

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES**

**MINUTES OF THE ONE HUNDRED FORTY-FOURTH MEETING OF THE
NATIONAL ADVISORY ENVIRONMENTAL HEALTH SCIENCES COUNCIL**

March 16, 2015

The National Advisory Environmental Health Sciences Council convened the Open Session of its one hundred forty-fourth regular meeting on March 16, 2015 in the Rall Building, Rodbell Auditorium, National Institute of Environmental Health Sciences, Research Triangle Park, NC. The Closed Session of the meeting was held February 19, 2015.

The meeting was open to the public on March 16, 2015 from 11:00 a.m. to 3:00 p.m. In accordance with the provisions set forth in Section 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), the meeting was closed to the public on February 19, 2015 from 8:30 a.m. to 11:30 a.m. for consideration of grant applications. Notice of the meeting was published in the *Federal Register*.

The Open Session of the meeting was a “virtual” meeting, with all Council members participating by telephone. Dr. Linda Birnbaum presided as Chair.

Participating Council Members

Habibul Ahsan, MD
Kim Boekelheide, MD, PhD
Kelly Brix, MD (*ex officio*)
Philip Brown, PhD
Lisa Conti, DVM
David Eaton, PhD
Kevin Elliot, PhD
Brenda Eskenazi, PhD
Kenneth Fasman, PhD
Andrew Feinberg, PhD
Tomás Guilarte, PhD
Howard Hu, MD
James Johnson, PhD (*ex officio*)
Norbert Kaminski, PhD
Randall Kramer, PhD
Linda McCauley, PhD, RN

Donna Mendrick, PhD (*ex officio*)

NIEHS Staff – Council Table

Joellen Austin
John Balbus, MD
David Balshaw, PhD
Linda Birnbaum, PhD
John Bucher, PhD
Gwen Collman, PhD
Christina Drew, PhD
Janet Hall, MD
Chip Hughes
Cindy Lawler, PhD
Alfonso Latoni, PhD
Chris Long
J. Patrick Mastin, PhD
Liz McNair
William A. Suk, PhD, MPH
Claudia Thompson, PhD
George Tucker
Rick Woychik, PhD
Darryl Zeldin, MD

NIEHS Staff

Kathy Ahlmark
Tremaine Baker
Martha Barnes
Linda Bass, PhD
Sharon Beard
Danielle Carlin, PhD
Kelly Chandler, PhD
Pamela Clark
Jennifer Collins
Yuxia Cui, PhD
Caroline Dilworth, PhD
Chris Duncan, PhD
Benny Encarnacion
Symma Finn, PhD
Barbara Gittleman
Kimberly Gray, PhD
Kristin Greiner
Astrid Haugen
Michelle Heacock, PhD
Jerry Heindel, PhD

Heather Henry, PhD
Michael Humble, PhD
Nina Jaitly, MD
Laurie Johnson
Bonnie Joubert, PhD
Helena Kennedy
Beth Lauderdale
Alicia Lawson
Kelly Lenox
Robin Mackar
David Malarkey, DVM, PhD
Kim McAllister, PhD
Steven McCaw
Roseanne McGee
Kirsten Mease
Mark Miller, PhD
Sri Nadadur, PhD
Aaron Nicholas
Liam O'Fallon
Jerry Phelps
Nicole Popovich
Molly Puente
Ericka Reid, PhD
Les Reinlib, PhD
Thad Schug, PhD
Daniel Shaughnessy, PhD
Carol Shreffler, PhD
Frederick Tyson, PhD
Bill Wade
Nigel Walker, PhD
Lori White, PhD
Leroy Worth, PhD

Members of the Public Present

Sandra Helverson, SSS
Ernie Hood, Bridport Services, LLC
Mike Phillips, RTI International

I. Call To Order and Opening Remarks

NIEHS/NTP Director and Council Chair Linda Birnbaum, Ph.D., welcomed attendees and called the meeting to order. She noted that this would be the first open session meeting for new Council members Drs. Ahsan, Brown, and Eskenazi. She also

recognized the retiring Council members, Dr. Boekelheide, Ms. Yeampierre, and Dr. Chesselet. She asked all present in the room to introduce themselves, which they did. She asked the Council members attending by telephone to introduce themselves. Following the introductions, NIEHS Division of Extramural Research and Training (DERT) Director and Council Executive Secretary Dr. Gwen Collman reviewed meeting logistics, including the voting process during the virtual meeting.

