Investigator initiated studies for the study coordinator: Some protocol issues that warrant special attention

Sarah Fowler-Dixon

Washington University School of Medicine in St. Louis

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Investigator Initiated Studies for the Study Coordinator: Some Protocol Issues that Warrant Special Attention (This is not all inclusive.)

Sarah Fowler-Dixon, PhD
HRPO Education Specialist
314-633-7456
fowlerds@wusm.wustl.edu
Objectives

- To identify what the regulations allow with regards to consent. To identify which type of consent is best for various types of studies. To understand when HIPAA, conflicts of interest and re-consent apply to a study’s consent process.

- To delineate criteria in determining what type of data and safety monitoring is best for a study. To understand what information is necessary in developing a data monitoring plan for a study.

- To know the criteria used in determining if an investigational drug or device exists. To understand the requirements of IND or IDE holders. To know when one is the IND or IDE holder. To understand FDA processes regarding INDs and IDEs.
Issues I will talk about

- Consent including Assent
- Data Monitoring
- Investigational Drugs and Devices
- Placebo
When thinking about consent, think about the entire process:

- Will our initial contact be through recruitment material?
  - What form will this take?
- Who will obtain consent
- Where
- How long will we give the participant to think about whether or not he/she wants to participate?
- Will we re-consent? How and when?
What is an appropriate consent type for your study?

- Full written consent
  - All 8 elements needed?

- Oral or telephone consent or information sheet
  - Waiver of Written Consent

- Waiver of consent (no consent obtained)
  - No follow-up
How to decide

1. What is your population?
   - Native English speakers or Non-English speakers
     - For non-English speakers do you have translators? Are you prepared to pay to have the consent and other materials translated?
     - Is there a chance non-English speakers will ever be enrolled? Are you prepared to handled this?
   - Capable of providing consent or will a legally authorized representative be needed as in the case of minors or cognitively impaired
     - What type of assent process will be used?
2. What is best for your study design?

- What will best inform the participants?
  - Complicated study design probably needs a written consent document
  - You can propose more than one consent process for your study, if appropriate given your populations.

- Will there possibly be follow-up in the future?
  - Obtain consent. Do not ask for a waiver of consent.

- What will help keep anonymity of participants?
  - No participant identifiers are being collected.
    - May want to use an information sheet (Waiver of Written Consent available to non-FDA regulated studies)
Is your study FDA regulated?

- Any use of a drug (a pharmaceutical preparation), other than the use of a marketed drug in the course of medical practice.

- Any protocol where a drug is administered as part of the protocol is FDA “research.”
  - For example, the protocol says all individuals will take 325 mg of aspirin. The exception is when the drug is up to physician discretion. For example, the protocol states: “Subjects who get a headache may take an aspirin at the direction of their physician.” This is without regard to “research” intent as defined by DHHS regulations. Administration of any non-approved drug (for any purpose – investigational or treatment) is “research” as defined by FDA. Use of a FDA-approved drug for a non-approved purpose is ordinarily classified as research. This includes “off-label” uses for research purposes.
Is your study FDA regulated?

• Any activity undertaken to determine the safety or efficacy of a medical device.
  – For example, oncology studies that involve external beam radiation are FDA “research” because they evaluate the safety and effectiveness of a device (radiation therapy machine) for treating a specific cancer.

• A comparison of two diagnostic imaging modalities is FDA “research”.
  – For example, all patients getting a CT scan will also undergo diagnostic ultrasound and the results of the two will be compared.

• Any activity whose results will be submitted to or held for inspection by FDA in support of a marketing permit.

• Any collection of data that is supported by a drug or device company should be assumed to be FDA “research” unless the sponsor has indicated in writing that the data will not be provided to FDA and will not be held for inspection by FDA.
If your study is FDA regulated:

- You need to use full written consent.
  - Include all 8 elements of consent
    - Purpose
    - Participation
      - include a description of investigational procedures
    - Costs/Payments
    - Risks
      - Include the appropriate injury language
    - Benefits
    - Alternatives
    - Confidentiality
      - Include HIPAA authorization language
    - Contacts
Are there any other consent options for FDA regulated studies?

