

MEETING SUMMARY
PRESIDENT'S CANCER PANEL
ENVIRONMENTAL FACTORS IN CANCER

September 16, 2008
East Brunswick, New Jersey

OVERVIEW

This meeting was the first in the President's Cancer Panel's (PCP, the Panel) 2008/2009 series on *Environmental Factors in Cancer*. The meeting focused on industrial and manufacturing exposures as they relate to cancer risk. The agenda for the meeting was organized into three discussion panels.

PARTICIPANTS

President's Cancer Panel (PCP)

LaSalle D. Leffall, Jr., M.D., F.A.C.S., Chair

Margaret Kripke, Ph.D.

National Cancer Institute (NCI), National Institutes of Health (NIH)

Abby Sandler, Ph.D., Executive Secretary, PCP, NCI

Panelists

Richard Clapp, D.Sc., M.P.H., Professor, Department of Environmental Health, Boston University School of Public Health

Devra Lee Davis, Ph.D., M.P.H., Head, Center for Environmental Oncology, University of Pittsburgh Cancer Institute, and Professor of Epidemiology, University of Pittsburgh Graduate School of Public Health

Adam M. Finkel, Sc.D., Professor of Environmental and Occupational Health, University of Medicine and Dentistry of New Jersey, School of Public Health, and Fellow and Executive Director, Penn Program on Regulation, University of Pennsylvania Law School

Elizabeth T.H. Fontham, M.P.H., Dr.P.H., Dean, School of Public Health, Louisiana State University, Health Sciences Center

David Kriebel, Sc.D., Professor of Work Environment, School of Health and Environment, University of Massachusetts Lowell

Philip J. Landrigan, M.D., M.Sc., Ethel H. Wise Professor and Chair, Community and Preventive Medicine, Mount Sinai School of Medicine

Frank E. Mirer, Ph.D., C.I.H., Professor, Environmental and Occupational Health Sciences, Hunter College School of Health Sciences

Christopher J. Portier, Ph.D., Associate Director, National Institute of Environmental Health Sciences, and Director, Office of Risk Assessment Research

Jeanne Rizzo, R.N., President and CEO, Breast Cancer Fund

Paul Schulte, Ph.D., Director, Education and Information Division, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention

Jeanne Stellman, Ph.D., Professor and Chair, Environmental and Occupational Health Sciences, SUNY-Downstate Medical Center

Daniel Wartenberg, Ph.D., Professor, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School Department of Environmental and Occupational Medicine, Environmental and Occupational Health Sciences Institute

OPENING REMARKS—DR. LaSALLE D. LEFFALL, JR.

On behalf of the Panel, Dr. Leffall welcomed invited participants and the public to the meeting. He introduced Panel members, provided a brief overview of the history and purpose of the Panel, and described the aims of the current series of meetings.

PANEL I

DR. ELIZABETH T.H. FONTHAM:

OCCUPATIONAL CARCINOGENS – ENVIRONMENTAL CARCINOGENS: A FINE LINE

Background

Dr. Fontham is the first Dean of the Louisiana State University (LSU) School of Public Health and Professor of Epidemiology, as well as Professor of Pathology in the LSU School of Medicine. A graduate of Tulane University School of Public Health and Tropical Medicine, Dr. Fontham has been on the faculty in the LSU Health Sciences Center since 1980. She is Associate Director of the Stanley S. Scott Cancer Center and Senior Consultant Epidemiologist to the Louisiana Office of Public Health, Environmental Epidemiology and Toxicology. Dr. Fontham has served as a member of the NCI Board of Scientific Counselors; a member of the Board of Directors of the American College of Epidemiology, of which she is a Fellow; inaugural Assistant Editor of *Cancer Epidemiology Biomarkers and Prevention*; Chairman of the Scientific Editorial Board of the North American Association of Central Cancer Registries; and a contributing author for both the Surgeon General's Reports and the International Agency for Cancer Research (IARC) Carcinogenesis Monograph series.

Key Points

- There is a fine line between occupational and environmental carcinogens. Occupational exposures tend to be at a higher dose and affect a smaller population, whereas environmental exposures tend to occur at a lower dose and affect a larger population. High exposure levels in the workplace typically lead to the identification of human carcinogens, many of which are also found in soil, air, water, and consumer products.
- The process by which environmental exposures (i.e., any external exposure other than inherited germ line mutations) cause cancer is a complex, multistage process that may involve structural damage to DNA; alteration of gene function; interference with natural DNA repair; accelerated cell turnover; clonal proliferation; and reversion of damaged cells to primitive behavior. However, every opportunity for a molecular process to go awry is an opportunity for intervention, change, and prevention.
- Agencies responsible for both assessing risk and regulating occupational and environmental carcinogens include the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA).
- Cadmium exemplifies the overlap between occupational and environmental exposures—in this case, an occupational carcinogen which has found its way into the environment. The primary means by which this toxic chemical enters air, soil, and water is through manufacturing operations and products (e.g., electroplating, production of refined metal,

batteries, and phosphate fertilizers). Fertilized soils can contain four to six times higher levels of cadmium than neighboring unfertilized soils; seafood and grains tend to be a primary exposure source depending on where in the United States you live.

