PROTECTING HUMAN SUBJECTS

U.S. DEPARTMENT OF ENERGY • OFFICE OF BIOLOGICAL AND ENVIRONMENTAL RESEARCH

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DOE Conference Strengthens Link Between Genetics Research and Human Subjects Communities

"Genetic Research and Human Subjects: The Changing Land-scape," a two-day technical and educational conference held June 25-26, 1997, in Bethesda, Md., at National Institutes of Health (NIH) facilities, provided opportunity for exploration and discussion of new concepts, latest bioethical concerns, and complex difficult-to-resolve issues related to genetics and human subjects. DOE and NIH, because of their sponsorship of the Human Genome project and their commitment to strong human subjects protection, were particularly excited about the ground breaking opportunity to bring together these communities which have an ever-expanding need for collaboration. A full-house of over 170 federal staff, administrators, researchers, and others interested in the issue were enthusiastic participants.

The meeting developed out of the need to educate both Institutional Review Boards (IRBs) and genetic researchers about not only the latest genetics research, but also how this research relates to the protection of human subjects, specifically, how to ethically involve human subjects in genetic research. Dr. Susan L. Rose, the DOE Protection of Human Subjects Manager, organized the meeting with co-chair Elizabeth Thomson of the NIH Human Genome Program. According to Dr. Rose, the educational conference was "an ideal setting to bring together genetics and human subject's -- to increase the technical and ethical understanding of the other's job, and to discuss unresolvable issues for IRBs." She also expressed how important it is for different agencies to work together in creating ethical standards for using human subjects in genetic research.

Researchers involved in genetics face special ethical issues and challenges in dealing with human research subjects. At the same time, public interest in genetic issues continues to increase with the advances in large-scale DNA sequencing in humans, and with genetics rapidly becoming an integral part of most medical care. Genetic information affects people in unique ways. It may predict events that will occur years in the future, or

not at all. It may predict the future of their family members or have a potential impact that may challenge and stigmatize both individuals and families.

To address some of these complex issues conference attendees actively participated in provocative sessions. There was also opportunity for participants to share numerous resources from their organizations and to interact informally sharing current projects and lessons learned. The spirited agenda included:

Congressional Interest in Human Subjects and Genetics
Mr. Christopher R. Kline, Minority Senate Governmental Affairs Committee

The Human Genome Project: Implications for Future Research
Dr. David Cox, Stanford University School of Medicine

The National Bioethics Advisory Commission: Human Subjects Issues in Genetic Research
Dr. Alta Charo, University of Wisconsin

Scientific and Ethical Issues in Large-Scale DNA Sequencing in Humans
Dr. Pieter deJong and Dr. James P. Karr, Roswell Park Cancer Institute

Gene Discovery Research in Families: Technology, Volunteer Recruitment, and Privacy
Dr. David Valle, Johns Hopkins University School of Medicine
Professor Bartha M. Knoppers, University of Montreal

Psychosocial Impact of Genetics Research
Dr. Kimberly Quaid, Indiana University Medical Center
Dr. Barbara Handelin, Handelin Associates

Using Stored Tissues for Genetic Research
Dr. Ellen Wright-Clayton, Vanderbilt University
Dr. David Korn, Stanford University

Design of Genetics Research: When to Disclose Results
Ms. Judith Yost, Health Care Financing Administration
Dr. Gail Geller, Johns Hopkins University

Neuropsychiatric Genetics Research and other Non-medical Genetics Research: What are the Controversies
Dr. Dean Hamer, National Cancer Institute

Research Issues in Special Populations
Dr. Karen Rothenberg, University of Maryland
Dr. Ben Wilfond, University of Arizona
Dr. Georgia Dunston, Howard University

Educating the Nation's IRBs
Dr. Christopher Hook, Mayo Clinic
Mr. Steve Peckman, University of California, Los Angeles

Rev. William Nebo, Senior Pastor, First Presbyterian Church, Livermore, California
Ms. Ruth Michels, St. Mary's Hospital, Grand Junction, Colorado
Where does this leave IRBs and others involved with genetics research and human subjects? Until regulations covering these new technologies are in place, education and communication are the keys. This conference offered a positive first step toward resolving seemingly unresolvable issues.

