of spirometer manufacturers have routinely provided it to customers together with new spirometers. Due to international interest, it has also been translated into a number of languages, most recently Turkish in September, 2013. Original version in English from 2011 available here: http://www.cdc.gov/niosh/docs/2011-135/. Turkish translation from 2013 available here: http://www.cdc.gov/niosh/docs/2011-135/2011-135turk.html.

Information sheet for employers, published jointly with OSHA, provides guidance to employers about how to obtain high quality spirometry from medical providers. Original version in English from 2011 available here: http://www.cdc.gov/niosh/docs/2011-133/. Spanish translation from December, 2012 available here: http://www.cdc.gov/spanish/niosh/docs/2011-133_sp/

Appendix 5

Work-Related Asthma
(September, 2012 – July, 2014)

Publications (also, see asthma surveillance publications in Appendix 1, which are not repeated here)

General Issues in Work-Related Asthma / Various Work Settings

Aasen TB, Burge PS, Henneberger PK, Schlunssen V, Baur X.: Diagnostic approach in cases with suspected work-related asthma. Journal of Occupational Medicine and Toxicology. 2013; 8:17. doi:10.1186/1745-6673-8-17 http://www.occup-med.com/content/8/1/17

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Fedan JS, Thompson JA, Ismailoglu UB, Jing Y. Tracheal epithelium cell volume responses to hyperosmolar, isosmolar and hypoosmolar solutions: relation to epithelium-derived relaxing factor (EpDRF) effects. Front Physiol. 2013 Oct 11;4:287. doi: 10.3389/fphys.2013.00287. eCollection 2013. PubMed PMID: 24130533; PubMed Central PMCID: PMC3795350.

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Henneberger PK, Liang X, Lemière C.: A comparison of work-exacerbated asthma cases from clinical and epidemiological settings. Can Respir J, 2013; 20(3):159-164.

Henneberger-PK; Wagner-GR; Lemiere-C. Asthma exacerbated at work. In: Asthma in the workplace, fourth edition. Malo J-L, Chan-Yeun M, Bernstein DI, eds. New York: CRC Press, 2013.

Lemiere C, Chaboillez S, Bohadana A, Blais L, Maghni K. Noneosinophilic responders with occupational asthma: a phenotype associated with a poor asthma prognosis. J Allergy Clin Immunol. 2014 Mar;133(3):883-5.e3. doi:10.1016/j.jaci.2013.09.005. Epub 2013 Oct 18. PubMed PMID: 24139830

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Lemiere C, Bégin D, Camus M, Forget A, Boulet LP, Gérin M. Occupational risk

factors associated with work-exacerbated asthma in Quebec. Occup Environ Med. 2012 Dec;69(12):901-7. doi: 10.1136/oemed-2012-100663. Epub 2012 Sep 21. PubMed PMID: 23000826.

Meza F, Chen L, Hudson N. Investigation of respiratory and dermal symptoms associated with metal working fluids at an aircraft engine manufacturing facility. Am J Ind Med. 2013 Dec;56(12):1394-401. doi: 10.1002/ajim.22253. Epub 2013 Sep 30. PubMed PMID: 24122918.

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Shurin MR, Yanamala N, Kisin ER, Tkach AV, Shurin GV, Murray AR, Leonard HD, Reynolds JS, Gutkin DW, Star A, Fadeel B, Savolainen K, Kagan VE, Shvedova AA. Graphene oxide attenuates th2-type immune responses, but augments airway remodeling and hyperresponsiveness in a murine model of asthma. ACS Nano. 2014 Jun 24;8(6):5585-99. doi: 10.1021/nn406454u. Epub 2014 May 23. PubMed PMID: 24847914; PubMed Central PMCID: PMC4072415.

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Indoor Environmental Quality / Dampness / Mold

Akpinar-Elci M, White SK, Siegel PD, Park J-H, Visotcky A, Kreiss K, Cox-Ganser JM.: Markers of Upper Airway Inflammation Associated with Microbial Exposure and Symptoms in Occupants of a Water-Damaged Building. Am J Ind Med. 2013; 56:522-530.