- An area in southern Louisiana called Acadiana or Cajun Country has long had high incidence rates of pancreatic cancer for all residents, regardless of ethnicity. There is a three- to four-fold higher level of cadmium in Louisiana-grown rice and at least a four-fold increased risk of pancreatic cancer associated with excretion of cadmium in urine. There are also substantial levels of cadmium in crawfish, which are pond-raised using the same farming area as the rice. However, while cadmium is regulated in the workplace, its presence in the food supply is not tested.
- Secondhand smoke, also known as “environmental tobacco smoke,” is an example of an environmental carcinogen that has created occupational risks and has not been well regulated in the workplace. In 2004, IARC noted that occupational exposure to secondhand smoke is associated with an approximately 20 percent increased risk of lung cancer. Some cities and states have passed clean indoor air laws, prohibiting smoking in buildings other than residences, but often with exemptions, most notably for bars and casinos. The U.S. lacks nationwide regulation, and exemptions place employees who are subjected to continuous 8-hour shifts of tobacco smoke from customers and other employees at risk; this “environmental carcinogen” is also an occupational carcinogen.
- Carcinogenicity and toxicity testing of chemicals should be conducted prior to their introduction into consumer use. Only 2 percent of the 80,000 to 100,000 chemicals currently in use have been tested; enhanced, fast-track methods of testing chemicals need to be adopted. This should be a high priority for regulators, as occupational and environmental exposures are both involuntary and preventable.
- Research methods development and increased federal funding of research (both intramural and extramural) are needed to assess occupational and environmental exposures. Cohort studies (i.e., occupational based, population based, case control, and prospective) need to continue to be strongly supported.
- High-risk groups (e.g., employees in small businesses, migrant and contract workers, women, children, and the international workforce) need to be addressed in research efforts; occupational exposure risks to these groups have historically been ignored.
- A policy to prevent rather than reduce exposures needs to be adopted whenever possible. In addition, it is necessary to educate the workforce and general public about known and suspected carcinogenic exposures, alternatives to these exposures, and accompanying cost-benefit tradeoffs.

DR. ADAM M. FINKEL:

THERE IS NO “WAR” ON OCCUPATIONAL CANCER

Background

Dr. Finkel is a Professor of Environmental and Occupational Health at the University of Medicine and Dentistry of New Jersey (UMDNJ) School of Public Health, and Executive Director of the Penn Program on Regulation at the University of Pennsylvania Law School. From 2000 to 2003, Dr. Finkel was Regional Administrator for the U.S. Occupational Safety and Health Administration (OSHA) in Denver, Colorado, responsible for regulatory enforcement, compliance assistance, and outreach activities in CO, MT, ND, SD, UT, and WY. From 1995 to 2000, he was Director of Health Standards Programs at OSHA headquarters and was responsible for promulgating and evaluating regulations to protect the nation’s workers from chemical,

radiological, and biological hazards. At OSHA, Dr. Finkel also negotiated several national “enforceable partnerships” bringing manufacturers, customers, and labor unions together to provide worker protections beyond what could have been achieved by command-and-control regulation.

Key Points

- An immediate, feasible, and long overdue action to reduce the cancer burden is to look at the workplace as a target of opportunity. It has been suggested that the annual cancer risk resulting from occupational exposures could range from 25,000 to 60,000 deaths per year, making it the eighth leading cause of death in the U.S.
- In the 38 years since the effort commenced, the federal government has done little to assess and reduce workplace exposures to carcinogens. There are two ways to view this problem: the number of people exposed to a carcinogen who succumb to cancer versus the risk of cancer faced by subgroups, e.g., individuals working in certain occupations. The individual probability of getting cancer faced by workers is much greater than what is accepted in the general population.
- EPA has a Congressional mandate to reduce lifetime excess cancer risks to below one in 100,000, whereas OSHA only regulates risk to one in 1,000; a 1,000-fold greater risk is accepted in the workplace. Furthermore, a new OSHA standard states that a 2.5 percent annual risk of lung cancer is acceptable for workers exposed to chromium.
- OSHA’s concern is health and safety in the workplace; unfortunately, the majority of resources are concentrated on safety problems (e.g., falling off buildings, electrical hazards) and not health hazards, which cause more occupational-related deaths per year. OSHA devotes roughly 90 percent of its resources to safety hazards and only 10 percent to health hazards. This asymmetry can partly be attributed to the fact that OSHA was a safety agency at its inception.
- It takes more time for OSHA to do a health inspection than a safety inspection. When OSHA is trying to increase inspection numbers it is more efficient to focus on safety. The number of OSHA health inspections in which samples (air, bulk, wipe) are collected nationwide each year appears to be well under 10,000.
- OSHA would benefit from adopting a health targeting system to enforce standards—i.e., a system that supported inspection of health hazards of special intensity or interest. For example, the last major new substance-specific health standard set by OSHA was in 1997 for methylene chloride. However, despite increased detection of methylene chloride over health standard limits during routine inspections, the number of inspections has declined. There is currently no system to focus inspection resources where they are most needed.
- Penalties for violating OSHA health standards appear to be far lower than penalties for violating safety standards.
- Congress should enact a Workplace Clean Air Act that includes reorganizing occupational health functions in the federal government. EPA and OSHA currently have a negating relationship and often end up moving pollution from the workplace to the environment and vice versa. Creating a structure for these agencies to work together would be good for workers, the environment, and industry.

DR. RICHARD CLAPP:

AVOIDABLE OCCUPATIONAL AND ENVIRONMENTAL CAUSES OF CANCER

Background

Dr. Clapp is a Professor of Environmental Health, Boston University School of Public Health, and Adjunct Professor at the University of Massachusetts, Lowell. He received his Masters degree in public health from the Harvard School of Public Health and his D.Sc. from Boston University School of Public Health. Dr. Clapp is an epidemiologist with over 30 years of experience in public health practice, teaching, and consulting. He served as Director of the Massachusetts Cancer Registry from 1980 to 1989 and Co-Chair of Greater Boston Physicians for Social Responsibility from 1999 to 2008. His research has included studies of cancer around nuclear facilities, in military veterans, in workers, and in communities with toxic exposures. He received an award for “Science for the Benefit of Environmental Health” in 2006.

