PROTECTING HUMAN SUBJECTS

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

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New technologies & international research

This issue of *Protecting Human Subjects* discusses several serious challenges that for the forseeable future will increasingly be a focus of the research ethics discussion.

New scientific endeavors, such as nanotechnologies, will require new ways to apply the ethical guidelines already in place. **Peter Lichty** of Lawrence Berkeley National Laboratory outlines the complexities of potential risks in this field and considers some of the ethical issues we will face.

Similarly, new understandings resulting from the Human Genome Project have created ethical and social issues that previously we have never had to consider. The haplotype map, or "HapMap," will be a tool that will allow researchers to find genes and genetic variations that affect health and disease. The HapMap will also, however, raise questions about the use of this information, a subject considered in another article featured in this issue.

Another challenge for Institutional Review Boards (IRBs) and the research community generally concerns internation research issues, which is discussed in a report by South African researcher **S. R. Benatar,** who writes about research in developing countries.

Human subjects risk in new nanotechnologies?

At less than 100 billionths of a meter, nanoparticles are the subject of increasing discussion among researchers, ethicists, and institutions

One of the hottest areas of scientific discovery today involves tiny particles with at least one dimension less than 100 billionths of a meter.

Peter Lichty

The enthusiasm generated by early discoveries has led to the formation of the National Nanotechnology Initiative, a multiagency research effort to be funded by the federal government with $5 billion during the next five years.

Applications of these new materials are expected to include better methods of drug delivery, more efficient solar cells, smaller integrated circuits, and better chemical reaction catalysts.

It is only a matter of time before nanoparticles are introduced into research on humans. To evaluate and understand the potential risk of these experiments, a few concepts should be understood.

No single nanotechnology

First of all, there is no single nanotechnology. A variety of technologies are used to produce nanoparticles, some new and some old. In fact, the new International Standards Organization committee writing standards for this field is referencing "nanotechnologies" in recognition of these multiple approaches.

By Peter D. Lichty, M.D., Occupational Medical Director Lawrence Berkeley National Laboratory

Production methods are often classified as top-down (micromilling, for example) or bottom-up (chemical synthesis), but this

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distinction is not important in human subjects research.

One important technological factor to be considered in human exposure experiments is that each synthetic method is associated with certain contaminants (exposure to which should also be evaluated) and some variations in particle size.

Nanoparticles are not new

"Natural" nanoparticles are widespread, including sea salt crystals and wind-blown dust. Many other nanoparticles in our environment are produced as byproducts of combustion, such as diesel exhaust particles or candle soot. Take a breath in the average office today, and you inhale about 30 million nanoparticles!

Current attention to particles in this size range is likely to reveal more facts about our past and current exposures to natural and byproduct nanoparticles, and will lead to additional scientific inquiries about those particles.

Not all nanoparticles are going to be in a form that can be released. Research on nanoscale circuits generally involves structures etched on or bound to silicon surfaces, which are not likely to become detached and lead to human exposure.

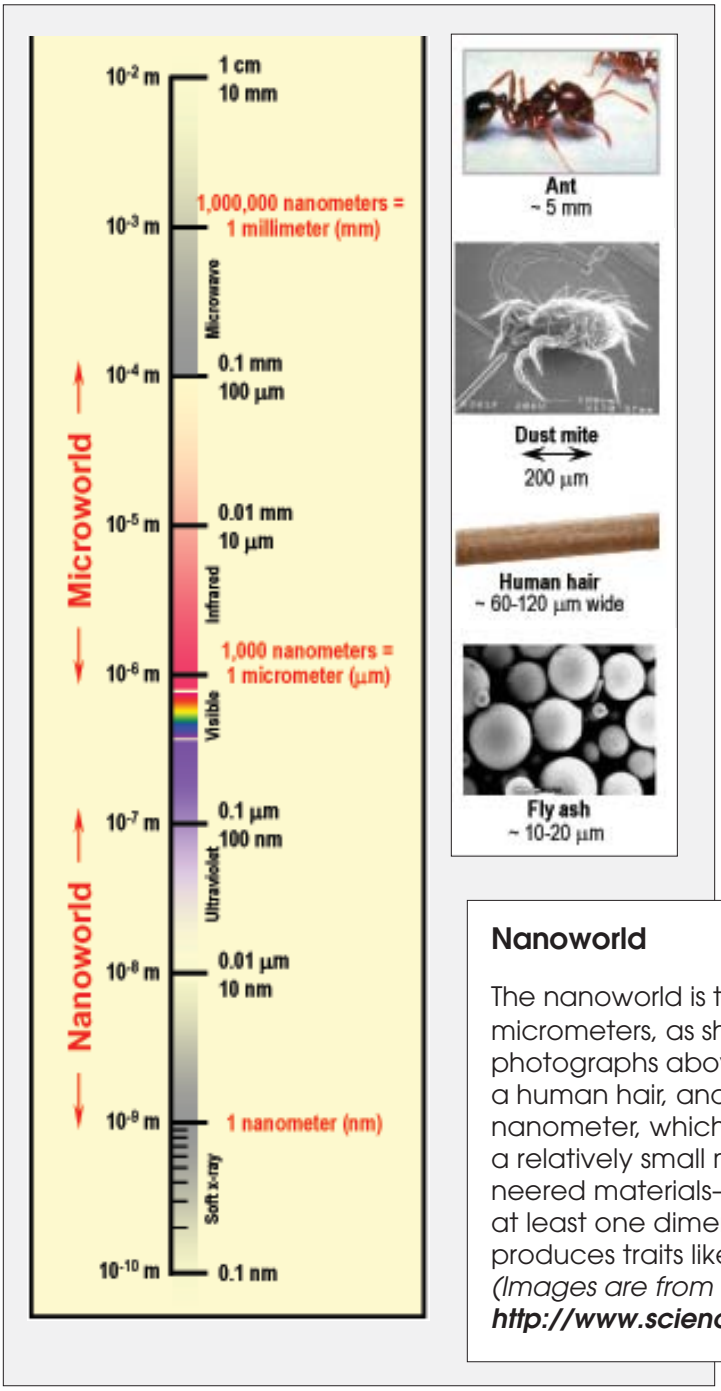
Take a breath in the average office today, and you inhale about 30 million nanoparticles

Finally, some products containing nanoparticles are already on the market, such as titanium dioxide sunscreens, stain-resistant fabric coatings, and carbon nanotube composite sports equipment. This means human exposures have already begun.

Some nanoparticles can be harmful

From past experience, we know that some nanoparticles can be harmful. Asbestos fibers are classified as nanoparticles because their diameters are in the nanoscale. Most combustion processes produce soot that has been shown, at least in animals, to be mildly carcinogenic.

Other nanoparticles seem to have very little toxicity. Carbon black (produced for automobile tires) is ➢



Nanoworld

The nanoworld is that part of the universe that is smaller than 10^{-8} micrometers, as shown in the graphic at left. For comparison, the photographs above show the approximate size of a dust mite, an ant, a human hair, and fly ash. The term nanotechnology comes from the nanometer, which is a billionth of a meter, or roughly the diameter of a relatively small molecule. The term is usually used to describe engineered materials—and the processes to manipulate them—for which at least one dimension is less than 100 nanometers and the small size produces traits like unusual strength or electrical performance.
(Images are from the DOE Office of Basic Energy Sciences Web site: ***http://www.science.doe.gov/bes/scale_of_things.html)***

relatively nontoxic, and a commercial product called Technegas® is used in medicine to follow gas movement, with no apparent ill effects. Generalizations about nanoparticles are inappropriate, and it is impossible to label them all as either "good" or "bad."