Conference Speakers Share Their Thoughts on Genetic Research and Human Subjects

Ellen Wright-Clayton
Vanderbilt University
Using Stored Tissues for Genetic Research

"The first question that should be asked about any research proposal, whether it involves active intervention with human subjects, record review, or the use of stored tissue samples for genetics research, is whether the research should be undertaken. Resolving this issue requires weighing such factors as the likelihood that the project will produce generalizable, useful knowledge, the likely importance of the knowledge to be gained, and whether the risks posed by the project are commensurate with the benefits to be gained."

Georgia M. Dunston
Howard University College of Medicine
Research Issues in Special Populations: Minority Populations

"Human genetic research, perhaps like no other discipline of scientific inquiry, uses diversity as a construct for defining human populations and a framework for understanding the biology of disease and health."

Dean Hamer
National Cancer Institute
Neuropsychiatric Genetics Research and Other Non-Medical Genetics Research: What are the Controversies?

"There is a steadily increasing evidence that genes influence many normal human characteristics from physical appearance to behavior. This research, which is bound to proliferate as the genome is sequenced, raises a variety of social, legal, and ethical issues. Should subjects be told if they have a predisposition to be fat or thin, happy or sad? What should their families, insurance companies, and employers know? When does genetics become eugenics?"

Bartha Maria Knoppers
University of Montreal
Gene Discovery Research in Families

"At a time of increased sensitivity to privacy and re-emergence of the biological' family for genetic research purposes, recruitment in families raises new issues. Different family forms mean that biological relatedness no longer coincides with sociological reality . . . this fact, coupled with the particular nature of genetic information, places several dilemmas before the researcher."

Steve Peckman
University of California, Los Angeles
Educating the Nation's IRBs

"The recent and ongoing revolution in the science and ethics of genetics research poses a moving target for biomedical IRBs. Current genetics research encompasses risks and requires analysis that may be uncomfortable, uncommon, or outside the experience and expertise of the multidisciplinary biomedical IRB."

Karen Rothenberg
University of Maryland School of Law
Genetics Research Studies: Implications for Women

"As genetics research projects are being undertaken, it is becoming increasingly clear that women are over-represented in many of these projects. Careful consideration must be given to the inclusion or exclusion of pregnant women . . . they should not be targeted for recruitment simply because they are particularly accessible, nor because they are more likely to participate. The potential impact of participation in genetics research on women's lives must be carefully considered as research projects are designed."

Genetic Testing and the Institutional Review Board

by Rev. William Nebo (LLNL IRB Citizen Representative)**

Genetic research has dramatically altered the landscape of the Institutional Review Board (IRB) of the Lawrence Livermore National Laboratory (LLNL). Before the legal and ethical implications of genetic research had been rigorously considered, it seemed as though approval of research on the human genome and other genetic studies would be easy. Samples involved exposing no one to anything radioactive, toxic, or particularly painful. Nonscientific individuals had not thought of their DNA being anything but such tiny bits of their identity that it seemed to matter little that someone was examining it and sorting out the genetic code it contained.

But soon the questions began to arise and the comfort level of this research diminished. The IRB stumbled over the issue of paternity (people discovering that their assumptions about who was parent to whom were wrong) and whether this should be defined explicitly on the informed consent form. The question of how much we should tell subjects about findings that were not clearly understood still surfaces, with varied answers depending on the case. We discovered that telling all--when all is not clear--can be more detrimental than telling nothing. In this case, we asked ourselves which moral principle applies: hold nothing back, or protect people from a detrimental rush to judgement by withholding what is unclear?

The issue of confidentiality became confused when the question arose regarding employers and insurance companies soliciting information about genetic testing. Counseling subjects to lie when asked if they had been part of genetic tests seemed morally questionable. Exposing subjects to risks in employment and insurance meant new revelations on consent forms, revelations that could effectively scare off subjects.

