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U.S. Department of Health & Human Services

DIRECTOR'S COUNCIL OF PUBLIC REPRESENTATIVES

# COPR Alumni

## CLASS OF 2001

- Theodore Castele (Ohio)
- Robin Chin (Rhode Island)
- Mary desVignes-Kendrick (Texas)
- David Frohnmayer (Oregon)
- Lydia Lewis (Illinois)
- Maurice F. Rabb (Illinois)

### Theodore Castele

Term: 1999–2001
Dr. Castele bridges the worlds of medicine, public health, media, business, higher education, and philanthropy. As a radiologist, he has a deep appreciation for and understanding of medical research. As "Dr. Ted" of Cleveland's TV Channel 5 (an ABC affiliate) and a television medical editor, he distills and translates that research into almost daily news reports that keep residents of Northeast Ohio abreast of breaking developments in medicine and science. A successful businessman, a community leader, and a physician, Dr. Castele brings a unique blend of skills to the work of boards, committees, and associations. He is known as a goodwill ambassador for his alma mater, the Case Western Reserve University School of Medicine, is the Chair for both the Dean's Technology Council and the CWRU Capital Campaign, and is an advisory board member of the school's Center for Aging and Health. He is Chairman of the Board for the Health Museum of Cleveland and the Centers of Dialysis Care, and he has served or is currently serving on the boards of the American Lung Association/Northern Ohio Division, the American Cancer Society, the National Osteoporosis Foundation?Ohio Chapter, and the Boy Scouts of America, the latter position continuing an involvement Dr. Castele traces back to his days as an Eagle Scout. He also serves on the Council of the American College of Radiology and Ursuline Nuns of Cleveland Advisory Board. Previous activities include serving as the Chief of Medical Staff at Cleveland's Lutheran Medical Center and as president of the Academy of Medicine of Cleveland, the Cleveland Radiological Society, the Medical Alumni Association, the Lutheran Medical Association, and the board of consultants for the Safety Department of the Cleveland Medical Bureau.

### Robin Chin

Term: 1999–2001
Ms. Chin is a pharmacist and the current chairperson of the National Asian Women's Health Organization's (NAWHO's) board of directors. She takes an active role in communicating health information to the 9.2 million Asian Americans living in the United States. She has a special commitment to improving conditions within medically underserved communities in Rhode Island and Massachusetts. This professional focus reflects her dedication to her local community and her determination to help end gender and ethnic health disparities. A breast cancer survivor, HIV/AIDS advocate, and diabetes educator, she shares her personal experience with breast cancer by speaking at conferences and community forums to dispel the view commonly held by Asian American women that breast cancer is a shameful disease and always fatal. In 1998, Ms. Chin participated in NAWHO's National Clinical Trials and Asian American Women Summit, which brought scientific and advocacy communities together at the National Institutes of Health, with the goal of making clinical trials more accessible to Asian American women. A preceptor of pharmacy practice at her alma mater, the University of Rhode Island, Ms. Chin is a pharmacy manager for CVS located in North Attleboro, an American Cancer Society board member, and a Reach to Recovery volunteer for the American Cancer Society.

### Mary desVignes-Kendrick

Term: 1999–2001
Dr. desVignes-Kendrick is Director of Health and Human Services for Houston, Texas, the fourth largest city in the nation. She is particularly interested in outcome disparities among various ethnic groups and in the process of narrowing those gaps. As a physician and Board-certified pediatrician, she is committed to providing excellent health care; as a public health practitioner, she is equally committed to preventing disease before its onset. Her vision of improving public health for the economically and culturally diverse population of Houston reaches beyond the realm of medicine to providing a range of social services through multi-service centers and to ensuring equal access to public health services. Under her leadership, Houston has reported significant improvements in infant mortality rates and infant immunization. Dr. desVignes-Kendrick has also led investigations of endemic and imported communicable disease outbreaks in Houston, and she is experienced in environmental investigations. She is past President of the National Association of County and City Health Officials, an organization that represents nearly 3,000 local health departments nationwide, and she is a member of the National Vaccine Advisory Committee. She earned her medical degree at Meharry Medical College and completed her pediatric residency at Baylor College of Medicine, where she served as assistant professor in the department of community medicine. She received a Master of Public Health degree from the University of Texas School of Public Health in Houston. A partial listing of her awards includes: the American Public Health Association's 1997 Milton and Ruth Roemer Award for creative local public health work, the National Forum for Black Public

Administrators' Certificate for Commitment to Excellence and Service to the Public, and the National Organization for the Professional Advancement of Black Chemists and Chemical Engineers' Top Doc Award. She and her husband, Ernest A. Kendrick, a psychiatrist that works with children and adolescents, have three children, Aziza, Jelani, and Shomari.

## David Frohnmayer

Term: 1999–2001

Dr. Frohnmayer is President of the University of Oregon, a major research institution with strong programs in biology and neuroscience. He and his wife, Lynn Diane Frohnmayer, co-founded the Fanconi Anemia Research Fund after their three daughters were diagnosed with this rare congenital disease. Dr. Frohnmayer has used his concern for his own children to assist other families affected by this complex medical condition, to stimulate a better understanding of the disorder, and to develop sources of financial support for medical research. The Fanconi Anemia Research Fund provides seed money to help scientists develop preliminary results needed to generate research proposals competitive for NIH funding. Dr. Frohnmayer estimates that laboratories whose early work was supported by the Research Fund have received more than $13 million in NIH support. He is a past member of the board of directors for the Fred Hutchinson Cancer Research Center and the National Marrow Donor Program and has participated actively in professional and civic associations, including the National Association of Attorneys General, the Governor's Special Commission Against Violent Crime, the Oregon Federation of Parents for a Drug-Free Youth, the Oregon Special Olympics, and the Children's Miracle Network Telethon. He has been elected to three terms in the Oregon Legislative Assembly and to three terms as Oregon Attorney General. On the national level, he was Assistant to the Secretary of what was then the U.S. Department of Health, Education, and Welfare and consultant to the Civil Rights Division of the U.S. Department of Justice. A graduate of Harvard College, Dr. Frohnmayer attended Oxford University as a Rhodes Scholar and earned his law degree from the University of California in Berkeley. The Frohnmayers are authors of Fanconi Anemia: A Handbook for Families and Their Physicians. In 2000 the Frohnmayers were honored with two national awards: Research! America's Advocacy Award and the Americans for Medical Progress Educational Foundation's Albert B. Sabin Heroes of Science Award. They have one surviving daughter and two sons.

## Lydia Lewis

Term: 1999–2001

Ms. Lewis, in her leadership position as Executive Director of the National Depressive and Manic-Depressive Association (National DMDA), has worked to remove the stigma from mental illness and to build public understanding of people with mood disorders. With more than 400 support groups across the United States and Canada, National DMDA is the country's largest patient-run, illness-specific nonprofit organization committed to advocating for research toward the elimination of mood disorders. National DMDA also works to inform patients, professionals, and the public that mood disorders are treatable; to foster self-help among people and families living with these illnesses; to eliminate discrimination and stigma against these individuals; and to improve access to care. Having joined the National DMDA staff in 1997, Ms. Lewis is credited with revitalizing the organization at a time when it seemed unlikely to continue and establishing strong cooperative relationships with other organizations, even though she had only worked with the organization less than two years. She currently serves on a joint task force of NIH's National Institute of Mental Health (NIMH) and National Center for Complementary and Alternative Medicine that is overseeing a clinical trial on St. John's wort, and she serves on the NIMH Oversight committees for the Star*D, TADS, and Step-BD clinical trials. She has published several articles in peer-reviewed journals and has presented at a wide range of mental health conferences. National DMDA was an active partner in NIMH's D/ART Program, promoting awareness of depression in the workplace. National DMDA's primary goal is to educate the general public, the media, medical professionals and legislators that mood disorders are treatable medical illnesses. Another goal is to ensure that the National DMDA provides strong links among mental health consumers, family members, and researchers and clinicians across the nation. Before joining National DMDA, Ms. Lewis worked at AT&T and was responsible for employee morale concerns during the period of its divestiture from the Bell Operating Companies. Ms. Lewis also served 11 years as Executive Director of The Committee of 200, an international nonprofit organization of preeminent women business owners and executives.

## Maurice F. Rabb

Term: 1999–2001

Dr. Rabb is Medical Director of Prevent Blindness America, a national volunteer eye health and safety organization serving millions each year through public and professional education, community and patient services, and medical research. A practicing ophthalmologist and clinical researcher, Dr. Rabb heads the Department of Ophthalmology and is President of the medical staff at Chicago's Mercy Hospital and Medical Center. Dr. Rabb is also Professor of Ophthalmology at the University of Illinois at Chicago. He has been active in the development of fluorescein angiography and has also made significant contributions to advancing public health through his service on advisory panels and committees. His research interests focus on understanding the effects of systemic diseases, such as diabetes, on the eye. Dr. Rabb has received support from NIH during his career and has served as a member of the Macula Society, the National Eye Institute's Eye Advisory Council, and as Chair of NIH's Sickle Cell Disease Advisory Council. He has also held positions as Acting Associate Chancellor and Interim Associate Vice Chancellor for Urban Health at the University of Illinois at Chicago. Dr. Rabb is active in the American Academy of Ophthalmology, the National Medical Association, and the Chicago Ophthalmological Society.

