NIOSH Respiratory Diseases Research Program Implementation Plan:

Responding to Recommendations in the National Academies Report,

Respiratory Diseases Research at NIOSH

DRAFT April 8, 2009

Executive Summary

The purpose of this document is to familiarize the reader with the National Institute for Occupational Safety and Health (NIOSH) Respiratory Diseases Research Program (RDRP) and its responses to recommendations arising from a recent program evaluation requested from the National Academies (NA). RDRP will seek scientific input on this document from NIOSH's Board of Scientific Counselors at its Spring 2009 meeting and stakeholder feedback through a public comment period.

The document has four main sections. The first section provides an overview of RDRP: what it is, how it operates, and its major strategic goals. The second section describes the program evaluation of RDRP conducted by the National Academies and provides comments and recommendations excerpted from the National Academies' report *Respiratory Diseases Research at NIOSH*, along with detailed responses from RDRP. The third section describes RDRP's highest priorities, which are based on the National Academies' recommendations and other inputs. The fourth section provides the reader with detailed information about the intermediate and activity/output goals that support each of RDRP's strategic goals, as well as lists of intramural projects and extramural grants currently underway in the various strategic goal areas.

RDRP is the program within NIOSH that is most directly responsible for meeting the challenge of preventing and reducing work-related respiratory diseases. It is a matrix management structure that provides programmatic leadership for activities relevant to occupational respiratory diseases across all of NIOSH's structural, supervisory organizational units (Divisions, Laboratories, and Offices). RDRP's ability to influence activities across NIOSH is derived in large part from its ability to set institute goals in the area of respiratory

diseases and to influence decisions about funding of project proposals submitted during an annual intramural National Occupational Research Agenda (NORA) funding competition. In this document, all individuals and groups supported by NIOSH to do work that is relevant to occupational respiratory diseases are included within RDRP. This inclusive view is the one most relevant to NIOSH's societal impact in the area.

The NA conducted its evaluation of RDRP during 2006 and 2007 and submitted an initial draft report early in 2008. 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 provided guidance in the form of recommendations for maintaining and improving RDRP.

The process of RDRP goal setting is depicted in the RDRP logic model. RDRP goals are updated annually and are influenced by a variety of inputs, such as surveillance data, stakeholder priorities, availability of expertise and resources, and the NA-RDRP committee's recommendations. Goals are established with a view towards ultimately achieving important end-outcomes.

RDRP goals are largely organized by disease and have a strong disease focus. However, RDRP recognizes that a broad spectrum of activities is needed to effectively address them. Thus, RDRP embraces a multidisciplinary approach that includes surveillance; research in exposure assessment methods, respiratory health assessment methods, epidemiology, engineering controls, respiratory protection, underlying disease mechanisms, and toxicology; risk assessment and development of authoritative recommendations; health communications; and training and education.

RDRP's five strategic goals are to prevent and reduce: work-related airways diseases, work-related interstitial lung diseases, work-related respiratory infectious diseases, and work-related respiratory malignancies; and to prevent respiratory and other diseases potentially resulting from occupational exposures to nanomaterials.

Within its strategic goal areas, RDRP has identified 3 high priorities for immediate attention: transition of film-based chest radiography surveillance to digital chest imaging; occupational respiratory disease surveillance, including innovations such as use of electronic health records; and flavorings-related lung disease. All of these were strongly recommended to RDRP by the NA-RDRP committee.

RDRP has identified additional high priorities within its strategic goal areas that will also need attention over time. These were also identified by the NA-RDRP committee as important, as is detailed in Section 2 of this document. Among the work-related airways diseases, work-related asthma induced by low and high molecular weight agents and irritants, and chronic obstructive pulmonary disease (COPD), are important priorities. Among the work-related interstitial lung diseases, issues related to coal workers' pneumoconiosis and silicosis are priorities. Asbestos causes a range of malignant and nonmalignant diseases and research identified in the NIOSH document *Asbestos Fibers and other Elongated Mineral Particles: State of the Science and Roadmap for Research* is an important priority. Within the strategic goal area of occupational respiratory infectious diseases, RDRP and NIOSH have special expertise in exposure assessment and in preventing transmission through engineering controls and personal protective equipment, especially respirators. Thus, these are important priorities. Within the area of respiratory malignancies, asbestos and elongated mineral particles have already been noted as priorities. Also, completion of a long-standing collaborative study being conducted by

partners at NIOSH and the National Cancer Institute that evaluates the role of diesel exhaust in lung cancer mortality is an important priority. Finally, RDRP has a keen interest in the potential adverse respiratory health impacts of nanomaterials, so contributing to and supporting the NIOSH Nanotechnology Program is also a high priority. Many other worthy areas of investigation were also endorsed by the NA-RDRP committee as is detailed in the current document.

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Supplemental Information: Cross-Cutting Issues - Surveillance, Exposure Assessment, and Emergency Response

Abbreviations

ATSDR	Agency for Toxic Substances and Disease Registry
BLS	Bureau of Labor Statistics
BRFSS	Behavioral Risk Factor Surveillance System
BSC	Board of Scientific Counselors
BWI	Brush-Wellman Inc.
CDC	Centers for Disease Control and Prevention
COPD	chronic obstructive pulmonary disease
CPT	clinical procedural terminology
CRC	Cancer, Reproductive, and Cardiovascular Diseases
CWHSP	Coal Workers' Health Surveillance Program
CWP	coal workers' pneumoconiosis
DHS	Department of Homeland Security
DLOs	divisions, laboratories and offices
DPM	diesel particulate matter
dNCO	diisocyanate
EC	evaluation committee
ECWHSP	Enhanced CWHSP Program
EP	evidence package
EPA	Environmental Protection Agency
FEV1	forced expiratory volume in 1 second
IARC	International Agency for Research on Cancer
ICD	International Classification of Diseases

IG	intermediate goals
ILO	International Labour Office
IOM	Institute of Medicine
LMW	low-molecular-weight
MSHA	Mine Safety and Health Administration
NA	National Academies
NCHS	National Center for Health Statistics
NCI	National Cancer Institute
NHANES	National Health and Nutrition Evaluation Survey
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute for Occupational Safety and Health
NNI	National Nanotechnology Initiative
NORA	National Occupational Research Agenda
NORMS	National Occupational Respiratory Mortality System
OG	output goals
OPA	Orthophthaladehyde
OSHA	Occupational Safety and Health Administration
PDM	personal dust monitor
PPT	Personal Protective Technology
RDRP	Respiratory Diseases Research Program
REL	Recommended Exposure Limit
SARS	severe acute respiratory syndrome
SENSOR	Sentinel Event Notification Systems for Occupational Risks

TB	tuberculosis
U.S.	United States
WoRLD	Work Related Lung Disease Surveillance Report
WRA	work-related asthma

Section 1. Overview of the Respiratory Diseases Research Program

Introduction

Purpose and Organization of Document: The purpose of this document is to familiarize the reader with the National Institute for Occupational Safety and Health (NIOSH) Respiratory Diseases Research Program (RDRP) and its responses to recommendations arising from a recent program evaluation requested from the National Academies (NA). RDRP will seek scientific input on this document from NIOSH's Board of Scientific Counselors at its Spring 2009 meeting and stakeholder feedback through a public comment period.

The document has four main sections. The first section provides an overview of RDRP: what it is, how it operates, and its major strategic goals. The second section describes the program evaluation of RDRP conducted by the National Academies and provides comments and recommendations excerpted from the National Academies' report *Respiratory Diseases Research at NIOSH*, along with detailed responses from RDRP. The third section describes RDRP's highest priorities, which are based on the National Academies' recommendations and other inputs. The fourth section provides the reader with detailed information about the intermediate and activity/output goals that support each of RDRP's strategic goals, as well as lists of intramural projects and extramural grants currently underway in the various strategic goal areas.

Definition of RDRP: RDRP is the program within NIOSH that is most directly responsible for meeting the challenge of preventing and reducing work-related respiratory diseases. RDRP was created in 2005 as a formal organizational component of the NIOSH matrix management structure. It functions to coordinate NIOSH efforts to prevent occupational respiratory diseases and to encourage multidisciplinary cooperation and collaboration by all

elements of NIOSH in this ongoing effort. RDRP is organized according to adverse respiratory health outcomes, which occur in every industrial sector: airways diseases (e.g., asthma and chronic obstructive lung disease [COPD]); interstitial lung diseases (e.g., coal workers' pneumoconiosis [CWP], asbestosis, silicosis, berylliosis); respiratory infectious diseases (e.g., tuberculosis, avian and pandemic influenza, severe acute respiratory syndrome [SARS], anthrax); respiratory malignancies; and potential adverse health effects that may be associated with exposures to nanomaterials and nanoparticles.

Because of RDRP's role in facilitating communication and collaboration across the NIOSH intramural and extramural operations, throughout this document the term "RDRP" will broadly describe all individuals and groups supported by NIOSH to do work that is relevant to occupational respiratory diseases. This inclusive view of all NIOSH respiratory diseases research is the one most relevant to NIOSH's societal impact in this area. RDRP shares interests with, and overlaps, other program areas. Where such overlaps exist, they will be noted.

RDRP Mission Statement: The RDRP mission is to provide national and international leadership for the prevention of work-related respiratory diseases. RDRP uses a scientific approach to gather and synthesize information, create knowledge, provide recommendations, and deliver products and services to those who can effect prevention.

Operational Aspects of RDRP

RDRP Structure: RDRP is a matrix management structure that provides programmatic leadership for activities relevant to occupational respiratory diseases across all of NIOSH's structural, supervisory organizational units (Divisions, Laboratories, and Offices). Almost every Division within NIOSH conducts respiratory research and is therefore a component of RDRP.

RDRP is led by a Cross-Sector Steering Committee. Members of this committee are drawn from all of the NIOSH divisions and laboratories, as well as from the NIOSH Office of the Director. A key component of the steering committee is representation from the NIOSH Office of Extramural Programs, to assure communication and coordination between intramural and extramural efforts. The steering committee has been empowered to mold activities in respiratory diseases through its ability to review and rank letters of intent submitted to an annual intramural National Occupational Research Agenda (NORA) funding competition. The steering committee has also been empowered to review all in-house projects relevant to respiratory diseases on an annual basis and provide feedback to divisions about each project's relevance and level of priority. The steering committee also engages in strategic planning guided by the RDRP logic model described in the next section of this document. The steering committee is a powerful force to coordinate and promote respiratory diseases research in both the intramural and extramural settings.

RDRP Planning and Logic Model: To help guide planning, RDRP has developed a logic model describing how a range of inputs and external factors can be synthesized into activities and outputs, and transferred to create intermediate and, finally, end outcomes.

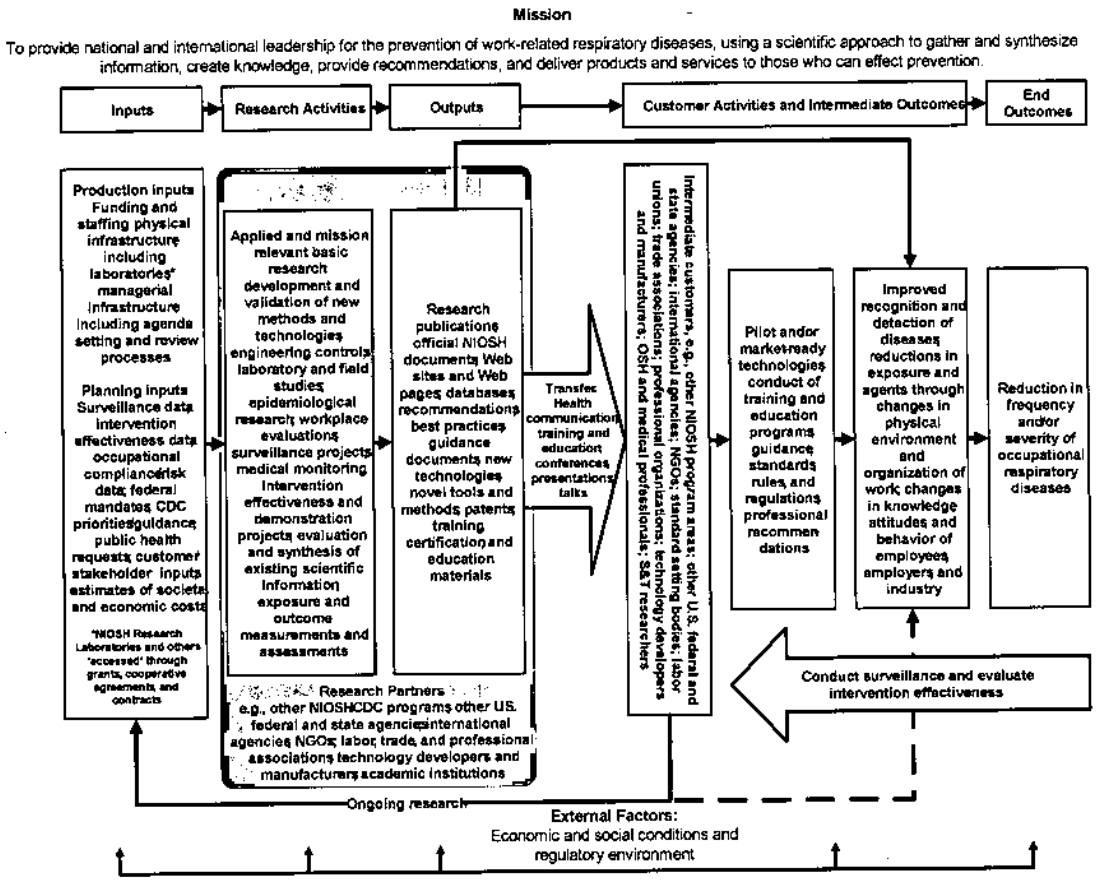

Figure 1. RDRP Logic Model

The operational logic model helps to assure that strategic planning activities are logical, appropriate, and optimize RDRP's relevance and impact (Figure 1). The logic model formally depicts the planning process. It moves from left to right across the chart, beginning with production and planning inputs. Those inputs lead to RDRP research activities. The outputs of RDRP research activities lead to customer activities. Some RDRP customers are intermediaries who use or adapt RDRP outputs before they reach the final customers: employers, employees, industries, educators, and regulators. Their actions help RDRP to contribute to the improvement of safety and health in the workplace. This process is affected by a variety of external factors including economic and social conditions and the regulatory environment.

At the far left of the logic model are planning inputs, which are data that guide RDRP to research action. Many sources, in addition to RDRP sources, provide input data. Data comes from workplaces, surveillance, risk assessments, intervention effectiveness studies, and from the Institute's stakeholders and customers. One of the major planning inputs for RDRP is ongoing occupational respiratory diseases surveillance conducted by RDRP. Major RDRP surveillance products can be accessed via the occupational respiratory diseases web home page at: http://www.cdc.gov/niosh/topics/surveillance/ords/. Two particularly important surveillance products include the Work-Related Lung Disease (WoRLD) Surveillance Report (http://www2a.cdc.gov/drds/WorldReportData/) and the National Occupational Respiratory Mortality System (NORMS; http://webappa.cdc.gov/ords/norms.html). Another important source of information about emerging occupational hazards is the NIOSH Health Hazard Evaluations Program (http://www.cdc.gov/niosh/hhe/).

An often-overlooked issue is that inputs do not only turn activities on. They also serve to turn off activities that have been completed, have become lesser priorities, or have otherwise outlived their usefulness.

Moving to the right of the logic model, activities encompass a broad range including many types of research; field investigations of work places; surveillance; policy development; training; and health communications.

Moving further to the right are outputs and transfer. The result of research is new knowledge. New knowledge serves society by providing practical guidance on matters of importance to the population. Research programs are obligated to contribute to the advancement of society by integrating this new knowledge into practice. RDRP carries out the responsibility to disseminate results of its research with a variety of outputs such as: reports, publications,

recommendations, workshops, databases, tools and methods, training and education materials, demonstration projects, best practices, developmental technologies, and licenses and patents. Testimony and criteria documents that recommend standards for controlling safety and health hazards in the workplace are uniquely important outputs for RDRP and NIOSH. These criteria documents represent the formal link between NIOSH and the Occupational Safety and Health Administration (OSHA) and Mine Safety and Health Administration (MSHA); and between research and rule-making.

Outcomes are found at the far right of the logic model. An outcome is a NIOSH contribution to reducing morbidity or mortality due to occupational injuries or diseases. These adverse health outcomes are "lagging indicators" that quantify a problem only after it has occurred. Especially for diseases of long latency, such as induction of cancer by carcinogens, "leading indicators" are useful surrogate outcomes. Leading indicators are measures that, if improved, suggest that lagging indicators such as long-term adverse health effects will subsequently be improved. Examples of leading indicator metrics include reduced causative exposures, increased use of control measures and appropriate work practices, establishment of improved standards and regulations, etc.

In many instances, it is difficult to effectively trace the contribution of NIOSH to particular outcomes. Many groups contribute to reducing occupational injuries and illnesses and to creating safer places to work. These groups are diverse and include employers and industry groups, workers and organized labor, public interest groups, academics and professional organizations, manufacturers of equipment for occupational safety and health, and other elements of local, state, and federal government, including regulatory agencies. The term

"intermediate outcome" refers to another type of surrogate outcome, evidence that RDRP influenced the actions of these groups, an important step toward real-world impact.

Overview of RDRP Strategic Goals

RDRP has five Strategic Goals. These goals are largely organized by disease and have a strong disease focus. However, it must be recognized that a broad spectrum of activities is needed to effectively address them. Thus, a multidisciplinary research program that includes surveillance; research in exposure assessment methods, respiratory health assessment methods, epidemiology, engineering controls, respiratory protection, underlying disease mechanisms, and toxicology; development of authoritative recommendations; health communications; and training and education is of critical importance in the prevention and reduction of work-related respiratory disease. RDRP Strategic Goals are as follows:

- Prevent and reduce work-related airways diseases
- Prevent and reduce work-related interstitial lung diseases
- Prevent and reduce work-related respiratory infectious diseases
- Prevent and reduce work-related respiratory malignancies
- Prevent respiratory and other diseases potentially resulting from occupational exposures to nanomaterials

Detailed descriptions of the intermediate and activity/output subgoals that support the strategic goals are found in Section 4. As will be apparent from Section 2, these are very consistent with recommendations made in the NA Report: *Respiratory Disease Research at NIOSH.* It should be noted that two of the strategic goal areas overlap extensively with other NIOSH cross-sector programs. The RDRP goal area related to respiratory malignancies overlaps with the NIOSH Cancer, Reproductive, and Cardiovascular Diseases (CRC) program. In the NA

report on NIOSH respiratory diseases research, it is noted that respiratory cancers are best approached within the context of a comprehensive cancer program. This is because a single type of carcinogenic exposure may cause many types of cancer. Also, many research and prevention approaches and issues are common to many types of cancer. Thus, it should be noted that the CRC program is the lead cross-sector program within NIOSH for issues related to cancer, including respiratory cancer. RDRP plays a secondary role in this area, supporting activities of special interest to RDRP. Similarly, the NIOSH nanotechnology research program, which was established after RDRP, is the lead program for issues related to nanotechnology. RDRP plays a secondary role. The NIOSH Board of Scientific Counselors (BSC) has recently conducted a separate review of the NIOSH nanotechnology research program.

Background and Significance of RDRP Strategic Goal Areas

Work-Related Respiratory Diseases: Work-related respiratory diseases are a problem of major magnitude. They cut across all industrial sectors and all elements of NIOSH, constituting approximately 60 percent of all disease and injury mortality and approximately 70 percent of all occupational disease mortality.

Airways Diseases: Airways diseases such as asthma and chronic obstructive pulmonary disease (COPD) are important occupational problems. In 2004, 11.4 million U.S. adults (aged 18 and over) were estimated to have COPD. For the 3-year period 2001-2003, an average annual 13.8 million adults had asthma. It has recently been suggested that about 24% of adult asthmatics experience exacerbation at work. A 2003 statement by the American Thoracic Society estimated that 15 percent of COPD and adult asthma were attributable to work, with a conservative annual estimated cost of nearly $7 billion in the U.S. alone.