- Your study is FDA regulated but it will qualify for expedited review,
  - therefore it most likely will receive a minimal risk designation

and the study involves no procedures for which written consent is normally required outside of the research context.

- Is a Waiver of Written Consent appropriate for your study?
  - Examples: telephone consent, oral consent, information sheet (consent document with no signature lines)
Choose the template that is right for your study.

- Normally all 8 elements of consent are included.
- WU includes 10 elements of consent in its biomedical consent template and 8 elements in its behavioral template, designed for minimal risk studies.

**Why?**

- Optional elements are included in the biomedical consent template such as the *injury language* which is not needed in minimal risk research.
Do we need to re-consent?

• Is your study a longitudinal study or does your study involve populations that may reach age of maturation or whose cognitive abilities may decrease over time?
  – Re-consent procedures may be appropriate for your study.

• Re-consent can take many forms: signing another consent document, a verbal conversation that is noted in the research record, a consent addendum, information sent via an information sheet/letter to the participant.
Will HIPAA Apply?

- Are you conducting the research at the medical school, or at Student Services or Psychological Services on the Danforth campus?
- Are you getting information out of, or putting information into a medical chart?
- If yes to either, HIPAA applies.
If HIPAA applies, what does this mean for consent?

- WU puts its HIPAA authorization language into the consent document under Confidentiality.
  - Delineate what PHI will be collected, from where, who will have access, who will it be shared with, and in what format.
  - If there are restrictions for contact those should be listed.
  - Include the Notice of Privacy box for treatment studies
What might be needed as part of the consent process?

- Will participants possibly be contacted in the future to participate in other studies?
  - Will need permission for future contact if HIPAA applies to your study.

- Will you want to access the data collected in this study for future studies?
  - Will need authorization to share data if HIPAA applies to your study.
What else might be needed as part of the consent process?

- Disclosure of any financial conflicts of interest that a study team member may have.

- Costs that may be incurred by the research participants.

- Payments given to participants.

- A statement regarding death if possible for the study.
What else might be needed as part of the consent process?

- Radiation exposure language, if applicable

- Authorization to send PHI via e-mail
  - WU discourages sending PHI via e-mail
  - Read and know HIPAA Security Policy #17 found on the HIPAA website at http://hipaa.wustl.edu

- Language for Siteman Cancer Center, if applicable

- Center for Applied Sciences language when any of their units are being used: Clinical Trials Unit, Pediatric Research Unit, Clinical Research Unit.
Consent is a process and begins with the initial participant contact, usually during recruitment, and continue throughout the study.

Regardless of the consent process utilized, federal guidelines tell us that the language used in materials going to research participants should be understandable to the target population.
Determine the best assent process or processes for your population.

Options:
- Waiver of Assent
- Oral Assent
  - Script or outline
- Written Assent
  - Separate assent document or have the individual sign an assent line placed on the consent document

You may propose more than one assent process for your study, this is especially important when a variety of ages are recruited.
Monitoring your study for participant safety and data integrity
Monitor adverse events for trends

Look at safety data to protect the participants

Consider the **size** and **risks** of the study, when determining the right plan for your study.
Consider

- How much risk is involved in your study.
  - Is there prior safety data that might suggest a higher volume of adverse events?
  - Current literature.
  - Is there something in the study design that would suggest that this study would place individuals at greater risk of harm?

Studies with more risk require more oversight.
Options for Oversight

Options:

- PI or research team member monitors the adverse events, for trends, alone.
- A group of research team members monitor the adverse events for trends.
- One or more individuals outside the research team monitor the study for trends.
- A data monitoring committee is formed:
  - field expert, unaffiliated member, statistician
    - Can use groups already in place with the distribution above.
What is reviewed?

