
University of Arizona Program in Research Integrity Education Monthly Newsletter

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A Message from the Director *Thomas P. Davis, Ph.D.*

This month we are fortunate to present Part I of three parts entitled, "Research Issues, Justice, and Conflict of Interest." Offered here is a section of an ethics module found at the Michigan State University website. This section is used with the permission of Dr. Howard Brody, Module Director, Center for Ethics & Humanities / Family Practice C208 East Fee or B118 Clinical Center (517) 355-7550. We thank Dr. Brody for granting permission to use this piece in the P.R.I.E. newsletter. The module may be viewed at http://www.msu.edu/course/hm/546/w8_intro.htm, and Dr. Brody may be reached at the follow email address: brody@msu.edu.

Research Issues, Justice, and Conflict of Interest Part I

There are two general sorts of ethical questions pertinent to medical research. First, we could ask about the ethical duties the investigator owes to the research subject. (This could be asked whether the subject of the experiment is a person, or a non-human animal). Second, we could ask what duties are incumbent upon all parties in order to maintain the integrity of the research enterprise generally. Some of the same principles pertinent to this second question may shed light upon the ethical relationship between physicians and industry, particularly the pharmaceutical industry.

For the purposes of this course, we situate the debate over research ethics within a larger question, conflicts of interest. The physician-investigator has a conflict of interest between serving the interests of the patient (getting personalized treatment which will cure the disease), society in general (increasing medical knowledge for tomorrow even if individual patients today do not benefit), and herself (getting more grants, getting promoted, etc.). We propose that physicians in practice today face two other very common conflicts of interest: 1) working within financial arrangements where reimbursement and

rewards sometimes rely upon saving money by denying patients some services that could be helpful to them; and 2) deciding which sorts of gifts to accept from pharmaceutical manufacturers, in the face of ethical arguments that such gifts may undermine the integrity of medicine, and factual arguments that physicians are often unduly influenced by these gifts without being aware of it. In this way the general ethical issue of how to manage conflicts of interest runs the gamut from highly dramatic cases like the Tuskegee syphilis study, to the most mundane questions of what drug company logo may be on the ball point pen in the physician's pocket.

Historical Aspects

Research ethics and the protection of the human subject are historically important in medical ethics because the modern "bioethics" movement is said to have begun by grappling with these questions. After World War II, the U.S. was outraged by accounts of experiments conducted by Nazi physicians upon concentration camp inmates, often subjecting the victims to great pain and death. The post-war trials of the Nazi war criminals, including some of the most prominent physicians under the Hitler regime, led to international statements of ethical principles for research, for the first time articulating the duty to obtain the informed consent of the research subject. Thus, recognition of a duty for informed consent in research preceded by at least a decade the formal recognition of a similar right of patients in medical therapy.

It was at first thought that these ethical problems in the conduct of research were restricted to totalitarian regimes like the Nazis. But this comfortable view was stripped away, first by an exposé by prominent investigator Dr. Henry Beecher in the *New England Journal of Medicine* in 1966, revealing more than 20 research studies conducted by prominent U.S. investigators in which subjects were put at substantial risk without their informed consent. This was followed in 1972 by the revelations of the Tuskegee syphilis study, in which the U.S. Public Health Service had kept black men in Alabama from

receiving effective antibiotic treatment for their syphilis for more than 25 years. Later it was revealed that many U.S. servicemen were subjected to experiments during and after World War II without their knowledge or consent. It gradually became clear that one need not be a Nazi in order to fall into the ethical trap of deciding that some presumed greater good overrode the health and well-being of the individual research subject – especially if the subject was poor or a member of a stigmatized minority group.

Principles of Protection of Human Subjects

Because of these revelations of abuse, research on human subjects was the first area within bioethics to be subjected to government regulation and the imposition of formal ethical guidelines and procedures. These consisted primarily of requirements for informed consent of subjects, and creation of institutional ethics review boards (IRBs) to monitor compliance with the ethical guidelines within all medical institutions conducting research.

The regulations embodied two basic principles of bioethics – respect for autonomy and justice. The principle of beneficence, often invoked in patient care settings, was specifically set to one side in research ethics, because the investigator sets out to do good for humankind generally, especially in the future, through obtaining useful new knowledge – and does not set out specifically to do good for the individual research subject. Thus a conflict of interest is presumed – the individual subject must be protected from possible exploitation in the name of the greater good of the larger society.