Key Points

- There is an historical imbalance in the allocation of resources to cancer control and prevention in the United States. The NCI budget has doubled in the past 10 years, with an enormous amount of funds going to genome-wide association studies and molecular mechanisms research. Conversely, the NCI Occupational and Environmental Epidemiology Branch has had level funding and is proposed to have a 3 percent cut in the next fiscal year. This Branch is a vital resource in the efforts to understand occupational and environmental carcinogenesis; the level of support for this kind of work needs to be increased.
- In 1981, Sir Richard Doll and Richard Peto published a paper on attributable causes of cancer, which minimized the attributable portion of cancer deaths due to occupational-related (then pollution-related) exposures. This resulted in a low priority attributed to occupational exposures or pollution. In recent years, researchers have looked at the limitations of Doll and Peto’s analysis and have found it to be inadequate. The focus needs to be taken off of trying to quantify exposures in terms of attribution to cancer risk—a nearly impossible task because exposures interact with one another and not all avoidable causes are known—and placed on preventable exposures.
- IARC has evaluated over 900 potential carcinogens; they have found 102 to be carcinogenic to humans, with 28 or 29 of those being occupationally-related.
- The current mechanistic understanding of cancer is that it is a multi-factorial, multi-causal, long-term process that can be influenced at various points by environmental exposures. This means there are multiple opportunities for prevention of exposure; researchers and policy-makers need to act on what they know.
- Childhood cancer incidence has been steadily rising in the last three decades, and there are a number of known environmental and occupational exposures that increase cancer risk—exposure to ionizing radiation through prenatal X-rays has been strongly linked to cancer; other links include pesticides, secondhand smoke, and solvents. Further information on the evidence of documented links to cancer can be found in the Toxicant and Disease Database at <http://database.healthandenvironment.org/>.
- As evidenced by tobacco control efforts in Canada, primary prevention has a positive effect on overall environmental health. That is, if people are less able to afford to buy cigarettes or cannot use tobacco in public places, exposure to tobacco-related carcinogens by smokers and others nearby is reduced. This has contributed to a decline in lung cancer in Canada, and to some extent in the United States.

- A generic carcinogens policy needs to be adopted. Such a policy would require new chemicals to be regulated at the outset if they are similar to a substance already classified as harmful and carcinogenic. Other needed prevention efforts include vigorously enforcing existing workplace and environmental carcinogen regulations and exposure limits, as well as promoting alternative research such as green chemistry.

DR. CHRISTOPHER PORTIER:

PRIORITIES FOR RESEARCH AND PREVENTION OF OCCUPATIONAL CANCER

Background

Dr. Portier is an internationally recognized expert in the design, analysis, and interpretation of environmental health data with a focus on carcinogenicity. In his career, he has managed a large research organization and developed a strategic initiative for the National Toxicology Program that is recognized for its innovation. He has contributed to the development of cancer risk assessment guidelines for national (EPA, FDA) and international (Organization for Economic Cooperation and Development, International Center for Pesticide Safety and Health Risk Prevention, IARC, and the governments of Australia, Korea, and Japan) organizations. Dr. Portier led the U.S. evaluation by national and international scientists of electromagnetic fields, the first comprehensive review in this field. He has received numerous awards including the prestigious Spiegelman Award from the American Public Health Association and Outstanding Practitioner of the Year Award from the International Society for Risk Analysis.

Key Points

- The World Health Organization (WHO) defines the environment as “all the physical, chemical, and biological factors external to the human host and all related behaviors, excluding those natural environments that cannot be reasonably modified.” This definition, which includes tobacco, food, infections, etc., as part of the environment, needs to be considered when determining how to address environmental carcinogenic risks.
- The evaluation of cancer risks is a complicated interplay of science, economics, society, and the overall translation among the three sectors. Numerous agencies evaluate evidence and set up identification of carcinogenic hazards, including IARC and its monograph series; the National Toxicology Program and its *Report on Carcinogens* (the U.S. official list of carcinogens in the environment, food, and the workplace); the U.S. National Academy of Sciences, which conducts evaluations of environmental and occupational hazards; and the EPA, which sets numerous limits in regard to carcinogenic exposures.
- IARC offers a simple example of the evaluation process of carcinogenic hazards. Its evaluation is divided into three steps. First, each epidemiology and toxicology study is evaluated for contributing evidence. Then in different groups (i.e., humans and animals), evidence is defined in terms of whether there is sufficient, limited, or inadequate evidence of carcinogenicity, or whether it suggests a lack of carcinogenicity. These evaluations, along with other mechanistic and relevant data, are then used in an overall evaluation through which it is decided whether a compound is a *known*, *probable* or *possible* human carcinogen; *not classifiable*, or *probably not* carcinogenic to humans.
- A current barrier to the effective prevention of environmental and occupational disease is the translation of information from molecular and genome-wide studies to the development of intervention strategies. With high-throughput screening technology, thousands of compounds can be screened at one time, but there is a gap between the data obtained from these screenings and immediate human relevance. To bridge this gap, molecular- and tissue-level

interaction data obtained from high-throughput screenings can be categorized as high, middle, or low priority for further testing. High-priority compounds should be taken through second tier testing (i.e., animal studies) and be evaluated in a functioning organism. If one of many similar compounds is found to be positive for carcinogenicity, then the whole class of compounds should be regulated.

- Information obtained through high-throughput screenings of specific targets in cells can be efficiently analyzed with the assistance of databases such as the National Institute on Aging's Genetic Association Database. This database contains approximately 29,000 records of human gene phenotype relationships and provides insight to the pathways involved and relationship between cancer and immune disease.
- In addition to genes, NIH's Comparative Toxicogenomics Database looks at chemicals that affect disease pathways. Genomic, proteomic, and metabolomic data related to chemical exposures are collected and studied to see how those chemicals are changing gene expression on an individual gene-protein level. These data on protein changes can be linked to disease pathways, the pathways linked back to the chemicals, and the chemicals linked back to the disease. This provides a prediction tool of how certain unstudied chemicals might relate to disease in humans. This methodology has been used to create a chemical-disease interactome, which provides priorities for studying specific diseases for specific chemicals.
- Humans are exposed to a broad spectrum of chemicals in the environment. The route of exposure for some of these compounds tends to be a single source and should be regulated as such. However, the current policy of regulating independent sources does not reflect the cumulative health concerns of being exposed to multiple, concurrent toxic chemicals.