Recently, the IRB had discussed the fact that to date we have seen none of these problems surface with insurance companies and employers. As genetic research becomes more common, it seems that both employers and insurance companies will soon have the capability of obtaining their own genetic testing through disclosed or surreptitious means. So why worry? Nonetheless, some IRB members still do worry.

In the era before full-blown genetic research, it was easy to categorize research using archived human material as exempt from IRB review. Conducting research on tissue pieces sitting in preservatives in pathology labs seemed akin to good recycling of waste products. But with the advent of robust genetic research, all of that has changed. Tissues can now be a road map to a pile of information about the donor and possibly the donor's identity and family. We now have to ask whether tissues gathered for one sort of genetic study could be used for more study without finding the donor and renewing his or her consent. To date, the policy is to obtain consent for each use of any specimen, but this policy may prove cumbersome and harmful to research in the future.

The results of genetic testing can impact family members as much as subjects. We are struggling with the question of how wide is the lab's responsibility to inform a subject's family of test results that might be of interest to their health. It would be easy to simply let the responsibility of informing family rest with the subject, but this leaves a moral shadow over research that produces genetic warnings for anyone sharing the subject's genetic background.

This changing landscape has burdened the LLNL IRB with long meetings, frustrated researchers, and a growing need to keep abreast of ethics in genetic research no matter how daunting the effort appears. The recent work to develop an LLNL IRB home page that will train both principle investigators and committee members alike in genetic research issues is an attempt to extend our sensibilities in this area before research is designed and approved. However, getting both committee members and principle investigators to do all of the reading and review that the questions seem to demand continues to be a formidable task.

Clearly, the thinking and the testing must continue for the benefit of all. To cease to extend our knowledge of how human genes help us and harm us is to ultimately fail to deliver relief from great suffering. But to extend this scientific knowledge without reaching to simultaneously extend our ethical sensitivity is to fail to grasp the significance of what the knowledge will do to the meaning of our lives. Science and ethics are partners not adversaries.

***The Rev. William Nebo is Senior Pastor of the First Presbyterian Church of Livermore, California. He has served as the community member of the Lawrence Livermore National Laboratory Institutional Review Board since 1990, and is currently a member of the National Human Genome Research Institute - Department of Energy - Ethical, Legal, and Social Implications Research Planning and Evaluation Group. Rev. Nebo was a featured speaker at the DOE sponsored conference "Genetic Research and Human Subjects: The Changing Landscape" held in Bethesda, MD, on June 26-27, 1997.*

A New Challenge For IRB's: Medical Surveillance for Former DOE Workers

*by Ms. Kitty Taimi***

The implementation of the Department of Energy's (DOE's) new pilot program for medical surveillance for former workers has created a unique and, at times, frustrating challenge for local DOE site Institutional Review Boards (IRBs). The fact that DOE's human subjects protection policies mandate that all projects undergo local IRB review has also, at times, challenged and frustrated the project teams as well as some DOE site managers and contractors. Overall, however, a general desire to have the program get off to a successful start has generated a broad spirit of cooperation that has allowed the concerns and interests of the involved parties to be addressed in positive ways.

Background

The medical surveillance program for former workers was developed by DOE with input from major unions representing DOE workers, government agencies such as the National Institute of Occupational Safety and Health (NIOSH), university health experts, occupational physicians, and other stakeholders. The program is being carried out under provisions of Section 3162 of the Defense Authorization Act of 1993. Six cooperative agreements totaling $2.8 million were awarded in September 1996 to teams of health and labor specialists. These teams are conducting pilot projects at the following sites: Hanford, Rocky Flats, Nevada Test Site, Oak Ridge, Paducah, and Portsmouth.

The first phase of each project is to conduct a needs assessment to determine whether medical surveillance for former workers from those sites is warranted. In other words, the teams are to evaluate existing information and recommend whether DOE should fund programs to monitor the health of former workers whose past occupational exposures have put their health at risk. If there is sufficient evidence that groups of former workers are at significant risk, targeted medical surveillance programs will be implemented.

