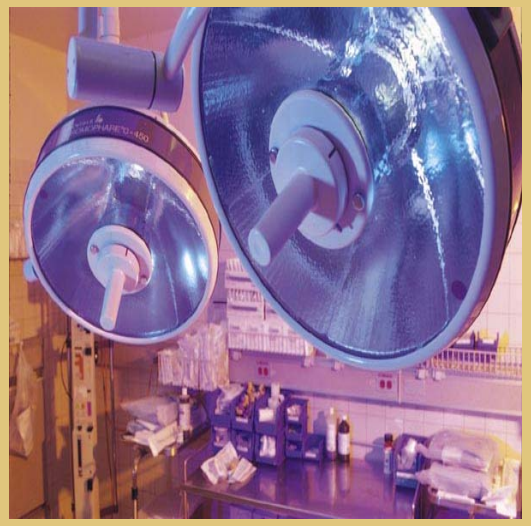

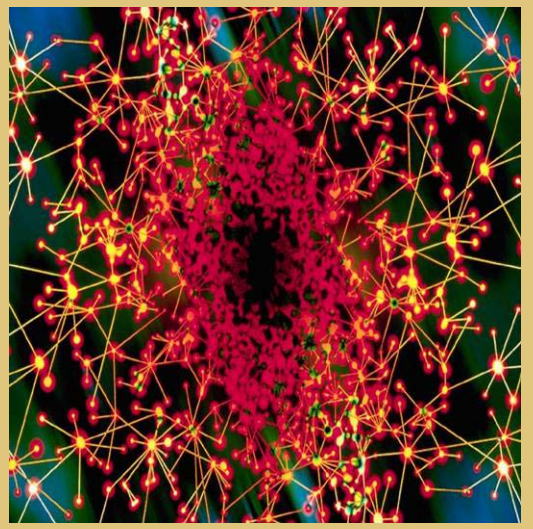

How I Would Revise the Human Subject Regulations

Tom Puglisi

Medical Research Summit 2004

Plenary Session, Day 2, 4:45

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Revising the Human Subject Regulations: Basic Assumptions

- Changes to the Common Rule will be extremely difficult without a clear legislative mandate
  - Published "Guidance" may be only realistic option for change
- Where possible, simplify & harmonize FDA / OHRP guidance to encourage compliance
- IRBs cannot do everything – Tradeoffs will be necessary to preserve the viability of the IRB system
- Efforts and resources should be targeted to research that presents the greatest risk of harm
- Different kinds of risks/harms need different protections
  - Physical vs Psychological vs Social vs Economic
- Protections should be proportional to the probability & magnitude of risks

Revising the Human Subject Regulations: Thru Joint FDA / OHRP Guidance

- Acceptable standards for scientific review
- Reporting of adverse events / unanticipated problems
- IRB / DSMB(DSM) relationships & responsibilities
- Safety monitoring for multi-center trials
- IRB review of sponsor safety reports
- Level of detail required in IRB minutes
- Level of detail required in written policies & procedures
- Standards for IRB diversity & expertise
- Informed consent & documentation of consent for persons who do not understand English or cannot read any language
- In research involving children, issues to consider / permissibility of:
  - **"No Benefit" Placebo Control "Treatment" Trials**
  - **Phase I "Treatment Research"**

Revising the Human Subject Regulations: Thru OHRP Guidance on "Research"

- "Systematic" investigation means an investigation that is conducted under a written or unwritten plan that permits drawing logical conclusions
- "Generalizable" knowledge means knowledge intended to be applicable beyond the institution or group of individuals about whom information is obtained in a systemic investigation
- Research under HHS Regulations does NOT include:
  - Course-related activities whose intent is primarily instructional
  - The usual activities of journalists reporting news or interviewing witnesses to news events
  - The usual activities of historians interviewing witnesses or participants in historical events
  - **Retrospective case reports on individual patients not identified (directly or indirectly) in the report**

Revising the Human Subject Regulations: Thru OHRP Guidance on "Human Subject"

- An individual "about whom an investigator … obtains information" does not include individuals who simply provide opinions about events external to themselves, in the absence of any environmental intervention or additional interaction on the part of the investigator
  - ie, opinion polling does not constitute human subject research
- "Identity ... may be readily ascertained … or associated with the information" means:
  - There are no codes or other linkers through which subjects may be identified, ***OR***
  - Investigators are prohibited by written agreement from (i) seeking or receiving the key to any such codes or linkers; (ii) attempting to identify subject identities; and (iii) releasing the information to anyone not bound by such a written agreement.

