2nd ANNUAL MEDICAL RESEARCH SUMMIT (March 26, 2002)

ACADEMIC MEDICAL CENTERS AND PHARMACEUTICAL COMPANIES: IMPROVING RELATIONSHIPS IN THE MEDICAL CENTER RESEARCH CONTEXT

Steven Peckman

"Regardless of whether one believes that the ultimate justification for government policies is the goal of promoting welfare and minimizing harms or respect for self-determination, one can agree that policies represent commitments to action and hence generate obligations."[1] - ACHRE

A. Trust & Responsibility

1. Federal government: OHRP (45 CFR 46), FDA (21 CFR 50 & 56)
2. Sponsors
3. Institutions
4. IRBs
5. Research Team

B. **Trust and the Therapeutic Misconception**[2]

1. Hippocratic Oath

2. Research = Treatment

3. OPRR/OHRP: "Research itself is not therapeutic; for ill patients, research interventions may or may not be beneficial. Indeed the purpose of evaluative research is to determine whether the test intervention is in fact therapeutic."[3]

4. OIG: "The line between research and therapy has become increasingly blurred."[4]

5. "It is ethically problematic if both investigators and patient volunteers see research from an exclusively therapeutic perspective… In the face of this potential divergence between pursuing patient-centered beneficence and scientific knowledge, the orientation of investigators as clinicians can promote a form of 'cognitive dissonance.'"[5]

6. ACHRE: "There is reason to worry that participants in research may have unrealistic expectations about the possibility that they will personally benefit from participation [in research]…"[6]

7. R. Alta Charo: "We have a society that tends to view everything that's new as better, and people are militating for access to theses drugs saying, 'Who are you to be protecting me against my own choices.'"[7]

C. Turnaround

1. Delays in IRB approval result in withholding "therapeutic research" from subjects and society

2. Delays cost sponsors $1.5 million per day

3. IRBs are too picky

4. FDA approved the study: IDE/IND

5. Amendments, Investigator Brochures, and the definition of a minor change

6. Education

7. James Bell & Associates: 73% of IRBs approved as submitted one quarter or fewer protocols. The report highlighted that IRBs could not approve protocols as submitted due to informed consent form deficiencies, such as technical language, understatement or omission or risks and benefits, omission of cost information, and omission of alternatives.

D. Study Design/Placebo Control

1. Declaration of Helsinki:
   a. "In any medical study, every patient-including those of a control group, if any – should be assured of the best proven diagnostic and therapeutic method."
   b. "The benefits, risks, burdens, and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic, or therapeutic method exists."

2. 21 CFR 312.126 cite five different types of control trials that may meet the requirements for NDA:
   a. placebo control
   b. dose comparison control
   c. no-treatment
   d. active-treatment
   e. historical control

3. ICH/GCP: every protocol should include a "Description of ethical considerations relating to the trial.[8]

E. Informed Consent

Every subject or his/her legally authorized representative should be presented with a consent document that is understandable to the subject.

1. What does "understandable mean"?

a. English v. non-English
b. Level of reading comprehension (One in 10 adults in Los Angeles has only six years of schooling).[9] National Institute of Literacy reported 20% of Americans read at or below the 5th grade level.

2. Avoid language that implies the therapeutic misconception
   Ex: Equating placebo with treatment

3. Technical language and jargon
   "Changes in lab results that monitor liver and bone changes can also occur. These changes are thought to be due to increased bone marrow (where blood cells are made) activity. The lab values return to normal after discontinuing treatment with drug X."

F. Recruitment

1. National advertising campaigns that do not meet FDA guidance

2. Campaigns that screen subjects without effective informed consent as required under 45 CFR 46.116 & 117.

G. Adverse Events

---

[1] Advisory Committee on Human Radiation Experiments, Final Report, Washington D.C: (1995) <http://tis.eh.doe.gov/ohre/roadmap/achre/chap4_2.html>.
[2] PS Applebaum, et.al., False Hopes and Best Data: Consent to Research and the Therapeutic Misconception, *Hastings Center Report*, v17, n2, 1987.
Alexander Capron, Statement of Commissioner Alexander M. Capron, LLB, in National Bioethics Advisory Commission, Research Involving Persons with Mental Disorders That May Affect Decisionmaking Capacity, Volume 1, www.bioethics.gov/capacity/TOC.html: 1998.
Evan G. DeRenzo, The Ethics of Involving Psychiatrically Impaired Person in Research, IRB, v16, n6; November-December 1994.
George Annas, Questing for Grails: Duplicity, Betrayal and Self-Deception in Postmodern Research, *Journal of Contemporary Health Law and Policy*, v12:100.
[3] Office for Protection from Research Risks (OPRR), The OPRR 1993 Protecting Human Subjects, Institutional Review Board Guidebook, US Government Printing Office: Washington DC, 1993, 1-2.
[4] June Gibbs Brown, Institutional Review Boards: A Time for Reform, Department of Health and Human Services/Office of Inspector General, June 1998.
[5] Franklin G. Miller, et.al., Professional Integrity in Clinical Research, *JAMA*, v280, n16, October 18, 1998
[6] Advisory Commission on Human Radiation Experiments, Final Report, Washington DC: Chapter 18, Section 2, 1995.
[7] Washington Post, August 1, 1998.
[8] International Conference on Harmonisation/Good Clinical Practice (ICH/GCP), FDA Guidance for Industry, Section 6, Clinical Trial Protocol. Section 6.12. <http://www.fda.gov/cder/guidance/959fnl.pdf>
[9] Nancy Cleeland, LA Workers Held Back by Education Rate, *Los Angeles Times*, February 5, 2002. "Nearly 25% of Los Angeles area adults never completed high school…."