Scientific Challenge

There are an estimated 600,000 individuals who have worked at DOE sites over the past 50 years, mostly in the development of nuclear weapons. Thousands have lost their jobs as DOE has continued to downsize with the end of the Cold War. The number of former workers potentially exposed to significant risks during their employment at DOE is not known. In general, workplace exposures were likely to be minimal and there may not be cause for concern. However, sometimes exposures can put workers at risk for diseases that may not show up for many years. The mandate of this new program is to determine whether some former workers are at significant risk due to past radiation and/or chemical exposures in the DOE workplace.

Although little is known today about methodologies that can effectively link diseases to past workplace exposures, DOE's goal is to provide a monitoring program that is both scientifically credible and cost effective. Scientific uncertainties, as well as difficulties in locating and accessing old site records and exposure data, are two major challenges facing DOE and project teams.

Site-Specific Projects

The six teams were selected from a national competition seeking innovative strategies for evaluating the health of former workers. Projects were selected based upon the results of an external merit review. Currently, there is a second round of applications under evaluation for funding this fall. Three more projects may be selected to begin a needs assessment at sites not hosting ongoing projects.

During the phase I needs assessments, investigators are to review existing information at the pilot sites and evaluate ways to effectively identify former workers who would most likely have had significant radiation and nonradiation exposures. The teams have been examining exposure and health data; developing methods for contacting potentially affected workers; estimating the most significant worker hazards, problems, and concerns; and identifying approaches for conducting site-specific medical surveillance programs for targeted workers. At the end of the needs assessment, a detailed plan and proposed budget for a potential second phase, the medical surveillance, will be submitted to DOE.

If there is sufficient documentation that medical surveillance is needed, phase II will be approved and a medical surveillance program will be implemented for targeted groups of former workers potentially at risk. Former workers will be located and asked to provide detailed occupational and medical histories. If determined to be warranted, medical screening tests will be offered to the workers. Participation throughout both phases of the program is strictly voluntary for all former workers.

During the first year of the program, DOE has obtained a great deal of assistance from NIOSH. With this support, and with the expertise of the pilot project teams--especially the labor organizations--the pilot program for medical surveillance for former DOE workers is off to a successful start.

IRB Challenges

The IRB review experience of each of the six projects has been unique. For the most part, IRB reviews have proceeded smoothly and the investigators have been able to address any issues identified by the local site IRBs with a minimal amount of additional work. However, there are lessons to be learned from the experiences of these first six projects. Highlights of several of these experiences are described below and in other articles in this newsletter.

In accordance with usual practices of research institutions, some of the former worker projects already had been reviewed by the applicant's IRB prior to being submitted to DOE for funding consideration. Consequently, the DOE policy requiring local site IRB review resulted in these projects being reviewed twice (by different IRBs). Although this was not generally a significant problem, it tended to cause some frustration on the part of the investigators who did not know that local site IRB review would be required and who ended up having to do additional work to satisfy concerns raised by the local site IRB. Project delays were minimized, however, through the issuance of temporary approvals to proceed (based upon the review conducted by the investigator's IRB) while the local IRB review was conducted.

During the application process, some other project investigators believed that phase I of the program (the needs assessment) did **not** require IRB review, and these applicants did **not** obtain their own institution's IRB approval. Consequently, these projects could not obtain temporary approval and could not proceed until the local DOE site IRB approval was obtained. This situation also was not generally a problem, because the local IRBs were in place and ready and willing to help. These IRBs determined that expedited reviews were warranted and thus project delays were minimized. However, it should be noted that most on-site work, including contact with individual workers, was not allowed until local IRB approval was obtained.