Bahnfleth-WP; Fisk-WJ; Burroughs-HEB; Persily-A; Martin-SB; Stanke-D; Li-YG. Shaping the next indoor air quality. ASHRAE J 2013 Aug; 55(8):50-52,54,56-58.

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Cho SJ, Cox-Ganser JM, Kreiss K, Park JH.: Evaluation of individual-based and group-based exposure estimation of microbial agents in health effects associated with a damp building. Journal of Exposure Science and Environmental Epidemiology. 2013; 23:409-415.

Cummings KJ, Fink JN, Vasudev M, Piacitelli C, Kreiss K. Vocal cord dysfunction related to water-damaged buildings. J Allergy Clin Immunol Pract. 2013 Jan;1(1):46-50. doi: 10.1016/j.jaip.2012.10.001. Epub 2012 Dec 2. PubMed PMID: 24229821.

Kreiss K. Dampness and mould in schools and respiratory symptoms. Occup

Environ Med. 2013 Oct;70(10):679-80. doi: 10.1136/oemed-2013-101641. Epub 2013 Aug 12. PubMed PMID: 23940192 (letter).

Rando RJ, Kwon CW, Lefante JJ. Exposures to thoracic particulate matter, endotoxin, and glucan during post-Hurricane Katrina restoration work, New Orleans 2005-2012. J Occup Environ Hyg. 2014;11(1):9-18. doi: 10.1080/15459624.2013.839879. PubMed PMID: 24283332.

Rando RJ, Lefante JJ, Freyder LM, Jones RN. Respiratory health effects associated with restoration work in post-Hurricane Katrina New Orleans. J Environ Public Health. 2012;2012:462478. doi: 10.1155/2012/462478. Epub 2012 Dec 9. PubMed PMID: 23365586; PubMed Central PMCID: PMC3529447.

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Isocyanates

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Mhike M, Chipinda I, Hettick J, Simoyi RH, Lemons AR, Green B, Siegel PD.: Characterization of methylene diphenyl diisocyanate haptenated human serum albumin and hemoglobin. Anal Biochem. 2013; 440(2):197-204.

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Agriculture / Food Production

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agricultural environment. Environ Sci Process Impacts. 2013 Sep;15(9):1760-7. doi: 10.1039/c3em00330b. PubMed PMID: 23896655.

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Appendix 6

Review of Progress Implementation Report for

NIOSH Respiratory Disease Research Program

Submitted by Board of Scientific Counselors

November 30, 2012

BSC Working Group Members

Dave Bonauto
Jackie Nowell
Michael Larranaga
Carol Rice

Respiratory Disease Research Program Score Sheet

Directions: For each recommendation listed below, please circle a score for each scoring element and provide a brief justification for the assignment of that score. The work group may provide scores in .5 increments where they deem appropriate. If the group chooses to do that, please put a .5 next to the corresponding number and circle that number.

Recommendations In Progress:

Recommendation
Systems for Surveillance: NIOSH should provide appropriate resources for and engage in high-priority occupational [respiratory] disease surveillance.(p136)

Relevance: 1 2 3 4 5 – **SCORE: 5**
Brief Justification: All of the activities being conducted are directly responsive to the recommendation. NIOSH surveillance products developed prior to 2008 have been maintained and improved (e.g. the NIOSH Work-related Lung Disease Report). NIOSH is leveraging existing population based surveys (e.g. NHANES, BRFSS, and NHIS) to better characterize the burden of occupational respiratory disease. NIOSH resources dedicated to the goal of including industry and occupation into the electronic medical record and other health surveys are of paramount importance. NIOSH is currently partnering with five states, up from four, for occupational asthma surveillance. Health hazard evaluation data are included in surveillance efforts related to flavorings related lung disease.