DISCUSSION AND CONCLUDING COMMENTS:

PANEL I

Key Points

- Economics and politics are both major barriers to the translation of research to regulatory application. Societal discussions about the implications of scientific findings also hinder the translation of science. The environmental and occupational risk assessment arena would benefit from the creation of an independent organization within the federal government that focuses solely on identification and quantification of hazardous exposures.
- New technologies are able to obtain data on biological reactivity in functioning cellular systems and will pave the way for more accurate prediction tools of disease and health risks.
- The literature already suggests an important link between heavy metal exposures (e.g., cadmium, arsenic) and pancreatic cancer. If and when IARC reevaluates cadmium, there should be enough human data complemented by animal and mechanistic studies for it to be classified as probably carcinogenic for humans in regard to pancreatic cancer.
- OSHA's predominant focus on safety rather than health is a regulatory problem born of structural and personnel issues; staff expertise is predominantly in the area of safety. This imbalance also stems from a public relations problem—it is difficult to attract public attention to silent epidemics of chronic disease, such as cancer.
- Doll and Peto's 1981 paper is no longer an accurate standard for assessing carcinogenic exposures; until a better standard is established, the IARC monograph panels are a balanced reference resource.

- Researchers and policy-makers need to aggressively pursue new research approaches (e.g., high-throughput screening) to efficiently identify and quantify carcinogens and to ensure that this information is incorporated into the regulatory process.

PANEL II

DR. PAUL SCHULTE:

PRIORITIES FOR RESEARCH AND PREVENTION OF OCCUPATIONAL CANCER

Background

Dr. Schulte is Director of the Education and Information Division and Manager of the Nanotechnology Research Center in the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC). From 1998-2005, he served as co-coordinator of the NIOSH Cancer Research Methods Team for the National Occupational Research Agenda. In 2005, he served as co-chair of the WHO Workshop on Mechanisms of Fibre Carcinogenesis and Assessment of Chrysotile Asbestos Substitutes. Dr. Schulte has served as a consultant to the International Agency for Research on Cancer and on the initial editorial board of the journal *Cancer Epidemiology Biomarkers and Prevention*. He has written numerous papers on the role of biological markers in cancer research and conducted extensive research on various occupational cancers and carcinogens.

Key Points

- The magnitude of the cancer burden related to occupation is still unclear; a better calculation of the amount of cancer attributable to occupation is needed. A recent study conducted by Leslie Rushton and colleagues in the U.K. found that 8 percent of cancers in men and 1.5 percent of cancers in women were attributable to occupation-related exposures. However, this approach only looked at six different types of cancer; the burden for all cancers due to occupational exposures is yet unknown. Also, areas where the occupational cancer burden particularly manifests itself—blue-collar, high-exposure industries such as mining, construction, manufacturing, and certain parts of the service sector—have not been specifically studied.
- The ongoing, uncontrolled occupational exposure to serious potential carcinogens identified by IARC poses harm to the health of workers and the greater public. There is a lack of regulation for many known and suspected occupational carcinogens, and the few permissible exposure levels or limits in place were based on acute toxic effects studies, not cancer studies. There are also numerous occupations for which an elevated cancer risk is documented, but for which a causal agent has not yet been identified (e.g., painters, rubber workers, dry cleaners, farmers, and welders). Investing resources and continuing to conduct research on occupational exposures is necessary because findings in the workplace are the basis for estimations of risks in the general environment.
- Methods to identify occupational carcinogens need to be improved; few new occupational carcinogens have been identified and strategic prioritization of data obtained from high-throughput screenings is necessary to improve carcinogenicity testing. Scientists should also consider the broader chemical environment when conducting high throughput screenings; people are exposed to myriad chemicals in the workplace and at home, and those mixtures need to be assessed.

- The lack of attention by clinicians to patient work history is a barrier to the assessment of occupational health risks. A systematic approach is needed to incorporate a person's work history into a broad range of health records, surveys, and medical care data systems. This enhanced surveillance also calls for disease tracking and long-term monitoring of specific high-risk groups (either known or emerging). For example, an area of potential high risk is working with nanoparticles; nanotechnology involves developing engineered fibers that may act similarly to asbestos (comprised of fibers in both the micron and nano range). Exposure registries of workers in this field, along with prospective studies, may be needed.
- Epidemiologic studies are critically important in identifying occupational hazards, but it is increasingly difficult to conduct these as the modern workforce changes job fields and locations frequently compared to the workforce of the 20th century. Studies designed to gather constant measures of exposures across different workplaces are needed to evaluate health risks associated with occupation. A useful approach would be to look at biologic changes that are precursors or intermediate markers on a path between exposure and disease, and use these endpoints to provide a strong indication of cancer risk in a population.
- Challenges in cancer risk assessment include translating the relevance of tumor changes in animals to humans, identifying mathematical models that consider a broad range of exposures and best predict low dose risks, and determining which mechanistic information can replace default assumptions regarding kinetics and metabolism as researchers extrapolate across species or groups.
- Improvements in the area of primary prevention entail designing processes to eliminate or minimize exposures, establishing standards to control exposures and monitor workers, and developing targeted control efforts for known and suspected carcinogens. NIOSH has recently embarked on a several-year initiative called Prevention Through Design with the purpose of designing out hazards for consumers and workers by modifying processes, tools, and buildings.