A third experience that deserves highlighting is a situation where the local IRB is not yet established, despite the DOE policy requiring local IRB review. Luckily, the project encountering this situation already had received IRB approval from the investigator's institution and temporary approval to proceed was granted. However, this temporary approval has had to suffice for the duration of phase I because the DOE site has not moved expeditiously to establish its IRB. There are now indications that the site is proceeding to set up an IRB, although this will probably take several more months. Hopefully, if this project is approved for phase II this fall, the site IRB will be in place and ready to conduct its review.

Other Lessons Learned

From the local IRBs' perspective, there are other experiences that are additional "lessons learned". The perspectives and experiences of site workers should provide additional valuable insights into how to make this

program responsive and successful. As new projects begin phase I, and the ongoing projects proceed into phase II, it is hoped that the local IRBs, the project teams, former workers, and the DOE sites will continue to work together cooperatively to address the new challenges that are sure to come.

***Ms. Kitty Taimi is now a federal consultant to the U.S. Department of Energy's Office of Environment, Safety and Health. Ms. Taimi has been involved in environmental and health issues at DOE since 1986. She is currently working on the Former Workers Medical Surveillance program. If you would like more information, please call Ms. Taimi at her DOE office number, (301) 903-0262.*

IRB Profile: The Oak Ridge Committee on Human Studies

The Oak Ridge Associated Universities (ORAU)/ Oak Ridge National Laboratory (ORNL) Committee on Human Studies (ORCHS) was established by ORAU in 1967--under National Institutes of Health (NIH) guidelines—to formalize efforts begun in 1950 by ORAU's predecessor, the Oak Ridge Institute for Nuclear Studies. The committee's mission was to ensure the protection of participants in studies being conducted in ORAU's Medical Division under its contract with the Atomic Energy Commission (AEC), DOE's predecessor. ORCHS' Multiple Project Assurance was approved by the NIH in 1969, and subsequently renewed for five-year periods, most recently in 1993. ORCHS was expanded in 1970 to include human studies conducted at ORNL, Paducah, and Portsmouth.

Current projects include the University of Cincinnati's research involving former construction workers at the Oak Ridge facilities, and the Oil, Chemical and Atomic Workers International Union (OCAW) study of former workers at DOE's gaseous diffusion plants in Oak Ridge, Paducah, and Portsmouth.

ORCHS chair, Dr. Shirley Fry, ORAU, noted that "the problems encountered and the issues raised during the site-specific review process of these non-institutional projects stemmed primarily from the novelty of the task and the urgency to complete the approval process. Differing perceptions of the IRB purpose, process, and motivations for approval were apparent. However, despite the difficulties that typically accompany new experiences, there were none that could not be resolved through the cooperation of all parties involved."

IRB Profile: Pacific Northwest National Laboratory

The Pacific Northwest National Laboratory (PNNL) Institutional Review Board (IRB) has been active since the late 1960s and holds a Multiple Project Assurance with the Department of Energy that was recently renewed until the year 2000. Its diverse membership includes three community members, a physician, a psychologist, and Battelle scientific staff with a long and involved history at the Hanford site. When additional expertise is desired, persons knowledgeable in that particular field are invited to participate in the review.

In August 1996, the PNNL IRB received a request from Dr. Susan Rose, Department of Energy Human Subjects Program Manager, to provide courtesy reviews of research programs being conducted by other agencies at the Hanford site. Current programs under PNNL IRB jurisdiction include two DOE work-related health studies involving former Hanford site workers. Sherry Davis-Cross, PNNL IRB Administrator, lists some

of the challenges encountered by project Principal Investigators (PI) and the site IRB on the road to final IRB project approval:

- *Unclear lines of responsibility and accountability* - initial problems at PNNL related to questions of funding for the site reviews. Just who is responsible for funding IRB site reviews is still an unanswered question.
- *Urgency and time constraints* - because Principal Investigators (PIs) were unaware that site IRB approvals were required, they were unprepared for the time and effort necessary to complete these reviews. This, in turn, led to confusion as to whether the work could or could not begin without site review.
- *Lack of time to plan and coordinate with PIs and their IRBs* - PIs dealing with two separate IRB reviews (their own institutional review and the project site review) found themselves besieged with meeting the requirements, sometimes unfamiliar procedures, and paperwork of both IRBs.