Sustainability: 1 2 3 4 4.5 5 – **SCORE: 4.5**
Brief Justification: NIOSH is dedicating personnel and other resources to improve occupational respiratory disease surveillance in the US and within selected individual states. Continued allocation of such resources will be necessary to sustain this recommendation. NIOSH should consider the NAS recommendation to develop an occupational respiratory disease surveillance plan (p. 146).

Progress: 1 2 3 4 5 – **SCORE: 5**

Brief Justification: The Respiratory Disease Research program (RDRP) has made substantial progress in implementing this recommendation. The relative absence of data characterizing the burden of occupational respiratory disease in the US was a notable concern in the NAS report and the initiated surveillance activities of the last several years are considerable.

Potential Impact: 1 2 3 4 5 – **SCORE: 4.5**

Brief Justification: More formal efforts to quantify the impact of NIOSH surveillance outputs are appropriate. The time frame for such an evaluation should be lengthy suggesting the evaluation of current outputs might best be viewed several years from now. The National Occupational Respiratory Mortality System appears to have high

utility based on web access data. If industry and occupational data are included within the medical record, the impact will be enormous and valuable for decades to come. State based surveillance programs have identified and promoted prevention of occupational asthma caused by cleaners and disinfectants. Other RDRP program activities relate to this surveillance recommendation and might be recognized as contributing to progress on this recommendation: medical screening programs, digital chest imaging, and the World Trade Center programs. The efforts to have industry and occupational data included in the medical record have fostered significant partnerships with the general public health community.

Recommendation
The committee recommends that the effectiveness of digital radiography in CWP surveillance should be an important continuing research priority, which will extend to all interstitial lung diseases. (p135)

Relevance: 1 2 3 4 5 **– <u>SCORE:</u> 5**

Brief Justification:

NIOSH has taken this recommendation very seriously and provided outstanding leadership in standardizing occupational chest radiography made with digital media. NIOSH has documented the equivalence between ILO classifications based on digital versus radiographic chest films. These research efforts were necessary given the evolving nature of medical care and its reliance on digital chest imaging. NIOSH should be commended in its timely and essential course of research activities in this area. The research effort complements the overall NIOSH support for electronic medical record.

Sustainability: 1 2 3 4 5 **– <u>SCORE:</u> 5**

Brief Justification:

The partnerships developed include the ILO and support from a group of B readers who participated in a collaboration to better understand impact of digital technology. This latter effort resulted in a solid basis for recommendations and products. In an effort to revise rules that specify use of films, NIOSH provided support for dedicated personnel to develop a Notice of Proposed Rulemaking (NPR) and monitor progress of rule-making.

Progress: 1 2 3 4 5 **– <u>SCORE:</u> 5**

Brief Justification:

Major accomplishments include the publication of findings regarding image quality, establishment of a chest image repository, provision of standardized digital images and B viewer software. Moreover, the NPR progressed to a rule in a very short period of time (https://www.federalregister.gov/articles/2012/09/13/2012-22253/specifications-for-medical-examinations-of-underground-coal-miners); this underscores the value of this activity to all stakeholders—industry, health care, workers and their representatives and government.

Potential Impact: 1 2 3 4 5 – **SCORE: 5**

Brief Justification:

The actions taken by NIOSH will substantially speed the transmittal of chest images, decrease time to diagnosis and aid in record retention by decreasing storage space and storage area design considerations.

Recommendation
In the flavoring industry, the RDRP response to the identification of diacetyl-induced bronchiolitis obliterans has led to surveillance efforts in multiple locations in an effort to detect and prevent disease. The evaluation committee agrees that continued surveillance, prevention of exposures, and mechanistic research to better understand this disease should continue to be a high priority for the RDRP. (p134)

Relevance: 1 2 3 4 5 – **SCORE: 5**

Brief Justification:

Diacetyl and its substitutes are important newly recognized hazards. Artificial food flavorings as a group are very broad and ever changing. To have limited inquiry to diacetyl would have been limiting. All of the activities since 2008 have high relevance. Field work is expanding the epidemiology, monitoring the increased use of substitutes, and evaluating controls for workplace exposure. Lab studies are providing the necessary research and models on the family of chemicals that make up food flavorings and their health effects. A criteria document has been produced for regulators and industry. Can guiding principles be identified from this course of inquiry that can be used in other settings, especially exposure prevention?

