

The Office of Health Assessment and Translation: A Problem-Solving Resource for the National Toxicology Program

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The National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) was established in 1998. CERHR served as an environmental health resource providing in-depth scientific assessments of effects on reproduction and development caused by agents to which humans are exposed. To our knowledge, CERHR was the only resource of its kind, producing evaluations that considered toxicity findings in the context of current human exposures to derive “level-of-concern” conclusions. This qualitative integration step is what distinguished CERHR documents from more traditional hazard evaluations prepared by other agencies.

When CERHR was established, the focus on reproduction and development was appropriate because of a strong interest in these health outcomes by the public, regulatory and health agencies, and the scientific community. In addition, a rationale for creating CERHR was the sense of a lack of uniformity across state and federal agencies in interpreting experimental animal studies of reproduction and development. CERHR was envisioned as a mechanism to apply a consistent strategy for interpreting these data. Although this need remains, we believe that the approaches used for CERHR evaluations should also be extended to other important health outcomes. Many chemicals display more than one type of toxicity, that is, carcinogens are often immunotoxicants, and reproductive and developmental toxicants may influence many endocrine-sensitive systems. A strict focus on reproductive and developmental end points evaluated in the context of current human exposures may not result in the most health protective levels of concern, and could be confusing to the public. From a public health perspective, understanding the implications of current human exposures should include consideration of all relevant health effects. Also, the NTP and the broader toxicology community need to confront the challenging scientific questions involved in utilizing information from the Toxicology in the 21st Century initiative (Collins et al. 2008). To do this we need a mechanism to systematically explore linkages between “toxicity pathways” and disease outcomes. To provide this, CERHR has spent the last 2 years in transition, laying the groundwork to become a more flexible scientific analysis program, while continuing to be grounded and recognized as a unique and important public health resource for the interpretation of reproductive and developmental hazards to humans.

This evolution of CERHR is a response to the changing and increasing demands on both the NTP analysis and research programs. “What does it mean?” is a question we increasingly want to answer, as our research and testing tools become more sophisticated and mechanistically based. A change in CERHR’s scope will also bring its work more in line with two recent initiatives established within the NTP that have mandates to address a broad range of health effects (Bucher 2008). In 2007 the NTP established a biomolecular screening program to administer its High Throughput Screening (HTS) Initiative in collaboration with our Tox21 partners (Schmidt 2009). This program takes advantage of technological advances in molecular biology and computer science to screen for mechanistic targets or “toxicity pathways” considered critical to adverse health effects. The host susceptibility program was also established in 2007 to study the genetic basis for differences in susceptibility that may lead to a better understanding of how substances in our environment may be hazardous to some individuals and not to others.



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On 11–13 January 2011, CERHR launched its expanded role by convening a diverse group of experts in toxicology, epidemiology, bioinformatics, and endocrinology to assess the strength of the literature linking selected environmental agents and exposures with diabetes and obesity (NTP 2011). Consideration was given to an array of information ranging from epidemiological findings and experimental animal and mechanistic data to screens of toxicity and disease pathways using HTS and literature curation methodologies. The use of several new analysis tools revealed novel linkages between a number of environmental agents and obesity or diabetes. These exciting findings are now being collated for publication.

To fulfill its mission, the NTP is developing more innovative and flexible approaches for information and data integration, both across different programs within the NTP and across the different types of data that are generated and utilized (i.e., mechanistic or high throughput; “hypothesis-driven” animal studies of the type undertaken by National Institute of Environmental Health Sciences (NIEHS)-funded extramural grantees; and toxicology studies conducted for the purpose of safety assessment). Recent experience with bisphenol A highlights the public’s confusion and the waste of scientific resources that can occur when these different types of scientific literature are developed on parallel, but separate, paths (Bucher 2009). The evolution of CERHR is an important part of this information integration effort, and CERHR’s new role calls for a new name: the Office of Health Assessment and Translation. Under the leadership of Kristina Thayer, the Office of Health Assessment and Translation will be the NTP focal point for the thoughtful and deliberative integration of relevant information of all types in health assessments for the protection of public health.

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John R. Bucher is the associate director of the NTP, an interagency program headquartered at the NIEHS. Along with participating programs at the National Center for Toxicological Research, Food and Drug Administration, and laboratories of the National Institute for Occupational Safety and Health in Morgantown, West Virginia, and Cincinnati, Ohio, the NTP is the nation’s principal comprehensive toxicology analysis, research, and testing effort. Bucher holds a Ph.D. in pharmacology from the University of Iowa, an M.S. in biochemistry from the University of North Carolina, and a B.A. in biology from Knox College, and he was an

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Kristina A. Thayer, director of the NTP Office of Health Assessment and Translation, holds a Ph.D. in biological sciences from the University of Missouri–Columbia. She has been with the NIEHS since 2003, serving in the NTP Office of Liaison, Policy, and Review and the NIEHS Office of Risk Assessment Research prior to assuming her current position. She has authored numerous NTP reports and manuscripts on the toxicological potential of environmental substances.

Linda S. Birnbaum, director of the NIEHS and the NTP, oversees a budget that funds multidisciplinary biomedical research programs and prevention and intervention efforts that encompass training, education, technology transfer, and community outreach. She recently received an honorary Doctor of Science from the University of Rochester, the distinguished alumna award from the University of Illinois, and was elected to the Institute of Medicine. She is the author of > 700 peer-reviewed publications, book chapters, abstracts, and reports. Birnbaum received

her M.S. and Ph.D. in microbiology from the University of Illinois, Urbana. A board-certified toxicologist, she has served as a federal scientist for 31 years, 19 with the U.S. EPA Office of Research and Development, preceded by 10 years at the NIEHS as a senior staff fellow, a principal investigator, a research microbiologist, and a group leader for the institute's Chemical Disposition Group.