Interstitial Lung Diseases: Even though the capability has existed for many years to prevent pneumoconioses such as silicosis, coal workers' pneumoconiosis (CWP), and asbestosis, pneumoconioses still cause or contribute to more than 2400 deaths per year in the U.S.A. and continue to be major causes of morbidity and mortality in developing countries. The threat of other interstitial lung diseases, such as chronic beryllium disease in beryllium processing or hypersensitivity pneumonitis in those exposed to metal working fluids, are also important concerns in specific industries.

Respiratory Infectious Diseases: Respiratory infectious diseases have become important occupational concerns. In the wake of the anthrax attacks of 2001, the potential for exposure to weaponized airborne microbiological agents has become a new reality for public service first responders and first receivers in healthcare facilities, as well as previously unanticipated at-risk groups such as postal workers. First responders and health care workers are also at risk for occupational exposure to naturally-occurring emerging infectious diseases. SARS-coronavirus (the causal agent of SARS), avian influenza, and pandemic influenza have all emerged as important concerns. New drug resistant strains of tuberculosis (TB), such as extensively drug-resistant-TB, have also emerged as important concerns. A particularly troubling aspect of these emerging respiratory pathogens is their often poorly defined potential for airborne transmission, an issue of obvious importance in designing prevention strategies.

Respiratory Malignancies: Respiratory malignancies can also result from occupational exposures. In 1996, it was estimated that approximately 9,000-10,000 men and approximately 900-1,900 women developed lung cancer annually in the U.S. due to past exposure to occupational carcinogens. More than half of these lung cancers were attributed to asbestos. Mesothelioma, a malignancy involving the layer of cells lining the lungs, heart and abdominal

cavity and caused by inhalation of asbestos fibers, was responsible for more than 2650 deaths in 2004.

Emerging Issues, Including Nanotechnology: New occupational respiratory diseases continue to emerge. Examples investigated by NIOSH in the last decade include severe obstructive lung disease due to constrictive bronchiolitis in those exposed to artificial butter flavorings, interstitial lung disease caused by respirable particles of nylon flock, and acute respiratory distress syndrome caused by leather conditioning spray. It is critically important for RDRP to maintain its ability to anticipate and respond rapidly to emerging problems. In this regard, the growth of nanotechnology and associated exposure to engineered nanoparticles is a particularly important emerging issue where anticipation may lead to prevention. Although occupational diseases have yet to be attributed to engineered nanoparticles, use of manufactured nanomaterials is projected to grow at an impressive pace with associated economic impacts. Laboratory-based RDRP studies already suggest that engineered nanoparticulate exposures represent potentially preventable occupational health hazards. Fiber-like elongated carbon nanotubes are a specific engineered nanomaterial of concern. Another potential emerging source of nanoparticle exposure is generation of combustion-related nanoparticles by newer, fuel efficient diesel engines.

Section 2. Program Evaluation of RDRP by the NA: Recommendations and Responses

RDRP Evaluation Process and Rating Scores

Expert peer review is one of the most valid and accepted methods of evaluating research programs. In 2005, NIOSH engaged the Institute of Medicine (IOM) and the Division of Earth and Life Studies (DELS) of the NA to conduct a series of evaluations of NIOSH research programs. Since then, 8 programs have been evaluated: Mining; Hearing Loss; Respiratory Diseases; Agriculture, Forestry and Fishing; Construction; Personal Protective Equipment; Health Hazard Evaluations; and Traumatic Injury.

Initially, the NA established a framework committee of 15 members to set the ground-rules for more specialized evaluation committees (EC) to evaluate the specific NIOSH programs. EC assessed the *relevance* of program activities to the improvement of occupational safety and health; and the *impact* of program research in reducing work-related hazardous exposures, illnesses, and injuries. Impact was assessed directly (e.g., reductions in illnesses or injuries) or, as necessary, by using intermediate outcomes to estimate impact. Relevance and impact were scored quantitatively, using integer scores from 1 (lowest) to 5 (best). EC also assessed program effectiveness in targeting new research areas and identifying emerging issues in occupational safety and health most relevant to future improvements in workplace protection. This area was not scored quantitatively; instead, EC provided a qualitative narrative assessment of program efforts and made suggestions about emerging issues that the program should be prepared to address.

The NA-RDRP evaluation committee consisted of the following members: Mark Utell (Chair), University of Rochester, New York, NY; John Balmes, University of California, San Francisco, CA; Paul Blanc, University of California, San Francisco, CA; Elisabeth Chamberlin,

Massey Coal Services, Charleston, WV; Rogene Henderson, Lovelace Respiratory Research Institute, Albuquerque, NM; David Manninno, University of Kentucky, Lexington, KY; James Merchant, University of Iowa, Iowa City, IA; Jacqueline Nowell, United Food and Commercial Workers International, Washington, DC; Charles Poole, University of North Carolina, Chapel Hill, NC; Richard Schlesinger, Pace University, New York, NY; Noah Seixas, University of Washington, Seattle, WA; Ira Trager, University of California, Berkeley, CA; David Wegman, University of Massachusetts, Lowell, MA.

For the review, RDRP scientists developed a detailed evidence package (EP) documenting RDRP operations and achievements over the decade following the beginnings of NORA in 1996, and RDRP plans for the future. The EP was submitted to the NA-RDRP committee on October 10, 2006. It remains available online at: http://www.cdc.gov/niosh/nas/RDRP/default.htm.

Subsequently, three reverse site visits were conducted. The first was on October 25, 2006. During this site visit, RDRP scientists presented an overview of RDRP and its activities relative to coal mine dust, silica, diacetyl and butter flavorings, work-related asthma, nanotechnology, and occupational respiratory disease surveillance. The second reverse site visit was on December 5, 2006. At the committee's request, Dr. David Weissman, the RDRP manager, made an additional presentation on respiratory infectious diseases. The final reverse site visit was held at the IOM on March 22, 2007 where, over a period of several hours, Dr. Weissman answered committee members' questions, many of which related to organizational and administrative aspects of RDRP.

In addition to the reverse site visits, the NA-RDRP committee also gathered information through written questions and requests for supplemental information; and through site visits by a

sub-group of the committee to Morgantown (January 16, 2007), Pittsburgh (January 17, 2007) and Cincinnati (January 18, 2007).

A draft version of the NA-RDRP report was provided to NIOSH in February, 2008. A debriefing was presented by the committee chairman, Dr. Mark Utell, at the NIOSH facility in Morgantown, WV on March 4, 2008. RDRP received a score of 5 for relevance and 4 for impact. The 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 final report is available online at: http://www.nap.edu/catalog.php?record_id=12171.

Overview of NA Recommendations and RDRP Responses

The NA report makes a range of recommendations to help RDRP maintain the relevance and impact of its research portfolio and achieve its goal of protecting workers from respiratory diseases. The NA-RDRP evaluation committee organized their recommendations according to the specific goals identified in the RDRP evidence package. Therefore, comments and recommendations excerpted from the report (identified by italics), and RDRP responses, are similarly organized. For each strategic area, NA-RDRP committee recommendations and responses are listed – first, general, overarching recommendations and then the more specific recommendations for the strategic goal area, as drawn from the evaluation committee's report. Note that the "subgoals" listed in this section reflect organization of the RDRP evidence package and have been superseded by the current intermediate and activity/output goals presented in Section 4.

Strategic Goal 1: Prevent and Reduce Work-Related Airways Diseases

NA-RDRP General Recommendations: Airways Diseases

Recommendation: *Improve detection of work related asthma, work-related fixed obstructive airway disease, and relevant exposures.*

RDRP Response: Preventing work-related airways diseases, including asthma and COPD, is one of RDRP's highest long-term priorities. Preventing flavoring-related lung disease, now documented in a number of cases to be associated with a pathological pattern of constrictive bronchiolitis, is also a high RDRP priority. These high priority areas are discussed in some detail in Section 3.

"Detection" of these conditions may refer either to detection at the population level, as in surveillance; or detection at the individual level, as in medical monitoring. Health and hazard surveillance are high RDRP priorities and presented in detail in Section 3. The surveillance role of the Health Hazard Evaluations Program in identifying emerging issues is also addressed in that section. From the standpoint of medical monitoring of individuals, several RDRP activities are relevant. In the case of asthma, several studies seek to improve secondary prevention through early recognition of specific immune sensitization to occupational asthmagens. In the case of fixed obstructive airway disease, an important area of RDRP research is development of guidelines and software tools for using spirometry to identify workers with accelerated loss of lung function. These workers may still have normal lung function, but still be at risk for future development of obstructive lung diseases such as COPD or flavorings-related lung disease. Early identification could facilitate secondary prevention efforts for affected workers.

Recommendation: *The RDRP should systematically evaluate whether its work-related asthma programs are being compromised under NIOSH's new priority-setting approach.*

RDRP Response: This recommendation is based on the concern that there is potential for respiratory disease to be under-recognized under an industrial sector-based approach to priority setting. For example, although approximately 13.8 million adults in the U.S. have asthma, and epidemiology suggests that about 15% of adult asthma is attributable to work, this work-association often goes unrecognized and/or is attributed to other causes. Other respiratory diseases, such as COPD, develop slowly and the effects of occupation may not be apparent for many years, often after the worker has retired. In these situations, putting emphasis on health and safety issues that occur immediately or with short latency and are obviously related to a particular industrial sector has the potential to result in under-emphasis of problems that are less apparent, even when they cause substantial morbidity and mortality.

For these reasons, RDRP is strongly committed to setting its priorities both to meet the needs of particular industry sectors and the needs of our society as a whole. A key requirement for setting these priorities is good data. As is described in Section 3, occupational respiratory disease surveillance that identifies associations between respiratory disease, occupation, and industry even when they are not obvious is an important priority of RDRP. This is, and will remain, an important area of investment. RDRP will also continue to participate in surveillance programs that identify respiratory problems in specific occupations and industries. A recent example was the identification in State-based surveillance of isocyanate-induced asthma in workers applying spray-on truck bed liners. Another example was recognition by the Health Hazard Evaluation Program of asthma in chloramine-exposed poultry workers.

RDRP maintains a wide range of multidisciplinary asthma research efforts in the intramural and extramural settings. Basic toxicological research evaluates issues such as sensitizing potential of chemical agents, mechanisms of airways toxicity, and human genetic

susceptibility. Epidemiological studies estimate incidence and prevalence and evaluate a range of risk factors, severity, and prognosis. Other studies seek to improve exposure assessment and engineering controls. An effort is underway to develop a revised recommended exposure limit (REL) for the asthmagen glutaraldehyde. All told, RDRP studies address a range of contemporary asthmagens of interest, including the glutaraldehyde substitute, orthophthaldehyde (OPA); aerosols generated in dental procedures; manicure products; isocyanates; cleaning materials; biodiesel; indoor air issues such as damp indoor environments, mold and other indoor air contaminants; and post-Katrina exposures.

RDRP also maintains active programs addressing other work-related airways diseases. RDRP played an important role in the recognition that COPD is an important adverse health outcome of occupational respiratory exposures. COPD remains an important focus of multidisciplinary study in both the intramural and extramural settings. Population-based and occupational-setting-focused epidemiological studies are evaluating risks for development of lung function abnormalities and COPD. Other studies are investigating mechanisms of airways toxicity. As previously noted, an important area of research is development of guidelines and software tools for early identification of workers with accelerated loss of lung function. These workers may still have normal lung function, but still be at risk for future development of COPD.

RDRP also played a key role in the recognition that worker exposures to the butter flavoring diacetyl were causing severe obstructive airways disease, documented by lung biopsy in a number of workers to be the result of constrictive bronchiolitis. RDRP continues to support multidisciplinary research to understand and prevent flavorings-induced lung disease. Current studies address the toxicology of diacetyl and other butter flavorings; approaches to exposure assessment; methods and guidance for engineering controls; documentation of respirator

performance for diacetyl; risk assessment in an effort to identify protective quantitative limits of exposure; and information dissemination to raise awareness of the condition. RDRP will continue to work closely with OSHA in an effort to support its efforts in this area.

Thus, RDRP continues to support a broad range of projects relevant not only to work-related asthma, but also to a number of other work-related airways diseases. Given the importance of these diseases, this is not expected to diminish. RDRP will continue a balanced approach to priority-setting that maintains relevance and impact by integrating a broad range of inputs, including sector-based inputs, health outcome-based inputs, inputs from the full range of stakeholders including labor, management, and other interested parties, and inputs from the full range of relevant disciplines.

Recommendation: *Because workplace exposures contribute highly to the likelihood of developing asthma, work in preventing and detecting asthma has the potential to greatly improve occupational safety and health among the U.S. workforce.*

RDRP Response: For reasons noted in the responses immediately above, and subsequently in Section 3, RDRP agrees.

Recommendation: *In addition, RDRP should continue to support population-based studies of associations between occupational exposures and chronic obstructive airway disease.*

RDRP Response: For reasons noted in the responses immediately above, and subsequently in Section 3, RDRP agrees. COPD is a major cause of morbidity and mortality in the U.S., and RDRP studies of this nature have contributed to increasing recognition of occupation and industry as risk factors.

NA-RDRP Detailed Recommendations: Airways Diseases

Subgoal: Preventing and reducing natural rubber latex asthma and allergy among healthcare workers.

Recommendation: *The RDRP's efforts to prevent latex allergy and asthma have been highly successful. RDRP investigators have documented that the prevalence of latex sensitization fell as a result of the intervention effort that began with the 1996 NIOSH Alert. The EC recommends that the RDRP assess how its successful work on latex and asthma can be extended to other high-molecular-weight sensitizers that cause occupational asthma and occupational rhinitis.*

RDRP Response: RDRP appreciates this comment. Extinguishing the epidemic of natural rubber latex-induced asthma that peaked in the late 1990s and was largely due to use of powdered natural rubber latex gloves was a great accomplishment to which many contributed, including RDRP. Although this was by no means easily accomplished, several features of the epidemic facilitated the response. Substitution of less hazardous medical devices, in particular non-powdered natural rubber latex gloves and non-latex gloves, was feasible. Because latex gloves were only really needed by those performing tasks such as medical procedures which required excellent tactile properties and preservation of dexterity, administrative controls were feasible. The occupational group affected by natural rubber latex allergy was healthcare workers, who rapidly became aware of the problem and, as a group, were accepting of solutions. Overall, the lesson of this episode is that occupational asthma due to a high molecular weight allergen such as natural rubber latex can be prevented.

A major focus of current RDRP research related to high molecular weight allergens is work to identify mold allergens, which are important concerns in indoor environments. Identifying, characterizing, and cloning these allergens will lead to the development of tools for

better diagnosis of mold allergy and objective assessment of mold allergen exposure. In addition, epidemiological studies are evaluating the respiratory impact of exposure to damp indoor environments, including risks associated with exposure to microbial constituents of the complex exposures in these environments. Studies are also evaluating the impact of correcting indoor water and dampness problems.

In addition, asthma induced by high molecular weight agents continues to be addressed via the Health Hazards Evaluation Program. For example, a current Health Hazard Evaluation addresses asthma at a soy packaging and distribution operation. It is supported by a parallel laboratory study identifying specific soy allergens in affected workers.

Subgoal: Preventing and reducing WRA in the isocyanate production industry.

Recommendation: *Previous RDRP work on diisocyanates directly addressed the most common low-molecular-weight sensitizing cause of asthma in the developed world and led to important knowledge that has been transferred to prevent disease. The EC recommends that the RDRP assess how its research on diisocyanates and asthma can be extended to other low-molecular-weight sensitizers that cause occupational asthma, especially in terms of mechanisms of disease.*

RDRP Response: RDRP appreciates this comment and agrees that many areas of its diisocyanate (dNCO) research may provide insight into the general knowledge leading to prevention of LMW asthmas; however, one should be cautious in extrapolating dNCO disease mechanisms to other LMW sensitizers. For example, dNCO-specific IgE can only be detected in approximately 20% of the dNCO asthmatics. This is in stark contrast to another group of significant occupational asthmagens that have been studied by RDRP, the organic acid anhydrides, where the association of IgE to disease is much stronger.

Despite the fact that most dNCO asthmatics do not exhibit IgE-sensitization, dNCO immunological animal studies conducted by RDRP have identified that the disease mechanism(s) are predominantly skewed toward a TH2 type mechanism with up-regulation of typical TH2 cytokines and chemokines. It is unclear to what degree the various LMW asthmas are IgE-independent but still represent a TH2-like asthma mechanism.

One issue potentially of concern for dNCO and other LMW sensitizers is the role of immunological sensitization via non-pulmonary routes of exposure. RDRP research has demonstrated that both dermal and nasal exposures can be potent routes for immunological LMW agent sensitization and subsequent asthmatic-like responses and rhinitis upon specific challenge. An active, continuing program takes advantage of sensitization via the skin to perform "local lymph node assays" to screen chemicals for sensitizing potential and identify LMW agents with the potential to cause asthma.

New approaches developed to address the chemistry of dNCO binding to carrier proteins may have applicability to other LMW agents. New monoclonal antibodies have recently been developed to identify and isolate dNCO-bound biomolecules. It is planned to use these agents, along with protein chemistry and mass-spectrometry based proteomic approaches to identify mammalian proteins susceptible to electrophilic attack/haptenation and possibly sites of haptenation within the proteins leading to immunological sensitization. Overall methods to be applied in this project are applicable for study of other LMW agents, and the proteins more susceptible to dNCO conjugation may be important targets to many LMW sensitizers.

Occupational asthma is one of the potential adverse effects of exposure to glutaraldehyde, an agent commonly used as a disinfectant in healthcare. NIOSH recommendations for exposure to glutaraldehyde are being reassessed in an ongoing project. One substitute for glutaraldehyde

is the LMW agent OPA, which represents a new emerging potential exposure in the healthcare setting. OPA like dNCO can readily react with functional groups on proteins (thiols and amines) to form potential neoantigens. Several RDRP studies are in progress addressing the degree to which this agent might also have the potential to also cause sensitization and asthma. In addition to this work, RDRP is also developing an epidemiological study to characterize exposures of healthcare workers to a range of potential LMW agents such as cleaners and disinfectants and to assess associations between these exposures, asthma onset, and asthma exacerbation.

Subgoal: Preventing and reducing WRA related to nonindustrial indoor environmental quality.

Recommendation: *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).*

RDRP Response: The general sense that indoor environmental quality work is not always related to work-related asthma is well taken. However, respiratory diseases are a prominent adverse outcome of indoor environmental quality problems. Building-related respiratory diseases include asthma, rhinosinusitis, building-influenced communicable respiratory infections, hypersensitivity pneumonitis, and nonspecific respiratory symptoms. In 1996, indoor environmental quality was identified by stakeholders as one of the original 21 occupational safety and health priorities for the first decade of NORA. An analysis published by the NORA Indoor Environment Team estimated that improving building environments could result in health benefits for more than 15 million of the 89 million U.S. indoor workers, with

economic benefits of $5 billion to $75 billion annually. A substantial proportion of these estimated benefits were respiratory (Mendell MJ et al. Am J Public Health 2002; 92:1430-1440). By far, the greatest proportion of asthma-related Health Hazard Evaluation requests reaching NIOSH come from nonindustrial building environments and are related to indoor air quality complaints. In fact, indoor environmental quality-related requests continue to be the largest source of Health Hazard Evaluations. Thus, research and service relevant to indoor environmental quality is an important and appropriate priority, whether it is pursued within RDRP or other elements of NIOSH.

RDRP work has focused on adverse respiratory outcomes of indoor environmental quality issues and made important contributions by expanding upon the conclusions of the Institute of Medicine in 2005 that damp indoor environments are associated with chest symptoms and exacerbation of preexisting asthma. RDRP has documented that some buildings are associated with new onset asthma and that biomass markers in dust are associated with building-related respiratory symptoms. In fiscal year 2000, RDRP initiated a Health Hazard Evaluation at a state government office building in Connecticut with significant dampness problems. Subsequently, a multi-year study was conducted in the building. The employees in this office building had a 7.5-fold increase in incidence of asthma after building occupancy compared to the incidence in adult years prior to building occupancy. Building-related lower respiratory symptoms were associated with biomass markers in dust including hydrophilic fungi and endotoxin. This study is now in its final stages, and should be concluded by 2010. An intervention study in three school locations in New England is currently in progress; this study should also conclude by 2010. Other studies are evaluating indoor air chemistry and the potential for consumer products used indoors such as cleaners to generate irritating, potentially

asthmagenic reaction products. Together, these studies will play an important role by informing public health prevention efforts relative to indoor environmental quality.

Subgoal: Improving detection of WRA and relevant exposures.