Many disciplines involved

Research on nanoparticles will involve a variety of disciplines, all with common difficulties. Most nanoparticles are invisible and require electron microscopes to view them. Nanoparticles tend to bind to each other, so it will be difficult to work with individual particles that have not formed agglomerate complexes.

As noted above, nanoparticles are not always pure, so separating the effects of the particles from the effects of contaminants will be difficult. Finally, nanoparticle preparations generally produce a bell-shaped size distribution—it is currently impossible to produce nanoparticles in a narrow size range, making the evaluation of size-related effects very difficult.

Interestingly, nanoscale research does not all require elaborate machines, a fact which encourages other countries to enter this field, increasing the likelihood of foreign collaboration in human subjects research.

Human experimentation will attempt to answer the following questions:

- **What happens to the nanoparticles we are already inhaling every day?** This question will help define the absorption, distribution, and elimination (if any) of background environmental nanoparticles. Attempts to use human tissue samples to extract and characterize nanoparticle burdens in the human body are likely. This may include surplus surgical tissues or autopsy samples.
- **Can we trace the path of nanoparticles in the body?** One type of nanoparticle, the quantum crystal, fluoresces at a frequency determined by the particle size. This type of particle has already been injected into the nude mouse and shown by transillumination to accumulate in the liver, spleen, and bone marrow. In humans, radioactively labeled particles likely will be used to trace the uptake and distribution of nanoparticles. The safety of using radiation in this type of experiment is well known, but the safety of injecting newly engineered nanoparticles in this type of experiment is not yet clear.
- **Can we extract nanoparticles from bodily fluids**? Using human samples, it may be possible to identify nanoparticles in blood or urine, to look for naturally occurring insoluble nanoparticles, or to check uptake and/or excretion in nanoparticle production workers.
- **Can we protect workers and the environment from released nanoparticles**? Once large-scale production of novel particles begins, it will be important to know how

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BES Scientific User Facilities include five focused on nanotechnology research

The Office of Basic Energy Sciences (BES) plans, constructs, and operates major scientific user facilities, including those primarily focused on nanotechnology. They serve researchers from universities, national laboratories, and industry. See http://www.science.doe.gov/Sub/Newsroom/News_Releases/DOE-SC/2006/nano/index.htm. The five user facilities are:

Center for Nanophase Materials Sciences
at Oak Ridge National Laboratory
Oak Ridge, TN
http://www.cnms.ornl.gov/

Molecular Foundry
at Lawrence Berkeley National Laboratory
Berkeley, CA
http://foundry.lbl.gov/

Center for Integrated Nanotechnologies
at Sandia National Laboratories and Los Alamos National Laboratory
http://cint.lanl.gov/

Center for Functional Nanomaterials
at Brookhaven National Laboratory
Upton, NY
http://www.cfn.bnl.gov/

Center for Nanoscale Materials
at Argonne National Laboratory
Argonne, IL
http://nano.anl.gov/

efficient filters are in capturing nano-particles. Some of this research can be done mechanically, using filtered air streams, but some of it will require workers wearing filtering respirators and measuring the nanoparticle protection factors for these devices. There will also be a need for human-worn devices to measure exposures to nanoparticles.

- **How do nanoparticles affect basic cellular processes**? This research has already begun, using the tools of genomics to see how nanoparticles change gene activity in human cell cultures. This type of human subjects research will probably use established, anonymous cell lines so that valid generalizations can be made.
- **Are nanoparticles absorbed through the skin**? One of the largest current applications for nanoparticles is nano-sized titanium dioxide sunscreens, which are cosmetically preferable due to their lack of color when applied. Early research suggested these particles are not absorbed, but some beryllium-oriented research suggests that particles in this size range can be absorbed when the skin is stretched. More experiments are needed.

All this research is designed to capitalize on the unique properties of newly created nanoparticles. A host of potential societal benefits await the use of these particles in medicine and technology. As always, the institutional review boards will need to keep up with the questions and controversies in this new field in order to protect the human subjects participating in research.Δ

Nanotech Web sites

Ethics in nanotechnology
http://bioethics.org/research/index.php?page_id=6

DOE Office of Science, nanoscience research
http://www.sc.doe.gov/Sub/Newsroom/News_Releases/DOE-SC/2006/nano/index.htm

Nanotechnology sources listing
http://www.zyvex.com/nano/

Foresight Nanotech Institute
http://www.foresight.org/Updates/Publications.html

Nanotech news discussion group
http://www.nanotech.50megs.com/

Nanotechnology journal
http://www.iop.org/EJ/journal/0957-4484

Richard Feynman on minitiarization
http://www.zyvex.com/nanotech/feynman.html

Nanotechnology debate: Drexler v. Smalley
http://pubs.acs.org/cen/coverstory/8148/8148counterpoint.html

Center for Responsible Nanotechnology
http://www.crnano.org/

Harvard University/Lieber Research Group
http://cmliris.harvard.edu/

University of North Carolina Nanoscience
http://www.cs.unc.edu/Research/nano/

International Society for Nanoscale Science
http://www.isnsce.org/

More nanotechnology links
http://sunsite.nus.edu.sg/MEMEX/nanolink.html

Project examines risks, implications of nanotechnologies

As nanotechnologies proliferate in laboratories, so have efforts to examine their implications and risks.

The Project on Emerging Nanotechnologies (**http://www.nanotechproject.org/**) was established in April 2005 to help "ensure that as nanotechnologies advance, possible risks are minimized, public and consumer engagement remains strong, and the potential benefits of these new technologies are realized."

A partnership between the Woodrow Wilson International Center for Scholars and the Pew Charitable Trusts, the project provides independent analysis by collaborating with researchers, government, industry, non-governmental organizations, policymakers, and others to "identify gaps in knowledge and regulatory processes, and to develop strategies for closing them," according to the project's Web site.

The database includes more than 200 research programs, including some financed by the European Union and other countries.

All research results, reports, and the outcomes of the project's meetings and programs are made available through publications and over the Web.Δ

Viola, Kirchner lead DOE's human subjects protection

Backgrounds in nuclear medicine, epidemiology, and genetics

Michael Viola, M.D., has been appointed Human Subjects Protection Officer for the Department of Energy (DOE), in the Office of Science, Office of Biological and Environmental Research (BER).

He will be assisted in human subjects protection activities by **Peter Kirchner**, M.D.

Michael Viola

Peter Kirchner

Viola said he and Kirchner would lead the program with the goal of "ensuring that the rights and welfare of human research subjects are protected while advances in biomedical, environmental, nuclear, and other research continue to lead to discoveries that benefit humanity."

Viola has been on the faculty of a number of medical schools, most recently at the State University of New York at Stony Brook where he was Professor of Medicine and Microbiology and Director of the University Cancer Center. He has been acting director of the Human Subjects Protection office for about a year.