II. Review of Confidentiality and Conflict of Interest

Designated Federal Official, Dr. Collman, reviewed the Conflict of Interest and Confidentiality procedures, which had been provided earlier to Council members in written form, and reviewed various other administrative matters.

III. Consideration of September 2014 Meeting Minutes

Approval of the September 2014 minutes was moved and seconded, and Council voted unanimously to approve the minutes. Dr. Collman noted the dates of the upcoming Council meetings for members to put on their calendars.

IV. Report of the Director, NIEHS

Dr. Birnbaum updated Council on Institute developments since the September 2014 Council meeting.

In her review of NIEHS-related budgetary matters, she noted that the institute actually received an appropriation from Congress this year, as opposed to the continuing resolutions that had been funding NIEHS for the past several years. She reported a 0.2% increase in the regular NIEHS budget, and a flat budget for Superfund. Although funding levels have not recovered fully since sequestration, she said they are still better than they were in FY 2013 or FY 2014.

She also related news about two rounds of unexpected funding recently received by NIEHS. First, the Centers for Disease Control and Prevention passed through \$10 million for up to five years to fund Ebola-related initiatives by the NIEHS Superfund Worker Training Program (WTP). Second, following the cancellation of the National Children's Study, NIH has elected to spend the intended funds to support children's health research activities. NIEHS and NTP will receive \$57 million in FY 2015. Tox21 will receive \$4 million to support developmental toxicity studies. Existing children's environmental health cohorts will see an additional \$5 million. The rest of the funding, \$48 million, will be allocated to support a new initiative called the Children's Health Exposure Analysis Resource (CHEAR).

In her legislative report, Dr. Birnbaum described several recent Congressional hearings and briefings, including her February 2015 first-time meeting with Senator Richard Burr (R-NC). She described the status of relevant pending legislation of interest to NIEHS, including unanimous Senate passage of the FOIA Improvement Act.

Turning to science advances, she briefly summarized several recent publications by NIEHS/NTP personnel or grantees. She also described recent publications from DERT, DNTP and DIR researchers, including collaborations fitting the “One NIEHS” concept. She also noted the landmark publication in *Nature* outlining an integrative analysis of 111 reference human epigenomes, which will eventually comprise more than 20 papers. The studies emerged from the NIH Roadmap Epigenomics Program, which is co-led by NIEHS and NIDA. The 200 authors included NIEHS personnel, under the leadership of Lisa Chadwick and Fred Tyson.

Dr. Birnbaum related several recent items of NIEHS news and highlights, including several events related to global environmental health. They included support of the WHO Chemical Risk Assessment meeting held in Paris in October. NIEHS also provides funding support for a new framework merging regional planning and ecosystem management called One Bioregion/One Health, which was developed by researchers at the University of California San Diego Superfund Research Center. NIEHS has signed a Memorandum of Understanding with Nanjing Medical University in China, supporting scientific exchanges. On January 15, representatives from Singapore’s Agency for Science Technology and Research visited NIEHS and met with Dr. Birnbaum and NTP staff regarding their intention to develop a program for 21st century toxicology.

Dr. Birnbaum recognized Commander Debra King from NTP and Lieutenant Commander John McLamb, who will be part of the Public Health Service contingent working to treat Ebola in Liberia over the next several months.

Among recent highlights regarding data and technology, she described the September 15-16 workshop co-sponsored by NIEHS, EPA, North Carolina State University, and others, which was devoted to development of a framework for environmental health science language.

NTP has been quite active in recent months, Dr. Birnbaum said, including release of the 13th Report on Carcinogens, a new vision and direction for the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), progress in the EPA’s Endocrine Disruptor Screening Program (with NTP participation), and publication of a handbook for conducting literature-based systematic review, which was developed by the NTP Office of Health Assessment and Translation (OHAT).

She went over several recent meetings and events with NIEHS participation, along with a rundown of upcoming meetings and events of NIEHS interest or sponsorship.