Recommendation: *The RDRP effort to improve the detection of WRA is of the highest relevance. While the quality of transfer activities to increase the awareness of WRA has been high, the EC recommends that greater attention be paid to irritant-induced asthma given its relative importance as demonstrated by Sentinel Event Notification Systems for Occupational Risks (SENSOR) data. Irritant-induced asthma warrants specific RDRP planning and goal setting that would build on accomplishments already made in this area. In addition, because of the key role of SENSOR data in surveillance for WRA, the RDRP should consider aggressively expanding this program beyond the collaborations that currently exist with four states as well as including "active" elements of surveillance.*

RDRP Response: RDRP appreciates this recommendation. State-based surveillance data clearly documents the importance of exposures to irritants such as cleaners and disinfectants in WRA. In response to this surveillance information, RDRP is involved or developing studies in several settings where exposures to irritants are an important issue. Two major efforts have already been described evaluating asthma in nonindustrial indoor environments (where there is exposure to cleaners, reaction products of indoor air chemistry, endotoxin and other biomass agents, etc) and in healthcare environments (cleaners, disinfectants, etc). Reviewing the intramural projects and extramural grants listed in Section 4, the reviewer will note many other examples, as well, such as wood smoke, diesel exhaust, welding fumes, and microbial agents.

RDRP also strongly agrees with the importance of surveillance for occupational respiratory diseases. Surveillance is identified as an important immediate priority for RDRP in

Section 3 and surveillance for occupational respiratory diseases in general was discussed earlier in this document. As was noted in the RDRP evidence package provided to the NA, only four states – California, Massachusetts, Michigan, and New Jersey – have been funded through NIOSH for occupational asthma surveillance as an enhancement to general occupational safety and health surveillance. Although partnership with and between these states has been highly successful in identifying major and emerging causes of work-related asthma, if funding permitted it would obviously be beneficial to engage more states in occupational asthma surveillance. For this reason, RDRP investigators are also working to build upon past collaborations with NCEH, a fellow component of CDC. Currently, CDC-NCEH funds 33 states, Puerto Rico and the District of Columbia to conduct comprehensive asthma control programs which include surveillance, partnerships and intervention implementation. Collaborations under discussion would increase activities relative to WRA in adults.

RDRP is also engaging in national surveillance for WRA. With financial support from RDRP in fiscal year 2006, the Behavioral Risk Factor Surveillance System (BRFSS) NCEH/Agency for Toxic Substances and Disease Registry (ATSDR) Asthma Call-back Survey included a 9-question WRA module. Results will be made available to the public, and also analyzed by RDRP researchers. RDRP is also funding the inclusion of work-related asthma questions within an occupational supplement to the National Health Interview Survey (http://www.cdc.gov/niosh/nora/symp08/posters/026.html). This will allow assessment of current asthma prevalence by occupation and industry. Finally, through the Health Hazard Evaluations Program, RDRP continues to investigate workplace settings where workers have complaints of asthma.

Subgoal: Establish the work-relatedness of COPD.

Recommendation: *The previous research of RDRP investigators on the risk of COPD due to exposure to coal dust has been cited by a number of investigators and policy makers in their assessment of the links between dust exposure and COPD, not only for this specific industry but also as a measure of biologic plausibility for COPD related to other exposures. RDRP studies using data from the National Health and Nutrition Examination Survey (NHANES) have contributed to a greater recognition of the role of occupational factors in the U.S. population burden of COPD. The EC strongly recommends that RDRP support for population-based studies of associations between occupational exposures and COPD continue in order to better define groups of workers at greatest risk and to assist in planning preventive strategies. RDRP efforts to retain spirometry and occupational exposure questions as components of NHANES are critical to better understanding of both the epidemiology of COPD in general and the occupational contribution to the population burden of this disease.*

RDRP Response: RDRP continues to actively pursue population-based studies examining the work-relatedness of COPD. For example, RDRP investigators are supporting the current round of NHANES, allowing it to better address COPD. In this effort, all adults participating in NHANES from 2007 to 2010 are being enrolled in a study of respiratory symptoms, occupational history, and spirometry. Exhaled nitric oxide is also being measured. RDRP designed the occupational questionnaire and is providing technical support for spirometry. The NIOSH Surveillance Program is going to provide occupation and industry coding as NCHS no longer has that capacity. These efforts will allow the study to provide updated population-based information about the prevalence of objectively-documented COPD and its relation to industry and occupation. RDRP investigators are also evaluating data from another large population-based study, the Multi-Ethnic Study of Atherosclerosis. This longitudinal study has

as its primary goal to study the characteristics of subclinical cardiovascular disease and the risk factors that predict progression to clinical cardiovascular disease. It involves more than 6,000 men and women from six US communities and is sponsored by the National Heart Lung and Blood Institute of the National Institutes of Health. RDRP investigators are collaborating with the study, which has evaluated subjects once with spirometry, to examine relationships between COPD, occupation and industry. Evaluating and tracking relationships between COPD, occupation, and industry is an important goal of enhanced occupational respiratory disease surveillance, which was discussed earlier in this document.

Subgoal: Develop tools and identify at-risk workers in industries and occupations to assess the extent, severity, and burden of work-related COPD.

Recommendation: *RDRP work on spirometry, especially the development of new reference equations for normative values, has had a major impact on respiratory disease research in general and, more specifically, on preventing COPD. The EC encourages the RDRP to continue its valuable work on the use of spirometry for longitudinal surveillance of populations known to be at risk for fixed obstructive airway diseases. The EC also recommends that RDRP surveillance activities for work-related COPD and fixed obstructive airways among the general population be established (e.g., there is no SENSOR activity for these conditions). Finally, the EC thought that methods development in the analysis of longitudinal studies of pulmonary function warrants more intense investigations.*

RDRP Response: RDRP thanks the NA-EC for this comment. RDRP contributions relative to the practice of spirometry had major impact not only on prevention of occupational respiratory disease, but also on diagnosis and treatment of nonoccupational respiratory diseases. RDRP efforts to improve the practice of spirometry have recently focused on approaches to

assessment of longitudinal spirometry. As adults age, it is normal for parameters measured by spirometry, such as forced expiratory volume in 1 second (FEV1) to decline. However, longitudinal spirometry may offer the opportunity to identify those with abnormally rapid decline, who may be at risk for the development of COPD or other pathologic conditions. RDRP research has identified some of the complexities in defining what constitutes abnormal decline. This threshold can vary depending on factors such as overall quality of a spirometry surveillance program and duration of follow up. RDRP has developed a software program called Spirometry Longitudinal Data Analysis (SPIROLA) that simplifies consideration of these issues and assists in longitudinal monitoring of spirometry. It can be freely downloaded from the NIOSH web site. Ongoing research in several cohorts seeks to further validate and refine approaches to performing and interpreting longitudinal spirometry for early, sub-clinical detection of pulmonary diseases, including COPD. These include a Danish cohort being studied primarily for heart disease; post-Katrina workers studied through in collaboration with Tulane University; and employers in a range of industries including construction, paper/pulp production, chemical production, beryllium production, and firefighting.

RDRP also remains strongly committed to its mandated role of certifying spirometry training courses. RDRP will continue to develop and update training materials, and evaluate new training programs for certification and existing programs at intervals for recertification. Needs for assessment of occupationally-related COPD in the general population and COPD surveillance are re-emphasized in this recommendation. RDRP agrees with the need to track the association of COPD with specific industries and occupations. Because of the long latency between exposure and COPD development, and because non-occupational COPD is common, occupational COPD surveillance will require monitoring of the general population with

statistical evaluation for associations between COPD and industry/occupation. As is described in Section 3, improved occupational respiratory diseases surveillance using innovative data sources such as electronic health records is an immediate, high priority for RDRP.

Subgoal: Develop, test, and disseminate recommendations for preventing COPD in the workplace.

Recommendation: *The RDRP should continue its efforts to support this important subgoal.*

RDRP Response: RDRP will continue its efforts in this area. Demonstration of the utility of SPIROLA and longitudinal assessment of lung function for early identification of COPD risk in cohorts such as coal miners, chemical workers, construction workers and fire fighters will continue. RDRP will evaluate the utility of spirometry being offered to coal miners participating in its Enhanced Coal Workers' Surveillance Program, which is discussed in more detail under the RDRP strategic goal for interstitial lung diseases. RDRP will continue its efforts to reduce exposures to silica and coal mine dust, also described in more detail under the strategic goal for interstitial lung diseases. Finally, RDRP will continue its efforts to enhance the recognition of occupation as a risk factor for COPD.

Subgoal: Prevent and reduce flavoring-related bronchiolitis obliterans.

Recommendation: *The RDRP response to the initial outbreak of diacetyl-induced bronchiolitis obliterans has led to surveillance efforts in multiple locations in an effort to detect and prevent disease. The committee agrees that preventing this disease, both in and of itself and as a model novel disease process, should be a high priority for the RDRP. Because RDRP inhalational toxicologic studies of agents newly recognized to cause airway diseases (e.g., diacetyl) have provided crucial information about mechanisms of disease, the EC strongly*

recommends that the capacity to conduct such studies be preserved. In addition, because work of the health hazard evaluation (HHE) and technical assistance program was key to identifying both diacetyl and nylon flock as agents that can cause respiratory disease, the RDRP should explore ways to systematically mine data from HHEs that share a common exposure and outcome focus.

RDRP Response: As previously noted, work in the area of flavorings-related lung disease is a very high immediate priority of the RDRP research program. Although this has been described previously, it bears repeating that RDRP will continue to bring multiple disciplines to bear in addressing a range of relevant issues, including basic toxicology, exposure assessment, engineering controls, personal protective equipment, medical monitoring and surveillance, and education/information dissemination. Using both the Health Hazard Evaluations Program and designed research studies, RDRP will continue to evaluate workplaces for flavorings exposures, measures to reduce flavorings exposures, and occurrence of flavorings-related lung disease. Finally, RDRP will support regulatory agencies such as the OSHA in their efforts to address this important problem.

RDRP agrees that the Health Hazard Evaluations Program is an important mechanism for recognizing emerging issues and that organized approaches to mining this data can improve this function. Computer searches of Health Hazard Evaluations can be performed by exposure and health complaint. This tracking system dates back to 1972 and will continue to be reviewed and updated, allowing those performing Health Hazard Evaluations to rapidly recognize if a sentinel focus of occupationally-related disease is an isolated event or is evidence of a recurring pattern. Data mining of health hazard evaluations can also serve another purpose. These evaluations are sometimes unique sources of human data that quantitatively relate occupational exposures and

health effects. In such cases, organized data retrieval can yield quantitative information useful for activities such as risk assessment.

Strategic Goal 2: Prevent and Reduce Work-Related Interstitial Lung Diseases

NA-RDRP General Recommendations: Interstitial Lung Diseases

Recommendation: *Continue and expand efforts to prevent coal workers' pneumoconiosis, silicosis, fiber-induced interstitial lung disease, chronic beryllium disease.*

Recommendation: *The activities related to interstitial lung diseases form a critical core of the RDRP and have provided well-documented improvements in occupational health. It is important that the RDRP continue to expand its activities in these areas so it can build on its earlier successes and respond to new challenges.*

RDRP Response: RDRP appreciates these comments and agrees that interstitial lung diseases remain an important occupational respiratory disease problem and remain an important priority. Details of current intramural projects, extramural grants, and strategic, intermediate, and activity/output goals for the area can be found in Section 4. Detailed responses to NA-RDRP recommendations in the specific areas are found below.

NA-RDRP Detailed Recommendations: Interstitial Lung Diseases

Subgoal: Coal workers' pneumoconiosis.

Recommendation: *NIOSH programs that were established in the 1970s, now under the purview of the RDRP, led to a marked reduction in miners' exposure to respirable coal dust and a decreased annual prevalence of pneumoconiosis through 1999. Despite progress in reducing CWP, surveillance reports have identified hot spots of rapidly progressive CWP in a geographic area that includes eastern Kentucky and southern West Virginia and, more alarmingly, an upward trend in disease prevalence in national data that may be accelerating. On the basis of these new surveillance data, 1) the EC recommends that the RDRP reexamine the organization and efficacy of the CWP surveillance effort, including the interaction between NIOSH and*

MSHA, with additional focus on the adequacy of exposure assessment and compliance determination. 2) The EC also recommends that the RDRP continue to conduct research to further support MSHA's adoption of the NIOSH recommended exposure limit of 1.0 mg/m^3 as the actual permissible exposure limit for coal mine dust. 3) The EC also recommends research on the possible role of coal rank and silica level in the rapidly progressive cases of CWP as well as other putative risk factors highlighted in NIOSH's hot spot research. 4) Finally, assessment of the strengths and limitations of digital radiography in pneumoconioses in general and its effectiveness in silicosis surveillance specifically should be an important continuing research priority.

RDRP Response: The four recommendations for CWP research will be addressed separately: 1) reexamination of the organization and efficacy of CWP surveillance, 2) continue to conduct research in support of MSHA rule making, 3) evaluate role of coal rank and silica exposure in mines, 4) evaluate digital x-ray technology for diagnosis of the pneumoconioses.

Reexamination of organization and efficacy of CWP surveillance: This recommendation refers to a federally-mandated screening program for CWP in active underground coal miners operated by RDRP. Regulations governing the CWHSP are found in the federal code of regulations at 42CFR37. Under these regulations, coal miners are entitled to a chest radiograph obtained at mine operator expense at entry into coal mining and at approximately 5 year intervals thereafter. Chest radiographs are generally obtained at local healthcare facilities approved to participate in the program. The radiographs undergo an initial evaluation locally to assure that no problems requiring immediate attention (such as lung cancer) are present. They are then sent to NIOSH to be "classified" for presence and severity of changes potentially associated with pneumoconiosis. Miners are notified of the results. If pneumoconiosis is present, miners are

entitled under MSHA regulations to move to lower-dust jobs, if available, and to undergo increased monitoring for exposure to coal mine dust. Chest radiograph data is also analyzed in aggregate by RDRP and used for CWP surveillance.

Several years ago, RDRP embarked upon a program to validate findings of the CWHSP and improve its performance. This "Enhanced CWHSP Program" (ECWHSP) obtains chest radiographs by sending a mobile examination unit to locations convenient to miners. It provided services to 1226 miners in fiscal year 2006, 1740 in fiscal year 2007, and 2143 in fiscal year 2008. Spirometry was also performed, allowing assessment for obstructive lung disease, a known adverse health outcome of coal mine dust exposure that usually cannot be diagnosed by chest radiograph. All tests are conducted at NIOSH's expense.

Initial efforts of the enhanced program have been focused on confirming findings of the CWHSP that there were "hot spots," or geographical areas of the country where risk was greatest for rapidly progressive CWP. The Appalachian area, including western Virginia, southern West Virginia, and eastern Kentucky was especially affected. The ECWHSP mobile examination unit was deployed to these areas, many of which had low participation rates in the conventional program. ECWHSP confirmed the continued occurrence of CWP, including an advanced form called progressive massive fibrosis (PMF) in miners as young as their 30s. These findings have been documented in two Morbidity and Mortality Weekly Reports (MMWR) and have validated the efficacy of the CWHSP in identifying regions affected by CWP. The enhanced program has also facilitated partnership with MSHA, which has played an important role in helping to promote the program to mine operators and miners; and to facilitate operations. Results of surveillance have been reported to MSHA, and the hot spots evaluations have provided MSHA with the foundation needed to further advance its efforts relative to coal mine dust.

We continue to work to improve the CWHSP. Enhanced operations will continue, especially in hot spot areas. Conversion of CWHSP and ECWHSP to digital radiography is described as an immediate high priority of RDRP in Section 3. This modernization effort will have important benefits for program operations, which will be modified as needed to accommodate the newer technology.

The NA-RDRP committee also recommended improvements in exposure assessment for coal mine dust. A major effort of the NIOSH Mining Program, which overlaps with RDRP and shares a strong interest in this area, is deployment of "personal dust monitors" (PDM) that can be used for real-time, continuous monitoring of coal mine dust exposure. NIOSH research played a key role in developing, validating, field testing, and transferring this technology to the private sector. These achievements, in turn, have allowed MSHA to move towards incorporating use of PDM into its regulations on monitoring coal mine dust exposures, with MSHA announcing a proposed rule for coal mine personal dust monitors in the Federal Register on January 16, 2009. Efforts will continue to facilitate dissemination of PDM into coal mines. This major advance will potentially improve the accuracy of exposure assessment and allow miners in real time to identify inhalation hazards and immediately take steps to correct them.

Conduct research to support MSHA adoption of 1.0 mg /m^3 permissible exposure limit: The efforts to introduce PDM described immediately above will hopefully improve upon current, intermittent sampling by mine operators and MSHA by providing real-time, continuous and hopefully more frequent sampling. This, in turn, will provide better exposure data for epidemiological studies examining coal mine dust exposure – disease response relationships.

Evaluate role of coal rank and silica exposure in mines: The NIOSH Mining Program and RDRP are collaborating on an ongoing project entitled, "Dust Control Technology for Black

Lung Hotspots." This project examines the types and applications of dust controls used by mines in regions identified by CWHSP and ECWHSP as hot spots for rapidly progressive CWP. Dust surveys are being conducted in selected mines to evaluate the relative effectiveness of the control technologies and to identify areas that are lacking in suitable control technologies. Sampling in the five mines surveyed to date has shown that a significant amount of silica-bearing rock is being cut. Mining thin seams of coal with large, powerful equipment can result in rock-cutting and generation of silica aerosols. RDRP is also conducting a case-control evaluation of miners with and without CWP in the hot spots regions in order to identify possible risk factors, such as coal rank, silica exposures, shift length, etc.

Evaluate digital x-ray technology for diagnosis of the pneumoconioses: RDRP strongly agrees with this recommendation and, as described in Section 3, has identified it as one of RDRP's top priorities. There is a critical need for screening programs for occupational lung diseases, including CWHSP and ECWHSP, to transition from film-based chest radiography to modern digital chest imaging. Due to the widespread adoption of digital radiography in US clinical settings, current public health use of older film-based technology is rapidly becoming unfeasible. That is why RDRP is moving aggressively to transition its radiologic surveillance programs to digital chest imaging, and why this activity is viewed as an immediate, high priority.

RDRP is also conducting research of the type noted in this NA-RDRP recommendation. Extramural research funded by RDRP has examined comparability of digital chest images and conventional screen-film chest radiographs for "classifying" the presence and severity of changes potentially related to pneumoconiosis according to the International Labour Office (ILO) classification system (http://www.cdc.gov/niosh/docs/2008-139/Manuscript-Franzblau-ClassificationComparison.html). In addition, RDRP is conducting a study to compare digital

images and conventional film-screen radiographs obtained during the same visit from participating coal miners. So far, approximately 2700 images have been collected for analysis. RDRP has assisted NCEH-ATSDR in another ongoing study comparing digital chest images and chest radiographs in asbestos-exposed residents of Libby, MT.

Subgoal: Silicosis.

Recommendation: *The RDRP has made significant contributions to mechanistic understanding of the toxicity of silica and prevention of silicosis. More work in both areas is needed. The evaluation committee recommends that the RDRP continue to support experimental studies of silica-induced cytotoxicity and fibrogenesis and the development of control technologies that include silica substitutes, particle surface coatings, and dust reduction measures. New or overlooked ongoing sources of silica exposure and silicosis should also receive appropriate programmatic attention from NIOSH. As for CWP, assessment of the effectiveness of digital radiography in silicosis surveillance should be an important continuing research priority.*

RDRP Response: RDRP appreciates the committee's comments. Basic mechanistic work focused on understanding silica toxicity and mechanisms of fibrosis will continue to be supported. However, it should be noted that RDRP's capacity for conducting such studies intramurally is limited and that, in recent years, personnel and resources formerly focused on this work have been redirected towards emerging issues such as nanoparticle toxicology. Thus, the volume of work in this area will likely be less than in the past. A number of projects have focused on measures for reducing dust exposures, including use of local exhaust ventilation for hand tools and during tuck pointing, use of enclosed cab dust filtration systems, and adding dust collection bags to coal mine roof bolting systems. Research involving other control technologies

will also be supported. Another area of research is development of improved methods for silica exposure assessment that would allow reliable quantification of lower levels of respirable crystalline silica than is currently possible. Efforts to improve disease surveillance, discussed in Section 3, will also help to detect new settings in which silicosis occurs. Performing Health Hazard Evaluations will also help to identify sentinel outbreaks of this ancient disease in new settings. Finally, as noted by the evaluation committee, transitioning from conventional to digital radiography will not just benefit coal miners, but also those exposed to silica.