He is founder and director of Medicine for Peace, an all–volunteer organization that has worked in Central America and the Middle East. He received an undergraduate degree from Princeton University and a medical degree from McGill University School of Medicine, followed by medical training at the Yale Medical Center and specialty training in medical oncology at the Sloan Kettering Cancer Center and the National Cancer Institute. His research interests are in the areas of epidemiology and genetics of melanoma and leukemia.

Kirchner is board certified in internal medicine and nuclear medicine. He came to DOE in 1998 from the University of Iowa where he was Director of Nuclear Medicine and Professor of Radiology and Medicine.

He is currently working on an Intergovernment Personnel Agreement from Oak Ridge National Laboratory to DOE-BER where he is a senior scientist. He is detailed part-time to the National Institute's of Health's Institute of Biomedical Imaging and Bioengineering where he is a senior advisor.

Kirchner earned a B.A. in physics at Yale University and an M.D. at Columbia University, with residency training in internal medicine at the National Naval Medical Center (NNMC) and fellowship training in nuclear medicine at Johns Hopkins University.

He subsequently established a residency program in Nuclear Medicine at NNMC and directed the nuclear medicine service. In 1977, he was an Associate Professor at the University of Chicago and the Associate Director of Nuclear Medicine. In 1981, he became Director of Nuclear Medicine at the University of Iowa.Δ

Lawrence Livermore's Web instructions for new investigators

New investigators at Lawrence Livermore National Laboratory in California now have available to them Web-based instructions outlining their responsibilities in research involving human subjects.

The site, which is required reading, provides the historical context of ethical conduct and discusses the mechanics and purpose of the IRB process. It includes an especially detailed range of activities that falls under the term "human subjects" research.

An IRB tutorial is among the features of the laboratory's site, which also includes all needed documents for IRB reviews.

The "New Investigators" site is part of a larger site created by Lawrence Livermore that provides detailed resources related to the IRB approval process, regulations, and research data.

The Web address is **http://www.llnl.gov/HumanSubjects/pi_instructions.html**

Reconsidering ethics in research

Some argue that conventional wisdom is wrong

As more public scrutiny focuses on human subjects research, scholarly analysis has also moved in the direction of raising questions related to fundamental ethical beliefs about research, whether those beliefs are still useful, and whether changes in the way these beliefs are implemented may be necessary.

The Hastings Center Report is at http://www.thehastingscenter.org/publications/hcr/hcr.asp

A series of articles published during the past few years by **The Hastings Center**, an influential bioethics think tank, has set the tone for the discussion, asserting either that accepted beliefs are wrong or should be applied in ways different from current practice.

For example, *The Hastings Center Report (HCR)* editor **Gregory Kaebnick** said in an editorial note that the trend several years ago toward stringent protection, with the federal government temporarily closing research at universities, has subsided. Now, he said, many believe "protections for subjects are too heavy-handed or are applied in clumsily sweeping ways, thereby getting in the way of good science." Throughout, Kaebnick added, "there appears to be a growing belief that some of the cornerstone concepts of the ethics of human subjects research, whether or not they provide adequate protections, are in need of rethinking" (*HCR*, 35:5, September-October 2005).

Several articles in the same issue develop the discussion of these questions. An article by **David Orentlicher** and another by **Lynn Jansen**, question the necessity of always requiring informed consent. They assert that coercion is sometimes understood too broadly and that "coercive" methods of recruiting new subjects may sometimes be acceptable.

An article by **Jennifer Hawkins** and **Ezekiel Emanuel** argues that coercion is often seen where there actually is none. Orentlicher points out that all cancer patients at the National Institutes of Health Clinical Center must agree to participate in a clinical trial in order to receive medical care.

Jeremy Sugarman discusses the issue of whether American researchers working in foreign countries should have to follow U.S. requirements on ethical conduct or the requirements of the host country. ". . . [T]he extent to which U.S. rules ought to apply in host countries remains unclear," Sugarman notes. He warns that "imposition of U.S. rules in other nations can seem hegeomonic to people who are desperately seeking assistance with devastating social and medical situations." The best course, he suggests, is to balance the competing considerations, a line he recognizes as tricky to follow.

In addition, several articles published in 2004 in *HCR* argue, again contrary to accepted beliefs, that it is not necessarily the case that when research conducted in foreign countries is proven effective, the benefits of that research must be made available in the country in which the research was conducted. See **John Arras**, "Fair Benefits in International Medical Research" (*HCR*, May-June 2004). Also see "Moral standards for research in developing countries: from 'reasonable availability' to 'fair benefits'" (*HCR*, May-June 2004).

"Coercive" methods of recruiting new subjects may sometimes be acceptable

The questions raised in these articles continue a line of questioning, Kaebnick says, that began in 2003 when *HCR* published an article by **Franklin Miller** and **Howard Brody.** In the article, the authors question the importance of adhering to "clinical equipoise." This refers to a situation in which "reasonable experts disagree about which treatment is best"—the experimental treatment or the treatment to which it is being compared. In his editorial, Kaebnick points out that researchers currently accept that clinical equipoise must exist if a trial is to be ethical. Miller and Brody say this is mistaken.Δ

". . . some of the cornerstone concepts of the ethics of human subjects research, whether or not they provide adequate protections, are in need of rethinking."

Research in developing countries

Recommendations include wider role for ethics committees, new ways of thinking about improving global health, and promoting moral progress in research

Ethical issues related to global health and medical research should be discussed in a world-wide debate extending beyond the traditional interpersonal level, according to an article by **S. R. Benatar**, director of the Bioethics Centre, University of Cape Town, South Africa (**"Reflections and recommendations on research ethics in developing countries," *Social Science & Medicine*, No. 54, 1131-1141**).

Problems such as that illustrated by the AIDS pandemic, he said, make it vital that the ethics debate "include the best interests of whole populations, the ethics of how institutions (including multinational drug companies) should function, and the ethics of international relations, especially those between rich/strong and poor/weak countries."

Re-evaluating ethical practices

The article argues that "When those in privileged positions and in wealthier countries consider undertaking collaborative research with colleagues in developing countries, it is necessary to understand both their own framework of thinking, and the implications of very different mind-set and environments in which research projects may be carried out . . ."

Problems such as the AIDS pandemic make it vital that the ethics debate include the best interests of whole populations

Benatar focuses primarily on ethical practices that may need to be re-evaluated in new circumstances. For example, he argues that simple principles and declarations provide insufficient direction when implemented without an understanding of context.

Recommendations

Similarly, he points out that researchers have tended to focus too much attention on informed consent and on reviewing research protocols, but provided inadequate attention to "monitoring studies, trying to improve the actual conduct of research, and promoting justice in the distribution of the burdens and benefits of research.

Benatar recommends that research ethics could be enhanced if ethics committees would focus more ➢

Clarification

The last issue of *Protecting Human Subjects* (No. 12, Summer 2005) included an account of a presentation by **Amaboo Dhai** at the 2005 PRIM&R meeting.