Ms. Davis-Cross notes that, "Communication and education are proving to be the answer to the expeditious handling of these often difficult and complex reviews. As many IRBs struggle with the issues of privacy and confidentiality related to data management and protection of personal and medical records, it is paramount that these projects receive the most careful and thoughtful review under the best of conditions--where the PI has time to prepare complete and proper documentation and the IRB has time to give it full and thorough review without constraints or extenuating pressures. Although the worker health studies have presented many challenges for both researchers and the PNNL IRB, it's apparent that all the participants have great concern and respect for the rights and welfare of the human subjects involved in these studies."

Update on the National Bioethics Advisory Commission

by R. Alta Charo, J.D.**

From the early 1980s to the mid 1990s, the United States was distinguished from most other developed countries by its lack of a national public body to assist the government in its policymaking on topics of biomedical ethics. While France, Canada, Spain, Denmark, and others regularly sought advice from public commissions on issues ranging from reproductive technologies to euthanasia, the United States relied on state commissions, court decisions, and academic bodies. The result was a pattern of policymaking that was slower and more unpredictable than that of its peers.

This changed with the 1996 appointment of a National Bioethics Advisory Commission (NBAC). According to its charter, its purpose is to "provide advice and make recommendations to the National Science and Technology Council, other appropriate entities, and the public, on bioethical issues arising from research on human biology and behavior, and the applications, including the clinical applications, of that technology." Its range extends to departmental and agency programs, policies, and regulations.

NBAC's first assignments focused on protection of human subjects and the management of genetic information. It was directed to accept other assignments suggested to it by the public or federal agencies based on the following criteria: the public health or public policy urgency of the issue; the relationship between the issue and the goals of federal investment in science and technology; the absence of another entity to deliberate appropriately on the issue; and the extent of interest within the federal government.

NBAC has 18 members of diverse professional backgrounds, and all its meetings are open to the public. Members are expected to make reports and recommendations on bioethics policy and can request that a department or agency respond to their suggestions within six months, but the NBAC itself has no power to force changes upon the federal government.

Currently, NBAC is reviewing all federal agencies and departments with respect to their management of human subjects research, and is spending much of 1997 in a detailed investigation of the adequacy of those protections and the possibilities for reform. To date, NBAC has noted that federal agencies are hampered in their efforts to protect human subjects by such things as inadequate numbers of employees assigned to the task; confused lines of authority or conflicts of interest arising from interagency cooperation; difficulties in implementing the common rule across widely varying research settings: complications due to national security concerns intrinsic to much research conducted by the military or intelligence services; and intertwining employment and research requirements in unique settings such as outer space.

NBAC is also interested in the changing nature of vulnerable populations. Current regulations provide special protections for human subjects who are children, pregnant, or prisoners. NBAC is looking into the prospect of developing additional protections for the emotionally or cognitively impaired, such as Alzheimer's patients, and for those who are living in institutionalized settings, such as nursing homes. NBAC is also examining the recent trend toward viewing those who are unable to gain access to trials of promising new therapies, such as fertile or pregnant women, or terminally ill patients, as equally "vulnerable," albeit in a different manner.

In a more overarching vein, NBAC is examining the general structure of human subjects protections. Many small research settings, such as *in vitro* fertilization and obesity clinics, are uncovered by federal law. Some have suggested extending human subjects protections, such as independent safety review of the experiment and assurances of informed consent by the subjects, to all such research settings. Senator John Glenn of Ohio has introduced legislation to that effect, which would provide penalties for those failing to ensure these basic protections.

NBAC is also examining the management and use of genetic information, and it has chosen to focus first on an issue of some urgency--the storage and use of human tissue. A growing number of protocols reviewed by Institutional Review Boards are proposing that stored tissue be sampled for genetic information. The value to this research is obvious, but, unfortunately, tissue currently in storage was rarely collected with this in mind. Thus, questions arise concerning the appropriateness of sampling this tissue without the informed consent of the tissue donors; methods for contacting and counseling tissue donors about the significance of the genetic information that might be found; and, for prospective tissue collection, rules governing information and commercial value sharing between investigators and donors.