Subgoal: Fiber-induced interstitial lung diseases

Recommendation: *The RDRP has played an important role in the epidemiologic evaluation of commercial products that contain asbestos. Despite the well-understood epidemiology of asbestos exposure and significant progress in the control of commercial asbestos exposures, more work needs to be done in this area, especially in terms of understanding fiber-specific cancer risk and the mechanisms of carcinogenesis. Fibers that are asbestiform, such as winchite and tremolite, which were found as contaminants of vermiculite mined in Libby, Montana, or of synthetic origin, such as nylon flock and refractory ceramic fiber, require continued study with attention to fiber characteristics, such as cleavage fragments, and low-level exposures, respectively. The RDRP has also contributed greatly to our understanding of a newly discovered interstitial lung disease among nylon flock workers. While RDRP-assisted control efforts in this industry have been effective, continued surveillance of the industry is needed as well as attention to other, emerging fiber-related respiratory health risks.*

RDRP Response: RDRP appreciates these recommendations. We also feel that there are many unresolved issues in this area. RDRP has drafted a Current Intelligence Bulletin titled *Asbestos Fibers and Other Elongated Mineral Particles: State of the Science and Roadmap for*

Research, which details current knowledge gaps and research priorities. It addresses fibers of asbestos minerals crystallized in an asbestiform habit; issues of mineral nomenclature, such as tremolite vs. winchite vs. richterite; and issues related to other elongated mineral particles with the dimensional characteristics of fibers, such as "cleavage fragments" and acicular or prismatic microscopic amphibole crystals. The *Roadmap* takes a multidisciplinary approach and addresses priorities in basic toxicology, exposure assessment, epidemiology, and early disease detection. The *Roadmap* is currently under review by a committee of the NA, with the results of the review expected late in 2009.

Current RDRP research is addressing a variety of issues in exposure assessment. Projects are developing and applying methods for improved competency testing of laboratories performing asbestos analysis by phase-contrast microscopy. A round robin laboratory evaluation of ASTM method D7200, *Standard Practice for Sampling and Counting Airborne Fibers, Including Asbestos Fibers, in Mines and Quarries, by Phase Contrast Microscopy and Transmission Electron Microscopy* is in progress. A proposed project will seek to develop and automate a scanning electron microscopy method for asbestos analysis. A proposed project will develop size-classified samples of asbestos fibers and non-asbestiform elongated mineral particles for use in toxicology and exposure assessment research. Finally, an epidemiology study is re-analyzing asbestos filter samples from a historical cohort of North Carolina chrysotile workers to determine the relationships between electron microscopy based parameters (such as fibers in size bins not apparent by light microscopy) and mortality from asbestos-related diseases. This will help in establishing exposure response relationships based on analysis of air samples by electron microscopy and help to identify fiber sizes most associated with risk of disease.

RDRP is developing an Alert to raise awareness of the dangers of exposure to flock in flocking industry employers and employees and to make recommendations for best practices in working with flock. RDRP is also pursuing research to evaluate toxicology of elongated engineered nanoparticles, such as single- and multi-walled carbon nanotubules. RDRP will continue to conduct surveillance and Health Hazard Evaluations and to identify emerging problems and track occupational health issues related to fibers.

Subgoal: Chronic beryllium disease

Recommendation: *The RDRP has made substantial contributions to our understanding of the risks of sensitization to beryllium and progression to chronic beryllium disease. RDRP epidemiologic studies have documented that the OSHA permissible exposure limit does not prevent sensitization or the onset of chronic beryllium disease. Current RDRP efforts are appropriate, but the committee recommends that work be targeted in support of a new recommended OSHA standard that would lead to improved controls to reduce airborne and dermal exposure in all workplaces where beryllium is used. Extending research to other, work-related granulomatous lung diseases is also encouraged.*

RDRP Response: RDRP is pursuing a range of activities that might eventually support establishment of an occupational exposure limit with the ability to prevent beryllium sensitization and chronic beryllium disease. In the meantime, a NIOSH Alert document is being developed that summarizes current knowledge and, based on what is currently known, makes recommendations for working more safely with beryllium. Since currently-existing exposure-response data do not document a safe level of exposure below which risk of sensitization and chronic beryllium disease is entirely eliminated, the draft Alert does not suggest a specific

occupational exposure limit. Instead, it states that because a safe level is not currently known, exposure levels should be kept as low as possible.

It may be that more sophisticated exposure metrics than airborne mass concentration will be required to identify a safe exposure limit. Exposure may need to take into account bioavailability issues, such as solubility of beryllium-containing particles in body fluids, and routes of exposure, considering both inhalation and skin exposure. Projects currently underway address these issues. For example, a collaborative project with Brush-Wellman Inc. (BWI), the major US producer of beryllium, assesses the effectiveness of a comprehensive preventive program that includes skin protection for prevention of beryllium sensitization in beryllium workers. A second collaborative project with BWI assesses and evaluates relative levels of beryllium skin exposure among beryllium workers, as well as surface migration patterns in beryllium production facilities. Another project addresses particle solubility in simulated body fluids as a risk factor for sensitization and chronic beryllium disease.

Knowledge gained from projects on physicochemical characterization, including solubility in body fluids, of various beryllium materials and the role of dermal exposure in sensitization will be applied into epidemiologic analyses of a cohort of beryllium workers already being followed by RDRP. Environmental data will be considered together with various genetic markers of susceptibility, allowing analysis of gene-environment interactions. Altogether, more sophisticated characterization of exposure, combined with deeper understanding of gene-environment interactions, will allow better determination of what exposure levels are safe, even for the most genetically susceptible individuals.

Although the work described above continues to be in progress, we have provided OSHA access to epidemiologic data from previously-completed studies for their risk analyses based on

currently-available exposure metrics. RDRP has also conducted a number of field evaluations of engineering controls for beryllium under an interagency agreement with OSHA.

An additional collaborative project with New York University seeks to validate a transgenic mouse model for chronic beryllium disease. It will also compare the relative toxicities of different chemical forms of beryllium (beryllium-metal versus beryllium oxide versus copper-beryllium alloy versus beryllium salts).

Work related to other granulomatous lung diseases will continue as driven by opportunity and surveillance data. For example, as already noted, RDRP maintains an active research program in indoor environmental quality. Hypersensitivity pneumonitis is a known adverse health effect of exposures such as microbial constituents within these environments. Although etiology is unknown, damp indoor environments have also been implicated in epidemiological studies as a risk factor for sarcoidosis. Although the major focus of current RDRP indoor air quality research is asthma, these additional adverse health effects will also be addressed, as possible. An additional granulomatous lung disease of interest is hypersensitivity pneumonitis induced by exposure to aerosols of metalworking fluids contaminated by growth of mycobacteria. RDRP has a long history of work in this area, and is currently funding an extramural project addressing this issue.

Strategic Goal 3: Prevent and Reduce Work-Related Respiratory Infectious Diseases

NA-RDRP General Recommendations: Respiratory Infectious Diseases

Recommendation: *Continue and expand efforts to protect workers from occupational exposures and to define mechanisms that make workers susceptible to respiratory infections.*

RDRP Response: RDRP appreciates this recommendation. RDRP recognizes that infectious diseases are an important concern for other parts of the federal government, in particular other parts of CDC and NIH. However, NIOSH is the federal agency with primary responsibility for occupational safety and health issues, which include prevention of work-related infectious diseases. RDRP recognizes the importance of cooperation, collaboration, and focusing its attention in particular on areas where it has special expertise and problems where it has unique interests not likely to be addressed by others. In this way, RDRP can leverage the capabilities of other agencies and benefit from their complementary strengths. As is described subsequently, RDRP areas of special expertise related to infectious diseases include exposure assessment; and reducing exposures through engineering controls and respiratory protection. RDRP also supports research that assesses the impact of noninfectious occupational exposures on respiratory host defense.

Recommendation: *Enhance surveillance for outbreaks of known and emerging occupational respiratory infections.*

RDRP Response: RDRP appreciates this recommendation. As is described in Section 3, RDRP has identified occupational respiratory disease surveillance, in general, as one of its immediate, high priorities. Such surveillance would also address occupational respiratory infectious diseases.

Recommendation: *Develop an overarching structure for the infectious disease program component and coordinate with other federal agencies to adopt technologies for the detection of bioterrorism agents for the protection of workers.*

RDRP Response: RDRP has responded, as recommended by the NA-RDRP committee, by re-structuring its strategic goals in the area. Instead of being organized by infectious agent, as was previously the case, they are now organized according to the overarching categories of exposure assessment; understanding host and pathogen characteristics important for transmission of disease; engineering controls; respiratory protection; and coordination and collaboration with other elements of CDC.

As recommended by the NA-RDRP committee, RDRP (and all of NIOSH) coordinate with other elements of CDC and other federal agencies to protect workers from bioterrorism agents. The major contact point for coordination is the NIOSH Office for Emergency Preparedness and the NIOSH Emergency Preparedness and Response Program, to which RDRP contributes. An example of a federal program that uses new technology for the detection of bioterrorism agents is the BioWatch program. This program places monitors that collect air samples for analysis by PCR at sites that might be targets for attack with biothreat agents. Many agencies, including the Department of Homeland Security (DHS), the Environmental Protection Agency (EPA), and CDC collaborate. The NIOSH role is to provide guidance for protection of workers involved in response to a bioterrorist event detected by BioWatch. Thus, BioWatch is an example of a program in which many federal agencies collaborate, each with specific responsibilities.

Recommendation: *The RDRP's efforts on infectious diseases appropriately concentrate on preventing infection through the use of respirators and understanding why certain people are susceptible to these infections.*

RDRP Response: RDRP appreciates this comment. Understanding why certain people are susceptible to occupationally-acquired respiratory infections is an important RDRP priority, especially when susceptibility can be prevented by limiting non-infectious occupational exposures that impair host defense or reversed through preventive measures such as vaccination. Use of respiratory protection to prevent transmission of respiratory infectious diseases is a shared interest of both RDRP and the NIOSH Personal Protective Technology (PPT) program, which has been very active in this area.

Recommendation: *In addition, more robust surveillance for disease outbreaks in occupational settings is needed.*

RDRP Response: As described in Section 3, occupational respiratory disease surveillance is an immediate, high priority for RDRP.

NA-RDRP Detailed Recommendations: Respiratory Infectious Diseases

Subgoal: Maintain reductions in occupational incidence of TB in high-risk work settings.

Recommendation: *The goal of the occupational TB program appears to be to prevent and reduce occupationally related TB in the context of the broader response of the Centers for Disease Control and Prevention to eliminate TB in the United States. This is appropriate, but the lack of specific occupational TB surveillance programs represents a major challenge. Given the continued immigration of documented and undocumented workers from areas with high prevalence of TB, the committee recommends that more specific occupational TB surveillance data be collected, along with exploration of improved methods for TB surveillance.*

RDRP Response: As described in Section 3, occupational respiratory disease surveillance is an immediate, high priority of RDRP. Such surveillance would include TB, and would supplement information already collected by the CDC national TB surveillance system. The current system collects information about verified cases of TB from state and local TB programs. The information is submitted electronically to CDC's Division of Tuberculosis Elimination. Occupational variables currently available in the surveillance system address industry of employment and include: correctional, healthcare, migratory agricultural, multiple, not employed, other, and not reported. This information can be accessed via the Online Tuberculosis Information System found at: http://wonder.cdc.gov/tb.html.

Subgoal: Protect workers from bioterrorism agents and from occupational acquisition of emerging diseases (including severe acute respiratory syndrome and avian and pandemic flu).

Recommendation: *The RDRP played a major role in the national effort to protect workers from the threat of anthrax-contaminated mail in 2001. Improved understanding of how workers became infected from the contaminated mail is needed to increase the "readiness" of government response to a future bioterrorism attack. The RDRP has also been responsive to the specific needs of stakeholders and the public with respect to extramural research on emerging infectious diseases. The committee recommends that research on bioterrorism and emerging infectious diseases be prioritized for extramural funding within the constraints of limited budgetary resources. In addition, NIOSH should coordinate with other federal agencies, such as the Department of Homeland Security, to adopt recently developed technologies for the detection of bioterrorism agents for the protection of workers.*

RDRP Response: RDRP appreciates and agrees with this recommendation. RDRP agrees that it is logical for this work to have a strong extramural focus. NIOSH laboratory

microbiology infrastructure is modest. Laboratory infrastructure appropriate for working with pathogenic infectious agents, particularly agents competent for transmission via the airborne route, is even more modest. To build a sustainable intramural program in this area would be very expensive. It would require recruitment of a significant number of new personnel and building laboratories capable of safely working with airborne human pathogens and animal models of relevant airborne infectious diseases. In view of these issues, it is most cost-effective for NIOSH to address occupationally relevant issues in bioterrorism and emerging infectious diseases that require working with the relevant human pathogens through its extramural program.

RDRP also agrees with the importance of working with other federal agencies, including DHS. The example of collaboration in the BioWatch program was previously discussed. Another example of collaboration across federal agencies is the recently published *Plan to Combat Extensively Drug-Resistant Tuberculosis Recommendations of the Federal Tuberculosis Task Force* (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5803a1.htm). RDRP was a major contributor to the section on infection control found in this document.

Subgoal: Protect workers from occupational exposures that make them susceptible to respiratory infections.

Recommendation: *The RDRP is to be commended for its work on personal respirators and engineering controls for preventing the transmission of infectious agents to workers. The committee recommends that support for these areas remains a high priority.*

RDRP Response: RDRP appreciates this recommendation. NIOSH is unique among the federal agencies for its strength in these areas. Thus, it is appropriate that NIOSH be a leader in developing and applying personal protective equipment and engineering controls to preventing occupational transmission of respiratory infectious diseases. The NIOSH PPT program plays a

leading role in issues related to respiratory protection, with RDRP in a supportive role. The PPT program is extensive, and its activities have been supported in several recent reviews by the NA. The PPT program is also being reviewed by the BSC in parallel to the RDRP program. Detailed information about PPT projects and plans are included within the PPT implementation plan provided separately to the BSC. Selected PPT projects most relevant to respiratory infectious diseases are listed in Section 4.

As previously noted, research that uses actual human pathogens to study respiratory protection and engineering controls will best be accomplished through engagement of the extramural community. However, a robust program of work involving modeling and use of simulant agents can and should be accomplished in the intramural setting. The high priority of this area is reflected in the goals for this area listed in Section 4.

Subgoal: Prevent outbreaks of occupational histoplasmosis by maintaining worker and employer awareness.

Recommendation: *The RDRP histoplasmosis research activity appears to be of historical interest, and the evidence package states that no new RDRP research is planned. In the absence of an operational definition of "awareness" and the documented lack of adequate resources for specific surveillance activities, it is unclear how the RDRP can achieve this subgoal. Given the limited budgetary resources of the agency, the committee recommends that consideration be given to dropping this subgoal.*

RDRP Response: The NA-RDRP committee's recommendation is well taken. A major focus of the RDRP evaluation was to assess relevance and impact of the RDRP program over the previous 10 years. Thus, issues were included in the RDRP evidence package that had achieved

impact during the previous 10 years, but were not necessarily areas of intense continuing activity. Histoplasmosis was one such area.

The restructuring of goals in the area of respiratory infectious diseases to address overarching issues instead of specific diseases has eliminated histoplasmosis as a specific subgoal area. Still, sporadic occupational outbreaks of histoplasmosis continue to occur. One example was an outbreak several years ago at an agricultural processing plant (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5343a6.htm). In view of this, should major advances occur in this area that might be applicable to preventing occupational transmission of histoplasmosis, RDRP might consider renewing activities in the area. RDRP will also respond appropriately as dictated by future outbreaks. In the meantime, even though histoplasmosis is not an active area of research, RDRP will continue to be a source of information for stakeholders including workers, employers, and others concerned about the disease.

Strategic Goal 4: Prevent and Reduce Work-Related Respiratory Malignancies

NA-RDRP General Recommendations: Respiratory Malignancies

Recommendation: *Develop a comprehensive plan for addressing respiratory malignancies in the workplace while assuring the integration of this plan with NIOSH and other federal agency efforts.*

RDRP Response: As previously noted, the lead program for work-related cancer research, including research related to work-related respiratory cancers, is the NIOSH CRC program (http://www.cdc.gov/niosh/programs/crcd/). RDRP plays a secondary, supportive role, with goals listed in Section 4 being those of special interest to RDRP.

Cancer research within NIOSH, respiratory or otherwise, is guided by a well-developed and comprehensive approach to priority setting. This approach is reflected in a paper developed by the NORA Cancer Research Methods Team during the first decade of NORA and published in 2003 (*Priorities for Development of Research Methods in Occupational Cancer*, http://www.ehponline.org/docs/2003/5537/abstract.html). For example, research that further elucidates the epidemiologic association of cancer with exposure to suspected (e.g., International Agency for Research on Cancer (IARC) Group 2A and 2B) carcinogens, many of which are not currently regulated as carcinogens in the U.S., is an important priority. Specific recommendations are made in several areas: identification of occupational carcinogens; epidemiological research in occupational cancer; improvements in risk assessment for occupational carcinogens; and prevention of occupational cancers.

NIOSH cancer research coordinates and collaborates with other federal agencies through a range of relationships. The NIOSH Director is a member of the National Cancer Advisory Board, along with leaders of a range of other federal agencies with an interest in cancer

(http://deainfo.nci.nih.gov/Advisory/ncabchr.htm). NIOSH is a core member of the National Toxicology Program (http://ntp.niehs.nih.gov/?objectid=720163E9-BDB7-CEBA-FB0157221EB4375F). NIOSH collaborates with other federal agencies in specific projects. For example, a NIOSH representative sits on the Executive Committee of the Agricultural Health Study (http://aghealth.nci.nih.gov/facts.html). Another example of collaborative research is a study of diesel exposure and lung cancer mortality being conducted by a team of NIOSH and NCI investigators. Thus, NIOSH cancer research is integrated with that of other federal agencies through relationships ranging from the institute level to collaborations between individual investigators.

Recommendation: *Refocus research on diagnostic tools to research on biomarkers of exposure or early detection of risk specific to occupational cohorts.*

RDRP Response: This recommendation is in response to information included in the RDRP evidence package about work to develop a microarray that detected alterations in gene expression and gene copy number that were identified as important in the development of murine lung adenocarcinoma as a potential tool for early detection of human lung adenocarcinoma. The NA-RDRP committee correctly noted that other agencies, such as NCI, were far better equipped than NIOSH to address non-occupational cancer issues. We agree with the evaluation committee recommendation that NIOSH should focus its efforts in the area of biomarkers of exposure or early detection of risk specifically on issues related to occupationally-induced human lung cancer.

Recommendation: *The program has had strong impacts in reducing and preventing respiratory cancers from exposures to hexavalent chromium, silica, (and) diesel exhaust and continues to address challenging problems related to occupational risk from lung cancer. RDRP*

should ensure that its research in these areas are well integrated into an overall program of occupational cancer research and not arbitrarily separated by these efforts.

RDRP Response: As previously noted, research related to occupational respiratory malignancies is well-coordinated across NIOSH. The lead program for work-related cancer research, including research related to work-related respiratory cancers, is the NIOSH CRC program, with RDRP playing a secondary, supportive role, focusing on issues of particular interest to RDRP.

NA-RDRP Detailed Recommendations: Respiratory Malignancies

Subgoal: Development of early diagnostic tools for lung cancer.

Recommendation: *The committee questions the relevance and impact of the research into biomarkers for early detection of lung cancer. While this area of investigation is relevant to lung cancer in general, there is little advantage to having this work located at NIOSH instead of at NCI and NIEHS, especially in light of available resources. Focusing the study of such biomarkers on workplace-specific prevention efforts would make these efforts more relevant to NIOSH's mission and would increase the likelihood of the program having a significant impact. The committee recommends that the RDRP consider refocusing the research of biomarkers for early detection to biomarkers of exposure or for early detection that addresses the needs of specific occupational cohorts at high risk of contracting lung cancer.*

RDRP Response: As noted previously, RDRP agrees with focusing its efforts in the area of biomarkers on problems specifically related to occupationally-induced human lung cancer. In response to this recommendation, goals in this area are focused on applying biomarkers to occupational settings; or evaluating biomarkers that have specific relevance to occupationally-related cancer. For example, current goals specify efforts such as evaluation of mineral dust-

induced gene (*mdig*) expression for the early detection of silica-induced lung cancer and the use of blood biomarkers such as serum osteopontin or soluble mesothelin-related peptide for the early detection of mesothelioma.