Respect for autonomy is honored by the requirements of informed consent. By being openly told about the nature of the research, and then freely consenting, the subject becomes (in a moral sense) a colleague and collaborator in the research. Trying to create a sense of moral equivalence between investigator and subject is the opposite of what was stated in one research scandal of the 1960's, the Jewish Chronic Disease Hospital case, in which elderly hospitalized men were injected with cancer cells without informed consent. The lead investigator, Dr. Southam, was asked by a reporter if he would agree to be a subject in this experiment himself. He replied that the risk was very low (although one of their subjects developed disseminated cancer as a result of the trial); but since highly trained cancer researchers were so rare, it would be wrong of him to take even this small risk. This claim of being morally superior to the research subject was exactly what the duty of informed consent and respect for the subject's autonomy was designed to reverse.

The second principle, justice, was invoked in response to the revelations that very often, risky experiments were conducted on subjects who were especially vulnerable and easily exploited. Prisoners and the mentally retarded, for instance, were disproportionately represented among the subjects of such research. The new government regulations specified additional safeguards, effectively raising the bar before research could be done on such populations. The principle of justice requires in particular that if one group of people within society stands to benefit the most from certain research studies, the risks and costs of those studies should be borne primarily by that same group. To subject prisoners or charity patients to risky experiments to develop new drugs or treatments which will benefit predominantly the well-to-do is unfair. Before a study is done on an easily exploited population, the investigators should show that it is for some reason not feasible to do the study on subjects more free to give or to withhold consent – as would be the case, for example, if a genetic disease exists predominantly within one minority racial group.

The Distinction: Research vs. Treatment

Clinical investigators, used to conducting their research in a largely unregulated environment, chafed at these new rules during the 1970's and 1980's. One argument they raised was that experimentation was hardly confined to research settings. In treating a patient with hypertension, for instance, one might have to try several different medications and dosages before one found the treatment that controlled blood pressure effectively with the least side effects. But it was not demanded that the physician treating the hypertensive patient get approval from an IRB and have the subject sign an 8-page consent form.

This objection led bioethicists to specify the fundamental distinction between research and treatment, or perhaps more properly, between the investigator-subject relationship and the physician-patient relationship. "Experimentation," they admitted, could apply equally well to both realms and so was not the critical moral point. What was critical, rather, was that the research enterprise exists primarily to produce new knowledge while treatment is administered primarily to help the individual patient. True, the lines may sometimes be blurred. A research subject, undergoing a thorough physical exam for enrollment in the study, may be discovered for the first time to have a heart murmur and may get prompt diagnosis and treatment of an important valvular defect. A patient undergoing treatment in the physician's office may develop a previously unreported adverse drug reaction, leading to

publication of an important case report. But the fact that a research subject may gain personal health benefits, or that a patient may generate new knowledge, is a secondary phenomenon which does not negate the fundamental ethical character of the two activities respectively.

The conclusion then drawn from this distinction is that, because the primary goal of medical therapy is the benefit of the individual, the patient can trust the physician in a way that it would not be rational for the research subject to trust the investigator. Regulations for informed consent and patient protection in the therapeutic realm can therefore be somewhat less complex and less strenuous, because they supplement rather than replace this basic individual trust. More stringent regulations and protections are needed in the research arena precisely because the well-being of the individual is not the investigator's first loyalty.

See Part II in the December 2004 issue.

Research on Research Integrity RFA Available

The new request for application (RFA) for the Research on Research Integrity Program focuses on three areas of interest: standards for responsible conduct of research, self-regulation of the research community, and factors that enhance or undermine research integrity. Submission deadline is November 19, 2004. See RFA on the ORI home page at <http://ori.hhs.gov>.

National Center for Ethics in Health Care Veterans Health Administration Integrated Ethics Program (IEP) Project

The IEP project is a major Center initiative that targets key institutional processes to improve the effectiveness of ethics programs at the facility level. The project aims to inspire systems change by applying principles of continuous quality improvement to better integrate clinical and organizational ethics "from the bedside to the boardroom."

The IEP project provides facility teams with educational resources they need to achieve four goals.

- create an environment that supports ethical practices;
- improve the quality of ethics case consultation;
- systematically address recurring ethical problems;
- use evaluation tools to foster improvement.

These resources include training materials, video and online courses, monthly process improvement tasks, a virtual community (IEP listserv), other web-based tools, and technical support.

More information on the IEP will be coming soon and may be viewed at the following web site: (http://www1.va.gov/VHAETHICS/education_1.cfm).