Dr. Birnbaum discussed several awards and recognitions recently gained by NIEHS personnel and grantees, including new grants to Dr. David Miller for his study of the blood-brain barrier in relation to ALS, Dr. Fred Miller for his research on myositis, and Dr. Lisa Rider for her work on dermatomyositis and polymyositis. She noted several recent NIEHS/NTP recipients of NIH Director's Awards, as well as personnel and grantees who received other NIH awards. She welcomed several new principal investigators in DIR and new NTP, DERT, and Office of Management staff members.

Dr. Hu referred to the funds made available since the phase-out of the National Children's Study, and noted the importance of funds going to children's cohorts for efforts such as infrastructure, including biorepositories and data management. Dr. Birnbaum said that there are certainly opportunities for such efforts related to the \$5 million supplement program. Dr. Collman said that NIEHS agrees wholeheartedly that epidemiologic studies, especially the longitudinal cohort studies, need infrastructure attention. She said that there would be a concept clearance related to that issue in the June meeting for Council's consideration.

V. Report of the Director, DERT

Dr. Collman reported to the council on recent activities and developments within DERT.

She welcomed several new DERT staff members, including George Tucker, MBA, the new chief of the Grants Management Branch.

She described several changes to the Council Delegated Authorities for FY 2015. Council voted unanimously in favor of accepting the changes as presented. She discussed the Biennial Report to Council on Gender/Minority Inclusion. Council voted unanimously to accept the report as written. She summarized several key points from the FY 2014 budget, noting that of 1409 applications received, 171 new RPG awards were made, with a total of 272 new awards. The pay line was 10% for R01, R21, and R03 grants. The success rate was 15% for RPGs and 16.7% for R01s. She also described several funding initiatives and the funding strategies for FY 2015.

Dr. Collman provided more details about the newly funded children's health initiatives Dr. Birnbaum had touched upon. She discussed the overall redistribution of the funding for the National Children's Study, totaling \$165 million.

She delineated the CHEAR program for the council, including the goals of the initiative and how it flows from the previous Genes, Environment and Health Initiative. She described the main parameters of the CHEAR program, which among other things is

intended to build a sustainable resource for characterization of the exposome within the children's health community. The CHEAR program will consist of a National Exposure Assessment Laboratory Network (using the U2C mechanism), an Exposure Data Repository and Resource for Statistical Analysis and Methods Development (also U2C), and a Coordinating Center (funded via a U24). She also detailed the \$5 million made available for administrative supplements in FY 2015 to support existing children's environmental health cohorts.

Dr. Collman noted the very rapid and intensive work done by the CHEAR team to develop the proposal to use the NCS funds and to issue the Funding Opportunity Announcements (FOAs) involved. The team consisted of 15 DERT people, co-led by Dr. David Balshaw and Dr. Claudia Thompson.

She described the infrastructure comprising the CHEAR initiative, and the workflow involved. She discussed the structure and workings of each of the three program elements. The \$48 million in funding will be spent in FY 2015 to run the CHEAR program for four years. She detailed the three FOAs, along with the FOA for the \$5 million in supplemental FY 2015 funding for existing cohorts.

Dr. McCauley asked about the issue of data sharing related to the CHEAR program's infrastructure, particularly in terms of communities who may have ethical concerns related to data sharing and privacy. Dr. Collman replied that NIEHS has been committed to engagement with communities with respect to children's environmental health research. She noted that availability of the CHEAR data from the repository will much depend on how information has been consented, and what the data access issues are for the parent studies involved. Dr. McCauley suggested that there might be a community review committee to review the issues, and that there may be template language available for all participants to use in their consent forms, in order to explain the data sharing process to communities. Dr. Collman mentioned that there has been recent discussion of the issue of re-consenting, and how the CHEAR program might develop template language for investigators to put into their consent forms.

VI. Worker Training Program Ebola Concept

Chip Hughes, chief of the Worker Education Training Branch, introduced the concept clearance on Ebola bio-safety and infection control training. The initiative emerges from the work the WTP has been doing for many years related to bio-agents and infection control as part of the WTP Hazardous Waste and Emergency Response program. Since last summer, he reported, NIEHS has been partnering with CDC, NIOSH, OSHA, and EPA on response to Ebola in the United States. He said that the heart of those efforts has been to build out in a whole community approach to the training process in each of the areas seen to be at high risk. That involves building from previous WTP

work in health care to the broader community areas where workers are potentially exposed to Ebola. The concept being presented to Council describes an FOA for the next three years to build an infrastructure around infectious disease response, to be carried out in partnership with other federal government agencies.

