Clinical Trials and Clinical Research Compliance

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Agenda

- Introduction
- Institutional Review Board (IRB)
- Investigational New Drugs
- Investigational New Devices
- Good Clinical Practice
- Clinicaltrials.gov Registration
- Conflict of Interest
- Protected Health Information (HIPAA)
- Clinical Research Billing Compliance
Introduction

• There are a number of laws, regulations, policies, etc. that govern clinical research
  • Federal
  • State and Local
  • University
Definitions

- Federal statutes: legislation enacted by Congress and signed into law by the President


- Example Citation: Title U.S.C. Part
  - 21 U.S.C. 321
  - 21 = Food and Drugs
  - 321 = Definitions, Generally

- http://www.gpo.gov/fdsys/search/home.action
Definitions

• Federal regulation: Rules created by federal agencies

• Code of Federal Regulation: Compilation of federal rules and regulations; referred to as CFR

• Example Citation: Title CFR Part.XXXX
  • 21 CFR 50.20
  • 21 = Food and Drugs (Title)
  • CFR = Code of Federal Regulation
  • 50 = Protection of Human Subjects
  • .20 = General Requirements for Informed Consent

• http://www.gpo.gov/fdsys/search/home.action
Michigan Laws

• Michigan Compiled Laws
• Example Citation: MCL Chapter.Section
  • MCL 722.1
  • 722 = Children (Chapter)
  • .1 = Definitions (Section)
University Policies

• MSU Human Research Protection Manual
  • Example: Section 6-4, Informed Consent
Institutional Review Boards
Introduction

• What?
  • Regulations that govern research and/or clinical investigations with human subjects
  • 45 CFR 46 (HHS, Common Rule)
  • 21 CFR 50, 56 (FDA)* additional requirements

• Requirements?
  • Review by an Institutional Review Board (IRB) or determination that the activity is exempt from IRB from review
Health and Human Services Regulations (Common Rule) = Research + Human Subjects
Definitions

*Research* means

- a systematic investigation, including research development, testing and evaluation,
- designed to develop or contribute to generalizable knowledge.

Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. 45 CFR 46.102 (d)
Definitions

Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains

- (1) Data through intervention or interaction with the individual, or
- (2) Identifiable private information.
Definitions

- **Intervention** includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

- **Interaction** includes communication or interpersonal contact between investigator and subject.

- **Private information** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.
Food and Drug Administration Regulations

= Clinical Investigation

+ Human Subjects
Definitions

Clinicale inversion means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part.” 21 CFR 56.102(c)
Definitions

- **For an activity involving drugs**: “Clinical investigation means any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice.” 21 CFR 312.3(b)

- **For an activity involving devices**: “Investigation means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device.” 21 CFR 812.3(h)

- **Test article** means any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act” (42 U.S.C. 262 and 263b-263n). 21 CFR 50.3(j)
Definitions

• “*Human subject* means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient.” 21 CFR 50.3(g)

• *For a clinical investigation involving drugs*: “Subject means a human who participates in an investigation, either as a recipient of the investigational new drug or as a control. A subject may be a healthy human or a patient with a disease.” 21 CFR 312(b)

• *For a clinical investigation involving devices*: “Subject means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease.” 21 CFR 812.3(p)
Informed Consent (FDA)

- Possibility that the Food and Drug Administration may inspect the records

- Clinicaltrials.gov statement

- Elements of consent cannot be waived

- Form must be signed and dated by the subject
Emergency Use (FDA)

- FDA provides an exemption from prior IRB review and approval for emergency use of an investigational drug or device
  - Emergency use of a test article, provided that such emergency use is reported to IRB **within 5 working days**. Any subsequent use of test article at institution is subject to IRB review. 21 CFR 56.102(c)
  - An activity must meet all of the following criteria for an emergency use exemption:
    1. Life-threatening situation or severely debilitating situation
    2. No standard acceptable treatment available
    3. Not sufficient time to obtain IRB approval
    4. Report to IRB within 5 working days of use
    5. Any subsequent use of test article is subject to IRB review
    6. Activity is not a systematic investigation designed to develop or contribute to generalizable knowledge

- Specific reporting requirements must be met
- **Contact the MSU IRB if this scenario arises**
Advertisements (FDA)