Recommendation: *An emerging issue that could inform research on the risk for work-related respiratory malignancies concerns the inverse relationship between lung cancer and endotoxin exposures. There are a variety of settings with complex exposures to chemical materials where endotoxin exposure occurs, ranging from agricultural settings to metal machining operations. NIOSH should consider whether its expertise in endotoxin positions it to contribute to understanding the role of endotoxin and cancer.*

RDRP Response: It has recently been reported that endotoxin exposure among Shanghai female textile workers may be protective against lung cancer (Astrakianakis et al. J Natl Cancer Inst. 2007; 99:357-64). A NIOSH extramural KO1 grant funded from August, 2008 through July, 2011 will follow up on this observation. The project will especially focus on whether healthy worker survivor effect contributed to the previously-documented association, since the study population included only subjects hired prior to the start of follow-up. In addition to further elucidating the relationships between endotoxin exposure and lung cancer, the project also seeks to develop and compare methods to control for healthy worker survivor effect.

Recommendation: *Despite significant contributions to technology for measurement of diesel particulate matter (DPM), NIOSH should continue efforts to develop and validate exposure methods for DPM, especially in the presence of other sources of carbon aerosols, and to provide validation of the methods used to measure DPM in coal mines.*

RDRP Response: RDRP agrees with the recommendation. This is an area of overlapping interest with the NIOSH Mining Program, which is actively pursuing efforts to

develop and validate exposure methods for DPM, especially in the presence of other sources of carbon aerosols, and to provide validation of the methods used to measure DPM in coal mines.

NIOSH has maintained that elemental carbon is a suitable surrogate for DPM exposure. The use of elemental carbon in metal/non-metal mines eliminates interferences from the most common non-DPM sources of carbon aerosols. In coal mines, there remains potential for elemental carbon interference due to submicrometer coal dust. However, NIOSH research has shown that the elemental carbon contribution from submicrometer coal dust can be largely eliminated with the use of an appropriate size selective sampler (Birch ME and Noll JD. J. Environ Monit 2004; 6:799–806). NIOSH is also developing a personal elemental carbon monitor. This personal monitor has been shown to accurately measure elemental carbon concentrations in mine air. This monitor is being commercialized by ICx Inc. and should be available to the mining industry by the fall of 2009..

NIOSH also continues to evaluate other metrics to measure DPM exposure. Two such metrics mentioned often in scientific literature are particle number and surface area. Studies completed at NIOSH Lake Lynn Laboratory have measured particle number concentration and particle surface area of diesel emissions in an effort to correlate these metrics with toxicity data. Analysis of this data is ongoing.

Recommendation: *Finally, it is noted that cancers related to asbestos exposure continue to rise. NIOSH should consider developing long-term follow-up studies of exposed workers and interventions, as appropriate, to reduce mortality among these groups. Continued surveillance for asbestos-related risks should receive additional attention.*

RDRP Response: RDRP agrees with this recommendation. Due to the long latency of asbestos-induced malignant and nonmalignant diseases, which can take decades to present, those previously exposed to asbestos remain at risk for long-term health effects.

A recent RDRP collaboration with external partners updated the vital status of a population of South Carolina chrysotile textile workers and assessed the role of fiber dimensions in exposure-response relationships for asbestosis and lung cancer (Stayner et al. Occup Environ Med. 2008 Sep;65:613-9). Transmission electron microscopy-based exposure estimates better predicted asbestosis and lung cancer mortality than previous phase-contrast light microscopy-based estimates. Lung cancer and asbestosis were most strongly associated with exposure to thin fibers (diameter <0.25 micrometers). Longer fibers (length >10 micrometers) were the best predictors of lung cancer. This study suggests that electron microscopy-based exposure measurements, which are able to detect thinner fibers than light microscopy, may provide improved estimates of risk. A new study that similarly re-evaluates a cohort of North Carolina chrysotile textile workers is currently in progress. It seeks to validate and extend upon previously-reported findings.

An additional NIOSH follow-up study is of interest. In a 1987 NIOSH study, Amandus et al published landmark studies documenting exposure-response relationships for asbestos-induced diseases in Libby, MT vermiculite miners. In a 2007 NIOSH study, Sullivan published an updated report describing malignant and nonmalignant respiratory mortality in the cohort. Based on this study, a partnership was formed with EPA. Data from the cohort is being augmented by EPA with additional information and being used by EPA to develop a risk assessment for asbestos-contaminated Libby vermiculite.

RDRP agrees with the importance of continued surveillance. The primary source of ongoing surveillance for asbestos-related disease is mortality surveillance. Because asbestosis and mesothelioma deaths are strongly related to past asbestos exposures, they allow national monitoring of the burden of disease associated with asbestos exposures. Updated mortality statistics can be viewed in the WoRLD Report, and customized queries of the data can be made via NORMS. Both of these resources can be accessed via the Occupational Respiratory Disease Surveillance (ORDS) website home page, found at: http://www.cdc.gov/niosh/topics/surveillance/ords/.

Strategic Goal 5: Prevent Respiratory and Other Diseases Potentially Resulting from Occupational Exposures to Nanomaterials

NA-RDRP General Recommendations: Nanomaterials

The growing recognition of the usefulness of nanomaterials in various industrial applications has created an urgent need to study the potential health effects of exposures to nanoparticles and methods to control exposures to nanoparticles during manufacturing processes. The RDRP has taken a lead at the national and international levels to address these questions. NIOSH should continue to play a leading role in informing and guiding national and international efforts to address potential occupational hazards and risks associated with the use of manufactured nanoparticles. NIOSH is particularly well suited to have an impact in continuing successful research into methods to monitor exposures to nanomaterials and to develop appropriate engineering controls to prevent such exposures. The following recommendations correspond to the three subgoals listed in the evidence package.

Recommendation: *NIOSH should continue to play a leading role in informing and guiding national and international efforts to address potential occupational hazards and risks associated with the use of manufactured nanomaterials.*

RDRP Response: RDRP appreciates this comment and also views this as a high priority area. As suggested in the recommendation, communication efforts are an important part of the NIOSH Nanotechnology Program. The NIOSH nanotechnology web site is a rich source of information and can be accessed at: http://www.cdc.gov/niosh/topics/nanotech/. A number of high profile and useful NIOSH publications can be downloaded from the website. These include publications such as Safe Nanotechnology in the Workplace (http://www.cdc.gov/niosh/docs/2008-112/) and Interim Guidance for Medical Screening and

Hazard Surveillance for Workers Potentially Exposed to Engineered Nanoparticles (http://www.cdc.gov/niosh/docs/2009-116/). A NIOSH Alert is currently under development with the tentative title of "Preventing occupational exposure to carbon nanotubes." It will present and discuss the implications of animal studies assessing the respiratory toxicology of single- and multi-walled carbon nanotubes.

Recommendation: *The report generally supports the RDRP's research efforts on nanomaterial toxicity, exposure, and dose-response. However, the committee is concerned that there may not be enough long-term data for risk assessments, and therefore the RDRP should consider other approaches for dealing with the potential health impacts of these new materials carefully.*

RDRP Response: This comment is well-taken. Fortunately, human occupational respiratory diseases specifically resulting from engineered nanomaterials currently have yet to appear. Thus, traditional risk assessment based at least in part on long-term human data is not yet possible. As a result, current public health guidance depends on other information, such as animal toxicology data, information about the ability of engineering controls and personal protective equipment to filter out nanoparticles, and professional judgment. As already noted, a NIOSH Alert on "Preventing occupational exposure to carbon nanotubes" that is based primarily on animal studies is under development.

NA-RDRP Detailed Recommendations: Nanomaterials

Subgoal: Determine the relative toxicity of nanomaterials.

Recommendation: *The RDRP can continue to support some respiratory studies on the toxicology of nanoparticles but because of limited funding should address only those issues that*

complement studies being supported by other organizations. Thus, there needs to be a continued close interaction with other organizations involved in nanotechnology health-related research.

RDRP Response: RDRP agrees that it is critical for NIOSH to form partnerships in this rapidly emerging area, especially under current economic conditions. NIOSH is currently partnering with a range of other institutes and organizations in the area of nanotechnology to leverage resources that would not otherwise be available. NIOSH actively participates in the National Nanotechnology Initiative (NNI). NNI is a federal research and development program established to coordinate the multiagency efforts in nanoscale science, engineering, and technology. NIOSH participates in NNI strategic and budget planning processes, resulting in coordination of research into occupational safety and health of nanotechnology with other government agencies. A partial list of the many partnerships that NIOSH has developed with governmental and non-governmental organizations can be seen at the following web page: http://www.cdc.gov/niosh/topics/nanotech/partners.html.

Subgoal: Conduct exposure assessments and engineering control evaluations in 10 nanomaterial production or use facilities by 2008.

Recommendation: *The committee agrees that this is an appropriate and high-priority intermediate goal for the RDRP nanomaterials component.*

RDRP Response: Since submission of the RDRP evidence package, this goal has been achieved. However, nanotechnology continues to evolve and there continues to be a need to conduct field studies to assess current workplace processes, materials, and control technologies associated with nanotechnology and to conduct on-site assessments of potential occupational exposures to a variety of nanomaterials. Thus, the NIOSH Nanotechnology Field Research Team continues to recruit research laboratories, producers, and manufacturers working with

engineered nanomaterials (1 to 100nm) to collaborate with field research. Details can be found at: http://www.cdc.gov/niosh/docs/2008-121/.

Subgoal: Produce dose-response data for carbon nanotubes sufficient to conduct a quantitative risk assessment by 2008.

Recommendation: *The committee agrees that this is an appropriate intermediate goal but is concerned that data may be insufficient to properly ground a quantitative risk assessment in this short time frame. In particular, data on human health effects are likely to be lacking. The RDRP should recognize that a quantitative risk assessment is not the only approach for dealing with the potential health impact of new materials in a precautionary manner.*

RDRP Response: As previously noted, RDRP appreciates the committee's recommendation. Sufficient data does not yet exist for such a risk assessment. It is likely that any data-based guidance for carbon nanotubes developed in the near future will depend heavily upon *in vitro* and animal *in vivo* toxicology models, because human occupational respiratory disease has not yet emerged from this new and growing exposure.

RDRP Cross-Cutting Issues: Surveillance, Exposure Assessment, Emergency Response, and Prioritization

In addition to commenting on strategic goal areas, the NA-RDRP evaluation committee also commented on several cross-cutting areas of importance to RDRP, including surveillance, exposure assessment, emergency response, and prioritization.

Surveillance

Recommendation: *NIOSH should provide appropriate resources for and engage in high-priority occupational disease surveillance.*

RDRP Response: We agree with this recommendation. RDRP has identified surveillance as an immediate, high priority area, as will be described in more detail in Section 3. In addition to occupational respiratory disease surveillance supported primarily by RDRP, the NIOSH Surveillance Program actively and comprehensively pursues occupational injury and illness surveillance. Information about the NIOSH surveillance program can be found at: http://www.cdc.gov/niosh/programs/surv/.

Recommendation: *The effectiveness of past NIOSH surveillance activities for coal-dust-related diseases highlights the importance of improved surveillance for other respiratory disorders.*

RDRP Response: RDRP appreciates this comment. By documenting rapidly progressive CWP in geographic 'hot spots" and the continued occurrence of advanced CWP in young miners, NIOSH chest radiograph-based surveillance has proven its continued relevance and impact. In order to survive, that program must be modernized. That is why transitioning NIOSH chest radiographic surveillance to digital chest imaging has been identified as an immediate, high priority need of RDRP, as will be described in Section 3.

Exposure Assessment

Recommendation: *Produce a programmatic approach to the development of sampling and analytic methods that include exposure assessment scientists as an integral part of RDRP activities. Exposure assessment is a core component of occupational respiratory disease research and prevention activities. The RDRP does not have specific, programmatic methods for exposure assessment, however.*

RDRP Response: RDRP embraces multidisciplinary approaches to preventing occupational respiratory diseases and agrees that exposure assessment is an integral element of RDRP activities. Without objective exposure assessment methods, there can be no quantitative understanding of exposure-response relationships, risk assessment, or occupational exposure limits. The science of sampling strategies is essential to accurate determination of exposure and accurate identification of occupational exposure limit exceedance. Development, validation, and dissemination of sampling and analytical methods for occupational agents are critical, core elements of the NIOSH mission.

RDRP integrates exposure assessment into its disease-based goals. Two recent examples are the chemical diacetyl; and asbestos and other elongated mineral particles. One of the RDRP activity/output goals is to develop and improve sampling and analytical methods for assessing exposure to diacetyl and other artificial flavorings. A method previously used when the problem of flavorings-related lung disease was first identified has been found to underestimate exposures in the presence of high humidity. Thus, the RDRP goal is motivated by the need to have a sensitive, reliable, validated exposure assessment method that works across usual ambient conditions in order to understand exposure-response relationships, conduct risk assessment, and develop recommendations for an occupational exposure limit.

Similarly, another RDRP activity/output goal is to develop improved sampling and analytical methods for assessing exposure to asbestos and other elongated mineral particles. This is one of the critical research needs identified in the draft NIOSH Current Intelligence Bulletin: *Asbestos Fibers and Other Elongated Mineral Particles: State of the Science and Roadmap for Research.* Research supported by RDRP has evaluated use of thoracic samplers to address dust overload problems in dusty environments; developed and tested new approaches to laboratory competence testing for performing asbestos analysis by phase-contrast microscopy; and worked to develop new asbestos dust standards for standardization of methods. A pending project seeks to develop improved, automated asbestos analysis using scanning electron microscopy.

RDRP scientists are also involved in institute-wide initiatives in exposure assessment, which are managed by the NIOSH Exposure Assessment Program: http://www.cdc.gov/niosh/programs/expa/. For example, NIOSH has recently embarked upon a Direct-Reading Method Initiative (DRMI) that seeks to advance the science of using direct-reading analytical techniques and direct-reading instruments that accurately assess exposures in real or near real time to protect workers and prevent disease. This is an area of great interest to RDRP, especially in view of MSHA's proposed rule to deploy PDMs in coal mines as a new alternative to traditional gravimetric filter sampling for coal mine dust. A workshop was held in November, 2008 to gather stakeholder input from academia, labor, management, developers, governmental agencies, and manufacturers on the research needs in the area of direct reading methods for assessing occupational exposures. Proceedings from the workshop are being developed and will be posted on the NIOSH website.

Emergency Response

Recommendation: *The RDRP is encouraged to explore research strategies in its emergency response efforts. The RDRP has made important contributions to the research and surveillance of respiratory disease in emergency responders to recent disasters, including the World Trade Center and anthrax terror attacks, and Hurricanes Katrina and Rita. However, much more can be learned about the relationship between exposure and disease response and ultimately about protecting emergency responders. In addition, the RDRP is encouraged to continue to develop cooperative work with other agencies that conduct research in infection and terrorism.*

RDRP Response: RDRP appreciates this recommendation. The main element of NIOSH involved in Emergency Preparedness and Response is the NIOSH Emergency Preparedness Group, based in Atlanta; and the NIOSH Emergency Preparedness and Response Program: http://www.cdc.gov/niosh/programs/epr/. RDRP has and will continue to play a supportive role, especially in areas relevant to occupational respiratory diseases. For example, RDRP has provided support to the Mt. Sinai WTC Responder Health Program to standardize spirometry in assessment of responders; and to analyze and report spirometry data from the WTC responder cohort. These studies have documented a high prevalence of abnormal spirometry (approximately 24%) in the cohort > 5 years after the disaster. In another example, RDRP researchers worked together with PPT Program researchers to study respirator use in post-Katrina New Orleans, documenting a high prevalence of improper N95 filtering facepiece respirator use by the general public. As previously noted in the section on occupational respiratory infectious diseases, RDRP will continue to work with the Emergency Preparedness and Response Program, with other elements of CDC, and with other federal agencies in this area.

Prioritization

Recommendation: *The RDRP should prioritize all research proposals under consideration for funding according to the RDRP strategic plan, which needs to be updated periodically. An emerging challenge is how research priorities for respiratory diseases that cut across sectors will be treated.*

RDRP Response: We appreciate this recommendation. RDRP updates its strategic plan at least annually. As a result, the plan has been updated twice since the RDRP evidence package was first submitted to the NA-RDRP evaluation committee. From the standpoint of funding decisions, RDRP has the most influence over investigator-initiated proposals submitted annually in competition for intramural NORA funding. RDRP funding recommendations are strongly based on its strategic priorities, which change from year to year based on inputs and external factors. Pursuit of this funding stream leverages investigators into research areas that are RDRP priorities, such as diacetyl and food flavorings research and asbestos research. Those responsible for managing other funding streams, such as the NIOSH Divisions and the NIOSH Office of Extramural Funding are also informed by RDRP strategic goals. RDRP appreciates the need to address occupational respiratory diseases that have societal impact, even if they are not recognized as problems by specific industry sectors because the diseases also have non-occupational etiologies or occur with long latency, potentially even after retirement. Examples would include occupationally-related asthma and COPD, which are massive problems from the societal standpoint. This issue speaks to the need for prioritization from both the industry sector and society-wide perspectives.

Recommendation: *The RDRP needs systems to govern the awarding of grants, contracts, and cooperative agreements and to integrate this external research into the NIOSH program to avoid duplication and inappropriate expenditure on low-priority research.*

RDRP Response: RDRP appreciates and agrees with this recommendation. Extramurally-funded activities are a critical component of the NIOSH effort to prevent occupational respiratory disease. Management of NIOSH extramural activities is housed within the NIOSH Office of Extramural Programs (OEP): http://www.cdc.gov/niosh/oep/. Although OEP management is independent of RDRP, a strong collaborative relationship exists. To ensure strong communication, one of the positions on the RDRP Steering Committee is reserved for a member from OEP. To assure appropriate consideration of programmatic issues in extramural funding, one of the positions on the NIOSH Secondary Review Committee (which conducts programmatic review of extramural grant proposals after peer review but before funding) is held by the manager of RDRP.

OEP funds extramural activities via a range of funding mechanisms. Examples of award mechanisms include grants and cooperative agreements [for investigator-initiated research in response to NIOSH's general program announcements and from specific Requests for Applications (RFAs)], consortia, Program Projects and Centers of Excellence, as well as the procurement of specific services through contracts. In addition, NIOSH supports extramural Centers in education, agriculture, Worklife, and construction. Programmatic priorities for funding via these mechanisms are informed by strategic goals established by the various NIOSH programs, including RDRP. Extramural proposals that address important goals which cannot be addressed by the intramural program due to limitations in expertise or infrastructure have special programmatic importance. That being said, it should be realized that, in some situations, overlap between intramural and extramural research may be desirable if it results in greater innovation or quicker achievement of research goals.

Section 3. Highest RDRP Priorities

The evidence package submitted to the NA-RDRP committee described a broad range of areas over a period of 10 years where RDRP could demonstrate relevance and impact. Based on input from the NA-RDRP committee, surveillance data, occupational health-related research, and the needs of stakeholders, RDRP has identified a subset of these areas as especially high priorities. An additional consideration for priority setting is whether an issue is likely to be addressed by others if it is not addressed by RDRP. The following description separates issues into immediate priorities to be addressed in the present (even if fully addressing them will take years); and intermediate to long-term priorities that require attention, but not with the same immediacy as the former group. In general, fully addressing these priorities will require the efforts of multiple disciplines carrying out many types of activities. This section is not intended to be a comprehensive list of all occupational respiratory disease issues that are appropriate to address. Clearly, a number of worthy issues are not included. This section seeks only to highlight a group of issues that are of particularly high priority.

Immediate Priorities

Digital Chest Imaging: There is a pressing need for RDRP and the public health community to have the tools and trained personnel necessary for transitioning from film-based chest radiography to modern digital chest imaging in screening programs for occupational and other lung diseases. Dust-induced lung diseases such as silicosis, asbestosis, and CWP continue to be important problems. Chest imaging is a necessary component of surveillance for these conditions and for targeting prevention efforts. However, due to the widespread adoption of digital radiography in US clinical settings, current public health use of older film-based

technology is rapidly becoming unfeasible. There is critical need to align such surveillance with mainstream imaging technologies used by the contemporary healthcare system.