DR. DAVID KRIEBEL:

CANCER PREVENTION THROUGH A PRECAUTIONARY APPROACH TO ENVIRONMENTAL CHEMICALS

Background

Since 1988, Dr. Kriebel has been on the faculty of the Department of Work Environment, University of Massachusetts, Lowell, where he holds the rank of full professor. He is also the Co-Director of the Lowell Center for Sustainable Production, which collaborates with industries, government agencies, unions, and community organizations on the redesign of systems of production to make them healthier and more environmentally sound. Dr. Kriebel's research focuses on the epidemiology of occupational injuries, cancer, and nonmalignant respiratory disease. Through his research and teaching, he seeks to improve the translation of scientific research into policies and practices for public health.

Key Points

- Many chemicals that are known to be toxic or carcinogenic, such as metal working fluids, are not being regulated in the environment. For example, millions of workers are exposed to metal working fluids in the United States, despite evidence of carcinogenicity. The OSHA standard for regulating metalworking fluids in the workplace has not changed since 1970 and does not effectively protect workers from related cancer risk. In addition to the hazards of known carcinogens not being acted upon, new hazards are created faster than scientists can study them; approximately 1,000 new chemicals are introduced into commerce each year.

Scientists do not have the ability to perform toxicity or carcinogenicity testing at this magnitude; as a result, there is little or no safety information on most chemicals in use.

- The current regulatory approach is guided by the “reactionary principle”: requiring evidence of harm before taking preventive action; placing the burden on the public and government to show that individual chemicals are harmful; failing to consider potential health and environmental impacts when designing new chemicals and technologies; and discouraging collaborative science as well as public participation in decision-making about control of hazards and introduction of new technologies.
- One solution to addressing the barriers impeding regulation is a precautionary approach that would require preventive action in the face of uncertainty. Precaution shifts the burden of proof to the proponents of an activity and requires the exploration of a wide range of alternatives to possibly harmful actions. It is a technology stimulating approach that controls potential hazards and encourages the search for safer alternatives.
- The determination of what is sufficient evidence for preventive actions depends on the context—the availability of alternative means of achieving the same social good and the consequences of inaction or acting in error. Scientific evidence must be integrated with societal, industry, and consumer interests when determining whether a precautionary regulation is necessary. Phthalates (plasticizers found in children’s toys) are one example. There is moderate, but not overwhelming, evidence that they are potentially harmful. Under the current regulatory model, phthalates will remain in products until scientists prove they cause harm. Under a precautionary model, phthalates, with moderate evidence of harm, might not be used in products used by children and, as a result, safer alternatives would be explored.
- As long as cancer prevention is a special interest group weighed against economic realities, it will have difficulty succeeding. Effective cancer prevention depends on development of inherently safe and clean technologies that are economically and energy efficient as well as sustainable. End of pipe controls, such as ordering a producer to install a filter on a smokestack or a ventilation system in the workplace, are non-productive costs. Government policies that encourage the elimination of hazardous chemicals and promote economic development based on sustainable production are necessary to make cancer prevention healthy for the economy as well as for the U.S. population.

DR. DANIEL WARTENBERG:

ENVIRONMENTAL FACTORS IN CANCER: TRICHLOROETHYLENE AND RELATED SOLVENTS: SCIENCE, REGULATION AND POLITICS

Background

Dr. Wartenberg is Professor and Director of the Division of Environmental Epidemiology in the Department of Environmental and Occupational Medicine at the Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey. He is immediate past President of the International Society of Environmental Epidemiology and has served on a variety of local, national, and international advisory committees for organizations including the World Health Organization, England’s Health Protection Agency, the Centers for Disease Control and Prevention, the National Academy of Sciences, the U.S. Environmental Protection Agency, and the New Jersey Governor’s Commission on Radiation Protection. Dr. Wartenberg’s primary research interests are the development and application of novel approaches to the study of environmental risk, pollution, and public health, with particular emphasis on geographic variation, disease clustering, and application of Geographic Information Systems.

Key Points

- Trichloroethylene (TCE) is a common organic solvent that has been in use since the early 1900s; it was used in dry cleaning until 1960 and is still used as a solvent and for cleaning metal. TCE is an example of an occupational hazard becoming an environmental issue. TCE is often improperly disposed of and this has resulted in groundwater contamination. This chemical is present at more than 850 Superfund sites across the country and in 34 percent of drinking water systems—mostly limited local supplies. The contaminated water supply can result in dermal and ingestion exposure. TCE is also highly volatile, causing vapor intrusion; TCE in groundwater rises through soil and cracks in the foundation of a house, also causing inhalation exposure to humans.
- A major research barrier to understanding TCE and other carcinogenic solvents is that there are multiple exposures in the workplace and it is difficult to isolate a particular chemical to study its direct risks. In a few cases where a direct exposure to workers has occurred, companies are reluctant to release data to state health departments. Similarly, in communities where there have been high exposures of TCE, states and localities are often unwilling to provide cancer-related information; data access is denied based on individual privacy and confidentiality protection. This lack of access to data is creating another barrier to understanding this problem.
- Regulatory delays also impede the protection of public health. Regulators need to be responsive to new data on health risks and take aggressive preventive action when evidence of possible carcinogenicity exists. Many occupational studies link TCE with various cancers, including kidney, liver, and non-Hodgkin lymphoma. The EPA conducted a state-of-the-science review in 1997, which was reviewed by EPA's Scientific Advisory Board in 2000. Subsequently, a report written by the National Academy of Sciences concluded that TCE is a complete kidney carcinogen. Eleven years later, there have been no regulatory decisions, and people continue to be exposed in the workplace and in their homes, raising the question of when the evidence will be strong enough to merit preventive action.