- All adverse events, regardless of whether or not they are submitted to the IRB.
- Other types of safety data depending on the study:
  - Efficacy information
  - Drug experiences in other studies
  - Toxicities
  - Literature that gives previous or current experiences with the drug, device, or agent
Based on what is right for your study determine:

- How often the data will be looked at.
- What types of reports will be generated.
- What the stopping criteria should be
  - Under what conditions would you stop the study?
  - A statistician can help define these.
Multi-site Study and WU is the coordinating center

You must also consider:

★ How will you obtain safety data from the other sites?
  ★ Set up agreements to ensure that you receive this data.

★ What requirements will you use for reporting?
  ★ If WU is the coordinating center, consider using the HRPO “What Should I Report to HRPO “ guideline in setting up reporting requirements
Sample Data Monitoring Plan

SAMPLE DATA MONITORING PLAN
For multi-center studies, your data monitoring plan should describe monitoring for the entire study as well as monitoring at WU.

Based on size and risks of the study, consider
- a plan where more than one individual monitors the study
- a plan with an independent monitor,
- a Data Monitoring Committee,
- individual(s) independent of sponsor and study.

**Study Monitoring.**
Who will monitor the study for safety at WU? For multi-center studies, who will monitor study-wide?
______ (PI, independent monitor, Research team, MD, PhD, biostatistician, BSN, RPh, etc) will monitor the study in accordance with the HRPO guideline titled “What Should I Report to HRPO?”.

**Reporting.**
All reportable events will be sent in accordance with timeframes specified in the HRPO guideline titled, “What Should I Report to HRPO?”.
Other reports that will be generated are________________. (Indicate if there will be other reports. Examples: safety reports, interim data analysis reports, summary reports, etc. What reports will be generated study-wide, for multi-center studies?)

These other reports will be sent to the HRPO (IRB) ________________________. (Indicate frequency for all reports generated. This includes those generated at WU and those generated study-wide for multi-center studies. Frequencies could include: annually, semi-annually, on an occurrence basis, after X number of weeks/months, after X number of subjects enrolled, after X number of adverse events, etc.)
______ will be reported to the sponsor. (Indicate which reports are sent to the sponsor. This includes reports generated at WU as well as those generated study-wide, for multi-center studies. All reports sent to the IRB must be sent to the sponsor, if one exists.)
Should there be an event or series of events that occur that increases the risks to the participants, the “following steps” will be taken_________________________ (Examples: conduct an investigation, modify the protocol, suspend the study, close the study, etc. Include examples that occur at WU as well as those that could occur study-wide for multi-center studies.) and will be reported to _____________. (Indicate who will receive the reports, e.g. IRB, sponsor, independent monitor, etc.) within_______. (Indicate the timeframe in which reports will be sent, eg. immediately, within 7 calendar days, within 24 hours, etc. At a minimum reporting timeframes to the IRB should be in accordance with the HRPO guideline, “What Should I Report to HRPO?”)
1. Changes in the status of the study due to safety concerns (such as a suspension or closure of enrollment)

2. Adverse Events:
   
   A. *Internal Adverse Events and External Adverse Events occurring in the same study if they are:
      
      - Serious (regardless of expectedness or relatedness) or;
      - Unexpected and reasonably related (regardless of seriousness)
   
   B. *External Adverse Events occurring in a different study if the adverse event places the participant(s) at a greater risk of harm than was previously known or recognized

3. Unanticipated Adverse Device Experiences (UADEs)

4. Protocol Exceptions (formerly Deviations or planned deviation)
5. Protocol Errors (formerly Violations/Errors or unplanned deviation)
6. Complex Complaints
7. Breaches of Confidentiality
8. Audit/Inspection/Inquiry
9. Participant Incarceration
10. New Information (Safety Monitoring, Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC) reports, interim analysis reports, progress reports or any event or new information that suggests the research places participants or others at a greater risk of harm than was previously known or recognized)

For more information see “What Should I Report to HRPO?” at http://hrpo.wustl.edu under Guidelines
What if my study uses an investigational drug or device?

