



IRB Process & Medical Devices

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IRB Review of Research: Criteria

- **Informed Consent** (*Respect for Persons*)
 - Will be sought prospectively
 - Includes required elements of information
 - Additional safeguards to protect vulnerable subjects
- **Risk are Balanced and Minimized** (*Beneficence*)
 - Sound research not to unnecessarily expose subjects to risk
 - Risks are minimized (e.g. - use data or proc. already available)
 - Risk to subjects is reasonable vs. potential benefits
 - Safety provisions & monitoring are adequate
 - Privacy & confidentiality provisions are adequate
- **Subject Selection is Equitable** (*Justice*)
 - Rationale for inclusion/exclusion criteria
 - Involvement of vulnerable populations justified



What The IRB Wants To Know



- **Understanding of ethical research**
 - **Training requirement (NIH + Medical Device Training)**
 - <http://phrp.nihtraining.com/users/login.php>
 - <http://www.fda.gov/training/cdrhlearn/ucm162015.htm>

- **What are you doing?**
 - **Procedures/Protocol**

- **Who are you doing it to?**
 - **Subject Population**
 - **Inclusion/Exclusion Criteria**

- **What are the risks and benefits?**

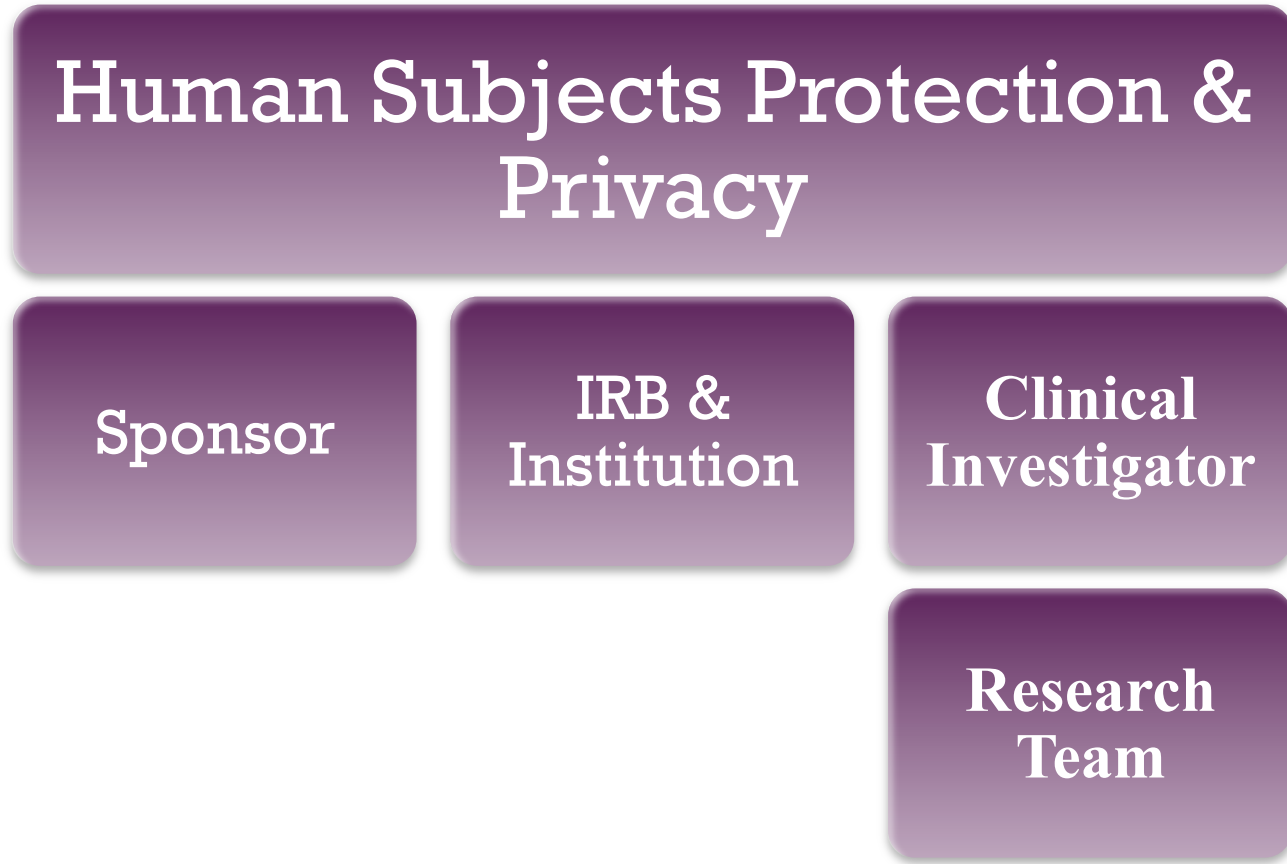
- **How will you ensure voluntary participation?**



What is Human Research?