The article we published discussing the presentation did not point out that Dhai's presentation and the narrative about the African woman, Ntombi, was based on an article published in the journal *Social Science & Medicine* (No. 54, 1131-1141) by **S. R. Benatar**, professor of medicine and director of the Bioethics Centre, University of Cape Town, South Africa.

Dr. Benatar's article, "Reflections and recommendations on research ethics in developing countries," discusses, among other things, the complexities of protecting human subjects in international research. A report discussing the article begins on this page. Additional articles by **Benatar** that discuss this topic include:

"A new look at international research ethics." *British Medical Journal* 321: 824-826.

"Avoiding exploitation in clinical research." *Cambridge Quarterly of Healthcare Ethics* 9(4): 562-565.

"Preventing vertical HIV transmission: the controversy in South Africa." *Journal of Women's Health and Law* 1(3): 313-318.

"Medical education and medical practice in the 21st century." *Brunei Medical Journal* 2: 15-16.

"Human Rights in the Biotechnology Era: A story of two lives and two worlds." Chapter in Bhatia, G.S., O'Neil, J.S., Gall, G.L. & Bendin, P.D. (eds) *Peace, Justice and Freedom: Human Rights challenges in the new millennium*: 245-257. Edmonton: University of Alberta Press, Edmonton.

Research in developing countries

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attention on their role as educators of researchers and the community. In addition, the committees should concentrate more effort on monitoring and auditing research, and providing accountability to the public. Because ethics "has received only patchy attention in many developing countries," Benatar notes, "there is little uniformity in the structure and function of research ethics committees and minimal, if any, public accountability."

An important first step in changing this situation would be for those who fund research to communicate sufficient concern and to approprite resources to develop more awareness of the importance of ethics in their endeavor.Δ

Ethical standards, laws, and Web links compiled for research protection in 72 countries

An *International Compilation of Human Subject Research Protections* has been published by the Office for Human Research Protections (OHRP), US Department of Health and Human Services.

The compilation was first released in June 2005, covering 54 countries, and then expanded in October to include 72 countries. Among other changes, the revised version adds standards issued by international organizations. It also provides the laws and regulations related to privacy/data protection, human biological materials, and genetic research.

OHRP's compilation even includes a list of countries for which no research standards could be identified. These included, among others, Afghanistan, Bhutan, Cambodia, Egypt, Iraq, Pakistan, Vietnam, Yemen, Bermuda, Ecuador, Paraguay, Suriname, Morocco, Mozambique, Sudan, and Zambia.

Web links to countries' research oversight agencies are included along with links to each country's documents related to oversight. A chart lists each country's key organizations, legislation, regulations, and guidelines. Web links are provided for all of these where available.

The compilation can be viewed at **http://www.hhs.gov/ohrp/international/index.html#NatlPol**

Useful Web sites

Free, Web-based course from the National Cancer Institute presents information about the rights and welfare of human participants in research
http://cme.cancer.gov/clinicaltrials/learning/humanparticipant-protections.asp

Human subjects research online training from the U.S. Department of Health and Human Services
http://www.hrsa.gov/humansubjects/

UCLA human research subjects training and certification
http://www.training.ucla.edu/

National Institute of Justice protecting human subjects training
http://www.ojp.usdoj.gov/nij/funding/humansubjects/index.html

National Center for Juvenile Justice Program for Protecting Research Subjects
http://ncjj.servehttp.com/irb/pages/Research_PHSH.html

Association of Research Libraries Policy on Research involving Human Subjects
http://www.arl.org/stats/privacy.html

Ethical and legal aspects of human subjects research on the Internet, from the American Association for the Advancement of Science
www.aaas.org/spp/sfrl/projects/intres/report.pdf

Assessing the system for protecting human research participants, Institute of Medicine of The National Academies
http://www.iom.edu/CMS/3740/4870.aspx

Bioethics topics–University of Washington
http://depts.washington.edu/bioethx/topics/

Research Integrity—a semi-annual newsletter published by Michigan State University
http://www.msu.edu/user/gradschl/integrity.htm

Research ethics program—courses and workshops at the University of California, San Diego
http://ethics.ucsd.edu/

Research ethics news
http://www.scidev.net/dossiers/index.cfm?fuseaction=dossierItem&Dossier=5&CFID=7625938&CFTOKEN=92486225

Policy paper on sponsors' obligations to human research subjects
http://www.scidev.net/dossiers/index.cfm?fuseaction=policybrief&dossier=5&policy=63

Clinical research training program—Albert Einstein College of Medicine
http://www.aecom.yu.edu/crtp/

Ethical concerns in HapMap project

While the HapMap project was completed last year, underlying ethical concerns linger as results of the mapping are applied in the clinic and the laboratory

When the first phase of the HapMap Project was completed last year, it marked the end of the least ethically delicate phase. The thorniest moral questions are more likely to arise as the data compiled is transformed into meaningful information about the groups of people whose DNA variations were identified by the project.

Ellen Clayton
(From photo by Dana Johnson)

The goal of the project was to explain how the 3 billion bits of DNA in the human genome are organized into sequence variants (haplotype blocks) that are shared by many people. The project's 200 or so researchers used DNA samples from Yoruba people in Ibadan, Nigeria; Japanese in Tokyo; Han Chinese in Beijing; and United States residents of Utah who have ancestry from northern and western Europe.

Once the haplotypes are mapped, the information should allow scientists to find inherited gene sequences linked to conditions such as cancer, diabetes, asthma, and heart disease. This, in turn, is expected to be used to develop treatments and cures (For more details, see the accompanying article on this page.)

Researchers were careful to guard against the obvious ethical problems, said **Ellen Clayton**, who headed the project's ethical component. For example, they incorporated ethical considerations into the initial design of the study, including ensuring that samples cannot be connected to individuals and that personal information is not linked to any sample. In addition, more samples were collected than were used, hence no specific individual is known to be included.

Stigmas and discrimination

The ethical problem most likely to arise would result from the fact that samples used to develop the HapMap are identifiable as coming from one of the study populations. This, in turn, means that comparisons can be made between populations. Studies employing the project's data could therefore lead to stigmatization and discrimination, said Clayton, who is a professor of pediatrics and law and director of the Vanderbilt University Center for Genetics and Health Policy. "A common characteristic of people throughout the world is that one group tries to prove that they are better than some other group," she said. "We must be careful not to provide support for those claims."

For example, if a disease-associated variant occurs more frequently in one group, the information could, mistakenly, be generalized to all or most of the group's members by suggesting that they have a higher-than-average risk of a disease. This would be

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What is the HapMap and how is it related to human research?

(The following includes information from the International HapMap Project, ***http://www.hapmap.org/abouthapmap.html****)*

The haplotype map, "HapMap," is a catalog of common genetic variants that occur in human beings. Genetic variants that are near each other tend to be inherited together. These regions of linked variants are known as haplotypes.

The map describes these variants, where they occur in DNA, and how they are distributed among people within specific populations and among specific populations in different parts of the world. Samples came from Yoruba people in Ibadan, Nigeria; Japanese in Tokyo; Han Chinese in Beijing; and United States residents of Utah who have ancestry from northern and western Europe.