1. How many here conduct investigator initiated studies that use investigational drugs or devices?

2. How many have applied for the IND or IDE for their study team or themselves?

3. How many prepare the drug or manufacture the device?
Is the drug investigational?

- Is the drug FDA approved but being used in an investigational fashion? (e.g. off label)

- The drug is investigational.

- You need to apply to the FDA for an Investigational New Drug (IND) number.

- If you are not following a sponsor’s guidelines, you must abide by the WU Investigational Drug/Device Accountability Policy
IND is not needed if all are true

- The drug is FDA-approved; AND
- The use is not intended to be reported to the FDA in support of a new indication for use or to support any other significant change in labeling of drug; AND
- The use is not intended to support a significant change in the advertising of the product; AND
- The use does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product; AND
- The study is conducted in compliance with the requirements for IRB review and informed consent (21 CFR parts 56 & 50); AND
- The study is conducted in compliance with the requirements concerning the promotion and sale of drugs (21 CFR 312.7); AND
- The study does not intend to invoke 21 CFR 50.24 (Emergency Use).
Implications for being the IND holder

- 21 CFR 312, subpart D
  - Responsible for selecting a qualified investigator
  - Provide the investigator with the key information needed to conduct the study.
  - Ensure proper monitoring of the investigation
  - Ensure that the investigation is conducted in accordance with the general investigational plan and protocols contained in the IND
Maintain an effective IND with respect to the investigations

Ensure that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug.
Go to the FDA website for directions:

Complete FORM FDA 1572 for sponsor-investigators

Complete FORM FDA 3674 to register with ClinicalTrials.gov

The Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85) was enacted on September 27, 2007. Title VIII of FDAAA added new Section 402(j) to the Public Health Service Act (42 USC § 282(j)) and expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices.
What if it’s a device study?
What is a medical device?

Medical devices include surgical lasers, wheelchairs, sutures, pacemakers, vascular grafts, intraocular lenses, and orthopedic pins. A longer list can be found in the **HRPO Investigational Drug (IND) and Investigational Device Exemption (IDE) Guideline** on the HRPO website, [http://hrpo.wustl.edu](http://hrpo.wustl.edu) under Guidelines.

Medical devices also include diagnostic products such as in vitro diagnostic reagents and test kits such as pregnancy test kits and imaging systems such as MRI.
Is the device investigational?

- The device is not FDA approved for the indication.
- The FDA approved device has been altered or a biologic has been added.

- If yes to either. The device is investigational.
- Is the device Significant Risk (SR)? If yes, an Investigational Device Exemption (IDE) is needed.
**Need for an IDE**

- Given a Significant risk device determination by an IRB.

- To obtain a FDA determination, you must apply to FDA.
21 CFR 812.40

- Responsible for selecting a qualified investigator
- Provide the investigator with the key information needed to conduct the study.
- Ensure proper monitoring of the investigation
- Ensure that IRB review and approval are obtained
- Submit an IDE application to FDA
- Ensure that any reviewing IRB and FDA are promptly informed of significant new information
Implications for IDE holders, subpart B

- Application
- Investigational Plan
- Report of prior investigations
- FDA action on the application: approval or disapproval
- Supplemental applications: all changes to the investigational plan require prior approval
- Treatment use of the investigational device
- Confidentiality of data and information
How do I apply for an IDE?