UNIVERSITY OF ARIZONA RESEARCH AND SERVICE GROUP (RSSG) Educational Opportunities

****This course satisfies the requirement for research ethics training by the N.I.H./N.S.F.****



Scientific Writing Strategies and Ethics PHCL 595b (PS 595b, BME 595b, CBIO 595b) Course Coordinators:

W. Daniel Stamer, Ph.D. – 626-7767 –
dstamer@eyes.arizona.edu, and
Thomas P. Davis, Ph.D. – 626-7643 –
davistp@u.arizona.edu

Purpose, Scope and Philosophy of the Course

The purpose of this course is to provide students with knowledge and skills to write/communicate effectively for a variety of scientific audiences; including scientific employers as well as administration in journals, funding institutions, potential academia and industry. The course will also cover the nine core instructional areas of the responsible conduct in research (RCR) and thus will satisfy the ethics requirement for many Federal grant programs. Content of the course will draw from the experience of 20 interdisciplinary faculty members with success in communicating ideas, hypotheses and data. The course will assist students in identifying and appropriately targeting scientific audiences and familiarize students with submission and peer-review processes.

For more details, contact Dr. Dan Stamer at: dstamer@eyes.arizona.edu or call 626-7767.



An FDA warning letter OAI (Official Action Indicated) was issued to the University of Arizona April 27, 2001 following an FDA audit in 2000. In essence, the citation was issued because a named study director and sponsor did not inform University Animal Care, The Office of the Vice President for Research or the campus Quality Assurance Unit that a GLP study was being conducted. A Form FDA-483 detailed the non-compliance items of the FDA regulations outlined in 21 CFR 58.

Subsequently, The Office of the Vice President for Research provided a point-by-point response to the audit results and initiated policies intended to assure such policy violations are not repeated. The

FDA re-audited the University in 2002 and found no violations or an NAI (No Action Indicated).

As is FDA's custom, the OAI warning letter will remain on the warning letter site, however the NAI is also clearly indicated, assuring private industry that The University laboratories are cleared to participate in projects in support of research or marketing permits regulated by the FDA.

To fulfill GLP standards and practices (as intended by 21 CFR 58), The University of Arizona appointed a Quality Assurance Officer (QAO) in June 2003 to report directly to The Director of Compliance, The Office of the Vice President for Research. All University generated GLP/IACUC protocols are now required to be reviewed by the Quality Assurance Officer and the Sponsored Projects routing sheet has a box to be checked for laboratories intending to undertake GLP studies.

UA HUMAN SUBJECT PROTECTION PROGRAM

≡Highlights≡

Human Subjects Protection Program

*The Belmont Report**

The Belmont Report was created as a result of a charge to the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (National Research Act of 1974). Part of The University of Arizona Federal-Wide Assurance is the agreement with the Office of Human Research Protections to abide by the principals in the Belmont Report (see the UofA Federal-Wide Assurance at www.irb.arizona.edu). This article outlines the basic principles of The Belmont Report and the application of those principles.

- 1) Respect for Persons – there are two basic ideas represented; 1) that individuals are to be treated as autonomous persons and 2) those with diminished autonomy deserve additional protection. The application of this principle is the use of an informed consent form and the opportunity for participants to choose what will or what will not happen to them. Consent for participation of individuals with diminished autonomy may require involvement of a surrogate or advocate.
- 2) Beneficence – the requirement that subject well-being is secured by reducing risk and maximizing the benefits to those individuals involved in research. The application of this principal is the risk / benefit analysis contemplated prior to the conduct of the study.

- 3) Justice – this principle requires that no single group of subjects unfairly bare the burden of research. The goal of equitable selection is to fairly distribute the risks and benefits of research among groups of individuals that stand to benefit from it. The application of this principal is in the scrutiny applied to selecting certain groups or individuals for participation. Subject selection should be related to the goals of the research and not merely on convenience or the manipulability of study subjects.

*Peckman, S. (2002). A Shared Responsibility for Protecting Human Subjects. In R. Amdur & E. Bankert (Eds.), Institutional review board: Management and function (pp. 17-21). Sudbury, MA: Jones and Bartlett.



News from HIPAA.....

Frequently asked questions on Privacy.....

Question:

Where can I find information about the flu and flu vaccinations?