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DIRECTOR'S COUNCIL OF PUBLIC REPRESENTATIVES

# May 1, 2001 Meeting Minutes

**5th Meeting of the Director's Council of Public Representatives**
**Tuesday, May 1, 2001**
**8:30 a.m.**
**Building 31C, Conference Room 6**
**National Institutes of Health**
**Bethesda, Maryland**

The Council of Public Representatives convened its fifth meeting at 8:30 a.m., Tuesday, May 1, Building 31C, Conference Room 6, National Institutes of Health, Bethesda, Maryland. The meeting was open to the public.

Dr. Ruth Kirschstein, Chair, Council of Public Representatives, and Acting Director, National Institutes of Health (NIH), presided.

## COUNCIL MEMBERS PRESENT:

- Luz Claudio
- Melanie C. Dreher
- Pam Fernandes
- Vicki Kalabokes
- Barbara Lackritz
- Joan Lancaster
- Debra R. Lappin
- Roland McFarland
- Isaac Montoya
- Rosemary Quigley
- Bob Roehr
- Thomas Vaalburg
- Douglas Yee

## COUNCIL MEMBERS ABSENT:

- Maurice Rabb

## AD-HOC PARTICIPANTS PRESENT:

- Marilyn Benoit
- Evelyn Bromet
- Ellen Grant
- Bob Martin
- Rodrigo Muñoz
- Leonard Tamura

### Executive Summary

Dr. Ruth Kirschstein began the 5th Meeting of the Director's Council of Public Representatives (COPR) by welcoming several ad hoc members and briefing the COPR on the President's budget request and anticipated appropriations hearings before Congress. She also provided a brief overview of important recent events, including NIH involvement in completion of a draft sequence of the human genome; new legislative authority granted to encourage health professionals, primarily physicians, to pursue clinical and basic science research careers; expanded NIH programs including the establishment of the NIH National Center for Minority

Health and Health Disparities Research, a new program to better enable 24 states to improve their infrastructures and make them more competitive for NIH grants; several efforts to explain to the public and Congress how NIH is allocating the funding it receives from Congress; and initial plans for establishing the recently mandated new NIH National Institute for Biomedical Imaging and Bioengineering. She also summarized several personnel changes among key NIH administrators.

Dr. Kirschstein said that the first meeting of the special NIH review committee, Human Pluripotent Stem Cell Review Group (HPSCRG), was postponed, pending a review of this entire area of research by the Department of Health and Human Services (HHS). She also said that she recently testified on this issue before Congress, reminding them that if such research is restricted to the private sector, it will not be subject to federal oversight.

COPR members presented a series of brief reports describing their recent NIH-related individual and working group activities on a range of topics, including efforts to make NIH Web sites more accessible to the visually impaired, efforts to coordinate NIH site visits in Tennessee and Hawaii, efforts to identify ways of streamlining regulatory burdens while strengthening protections for those who participate in clinical trials, and efforts to evaluate the overall performance of the directors of the NIH National Institute of Environmental Health Sciences (NIEHS) and the National Institute for Nursing Research (NINR).

Dr. Patricia Grady, Director of the NIH NINR, described her Institute's programs and priorities, including research focusing on chronic illnesses, end of life, genetics, and health disparities; completion of a strategic plan for the Institute, which emphasizes supporting research opportunities, disseminating findings, and training nurse researchers; and other targeted studies, such as low birth-weight babies, coping with chronic illness among teenagers, helping the elderly return home following hospital care, and developing bilingual tools for communicating with Hispanic populations. NINR's Division of Intramural Research sponsors several training programs each year, including one in human genetics and another to train nurses on how to launch their scientific careers.

Dr. Allen Spiegel, Director of the NIH National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), said that the Institute sponsors research in diabetes and six additional areas, adhering to a strategic plan that was developed following a public meeting held in October 1999. Noting that some 16 million individuals have diabetes and the high toll that it exacts in medical costs—which is estimated at $100 billion per year—this disease has a high priority within the Institute, according to Dr. Spiegel, who summarized a number of the complications associated with type 1 and type 2 diabetes and research efforts aimed at better understanding and combating them.

Dr. Duane Alexander, Director of the NIH National Institute of Child Health and Human Development (NICHD), said that, in terms of planning and conducting biomedical research or for purposes of determining appropriate therapeutic drug doses, children cannot be considered small adults. He also pointed out that many childhood diseases are dealt with by preventive vaccine treatments, thus making it essential to focus on children rather than adults when conducting research on such vaccines. Another important reason for conducting research on children is that they are the appropriate target population in efforts to delay the onset of diseases, conditions, and behaviors primarily affecting adults, including smoking, drug abuse, and obesity. Because of challenges in achieving informed consent, research on children was nearly abandoned during the 1970s. Although research on children is thriving again, researchers and administrative officials need to exercise considerable care in ensuring that children who participate are subjected to minimal risks and that extra effort is made to maintain high safety standards.

COPR members Ms. Debra Lappin, Dr. Isaac Montoya, Ms. Rosemary Quigley, and Dr. Melanie Dreher summarized efforts of the Human Research Protections Working Group, whose members prepared a draft report on this subject. That report describes the importance of having a public perspective and maintaining a careful balance between efforts to advance knowledge and those intended to protect patients who participate in clinical research programs. The members of this working group acknowledged the complex network of oversight and advisory boards and committees that are actively involved in these issues. They also plan to revise their own report based on COPR discussion.

Dr. Kirschstein and Dr. Wendy Baldwin, the NIH Deputy Director for Extramural Research, encouraged the members of the working group to continue developing a broad-based document that would help to educate the public about key patient-protection issues; to review prototype informed consent documents, such as one that has been developed by the NIH National Cancer Institute, for its potential usefulness in other biomedical research areas; and to consider other ways that COPR members can provide suggestions to help Institutional Review Boards do a better and more uniform job in protecting human subjects.

COPR members commented on future meeting agendas, requesting that Dr. Kenneth Olden, NIEHS Director, and Dr. Stephen Straus, Director of the NIH National Center for Complementary and Alternative Medicine, be invited to give presentations.

## NIH Director's Report

Dr. Ruth Kirschstein began the 5th Meeting of the Director's Council of Public Representatives (COPR) by welcoming several ad hoc members to the council whose formal appointments are pending, Marilyn Benoit, Evelyn Bromet, Ellen Grant Bishop, Robert Martin, Rodrigo Munoz, and Leonard Tamura. She congratulated COPR member Pamela Fernandes for winning a bicycling gold medal in the Para Olympic Games that were held in Australia.

Dr. Kirschstein reviewed President Bush's budget request for NIH for fiscal year (FY) 2002 that was released initially in outline form in February and later in full detail on March 9. That budget request calls for a 13.5 percent increase to $23 billion for NIH, representing the fourth installment in a plan that aims to double the NIH budget within a five-year period.

Dr. Kirschstein and other NIH Institute Directors typically are called on to testify on spending plans before appropriations subcommittees of both the House of Representatives, where Representative Ralph Regula (R-OH) chaired the Subcommittee on Appropriations for Labor, Health and Education, and the Senate, where Senator Arlen Specter (R-PA) chaired the corresponding Appropriations Subcommittee. Rep. Regula, who recently succeeded retired Rep. John Porter (R-IL), is holding a series of theme hearings on NIH budget-related issues instead of hearings intended to scrutinize closely NIH programs institute-by-institute. Dr. Kirschstein said that several members of Congress, including Rep. Regula recently visited NIH, as did Rep. David Obey (D-WI), who is the ranking minority member of the House Appropriations Subcommittee dealing with NIH. In addition, HHS Secretary Tommy Thompson visited the NIH campus, including the Clinical Center. Other noteworthy NIH events that are scheduled for June include the naming of the plaza in front of the NIH Shannon Building in honor of former Representative Paul Rogers and the dedication of a new laboratory building, named in honor of former Representative Louis Stokes of Ohio.

Formal appropriations hearings were scheduled for May 16 in the House of Representatives and May 23 in the Senate, according to Dr. Kirschstein. Among highlighted NIH programs and achievements are the completion of a full draft sequence of the human genome; rapid progress in efforts to sequence genomes of other organisms such as the mouse and rat; heightened emphasis on clinical research programs, including authorizing legislation from December 2000 that provides career development awards and also enables NIH to repay loans at a level of $35,000 per year (plus ancillary expenses) for medical students while they are being trained to conduct clinical research; new emphasis on infrastructure and enabling technologies, including support of 36,000 grants, the highest number in NIH history; and research on health disparities and underserved populations, including an increase in the proposed budget for the new NIH National Center for Minority and Health Disparities by 20 percent to $158 million.

Dr. Kirschstein said that NIH will begin the Biomedical Research Infrastructure Network (BRIN) Program in FY 2001 that is aimed at bolstering institutions in 24 states that receive relatively little funding from NIH to support research. The new program provides funding to help institutions within those states form consortia and take other steps to make future biomedical research proposals more competitive. NIH also recently increased stipends for predoctoral and postdoctoral researchers by 10 percent, and is developing a plan for adjusting those stipends systematically during the next five years.

Dr. Kirschstein reminded COPR members that legislation was enacted to establish the NIH Institute for Biomedical Imaging and Bioengineering (NIBIB). She pointed out that many NIH Institutes, particularly the National Cancer Institute and the National Heart, Lung, and Blood Institute, are sponsoring research in the areas in which the new Institute will specialize. The initial budget request for NIBIB in FY 2002 is for $40 million, and Dr. Donna Dean is serving as its interim director.