Much of this work on genetics and human subjects research was put aside when President Clinton directed NBAC to report back within 90 days of the announcement of Dolly (the first animal successfully cloned from an adult somatic cell) on the prospects for use of this technology in humans. The recommendations, published in the June 1997 report Cloning Human Beings (obtainable by calling the NBAC offices at 301-402-4242), call for the following: a five-year ban on efforts to use this technology to conceive an embryo that will be transferred to a womb for gestation; extension of human subjects protections to efforts to use cloning in the human species; coordination with the policies in other countries; and a review of the science in time for a fresh round of policy making on this topic in five years. The recommendations also called quite specifically for a clear demarcation between applications that involve making a baby and those that involve cloning DNA, cells, or embryos. For these, NBAC made no recommendations.

The effort to make recommendations on cloning highlighted the central dilemma faced by NBAC: is it to engage in pure ethics analysis, pure policy analysis, or some combination of the two? This uneasy tension between philosophy and policy is not unique to NBAC, however, as it is a problem shared with other national- and state-level commissions that focus on ethics. It remains to be seen how NBAC will balance these tensions as its next series of reports are issued.

***R. Alta Charo, J.D., is a Professor of Law at the University of Wisconsin in Madison, Wisconsin. She has served on the U.S. National Bioethics Advisory Commission since 1996. Prof. Charo was a featured speaker at the DOE sponsored conference "Genetic Research and Human Subjects: The Changing Landscape," held in Bethesda, Maryland, on June 26-27, 1997.*

Are Workers' Rights in Jeopardy?

Panel Convened to Develop an Ethical Framework for Studies Involving the Worker Community

"One thing is certain--an ethical framework for research on, with, or by workers does not exist. The worker community, a very important resource to DOE and the nation, deserves thoughtful and balanced guidance by consensus for all worker studies whether they are currently underway, being planned, or in the future." With these words, Dr. Susan Rose, manager of DOE's Human Subjects Program, opened a workshop on developing an ethical framework for studies involving the worker community. Dr. Rose explained that it is imperative to take an innovative, proactive approach to shedding light on and establishing guidelines on the ethical issues related to studies involving the worker community.

Over the years, many studies of DOE work related health effects have been undertaken, a number of which were epidemiologic in nature. Times have changed for both DOE and for worker studies. There is more knowledge about genetic susceptibility and variability, exposure monitoring and record keeping have changed, as have the policies and procedures for doing studies on human subjects. Yet, more questions are being raised than answers provided.

To help fill this void, DOE's Office of Energy Research, as the DOE office responsible for protecting human research subjects and as the home of the DOE Human Genome Program, sponsored a two-day workshop on June 15-16 to draft a white paper that will illustrate ethical issues that should be of interest to DOE-related worker studies. A group of distinguished professionals, representing the workers, workplaces, researchers, and others involved in worker issues from a variety of perspectives, was invited to participate on a panel to initiate the effort. The selection of panel members with diverse experience and relationship with worker studies was a deliberate process.

For this initiative to be successful, it was critical that the panel members represent the perspectives of the range of stakeholders impacted by worker studies—worker, union, Institutional Review Board, facility owners and management, federal oversight and management, occupational medical physicians, and researchers. Additionally, the issues need to be explored from a legal, ethical, social, and medical perspective.

Dr. Theodore Emmett from Thomas Jefferson University, along with Dr. Susan Rose, actively engaged the panel members in a spirited, informed discussion centering around a draft white paper developed for the meeting by Dr. Rose and Dr. Emmett entitled "Developing an Ethical Framework for Studies Involving the

Worker Community." The draft outlines ethical issues that need to be considered in research involving the worker community, which are additional to the accepted guidelines and principles involved in all biomedical research. It includes some of the more important issues and suggests mechanisms by which those issues might be addressed.