Answer:

- ✚ You may find out about the availability of flu shots in your region at the American Lung Association site (this site is not sponsored by the U.S. government):
<http://www.findaflushot.com/lungusa/>
- ✚ Be sure to check out HHS's new Flu information page: <http://www.hhs.gov/flu/>
- ✚ For information about the flu (influenza) and flu vaccinations, please visit the site of the Centers for Disease Control and Prevention:
<http://www.cdc.gov/flu/index.htm>
- ✚ Additionally, you may call the CDC Immunization Hotline at:
English: (800) 232-2522
Español: (800) 232-0233
- ✚ Medicare has *Frequently Asked Questions* about the flu:
http://medicare.custhelp.com/cgi-bin/medicare.cfg/php/enduser/std_alp.php?p_cat_lv1=66.
- ✚ Medicare.gov has info on fighting the flu at:
<http://www.medicare.gov/Health/FluDetails.asp>
- ✚ Additional info about the flu can also be found on the site of the Food and Drug Administration:
<http://www.fda.gov/oc/opacom/hottopics/flu.html>
- ✚ The NIH offers information on flu at:
<http://health.nih.gov/result.asp/370>
- ✚ The NIH National Library of Medicine has flu information at:
<http://www.nlm.nih.gov/medlineplus/influenza.html>

HIPAA VIDEOCONFERENCE TAPE AVAILABLE

The Society for Research Administrators (SRA) International Satellite Videoconference from January 23, 2003 is available on tape.

To request use of the tape, please contact *Alice Langen*, Director, Research Standards & Compliance, Office of the VP for Research (621-5196) or langena@u.arizona.edu. After viewing, you will receive a *Certificate of Completion* for your files and grant submissions.

OPPORTUNITIES FOR ON-LINE ETHICS TRAINING

On-Line Module or Short Course in "The Ethics of Research with Human Subjects"

The Least of My Brothers

Funded by the [National Institutes of Health](#)
(Grant Number 1 T15 AI07601)

The Least of My Brothers is an on-line module or short course in the ethics of research with human subjects. Please contact the following web site: <http://poynter.indiana.edu/sas/lb/>. You may also contact Kara Lochridge at: (812) 856-4968, or klochrid@indiana.edu.

Ethical Guidelines for Gifts to Physicians from Industry

Free educational modules now available

The AMA's national initiative on *The Communication of Ethical Guidelines for Gifts to Physicians from Industry* is now offering four free online modules for CME credit. Each educational module is available in two formats:

- Online self-study for CME credit; and
- Downloadable resources educators can use to build one-hour learning experiences.

The educational modules will help satisfy Accreditation Council for Graduate Medical Education (ACGME) requirements for education on pro-fessionalism and industry professional relationships as well as similar requirements by the American Board of Medical Specialties.

Physicians can earn AMA PRA category 1 credit for the online self-study version. Local sites can issue CME credit for the classroom version of the downloadable educational modules.

For more information visit the following site: <http://www.ama-assn.org/ama/pub/category/8405.html>.

Announcing the 1st Global Quality Assurance Conference and 21st Society of Quality Assurance (SQA) Annual Meeting

This precedent-setting conference and pre-conference training will be held Sunday through Thursday, 20 - 24 February 2005, in Orlando, Florida, USA, with the theme, "Committed to Quality in Research." The International Organizing Committee, through SQA, is accepting abstracts for the Conference. [Submit your abstract now](#) for a 30-minute topic, a complete 90-minute session (traditionally three 30-minute topics) or a poster. The submission deadline was September 13, 2004. The Program Committee will consider all regulatory QA topics: manufacturing (GMPs), preclinical (GLPs) and clinical (GCPs). Other areas of interest may include animal health, bioanalysis, biotechnology, computer validation, medical devices, scientific archiving, university issues and much more.

UPCOMING CONFERENCES/WORKSHOPS

November 12-14, 2004

ORI Research Conference on Research Integrity – 2004
San Diego, CA

Co-Sponsor: University of California – San Diego
http://ori.dhhs.gov/html/programs/conf_workshops_2004.asp

December 2-3, 2004

Developing Policy on Institutional Conflict of Interest
Las Vegas, NV

Co-Sponsor: University of Nevada – Las Vegas
http://ori.dhhs.gov/html/programs/conf_workshops_2004.asp

December 8, 2004

Ethics and Responsible Conduct of Research Workshop
Washington, DC

Co-Sponsor: Council of Graduate Schools
http://ori.dhhs.gov/html/programs/conf_workshops_2004.asp

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Words of Wisdom:

*The "silly question" is the first intimation
of some totally new development."*

——— *Alfred North Whitehead*