Sharon Beard presented details of the concept to the council. She described the background, mission, and history of the NIEHS Superfund Worker Training Program.

She noted that NIEHS WTP actively participates in a Federal Interagency Working Group on Ebola Training in order to develop worker training programs for populations identified to be at risk of Ebola exposure, including health care workers. The effort will be supported by \$10 million in new funding, as Dr. Birnbaum had mentioned. The training resources in development include Ebola awareness orientation and Ebola operations-level training. The training plan will continue collaborations and consultations with Federal, state and local partners, will provide supplemental funding to existing awardees, and will fund a full FOA for extensive Ebola training to reach additional target populations, with a “Whole Community” approach to bring together multidisciplinary expertise and promote communication and coordination with local response organizations.

Dr. Conti was the first Council reviewer. She noted that Ebola training is an urgent need at this point, as the disease has “touched our shores.” She mentioned that there is also a pet component and an animal component when Ebola exposures are considered, said that those aspects should be included in the training. She said that the strength of the proposal is the interagency group, with its “all-hazards” approach. It will represent an important resource if state and local organizations should become overwhelmed, and will provide consistency in guidelines. She stated that the concept is definitely needed and that she and her organization would “whole-heartedly support.”

Dr. McCauley was the second Council reviewer. She agreed with Dr. Conti’s suggestion that the concept is quite important. As a nurse, she said she was particularly concerned with the nursing community’s risk of exposure when caring for Ebola patients. She also approved of the strong focus on some of the other professional groups that perhaps have not had the level of training that is available to the actual direct-care providers. She particularly liked the emphasis on attitudes in the proposed program, especially among groups such as veterinarians, laboratory workers, day care workers, transportation services, and similar groups. She said she was “highly supportive” of the concept.

Dr. Collman opened the floor for general discussion. There being none, she requested and received a motion and second to approve the concept. Council voted unanimously in favor of the concept.

VII. Concept Clearance: Household Air Pollutants, Tobacco, and Lung Exposure: Interventions among LMICs

Drs. Claudia Thompson and Kimberly Gray, members of the NIH Trans-Working Group on Cookstoves, presented the concept clearance on cookstoves to the council.

Dr. Thompson first provided Council members with background information about the scope of the cookstoves problem and the NIH/NIEHS investment in the area, which has been substantial. Currently NIEHS supports 32 grants in 17 different countries. She also presented some of the relevant science on the health effects of cookstoves, including interventional and observational studies. She described the 2014 NIEHS Cookstove Symposium, titled “Assessing Exposures and Health Effects Related to Indoor Biomass Fuel Burning,” which brought together researchers working in the area to discuss the latest science, policy, and future directions. The current research agenda includes further investigation of stoves and fuels, adoption and sustainable use, exposure assessment, health outcomes, and improved prediction of acute and chronic health outcomes.

The goal of the proposed FOA is to support a multi-country trial with clean fuels vs. traditional methods, while controlling for tobacco and ambient air quality, monitoring household and personal exposures, and leveraging applied stove and fuel interventions to conduct a phase 3 efficacy trial targeting improvements in health outcomes in Low- and Middle Income Countries (LMICs). The basic metric of the initiative (to be led by the National Heart, Lung, and Blood Institute; NHLBI) will be the successful completion of an intervention study, tailored to the LMIC sites investigated but with common primary health outcome measurements. The project will use a U01 mechanism – a single award with coordinating functions.

With a total five-year budget of \$20 million, NIEHS would commit to \$500 thousand in funding per year, or a total of \$2.5 million.