DR. JEANNE STELLMAN:

DELUSIONS, ILLUSIONS, AND ONGOING NEGLECT OF HAZARD RECOGNITION, REGULATION, AND CONTROL OF INDUSTRIAL CARCINOGENS

Background

Dr. Stellman recently joined the State University of New York-Downstate Medical Center in Brooklyn, NY, as Professor and Chair of Environmental and Occupational Health Sciences and Associate Dean for Research in its newly established School of Public Health. She served for many years as Assistant Director for Cancer Control of the Comprehensive Cancer Center at Columbia University and founded and directed the Women's Occupational Health Resource Center, which served as a major center of research, education, and training, with support from the Occupational Safety and Health Administration and other funders. Dr. Stellman is currently actively engaged in research on herbicides in Vietnam and was director of a multimillion-dollar study for the National Academy of Sciences to develop exposure methodologies for epidemiological studies of military herbicides.

Key Points

- One of the first strong standards regulating a carcinogen was for polyvinylchloride (PVC) in the 1970s. Trade unions, advocates, and an alert practitioner who identified a rare signal

tumor in PVC workers helped enact this regulation; within 6 months, industry had developed alternatives that protected workers. The trade union movement has been responsible for almost every occupational safety and health standard in place today; once the unions lost their strength, so did the standards-making process. Advocacy is key to regulation and control and to funding of scientific studies.

- Highly reactive biological materials will interact with humans; it should be a fundamental principle of processing that if a chemical or industrial process involves a biological material, aggressive preventative measures must be taken to prohibit contact between humans and the biological material, regardless of the state of the science.
- The chemical-by-chemical approach to testing and regulation ignores the changing vulnerability of workers over time. Workers are concurrently exposed to multiple chemicals over time, in addition to their own genetic susceptibilities. The purpose of regulation should be to protect at the “least vulnerable” levels of exposure rather than identifying the most vulnerable and setting standards that require more endurance.
- A set of alternate criteria for higher-level studies is needed to better regulate and control workplace hazards. There is no good methodology for obtaining or reconstructing a lifetime occupational history; this is a significant barrier to conducting higher-level carcinogenicity studies. Most medical records are inaccessible due to privacy regulations; even if they can be accessed, they rarely contain information on occupational history. Records such as tumor registries and death certificates may contain occupational data, but these data are not coded. The changing nature of the workplace also makes it difficult to find isolated instances of toxic exposures or a large enough population sample for statistical relevancy.
- The United States has fallen behind in both precautionary principles and regulation. The European Union’s REACH (Registration, Evaluation and Authorization of Chemicals) regulatory system has eliminated suspicious chemicals from consumer products sold in Europe (although these chemicals still remain in products sold in the United States).
- It has been approximately 30 years since NIOSH has inventoried chemicals that are in use in the United States; a new industry-wide study needs to be done. While knowing “what is out there” may not be important scientifically, it will assist advocates in lobbying for regulations.
- Thorough engineering and process controls to minimize effluents (i.e., end-of-pipe controls) are needed. There is no harm in preventing exposure when toxicity or carcinogenicity is unclear.

DISCUSSION AND CONCLUDING COMMENTS:

PANEL II

Key Points

- Identifying markers that are early indicators of cancer (e.g., cytogenetic changes, activated signaling pathways, gene mutations) and could be used as endpoints in epidemiologic studies could save time and money in cancer hazard identification efforts. However, this methodology requires agreement on which intermediate markers are actually indicative of cancer risk.
- Industry has little incentive to adopt clean and safe processes up front, creating the need for end-of-pipeline toxin controls. The precautionary approach to regulation might incentivize a more proactive approach to developing safer chemical processes. A successful example of this approach is the Toxic Use Reduction Act in Massachusetts, which has been in place for approximately 20 years. This law does not ban or require industry control of chemicals, but

does require companies that use toxic chemicals to “plan” for their elimination. This non-punitive approach has resulted in at least a 40 percent reduction in the use of toxic chemicals over that time period.

- The myth that it will be overly expensive and disruptive to “design out” a hazard is untrue. Companies have found it cost-effective to create new technologies to reduce toxic hazards. It might be useful to collect and publish examples of the return-on-investment resulting from designing out occupational hazards.
- It would be helpful for companies that have employed individuals who have been exposed to occupational chemicals to share the names of those workers and years they worked. This information could be compared with state cancer registries and the death index, providing at least some measure of exposure risk.
- Stopping rules—such as those that exist for clinical trials—are needed relative to production of environmental chemicals. These are a pre-existing set of rules that would prohibit further production of a chemical if it appears to be dangerous. The FDA has a series of precautionary rules to oversee the introduction of new drugs, and the chemical industry should establish a similar set of rules for the introduction of new chemicals into the environment.
- Better communication between epidemiologists, toxicologists, and chemical engineers is necessary to understand the driving forces behind industry. Toxicity and limitation of exposure need to be as important as profit.

PUBLIC COMMENT

Key Points

- The regulatory method does not work because many aspects of it are being institutionalized (e.g., the Office of Management and Budget Data Quality Act, the Paperwork Reduction Act), thus stymieing the process. In the absence of regulation and sometimes information, scientists need guidance when making decisions or recommendations affecting public health.
- When all costs are considered, regulation tends to pay for itself. Industry is very successful at externalizing all the costs of proper waste disposal or exposing workers carelessly, and these costs must also be taken into account when determining the cost of regulation.
- Construction workers should not be neglected as an occupational group worth studying for hazardous exposures. Fiberglass and vermiculite are some of the chemicals these workers are exposed to and for which adequate toxicity and carcinogenicity data are not known.
- Public health data must be made available to the scientific community, and also within government agencies, so that both researchers and policy-makers can competently serve and protect the public health. There is no warranted justification for not making public health data available to people who have the necessary knowledge and experience to protect confidentiality and privacy. The National Academy of Sciences will be issuing a report in the near future on the difficulties of conducting epidemiologic studies in the face of privacy protections.
- North America has one of the best cancer surveillance systems in the world and has amassed a great deal of data that can elucidate many aspects of cancer. In the future, an increasing amount of data will be made available through electronic means with increased linking capabilities; the scientific community needs to consider how to make all these databases interoperable.
- Advocacy is often needed to push for legislation when government is unresponsive. It is important to have the right leadership to apply effective public pressure. Alliances and

coalitions also need to be built; no progress will be seen as long as cancer prevention is seen as a special interest.