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Health Impact from Air Pollution in Thailand: Current and Future Challenges

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Emerging from an agricultural base to more industrialization, Thailand now faces many environmental problems, particularly air pollution, resulting in adverse health consequences. The three major sources of air pollution are vehicular emissions in cities, biomass burning and transboundary haze in rural and border areas, and industrial discharges in concentrated industrialized zones.

Recent air quality data suggest that particulate matter < 10 μm in aerodynamic diameter (PM_{10}) is the most important air pollutant in urban and rural areas. In cities such as Bangkok, air quality monitoring performed by the Pollution Control Department (PCD) for the past 10 years revealed that the levels of PM_{10} have exceeded both annual (50 $\mu\text{g}/\text{m}^3$) and 24-hr (120 $\mu\text{g}/\text{m}^3$) national standards (PCD 2010). The main source of PM_{10} in Bangkok is vehicular emissions (Chuersuwan 2008; Parsons International Ltd. 2001).

In the rural and border areas, most notably Chiangmai, agricultural burning and forest fires, including transboundary haze from Myanmar, have contributed to high levels of PM_{10} , which have increased to critical levels since 2006 [250 $\mu\text{g}/\text{m}^3$, 300 $\mu\text{g}/\text{m}^3$, 175 $\mu\text{g}/\text{m}^3$, and 220 $\mu\text{g}/\text{m}^3$ in 2006, 2007, 2008, and 2009, respectively (PCD 2010)]. More importantly, many consecutive days of high PM_{10} levels resulted in increases in hospital admissions and outpatient visits (Chiangmai Provincial Public Health Office 2007).

Moreover, the Southeast Asian haze that originated in Indonesia has continually affected the health of residents of the southern provinces, particularly in 1996 and 1997, where the maximum PM_{10} levels reached as high as 314 $\mu\text{g}/\text{m}^3$ (PCD 2010). The most severe haze episode occurred in 1997 and resulted in sharp increases in outpatient visits (26%)



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and hospital admissions (33% for all respiratory, 36% for pneumonia, 40% for bronchitis/chronic pulmonary obstructive disease, 12% for asthma) within a period of a few months (Health Systems Research Institute 1998).

Several studies worldwide have demonstrated that PM_{10} is associated with premature mortality and a wide range of morbidity outcomes. As part of the Public Health and Air Pollution in Asia (PAPA) multicities study, results for Bangkok showed that each 10- $\mu\text{g}/\text{m}^3$ increase in PM_{10} is associated with a 1.25% increase in all-cause mortality, which is higher than for the three other participating cities [0.53% for Hong Kong, 0.26% for Shanghai, and 0.43% for Wuhan (Wong et al., 2008)] and higher than multicities studies conducted in Western countries (Katsouyanni et al. 2001). The higher effects in Bangkok may be related to high temperatures in Bangkok throughout the year, higher exposures to air pollution from longer periods of time spent outdoors, and less availability and use of air-conditioning.

As a developing country, Thailand strives for a continual economic growth. Consequently, expansion of petrochemical plants rose sharply, particularly in the coastal province of Rayong, with > 73 million tons of chemicals used annually (Department of Industrial Works 2010). Although environmental management has been instituted, levels of volatile organic compounds (VOCs) continue to exceed Thailand's standards (PCD 2010).

Epidemiological studies have been limited, with only sporadic reports of respiratory symptoms and illnesses after episodic events of accidental releases from industries. However, a recently completed large-scale population-based epidemiology study with > 26,000 subjects indicated that residents who live near the petrochemical industrial estate have higher risks in adverse pregnancy outcomes, neuropsychological symptoms, and poor performance on neuropsychological tests (Vichit-Vadakan et al. 2010). In particular, results show significant excess risk of preterm birth before < 34 weeks among mothers residing < 4 km

from the industrial estate [odds ratio (OR) = 3.34; 95% confidence interval (CI), 1.18–9.47]; nonsignificant increased risks were found for all pregnancy outcomes (OR = 1.60; 95% CI, 0.87–2.93), preterm birth before 37 weeks (OR = 1.68; 95% CI, 0.85–3.30), low birth weight (OR = 1.42; 95% CI, 0.52–3.78), and small for gestational age (OR = 1.24; 95% CI, 0.31–4.90). Generally, the excess risk decreases with increased distances.

Obtaining sustainable development that balances environmental conservation and the well-being of the population remains a challenge for Thailand. In national strategies for development, policy makers often rely only on economic information because of the lack of empirical data on health, social, and environmental impacts from developmental policies and projects. Fostering and strengthening epidemiological research in Thailand not only provides the necessary perspective for policy development but contributes to the larger body of knowledge in environmental health.

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Nuntavarn Vichit-Vadakan currently serves as the dean of the Faculty of Public Health, Thammasat University. She continues to participate in numerous important environmental epidemiological studies as the principal investigator. Results of her studies have led to policy development, such as the setting of Thailand's national standard for PM_{2.5}.

Nitaya Vajanapoom has a Ph.D. in epidemiology from the University of North Carolina and is an environmental epidemiologist at Thammasat University in Bangkok. Her studies on the health effects of air pollution include the PAPA project and a 5-year population-based study that examined the health effects of air pollution from a lignite power plant and petrochemical industrial estate in Thailand.

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