Federal law mandates that NIOSH maintain a surveillance program for underground coal miners that includes chest radiographs obtained at entry into mining and at about 5 year intervals thereafter. This Coal Workers' Health Surveillance Program (CWHSP) identifies coal miners with early CWP. Miners with evidence of CWP are entitled under the law to certain secondary prevention measures, such as transfer to jobs with lower dust exposure and more intensive monitoring for dust exposure. Under the law, radiographs are paid for by the coal mine operators that employ the miners. Ideally, the radiographs are obtained in conveniently-located local healthcare facilities approved to participate in the program.

To assure consistent, reproducible evaluation of chest radiographs, federal regulations mandate that radiographs submitted to CWHSP be evaluated for the presence and severity of changes possibly associated with pneumoconiosis using a classification system developed by the International Labour Office (ILO). The ILO classification system is the standard approach throughout the world for systematic, reproducible evaluation of chest radiographs in a range of public health and other settings. It requires the use of film-based chest radiographs.

Because the ILO classification system is not used for clinical diagnosis, RDRP operates a training and certification program that teaches physicians to use it and documents competence through testing. This program is called the B Reader Certification Program. B Reader certification has become an internationally recognized standard of competence in use of the ILO classification system. Other Federal agencies have looked to NIOSH guidelines and B Readers when setting up their own programs addressing silicosis, asbestosis, and CWP.

The impact of the healthcare system's near-complete migration to digital radiography on public health surveillance is demonstrated by its effect on the CWHSP. Over the last 10 years, the number of medical facilities approved to participate in the coal workers' radiographic screening program has progressively declined from 187 in 1998 to 131 in 2008. Of these, only 48/131 actually participated. Many facilities have cited transition to digital radiography as the reason for termination of participation. Coal miners are often unable to obtain conventional chest radiographs in their communities and must travel long distances to participate in screening. Numbers of B Readers have also declined from 682 in 1998 (average age 51) to 337 in 2009 (average age 58), in part due to unwillingness or inability to deal with older film technology.

In view of these issues, RDRP has undertaken an initiative to transition service, education, and physician certification programs to use of digital imaging. We have funded research to document equivalency of digital and film-based ILO classification results. We have held an expert and stakeholder public meeting for input on operational issues (http://www.cdc.gov/niosh/docs/2008-139/default.html). We have worked with ILO to establish a process by which digital chest imaging will be accepted under the ILO classification system. We have engaged contractors to analyze CWHSP operations and develop a plan for transition.

Next steps for addressing this immediate, high priority issue include: acquisition of necessary hardware and software; acquisition of appropriate professional support, including systems integration and training/technical support for intramural staff and outside participating healthcare facilities; initiation of a demonstration project to stand up the new digital surveillance program; updating regulations and issuance of guidelines to fully implement the digital surveillance program; development and provision of physician training in classification of chest images and the B Reader certification examination in digital format; identification, recruitment

and certification of more healthcare facilities as participants in CWHSP; and training and certification of more physicians as B Readers. In addition, a program of research is needed to document equivalence of film-based and digital chest imaging for a range of conditions; to fully modernize technology and address issues such as computer-assisted film classification; and to develop guidelines for integration of other modern chest imaging modalities, such as computerized axial tomography, into chest-imaging based surveillance schemes.

Occupational Respiratory Disease Surveillance: Improving occupational respiratory disease surveillance was an important recommendation of the NA-RDRP committee. Surveillance is critical for planning, priority setting, and tracking progress. Unfortunately, major sources of occupational surveillance data such as the Bureau of Labor Statistics' (BLS) Survey of Occupational Injury and Illness and Census of Fatal Occupational Injuries do a far better job of identifying occupational injuries than occupational diseases, including respiratory diseases. One major problem is undercounting of occupational diseases such as work-related asthma (WRA). These diseases are often attributed to non-occupational causes and the occupational contribution is not recognized or recorded. Another important problem is diseases of long latency. Because these may not have onset for years, often after the worker has moved to a new job or even retired, they are not captured in BLS data. Occupational diseases of long latency are also often attributed to non-occupational causes, compounding the difficulty in recognizing and accurately tracking them.

Historically, a major source of data for ongoing occupational disease surveillance, including occupational respiratory disease surveillance, has been mortality data from the National Center for Health Statistics (NCHS). From 1985-1999, a number of states coded information from death certificates, including multiple-cause-of-death and usual industry and

occupation. A list can be found at:

http://www2a.cdc.gov/drds/WorldReportData/html/AppendixE.html. These data were entered into an electronic database, which allowed ongoing statistical evaluation of relationships between usual industry and occupation and mortality from specific diseases. In the case of diseases that often occur from non-occupational causes, such as asthma, COPD, and lung cancer, these mortality data were extremely useful for documenting risks associated with various industries and occupations. Unfortunately, since 2000, relatively few states have coded usual occupation and industry from death certificates and it has not been possible to do this type of analysis using nationally representative data. However, mortality surveillance remains a useful tool for tracking diseases strongly associated with occupational exposures, such as CWP, asbestosis, silicosis and mesothelioma.

As recognized by the NA-RDRP committee, developing new approaches to comprehensive morbidity and mortality surveillance for occupational respiratory diseases is an important need. To improve mortality surveillance, RDRP has strongly endorsed and supported efforts by the NIOSH Surveillance Program to develop methods for automated coding of industry and occupation data, such as that reported on death certificates. When developed, RDRP will also strongly support deploying these methods so that death certificate data from a larger, more nationally representative group of states will again be coded for usual industry and occupation. In addition, as a stopgap solution to fill the vacuum left by cessation of death certificate coding in 1999, the RDRP program has proposed to undertake case-control studies evaluating associations between selected respiratory disease mortality outcomes and industry/occupation. These studies will require less death certificates to be coded for industry

and occupation than was the case in routine, ongoing surveillance and thus will make nationally representative data for a few occupational respiratory conditions available at an affordable cost.

It is also important to develop new data streams for occupational respiratory disease surveillance, particularly morbidity surveillance. Workers' compensation data and data from the healthcare system are particularly important potential sources of information. While workers' compensation data suffers many of the same limitations as the BLS with regards to occupational respiratory disease, RDRP is working with the NIOSH Surveillance Program to develop mechanisms with insurance carriers to assess patterns and trends within their data. With regard to the healthcare system, if industry and occupation information could be crossed with information such as International Classification of Diseases (ICD) code, Current Procedural Terminology (CPT) code, and/or pharmaceutical usage data, important new data streams for occupational respiratory disease surveillance could be created. Sources of healthcare data might include groups such as healthcare payers (e.g., insurance companies or Centers for Medicare and Medicaid Services); healthcare providers (e.g., hospitals, health maintenance organizations, provider networks); and states.

Electronic health records provide a particularly important new opportunity. In recent years, healthcare providers have moved to convert health records to electronic format. Electronic health records have many important advantages over paper records, including improved ability to transfer clinical information between providers and improve quality of care. In 2004, the President set a goal for every U.S. citizen to have an electronic health record by 2014. In 2009, this goal was codified by the U.S. Congress (Steinbrook R. New Engl J Med 2009; 360:1057-1060). In 2005, the Office of the National Coordinator for Health Information Technology established the Health Information Technology Standards Panel (HITSP) to

harmonize and integrate health information standards to facilitate sharing information among organizations and systems (http://www.HITSP.org). Implementation testing of an initial set of standards began in January, 2008. If an approach to coding electronic health records for patient industry and occupation that was easy to use for the healthcare system could be developed and adopted as a standard, it would make these records a powerful tool for occupational respiratory disease surveillance. Thus, it is of critical importance for RDRP and other elements of NIOSH with an interest in surveillance to work with the public and private organizations engaged in developing standards and processes for electronic health records to develop efficient methods of recording information on industry, occupation, and employment status. RDRP is actively engaging with partners in this area and has representatives on a vital statistics group focused on the electronic processing of birth and death records. It also is represented on the Public Health Data Standards Consortium, an important group for developing standards for electronic health records.

RDRP must continue to collect and enhance surveillance data from a range of other sources. State-based surveillance is especially important. NIOSH currently funds 15 states to conduct "fundamental" surveillance, which includes pneumoconiosis hospitalization and mortality. Four of these states have funding to conduct enhanced surveillance for work-related asthma, and two for silicosis. Were funding to permit, it would be highly desirable to engage more states in these activities. RDRP is also involved in several national, population-based studies including the National Health and Nutrition Evaluation Survey (NHANES), the National Health Interview Survey (NHIS), and the Behavioral Risk Factor Surveillance System (BRFSS). These surveys are based in other parts of CDC, which charge RDRP to include questions in the surveys. Funding permitting, it would be desirable to have questions about industry, occupation,

workplace exposures and respiratory disease included in these surveys on an ongoing basis. Simply acquiring information as to the year of onset of respiratory diseases such as asthma would make the surveys more useful in assessing patterns of illness within occupations and industries.

In addition to respiratory health surveillance, tracking of potentially hazardous occupational respiratory exposures through hazard surveillance is also an important need. Such data is currently limited. The OSHA Integrated Management Information System (IMIS) is often used as a source of current exposure information. It includes data collected from workplaces undergoing compliance inspections and consultation surveys. Because these workplaces may not be representative of other workplaces not undergoing compliance inspections or requesting consultations, IMIS exposure data also may not be representative. Other compliance data may suffer from similar selection bias. Other surveillance systems, such as the Hazardous Substances Emergency Events Surveillance (HSEES) system, are more oriented to general environmental than occupational exposures. In an effort to collect nationally representative exposure information, NIOSH conducted the National Occupational Hazard Survey (NOHS) from 1972 to 1974, the National Occupational Exposure Survey (NOES) from 1981 to 1983, and the National Occupational Health Survey of Mining (NOHSM) from 1984 to 1989. Although these surveys have played a critical role in associating specific hazards with industries and occupations, they are now very dated. RDRP strongly supports efforts of the surveillance program to conduct updated, innovative, nationally representative hazard surveillance. An example of such surveillance is a current project (http://www.cdc.gov/niosh/docket/nioshdocket0135.html) that is focusing on the healthcare industry. It is using an online survey to collect information about work practices and hazardous

exposures, including respiratory exposures such as aerosolized medications (ribavirin, pentamidine, tobramycin), chemical sterilants (ethylene oxide, hydrogen peroxide gas plasma), high level disinfectants (glutaraldehyde, OPA, peracetic acid, hydrogen peroxide), and surgical smoke. If successful, similar surveys should be pursued in other industrial sectors.

Although the NIOSH Health Hazard Evaluations Program is not primarily a surveillance program, it plays a very important role in identifying new and emerging hazardous exposures and occupational respiratory diseases. Thus, it has a unique and important surveillance role. Maintaining this program and following up on the risks that it identifies are important RDRP priorities.

Whatever its source, dissemination of surveillance data to those who can use it is also an important RDRP priority. RDRP will continue to make extensive use of web-based communication. It will maintain the WoRLD report and develop new pages on the NIOSH website. It will also seek to communicate information via a range of other media.

Flavorings-Related Lung Disease: Since 2001, flavorings-related lung disease has been an important emerging occupational respiratory disease problem and an important focus of activity for RDRP (http://www.cdc.gov/niosh/topics/flavorings/). It is a previously unrecognized cause of severe and even fatal obstructive lung disease. In many of those with the condition who have undergone lung biopsy, the pathology has been that of constrictive bronchiolitis obliterans. Recent studies document that diacetyl, which is an important butter flavoring chemical, is a respiratory epithelial toxin. These studies support the ability of diacetyl vapor inhalation to cause flavorings-related lung disease. Other flavoring chemicals might also play a role.

Perhaps because RDRP first described severe disease in workers who made butter flavored microwave popcorn, a popular and seemingly harmless product, this occupational

disease has generated much attention from a range of stakeholders. On September 26, 2007, the House of Representatives passed H.R. 2693, the "Popcorn Workers Lung Disease Prevention Act." The act specified that the Secretary of Labor would be responsible for promulgation of a final standard not later than 2 years after enactment. The act did not become law, but it demonstrates the desire of stakeholders for regulations to protect workers from flavorings-related lung disease. On March 16, 2009 Secretary of Labor Hilda Solis made the following statement: "I am alarmed that workers exposed to food flavorings containing diacetyl may continue to be at risk of developing a potentially fatal lung disease. Exposure to this harmful chemical already has been linked to the deaths of three workers…These deaths are preventable, and it is imperative that the Labor Department move quickly to address exposure to food flavorings containing diacetyl…"

Thus, there is an immediate, high priority need for RDRP to provide the scientific information needed by OSHA for its efforts to regulate diacetyl in the workplace. A core need is to perform a quantitative risk assessment and recommend an appropriately protective exposure limit to OSHA. One issue to be addressed in this risk assessment is that the exposure assessment method previously used by NIOSH for diacetyl is known to underestimate exposures in the presence of high humidity. Thus, efforts are underway to develop a factor that corrects for this underestimation when epidemiological data that used the older exposure assessment method are applied to risk assessment. In addition, efforts are underway to develop, validate and recommend new exposure assessment methods that are more sensitive and not affected by humidity. Other work of immediate importance is to assess exposures to flavoring chemicals, including diacetyl, in a range of work settings where such chemicals are used; and to develop specific recommendations for engineering controls and personal protective equipment. Finally, a

number of basic toxicological questions remain to be elucidated. The mechanism of action of diacetyl remains unclear, as are the respiratory toxicities of other many other flavoring chemicals. Exploration of structure activity relationships might help to identify additional potential respiratory toxins and prioritize them for study. In addition, the effects of combined exposures need to be studied. For example, a recent study in animals suggests that combined exposure to another flavoring agent, butyric acid, might slightly increase the penetration of diacetyl into the lung.

Intermediate to Long-Term Priorities

This section will briefly address other high priorities according to RDRP strategic goal area. As previously noted, these high priorities were identified based on the NA-RDRP committee report, other inputs of the sort detailed above in the section on background and significance of the RDRP goals, and considerations of whether other groups would take on these issues if RDRP/NIOSH did not.

Prevent and reduce work-related airways diseases: Work-related asthma (WRA) is an extremely high priority. Within WRA, research to understand and prevent asthma induced by low molecular weight agents (LMW) such as isocyanates remains a very high priority. Relative to high molecular weight agents, the mechanism of action of low molecular weight agents is far less well understood. Mechanistic understanding might lead to improved diagnostic tools to document sensitization, which would greatly benefit secondary prevention. Also, practical issues of exposure assessment, exposure control, and medical monitoring are of great importance. A key consideration for asthma induced by low molecular weight agents is that these agents have primarily been studied by scientists interested in occupational disease. Thus, if RDRP did not address these, progress might be greatly slowed.

Other priorities in WRA include asthma in several occupational settings where the burden of asthma is high and the exposures complex, often including both sensitizers and irritants. These include asthma in healthcare settings and asthma associated with indoor air quality problems and damp buildings, the most frequent source of asthma-related Health Hazard Evaluation requests. Work-exacerbated asthma also remains a high priority area, as a large proportion of asthmatics experience exacerbation at work and prevention of this problem remains less well studied than prevention of asthma where work exposures are an etiological cause (a condition termed "occupational asthma").

Prevention of work-related COPD also remains an important priority. As suggested by the NA-RDRP committee, there is still a need for population-based studies documenting associations between industry, occupation, and COPD. There is also an important need for early, pre-clinical detection to provide opportunities for secondary prevention and for primary prevention among coworkers. In this regard, further development and validation of decline in spirometry performance over time as an early marker of COPD remains a priority. Development of other disease markers allowing preclinical detection would also be very desirable.

Prevent and reduce work-related interstitial lung diseases: Documentation that CWP continues to exist, and that severe CWP is occurring in miners as young as their 30s, makes CWP a high priority area. It is important to understand what is different about geographical "hot spots" for CWP and use this information to tailor prevention activities to those areas. The need for transitioning chest imaging surveillance to digital technology has already been discussed as an immediate, high priority.

Silicosis also continues to be a high priority condition. Exposure to crystalline silica is spread across many industries and is an emerging hazard in construction, where exposures in

jobs such as concrete grinding, masonry tuckpointing, highway repair, and concrete roof tile-cutting have been of great concern. Understanding relative toxicities of silica and potential abrasive blasting substitutes remains important, as is documentation of exposures and developing solutions where overexposures exist. Transitioning chest imaging surveillance to digital technology will benefit programs screening for silicosis.

Prevent and reduce work-related respiratory infectious diseases: Although work-related respiratory infectious diseases are of great importance, other agencies and parts of the Centers for Disease Control and Prevention (CDC) with a primary focus on infectious diseases in general are better equipped than RDRP to address issues of general clinical interest. The RDRP and NIOSH role is therefore to contribute to prevention in areas where NIOSH has special interest and expertise. The NA-RDRP committee especially identified respiratory protection for occupational respiratory infectious diseases as such an area. RDRP agrees with this recommendation and will work to support the NIOSH Personal Protective Technology (PPT) Program, which has the primary leadership role in the area of respiratory protection, to conduct research that improves prevention of work-related respiratory infectious diseases through respiratory protection. RDRP also highly prioritizes research in the areas of infectious agent exposure assessment and preventing occupational respiratory infectious disease transmission through engineering controls, since exposure assessment and engineering controls are areas of great strength in NIOSH.

Prevent and reduce work-related respiratory malignancies: As noted elsewhere in this report, the NIOSH Cancer Research Program has the primary leadership role in this area and RDRP plays a secondary, supportive role. Notwithstanding, RDRP has a particularly strong interest in two areas. The first is asbestos-related research. In part because of long latency,

asbestos continues to be an important cause of lung cancer, mesothelioma, and nonmalignant respiratory conditions including asbestosis and several types of pleural disease. There is important need to determine the usefulness of early disease markers for secondary prevention, such as the use of serum levels of soluble mesothelin-related peptide and osteopontin for early detection of mesothelioma. There is also an important need to modernize exposure and risk assessment for asbestos to utilize electron microscopy-based exposure metrics, thereby eliminating the need to assume that thin fibers not visible by light microscopy are present in fixed ratios to larger fibers that are visible by light microscopy. These and other issues of high priority are addressed in the NIOSH draft document, *Asbestos Fibers and Other Elongated Mineral Particles: State of the Science and Roadmap for Research* (http://www.cdc.gov/niosh/docket/NIOSHdocket0099B.html).

Another high priority is to complete a long-standing collaborative study being conducted by partners at NIOSH and the National Cancer Institute (NCI) to evaluate the role of diesel exhaust in lung cancer mortality. Over the years, stakeholders have expressed great interest in this study.

Prevent respiratory and other diseases potentially resulting from occupational exposures to nanomaterials: As noted elsewhere in this document, the NIOSH Nanotechnology Program plays a leading role in this area and RDRP plays a secondary, supportive role. The BSC has recently reviewed the NIOSH Nanotechnology Program and expressed its support for the program's activities. RDRP agrees with the BSC assessment of the importance of this area, particularly in light of emerging toxicology research documenting the respiratory tract as a potential target for inhaled nanoparticles, and will continue to engage with, and support, the program.

Section 4. Strategic Plan, Intramural Projects, and Extramural Grants by RDRP Strategic Goal Area

This section provides detailed information about intermediate and activity/output goals supporting each of the RDRP strategic goals. The hierarchy of goals is as follows: strategic goal supported by intermediate goal, intermediate goal supported by activity/output goal. These current goals reflect the NA review recommendations, which first started to be implemented by RDRP in fiscal year 2008. In addition, for each strategic goal area, current intramural projects and extramural grants are listed. Most extramural grant information was obtained directly from the NIH Computer Retrieval of Information on Scientific Products (CRISP) web page (http://crisp.cit.nih.gov/crisp/crisp_query.generate_screen) and is shown here as displayed in that system.

Although the strategic goal areas are largely organized according to disease types, RDRP recognizes that many types of activities and multidisciplinary engagement are needed to successfully address them. For example, surveillance is critically needed to document baseline conditions and the impact of intervention and prevention efforts. Research, education, communication, information dissemination, and providing support to standard-setting and regulatory groups are other examples of activities critical to addressing problems, influencing those that can make a difference, and achieving impact.

Strategic Goal 1: Prevent and reduce work-related airways diseases.