Phase one of the project was completed late in 2005. Phase two will be an ongoing effort to develop more understanding about the variants in genetic sequences. The HapMap itself does not establish connections between particular genetic variants and diseases. Rather, it pro-

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unfortunate because, while the population may include people with the disease-associated variant, not all people in the population have the variant and, in addition, many people outside the population may bear similar risks.

Especially vexing

The inevitable making of inferences about population relatedness may have good and bad results, which makes the issues especially vexing. The purpose of identifying the variants is to create shortcuts to find remedies for many debilitating diseases, and yet the information can also be used to stigmatize an entire group by characterizing them in ways that result in discrimination. This result could take the form of compromising medical insurance coverage, access to health care, and social stigmatization. (For a discussion of aspects of this issue, see Ellen Clayton, "The complex relationship of genetics, groups, and health: what it means for public health," *The Journal of Law, Medicine & Ethics* 30, 290–297, 2002.)

Genetic findings could undermine established cultural or religious traditions or legal or political status

Clayton said the optimistic view of long-term benefits from the project is that "in a world characterized by unequal distribution, what we learn from information in the HapMap may allow us to develop treatments that can accomplish more equal distribution of health care."

The project's Web site (**http://www.hapmap.org/**), which discusses many of these issues, points out that "genetic findings could undermine established cultural or religious traditions or legal or political status." This could happen because groups "have firm beliefs about the origin of the group or about the relationship of the group to other groups, and these beliefs may be challenged by findings built on the use of the HapMap. In addition, genetic findings may conflict with the social and cultural methods that groups have developed to determine who is a member of that group." Clayton said it is thus especially important that findings from the HapMap not be superficially interpreted in ways that could perpetuate social and historical stereotypes.

Another concern is that the mapped variants may be used wrongly to suggest that constructs such as "race" have significant biological meaning. To assume biological significance could lead to erroneous claims about racial differences in genetic and ancestral predispositions. The information emerging from the project suggests just the opposite, indicating that race is only loosely connected to biological ancestry. (For a discussion of this issue, see M. W. Foster and R. R. Sharp, "Beyond race; towards a whole-genome perspective on human populations and genetic variation," *National Review of Genetics*, 2004, Oct. 5, 790-6.)

The widespread debate about the biological relevance of group identity typically takes two forms. One side argues that genetic variants between groups contributes negligibly to health disparities related to social identity and therefore the possibility of stigmatization is too great to justify the risk. The other side insists that we should not ignore the scientific implications of population-specific variants. Clayton argues that to prevent stigmatization, researchers using the HapMap must be careful not to generalize in describing groups.

Taking steps to avoid ethical mistakes

Seeking to avoid anticipated ethical mistakes inherent to this debate, the project took a variety of steps, including close collaboration with bioethicists and community groups.

Teams of geneticists and ethicists worked with community groups to explain the project and discuss questions about how samples would be collected and described and how the resulting information

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HapMap Web sites

International HapMap Project
http://www.hapmap.org/

National Human Genome Research Institute HapMap
http://www.genome.gov/10001688

Gene expression blog—Ethics of the Hapmap
http://www.gnxp.com/MT2/archives/002343.html

Practical Guide to the HapMap
http://www.the-scientist.com/article/display/23052/

***Nature Genetics* article**
http://www.nature.com/ng/journal/v37/n11/abs/ng1653.html

"Toward a new vocabulary of human genetic variation," in* Science *magazine.
http://www.sciencemag.org/cgi/content/full/298/5597/1337

would be used. Consent forms were modified and approved by local ethics committees as a result of these interactions so that they would be appropriate for each community.

Community advisory groups
Each community also formed a community advisory group (CAG) that will continue to exist for the foreseeable future. The group will function as a liaison between the community and the Coriell Institute, where the samples will be stored. In addition, Coriell will prepare quarterly reports and periodic newsletters telling the communities about how the project is proceeding and how the samples are being used.

Built into the study's design was a prohibition on developing drugs or other commercial products as a part of the project. Other studies, however, are expected to use the information to develop diagnostic and pharmaceutical products.

For additional discussion about ethical issues related to the projects, see the following:

A report by the HapMap Consortium, "A haplotype map of the human genome," *Nature,* Oct. 27, 2005, **http://www.nature.com/nature/journal/v437/n7063/abs/nature04226.html**.

Richard Gibbs, "Deeper into the Genome, *Nature,* Oct. 27, 2005, **http://www.nature.com/nature/journal/v437/n7063/full/4371233a.html**.

"The International HapMap Consortium. Integrating ethics and science in the International HapMap Project." *Nature Reviews Genetics* 5, 467-475. 2004, **http://www.nature.com/nrg/journal/v5/n6/full/nrg1351_fs.html**Δ

What is the HapMap? (*continued from page 9*)

vides information that other researchers can use to link genetic variants to the risk for specific illnesses, with the goal of developing new methods of preventing, diagnosing, and treating disease. For example, studies published last year in the journal *Science* reported that scientists used HapMap data to find a genetic variant that substantially increases the risk of macular degeneration, the leading cause of vision loss in the elderly.

Influencing physical traits, responses
Genetic sequences contain information that influences our physical traits, our likelihood of suffering from disease, and the responses of our bodies to substances that we encounter in the environment.

The sequences of different people are remarkably similar. When the chromosomes of two humans are compared, their DNA sequences are identical for hundreds of bases. But at about 1 in every 1,200 bases, on average, the sequences will differ. Differences in individual bases are the most common type of genetic variation. These differences are known as single nucleotide polymorphisms, or SNPs (pronounced "snips").

Genetic diversity
By identifying most of the approximately 10 million SNPs, the HapMap charts the basis for a large fraction of human genetic diversity. For geneticists, SNPs act as markers to locate genes in DNA sequences. If, for example, a change in the makeup of a gene increases the risk of suffering from high blood pressure, researchers need to find out where in the chromosomes that particular gene is located. To do this, they could compare the SNPs in people who have high blood pressure with the SNPs of people who do not. If a particular SNP is more common among people with hypertension, that SNP could be used as a pointer to locate and identify the gene involved in the disease.

However, testing all of the 10 million common SNPs in a person's chromosomes would be extremely expensive. The development of the HapMap will enable geneticists to take advantage of how SNPs and other genetic variants are organized on chromosomes. It provides a shortcut to identifying the causes of certain diseases.

In many parts of our chromosomes, just a handful of haplotypes are found in humans. In a given population, 55% of people may have one version of a haplotype, 30% may have another, 8% may have a third, and the rest may have a variety of less common haplotypes.

The HapMap identifies these common haplotypes, along with the "tag" SNPs that uniquely identify them. By testing an individual's tag SNPs (a process known as genotyping), researchers will be able to identify the collection of haplotypes in a person's DNA.Δ

No regulations for "IRB shopping"

Problem may be more serious for pharmaceutical companies

The U.S. Food and Drug Administration (FDA) announced on February 28, 2006, that it would not regulate a practice in which researchers conducting clinical trials submit proposed protocols to IRBs believed to be more likely to grant approval. The FDA said so-called "IRB shopping" either does not occur or is not a significant problem.

The proposed regulation had been criticized by many large research institutions as unnecessarily cumbersome and unlikely to provide real protection for human subjects.