Sustainability: 1 2 3 4 5 – **SCORE: 4.5**

Brief Justification:

Continued priority status for diacetyl must be balanced against other emerging issues and changes in the flavoring industry. Alternative surveillance activities may be considered,

such as a disease registry for obstructive lung disease, including bronchiolitis obliterans. Expanding field studies and laboratory research on substitutes and restrictive disease etiology will be of use to regulators, health care providers and other researchers.

Progress: 1 2 3 4 5 – **SCORE: 5**

Brief Justification:

The progress to date has been impressive. Major accomplishments include progress in assessing the toxicology of food flavoring chemicals being substituted by the industry for diacetyl, assistance to California in development of a CalOSHA standard on artificial food flavorings, a correction procedure to adjust diacetyl concentrations previously measured using the NIOSH Method to account for humidity and a criteria document which includes state-of-the-art control technologies due for publication in the coming months.

Potential Impact: 1 2 3 4 5 – **SCORE: 5**

Brief Justification:

The potential impact is far reaching. The NIOSH criteria document recommends an exposure limit for diacetyl and 2,3-pentanedione and preventive measures designed to reduce or eliminate the adverse health effects of these chemicals. As well, is serves as a tool for the food industry in controlling exposures. It is an evaluation of all known and available scientific information relevant to them. The recommendations are intended for use by OSHA in promulgating a standard. NIOSH's contributions led to development of California's CalOSHA standard and Federal OSHA's enforcement program for popcorn manufacturing. NIOSH's contributions could well lead to elimination of substitute food flavorings. In order to facilitate exposure reduction, it is recommended that specific, proven engineering controls be added to the NIOSH Flavorings website.

Recommendation
In terms of chronic obstructive pulmonary disease (COPD), understanding the contribution of occupational exposures is difficult. To understand this issue, the evaluation committee strongly recommends that, for planning preventive strategies, the RDRP continue to support population-based studies of associations between occupational exposures and COPD to better define groups of workers at greatest risk. (p134)

Relevance: 1 2 3 4 5 – **SCORE: 4.5**

Brief Justification: All of the activities being conducted are directly responsive to the recommendation. NIOSH surveillance products developed prior to 2008 have been maintained and improved (e.g., the NIOSH Work-related Lung Disease Report). NIOSH is leveraging existing population based surveys (e.g., NHANES, MESA, Copenhagen City Heart Study) and other studies on coal mine dust, beryllium, endotoxin, and World Trade Center dust exposures. NIOSH led the effort to collect spirometry data from participants in studies initiated prior to 2008, including NHANES III and MESA. NIOSH plans to analyze current NHANES data to evaluate associations between work-related COPD and determine other attributable risks, including industry-and occupation-specific trends in tobacco use since NHANES III. NIOSH partnered with other CDC divisions to produce the report "Public Health Strategic Framework for COPD Prevention" in 2011. NIOSH has posted software on its website to help surveillance programs evaluate and monitor longitudinal data and engaged external partners to target secondary prevention from both occupational and non-occupational causes of COPD. NIOSH should consider increasing the emphasis on conducting longitudinal studies on high risk populations and developing spirometric reference standards for specific ethnic and racial minorities common in the US population.

Sustainability: 1 2 3 4 5 **– <u>SCORE:</u> 4**

Brief Justification: NIOSH is dedicating personnel and other resources to conduct research, develop education materials (Spirometry posters and training manual, "Public Health Strategic Framework for COPD Prevention", information sheets), and provide tools for longitudinal data analysis (software). NIOSH has worked with spirometer manufacturers to include educational posters with every spirometer shipped. Over 60,000 posters have been delivered and the poster is available in five languages with plans to develop an additional six translations. NIOSH should consider developing metrics to evaluate the impact of their spirometry poster on clinical practice. This is also a research area requiring both the resources of intra- and extra-mural funding programs.