Dr. Kirschstein said that the first meeting of the special NIH review committee, Human Pluripotent Stem Cell Review Group (HPSCRG), will review compliance documents related to conducting research on human embryonic stem cells. The meeting, which was scheduled for April, was postponed while HHS officials conduct a broader review of such research. In response to a question from Ms. Rosemary Quigley, Dr. Kirschstein said that both scientific and legal reviews of stem cell research are under way, and that NIH plans to have its scientific report completed early in June. She said that an announcement of that initial meeting was being postponed to coincide with the release of President Bush's FY 2002 budget request but there was no link between these two activities. She also said that during a hearing before the House Appropriations Subcommittee, she responded to Rep. Roger Wicker (R-MS), telling him there is a need to compare results from studies on human stem cells from adult and embryonic sources. She also told him that, if all such research is being done in the private sector, there is no requirement for information about it to be published or for researchers to adhere to federal guidelines.

Dr. Kirschstein mentioned several recent NIH personnel changes, including the appointment of Dr. Paul Sieving from the University of Michigan to Director of the NIH National Eye Institute (NEI) as of June 1; the departure of Dr. Gerald Fischbach, who was Director, NIH National Institute of Neurological Diseases and Stroke, for which a position search is under way; and a search is under way for Director of the NIH Office of AIDS Research.

*Discussion*

In response to a question from Dr. Isaac Montoya, Dr. Kirschstein said that the BRIN program already has conducted workshops and provided technical assistance to help the 24 designated states build infrastructure at local research institutions.

In response to questions from Mr. Douglas Yee about NIH budgets after the five-year doubling period, Dr. Kirschstein said that continued increases of 15 percent per year should not be expected, but some increases will be needed to accommodate expanding scientific opportunities. A concern is that federal support for research in the allied physical sciences is not being expanded at other agencies.

## COPR Members Report to NIH Director on COPR Activities

Ms. Barbara Lackritz, who said that her book, *Adult Leukemia*, is now in its second printing, has been speaking to groups concerned about cancer. She will visit with officials in the Department of Defense to discuss tumor registries, and with officials at the NIH National Institute of Dental and Craniofacial Research to discuss its programs. Moreover, she was appointed to the NIH National Cancer Institute (NCI) public forum for advocates.

Ms. Pam Fernandes said that she is working with information technology specialists at NIH to make NIH Web sites more accessible to people with impaired vision. She said that NIH is making good progress in this effort, and its specialists are going beyond current legislative mandates to improve accessibility.

Mr. Doug Yee said that he is meeting with researchers at several institutions in Hawaii to develop ways of making them more competitive when seeking support from NIH for their biomedical research programs. Already, administrators from the medical school at the University of Hawaii have appointed a new dean and are holding broad-based meetings to address such issues. These meetings also are leading to new developments involving nonprofit organizations that provide resources to support researchers at the medical school and elsewhere in Hawaii. Dr. Kirschstein said that NIH officials have and will continue to work with Senator Daniel Inouye (D-HI) on these issues.

Dr. Melanie Dreher mentioned three COPR-related assignments, the first involving her effort to espouse a broader view being taken while developing evidence-based practices in medicine. For instance, she was appointed to a committee advising the NIH Office of Medical Applications of Research (OMAR), where she is urging OMAR to consider evidence other than from randomized clinical trials and to design alternative types of clinical trials. Her second assignment involves finding relief from federal regulatory burdens for researchers and institutions, and she is working with a committee that advises Dr. Wendy Baldwin, NIH Deputy Director for Extramural Research. The committee mandate is to increase efficiency and reduce costs from regulatory burdens associated with NIH-supported biomedical research—for instance, that arise while administering IRBs that protect human subjects participating in such research.

Dr. Dreher said that her third assignment led her to participate in an evaluation of the NIH National Institute for Environmental Health Sciences (NIEHS). She said that the concept of environmental justice pervades its programs, and she praised its efforts to protect public health broadly, focusing not so much on specific diseases but on environmental forces that can affect many diseases. She recommended that Dr. Kenneth Olden, Director of NIEHS, be invited to speak to COPR members.

Ms. Debra Lappin said that she attended the first meeting of the council that is advising the HHS Office for Human Research Protections (OHRP). During that

meeting, two issues were foremost: i) conflicts of interest as they may affect clinical trials and ii) protective measures that pertain to subjects participating in behavioral and social science research projects. Also, when Ms. Lappin gives talks on medical ethics or women's health issues, she often is asked about COPR.

Mr. Bob Roehr, who belongs to the Association of Health Care Journalists, is exploring whether its members can work with Dr. Barry Kramer, Director of the NIH Office of Medical Applications of Research, to develop continuing education programs for journalists specializing in health care issues. Dr. Kirschstein noted that Dr. Kramer is also being appointed Director of the NIH Office of Disease Prevention to replace Dr. Bill Harlan, who has retired. Mr. Roehr is exploring other ways to forge relationships between NIH and the Association, while planning events for its 2002 meeting, to be held next April in Washington, DC.

Ms. Rosemary Quigley said that she accepted a faculty position at the Baylor College of Medicine, Center for Medical Ethics and Health Policy. She described her involvement in efforts to revise NIH guidelines for reporting adverse clinical events during gene transfer procedures.

Ms.Vicki Kalabokes, as a member of the Coalition of Autoimmune Patient Groups, met with officials at the National Institute of Allergy and Infectious Diseases (NIAID) to review research efforts in this area that are sponsored elsewhere at NIH. She also was part of a team that conducted a comprehensive review of the NIH National Institute of Nursing Research.

Mr. Roland McFarland said that members of the film and television community in Hollywood met with former HHS Secretary Donna Shalala and with Surgeon General David Satcher to consider how to interject public health messages in films and television programs. In addition, the NIH National Institute on Drug Abuse participates in sponsoring the Prism Awards that recognize creative themes and messages within entertainment programs that address the problem of substance abuse. He also said that many production studios now sponsor medical research fund raising events. In response to a comment from Ms. Lackritz about the depiction of smoking in movies, Mr. McFarland said that there are ongoing discussions about this issue, with greater control over television programming than over feature films.

Dr. Isaac Montoya said that through the Health Resources and Services Administration (HRSA), he frequently visits community-based clinics in Texas that serve low income, migrant laborers, and other underserved population groups and provides them with NIH informational materials. Also, whenever he visits universities, he reserves time to visit neighboring clinical centers and to provide them with such materials.

Dr. Luz Claudio has worked with NIEHS to develop community outreach and education programs.

Ms. Joan Lancaster hosted a visit by NIH officials to East Tennessee State University Medical School. Ms. Lancaster expressed frustration that this institution is not eligible for support under the NIH BRIN program. Dr. Kirschstein noted that other NIH programs through the National Cancer Institute and the NIH National Center on Minority Health and Health Disparities can provide research-funding opportunities for that and other institutions in the Appalachian region. Ms. Lancaster said that she has worked with Senator Bill Frist (R-TN) to find federal support for the medical school and she also is involved with a regional council on tobacco and health that is seeking support for health care and health-related research activities.

Dr. Kirschstein said that Dr. Maurice Rabb, who could not attend the COPR meeting, made a formal presentation about the COPR to the national advisory committee of the NIH National Eye Institute (NEI).

## Important Aspects of Nursing Research

Patricia Grady, Ph.D., R.N., F.A.A.N., Director, National Institute of Nursing Research (NINR), said that the Institute's mission is to support research contributing to the knowledge base for nursing care. NINR-supported research is broad based, including chronic illnesses, end-of-life care issues, palliative care, disease prevention, genetics, quality of life, and health disparities. NINR supports individual researchers, workshops, an annual roundtable on nursing research, and smaller advisory meetings to reevaluate research priorities. Many of these activities entail collaborative efforts with sister NIH Institutes and centers.

The NINR strategic plan calls for high quality research, collaborative efforts with other disciplines, disseminating research findings to the wider community, training and career development programs, and support for health disparities research, which includes outreach and infrastructure development. Targeted study efforts include: a cost-savings study of a healthy newborn community intervention program; a program to reach diabetic teenagers to help them with comprehensive blood-sugar control efforts to ameliorate the long-term impacts of this disease; a study of accelerating hospital-to-home transitions for elderly patients as a way of reducing overall health care costs; and interventions to improve the quality of life for arthritis patients in a Spanish-speaking population group.

Another continuing concern for NINR is the nursing shortage, along with a shortage of nurse researchers, according to Dr. Grady. The NINR Intramural Program sponsors several training programs each year, including one in human genetics and another to train nurses on how to conduct research projects. Dr. Grady also pointed to several priority programs, including the Institute's focus on end-of-life care research. Finally, she invited COPR members to attend the NINR 15th anniversary celebration on September 20-21, 2001.

*Discussion*

Ms. Lappin said that because the name of the Institute belies the breadth of its programs, NINR leaders face an important challenge in communicating to the public the full extent of the Institute's mission. Dr. Grady agreed that NINR's name does not adequately describe its activities but indicated that a name change is unlikely. Dr. Kirschstein agreed, pointing out that members of the nursing community and of Congress who helped to establish the Institute would likely resist changing its name.

Ms. Lackritz suggested that NINR develop outreach programs for youth as a way of encouraging them to consider nursing careers. In response, Dr. Grady said that NINR officials are working to provide information about careers in health research and allied areas to ever-younger groups of people. Other efforts are directed at undergraduate students, including those in minority groups and attending universities that traditionally serve such communities, encouraging them to work in research programs during summers and to pursue additional opportunities in biomedical research.