The Department of Health and Human Services' inspector general in 1998 recommended regulation because of "a few situations where sponsors and/or research investigators who were unhappy with one IRB's reviews switched to another without the new IRB being aware of the other's prior involvement."

University researchers are required to use their own IRB. The problem is thought to be more serious among pharmaceutical companies, which hire for-profit IRBs.

Some of the comments received by the FDA suggested the problem could be solved by requiring that IRBs ask clinical-trial sponsors if their proposals had previously been considered by or rejected by other IRBs. Another suggestion was to place protocols rejected by an IRB on a federal Web-based registry.

One registry, **ClinicalTrials.gov**, is currently operating but without requirements that rejections be announced. Other commenters suggested that clinical-trial sponsors intent on IRB shopping could get around the registry by simply giving a rejected research proposal a new title and details to make it appear novel.Δ

News notes

Duke uses Office of Science grant to develop Web-based ethics training

Duke University Medical Center has used a $597,000 grant from the DOE Office of Science to develop a Web-based ethics training program for scientists and medical investigators involved in genetics research as well as those who are responsible for reviewing this research.

A panel of scientists, ethicists, attorneys, and philosophers developed the program, Accessible Genetics Research Ethics Education (AGREE). The effort was led by **Jeremy Sugarman**, Director of the Duke Center for the Study of Medical Ethics and Humanities. He continues to be the principal investigator for AGREE (**http://agree.mc.duke.edu/**).

Duke does not charge a fee to use the education modules, although users must register to get access. A fee of $25 per module is charged to get the optional Continuing Medical Education (CME) credit. The CME credits are available for purchase after completion of each module.

The site also includes selected presentations from the conference, *Working at the frontiers of law and science: applications of the human genome*, which was held at the University of North Carolina, Chapel Hill, in 2003. The educational modules range in topics from "ethics and genetics research in populations" to "ethical issues in behavioral genetics research."

A comprehensive listing of other resources is also available on the site, including links to general research ethics information, links specific to ethics in genomics, information about genomics, and contact information for a variety of agencies and organizations involved in genomic research ethics.Δ

When things go wrong . . .

Who enforces? Who pays? How ensure it's not repeated?

By Sherry Brewer, Director
Office of Research Integrity
University of Tennessee
Graduate School of Medicine

Increasingly, the light of public scrutiny is shining upon the world of biomedical research. From the highly publicized tragedy of the Gelsinger family in 1999 to the more recent death of a study volunteer in an Eli Lilly trial, the media, the public, and the government are asking tougher questions about research.


Sherry Brewer

Concerns about safety, privacy, and conflicts of interest are at the heart of the public scrutiny. Who is paying for the research? What else is affecting this investigator's decisions other than the safety of the participants? Does the design of the study protect the participants?

Concerns about protection of the privacy of the participants have also been expressed. Who sees the data from the study? Who is making sure that the study is conducted as planned? What happens when something goes wrong? Who enforces? Who pays? How do we ensure that mistakes are not repeated?

Good news and bad news

The good news and the bad news (depending upon point of view) is that legal expertise is rapidly developing to help research subjects, investigators, IRB members and sponsors answer some of these tangled questions related to research.

The media, the public, and the government are asking more questions about research

By its very nature, the U.S. legal system is fluid, giving constantly changing responses to the issues facing our society. As biomedical research is subject to greater and greater public criticism, the legal system will respond with emerging laws, understandings, advice, and expertise.

Headline-grabbing stories about multimillion dollar private lawsuits have received the greatest attention in the past six years. The full range of possible consequences is broad, including voluntary shut-downs, loss of academic privileges, involuntary shut-downs, regulatory fines, exclusions from future research, civil lawsuits, or even criminal sanctions for the most egregious cases.

How does an IRB respond to the heightened legal stakes?

First, we must recognize that the IRB mission is to protect research subjects, not institutions or investigators.

An IRB with a defensive posture may not have the interests of research subjects as its highest priority.

An IRB with a defensive posture may not have the interests of research subjects as its highest priority. Institutions and individual researchers must take measures to avoid unnecessary exposure to lawsuits and other negative consequences; overseeing these measures, however, is not the IRB's *raison d' etre*.

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Alden March Bioethics Institute

The Alden March Bioethics Institute maintains a comprehensive listing of conferences, educational programs, and other activities related to research ethics and related issues.
For information, see:
http://www.bioethics.net/events.php?page=1

For a listing of bioethics news generally, see the institute's site at:
http://www.bioethics.net/

Administrators who understand the current legal environment are more likely to support the necessary educational, oversight and organizational infrastructure . . .

Second, the IRB can respond by ensuring that mistakes are not needlessly repeated. Your IRB should review information about each lawsuit, shutdown, or sanction from a government agency for the "lesson learned." What systems or processes failed or appeared to fail? Is there a safety net within your own organization to protect against the same kind of scenario? Does the human subject protections education offered at your institution prepare research staff to anticipate a similar situation?

The warning letters and determination letters found at the U.S. Food and Drug Administration and Office for Human Research Protection Web sites are helpful sources that may help your institution identify holes in its system. At our institution, we use a mock trial format for an education conference to accentuate the everyday scenarios that may result in harm to a research subject.

Third, your IRB can respond by educating key decision makers. Administrators who understand the current legal environment are more likely to support the necessary educational, oversight, and organizational infrastructure required to prevent similarly problematic scenarios.

Your organization could consider preparing a one-page monthly or bi-monthly newsletters for administrators, legal counsel, and other key players who have ultimate responsibility for human subject protections. This newsletter could include information on key issues from current cases.

While an overly defensive legal posture is not the role of the IRB, a proactive IRB can serve to keep administrators aware of emerging issues.

Staying informed about the legal environment for research could make the difference in planning ahead or looking back to see what went wrong.Δ

Networking resources for IRBs

IRB forum, local consortiums, continuing education

IRB administrators and members often hear the complaint from investigators, coordinators, and study staff that "no other IRB requires this."

That's when the creeping questions begin—are we out of line with other IRBs? Is there a better way to do this?

By Sherry Brewer, Director
Office of Research Integrity
University of Tennessee
Graduate School of Medicine

Reality check

The on-line IRB Forum (www.irbforum.org) provides a readily accessible "reality check"—a way of finding out whether your practices, policies, and problems are in line with those of other IRBs. On the whole, information gained through the forum is valuable. However, the usual caveats for Internet information apply—do not act solely upon information or advice given through this channel.

The DOE Human Subjects Working Group (HSWG) also offers networking with IRBs working within the same agency. Both the online forum and the HSWG are helpful in gauging whether local IRB practices are in sync with other institutions nationally. But what about local IRBs? How are they dealing with the same issues, questions, and problems—or even with the same investigators?

Convene a local consortium

In East Tennessee, one solution we have found is to convene a consortium of local IRB administrators. While a loose connection between a few of the administrators had existed (perhaps a telephone conversation when an investigator was conducting the same protocol in two different sites), there was no formal organization that pulled together local IRBs.