- 21 CFR 812, *Investigational Device Exemptions*, covers the procedures for the conduct of clinical studies with medical devices including application, responsibilities of sponsors and investigators, labeling, records, and reports.
“A sponsor shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.”
Includes and is in addition to investigator reports:

- Unanticipated adverse device effects
- Withdrawal of IRB or FDA approval
- Current investigator list
- Progress reports
- Recall and device disposition
- Final report
- Informed consent
- Significant risk device determinations
What do Investigational Device Exemption regulations cover?
21 CFR 812 covers 3 types of devices:

- Significant Risk
- Non-significant Risk
- Exempt
A significant risk device poses a “potential for serious risk to the health, safety, or welfare of a subject.” Such devices may only be studied under an Investigational Device Exemption (IDE) granted by the FDA. A device is SR (and requires an IDE) if it:

- is intended as an implant, or
- is purported or represented to be for a use in supporting or sustaining human life, or
- is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health; or
- otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
Non-Significant Risk

- IRB makes this determination. In doing so, the IRB needs the following:
  - Description of why the device is not significant risk
  - The proposed use of the device, as well as any protocol related procedures and tests
  - Additional information regarding the device from the sponsor, if needed.
Exempt studies still need IRB review

- Examples: Humanitarian Use Devices
- Those with a 510K submission
Humanitarian Use Devices

- Intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year.
  - affects a small patient populations.
  - A Humanitarian Device Exemption enables the provision of humanitarian use devices (HUDs) in the population described above faster than the traditional FDA approval process.

- An approved HDE authorizes marketing of the HUD. However, a HUD may only be used after IRB approval has been obtained for the use of the device for the FDA approved indication.
  - The labeling for a HUD must state that the device is a humanitarian use device and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.
Some type of consent is still needed.

21 CFR 814.124 requires IRB review and approval.

This device is not considered investigational as FDA approval of the Humanitarian Device Exemption is a marketing approval.
Most stringent type of device marketing application

For a PMA to be approved, FDA must determine that sufficient valid scientific evidence exists to assure that the device is safe and effective for its intended use(s).

For more information, go to www.fda.gov/cdrh/devadvice
During the FDA review of the premarket notification, the device remains investigational and is still subject to:

- IRB review and regulations
- Informed consent processes
- Safeguards for research participants, including additional safeguards for vulnerable populations such as children
- IDE regulations
Responsibilities of the IND or IDE holder
Implications for being the IND or IDE holder:

- You function as the sponsor.
- You will have the responsibilities of the investigator and the sponsor.
You are responsible for:

- All aspects of the clinical study including:
  - Communication with FDA
    - Safety reports, annual reports, protocol amendments etc.
  - Ensuring proper infrastructure is in place to perform the clinical investigation
    - Staff training, development of study, SOPs, proper informed consent process, protocol adherence, adverse event reporting, maintenance of regulatory files, drug and/or device accountability records, maintenance of complete case histories, etc.
You are also responsible for:

- Monitoring the conduct and progress of the study
- Reviewing and evaluating any information relevant to the safety of the drug/biologic or device
You also have Investigator Responsibilities

Which include:

- Ensuring the study is conducted according to
  - the signed investigational statement (eg. Form 1572)
  - The investigational plan
  - Applicable regulations for informed consent
- IRB approval is met
- Rights, welfare, and safety of participants in the study are protected
- Ensuring that all other responsibilities listed in the applicable FDA regulations are met
Regardless of whether it’s a drug or device study.
FDA should get back to you within 30 days regarding its decision.

The drug/device must be listed as “investigational” in the consent document.
If you prepare the drug or manufacture the device, you must abide by Good Manufacturing Practices.
**Good Manufacturing Practices**

- **Good Manufacturing Practice** or GMP (also referred to as 'cGMP' or 'current Good Manufacturing Practice') is a term that is recognized worldwide for the control and management of manufacturing and quality control testing of foods, pharmaceutical products, and medical devices.

- In the US, the phrase "current good manufacturing practice" appears in 501(B) of the 1938 Food, Drug, and Cosmetic Act (21USC351). US courts may theoretically hold that a drug product is adulterated even if there is no specific regulatory requirement that was violated as long as the process was not performed according to industry standards. By June 2010, the same cGMP requirements will apply to all manufacture of dietary supplements.[1]
GMP

- GMP takes the holistic approach of regulating the manufacturing and laboratory testing environment itself.