Dr. Claudio noted that in many of Dr. Grady's examples, evidence was provided as to the cost-effectiveness of various interventions. In response, Dr. Grady said that providing such information is part of a broader trend to indicate where and how a specific intervention might affect costs, sometimes increasing short-term costs of care while providing overall savings and improved quality of life. Dr. Kirschstein said that Rep. Ernest Istook Jr. (R-OK) regularly requests information from NIH as to how new technologies and interventions affect the health care costs.

In response to a question from Dr. Benoit about cutbacks affecting school nurses, Dr. Grady said that some research projects indicate that nurses can provide information to teachers about behaviors that would enable children to improve their overall health—for instance, in ways that could reduce their long-term risk for developing cardiovascular illness. Some of these programs are directed at students from minority groups.

Dr. Dreher said that she is proud to be a nurse scientist, and that Dr. Grady's report reinforces her sense of professional pride. She also said that, although much of the research being sponsored by NINR is not glamorous, it is of fundamental importance to the American public.

Dr. Montoya said that he has helped to improve communications between NINR and organizations representing those working in clinical laboratories, another profession with an acute shortage of trained personnel.

## Recent Advances in Diabetes Research

Ms. Fernandes introduced Allen Spiegel, M.D., Director, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), noting that he came to NIDDK in 1973, and served as Scientific Director for the Institute for nine years before being appointed Institute Director on November 15, 1999.

Dr. Spiegel referred COPR members to written materials and to the NIDDK Web site for additional information describing the Institute's mandate and its programs. Spanning a broad range of internal medicine and chronic disease, the research portfolio includes investigations in diabetes, endocrinology, metabolic and genetic diseases, digestive and nutritional disorders, and kidney, urinary tract, and blood disorders. In addition to providing extensive support to researchers outside of NIH, the Institute supports an intramural program at NIH in Bethesda and one in Phoenix, Arizona, where the focus is on type 2 diabetes and obesity in Pima Indians of the Gila River Indian Community.

Like many other NIH Institutes and centers, NIDDK developed a strategic plan several years ago through a process that included substantial public input, according to Dr. Spiegel. Diabetes research is naturally a pivotal component of NIDDK programs, and its impact is felt across other specific areas and involves other NIH Institutes, such as the National Heart, Lung, and Blood Institute, the National Eye Institute, and the National Institute of Child Health and Human Development. For example, diabetes is the main cause of kidney failure, necessitating dialysis and transplantation procedures; blindness is a common complication of diabetes; and heart disease remains the main cause of death among individuals with diabetes. Diabetes costs the Nation an estimated $100 billion each year.

Diabetes is a complex disease involving dysfunction of the hormone insulin, which is secreted by specialized islet cells within the pancreas, and that acts on fat, liver, and muscle cells to regulate sugar transport and metabolism, according to Dr. Spiegel. There are two distinct forms of diabetes but, in both cases, maintenance of good blood sugar control helps to mitigate or avert complications. Type 1 diabetes, an autoimmune disease, leads to destruction of the pancreatic islet cells that ordinarily produce insulin. It often strikes the very young, and insulin treatment is essential. Type 2 diabetes results from reduced sensitivity to, and reduced secretion of, insulin but generally is not due to autoimmune destruction of islet cells of the pancreas. Although weight loss, diet, and exercise are helpful initially in controlling type 2 diabetes, individuals often require treatment with a variety of non-hormonal medications and insulin.

Population figures indicate that the incidence of type 2 diabetes is rising sharply within the U.S., even among young people, according to Dr. Spiegel. This disease is especially widespread among Pima Indians, affecting 65 percent of this group, and among other minority groups, such as African Americans and Mexican Americans. Obesity is a major risk factor for developing this type of diabetes. Moreover, recent studies indicate that lifestyle changes to control weight and blood glucose levels can prevent the development of frank diabetes among specific population groups, and large-scale studies are under way in the U.S. to determine whether interventions such as diet, exercise, and therapeutic drugs are applicable to preventing diabetes among broader-based population groups.

Other studies are probing the genetic and environmental factors that predispose people to develop type 2 diabetes. For example, researchers in 1995 described the hormone leptin in obese mice and now believe that it contributes to the development of insulin resistance, a key intermediate step en route to developing type 2 diabetes.

Precisely what gives rise to type 1 diabetes remains unknown, according to Dr. Spiegel. Studies of identical twins indicate that both genetic and environmental factors come into play, triggering the autoimmune destruction of the pancreatic islet cells that ordinarily produce insulin. NIDDK is sponsoring research to identify more of the factors that contribute to this early-stage development of the disease, hoping to find new ways of blocking deterioration before frank diabetes is established.

In more severe, or "brittle," cases of type 1 diabetes, it can be very difficult to regulate blood sugar levels, according to Dr. Spiegel. However, a small number of such individuals have been cured of their disease after receiving transplanted pancreatic islet cells from non-diabetic donor pancreases. Because results following this procedure are not uniformly successful, Dr. David Harlan of NIDDK is beginning a follow-up transplant study to refine and further evaluate this procedure, which is accompanied by chronic immunosuppressive therapy to maintain the transplanted cells. Another problem is that the supply of islet cells from pancreases obtained from cadavers is woefully inadequate.

NIDDK is also involved in extensive public education and outreach efforts to inform various population groups about the signs and risks of diabetes, particularly those associated with the epidemic of type 2 disease that is especially rampant in Hispanic, Native American, and African American communities. Information about materials available through the National Diabetes Information Clearinghouse and education programs and awareness campaigns of the National Diabetes Education Program are on the NIDDK home page.

*Discussion*

Ms. Fernandes described her own recent disturbing encounter with a physician who appeared to be wholly unaware of her health history, including some 35 years as a diabetic. She said that this incident and others like it indicate that NIDDK faces a major public communications challenge. In response, Dr. Spiegel said that NIH has an important role to play in educating the public but that it needs help from other organizations to deal with challenges such as health care fragmentation. This public education effort will also benefit from involvement of additional members of the health care professions, such as pharmacists and nurses, to deliver broad-based messages about diabetes and other complex diseases.

In response to a question from Dr. Dreher, Dr. Spiegel said that several NIDDK-sponsored programs are aimed at evaluating behavioral interventions in the context of diabetes disease research, particularly as a way of helping obese individuals to lose weight and reduce their risk of type 2 diabetes. Other diet-and-behavior programs are directed at school-age children, such as Hispanic Americans in the San Antonio area. However, because these issues are more complex and involve the interplay of the hormone leptin with diet, research is under way to delve more deeply into how individuals may more effectively control weight over the long term.

In response to a question from Ms. Lappin about what might trigger the autoimmune responses that lead to type 1 diabetes, Dr. Spiegel said that there are many unproved ideas about viruses—such as enteric viruses—or other infectious agents being the triggering agents. For example, in both Finland and Sardinia, where public health officials maintain registries of diabetes cases, there seems to be a seasonal incidence of the disease, suggestive of an infectious disease trigger. There is another unproven hypothesis linking diabetes to the consumption of cow's milk. In addition, there is evidence of a broader susceptibility among diabetics to other autoimmune conditions, suggesting a broader genetic predisposition for such diseases, which leaves open the question of why the pancreas is the target organ for some individuals, whereas other organ systems are the targets in other cases. Nonetheless, if type 1 diabetes is indeed triggered by autoimmunity, it may be possible to block its onset with drugs that interfere with immune system responses.

In response to a question from Dr. Montoya about a vaccine-based approach, Dr. Spiegel said that, if a particular virus proves to be the triggering event for type 1 diabetes, then perhaps a conventional vaccine could help prevent that infection and subsequent autoimmune responses that appear to lead to this long-term disease. Another quasi-vaccine approach, more accurately termed an immune tolerance approach, would be to redirect the autoimmune response as a way of preventing the steps leading to destruction of the pancreatic islet cells that produce insulin. One such approach being tested in animals involves administering to them a part of the insulin molecule, much as a vaccine would be, as a way of preventing destructive immune system responses to this hormone.

In response to a comment from Dr. Benoit about sedentary school children, Dr. Spiegel agreed that there is a widespread problem and said that some children are the target of discriminating advertisements that further encourage bad eating habits and inactive lifestyles. The National Diabetes Education program has established a Work Group on Diabetes in the Schools and another Work Group on Diabetes in Children to address this problem.

In response to a question from Dr. Martin about the Tribal Nations and the Indian Health Service, Dr. Spiegel said that NIH is working on multiple levels to reach this population group—at different ages and in many different settings. Some of these efforts are aimed at encouraging such children to pursue scientific careers, whereas other efforts are include working with tribal leaders. In response to related questions from Dr. Bishop about the entertainment industry providing a means to reach certain population groups, Dr. Spiegel said that high-profile individuals from professional sports teams and from the television and film industries are very helpful in developing and then delivering diabetes-related messages to hard-to-reach population groups.

## Research Involving Children

Duane Alexander, M.D., Director, National Institute of Child Health and Human Development (NICHD), described three major reasons for conducting biomedical research on children. First, because children are not merely small adults, researchers cannot simply extrapolate research findings in adults and apply them to children. Based largely on this argument, pediatricians, led by Dr. Robert Cook in 1960, convinced then newly-elected President John Kennedy to establish NICHD at NIH. Although NICHD has a special focus on children's health issues, virtually all the other NIH Institutes conduct research involving children.