A loosely defined "consortium" of local IRB administrators now exists, meeting every other

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Networking resources (Continued from page 14)

month for discussion and continuing education directly tailored to the needs of the group. Programs have included:

- How each institution addresses conflict of interest questions (IRB requirements for information, language in consent forms, institutional committee structure)
- "Form" swap in which members brought copies of effective office forms
- IRB software management demonstrations
- Reports from members who attended national conferences (PRIM&R, etc.)
- Investigator training requirements for each institution
- Advice/recommendations/experiences in taking either the Certificate of IRB Professional (CIP) exam or the Certificate of IRB Manager (CIM) exam

Recommendations
Based upon our experiences, here are a few recommendations for starting a consortium:

- Start by compiling a list of all the local IRBs that you can identify. Include colleges, univer-sities, and hospitals. IRBs typically aren't listed in the institution's phone book, so some Internet research and/or phone calls may be required in order to locate the IRBs.
- Invite IRB administrators, chairs, compliance officers and/or representatives from the IRB to attend an organizational meeting.
- At the first meeting, determine:
  - Level of members' interest
  - Frequency of meetings
  - Place for meetings (deciding on a set meeting place will facilitate attendance)
  - Topics of interest
  - Whether to divide into a biomedical group and a social/behavioral group or keep a combined group
  - Who will serve as facilitator
  - Topics of interest and possible speakers

Benefits of networking
Whether or not you want to pursue accreditation of your meetings for Continuing Education Units (CEUs), administrators and IRB members will benefit from the local "reality check" in many ways, including knowing people who might be able to serve as

- Consultants for your IRBs questions
- Speakers for local IRB and investigator training
- Interested audiences for local research ethics conferences

These benefits—education, problem solving, and improved professionalism—can be helpful for any IRB.Δ

Human subjects Web sites

Bioethics resources for health care organizations
http://www.mcw.edu/bioethics/presentation.html

DOE Office of Human Radiation Experiments
http://www.eh.doe.gov/ohre/

National Institutes of Health (NIH) Office of Extramural Research, Human Subjects Web site
http://grants.nih.gov/grants/policy/hs/index.htm

NIH stem cell information
http://stemcells.nih.gov/policy/guidelines.asp

Consortium to examine clinical research ethics
http://csmeh.mc.duke.edu/cecrelndex.htm

University of Minnesota Research Subjects' Protection Programs
http://www.research.umn.edu/subjects/

Resource for people considering participation in research
http://www.med.umich.edu/irbmed/research.htm

The Center for Information & Study on Clinical Research Participation
http://www.ciscrp.org/about/who.asp

Program on ethical issues in international health research, Harvard School of Public Health
http://www.hsph.harvard.edu/bioethics/

New books on human subjects research

U.S. Department of Energy (DOE), *Federal Human Subjects Protection Resource Book* (2006). The book will be available to DOE offices and laboratories in the spring/summer of 2006. It was a joint project of DOE, the U.S. Department of Defense, and the U.S. Department of Veterans Affairs. However, it does not represent the official views or policies of these or any other agencies. Rather, it is an attempt to synthesize the information currently available on the protection of human subjects in research. The book itself does not constitute regulations or formal federal agency guidance, but existing regulations and agency guidance are cited when appropriate.

The manual contains chapters that provide background information on the history and development of the federal regulations, chapters that discuss procedural and substantive issues regarding the review and conduct of human subjects research, and chapters that are specific to one type of research (e.g., genetics, biological samples) or research in specific populations (e.g., international settings, children, workers).

The book will be available in limited supplies in hardcopy and in CD version. DOE will send a notice out to the DOE and DOE laboratories giving them the opportunity to order copies when it is available.

Chastain, Garvin and **Landrum, R. Eric**, editors, *Protecting Human Subjects—Departmental Subject Pools and Institutional Review Boards*. Published by APA Books, this is a compilation of articles related to the use of human research subjects by university psychology departments.

They say psychology departments conduct innumerable research studies annually and rely heavily on departmental subject pools for their experiments. How are the rights and welfare of those subjects protected? How can universities improve their administrative practices so that their research programs are successful and ethically run?

This volume reviews empirical evidence on the structure and functioning of departmental subject pools nationwide and of the institutional review boards that oversee them. The case studies and practical lessons offered by this book may be a useful resource.

Amdur, Bankert, *Institutional Review Board: Management and Function*, 2nd Edition (2006). The "go to" reference for daily IRB management has been updated with a second edition, which includes seven new chapters:

- IRB closure of study files
- Internet research
- Research in public shools
- Phase I clinical trials in healthy volunteers
- Vulnerability in research
- Balancing the risks and potential benefits
- HIPPA

Coleman, Menikoff, Goldner, and Dubler, *Ethics and Regulation of Research with Human Subjects* (2005). Designed as a set of teaching materials and patterned after a traditional law school "casebook" this 746-page tome provides background information, as well as analysis of current issues and reprints of relevant articles. Chapters include "The Changing Face of Research," "Monitoring of Ongoing Research," and "Genetics Research." Additionally, the end of each chapter includes notes and questions that are helpful in generating discussions in IRB meetings, training, or classroom settings.

Steiner, John, *Clinical Research Law and Compliance Handbook* (2006). John Stein, Chief Compliance Officer for the Cleveland Clinic Health System, has authored a guidebook which serves as an excellent overview and operational guide for research compliance. The book is geared toward compliance officers, but chapters such as "Key Compliance Issues for Institutional Review Boards," "Clinical Research Trials in the Courtroom," and "Legal Issues in the conduct of multinational Clinical Trials" will provide valuable information for IRB members and administrators.Δ

News notes

Bioethics blogs

Blogs have developed on the Internet for thousands of topics, and now a few have been created to discuss bioethics, including the ethics of research with human subjects. The following are some that seem particularly interesting:

• Bioethics blog, written by the editors of *The American Journal of Bioethics*
http://blog.bioethics.net/

• The Hastings Center bioethics forum
http://www.bioethicsforum.org/whatis.asp

• Women's bioethics project
http://womensbioethics.blogspot.com/

• Business ethics (includes discussion of the bioetch industry in the developing world)
http://www.businessethics.ca/blog/

Canadian review board has federal-wide assurance with OHRP

An independent ethics committee operated by Institutional Review Board Services has secured a federalwide assurance (FWA) with the U.S. Office of Human Research Protections. The committee is designed to expedite ethics reviews of proposed research in Canada and other countries.

It is limited to research on human subjects conducted or sponsored by credible organizations that will operate in accordance with applicable local, national, and international laws and standards. The committee says it will not approve research that has previously rejected by any other IRB/REB unless in conformance with regulatory requirements and the IRB's standards. In general, research involving cloning, fetal tissue, gene transfer, some kinds of population or other genetic research and prisoners are not accepted for review. The IRB will review anonymous tissue samples to be obtained from the U.S. National Institutes of Health or other government agencies, so long as it conforms to generally accepted ethical precepts.
For information, see **http://www.irbservices.com/**

Research misconduct more likely when IRBs are seen as unfair

When researchers perceive that IRBs make unreasonable demands or are otherwise acting unfairly, they sometimes find ways to circumvent the boards and proceed with their projects. The phenomenon was reported in the November 10, 2005, issue of *Nature* in a report by **Jim Giles**, who discusses a series of papers documenting the misconduct.