Progress: 1 2 3 4 5 **– <u>SCORE:</u> 4**

Brief Justification:

NIOSH has dedicated personnel and other resources to the prevention, early detection, and management of work-related COPD. NIOSH should consider identifying at-risk populations and developing prevalence data for smoking status by industry and occupation and address smoking in future longitudinal studies. NIOSH has engaged with partners to target secondary prevention from non-occupational causes (smoking, weight gain, sedentary lifestyle and occupational causes (hazardous exposures) but the results of these partnerships have yet to be realized. It is unclear how NIOSH determines which groups of workers are appropriate for targeted studies intended to prevent the onset of COPD.

Potential Impact: 1 2 3 4 5 – **SCORE: 5**

Brief Justification: The changing nature of work (multiple employers, new materials, novel exposures, short-term jobs, multiple jobs at the same time) pose a real challenge to area of research. In 2009, COPD was the 3rd leading cause of death, with 137,353 deaths attributable to the disease. The American Thoracic Society estimates that approximately 15% of COPD cases are attributable to the work environment, highlighting COPD's significance as a major work-related health issue. For these reasons, the potential impact of primary prevention activities, early disease detection, and appropriate management of COPD can have long-lasting positive impacts on the workforce. NIOSH should consider follow up to determine if the training and disseminated tools to improve spirometry have actually improved the quality of surveillance programs using spirometry.

Recommendation
Because the contribution of occupational exposures to the burden of adult asthma is high, work in pursuit of the four WRA subgoals can have a potentially large impact on improved occupational safety and health among the U.S. workforce. (p134)

Relevance: 1 2 3 4 5 – **SCORE: 5**

Brief Justification: The activities conducted since 2008, directly respond to the recommendation. Since 2008, NIOSH has expanded both extramural and intra-mural work-related asthma (WRA) research activities as well as the state-based surveillance co-operative agreement programs. These activities have identified potential and emerging causes of WRA, and led to better estimates of the burden of WRA in the general working population through the BRFSS Asthma Call Back Survey. Special studies were undertaken to characterize exposures and health effects of particular asthma causing agents (e.g. diisocyanates), to evaluate the effects of poor indoor air quality, dampness and mold on the respiratory tract, as well as assessing the health effects of irritant inhalational exposures encountered during natural or man-made disasters. Laboratory work has identified methods for identifying novel indoor air contaminants, and the development of monoclonal antibodies for diisocyanate protein adducts. Concerns from the subgroup suggest some efforts might be undertaken to enhance the recognition among medical clinicians of workplace exposures as a cause of asthma as well as the subsequent clinical evaluation and care of work-related asthma.

Sustainability: 1 2 3 4 5 – **SCORE: 4**

Brief Justification: The current WRA research efforts at NIOSH represent an exemplary partnership between extramural research, state-based surveillance, and NIOSH's intramural research and surveillance program activities. The activities reflect effective

utilization of currently available inputs. There is not a clear sense regarding the prioritization of the limited resources for work-related asthma surveillance and prevention activities. Second, some consideration might be given to emphasizing partnerships with health care provider groups for work-related asthma recognition and clinical care, medical screening programs for other specific exposures, and developing a long-term strategic research plan addressing indoor air quality.

Progress: 1 2 3 4 5 **– <u>SCORE:</u> 4**

Brief Justification: Substantial progress has been made in addressing the recommendation. A range of surveillance and research programs have been launched or enhanced since 2008 to further advance progress on this recommendation. Resource constraints limits further progress.

Potential Impact: 1 2 3 4 5 **– <u>SCORE:</u> 5**

Brief Justification: Better population-based estimates of the prevalence of work-related asthma will increase recognition of WRA as a public health problem. The large number of publications within the scientific peer-reviewed literature demonstrates NIOSH success in disseminating its research finding to the scientific community. These publications documenting research characterizing emerging or known causes of WRA and contaminants in indoor air will provide the foundation for evidence-based clinical decision making for WRA causation and workplace exposure assessment.