Dr. Alexander made a point about food intake per body weight to illustrate the folly of extrapolating—in this case, food intake—from adults to children. The extrapolation becomes increasingly absurd the smaller and younger the child, eventually breaking down altogether when applied to infants, whose nutritional needs are very high and would not be met at all if they were given low amounts of food on the basis of such extrapolations.

Similar principles apply when trying to assign appropriate drug doses for children by extrapolating from values that are based strictly on weight differences from those drug doses that are appropriate for adults of a given size, according to Dr. Alexander. The fact that children typically metabolize drugs at very different rates because they produce lower levels of specialized enzymes needed for doing so further complicates this picture.

For example, during the 1960s, the antibiotic chloramphenicol was routinely administered to babies in doses that were determined by extrapolating from adult-appropriate doses. However, because babies lack a liver enzyme that chemically modifies the drug to ease its excretion, they would develop 10- to 100-fold higher than normal doses during a course of treatment, inducing gray baby syndrome. Once the medical community realized what was happening, dosing regimens for babies were reconfigured at levels tenfold lower than those for adults. Despite such experiences, initial dosing of new drugs for children is still sometimes based on extrapolated values, except for drugs belonging to certain chemical classes. However, the Food and Drug Administration (FDA) now requires manufacturers to test new drugs in children, and NICHD has established a network of pediatric pharmacology research units to assist in such testing.

A second major reason that research is conducted in children is that many diseases, including neonatal respiratory distress syndrome, sudden infant death syndrome, and birth defects such as spina bifida and congenital heart disease, are manifest in children but not adults, according to Dr. Alexander. Moreover, to study growth and development, researchers need to study children.

Dr. Alexander said that a third major reason for conducting biomedical research on children is that insights about specific diseases can lead to interventions that prevent or delay the onset of those diseases among adults. For instance, calcium intake for long-term storage is essentially completed by age 20, meaning that early childhood consumption of this nutrient is a critical factor for forestalling osteoporosis much later in life. Other familiar examples include smoking or alcohol and drug abuse, which typically begin early in life but have long-term consequences for health.

Despite the obvious need for conducting research on children, during the 1970s extremists voicing ethical concerns came close to prohibiting such activity when they insisted on a very strict interpretation of the need for informed consent, according to Dr. Alexander. However, a national commission carefully examined this issue along with other ethics-based concerns about biomedical research and concluded that research with children is essential and that permission from parents and assent from participating children, where possible, were sufficient ethical criteria for moving forward with research.

In addition, the commission established several categories of research, each of which requires different levels of protection when children are involved. For instance, research posing a minimal risk to children, regardless of whether a particular child might benefit from it, could proceed so long as one parent agreed and the child assented. If the research involved greater than minimal risk but is intended to benefit the child, it could proceed, so long as the benefits were equal to or outweighed the risks—again, also with permission from a parent. For the category called minor increase over minimal risk, the commission recommended that in such cases, permission from both parents as well as assent from children is required before proceeding. Finally, for research that does not fit these risk categories but is considered worth pursuing, the HHS Secretary is to appoint a special panel to review that research and to advise whether it should be pursued. This system has been in effect since 1983.

More recently, since the 1990s, interest is increasing to conduct research involving women, members of minorities, and children, populations who were once thought to be too vulnerable to participate, according to Dr. Alexander. Indeed, Congress mandates inclusion of women and minorities in many kinds of biomedical research, as well as children, unless their exclusion can be justified.

Meanwhile, researchers and those charged with implementing the commission's guidelines from the 1980s are challenged by efforts to interpret the categories of risk and how to apply them to specific situations. Dr. Alexander said that a current debate over whether minimal risk applies equally to healthy and sick children is misapplied. He said that the commission established the category of minor increase over minimal risk to cover sick children who are routinely exposed to risks as part of their necessary medical treatment and who may thus bear some additional risks to gain knowledge to help other children with similar conditions. Other current issues include concern over whether several minimal risks are cumulative or should be considered separately and whether adolescents should be treated differently from younger children in terms of seeking consent versus assent.

*Discussion*

Dr. Kirschstein pointed out that Dr. Alexander and Ms. Anne Thomas served as staff members to the commission during the 1970s.

In response to a question from Mr. Roehr about the applicability of animal studies, Dr. Alexander said that the same difficulties pertain to children as to adults, namely that studies in animals are useful but not definitive for predicting what happens in humans. In any case, researchers interested in studying children consider it useful to study young animals, and when concerns revolve around pregnant women, researchers consider it useful to study pregnant animals.

Mr. Roehr asked about the need for and the standard procedures for conducting studies in children or in pregnant women to evaluate drugs. Dr. Alexander said that FDA officials and industry representatives typically conduct adult studies first and only later consider studies in women and children, provided the candidate drug is seen as eventually useful for treating conditions that they may develop and only after tests in young and in pregnant animals are completed. Moreover, in general, proof of efficacy may be waived for children as long as safety and dosing studies are completed.

In response to a question from Dr. Benoit about dividing children into gender groups for the purposes of biomedical research studies, Dr. Alexander said that, although little attention was paid to this question, it seems likely that researchers will look more carefully at potential gender differences in their results from biomedical studies involving children.

Ms. Quigley commented on her experiences in clinical trials as a young child with cystic fibrosis, including low-fat diets and sleeping in a high-humidity tent. She also recalled not being consulted about participating in certain contemplated protocols and said that pediatric investigators should routinely explain to children that they might not benefit from participating in research. Dr. Alexander said that researchers owe it to children to try to explain what the research is about and to treat assent-related issues as seriously as informed consent. He also noted that many children are altruistic and are willing to participate in research because it can benefit others.

In response to a question from Dr. Evelyn Bromet about long-term cohort studies that start with young children and may follow them through adolescence and adulthood, Dr. Alexander said that one such study of cerebral palsy from the 1950s and 1960s came to a halt because investigators concluded that most of the questions they needed to address required following children only to the age of seven. The study indicated that the disease reflects abnormalities that arise before birth, either from genetic abnormalities or other developmental problems that occur in utero. He also pointed out that such studies can be extremely expensive to continue. Dr. Kirschstein said that such long-term studies are begun with considerable interest, but sometimes that interest fades over the years.

On a related matter, NICHD is planning a major long-term study under the auspices of the President's Task Force on Environmental Health Safety Risks for Children. The study is endorsed widely by Congress, the Secretary of Health and Human Services, the Administrator of the Environmental Protection Agency, and the Surgeon General among others. Plans now call for beginning the study in 2003 and completing it by 2030.

## COPR Human Research Protections Working Group Presentation

**Presentation by Debra R. Lappin**

Ms. Lappin said that, with increasing budgets for NIH-supported clinical research, protecting those who participate as subjects in those projects represents a growing challenge. During the past year, several members of COPR have participated as part of a working group to review protections for human subjects of research. A guiding principle for this review group is that "...clinical research must not only lead with the high-tech cutting edge of science but also with the high-touch of human interactions that value and empower participants as full partners in the research process..." she said, quoting a statement from the draft report by another COPR member, Mr. Roehr.

Ms. Lappin briefly reviewed federal administrative activities and programs throughout HHS that are relevant to patient protection efforts. She referred to the HHS Office of Human Research Protections (OHRP) and its advisory council; the HHS Office of Inspector General, which completed several reports on this subject; the National Bioethics Advisory Commission, which has issued several major reports and is expected to issue another report in June 2001; the Institute of Medicine (IOM), which is reviewing plans to accredit institutional review boards; Public Responsibility in Medical Research (PRIM&R), which is concerned over the public's growing skepticism regarding clinical research; and the American Association of Medical Colleges, which is looking at financial conflicts of interest and how they might affect the objectivity of investigators.

Ms. Lappin said that she and other COPR members who participated in this working group effort were particularly intent on representing the public's interest and being its voice as a way of building public trust in clinical research efforts. In doing so, they identified three specific project goals: to offer the public perspective in establishing a balance between protecting human subjects and achieving research progress; to advise NIH on empowering the public to be a partner in such research; and to identify related issues and set forth patient protection guidelines for NIH researchers and the public to follow.

Within NIH, there is a complex network of reviews and evaluations for any extramural research proposal, and there are other oversight mechanisms involving OHRP; FDA becomes involved when drugs or vaccines are being evaluated. Ms. Lappin said that there are multiple points within these networks where patients could have a greater voice to assure that patient protections represent their needs.

Ms. Lappin said the working group's draft report has six sections, including recent events, background information about COPR and its involvement, areas of concern and the public's role, conflict of interest, confidentiality and privacy, and health disparities along with social science and behavioral medicine.

Ms. Lappin said that recent events involving clinical trials, particularly the death of Jessie Gelsinger during a gene transfer experiment, call into question the effectiveness of institutional protections for human subjects, making it important for the public to voice its concerns. Also important is the ability of individual participants in clinical trials to have a voice and adequate power to protect their own interests. She said that it will be critical for COPR to shore up faith in the research enterprise.

**Presentation by Rosemary B. Quigley**

Ms. Quigley reminded other COPR members that the council is a diverse public group whose members appreciate the importance of clinical research and the need to protect individuals who participate in such studies. Although almost any research comes with some risk, it is important to favor protections while balancing those risks against what is necessary to further the research. Indeed, research can change the standard of care for patients with a particular disease, and those changes may themselves carry additional risks. Hence, it is important for the public to better understand the inherent risks of research.