Revising the Human Subject Regulations: Thru OHRP Guidance on Exemptions

- "Public behavior" means behavior in any context in which persons may reasonably expect to be observed
  - Ie, any gathering of 10 or more persons in the absence of an pledge of confidentiality – including classroom settings
- "Publicly available" means:
  - Freely available to any adult
  - Commercially available, even where credentialing restrictions may apply
- "Recorded in such a manner that subjects cannot be identified" means"
  - There are no codes or other linkers through which subjects may be identified, ***OR***
  - Investigators are prohibited by written agreement from (i) seeking or receiving the key to any such codes or linkers; (ii) attempting to identify subject identities; and (iii) releasing the information to anyone not bound by such a written agreement.

Revising the Human Subject Regulations: Thru OHRP Guidance on Minimal Risk

- Clarification that the definition of "minimal risk" requires consideration of both the *probability* and the *magnitude* of harm or discomfort anticipated in the research
- Study conditions may impact the *probability* of harm
  - Probability of psychological harm may be reduced by (i) screening or "warning away" subjects who may experience undue stress; (ii) requiring that investigators be trained clinicians; (iii) providing counseling
  - Probability of social or economic harm may be reduced by increased confidentiality protections that make a breach of confidentiality highly unlikely

Revising the Human Subject Regulations: Thru OHRP Guidance on Informed Consent

- Permit Layering of Informed Consent Documents
- Layer 1: Generic Outline of Subjects Risks (similar to written text for short form oral consent) = 1-2 pages
  - Contains Reference to Layer 2
  - Witness Required If Signed Documentation Uses This Form
- Layer 2: Informed Consent Document with Study-Specific Information Sufficient for Documentation of Consent
  - Target Length Fewer than 10 pages
  - Reference to Attachment with Detailed Information About All Aspects of the Research May Run 20-30 Pages for Complex Research

Revising the Human Subject Regulations:
Thru OHRP Guidance on Review of Multi-Site Rsch

- Permit Layering of IRB Oversight Responsibilities Under Written Agreements
- Central IRB Responsible For
  - Risks Minimized Thru Sound Design; Risks Reasonable Relative to Benefits; Enrollment Criteria; Privacy & Confidentiality; Safety Monitoring; Study-wide Protections for Vulnerable Subjects; Investigator Qualification Standards
  - Informed Consent Text Regarding Research Procedures, Risks, Benefits, Alternatives, Confidentiality, Voluntary Participation
- Local IRB
  - Availability of Local Resources, Suitability of Local Research Context, Informed Consent Text Regarding Confidentiality, Compensation, Contacts, Oversight of Local Researchers

Revising the Human Subject Regulations: Regulatory Reform

- Separate Oversight of Research Involving Interaction or Intervention from Research Involving Private Information
  - Regulations for Intervention / Interaction Research Comparable to Current Human Subjects Regulations
  - Create Simplified Research Privacy Rule Applicable to All Identifiable Private Information
- Requires Legislation:
  - Create Single Office / Agency to Enforce All Human Subject Regulations: Common Rule, 45 CFR 46, 21 CFR 50, 21 CFR 56, Research Privacy, Financial Conflict of Interest
  - Bring All Human Research Under Federal Regulation
  - Provide National Liability Protection Program for IRBs and Institutions Conducting IRB-Approved Research
  - Provide National Compensation Plan for Injury in IRB-Approved Research

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