Intermediate Goal 1.1: prevent and reduce the full range of WRA, including work-exacerbated asthma; occupational asthma; and irritant-induced asthma.

Activity/Output Goal 1.1.1: assess the extent, severity, burden, and risk factors for WRA and approaches to prevention across a broad range of industries and occupations.

Activity/Output Goal 1.1.2: develop improved tools for detection of WRA by questionnaire or ambulatory spirometry.

Activity/Output Goal 1.1.3: 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.

Activity/Output Goal 1.1.4: 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.

Activity/Output Goal 1.1.5: evaluate the impact of indoor air quality on WRA and the effectiveness of building remediation in preventing WRA associated with poor indoor air quality.

Activity/Output Goal 1.1.6: develop and implement demonstration projects that address the role of screening and surveillance for WRA in occupational settings.

Activity/Output Goal 1.1.7: conduct basic research to better define the mechanisms of action of low molecular weight sensitizers and irritants capable of inducing WRA and to better characterize high molecular weight occupational allergens and their health effects.

Intermediate Goal 1.2: prevent and reduce work-related COPD.

Activity/Output Goal 1.2.1: conduct surveillance and epidemiological studies to assess the extent, severity, and burden of work-related COPD and identify industries and occupations associated with COPD.

Activity/Output Goal 1.2.2: conduct systematic population-based studies to better define groups of workers at greatest risk of COPD and guide development of preventive strategies.

Activity/Output Goal 1.2.3: improve tools such as longitudinal spirometry and respiratory questionnaires for early detection of occupationally-related COPD.

Activity/Output Goal 1.2.4: develop and improve methods for collecting, analyzing, and responding to the results of longitudinal pulmonary function testing to optimize identification and secondary prevention for individuals at risk of developing severe COPD.

Activity/Output Goal 1.2.5: promote the implementation of longitudinal pulmonary function testing in the workplace for surveillance and intervention in populations at risk for fixed airways obstruction.

Activity/Output Goal 1.2.6: study associations between irritant inhalation exposures during disasters, such as dust at the site of the World Trade Center (WTC) collapse, and development of obstructive lung disease (this objective overlaps with asthma prevention, since many affected individuals have reactive airways disease; and potentially will overlap with other long-term effects of WTC-related exposures).

Intermediate Goal 1.3: prevent and reduce flavorings-induced obstructive lung disease, including bronchiolitis obliterans.

Activity/Output Goal 1.3.1: conduct surveillance, epidemiological studies, and field studies to identify the full range of food production industries at risk for flavorings-induced lung disease.

Activity/Output Goal 1.3.2: develop and improve sampling and analytical methods for assessing exposure to diacetyl and other artificial flavorings.

Activity/Output Goal 1.3.3: develop protective recommendations for exposure assessment and engineering controls in work settings using artificial flavorings; disseminate information to improve recognition of flavorings-induced lung disease by a range of groups, including clinical practitioners, public health officials, facilities using artificial flavorings, and

workers using artificial flavorings; disseminate information and encourage healthcare providers to report cases of flavoring-induced lung disease to state health departments and NIOSH.

Activity/Output Goal 1.3.4: provide regulators with information needed to address current requests for Emergency Temporary Standards for diacetyl and the data and risk assessments they will need for worker protection over the long term.

Activity/Output Goal 1.3.5: 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.

Current RDRP Intramural Projects: Airways Diseases

	Name of Project	Project Officer
1	*Effect of Stainless Steel Welding Fume Particulate on Lung Immunity in Mice	Anderson, Stacey
2	*Lung Effects of Resistance Spot Welding Using Adhesives	Antonini, James
3	*Worker Monitoring Using Pulmonary Function Testing	Attfield, Michael
4	Multi-Ethnic Study of Atherosclerosis: Occupational Analysis (COPD component)	Baron, Sherry
5	*Spirometry Training Course Certification	Beeckman-Wagner, LuAnn
6	Development of New Immunodiagnostic and Detection Techniques for Indoor Fungi	Beezhold, Donald
7	Identification of Occupational Allergens	Beezhold, Donald
8	*Validation Studies in Occupational Immunotoxicology	Biagini, Raymond
9	Orthophthaladehyde (OPA) Hazard Assessment	Chen, Lilia
10	Building Related Asthma Research: Maine Public Schools	Cox-Ganser, Jean
11	Flavoring Risk Assessment	Dankovic, David

12	Diacetyl Engineering Controls Research	Dunn, Kevin
13	Isocyanate Method Development and Exposure Assessment	Ernst, M. Kathleen
14	Indoor Environment Nitrate Radical Chemistry	Ham, Jason
15	Work-related Asthma Research and Prevention	Henneberger, Paul
16	The Occupational Burden of COPD	Hnizdo, Eva
17	Criteria Document: Diacetyl	Hodson, Laura
18	Pathophysiology of Popcorn Workers' Lung	Hubbs, Ann
19	Immune and Inflammatory Aspects of Occupational Rhinitis	Johnson, Victor
20	Orthophthaladehyde (OPA) Hazard Assessment	Johnson, Victor
21	*Prevention of Occupational Respiratory Disease in Ag	Kullman, Greg
22	Survey of Chemical Exposure in the Biodiesel Industry	Law, Brandon
23	Exposure Assessment by Exhaled Breath/ Physiological Sampling	Lee, Emily
24	Revised REL for Glutaraldehyde	MacMahon, Kathleen
25	Information Campaign to Prevent Flavoring-Induced Lung Disease	Okun, Andrea
26	Worker Respiratory Health Post-Remediation of Water Damage	Park, Ju-Hyeong
27	Direct Reading Instrument Metrology	Pearce, Terri
28	Manicurists' Exposure, Health, & Exposure Interventions	Reutman, Susan
29	Cutaneous Bioactivity of Xenobiotics: Hapten vs. Prohapten	Siegel, Paul
30	Trimilletic Anhydride-Induced Late Phase Airway Responses	Siegel, Paul
31	Medical Monitoring for Workers Using Isocyanates	Storey, Eileen
32	Diacetyl Exposure Assessment Research Study	Streicher, Robert
33	Exposures and Engineering Controls in the Flavoring Industry	Taylor-McKernan, LauraLynn

34	Dermal Sensitization Testing	to be named
35	Orthophthaladehyde (OPA) Hazard Assessment	Toraason, Mark
36	Indoor Chemistry of Consumer Product Mixtures	Wells, John
37	Ozone Chemistry on Indoor Surfaces	Wells, John
	Genetics in Occupational Diseases	Yucesoy, Berran
38	Immunotoxicity of Workplace Xenobiotics in Humans	Yucesoy, Berran
39	Occupational Asthma: Inflammation and Workplace Diseases	Yucesoy, Berran

*Denotes project listed for >1 strategic goal

Current RDRP Extramural Grants: Airways Diseases

	Grant Title	PI	Institution	Dates
1	Bioaerosols in Midwest greenhouses and respiratory symptoms among workers	Adhikari, Atin	University of Cincinnati	(08/08-07/10)
2	*Control of Workplace Diesel Exhaust Particulate	Armendariz, Alfredo	Southern Methodist University	(08/05-07/09)
3	Genetic susceptibility to occupational asthma	Bernstein, David	University of Cincinnati	(09/06-08/10)
4	Lung Disease in Chinese Textile Workers	Christiani, David	Harvard University	(09/95-06/10)
5	Respiratory Effects in Workers From Post-Katrina Related Airborne Exposures	Glindmeyer, Henry	Tulane University	(08/07-07/12)
6	Longitudinal Study of Respiratory Function in Aluminum Smelter Workers	Gulati, Mridu	Yale	(09/06-08/09)
7	Screening for Obstructive Sleep Apnea in Commercial Drivers	Gurubhagavatula, Indira	University of Pennsylvania	(08/07-07/10)
8	Towards a better understanding work-aggravated asthma	Lemiere, Catherine	Hospital du Sacre-Coeur de Montreal	(09/05-08/10)
9	*Design/Advanced Electrostatic Sampler for Total Bioaerosols	Mainelis, Gediminas	Rutgers	(08/06-07/09)
10	*Microbiological Characterization and Mitigation of Bioaerosols in CAFOs	Pace, Norman	University of Colorado, Boulder	(09/06-09/10)
11	*Respiratory protection against bioaerosols in agriculture	Reponen, Tina	University of Cincinnati	(08/07-07/10)
12	Organic dust epithelial PKC activation and airway disease	Romberger, Debra	University of Nebraska Medical Center	(08/06-07/10)
13	*Occupational injury and illness surveillance	Rosenman, Kenneth	Michigan State University	(07/05-06/10)

14	Farm worker family health cohort study	Schenker, Marc	University of California	(04/08-03/13)
15	Development and validation of a woodsmoke biomarker in urine	Simpson, Christopher	University of Washington	(09/07-08/09)
16	*HSPH center for excellence to promote a healthier workforce	Sorensen, Gloria	Harvard	(09/07-08/11)
17	*Antibiofilm tubing to reduce occupational exposure to biohazards in dentistry	Sun, Yuyu	University of South Dakota	(06/08-05/10)

*Denotes project listed for >1 strategic goal

Strategic Goal 2: Prevent and reduce work-related interstitial lung diseases

Intermediate Goal 2.1: prevent and reduce coal mine dust-induced respiratory diseases, with primary focus in this intermediate goal on CWP.

Activity/Output Goal 2.1.1: improve technologies for dust assessment and dust control in coal mining. Provide technical guidance for the use of a personal dust monitor for real-time assessments of dust exposure.

Activity/Output Goal 2.1.2: identify state-of-the-art technologies for controlling coal mine dust exposures and transfer this information to industry through a series of regional dust control workshops by October 2012.

Activity/Output Goal 2.1.3: perform x-ray surveillance for CWP to monitor the extent and severity of the problem. Investigate the nature and causes of geographic "hot spots" of pneumoconiosis, in part by completing a comprehensive program of mine-site sampling to assess the impact of geology, control technology and mining practices. Survey mines in hot-spot and non-hot-spot areas of the coal fields to assist in identifying factors associated with rapid disease development and progression.

Activity/Output Goal 2.1.4: engage MSHA in a dialogue with the aim of adopting the NIOSH REL of 1.0 mg/m3 as the actual permissible exposure limit (PEL) for coal mine dust

exposure. As the enactment of such a PEL would be solely the domain of MSHA, we have no control over the process or timeframe.

Activity/Output Goal 2.1.5: 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 Office classification system. Transition NIOSH's mandated surveillance activities, including the B reader certification program, to use of digital chest imaging.

Intermediate Goal 2.2: prevent and reduce silica-induced respiratory diseases, with primary focus in this intermediate goal on silicosis.

Activity/Output Goal 2.2.1: conduct hazard surveillance to track silica exposures and seek new or overlooked sources of silica exposure to workers.

Activity/Output Goal 2.2.2: reduce hazards associated with abrasive silica sand blasting by evaluating the relative respiratory toxicities of silica vs. abrasive blasting alternatives such as coal slag, garnet, steel grit, crushed glass, and specular hematite.

Activity/Output Goal 2.2.3: develop, improve and validate sampling and analytical methods for assessing exposures to silica.

Activity/Output Goal 2.2.4: develop mining control technologies to reduce or eliminate silica exposure, which would include dust reduction or particle coating. Transfer information on these silica control technologies to the metal/non-metal mining industry through a series of regional workshops.

Activity/Output Goal 2.2.5: develop and improve control technologies to reduce or eliminate silica exposures across a range of occupational settings where silica is a known

problem (mining, construction, abrasive blasting, foundries, dental laboratories, etc.) and in new occupational settings where silica exposure may appear as an emerging problem.

Activity/Output Goal 2.2.6: develop and validate approaches to early detection for silicosis such as new approaches to chest imaging and assessment of biomarkers associated with silica exposure and interstitial lung disease.

Intermediate Goal 2.3: prevent and reduce "fiber"-induced respiratory diseases.

Activity/Output Goal 2.3.1: obtain public and stakeholder comment and finalize a document that identifies current research gaps and priorities in the area of respiratory diseases caused by inhalation exposure to asbestos and other elongated mineral particles ("Asbestos and other mineral fibers: a roadmap for scientific research").

Activity/Output Goal 2.3.2: develop improved sampling and analytical methods for assessing exposure to asbestos and other elongated mineral particles.

Activity/Output Goal 2.3.3: conduct hazard surveillance to document workers, job tasks, and industries in which workers are exposed to various types of elongated mineral particles, including elongated cleavage fragments of amphibole minerals.

Activity/Output Goal 2.3.4: conduct epidemiological investigations to better characterize the relationships between exposures to asbestos and other elongated mineral particles, including elongated cleavage fragments of amphibole minerals, and health effects such as interstitial lung disease, lung cancer, and mesothelioma.

Activity/Output Goal 2.3.5: perform basic toxicological research to elucidate the important determinants of toxicity for asbestos fibers and other elongated mineral particles and to improve the ability to predict the toxic potential of natural and man-made inorganic fibers.

Activity/Output Goal 2.3.6: develop and publish a NIOSH Alert on flock and flock workers' lung.

Intermediate Goal 2.4: prevent and reduce beryllium sensitization and chronic beryllium disease.

Activity/Output Goal 2.4.1: evaluate the effectiveness of a comprehensive preventive program that includes reduction of skin exposures at a copper-beryllium alloy facility in reducing immunological sensitization to beryllium and chronic beryllium disease.

Activity/Output Goal 2.4.2: evaluate the effectiveness of a comprehensive preventive program that includes reduction of skin exposures at a beryllium manufacturing facility in reducing immunological sensitization to beryllium and chronic beryllium disease.

Activity/Output Goal 2.4.3: perform a cohort study assessing the longitudinal development of immunological sensitization to beryllium and chronic beryllium disease in workers at a beryllium oxide/ceramics plant over an eleven-year follow-up period.

Activity/Output Goal 2.4.4: develop, refine and validate improved methods to assess exposure to beryllium; and determine whether complex exposure metrics taking estimated dissolved beryllium dose and dermal exposure into account are better predictors of adverse health effects than simple mass-based exposure metrics.

Activity/Output Goal 2.4.5: perform epidemiological and laboratory studies to elucidate mechanisms of beryllium-induced disease, including studies that clarify the role of genetic susceptibility in developing immunological sensitization to beryllium and chronic beryllium disease; and the role of gene-environment interactions.

Current RDRP Intramural Projects: Interstitial Lung Diseases

	Name of Project	Project Officer

1	*Worker Monitoring Using Pulmonary Function Testing	Attfield, Michael
2	Worker Monitoring Using Imaging Techniques	Attfield, Michael
3	*Spirometry Training Course Certification	Beeckman-Wagner, LuAnn
4	Reducing Silica Hazards in the Metal/Nonmetal Industry	Chekan, Gregory
5	State-of-the-Art Technology for Controlling Coal and Silica Dust	Colinet, Jay
6	Dermal Exposure and Sensitization Risk (beryllium program)	Day, Gregory
7	Preventing Silicosis in Highway Construction Through a State-based Partnership	Echt, Alan
8	Differential Toxicity of Beryllium Materials	Hubbs, Ann
9	Core and Research-to-Practice Coordination (beryllium program)	Kreiss, Kathleen
10	*Risk Assessment Methods for Particles and Fibers	Kuempel, Eileen
11	*Prevention of Occupational Respiratory Disease in Ag	Kullman, Greg
12	Controlling Respirable Dust on Continuous Mining Operations	Listak, Jeffery
13	Induction of Lung Fibrosis by Cerium Oxide in Diesel Exhaust	Ma, Jane
14	Surface Silanol Detection in Silicon-containing Materials	Murray, David
15	*Silica, Lung Cancer & Respiratory Disease Quantitative Risk	Park, Robert
16	Dust Control Technology for Black Lung Hot Spots	Pollock, Douglas
17	Dust Control for Longwall Mining	Potts, Drew
18	Global Silica Information Dissemination	Rice, Faye
19	Beryllium Disease Surveillance/ Research	Schuler, Christine

20	Computational Studies of Mineral Dust Properties	Snyder, James
21	Bioavailability Estimates and Health Outcomes (beryllium program)	Stefaniak, Aleks
22	Exposure Assessment Tools for Airborne Sensitizers	Stefaniak, Aleks
23	Tungsten Oxide Fiber Dissolution in Artificial Lung Fluids	Stefaniak, Aleks
24	Long-Term Efficacy of a Preventive Program (beryllium program)	Thomas, Carrie
25	Workplace Solutions for Silica Control in Construction	Topmiller, Jennifer
26	Potential Biomarkers for Pulmonary Effects from Exposure to Iraq Ambient Air Dust	Vallyathan, Velayudhan
27	Lake Lynn Lab	Weiss, Eric
28	Coal Workers' Health Surveillance Program	Wolfe, Anita
29	Enhanced Coalworkers Health Surveillance Program	Wolfe, Anita
30	Respirable Silica Measurements with High Flow Rate Samplers	Wu, Yi-Hsuan

*Denotes project listed for >1 strategic goal

Current RDRP Extramural Grants: Interstitial Lung Diseases

	Grant Title	PI	Institution	Dates
1	Crystalline Silica and RSP Control Methods Effectiveness during Concrete Grinding	Akbar-Khanzadeh, Farhang	University of Toledo	(09/07-08/09)
2	Preventing falls, silica exposure with Latino construction workers	Azaroff, Lenore	University of Massachusetts, Lowell	(08/07-07/12)
3	*Occupational injury and illness surveillance	Rosenman, Kenneth	Michigan State University	(07/05-06/10)
4	*Improved Spray Scavenging of Particulates via Acoustical Excitation of Drop Oscillations	Saylor, John	Clemson	(08/08-07/11)
5	*HSPH center for excellence to promote a healthier workforce	Sorensen, Gloria	Harvard	(09/07-08/11)
6	Mycobacteria in metalworking fluids	Yadav, Jagiit	University of Cincinnati	(09/01-06/09)

*Denotes project listed for >1 strategic goal

Strategic Goal 3: Prevent and reduce work-related respiratory infectious diseases

Intermediate Goal 3.1: Develop improved approaches to detect and quantify exposures to airborne infectious agents and settled infectious agents with the potential to cause respiratory infection.

Activity/Output Goal 3.1.1: develop database of methods for anthrax exposure assessment.

Activity/Output Goal 3.1.2: develop and validate novel sampling and analytical methods for assessing exposures to airborne infectious agents such as influenza virus.

Activity/Output Goal 3.1.3: develop, improve and validate direct-reading methods for assessing exposures to airborne and settled infectious agents with the potential to cause respiratory infection.

Intermediate Goal 3.2: Elucidate pathogen and host factors underlying susceptibility to transmission of occupational respiratory infectious diseases.

Activity/Output Goal 3.2.1: evaluate the impact of occupational exposures on susceptibility to respiratory infection, including underlying mechanisms. Occupational exposures of current concern include welding fume and its constituents; diesel exhaust; residual oil fly ash (ROFA); silica; and potentially others, if evidence suggests that exposure increases risk of respiratory infection.

Activity/Output Goal 3.2.2: evaluate the impact of pathogen characteristics on airborne disease transmission, including aerosol size distribution; impact of factors such as temperature, humidity and UV irradiation on aerodynamic properties, viability and infectivity; and pathogen/environmental factors that affect re-aerosolization of settled agents. Use these findings

to develop approaches for predicting the relative importance of airborne and contact disease transmission.

Activity/Output Goal 3.2.3: Apply available basic and epidemiologic data to developing approaches to risk assessment for airborne transmission of occupational infectious agents.

Intermediate Goal 3.3: Reduce exposure to airborne occupational infectious agents through engineering controls.

Activity/Output Goal 3.3.1: Develop and disseminate information to improve engineering controls applicable to TB and other agents, including ventilation and modeling of air flow, air filtration, and disinfection via UV germicidal irradiation.

Activity/Output Goal 3.3.2: Develop, demonstrate, and disseminate methods for "expedient airborne isolation" that can be deployed in settings such as epidemics where there is high demand for airborne isolation rooms.

Intermediate Goal 3.4: Reduce exposure to airborne occupational infectious agents through respiratory protection.

Activity/Output Goal 3.4.1: develop respirators with better sealing characteristics through improved anthropomorphic facial panels; develop a total inward leakage standard that would provide consumers with an assessment of the fitting characteristics of respirators; and perform research to assess the optimal methods and frequency of fit-testing.