- The New York State Breast Cancer Network is a coalition of 24 breast cancer organizations that has a legislative agenda; they meet monthly by telephone and lobby every day in Albany. It is one of the only such networks in the country and has been a very effective grassroots effort.
- The Collaborative on Health and the Environment—a project based out of the nonprofit organization Commonweal in California—is a network that engages scientists, health professionals, advocates, government officials, and the general public to work together and communicate science to constituencies. More information can be found at the Web site healthandenvironment.org.
- A change in the Presidential administration will not automatically result in changes in policy in this area; industry will continue to oppose regulation of toxic chemicals based on potential loss of jobs overseas and cost concerns. A good economic justification will need to be made in order to begin moving industry to “green” production.

PANEL III

DR. DEVRA DAVIS:

THE CASE FOR ENVIRONMENTAL ONCOLOGY: MAKING PREVENTION THE CURE FOR CANCER

Background

Dr. Davis is Director of the world’s first Center for Environmental Oncology at the University of Pittsburgh Cancer Institute and Professor of Epidemiology at the University of Pittsburgh’s Graduate School of Public Health. Her recent book, *The Secret History of the War on Cancer*, was a top pick by *Newsweek* and is being used at major schools of public health, including Harvard, Emory, and Tulane University. She has also authored more than 190 publications in books and journals ranging from the *Lancet* and the *Journal of the American Medical Association* to *Scientific American* and the *New York Times*. Dr. Davis is the recipient of a Women’s Leadership Exchange Compass Award, presented by OPEN: The Small Business Network from American Express, for breaking the paradigms of how women are perceived. She also received the first Lisa Zhang Environmental Award from the United Nations in 2008.

Key Points

- In 1936, the world’s leading cancer scientists knew that synthetic hormones, X-rays, solar radiation, coal tars/soots/dusts, benzene, and cobalt-uranium mining all caused cancer. However, the public was not made aware of these hazards; it was a time before the Internet and information was not widely shared.
- Asbestos—a known carcinogen—is not banned or even monitored in the United States; it is still found in cement pipes, brakes, sand, and insulation. Additionally, 30 million U.S. homes are insulated with zonolite, which can be contaminated with tremolite containing asbestos fibers. The pervasive effects of asbestos are evident in the fact that one in three cases of mesothelioma—a tumor thought to be uniquely associated with asbestos—occurs in people with no known history of working with the toxic substance. WHO, the World Bank Group, the International Labor Organization, and other public health-related organizations and policy makers have recommended a global ban on asbestos. Yet the United States tripled imports of

asbestos sheet insulation from Mexico in the beginning of this century, and asbestos use continues throughout Latin America.

- Production of a number of known industrial carcinogens (e.g., benzene, vinyl chloride) increased exponentially from the 1960s to the 1980s. The 1981 Doll & Peto analysis of cancer risk could not have accurately reflected the impact of this exponential increase in industrial use of synthetic organic chemicals; cancer has a latency of 10 to 30 years. Demographics (e.g., race/ethnicity) were also ignored, resulting in an underestimation of cancer risk.
- When assessing the change in cancer rates by birth cohort (beginning in 1893), smoking-related cancers continue to increase in women, breast cancer risk is approximately double in women today than for their grandmothers, and cancer risk not related to smoking is approximately 50 percent higher for women today. For men, there has been a decline in smoking-related cancers; however, cancers in men not related to smoking (or screening) are continuing to increase.
- Prenatal exposure to the synthetic estrogen diethylstilbestrol (DES) increases cancer risk in offspring. NCI's National Cooperative DES Project found that women whose mothers took DES had an almost doubled risk of breast cancer by age 40. Based on emerging data, this risk may extend to grandchildren of women who took DES. Men between the ages of 15 and 44 whose mothers had unusual exposures to either synthetic hormones, phytoestrogens, or persistent organochlorine pesticides face an increased risk of testicular cancer.
- Another area of concern is the inappropriate and growing use of computed tomography (CT) scans—particularly in children. The amount of radiation for a CT scan must be adjusted for size and age of the body; unfortunately, many unadjusted scans are being performed in places such as shopping malls. Federal standards for CT technologists, including licensing, training, and testing, as well as a national database on radiation doses, are needed to ensure appropriate use and procedures.
- An exciting theory of carcinogenesis is the idea that common inflammatory pathways could be involved in linking obesity, cardiovascular disease, and cancer. Obesity may be an inflammatory condition linked to rapid expansion of adipose (fat) tissue; the more frequent and rapid the cell growth, the greater the probability of error linked to other disease. Polychlorinated biphenyls (PCBs) can accumulate in fat tissue and lead to both obesity and obesity-associated atherosclerosis. Studies of PCBs' chemical cousins, polybrominated biphenyls (PBBs), suggest an association with increases in breast cancer, non-Hodgkin lymphoma, and digestive system cancers.
- The National Toxicology Program asserts there is cause for concern from exposure to bisphenol-A (BPA). BPA has been associated with prostate and breast cancers, obesity, miscarriages, brain disorders, and reproductive abnormalities, including feminization of males and masculinization of females. Interestingly, exposure to nutritional supplements (e.g., genistein, folates, Omega 3 fatty acids, vitamin D, calcium) prior to BPA exposure may negate its detrimental effects. However, the public should not have to guard themselves from a chemical that can be eliminated from the environment.
- A patient history database—a set of core clinical and epidemiologic data—needs to be cultivated, supported, and piloted nationwide. The database should identify high-risk patients and link them with tissue repositories and clinical databases. It would facilitate clinical and translational research and capitalize on emerging technologies, including lifetime use of diagnostic technology. Such a database would revolutionize the effectiveness of epidemiologic studies.