Educational efforts are very much needed, according to Ms. Quigley. For example, some research follow-up studies, such as one conducted by the Advisory Committee on Human Radiation Experimentation, indicate that some people who participated in research projects sometimes do not fully realize that they have done so. Moreover, sometimes participants do not appreciate that they may not benefit from participating in research inasmuch as the therapy under investigation has not been proven effective. There is also considerable confusion over what distinguishes medical care from research participation. Typically, she said, the sicker people are, the more likely they are to expect the experimental therapy to be effective.

Ms. Quigley said that Code of Federal Regulations and the Common Rule apply to the majority of individuals who participate in federally-sponsored research. These regulations specify standards for IRBs in terms of their composition—for example, they require public representation among their membership—and outline the scope of their reviews. They also specify standards for informed consent, the need to disclose benefits and risks and to maintain confidentiality, and the applicability of these rules to certain vulnerable population groups such as prisoners, pregnant women, and children.

Ms. Quigley noted that, especially since the early 1980s when the Bayh-Dole Act was signed into law, biomedical research has flourished in both the public and private sectors. That law encourages the transfer of technology developed with federal support at universities and other such institutions into the private sector for commercialization. One major impact has been a sharp rise in therapeutic product development and in the clinical trials needed to test whether such products are safe and effective. These developments have prompted various questions—among them, some having to do with perceptions within the public that there are increased opportunities for conflicts of interest because doctors and researchers derive some of their support from industry.

In addition, there are perceived and possibly real threats to the autonomy of individuals who participate in research because of the way data are collected, because of new ways with which the genetics of patients may be probed, and the involvement of families rather than single individuals in some protocols, according to Ms. Quigley. Amid this voluminous information gathering, the fine points of informed consent can be overlooked, particularly those that speak to it being an ongoing process throughout the research project, not simply a one-time signing of a particular document. Nonetheless, participants and the public increasingly are demanding to know more about what goes on in particular clinical trials, much as they demand to know more about medical developments and current research. This momentum leads the public and research participants to want to be involved in partnerships with the clinical research team—to be empowered.

**Presentation by Dr. Isaac D. Montoya**

Dr. Montoya said that the COPR working group identified as its two core issues: i) statements from it to NIH representing the public voice in terms of protecting research participants and ii) empowering patients and the public to be partners in research. He said that there are challenges to understanding what is required for a participant to be fully informed before giving consent to participate in a protocol. A major component of this process is the transparency of information provided to candidate participants. Another component is the extent of participation of the public in the IRB review process and in understanding conflicts of interest.

On the issue of health disparities, matters are so complex that a separate working group will address them, according to Dr. Montoya. Similarly, although COPR is interested in participant protections in the context of the behavioral and social sciences, the working group decided to leave this problem with an advisory committee of OHRP that is reviewing these issues and anticipates completing a report in the first half of 2002.

**Presentation by Dr. Melanie C. Dreher**

Dr. Dreher reviewed several broad principles and conclusions of the working group. First, COPR believes that research participants should be equal partners with researchers in a protocol, and NIH has a responsibility for preparing participants for this role. She asked NIH to prepare an inventory of projects where it is doing so. She also urged NIH to continue various discussions with the public on difficult issues, such as the disposition of stored tissue samples from genetics research projects.

Dr. Dreher recommended that NIH monitor its public communication efforts and its public image while continuing its public education efforts. NIH also should periodically investigate the complex relationship between researchers and research participants through surveys and other instruments. For instance, it might develop a survey to determine why individuals sometimes choose not to participate in research projects.

*Discussion*

Ms. Cate Timmerman said that she would moderate the discussion of the COPR working group report. She said that the issues surrounding human research protection are complex and interconnected, making it difficult for COPR members to agree on a statement or even a format for what they want to deliver to NIH officials. She reminded COPR members that they are mandated to advise NIH and to provide a perspective representing the public interest.

Dr. Benoit said that she had strong views on the process of developing informed consent, particularly when it involves individuals from the inner city who may be illiterate. She later said that these communication challenges also pertain to routine situations that can arise when delivering health care. In response, Ms. Lappin said that some researchers still do not believe that they can or need to explain complex material to potential research participants, accentuating the need for COPR to emphasize the importance of the informed consent process.

In response to a comment from Dr. Bishop about the role played by money paid to participants, Ms. Lackritz said that this issue further complicates efforts to obtain genuine informed consent. She later said that the whole process in which informed consent comes up can be intimidating and confusing, making it difficult for would-be participants to understand issues and frame appropriate questions. In response to a later question from Dr. Montoya, Dr. Kirschstein said that there is a broad debate over whether it is ethical to pay research participants; she also offered to provide COPR members with copies of a report on this topic prepared by Dr. Christine Grady, Department of Clinical Bioethics at the Warren G. Magnuson Clinical Center of the NIH. Several COPR members engaged in a brief follow-up discussion of this topic.

Mr. Thomas Vaalburg said that, based on his experience as a participant in two separate clinical trials, informed consent procedures do not work well. He questioned whether information about the relative success of the informed consent process should come from NIH or the institutions conducting the research. Ms. Fernandes said there are concerns on several levels, with some of them focused on the administrative completion of required paperwork and others focused on taking a multi-level approach to educating each patient-participant. Although it is relatively easy to determine whether consent forms are duly completed, it is far more difficult to determine whether a participant is fully informed about the experimental procedures, she added.

Mr. Yee said that it will be necessary to change the mind-set of researchers. However, he added, if patient protections are made too strong and unwieldy, they could discourage researchers from undertaking projects.

Dr. Tamura said that any considerations regarding informed consent should take into account the specific family, community and cultural context. Dr. Bromet said that the concept of respect is equally important when investigators have discussions with patients and with their families about participating in research. Later during the discussion, she recommended that researchers routinely meet with participants once a study is completed to explain fully what it determined. In response, Dr. Baldwin said the responsibility lies with NIH for convincing researchers to inform participants in a timely manner about research findings. Dr. Montoya later suggested that simply adding the word respect would not be enough and that more fully educating participants about the research process would be a better approach. Dr. Claudio later said that prospective research participants should be furnished with questions that would help them decide whether to provide informed consent.

Mr. Roehr said that there is an extensive, institutionalized system for the research and health care establishment presiding over informed consent, but that the infrastructure on the patient-participant side is considerably less developed. He recommended developing an inventory of components within the latter system as a first step toward strengthening it.

*Discussion on Document Development*

Ms. Timmerman suggested that COPR members evaluate the type of document that should be presented to NIH and how to bring the public viewpoint to the attention of NIH for the purpose of improving patient protections. For example, COPR might produce a document specifying points to consider; a handbook for educating researchers; a white paper outlining issues, problems, and potential solutions; or an agenda for NIH to follow in promoting public and participant education. She later reminded COPR members that whatever product is presented to NIH, it needs to come with approval from the full council, not merely from a working group.

Dr. Kirschstein reminded COPR members of the handbook on informed consent described during the October 2000 meeting by Ms. Mary McCabe, R.N. of NCI. Ms. Lappin agreed that the NCI handbook provides a good example of how to engage people in the informed consent process but she also voiced concern that the handbook might not be read by researchers. Mr. Vaalburg later said that research participants might want a booklet describing the research, alternative procedures, and other useful information about what might arise during a clinical trial. Dr. Kirschstein urged him to review the NCI prototype.

Ms. Fernandes said that an important informed consent challenge is to reach potential research participants who come from widely varied backgrounds. Mr. Roehr agreed, saying that it is relatively easier to reach researchers and a comparable system is needed to reach and empower would-be research participants. In response to a subsequent question from Dr. Dreher, Mr. Roehr said that one component of such a system would be a training program aimed at educating members of the public to serve on local IRBs. In response to a question from Dr. Bromet about the involvement of patient advocates in research protocols, he said that

patient advocacy and other elements for assisting research participants to be better informed and empowered need to be systematically strengthened and institutionalized.

Other COPR members agreed and said that research participants should be entitled to have full copies of research protocols as a normal part of the informed consent process. Both Dr. Kirschstein and Dr. Baldwin agreed that this practice should be followed except in rare cases where disclosing certain details of the protocol would interfere with the research itself.

Dr. Baldwin suggested that COPR members consider whether they want to produce additional documents or recommend how NIH might better distribute some of the informed consent or other materials that are already available. She also asked for guidance on whether the focus is on researchers or on research participants. Her own view is that the informed consent process itself needs to be more fully studied as a key step toward improving it. Dr. Dreher said that one recommendation of the working group is for further research on the informed consent process.

In response to questions from Mr. Yee about courses being given to researchers on informed consent and related accreditation issues, Dr. Baldwin said that it is too soon to know what the impact of these efforts will be, although anecdotal reports are positive. She added that requiring researchers to take such courses appears to be an appropriate step for NIH to take.

In response to a question from Dr. Benoit about surveying patients in clinical trials, Dr. Baldwin said it would be helpful to have some way of knowing more fully what research participants understand about the research during the course of a clinical trial.

Dr. Kirschstein suggested that COPR members consider the role of patient advocates in the NIH-sponsored Women's Health Initiative, a long-term and broad-based study of women's health issues.