Activity/Output Goal 3.4.2: perform research to assess the possibility of decontamination and re-use of disposable N95 filtering face piece respirators under conditions of respirator shortage.

Activity/Output Goal 3.4.3: complete the development of Chemical, Biological, Radiological, and Nuclear respirator certification standards

Activity/Output Goal 3.4.4: develop and disseminate information products to improve the use of respirators

Intermediate Goal 3.5: Reduce the burden of airborne occupational respiratory infectious disease through improved medical screening methods.

Activity/Output Goal 3.5.1: develop and evaluate new methods in medical screening and surveillance for TB infection as an alternative to tuberculin skin testing.

Activity/Output Goal 3.5.2: develop improved strategies for early identification and isolation of infectious cases.

Intermediate Goal 3.6: Reduce the burden of airborne occupational respiratory infectious disease through coordination and collaboration with other elements of CDC.

Activity/Output Goal 3.6.1: continue to work with other elements of CDC in the implementation of the Federal Interagency TB Prevention Plan.

Activity/Output Goal 3.6.2: continue to work with other elements of CDC in the development and implementation of a pandemic influenza prevention plan including outreach to multiple industries.

Activity/Output Goal 3.6.3: continue to work with other elements of CDC in the development and implementation of a cross-CDC environmental microbiology research program.

Current RDRP Intramural Projects: Respiratory Infectious Diseases

	Name of Project	Project Officer
1	*Effect of Stainless Steel Welding Fume Particulate on Lung Immunity in Mice	Anderson, Stacey
2	*Lung Effects of Resistance Spot Welding Using Adhesives	Antonini, James

3	Computational Fluid Dynamics (CFD) in Control Technology	Bennett, James
4	*Validation Studies in Occupational Immunotoxicology	Biagini, Raymond
5	Assessing the TB Education Needs for Hispanic Immig. Workers	Eggerth, Donald
6	New Approaches to Medical Screening for Latent TB	Hettick, Justin
7	*Welding Fume Metals Exposure Matrix Determination	Keane, Michael
8	Aerosol Generation by Cough	Lindsley, William
9	Respirator & Surgical Mask Efficacy from Cough Aerosols	Lindsley, William
10	Pandemic Influenza Guidance and Educational Products	MacMahon, Kathleen
11	Expedient Airborne Isolation for Emergency Response Exercises	Mead, Kenneth
12	Demonstration and Surveillance Systems in Healthcare	Oke, Charles
13	N95 and P100 TIL Testing	Peterson, Jeffrey
14	Project BREATHE (Better Respirator Equipment Utilizing Advanced Technologies for Healthcare Employees)	Roberge, Raymond
15	No Fit Test Filtering Facepiece Workshop and Research Roadmap	Shaffer, Ronald
16	Reusability of Filtering Facepiece Respirators	Shaffer, Ronald
17	Metabolic Evaluation of N95 Respirator Use with Surgical Masks	Sinkule, Edward
18	Respirator & Surgical Mask Efficacy from Cough Aerosols	Szalajda, Jonathan
19	Respiratory Protection for Terrorist Threat / Standards Development	Szalajda, Jonathan
20	Total Inward Leakage	Szalajda, Jonathan
21	Total Inward Leakage - Other Classes of Respirators	Szalajda, Jonathan
22	Development of Computer-Aided Face-Fit Evaluation Models	Viscusi, Dennis and Zhuang, Ziqing
23	Frequency of Fit Testing	Viscusi, Dennis and Zhuang, Ziqing

24	Powered Air Purifying Respirator (PAPR) Standard	Vojtko, Richard
25	The Impact of Respirator Use on CO2 levels and O2 Saturation	Williams, Warren (Jon)

*Denotes project listed for >1 strategic goal

Current RDRP Extramural Grants: Respiratory Infectious Diseases

	Grant Title	PI	Institution	Dates
1	Experimental and Theoretical Study of Early Detection and Isolation Influenza	Celik, Ismail	West Virginia University	(08/06-07/09)
2	Development of a Highly Efficient Personal Sampler to collect Viable Bioaerosols	Cheng, Yung-Sung	Lovelace Biomedical and Environmental Institute	(09/07-08/10)
3	Particle sizes associated with airborne viruses	Goyal, Sagar	University of Minnesota Twin Cities	(09/08-08/12)
4	*Design/Advanced Electrostatic Sampler for Total Bioaerosols	Mainelis, Gediminas	Rutgers	(08/06-07/09)
5	Durable Visible Light-activated Antiviral Coatings for Fabrics Used for Personal	Mize, Patrick	Laamscience Inc. NC	(07/08-12/08)
6	Testing Interventions to Human-Generated Occupational Airborne Infections	Nardell, Edward	Brigham and Women's Hospital	(08/06-07/11)
7	*Microbiological Characterization and Mitigation of Bioaerosols in CAFOs	Pace, Norman	University of Colorado, Boulder	(09/06-09/10)
8	*Respiratory protection against bioaerosols in agriculture	Reponen, Tina	University of Cincinnati	(08/07-07/10)
9	*Antibiofilm tubing to reduce occupational exposure to biohazards in dentistry	Sun, Yuyu	University of South Dakota	(06/08-05/10)

*Denotes project listed for >1 strategic goal

Strategic Goal 4: Prevent and reduce work-related respiratory malignancies

The lead program for work-related cancer research, including research related to work-related respiratory cancers, is the NIOSH CRC program. As noted in the NA report on NIOSH respiratory diseases research, respiratory cancers are best approached within the context of a comprehensive cancer program. This is because a single type of carcinogenic exposure may cause many types of cancer. Also, many research and prevention approaches and issues are

common to many types of cancer. The goals specified in this section are those of special interest to the RDRP.

Intermediate Goal 4.1: reduce the incidence of work-related cancer through research, promotion of carcinogen-free workplaces, and international collaborations.

Activity/Output Goal 4.1.1: develop a national research plan for fiber-induced lung cancer by obtaining public comment, completing, disseminating and implementing priorities described in the document, "Asbestos and Other Mineral Fibers: A Roadmap for Scientific Research."

Activity/Output Goal 4.1.2: complete a reanalysis of respiratory malignancies in a cohort of chrysotile asbestos textile workers, previously studied only by light microscopy, whose exposures will be reanalyzed by EM. This will allow modeling of exposure-response that takes into account the vast majority of fibers that cannot be seen by the light microscopy-based methods previously used to study the cohort.

Activity/Output Goal 4.1.3: conduct epidemiological investigations to better characterize the relationships between exposures to asbestos and other elongated mineral particles, including elongated cleavage fragments of amphibole minerals, and health effects such as interstitial lung disease, lung cancer, and mesothelioma (same as in the interstitial lung diseases section).

Activity/Output Goal 4.1.4: Elucidate mechanisms of silica-induced lung cancer and reduce silica exposures (exposure reduction is discussed in the interstitial lung diseases section).

Activity/Output Goal 4.1.5: Evaluate a cohort of workers at three beryllium processing facilities to assess the association between lung cancer mortality and quantitative metrics of cumulative, average and peak exposures.

Activity/Output Goal 4.1.6: continue to follow the Colorado Plateau uranium miners' cohort to assess lung cancer risk associated with radon exposure 20 to 40 years after exposure, as well as interactions between radon exposure and smoking.

Activity/Output Goal 4.1.7: prevent and reduce respiratory diseases associated with exposure to diesel particulate matter (DPM), including lung cancer by: a) improving technologies for DPM assessment and control in underground mining; b) providing technical guidance, through workshops and intervention studies, for the use of control technologies and monitoring to reduce DPM exposure in miners; c) evaluating the relationship between a miner's exposure to DPM and mortality, including lung cancer mortality, in a large cohort study.

Activity/Output Goal 4.1.8: Evaluate the ability of single-walled and multi-walled carbon nanotubes to cause chromosomal abnormalities in target cell populations in vitro and in vivo.

Intermediate Goal 4.2: reduce mortality from work-related cancer by developing, testing, and implementing methods for early detection of work-related cancer.

Activity/Output Goal 4.2.1: evaluate whether a high density chromosomal marker array is able to identify patterns of deletions and duplications that are specific for occupationally-induced murine lung cancer and have potential utility for detection and/or diagnosis.

Activity/Output Goal 4.2.2: develop and validate biomarkers of exposure to occupational carcinogens or biomarkers for early detection of occupational respiratory cancer that address the needs of specific occupational groups at high lung cancer risk. Examples include evaluation of mineral dust-induced gene (*mdig*) expression for the early detection of silica-induced lung cancer and the used of blood biomarkers such as serum osteopontin or soluble mesothelin-related peptide for the early detection of mesothelioma.

Current RDRP Intramural Projects: Respiratory Malignancies

	Name of Project	Project Officer
1	Mortality Among Independent Owner-operator Truck Drivers	Alterman, Toni
2	Case Control Study of Lung Cancer & Diesel Exhaust in Mines	Attfield, Michael
3	Ultrafine Aerosols from Diesel-Powered Equipment	Bugarski, Aleksandar
4	Mineral Dust-Induced Gene (MDIG) & Occupational Lung Disease	Chen, Fei
5	*Welding Fume Metals Exposure Matrix Determination	Keane, Michael
6	*Risk Assessment Methods for Particles and Fibers	Kuempel, Eileen
7	Evaluation and Implementation of Diesel Emission Controls	Mischler, Steven
8	Measuring Diesel Particulate Matter in Underground Mines	Noll, James
9	*Silica, Lung Cancer & Respiratory Disease Quantitative Risk	Park, Robert
10	Genetic Fingerprint of Mouse Lung Cancer	Reynolds, Steve
11	Beryllium and lung cancer risk at seven beryllium processing facilities	Schubauer-Berigan, Mary
12	Development of Epidemiology Research Methods	Schubauer-Berigan, Mary
13	Radon exposure and lung cancer risk with extended follow-up of the Colorado Plateau miners cohort	Schubauer-Berigan, Mary
14	Fernald Mortality Update	Silver, Sharon
15	Collection and Analysis Techniques for IC Engine Exhaust Particulate Matter	Original PI deceased - PI TBD

*Denotes project listed for >1 strategic goal

Current RDRP Extramural Grants: Respiratory Malignancies

	Grant Title	PI	Institute	Dates
1	Endotoxin and Lung Cancer: Separating Healthy Worker Bias From Biologic Mechanism	Applebaum, Katie	Boston University	(08/08-07/11)
2	*Control of Workplace Diesel Exhaust Particulate	Armendariz, Alfredo	Southern Methodist University	(08/05-07/09)

3	National Mesothelioma Virtual Bank for Translational Research	Becich, Michael	University of Pittsburgh	(09/08-08/11)
4	P53 Biomarker and Intervention in Occupational Cancer	Brandt-Rauf, Paul	Columbia University, NYC	(07/06-06/10)
5	Causal and Nonlinear Models of Cancer Risk Among Autoworkers	Eisen, Ellen	University of California Berkley	(08/07-07/10)
6	Chrysotile and lung cancer: time-related effects and pooled analysis	Loomis, Dana	University Nevada Reno	(08/08-07/09)
7	*Improved Spray Scavenging of Particulates via Acoustical Excitation of Drop Oscillations	Saylor, John	Clemson	(08/08-07/11)

*Denotes project listed for >1 strategic goal

Strategic Goal 5: Prevent respiratory and other diseases potentially resulting from occupational exposures to nanomaterials

Anticipating the potential hazards of nanomaterials and responding through a program of research, development of authoritative recommendations, and international collaborations has been a high priority NIOSH initiative for approximately 5 years. In the period since the RDRP evidence package was developed and the NA-RDRP evaluation conducted, nanotechnology-related activities at NIOSH have developed into a separate program with a separate intramural NORA funding stream. RDRP has a strong interest in nanotechnology, since the respiratory tract is an important route of entry and potential target for pathology induced by nanoparticles, whether engineered or the by-product of other processes. However, the NIOSH nanotechnology program has now matured into a separately managed, comprehensive program of research and service that has recently been reviewed by the BSC. Comments on nanotechnology research noted in the NA-RDRP review have previously been provided to the BSC as a component of the BSC review of nanotechnology. RDRP will continue to maintain a keen interest in nanomaterials and their potential impact on respiratory health, but will play a secondary, supportive role in the multidisciplinary and diverse NIOSH nanotechnology program. Full details of the NIOSH nanotechnology program, including intramural projects, extramural grants,

and strategic plan can be accessed via the NIOSH nanotechnology home page found at: http://www.cdc.gov/niosh/topics/nanotech/.

Intermediate Goal 5.1: determine the potential respiratory toxicities of nanomaterials.

Activity/Output Goal 5.1.1: perform basic in vitro and in vivo toxicology studies to evaluate for respiratory toxicity of nanoparticles and, if present, to identify the responsible nanoparticle characteristics and mechanisms of action underlying toxic effects.

Intermediate Goal 5.2: characterize respiratory exposures and measures used to reduce exposures, including engineering controls and respiratory protection, in work settings where engineered nanomaterials are produced or used.

Activity/Output Goal 5.2.1: develop partnerships and conduct field evaluations of facilities where nanomaterials are produced or used.

Intermediate Goal 5.3: develop guidance for facilities that produce or use nanomaterials.

Activity/Output Goal 5.3.1: continue to provide up to date guidance documents for primary and secondary prevention of respiratory diseases potentially caused by nanomaterials.

Current RDRP Intramural Projects: Nanomaterials

	Name of Project	Project Officer
1	Workplace Monitoring of Carbon Nanofibers/Nanotubes	Birch, Eileen
2	Nanoaerosol Monitoring Methods	Birch, Eileen and Evans, Douglas
3	Systemic Microvascular Dysfunction: Effects of Ultrafine vs. Fine Particles	Castranova, Vincent
4	Determination of Diameter Distribution for Carbon Nanotubes by Raman Spectroscopy	Chirila, Madalina
5	Titanium Dioxide and Other Metal Oxides Exposure Assessment Study	Curwin, Brian
6	WC-Co Nanoparticles in Initiating Angiogenesis by Reactive Oxygen Species	Ding, Min

7	Dustiness of Nanomaterials	Evans, Douglas
8	NIOSH Alert "Preventing occupational exposure to carbon nanotubes"	Geraci, Charles
9	Development and Evaluation of Nanoaerosol Surface Area Measurement Methods	Ku, Bon-Ki
10	Nanoaerosol Surface Area Measurement Methods	Ku, Bon-Ki
11	Nanoparticles-Dosimetry and Risk Assessment	Kuempel, Eileen
12	Potential Effects of Silicon-based Nanowires on Lung Toxicity	Leonard, Stephen and Roberts, Jenny
13	Evaluation of the Pulmonary Deposition and Translocation of Nanomaterials	Mercer, Robert
14	Field Research Team	Methner, Mark and Geraci, Charles
15	Calm Air Chamber and Wind Tunnel Evaluation of Personal Aerosol Samplers for Nanoparticle Exposure Assessment	Pearce, Terri
16	Investigations of Multi-Walled Carbon Nanotube Toxicity	Porter, Dale
17	Pulmonary Toxicity of Metal Oxide Nanospheres and Nanowires	Porter, Dale
18	Cell-Based Assessment for Iron Nanoparticle-Induced Health Risks	Qian, Yong
19	Penetration of Nanoparticles through Respirators	Rengasamy, Samy
20	Specific Biomarkers for Unusual Toxicity of Nanomaterials	Rojanasakul, Liying
21	Potential Aneuploidy Following Exposure to Carbon Nanotubes	Sargent, Linda
22	Assessing the Feasibility of Industrywide Exposure and Epidemiology Studies of Workers Exposed to Engineered Nanomaterials	Schubauer-Berigan, Mary
23	Assessment of Carbonaceous Materials on Mutagenicity	Shvedova, Anna
24	Occupational Exposures and Potential Neurological Risks	Sriram, Krishnan
25	Nanoscale Reference Materials for Health Protection	Stefaniak, Aleks
26	Standard Determination of Nanoparticle Size	Stefaniak, Aleks
27	Ultrafine TiO2 Surface and Mass Concentration Sampling Method	Stefaniak, Aleks

Current RDRP Extramural Grants: Nanomaterials

	Grant Title	PI	Institute	Dates
1	Role of Surface Chemistry in the Toxicological Properties of Manufactured Nanoparticles	Dutta, Prabir	Ohio State University	(09/06-08/09)
2	Integrated approach to understanding toxicity of inhaled nanomaterials	Grassian, Vicki	University of Iowa	(04/08-03/12)
3	Lung Oxidative Stress/Inflammation By Carbon Nanotubes	Kagan, Valerian	University of Pittsburgh	(07/05-06/09)
4	Personal Exposure to Engineered Nanoparticles	Peters, Thomas	University of Iowa	(09/07-08/10)
5	A Personal Sampler for Assessing Inhaled Nanoparticle Exposures	Volkens, John	Colorado State Fort Collins	(07/08-06/10)
6	Monitor & Characterize Airborne Carbon Nanotube Particles	Xiong, Judy	NYU School of Medicine	(08/05-07/09)

Supplemental Information: Cross-Cutting Issues - Surveillance, Exposure Assessment, and Emergency Response

In addition to commenting on strategic goal areas, the NA-RDRP evaluation committee also commented on several cross-cutting areas of importance to RDRP, including surveillance, exposure assessment, and emergency response.

The following table shows some of the intramural projects in these areas that are not classifiable into individual RDRP disease-specific goal areas, but contribute instead to prevention of respiratory disease across a range of disease types. It should be recognized that additional NIOSH intramural projects, such as those related to general emergency response issues, contribute to respiratory disease prevention, but not as a primary focus.

Cross-Cutting Intramural Projects of Particular Interest to RDRP: Surveillance, Exposure Assessment, and Emerging Issues

	Name of Project	Project Officer
Surveillance		
1	State-Based Surveillance Activities	Filios, Margaret
2	Occupational Lung Disease Surveillance Dissemination	Mazurek, Jacek
3	Health & Hazard Surveillance Systems: Development & Analysis	Schleiff, Patricia
Exposure Assessment		
1	Analytical Method Development for Emerging Problems	Brown, Kenneth
2	Methods Development and Analytical Support for Field Research	Key-Schwartz, Rose
3	NIOSH Manual of Analytical Methods Cooperative Research	Schlecht, Paul
4	Aerosol Exposure Assessment	Volkwein, John
Emerging Issues		
1	Emerging Issues in ORD Surveillance	Attfield, Michael
2	Emerging Issues in Occup Respiratory Disease Lab Research	Coffey, Christopher
3	Emerging Issues in Occup Respir Dis Epidemiology	Kreiss, Kathleen

The following table shows extramural grants in the area of exposure assessment that are not focused on a specific agent and thus are not classifiable into one of the specific RDRP goal areas. Exposure assessment grants focused on specific agents have already been presented in association with their RDRP goal areas. The table also shows World Trade Center-related

extramural grants, which are of great interest to RDRP because of the high prevalence of respiratory problems in World Trade Center responders.

Cross-Cutting Extramural Grants of Particular Interest to RDRP: Exposure Assessment (not focused on a particular agent / disease) and World Trade Center (WTC) –Related

	Grant Title	PI	Institute	Dates
Exp. Assess				
1	Computational fluid dynamics of particle inhalability at low windspeeds	Anthony, Theresa	University of Arizona	(06/08-05/13)
2	Work, neighborhood, commuting and occupational health disparities	Chen, Jarvis	Harvard	(09/08-08/10)
3	Workplace Aerosol Sampling at Realistic Low Windspeeds	Vincent, James	University of Michigan Ann Arbor	(09/04-08/09)
4	Lung deposition sampler for inhalable aerosol	Volkens, John	Colorado State Fort Collins	(08/07-07/09)
WTC				
1	Occupational Safety and Health Surveillance in New York	Gelberg, Kitty	Center of Environmental Health	(07/05-06/10)
2	WTC RHC Data and Coordination Center	Herbert, Robin	Mount Sinai School of Medicine, NYC	(06/04-05/09)
3	NYC Fire Dept. Clinical Center for WTC Medicals	Kelly, Kerry	NYC Fire department	(07/04-06/09)
4	WTC Responder Health Consortium Clinical Center	Moline, Jacqueline	Mount Sinai School of Medicine, NYC	(07/04-06/09)
5	WTC Non-responder Program NYC Health and Hospitals Corp.	Reibman, John	NYC Health and Hospitals Corp.	(09/08-09/11)