- No claims (explicit or implicit) that drug or device:
  - Safe or effective for purpose under investigation
  - Known to be equivalent or superior to any other drug, device

- Not use terms such as (without explaining that the test article is investigational):
  - "new treatment"
  - "new medication"
  - "new drug"

- Not promise "free medical treatment," (when intent is to say subjects will not be charged for taking part in the investigation)

- Advertisements may state that subjects will be paid, but should not emphasize payment or amount to be paid, by such means as larger or bold type.
Screening and Enrollment (FDA)

- Informed consent must be obtained prior to initiation of any clinical procedures that are performed solely for the purpose of determining eligibility for research
  - Includes wash-out

- Clinical screening procedures for research eligibility are considered part of subject selection and recruitment process and, therefore, require IRB oversight
Record Keeping (FDA)

• Records required by FDA shall be retained for at least 3 years after completion of research, and records shall be accessible for inspection and copying by authorized representatives of the FDA at reasonable times and in a reasonable manner. 21 CFR 56.115 (b)

• Longer record retention periods may be required by clinical trial agreement
Unanticipated Problems Involving Risks to Subjects or Others

• Report potential unanticipated problems involving risks to subjects or others
  • **Unexpected** (in terms of nature, severity or frequency) given research procedures described in protocol-related documents, such as IRB approved research protocol and informed consent document and characteristics of subject population being studied; and

  • **Related:** Whether adverse event is related or possibly related (there is a reasonable possibility that adverse event may have been caused by procedures) to participation in research

  • **Risk:** Suggests that research places subjects or others at a **greater risk of harm** (including physical, psychological, social, legal, or economic) than was previously known or recognized
Protocol Deviations or Violations

• Report protocol deviations or violations
  • **Protocol Deviation**: Any change, divergence, or departure from study design or procedures of research protocol that is under investigator's control and that has not been approved by IRB. A protocol deviation does not impact subject safety, compromise integrity of study data and/or affect subject’s willingness to participate in study

• **Protocol Violation**: Deviation from IRB approved protocol that may affect the subject's rights, safety, or well being and/or completeness, accuracy, integrity and reliability of study data and/or affect subject’s willingness to participate in study
Protocol Deviations or Violations

- Protocol deviations can be reported to IRB at time of renewal or after four occurrences have accumulated.

- Protocol deviations which meet definition of an UPIRSO must be reported immediately.

- Protocol violations must be submitted promptly to IRB.

- Reported via protocol deviation form available on HRPP website.
Where to Find MSU Requirements

• MSU Institutional Review Board Office

• http://hrpp.msu.edu/
Investigational New Drugs
Investigational New Drugs

• What?
  • Regulations that govern clinical investigations with drugs involving human subjects
  • 21 CFR 312 (FDA)

• Requirements?
  • Requires filing an investigational new drug application and complying requirements unless exempt
Definitions

“Drug” means:

• (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and

• (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and

• (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and

• (D) articles intended for use as a component of any article specified in clause (A), (B), or (C).

*Federal Food Drug and Cosmetic Act 21 U.S.C. § 321(g)*
Definitions

"Clinical investigation" means any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects.

- Experiment is ANY use of a drug except for the use of a marketed drug in the course of medical practice.” (21 CFR 312.3(b))

- “Off Label Use” or “Unlabeled Indication”
  - 21 CFR 312 does not apply to use in practice of medicine for an unlabeled indication of a new drug product approved or of a licensed biological product
Definitions

• **IND** is an Investigational New Drug Application

• Submitted by a sponsor to the FDA

• If subject to an IND, required before a clinical investigation can begin
IND Assessment for Drugs

Drug?
- Does the activity involve a drug?
  - If no, stop. Not FDA regulated (for a drug).
  - If yes, continue.

Clinical Investigation?
- Does the activity involve a clinical investigation?
  - If no, stop. Not FDA regulated as a clinical investigation.
  - If yes, continue. FDA regulated.

IND?
- Does the clinical investigation have an IND?
  - If yes, verify IND number.
  - If no, continue.