Dr. Kramer was the first Council reviewer. He noted that indoor air quality is a huge public health problem in LMICs, and that it is “finally beginning to get the public policy and research funding attention that it deserves.” He felt that the concept clearance is an important step forward in calling for a transagency approach to funding and research coordination. He approved of the emphasis on working closely with scientists in LMICs. He also liked the emphasis on leveraging existing research projects, and the relatively long time frame selected for the project. He said he was concerned about the large attention paid to tobacco smoking. He acknowledged the importance of examining multiple exposures in the home environment, but felt that the concept placed too much

emphasis on second-hand tobacco smoke exposure. He said he would prefer to see tobacco smoke treated as a confounding factor rather than a main point of emphasis. He also expressed concern about the great variation in design in improved cookstoves. He said it would be important to determine study designs to account for the many differences in improved cookstoves, as well as the cultural and behavioral differences in the multi-country study. Overall, he said, he very much liked the proposed approach, including use of the U01 mechanism, and would support NIEHS joining this multi-institute initiative.

Dr. McCauley was the second Council reviewer. She agreed with Dr. Kramer's comments, and felt that it is "a wonderful concept." She said she was particularly impressed with the transagency collaboration, and was excited about NIEHS being involved in the multi-site intervention trial. She shared Dr. Kramer's concern about how secondhand smoke would be handled within the study. She found Dr. Thompson's slide depicting a flow chart to be extremely helpful. She felt that translation from the lab to the field and accounting for behavioral aspects were both important.

Dr. Thompson responded to the reviewers' comments. She said that secondhand smoke and smoking represented significant confounding factors in any of these studies. She noted that the NCI partners are particularly interested in the role of cigarette smoke in indoor air pollution. She said that the current thought in cookstove technology is to advance the cleanest possible fuels. She added that the practice of fuel "stacking" has also hindered progress toward improved outcomes. She said that cleaner fuels will be driving interventions, and there will be discussion about which is the best cleaner technology to use in the context of cultural acceptance within countries in many different regions of the world.

Dr. Birnbaum mentioned that one of the findings that emerged from the 2014 workshop was that even with improvements in biofuel burning, too often the indoor air pollution is still above a level of concern. She added that 5-15 million Americans use cookstoves and biofuel burning, so there is concern within the U.S. as well.

Dr. Eaton said that he serves on a global health alliance foundation that has funded a number of studies in LMICs on cookstoves, and he reiterated that it is as important, if not more important, to make sure that the technology is culturally acceptable to be adopted. He recommended involving cultural anthropologists and sociologists in the research to help make sure that the technology is actually culturally acceptable.

Dr. Kaminski observed that a half-million dollars is not a large sum per year, and asked how many U01s are being anticipated. Dr. Thompson noted that with the contribution of other entities, the total is actually roughly \$4 million per year. Also, there is currently conversation with the Bill and Melinda Gates Foundation, who are interested in these

activities. Thus, there may be additional funds for the program. She said the current funding would support one or two programs, with multiple sites and a coordinating center.

Dr. Elliot supported the idea of incorporating anthropologists and social scientists into the research program. He noted the importance of sensitivity to issues of cultural acceptance. Dr. Collman mentioned that the 2014 workshop included several demographers and anthropologists who reported on research in those areas. She said they had spoken about other health outcomes, particularly those related to women and their exposure to violence as a result of collecting their burnable fuels. Thus, there are many possible positive outcomes of improving the technologies, such as girls having more opportunity to attend school, women being less exposed to violence due to reduced collection times, and more.

Dr. Collman asked for and received a motion and second to approve the concept clearance. Council members voted unanimously in favor of the motion.

VIII. Nanotechnology Environmental Health and Safety Research: Funding Opportunities Concept

Dr. Sri Nadadur from the DERT Exposure Response and Technology Branch presented the nanotechnology concept clearance to the council.

He provided background and historical information about nanotechnology and associated health and safety research, noting that nano environmental health science is a complex issue given the many applications and types of materials involved. The overarching goals of the NIEHS program are to gain fundamental understanding on the interactions between engineered nanomaterials (ENMs) and biological systems, to develop comprehensive toxicological data, and to serve as a resource for reference data to address public health issues and regulatory needs. He shared some of the results of studies conducted by the NIEHS centers for Nanotechnology Health Implications Research (NCNHIR) consortium. He also described the research gaps and needs to be addressed under a new FOA that he proposed, which include expansion of the knowledge base and establishment of comprehensive toxicity profiles.

