

Protecting Human Subjects at KUMC

From Principle to Practice

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Research Compliance Division



Purpose of this session...

- Discuss regulations and principles governing human research
- Explain our protection program
- Outline consequences of noncompliance
- Explore practical implications for conducting human research at KUMC
- Identify your internal resources



Rules, regulations, policies and procedures...

- HIPAA
- Controlled Substances Act of 1970
- Public Health Service Act
- Public Health Security and Bioterrorism Preparedness and Response Act
- Federal Food, Drug and Cosmetic Act
- Federal Policy on Recombinant DNA
- Bayh-Dole Act of 1980 (Patent Rights in Inventions Made with Federal Assistance)
- Numerous state laws



Wait, there's more...

- 21 CFR 50 and 21 CFR 56 (FDA Human Subjects Regulations)
- 21 CFR 312 (FDA Investigational Drug Regulation)
- 21 CFR 812 (FDA Investigational Device Regulation)
- 45 CFR 46 (DHHS Human Subjects Protection Regulation)
- Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research
- Nuremberg Code
- World Medical Association Declaration of Helsinki
- International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)
- Public Law 103-43: Transplantation of Fetal Tissue



We're not through yet...

- Interstate Shipment of Etiologic Agents (CDC)
- Laboratory Registration and Select Agent Transfer Program (CDC)
- Importation Permits for Etiologic Agents (CDC)
- Packaging and Shipping Instructions (CDC)
- OMB Circulars
- OSHA Bloodborne Pathogens Standard (OSHA)
- Introduction of Genetically Engineered Organisms (NIH)



Confused? Of course you are...

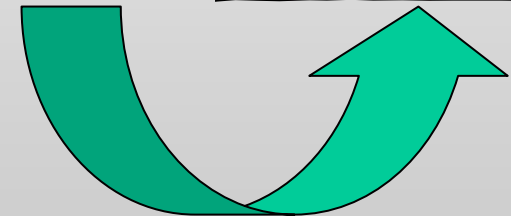
- The list of external mandates is extensive and in a constant state of flux
- To make matters worse, scrutiny has increased significantly
- Who is watching?



Who's watching us?

FDA OSHA
 ORI OCR
 USDA
 DOT FAA
NRC OHRP EPA
 OIG CDC
 NIH OMB
 DOJ DEA

And, of course, the court of public opinion...



Consequences of Noncompliance

- Physical/monetary/psychological harm to employees, research subjects, students or trainees
- Degradation of KUMC reputation, loss of public trust
- Additional regulatory oversight resulting in greater scrutiny, expanded programmatic requirements and greater institutional investments
- Suspension/disqualification of individual researchers
- Fines, penalties, punitive/compensatory damages, debarment and legal defense costs



About those costs...

University of Minnesota
Misuse federal grants
\$2.5-32 mil

University of Michigan
Chief Urologist charged with
Conflict of Interest
\$100,000 penalty
1 year probation

Thomas Jefferson University
Medicare over-billing
\$12 mil

Miscellaneous Scientific Misconduct
Johns Hopkins
Harvard (2)
Yale

**Public Demand
for
Improved Control**

New York University Medical Center
Inflated research grant costs
\$15.5 mil

Yale University
Medical over-billing
\$5.6 mil

Stanford University
Inflated research overhead costs
\$1.2 mil

University of Chicago
Research fraud and abuse
\$650,000

University of Texas
Underpayment of royalties
whistle blower
\$12 mil

Duke University
Sexual harassment
\$0.5 mil



The bottom line

- KUMC, the researcher and all research staff share responsibility for complying with this maze of requirements
- Mistakes and noncompliance, even if not intentional, can have drastic consequences
- We can't expect you to know all the regulations, but you **must** know the basic principles upon which they are based
- The principles will help simplify the practice



Principle #1: Institutional Review and Approval

- **Initial:** before commencing any part of any research study and sometimes before submitting funding proposal
- **Continuing:** required at pre-determined intervals (generally at least yearly)
- **Critical event:** serious & non-serious adverse events, protocol deviations, consent form changes, study amendments, recruitment efforts, agency site audits, subject complaints
- **Transactions:** proposal submissions, contracts, patents, material transfers



Practical Implications

- Never begin a research study without institutional review and approval
- Never make a change in your study without checking to see if needs review and approval
- Report critical events
- Transact through university avenues
- Meet continuing review requirements. Each compliance committee is empowered to terminate your approval if you miss the review deadline.



Principle #2

KUMC operates a comprehensive human research protection program



- Ethics and Privacy (HSC)
- Safety (Biosafety and Radiation Safety)
- Conflict of Interest
- Data Integrity (DSMB)
- Compliance Oversight
- Certification/Training

Practical Implications

- Approval from one body does not necessarily enable you to begin research
- Each required approval must be completed before you enroll a subject or commence your project
- Use your internal resources to determine what reviews are necessary



Principle #3: Consent is Critical

- Informed consent is an inherent component of the research process, not an adjunct exercise
- Informed consent can't occur without an approved current form containing signatures obtained from a legally authorized representative before a subject participates in any aspect of the study, including screening
- Consent forms are complicated
- When the protocol changes or new study-related information arises, the consent process starts all over again
- The form is important but it is only one part of a meaningful and on-going process



Practical Implications

- Recognize the complexity of the consent form and seek expert advice to create it
- Never use an unapproved or expired consent form
- Acquire and maintain evidence of consent
- Delegate responsibility for this part of your research very judiciously



Principle #4: Documentation Counts



- Committee Submissions
- Case Report Forms
- Consent Documents
- Signatures!
- Laboratory Records
- Regulatory Binders
- AE/SAE Reports
- Protocol Deviations
- Contracts
- Dates Are Important!

Practical Implications

- Use current application forms, complete all required sections and ensure your submission packet is complete....incomplete submissions will delay the review/approval process
- Understand documentation requirements associated with your research – use checklists from your internal resources or sponsors
- Separate research records from patient care records



Principle #5: Disclose and Manage Potential Conflict of Interest

- Any tie to a project's funding source is suspect
- COI can be time OR financial interest
- Disclosure of potential conflicts by the PI and all project-related personnel is the key to protection



Practical Implications

- Reassess your potential for COI with every research project; when in doubt, disclose
- Most individual COI's can be mitigated or managed, but not without university involvement
- Potential COI's must be disclosed in the consent form
- Seek advice from your internal resources



Principle #6: Research Integrity

- No amount of institutional oversight can compensate for lack of integrity on the part of a researcher or administrator
- Serious misconduct includes fraud, plagiarism and fabrication
- Failure to meet institutional and sponsor requirements constitutes misconduct



Practical Implications

- Know your responsibilities as a PI, Research Staff or Chair/Director
- When in doubt, report...
 - suspected noncompliance
 - mistakes, complications, subject concerns
 - documentation errors
 - sponsor monitoring outcomes that reveal deficiencies
 - failure to apply the previous principles



Your internal resources...

Training

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HSC

Allison Greig x8-1422 agreig@kumc.edu

Sharon Grable x8-5712 sgrable@kumc.edu

Radiation Safety

Safety Office x8-6126 rschukma@kumc.edu

All other Research Compliance Questions

Jo Denton x8-5492 jdenton@kumc.edu

<http://www2.kumc.edu/researchcompliance/>



More Internal Resources

KUMC Research Institute

- Clinical Research Administration
- Finance and Administrative Services
- Legal Counsel and Contracts Office
- Sponsored Programs Administration
- Technology Transfer, Intellectual Property & Commercialization

Phone: x8-1261

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