IND Exempt?
- Is the clinical investigation IND Exempt?
  - If no, IND required.
  - If yes, verify IND exemption. STILL FDA REGULATED for IRB REQUIREMENTS
Examples of IND Exemption

- Clinical investigation of drug product lawfully marketed in US
- Not intended to be reported to FDA as well-controlled study in support of new indication for use nor intended to be used to support any other significant change in labeling for drug
- If lawfully marketed as prescription drug product, not intended to support significant change in advertising for product
- Does not involve a route of administration or dosage level or use in patient population or other factor that significantly increases risks (or decreases acceptability of risks) associated with use of drug product
- Conducted in compliance with requirements for IRB review; and
- Conducted in compliance with requirements for promotion
  - Cannot represent in promotional context that investigational new drug is safe or effective for purposes under investigation or otherwise promote drug (meant to preclude commercialization before approved)
  - Cannot commercially distribute or test market an investigational new drug.
  - Cannot unduly prolong an investigation after finding that the results of the investigation appear to establish sufficient data to support a marketing application
Investigational New Devices
Investigational New Devices

• What?
  • Regulations that govern clinical investigations with devices involving human subjects
  • 21 CFR 812

• Requirements?
  • Requires filing an investigational new device exemption and complying requirements unless exempt (or meets requirements for an abbreviated IDE)
Definitions

“Device” (except when used in paragraph (n) of this section and in sections 331(i), 343(f), 352(c), and 362(c) of this title) means:

• an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is—
  • (1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
  • (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
  • (3) intended to affect the structure or any function of the body of man or other animals, and
• which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

*Federal Food Drug and Cosmetic Act, 21 U.S.C. 321(h)*
Definitions

"Investigation" means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device. (21 CFR 812.3(h))
Definitions

• **IDE** is an Investigational Device Exemption Application

• Submitted by a sponsor to the FDA

• If subject to an IDE, required before a clinical investigation can begin
Assessment for Devices

- **Device?**
  - Does the activity involve a device?
  - If no, stop. Not FDA regulated (for a device)
  - If yes, continue.

- **Clinical Investigation?**
  - Is the activity a clinical investigation involving a human subject?
  - If no, stop. Not FDA regulated as a clinical investigation.
  - If yes, continue. FDA regulated.

- **IDE?**
  - Does the clinical investigation have an IDE?
  - If yes, verify.
  - If no, continue.

- **Abbreviated IDE**
  - Does the clinical investigation qualify for an abbreviated IDE?
  - If yes, verify. SUBJECT TO ABBREVIATED REQUIREMENTS and STILL FDA REGULATED for IRB REQUIREMENTS
  - If no, continue.

- **IDE Exempt**
  - Is the clinical investigation IDE exempt?
  - If yes, verify. STILL FDA REGULATED for IRB REQUIREMENTS
  - If no, IDE required.
Example of Abbreviated IDE Requirements

- **Labeling** – The device must be labeled in accordance with the labeling provisions of the IDE regulation and must bear the statement “CAUTION – Investigational Device. Limited by Federal (or United States) law to investigational use.”;
- **IRB Approval** – The sponsor must obtain and maintain IRB approval;
- **Informed Consent** – The sponsor must assure that investigators obtain and document informed consent;
- **Monitoring** – All investigators must be properly monitored to protect human subjects and assure compliance;
- **Records and Reports** – Sponsors are required to maintain specific records as required by IDE regulation
- **Investigator Records and Reports** – The sponsor must assure that participating investigators maintain records and reports;
- **Prohibitions** – Commercialization, promotion, test marketing, misrepresentation of an investigational device, and prolongation of the study are prohibited.
Examples of IDE Exemptions

- Preamendment (pre-1976) devices
- 510(k) – cleared or PMA-approved devices, if used in accordance with approved labeling
- In vitro diagnostic devices (most of the time)
- Consumer preference testing
- Combinations of legally marketed devices
- Custom devices, unless the device is being used to determine safety or effectiveness for commercial distribution.