In response to questions from Mr. Yee about research that is not supported by NIH, Dr. Kirschstein said that the primary task for COPR members is to advise NIH as a way of influencing NIH-supported research. Beyond that, NIH has no jurisdiction over clinical research by other sponsors, except for setting a moral tone. Dr. Baldwin added that officials outside NIH are looking more broadly at the U.S. system for protecting research participants. Mr. Roehr said that, by training researchers as to appropriate practices when dealing with patient participants in NIH-sponsored clinical trials, NIH can additionally influence researchers in the private sector and thereby improve the informed consent process more generally.

Dr. Yvonne Maddox, NIH Acting Deputy Director, asked about making the content of informed consent documents more user-friendly and informative, and about meeting with IRB chairs. In response, Ms. Quigley said that, during her service as a representative of the public on an IRB, other members came to expect her to help make documents more accessible to research participants and to add certain kinds of information that often was missing from draft documents but would help would-be participants decide whether to join a research protocol.

Ms. Thomas said that another means for empowering the public as well as public members of IRBs is through better use of the many documents on these subjects that are maintained on the NIH Web site, many of which are found within the "clinicaltrials.gov" section.

Ms. Lancaster alluded to patient confidentiality needs and to recent legislation that could complicate this issue for many people. She also said that those who recruit research participants could play an important role in informing them about the research being planned.

In response to a suggestion from Ms. Timmerman that COPR members not try to settle the issue of what type of document to prepare for NIH but instead focus on defining key issues, Ms. Lappin said that COPR might consider new ways, such as through informed recruiters and patient advocates, of reaching and educating prospective research participants.

In response to a question from Dr. Dreher about recommendations for changing the informed consent process, Ms. Fernandes said more time is needed before beginning a protocol for the prospective participants to consult with family members and, once begun, time is needed for participants to reevaluate their experiences within the clinical trial and perhaps serially re-consent to participating. Dr. Bromet said that the possibility of participants re-consenting poses difficulties for researchers managing clinical trials.

Several other COPR members joined the discussion, examining what informed "re-consent" really would mean. Ms. Quigley said that some researchers might see re-consent as a hurdle for transmitting any new, important information to participants. But Ms. Lappin said that the NCI prototype document presents re-consenting as part of an ongoing process in which researchers and participants communicate about progress during the protocol. Several others suggested that the NCI document be more widely adopted throughout NIH.

Dr. Tamura suggested that COPR endorse the recommendation that NIH research further the informed consent process. In response to a comment from Dr. Bromet, Ms. Lappin said that the working group draft report comments on NIH efforts in this area. Dr. Baldwin offered to transmit summaries of ongoing NIH-sponsored studies in this area. She also urged COPR members not to specify types of research projects for NIH to support but to provide more general recommendations in this area.

*Concluding Discussion of Patient Protection-Related Issues*

Eventually, COPR members agreed to circulate a revised working group draft by e-mail for further discussion at the council's next meeting. Ms. Timmerman said that, although the working group identified several core issues, other members of COPR did not say whether they endorsed the working group's views of patient protections-related issues. Mr. Roehr said that public participation in IRBs and broader questions about implementing COPR recommendations needed to be addressed. Although Ms. Kalabokes said that informed consent might be the general heading under which most other issues fell, Ms. Quigley and Ms. Lackritz disagreed, saying that there were several broader, separate issues under consideration.

Ms. Timmerman asked COPR members whether they agreed on pursuing five topics: conflict of interest, informed consent, transparency of information, IRBs, and privacy. Mr. Roehr said that research participants should decide for themselves how much they want to learn about financial conflicts of interest among

investigators overseeing particular protocols. Ms. Lappin said that only about 25 percent of IRBs require investigators to disclose such information, but she was not sure whether COPR should pursue this issue or table it. Mr. Roehr said that, in principle, patients should have the same access as the host institution and its investigators to such information.

Dr. Belinda Seto noted that, following a meeting on conflicts of interest in August 2001 that was sponsored by HHS and held at NIH, a draft document was prepared to capture the breadth of discussion rather than to provide interim guidance on this topic. She also said that IRBs often lack the expertise to evaluate conflict-of-interest disclosures. Mr. Yee noted that his organization stopped collecting disclosure statements because the task proved too burdensome and uninformative.

Ms. Timmerman said that the working group would like to know what to do next with its draft report. She said that COPR members appeared to endorse its portrayal of core issues, project goals, and plans to present a statement containing recommendations for NIH to pursue, such as empowering patients, the public, and research participants. She urged COPR members to transmit further recommendations to the working group. Dr. Tamura said he would like additional information about these issues before going forward with refinements to the draft report. Other COPR members said that the draft report provides a strong basis to work from, even if it might not encompass all of the relevant issues.

## COPR Business Items

Ms. Fernandes said that some COPR members would like to have a stronger say in setting meeting agendas. Ms. Lackritz said it would help to see the tentative agenda earlier before a meeting, thereby enabling COPR members to amend it. Ms. Quigley said that some COPR members would like to review NIH priority setting and how research budgets are set, with one aim being for those priorities to reflect more closely the burdens of disease. COPR members would also like to bring in external (to the NIH) consultants to define and assess burdens of disease. Dr. Bishop agreed, saying COPR members should have a stronger say in helping NIH set research priorities. Ms. Fernandes added that COPR would prefer fewer and briefer presentations by Institute Directors, allowing more time for discussions with them.

In response to a question from Ms. Thomas, COPR members agreed that Dr. Straus, Director of the NIH National Center for Complementary and Alternative Medicine, and Dr. Kenneth Olden, Director of the NIH National Institute of Environmental Health Sciences, should be invited to speak at a future COPR meeting. Ms. Thomas also noted that the topic of using burdens of illness as a mechanism for setting NIH research priorities is a very complex subject, and she urged COPR members to refer to several documents describing how NIH sets priorities. She cautioned them against trying to take on several complex topics, such as patient protections, priority setting, and health disparities, simultaneously.

When several COPR members suggested involving members of Congress in their activities, Ms. Thomas reminded them that, during those days that they are actively serving as COPR members, they are considered special government employees and thus are prohibited from activities that could be construed as lobbying Congress.

*Scheduling of future meetings*

Ms. Thomas led a discussion about when to hold the next COPR meetings, deciding on October 22-23, 2001; April 15-16, 2002; and October 21-22, 2002.

## Summary and Conclusions

The Director's Council of Public Representatives (COPR) of the National Institutes of Health (NIH) met on May 1, 2001, to learn of recent events including budget deliberations that affect NIH, several programs within three specific Institutes, and to discuss a draft report prepared by a working group of COPR members on the issue of human subject protections.

The COPR acknowledged and commented on these presentations, made several specific recommendations about patient protection measures to guide those who will revise the working group draft report, and discussed setting the agenda for the council's future meetings.

## Table of Abbreviations

- **ACD—**Advisory Committee to the Director
- **BRIN—**Biomedical Research Infrastructure Network
- **CDC—**Centers for Disease Control and Prevention
- **COPR—**Council of Public Representatives
- **CSR—**Center for Scientific Review
- **DHHS—**U.S. Department of Health and Human Services
- **FDA—**Food and Drug Administration
- **FY—**Fiscal Year
- **GPRA—**Government Performanceand Results Act
- **HRSA—**Health Resources and Services Administration
- **HPSCRG—**Human Pluripotent Stem Cell Review Group
- **IHS—**Indian Health Service
- **IOM—**Institute of Medicine
- **IRB—**Institutional Review Board

- **NBAC—**National Bioethics Advisory Commission
- **NCI—**National Cancer Institute
- **NCRR—**National Center for Research Resources
- **NCMHD—**National Center on Minority Health and Health Disparities
- **NEI—**National Eye Institute
- **NIAMS—**National Institute of Arthritis and Musculoskeletal and Skin Diseases
- **NIBIB—**National Institute for Biomedical Imaging and Bioengineering
- **NICHD—**National Institute of Child Health and Human Development
- **NIDA—**National Institute on Drug Abuse
- **NIDCR—**National Institute of Dental and Craniofacial Research
- **NIDDK—**National Institute of Diabetes and Digestive and Kidney Diseases
- **NIEHS—**National Institute of Environmental Health Sciences
- **NIH—**National Institutes of Health
- **NIMH—**National Institute of Mental Health
- **NINDS—**National Institute of Neurological Disorders and Stroke
- *NINR—*National Institute of Nursing Research
- **NHGRI—**National Human Genome Research Institute
- **NLM—**National Library of Medicine
- **NSF—**National Science Foundation
- **OCPL—**Office of Communications and Public Liaison
- **OHRP—**Office for Human Research Protections
- **OMAR—**Office of Medical Applications of Research
- **OSP—**Office of Science Policy
- **OTT—**Office of Technology Transfer
- **PI—**Principal Investigator
- **RFA—**Request for Applications

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This page last reviewed on November 28, 2011

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DIRECTOR'S COUNCIL OF PUBLIC REPRESENTATIVES

# October 2, 2001 Meeting Minutes

## FULL MEETING OF THE DIRECTOR'S COUNCIL OF PUBLIC REPRESENTATIVES TO DISCUSS DRAFT HUMAN RESEARCH PROTECTIONS REPORT

*Conference Call*

National Institutes of Health
Bethesda, Maryland

### Summary Report

National Institutes of Health (NIH) Acting Director, Dr. Ruth Kirschstein, welcomed members of the Director's Council of Public Representatives (COPR) and thanked them for participating in this official, full meeting by means of telephone conference to discuss a COPR working group's draft report on human research protections. She then asked Ms. Debra Lappin, who chaired the working group, to lead the discussion.