- An extremely important part of GMP is documentation of every aspect of the process, activities, and operations involved with drug and medical device manufacture. If the documentation showing how the product was made and tested (which enables traceability and, in the event of future problems, recall from the market) is not correct and in order, then the product does not meet the required specification and is considered contaminated (adulterated in the US).

- Additionally, GMP requires that all manufacturing and testing equipment has been qualified as suitable for use, and that all operational methodologies and procedures (such as manufacturing, cleaning, and analytical testing) utilized in the drug manufacturing process have been validated (according to predetermined specifications), to demonstrate that they can perform their purported function(s).
GMP regulations

- GMP for drugs, 21 CFR 210 & 211
- GMP for biologics, blood and blood components, 21 CFR 600 & 606
- GMP for devices, 21 CFR 820
- GMP for human cells, tissues, cellular and tissue-based products, 21 CFR 1271
Good Clinical Practices

- **Good Clinical Practice** is an international quality standard that is provided by International Conference on Harmonisation (ICH), an international body that defines standards, which governments can transpose into regulations for clinical trials involving human subjects.

- Good Clinical Practice guidelines include protection of human rights as a subject in clinical trial. It also provides assurance of the safety and efficacy of the newly developed compounds.
Good Clinical Practice Guidelines include:

- standards on how clinical trials should be conducted,
- define the roles and responsibilities of clinical trial sponsors,
- Define the roles and responsibilities of the clinical research investigators,
- Define the roles and responsibilities of the clinical monitors. (In the pharmaceutical industry monitors are often called Clinical Research Associates.)
21 CFR 50, *Protection of Human Subjects*, provides the requirements and general elements of informed consent;

21 CFR 56, *Institutional Review Boards*, covers the procedures and responsibilities for institutional review boards (IRBs) that approve clinical investigations protocols;

21 CFR 54, *Financial Disclosure by Clinical Investigators*, covers the disclosure of financial compensation to clinical investigators which is part of FDA’s assessment of the reliability of the clinical data.

21 CFR 820 Subpart C, *Design Controls of the Quality System Regulation*, provides the requirement for procedures to control the design of the device in order to ensure that the specified design requirements are met.
WU Investigational Drug/Device Accountability Policy

- You either abide by the sponsor’s guidelines for handling or you must abide by the WU Investigational Drug/Device Accountability Policy.
WU Investigational Drug/Device Accountability Policy

Found on the Vice Chancellor for Research page at

http://research.wustl.edu/PoliciesGuidelines/Pages/IDDA.aspx
Investigational/Device Accountability Policy

- What it specifies;
  - Receipt and inventory of investigational drugs/devices
  - Storage of investigational drugs/devices
  - Dispensing of investigational drugs/devices
  - Return or disposal of investigational drugs/devices
Other Policies you may need to know about
Depending on your study, and if an industry sponsor is involved, you may be asked to abide by:

- Good Lab Practices
- Good Tissue Practices

  E.g. Blood banking, cell suspensions, manufactured or manipulated in a closed system or allergens prepared or manipulated in a closed system. Closed systems are not open to the environment.
**Good laboratory practice** generally refers to a system of management controls for laboratories and research organizations to ensure the consistency and reliability of results as outlined in the *Organisation for Economic Co-operation and Development* (OECD) Principles of GLP and national regulations.

GLP applies to non-clinical studies conducted for the assessment of the safety of chemicals to man, animals and the environment. The internationally accepted definition is as follows:
Good Laboratory Practice (GLP) embodies a set of principles that provides a framework within which laboratory studies are planned, performed, monitored, recorded, reported and archived. These studies are undertaken to generate data by which the hazards and risks to users, consumers and third parties, including the environment, can be assessed for pharmaceuticals (only preclinical studies), agrochemicals, cosmetics, food additives, feed additives and contaminants, novel foods, biocides, detergents etc.... GLP helps assure regulatory authorities that the data submitted are a true reflection of the results obtained during the study and can therefore be relied upon when making risk/safety assessments.