21 CFR 812.2(c)
Investigational Drug and Device Requirements
Administration (IND or IDE)

- **Drug**
  - An investigator shall administer drug only to subjects under investigator's personal supervision or under supervision of a sub investigator responsible to investigator.
  - Investigator shall not supply investigational drug to any person not authorized under this part to receive it. 21 CFR 312.61

- **Device**
  - An investigator shall permit an investigational device to be used only with subjects under the investigator’s supervision.” 21 CFR 812.110(c).
Storage and Accountability (IND or IDE)

- **Control**
  - Investigator is responsible for ensuring control drugs and devices

- **Disposition**
  - **Drug**
    - An investigator is required to maintain adequate records of disposition of drug, including dates, quantity, and use by subjects.
    - If the investigation is terminated, suspended, discontinued, or completed, investigator shall return unused supplies of drug to sponsor, or otherwise provide for disposition of the unused supplies of the drug under 312.59.
  - **Investigational Devices**
    - Upon completion or termination of a clinical investigation or investigator's part of an investigation, or at the sponsor's request, an investigator shall return to sponsor any remaining supply of device or otherwise dispose of device as the sponsor directs. 21 CFR 812.110(e)
Storage and Accountability (MSU)

- Investigator must describe plan for storage, handling, and control of test article.

- If clinical investigation is being conducted at a clinical facility, facility’s procedures for control of pharmaceuticals, medical devices, and controlled substances should be followed.

- IRB members will evaluate investigator’s plan, including assessment of:
  - Storage and security of test article
  - Administration by appropriate individuals
  - Plans for documentation and maintenance of records

- Proper handling and storage may also be assessed during site visits by the human research liaisons.
Record Keeping (IND or IDE)

Drugs
- Investigator shall retain records required to be maintained for a period of:
  - 2 years following date marketing application is approved for drug for indication for which it is being investigated; or,
  - if no application is to be filed or if application is not approved for such indication, until 2 years after investigation is discontinued and FDA is notified. 21 CFR 312.62(c)

Devices
- Investigator or sponsor shall maintain records required during investigation and for period of 2 years after latter of following two dates:
  - Date on which investigation is terminated or completed, or
  - Date that records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol. 21 CFR 812.140
- Investigator or sponsor may withdraw from responsibility to maintain records and transfer custody of records to any other person who will accept responsibility for them, including requirements of 812.145. Notice of transfer shall be given to FDA not later than 10 working days after transfer occurs. 21 CFR 812.140
Monitoring (IND or IDE)

Drugs

- Sponsors are responsible for ensuring proper monitoring of investigation(s), ensuring that investigation(s) is conducted in accordance with general investigational plan and protocols contained in IND. 21 CFR 312.50

Sponsors . . .

- **Shall** monitor progress of all clinical investigations being conducted under its IND.
- **Who** discovers that investigator is not complying with signed agreement (Form FDA-1572), general investigational plan, or requirements shall promptly either secure compliance or discontinue shipments of investigational new drug to investigator and end investigator’s participation in investigation (and require investigator dispose of or return investigational drug and notify FDA).
- **Shall** review and evaluate evidence relating to safety and effectiveness of drug as obtained from investigator.
- Shall make reports to FDA regarding information relevant to safety of drug and make annual progress reports.
- **Who** determines that its investigational drug presents an unreasonable and significant risk to subjects shall discontinue those investigations that present risk, notify FDA, all IRBs, and all investigators who have at any time participated in investigation of discontinuance, assure disposition of all stocks of the drug outstanding, and furnish FDA with a full report of sponsor’s actions.
Monitoring (IND or IDE)

Devices

- **Entry and inspection.** A sponsor or an investigator who has authority to grant access shall:
  - Permit authorized FDA employees,
  - At reasonable times and in a reasonable manner,
  - To enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept). 21 CFR 812.145

- **Records inspection.** A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, shall
  - Permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation. 21 CFR 812.145

- **Records identifying subjects.** An investigator shall permit
  - Authorized FDA employees to inspect and copy records that identify subjects,
  - Upon notice that FDA has reason to suspect
    - that adequate informed consent was not obtained, or
    - that reports required to be submitted by investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading. 21 CFR 812.145
Monitoring (MSU)

- The following entities may conduct site visits of the investigator’s research:
  - Study sponsor
  - U.S. Food and Drug Administration (FDA)
  - Office for Human Research Protections (OHRP)
  - Federal agencies
  - MSU Human Research Protection Program (HRPP)
Monitoring (MSU)

• Human Research Liaison Office
  • Conducts site visits for compliance, education and oversight.