Giles reports that the authors of the papers "say they have evidence that some ethics panels are alientating researchers and inadvertently promoting deceit." The issue is also examined in a survey of misconduct rates among 3,000 researchers funded by the U. S. National Institutes of Health. The survey, also reported in *Nature*, found that a third of respondents had engaged in one of ten types of misconduct in the past three years (see *Nature* **435,** 718–719; 2005, and B. C. Martinson *et al., Nature* **435,** 737–738; 2005).

Giles reported that further analysis of the survey data, to be published in 2006 in the *Journal of Empirical Research on Human Research Ethics*, shows that misconduct rates were highest among researchers who felt that they had been unfairly treated by other governing bodies in science, such as funding review panels.

Revisions, new guidance, & updates

The following is a brief list of a few of the important recent changes and possible changes in regulations, guidance, and review requirements related to IRBs and human research issues.

1. The Office for Human Research Protections (OHRP) has issued guidance about how to report problems to OHRP, especially those involving risks to human subjects or serious noncompliance with Health and Human Services (HHS) regulations. See **www.hhs.gov/ohrp/policy/incidreport_ohrp.html**
2. OHRP also issued a new guidance, "Children Involved as Subjects in Research: Guidance on the HHS45CFR 46.407 ('407') Review Process." See **www.hhs.gov/ohrp/children/guidance_407process.html**
3. The National Cancer Institute and the National Institutes of Health are seeking to change the way IRBs review cancer research protocols. See **www.nih.gov/news/pr/jun2005/nci-07.htm.**
4. The U.S. Senate passed rules regulating testing of pesticides on humans by the Environmental Protection Agency. This occurred after it was alleged that several human pesticide studies violated ethical guidelines. See **http://www.epa.gov/pesticides/**
5. OHRP has updated more than 30 Q&As on human research protection involving the assurance process and the IRB registration process. See **http://www.hhs.gov/ohrp/**
6. An interim final rule on research misconduct went into effect late in July 2005 affecting all research projects conducted or financed by DOE. See **http://www.epa.gov/fedrgstr/EPA-IMPACT/ 2005/June/Day-28/i12645.htm**
7. The federal Office of Research Integrity updated its FAQ list regarding the final rule on research misconduct. The rule went into effect June 16, 2005. See **http://ori.dhhs.gov/policies/faq.shtml**
8. The U.S. Congress is considering a bill, Fair Access to Clinical Trials, which would, among other things, require researchers to enter their clinical trials into a federal registry before starting them and to report the results of the trials at their conclusion. See **http://olpa.od.nih.gov/tracking/house_bills/session2/hr-5252.asp**

Web sites

International ethical guidelines, codes, declarations
http://www.nih.gov/sigs/bioethics/internationalresthics.html

Ethics of research related to healthcare in developing countries
http://www.nuffieldbioethics.org/go/ourwork/developingcountries/introduction

Research involving individuals with questionable capacity to consent: points to consider
http://grants.nih.gov/grants/policy/questionablecapacity.htm

IRB forum—discussion and news forum
http://www.irbforum.org/

Fred Hutchinson Cancer Research Center—Institutional Review Office
http://www.fhcrc.org/admin/iro/irb/

Certification as an IRB professional
http://www.primr.org/certification/overview.html

Bioethics and the National Institutes of Health (NIH)
http://www.nih.gov/sigs/bioethics/withinnih.html

NIH National Human Genome Research Institute, Ethical, Legal and Social Implications Research Program
http://www.nhgri.nih.gov/10001618

Centers for Disease Control and Prevention—Human Research Protection Office
http://www.cdc.gov/OD/ads/hsr2.htm

The President's Council on Bioethics
http://www.bioethics.gov/

Office for Human Research Protection
http://www.hhs.gov/ohrp/

Department of Health and Human Services (HHS) Office of Research Integrity
http://ori.dhhs.gov/

HHS Office of Research on Women's Health
http://www4.od.nih.gov/orwh/

Kennedy Institute of Ethics–Library and Information Services (with link to bioethics literature)
http://www.georgetown.edu/research/nrcbl/

HHS posts revised regulations for protecting human subjects

The Office for Human Research Protections (OHRP) has posted a revised, up-to-date version of the Health and Human Services (HHS) regulations for the protection of human subjects, 45 CFR part 46, at **http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm** on the OHRP Web site.

Among other things, this updated version includes the following technical amendments to the federal policy for the protection of human subjects that were announced in the *Federal Register* in 2005:

• Changing references from the "Office for Protection from Research Risks" to "Office for Human Research Protections, or any successor office"

• Changing the Office of Management and Budget (OMB) control number for the Paperwork Reduction Act clearance from "9999-0020" to the current number "0990-0260"

• Rewording the footnote to section 45 CFR 46.101(i) to reflect the 2001 change in subpart B of 45 CFR part 46 that made the exemptions described in section 101(b) applicable to research covered by subpart B.h.

International/cross-cultural research

The University of Minnesota has developed a comprehensive Web site offering guidance on international and cross-cultural research. It is at **http://www.research.umn.edu/irb/guidance/international/index.cfm**

The site includes reports and articles related to international research. It also has extensive listings about and connections to other resources related to international research ethics.

OHRP launches Spanish site

The U.S. Department of Health and Human Services Office of Human Research Protections has recently launched its new Spanish-language Web site at **http://www.hhs.gov/ohrp/espanol/intro.htm**

The site includes links to Spanish versions of

- 45 CFR 46, subparts A, B, C, and D
- Step-by-step instructions for registering an IRB
- Instructions to receive IRB updates
- The Federalwide Assurance (FWA)
- Instructions for an FWA application
- Instructions for FWA updates.

Protecting Human Subjects

This newsletter is designed to facilitate communication among those involved in emerging bioethical issues and regulatory changes important to both DOE and the human subjects community.

DOE Human Subjects Protection
Program Manager, Michael Viola, M.D.
Assistant Program Manager, Peter Kirchner, M.D.

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http://www.science.doe.gov/ober/humsubj/newslett.html

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Meetings

8th Annual "Ethical Issues in International Health Research Workshop"
June 12–16, 2006
Boston, MA
This meeting will be held at the Harvard School of Public Health. For information, see **http://www.bioethics.net/events.php?viewEvent=211**

Creative Ethical Problem Solving in Human Research
July 28, 2006
California State University East Bay Conference Center, Oakland, CA
Registrants for this educational program have the option of attending the entire program or of selecting one of the two courses. For details, see **http://www.bioethics.net/events.php?viewEvent=198** or see **http://www.csueastbay.edu/JERHRE/conference/index.html**. Contact Linda Eick, linda.eick@csueastbay.edu

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2006 Annual Human Research Protection Programs
November 15–18, 2006
Marriott Wardman Park Hotel, Washington, D.C.
Pre-conference education program will be held on Nov. 15. PRIM&R/ARENA's annual conference will be Nov. 16–18. For information, see **http://www.healthra.org/**

4th Research Conference on Research Integrity—U.S. Public Health, Office of Research Integrity
December 1, 2006
Tampa, FL
The conference will gather scholars from different disciplines to discuss problems relating to research integrity. For information, see **http://www.bioethics.net/events.php?viewEvent=200 or contact Mary Scheetz, mscheetz@osophs.dhhs.gov, (240) 453-8438.**