The renewal program would focus on a limited set of ENMs, and would consist of a U24 materials resource core center and U01 basic research projects. There would be formation of a consortium, with annual meetings, encouragement of new collaborations, and opportunities for collaborative efforts. Data from the NIEHS nano research programs would all be fed into the Chemical Effects in Biological Systems (CEBS) database.

The U24 center RFA would involve one grant totaling approximately \$800 thousand, and the U01 program would fund 8-10 grants with approximately \$3 million.

The first Council reviewer was Dr. Kaminski. He cited several aspects of the program as being “real strengths,” such as the fact that it is coordinated and employs a comprehensive approach. He said that he likes the consortium approach as a means of maximizing productivity. He felt that the regular communications among consortium members would increase the likelihood of adjustments in the research directions. He said that having a U24 center as the provider of materials is “absolutely critical.” He also approved of the nano CEBS database. He also recognized some challenges. First, he noted that ENMs are highly diverse materials with respect to their size, shape, chemical composition, and other attributes. Thus, he felt it would be likely that only a small set of materials would be identified for the studies, meaning that a lot would be learned about just a few materials, with the challenge being how much that information could be extended to the broader set of ENMs. He said that the program as described seems to be fairly ambitious, with emphasis on several routes of exposure, both chronic and acute exposures, *in vivo*, *in vitro* and *in silico* models to be profiled, and several other factors, posing a challenge for the program. He also felt that it would be critical to identify the materials to be studied prior to issuance of the RFA. He noted that 8-10 U01 grants would not involve a huge amount of money, and he suggested going more for the lower number of 8, which would provide the grantees with adequate funding to do a good job.

The second Council reviewer was Dr. Eaton. He noted that the one thing that has been learned from the work of the consortium so far has been that the toxicology of ENMs is truly different. “It’s not a matter of what their composition is, it’s the matter of how they are made and how they’re put together in their physico-chemical characteristics.” He felt that NIEHS was already invested in the area and that it would be important for that investment to continue. He approved of the concept of a single U24 for the materials, allowing a common source of ENMs to study. He noted that one area where information is lacking is the actual human exposure to nanomaterials – how people are actually exposed and the characteristics of those exposures.

Dr. Kaminski added that he did in fact support the concept proposal.

Dr. Nadadur said that the types of nanomaterials to be provided by the core center to the investigators will be determined before the funding opportunity is issued, and that the list will be included in the FOA. He elaborated on the reasoning behind the decision to have just one core center.

Dr. Birnbaum asked Dr. Bucher to discuss what NTP is doing related to human exposure to nanoparticles. Dr. Bucher said that over the last few years, NTP has been

working with NIOSH to gain access to workplaces where ENMs are being manufactured and used. The focus has been on some of the issues associated with carbon nanotubes. In general, he said, the exposures seen have not been terribly high, in that most of the sites involved have been open to installing exposure prevention measures, which NIOSH has found to be relatively effective.

Dr. Collman added that about a year-and-a-half ago, NIEHS held a workshop where information was presented about the NIOSH studies, along with several other reports from experts in the field. She said that the current initiative was designed to continue that work that NIEHS has done at the biological level, while encouraging development of new exposure assessment methods. She agreed that the ultimate transfer would be to go from the laboratory to human populations, but was not sure that it was quite ready for that to happen. Dr. Eaton agreed, and said he was glad to hear about the close collaboration with NIOSH.

Dr. Guilarte asked about how the concept might be associated with research on nanomedicine. Dr. Nadadur described some of the current nanomedicine initiatives, and discussed how they fit in with the NIEHS program.

Dr. Collman requested a motion to approve the concept. A motion was made and seconded. The Council members voted unanimously in favor of the concept.

XIII. Adjournment

Dr. Collman thanked all of the Council members and staff for their participation in the meeting. Dr. Birnbaum added her thanks, noting that it was amazing what could be accomplished when circumstances prevented a real meeting.

The meeting was officially adjourned at 11:00 a.m., March 16, 2015.

CERTIFICATION:

/s/
Linda S. Birnbaum, PhD, DABT, ATS
Chairperson
National Advisory Environmental
Health Sciences Council

/s/
Gwen W. Collman, PhD
Executive Secretary
National Advisory Environmental
Health Sciences Council

Attachment:
Council Roster