  • Routine site visits occur for:
    • All full board initial applications that have enrolled and are recruiting subjects
    • A sample of expedited and exempt

  • Performs internal monitoring of HRPP and IRB to assure compliance.

  • Serves as a resource for researchers regarding regulatory compliance.
International Conference on Harmonisation – Good Clinical Practice (E6)
International Conference on Harmonization - Good Clinical Practice (E6)

• What?
  • International standard for conduct of clinical trials involving human subjects

• Requirements?
  • May be required by contract or other means
Examples of ICH-GCP Requirements

- **Sponsor**
  - When using electronic trial data systems the sponsor should maintain SOPs for using these systems.
  - Report all adverse drug reactions that are both serious and unexpected.

- **Investigator**
  - It is recommended that the investigator inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.
  - Responsible for giving subjects or their legally authorized representatives a signed and dated consent form.

- **IRB**
  - Retain all relevant records (e.g. written procedures, membership lists, lists of occupations/affiliations of members, submitted documents, minutes of meetings, and correspondence) for a period of 3 years after completion
FDA Good Clinical Practice (GCP)
FDA Good Clinical Practice (GCP)

- **What?**
  - FDA regulations that govern the conduct of clinical trials

- **Requirements?**
  - If conducting FDA regulated research
FDA Good Clinical Practice (GCP)

- There are many requirements that may be applicable depending on the research
  - Electronic Records; Electronic Signatures (21 CFR Part 11)
  - Protection of Human Subjects (Informed Consent) (21 CFR Part 50)
  - Financial Disclosure by Clinical Investigators (21 CFR Part 54)
  - Institutional Review Boards (21 CFR Part 56)
  - Investigational New Drug Application (21 CFR Part 312)
  - Foreign Clinical Trials not conducted under an IND (21 CFR Part 312.120)
  - Form 1571 (Investigational New Drug Application)
  - Form 1572 (Statement of Investigator)
  - Applications for FDA Approval to Market a New Drug (21 CFR Part 314)
  - Bioavailability and Bioequivalence Requirements (21 CFR Part 320)
  - Applications for FDA Approval of a Biologic License (21 CFR Part 601)
  - Investigational Device Exemptions (21 CFR Part 812)
  - Premarket Approval of Medical Devices (21 CFR Part 814)

- For complete information, visit http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm114928.htm
Clinicaltrials.gov Registration
Clinicaltrials.gov Registration

• What?
  • Registration of clinical trials through clinicaltrials.gov

• Requirements?
  • Applicable clinical trials (FDAAA 801)
  • Clinical trials to be published in an ICMJE journal (International Conference of Medical Journal Editors)
  • Sponsored research requirement (e.g. NIH)
Clinicaltrials.gov Registration (FDAAA 801)

• “Responsible party” register and report results of the trial.
  • A “responsible party” is typically the sponsor of the research.
  • However, the sponsor, grantee, contractor, or awardee can designate the principal investigator as the responsible party under certain conditions.
  • If the principal investigator is designated as the responsible party, he or she becomes responsible for registering and reporting results of the clinical trial.

• Must have the study registered no later than 21 days after enrolling the first subject.
Clinicaltrials.gov Updates (FDAAA 801)

• Responsible party must update:
  • No less than once every 12 months
  • Recruitment status not later than 30 days after the recruitment status of the trial has changed; and
  • Primary completion date of the applicable clinical trial not later than 30 days after the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated.
Clinicaltrials.gov Reporting (FDAAA 801)

- Responsible party must submit summary results information (including adverse events) no later than 1 year after the primary completion date for registered applicable clinical trials
Clinicaltrials.gov

- Terms and conditions accepted by all ClinicalTrials.gov account holders require that clinical trial records be **reviewed and verified at least once every 12 months**
Where to Find MSU Requirements

- MSU Human Research Liaison Program

http://hrpp.msu.edu/
Where to Find MSU Information

- Conflict of Interest Office

http://coi.msu.edu
Protected Health Information
Protected Health Information (HIPAA)

• What?
  • Define and limit the circumstances in which an individual’s protected health information (PHI) may be used or disclosed by covered entities
  • 45 CFR 160, 162, 164

• Requirements?
  • A covered entity may use or disclose PHI for research provided that the activity meets specified HIPAA requirements for the release of PHI
Definitions