- The current regulatory system does not work. The government needs to grant immunity against punitive damages to companies that agree to provide confidentially protected evidence on toxic hazards; fund worker and community recovery and repair through fees on carcinogen producing industries; and support systematic surveillance of worker and community health.

DR. PHILIP LANDRIGAN:

CHILDHOOD CANCER AND THE ENVIRONMENT

Background

Dr. Landrigan is a pediatrician, epidemiologist, and internationally recognized leader in public health and preventative medicine. He has been a member of the faculty of Mount Sinai School of Medicine since 1985 and Chairman of the Department of Community and Preventive Medicine since 1990. He is known for his many decades of work in protecting children against environmental threats to health, most notably lead and pesticides. He has been a leader in developing the National Children's Study, the largest study of children's health and the environment ever launched in the United States. Dr. Landrigan has been centrally involved in the medical and epidemiologic studies that followed the destruction of the World Trade Center on September 11, 2001. He has also consulted extensively to the World Health Organization.

Key Points

- While mortality from childhood cancer has gone sharply down, incidence rates are increasing. There has been a 55% increase from 1975 to 2005 in the incidence of leukemia in 0 to 14-year-olds and an 81% increase for acute lymphocytic leukemia—the most common type of leukemia. Incidence of cancer of the brain and nervous system has increased 39%. Testicular cancer, which primarily occurs in 15 to 30-year-olds, has increased by 51% in white males and by 45% in black males. The explanation for this increase may be due in part to better diagnostics, but this alone does not account for the continued inexorable rise. Serious consideration must be given to the possibility that environmental factors are involved.
- Detectable levels of several hundred synthetic chemicals are found in the bodies of all Americans. There are 80,000-plus chemicals in use in commerce, and basic toxicity is available for fewer than half of high production volume (HPV) chemicals. Even more disturbing is that information on developmental toxicity is available for fewer than 20% of HPV chemicals.
- Children have unique vulnerabilities and are surrounded by chemicals that have not been properly tested. They are more heavily exposed to toxins, pound-for-pound, than adults. In the first 6 months of life, infants drink seven times as much water per pound of body weight per day as the average American adult. Children breathe three to four times as much air and eat several times as much food (pound per pound) as adults. They have a diminished ability to detoxify and excrete many chemical toxins. Additionally, children have more years of future life—if they are exposed to a toxic chemical *in utero* or in the first years after birth, they have a longer latency period for the resulting damage to manifest.
- The worldwide epidemic of phocomelia—defects of the arms and legs occurring in babies exposed *in utero* to thalidomide—painfully exemplifies the vulnerability of fetuses, infants, and young children to toxic chemicals. Thalidomide, developed in Germany and Switzerland in the 1950s and 1960s, was found to be extremely effective at suppressing morning sickness in pregnant women in the first trimester of pregnancy. It was widely prescribed in Europe ; by the time it was found to be the cause of phocomelia, 15,000 babies were born with this birth defect.

- The European Ramazzini Foundation has recently shown that the artificial sweetener aspartame is a chemical carcinogen; when exposure to the fetus occurs *in utero*, a much lower dose is required to produce malignancy compared with an adult dose. The FDA has not been swayed by these studies, but they should be taken more seriously considering that approximately 80 percent of children in the United States are exposed to aspartame on a regular basis.
- Elements of a national strategy for the discovery of the environmental origins of childhood cancer would include enhanced testing of chemicals for developmental carcinogenesis; epidemiologic prospective studies of children, especially large, multi-year birth cohort studies that incorporate careful measures of chemical exposures and genetic susceptibility (e.g., the National Children's Study); and development of a new paradigm for cancer prevention that explicitly recognizes the unique vulnerability of fetuses, infants and children.
- The U.S. National Children's Study, to be launched in 2008, will follow 100,000 children from early in pregnancy to at least 18 years of age. This multi-year prospective epidemiological study will examine the influences of exposures in early life on health—chemical, physical, social, and behavioral exposures.

DR. FRANK MIRER:

PREVENTING CANCER BY CONTROLLING OCCUPATIONAL AND ENVIRONMENTAL EXPOSURES

Background

Dr. Mirer is a toxicologist and certified industrial hygienist serving as Professor of Environmental and Occupational Health in the Urban Public Health Program at Hunter College of the City University of New York. His primary scientific interest is exposure and risk assessment in the occupational environment, and regulatory policy. Dr. Mirer previously served as Director of the United Auto Workers Health and Safety Department and participated in each round of automobile industry collective bargaining from 1976 to his retirement. He was inducted into the National Safety Council's Health and Safety Hall of Fame, received the Alice Hamilton Award for Lifetime Service from the Occupational Safety and Health Section of the American Public Health Association, and received the President's Award for Health and Safety from Ford Motor Company. He is a Fellow of the Collegium Ramazzini and the American Industrial Hygiene Association.

Key Points

- A major fraction of known and probable human carcinogens have been identified by studies in the occupational environment.
- Women have not been heavily employed in chemical exposure industries, (and studied even less). As a result, there is a lack of information about the effects of chemical exposures on breast, uterine, and other cancers.
- Community particulate air pollution has emerged as a risk factor for lung cancer; however, the risk of fine particles such as silica, soot, wood dust, formaldehyde, and diesel particulate matter remains under recognized. A higher priority needs to be placed on regulating these materials, given high exposures to the public and status of some of these as known human carcinogens.
- Variation is needed to detect carcinogens. For example, if everyone smoked the same amount it would be difficult to identify tobacco smoke as a carcinogen in humans. Exposure to chemicals outside of occupational settings is at fairly uniform levels (e.g., gasoline at the

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