Ms. Lappin said the working group—other members include Dr. Melanie Dreher, Ms. Barbara Lackritz, Ms. Joan Lancaster, Mr. Roland McFarland, Dr. Isaac Montoya, Ms. Rosemary Quigley, Mr. Bob Roehr, and Mr. Tom Vaalburg—is seeking comments, changes, and approval from COPR members for its draft report. She thanked NIH officials for supporting the working group in these efforts and also praised NIH more broadly for supporting research-related patient protections; she additionally thanked the COPR working group members in preparing the draft report.

Ms. Lappin said the draft report consists of a lengthy supporting document and an executive summary, which contains recommendations. A commitment to consider the subject of human research protections was made about two years ago; plans evolved as the working group sought an appropriate means to express COPR's views on these issues, recognizing that COPR represents the interests of the general public.

One major thrust of the working group report is an emphasis on the value of human life in the context of medical research, making it crucial for researchers to observe high ethical standards when conducting that research. Another major thrust entails ensuring that patients have a greater voice in key decision-making that will affect the course of medical research, according to Ms. Lappin. The working group believes that NIH leadership in promoting this latter "patient empowerment" effort is vital.

In framing its recommendations, the working group considered six key areas: 1) informed consent, 2) transparency of information, 3) institutional review boards (IRBs), 4) conflicts of interest, 5) confidentiality and privacy, and 6) enhanced education and training of the public. Informed consent, for example, should be considered a continuing process, not a single event at the outset of a clinical research project, and should allow potential participants broad freedom to learn fully about the research being planned. In the same vein, information about such research—-including data about adverse events, relevant information in the published literature, and eventual outcomes of the research—should be available and made "transparent" to active and potential participants.

The working group recognizes that many individual IRBs are under severe strain. Therefore, the report urges NIH to critically reexamine the entire system of IRBs and review the impact of conflicts of interest on IRB performance. The working group also recommends that NIH encourage appointments of independent members to the review boards. It also urges that IRBs more fully disclose conflicts of interest to potential and actual study participants and that NIH considers weighting its funding awards in a way that will encourage institutions whose IRBs make such disclosures fully and consistently.

Under its fifth recommendation, the working group suggests that measures to protect patient confidentiality be fully woven into the informed consent process. The group also urges NIH to develop model programs for educating the public about participating in biomedical research and improve the training and sensitivity of investigators who conduct such research.

**DISCUSSION OF WORKING GROUP DRAFT RECOMMENDATIONS**

Dr. Luz Claudio asked how COPR might assess NIH's eventual implementation of these recommendations. Ms. Lappin suggested that NIH could identify milestones to mark progress in implementing the COPR recommendations.

Dr. Evelyn Bromet asked whether the draft report recommendations apply broadly to research involving human subjects or more narrowly to clinical research. She also asked whether there is a suitable title for the report. In response, Dr. Isaac Montoya indicated that the working group members focused on developing recommendations applicable primarily to clinical research situations and deferred non-clinical matters to a future working group. Dr. Bromet then recommended that the report delineate its scope more clearly from the outset. Her comment prompted Ms. Lappin to suggest the report be called, "Human Research Protections in Clinical Trials: A Public Perspective."

In response to a question from Mr. Doug Yee, Ms. Lappin said informed consent needs to be conducted on multiple levels and that documents used for this purpose

should be written simply and, if need be, in languages other than English. Ms. Lackritz said the draft describes a wide variety of situations that need to be dealt with to achieve informed consent. Dr. Montoya added that the report encourages NIH to be innovative in developing better means to inform participants about current clinical research.

Dr. Bromet asked about making previously published reports (before 1966) and non-English language reports available to meet recommendations calling for the informed consent process to be fully transparent. In response, Dr. Kirschstein indicated that the National Library of Medicine (NLM) staff can provide selected publications in translation but a comprehensive selection may not always be available. Mr. Bob Roehr said the draft report should recommend the use of the NLM Medline system "and its successors" to incorporate any forthcoming improvements in that system.

In response to comments from Rosemary Quigley, Ms. Lappin suggested the report should say updated information will be made available to research participants without recommending that specific FAQ (Frequently Asked Questions) segments be updated.

Dr. Bromet asked whether or not NIH takes the lead in setting IRB policies. Dr. Kirschstein said many IRB practices are determined at the local institutional level but NIH will soon be providing additional financial support to IRBs, which would serve to improve practices. She also noted that the Office for Human Research Protections within the U.S. Department of Health and Human Services reviews IRB performance—a task that was formerly conducted by the NIH Office of Protection from Research Risks.

Dr. Kirschstein said NIH relies on local institutions to appoint and train its members who represent the public but is considering ways to strengthen its role in advising local IRBs about involving the public. Ms. Quigley said that ways are needed to strengthen public members role's at individual IRBs. She further noted the working group did not make specific recommendations about improving the training of IRB members because it recognizes that such efforts are underway elsewhere. Ms. Lappin said, in effect, the working group's first recommendation calls for wholesale reevaluation of the system as a basis for improving IRBs, including better training of IRB members.

Mr. Yee, Mr. Roehr, and Ms. Lappin considered whether the draft report recommendations are aimed to extend beyond NIH-supported research. They concluded that COPR's mandate restricts the council to making recommendations to NIH.

Dr. Len Tamura asked whether the draft report specifically makes a recommendation about incentives for better handling of conflicts of interest by institutions. Dr. Bromet said that improved performance in handling conflicts of interest might be added as a criterion for evaluating and reviewing grants. Ms. Lappin said that perhaps incentives should be based on institutions improving their overall performance against a checklist of patient protection measures rather than restricting incentives to improvements in handling conflicts of interest. Mr. Roehr suggested that such incentives be viewed as tools for measuring implementation of the recommendations embodied in the forthcoming COPR report.

Dr. Bromet said it may be important to make handling of conflicts of interest a criterion since it is not currently a specific criterion during grant reviews. After some additional discussion, Dr. Kirschstein urged COPR members to review this suggestion very carefully before finalizing it. Dr. Montoya also urged special care in this area, saying that COPR would do better to frame general, rather than detailed, recommendations in this context. He pointed out that reviewers are told to focus on the scientific merit of proposals. Dr. Bromet differed on this point, stating that evaluating how human subjects will be treated during clinical trials is an integral part of the scientific review.

Dr. Kirschstein interjected that NIH routinely conducts reviews on two levels—the first focuses on scientific merit and the second, by advisory councils, on broader issues, including potential conflicts of interest. Dr. Kirschstein also indicated that councils delay funding of proposals until any concerns over such issues are satisfactorily addressed. She further pointed out that NIH is studying a report indicating that some 25 percent of all IRBs have mechanisms for disclosing and examining conflicts of interest. In light of this discussion, Dr. Montoya recommended changing the working groups draft to say that conflict of interest review practices should be considered but not invoked, so approval of otherwise acceptable clinical research proposals would not be delayed. Ms. Lappin and Mr. Roehr agreed to modify the draft report to include milder language recommending that NIH review panels may include a criterion about conflicts of interest. Namely, that review panels could include a criterion that institutions submitting a proposal have systems in place for disclosing conflicts of interest and that such review panels indicate that this criterion could become a factor in the allocation of resources.

Dr. Tamura suggested that, as with informed consent, ensuring confidentiality and privacy of clinical research participants should be explicitly described in the working group report as an ongoing process, not a static event. In response, Mr. Roehr and several other COPR members said that the draft could be reworded to reflect his suggestion.

## CONCLUSION

Ms. Lappin requested NIH to circulate the amended working group document among COPR members for final changes and approval, and that the completed report be submitted to Dr. Kirschstein at the COPR meeting scheduled for October 23, 2001.

Mr. Yee expressed concern about how additional comments from the public might be handled. Dr. Kirschstein said that the agenda for the next meeting will be made public and that members of the public will have the opportunity to send comments on the document, once it's available. She said that after COPR officially submits the working group report, NIH will review it to determine how to implement the recommendations. The final report also may be posted on the NIH Web site—and certainly on the COPR Web site—as one way for COPR to share its recommendations.

Dr. Kirschstein noted that once the report is presented to NIH by COPR, the typical process is for NIH senior staff to review the report and determine how to integrate the recommendations, including taking into consideration actions being taken by sister agencies, such as the Office for Human Research Protections and the Food and Drug Administration. She indicated that asking NIH for measurable results, as mentioned earlier in the discussion, could prove difficult. NIH could more readily update COPR periodically on progress in implementing the forthcoming recommendations.

COPR members and Dr. Kirschstein briefly discussed the need for heightened sensitivity to language in matters concerning human research protection in the

aftermath of the September 11, 2001, attacks.

I hereby certify that, to the best of my knowledge, the foregoing minutes are accurate and complete.

Ms. Jennifer Gorman Vetter, Executive Secretary, Director's Council of Public Representatives

Ruth L. Kirschstein, M.D., Acting Director, NIH

**Acronyms**

- **COPR**—Council of Public Representatives
- **DHHS**—U.S. Department of Health and Human Services
- **IRB—**Institutional Review Board
- **NBAC—**National Bioethics Advisory Commission
- **NIH**—National Institutes of Health
- **NLM—**National Library of Medicine
- **OHRP—**Office for Human Research Protections
- **OPRR—**Office of Protection from Research Risks

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