The draft also clarifies the context of many worker studies, pointing out that the legal requirements to protect human subjects apply to a much broader range of research than many investigators and program managers realize. In addition to traditional biomedical studies, regulations cover, for example, research that:

- uses humans to test devices or products that have been developed through research
- uses data collected through intervention or interaction with individuals (including non-traditional considerations like manipulation of a subject's environment)
- uses private information that can be readily identified with individuals, even if the information was not collected specifically for the study in question
- uses bodily materials such as cells, blood or urine, tissues, organs, hair, and nail clippings, even if the material was not collected by the investigator
- uses humans to evaluate environmental alterations

The draft white paper has been developed and is under review by panel members. Ultimately, it is hoped that these guidelines may be adopted by other federal agencies and the private sector. Look for an update in the next issue.

OCAW Holds Public Ethics Discussion in Oak Ridge

The Oil, Chemical, and Atomic Workers International Union (OCAW) was host to a small public meeting on the ethical, social, and legal issues relating to health studies for former Department of Energy (DOE) construction workers on February 10-11, 1997, at the Oak Ridge Institute for Science and Education (ORISE) in Oak Ridge, Tenn.

The workshop brought together former union workers, researchers, DOE officials, ORISE staff, and local citizens interested in an open dialogue on the ethical issues involved in medical surveillance of workers employed by the federal government and its contractors during the developing years of the nuclear program. In 1996, DOE announced the award of six cooperative agreements to fund pilot health studies for these former workers.

Dr. Eula Bingham, a researcher at the University of Cincinnati, and Sheldon Samuels, Vice President, The Ramazzini Institute for Occupational and Environmental Health Research, served as coordinators for the public workshop. Dr. Bingham, the Principal Investigator for one of the six DOE medical surveillance awards, explained that the project would involve the collection of any existing past medical records and the reconstruction of medical records that do not exist. This data will be gathered through interviews with former construction workers and their families.

It is the handling of these medical records and medical exams that gives rise to some of the ethical questions under discussion. Many of these complex issues involve data confidentiality, voluntary and involuntary informed consent, fear of discrimination by employers and insurance companies, and the stigma attached to past

employment at these sites. Mr. Samuels announced that the workshop will result in a list of recommendations that address the concerns regarding the handling of this very sensitive data.

Biological and Environmental Research Program Celebrates 50 Years

The U.S. Department of Energy and the National Research Council of the National Academy of Sciences jointly sponsored a symposium celebrating the legacy and exploring the promise of 50 years of achievements in the department's Biological and Environmental Research Program (BER). The two-day celebration was held May 21-22, 1997, at the National Academy of Sciences in Washington, D.C.

BER programs cross traditional research boundaries to seek revolutionary solutions to energy-related biological and environmental challenges. Research areas include health effects, genome, global environmental change, nuclear medicine, and bioremediation. One important DOE legacy is the establishment of the first Human Genome Program. In addition, DOE's Protection of Human Subjects Program, which oversees **all DOE research involving human research subjects,** is part of BER. All research funded by DOE, performed by DOE workers, or performed at a DOE site is required to comply with human subject regulations.

The program's keynote speaker, Dr. Leroy F. Hood, University of Washington, spoke on the "Impact of Biotechnology and Environmental Research on Science and Society in the 21st century." His presentation included a discussion of the study of diseases as a systems problem and how the deciphering and manipulation of systems information will bring together diagnostics, therapy, and prevention.

The celebration was attended by personnel across the DOE complex. The audience included influential representatives from science, government, industry, academia, and the media--all invitees who helped shape the policies that determined the future of the BER program. A poster session highlighted exhibits from national laboratories and DOE facilities across the country.

Newsletter Information

This bulletin is designed to facilitate communication among those involved in human subjects research and to inform persons interested in human subjects research activities.

DOE Human Research Subjects Program

- **Program Manager**: *Dr. Susan L. Rose*
- **Editors**: *Dotty Roberts, Linda Sharp*
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