- **Individually identifiable health information** is information that is a subset of health information, including demographic information collected from an individual, and employer, or health care clearinghouse; and (2) Relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual; and (i) That identifies the individual; or ii) With respect to which there is a reasonable basis to believe the information can be used to identify the individual.
Protected Health Information (HIPAA)

• When May PHI be Released?
  • Research Use or Disclosure with Individual Authorization
  • Board approval of an alteration of the use or disclosure with Individual Authorization
  • Board approval of a waiver of authorization
  • Limited Data Sets with a Data Use Agreement
  • Reviews preparatory to research
  • Research in decedent’s information
  • De-identification
Research Use of Disclosure with Individual Authorization

• Authorization form must include 6 elements and 3 statements
• Original signed authorization form must be kept for 6 years after the expiration date
• Copy of signed authorization must be given to the subject
Where to Find MSU Requirements

- MSU Human Research Liaison Office

- [http://hrpp.msu.edu/](http://hrpp.msu.edu/)
Clinical Research Billing Compliance
Clinical Research Billing Compliance

• What?
  • Requirements that govern what patient care costs can be billed to insurance
  • Centers for Medicaid and Medicare, National Coverage Determination
  • Affordable Care Act

• Requirements?
  • Applicable if a billable event may occur
Where to Find MSU Information

- Clinical Research Billing Compliance Office

http://ora.msu.edu/crbc-office
Conflict of Interest
Conflict of Interest

• What?
  • Disclosure of significant financial interests for review and management
  • 21 CFR 54 (FDA)
  • 42 CFR 50, Subpart F and 45 CFR 94 (PHS)
  • Affordable Care Act, Physician Payments Sunshine Act

• Requirements?
  • FDA clinical investigations
  • Research funded by PHS/NSF, or other sponsored research as applicable
  • Manufacturers of drugs, devices that participate in US federal health care programs
  • University requirements
Conflict of Interest (PHS)

- Requires investigator training
- De minimus threshold of $5,000 (instead of $10,000)
- Annual reports plus additional reporting requirements
- Public accessibility under certain circumstances
- Retrospective review
Conflict of Interest
(Physician Financial Transparency Reports – Sunshine Act)

• Require manufacturer’s of drugs, medical devices to report payments and items of value given to physicians and teaching hospitals

• Known as the Open Payments Program

• Data now available on http://cms.gov/openpayments/
Resources
Where to Find Federal Laws

- Federal Digital System

• [http://www.gpo.gov/fdsys/search/home.action](http://www.gpo.gov/fdsys/search/home.action)
Where to Find Michigan Laws

- **Michigan Legislative Website**


- [Welcome!](http://www.legislature.mi.gov/)
  - A free service of the Michigan Legislative Council, the Michigan House of Representatives, and the Michigan Senate.
  - Bills and resolutions reported out of committee with substitute/amendment will contain a link to the substitute/amendment.
  - Meeting dates are now included in Senate Committee Bill Records.
  - Michigan Manual searching is now available.
  - Check out the new Public Act archive.

- **Recent Activity** (current news cycle has 0 items) [All recent bill activity]
  - No bill activity within the last 24 hours. - House: Adjourned until Wednesday, October 22, 2014 10:00:00 AM

- **Legislative Bill Search for 2013-2014 Session**
  - **Bill Number**: (ex. "4001" or "4001-4005")
  - **Bill Content**: (ex. "environment")

- **Bill Category**
  - Please Select a Category (2013-2014)...
  - (ex. select 'weapons' to show related bills even if 'weapons' is not found in the text of the bill.)

- **Michigan Compiled Laws Search**
  - **MCL Section**: (ex. "2.29" or "8.40-8.50")
  - **MCL Content**: (ex. "tenant")

- **Legislative Activity**
  - **How do I...**
    - Today's Calendars
    - Today's House Meetings
    - ...get notified when a bill status changes?
    - ...find a Public Act?
Where to Find MSU Requirements

- MSU Human Research Protection Program Website

http://hrpp.msu.edu/
Where to Find MSU Requirements

• MSU Human Research Protection Program Manual

• http://hrpp.msu.edu/msu-hrpp-manual-table-contents