GLP can be confused with the standards of laboratory safety - wearing appropriate gloves, glasses and clothing to handle materials safely.
Current Good Tissue Practice (cGTP), also known as Good Tissue Practice (GTP), is a term that is one of the "GxP" requirements derived from cGMP. The rule was written and is enforced by the U.S. Food and Drug Administration (FDA), specifically the Center for Biologics Evaluation and Research.

It is generally used to mean the requirements of section 1271 of chapter 21 of the US Code of Federal Regulations, though the rule itself specifies that the GTPs are only subpart D of that section.[1]

The rules cover a broad variety of articles referred to as "HCT/Ps" for Human Cellular, Tissue, and Tissue-based Products and the regulations cover more or less any cellular entity taken from a human and transplanted into another human. There are several exceptions in the rules for Organ transplants, blood for transfusion, and other articles which already have established requirements.
The rules are an expansion and revision of the section 1270 of the same chapter and now cover a larger group of products. The most controversial products covered in these rules include stem cells and tissue used in reproductive medicine (assisted reproductive technology): sperm, oocytes, and embryos.

These rules only cover tissue which has not been significantly modified. Any major changes will make the product into either a drug or a medical device, though some of the rules in this section still apply to human-sourced drugs and medical devices.

The rules only affect products collected after May 25, 2005.
What if I use a Placebo?
Placebo

- No proven therapy exists
- A proven therapy exists but:
  - There is compelling and scientifically sound reasons for its use
  - The toxicity of the treatment is such that patients commonly refuse it
  - Patients who receive placebo will not be subject to any additional risk of serious or irreversible harm
  - Denial of active treatment may not pose an increased risk of death, severe morbidity or disability or severe discomfort
Participants must be informed that they may receive a placebo

- Any viable alternatives, if applicable
- Rationale for using placebo
- Duration of time, discomfort, and potential effects of receiving a placebo
- Consequences of delayed active treatment

HRPO Use of Placebo Guideline and Form S
IRB Submission Basics
Basics for your IRB Submission

- Appropriate submission form
  - List engaged members of your team
    - Those under WU auspices need CITI training
    - See the Human Subjects Education Policy at [http://www.wustl.edu/policies/humansubjectseducation.html](http://www.wustl.edu/policies/humansubjectseducation.html)
  - List engaged sites – Federal Wide Assurance (FWA) numbers needed. (Form B)
    - If using community agencies, physicians, etc.
      - Be aware: We need their FWA number. If they do not have one, they will need either the FWA or an individual investigator agreement (IAA).
Basics for your IRB Submission

- Protocol with data safety monitoring plan
- Consent process with appropriate documents, outlines, letters, forms,
- Grant with salaries blocked out, if WU is the primary awardee
- Recruitment materials, if available
- Form T, Financial Conflict of Interest (if applicable)
Basics for your IRB Submission

- Investigational drugs/devices
  - Form C, IND/IDE includes radioactive drugs, other biologics and dietary supplements
  - IND/IDE number or exemption letter (if obtained prior to IRB review)
  - Description of the device and its intended use, if applicable
  - Any investigational drug brochures or device pamphlets
This list is not all inclusive. HRPO forms will guide you to any auxiliary forms or approvals you may need.

- Form E, Minors (0-17 yrs in MO)
- Form P, Research Related Radiation, if applicable
- Form N, Stored Data or Tissue for Future Research, Research Involving
- Form S, Justification for Use of a Placebo
HRPO website, [http://hrpo.wustl.edu](http://hrpo.wustl.edu)

Guidelines page:
[http://hrpohome.wustl.edu/default.aspx](http://hrpohome.wustl.edu/default.aspx)

Drug/Device Guidelines:

Vice Chancellor for Research website,
[http://research.wustl.edu](http://research.wustl.edu)