- **Research** - *a systematic investigation ..., designed to develop or contribute to generalizable knowledge.*
- **Human subject** - *a living individual about whom an investigator conducting research obtains:*
 - Data through intervention or interaction with individual, or
 - Identifiable private information
 - individually identifiable;
 - reasonably expect not to be observed, recorded or made public

+ FDA-Regulated Research





Determination of What Needs an IRB Review



- Research Office website: <http://www.pacificu.edu/research/>
- IRB website: <http://www.pacificu.edu/irb/index.cfm>
- Use request for determination form
- Accurate, complete information
- Educate yourself about medical devices, drug studies, and the IRB process to demonstrate that you are concerned for the safety of the participants
- Be prepared to provide additional data
- <http://www.hhs.gov/ohrp/> & <http://www.fda.gov/>

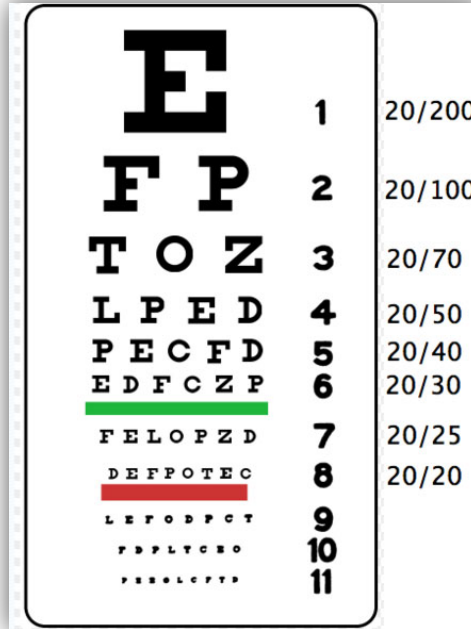
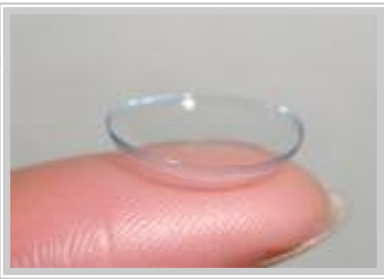


What are the IRB review categories?



- Types of review
 - Exempt from IRB review (less than minimal risk but not NO review)
 - Expedited IRB review (minimal risk)
 - Full board (convened) IRB review (more than minimal risk, involve special/non-autonomous populations, prisoners, pregnant women)
- Affected by the level of risk and the type of project
- Minimal risk = ***the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.***

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Medical Devices or Not?

Classify your device
Ophthalmic Devices

+ Medical Device

- An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent or other similar or related article (including any component, part, or accessory) which is:
 - Recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
 - 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
 - Intended to affect the structure or any function of the body of man or other animals, and which **does not achieve any of 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 any of its primary intended purposes.





Statutes and Regulations that Apply



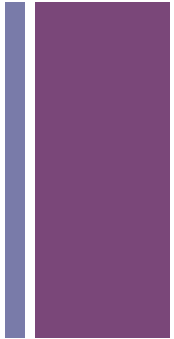
- Code of Federal Regulations (CFR)
 - 21 CFR Part 50 (informed consent & safeguards for children)
 - 21 CFR Part 812 (IDE requirements)
 - 21 CFR Part 54 (Financial disclosure)

+ Clinical Investigations

- **Clinical Investigation:** 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 FDA under section 505(i) [investigational drugs] or 520(g) [investigational devices] of the [FD&C] Act, or
 - need not meet the requirements for prior submission to the FDA under these sections of the Act, but the results of which are **intended to be later submitted to, or held for inspection by, the FDA as part of a research or marketing permit.**
- The terms *research*, *clinical research*, *clinical study*, *study*, and *clinical investigation* are synonymous in **FDA** regulations.
- **Test Article:** Any drug, biologic, device, etc. for human use that is subject to regulation under the Act.
- **Human Subject:** An individual who is or becomes a participant in research, either as a recipient of the test article or as a control.



Summary of Device Classification and Marketing Approvals



Risk-Based Classification	Most Common Path to Approval
Class I – Lowest Risk (exam gloves)	510(k) exempt – no FDA approval required
Class II – Moderate Risk (orthopedic plate)	510(k) – pre-market notification to FDA of intent to market
Class III – Highest Risk (cardiovascular stent)	PMA – pre-market approval from FDA

- Devices are defined and classified based on their **intended use**. That means that the same device, used in different ways, can require more than one notification or approval.
- These classifications are made by the FDA and are separate from determinations of risk by an IRB (more on that shortly).

+ Definitions – IDE Regulations

- **Investigational Device** means a device that is the object of an investigation.
- **Investigation** means a **clinical investigation** or research involving one or more subjects to **determine the safety or effectiveness of a device**.
- An **Investigational Device Exemption (IDE)** allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application or a Premarket Notification 510(k) submission to FDA.
 - It permits the device to be **shipped lawfully** for the purpose of conducting a clinical investigation.
 - **Exempt from what?** The requirements (FD&C Act) of placing a device in interstate commerce (commercial distribution):
 - PMA or 510(k)
 - Establishment registration
 - Device listing



Devices covered under IDE Regulations (21 CFR Part 812)



- Three (3) types of device studies are covered:
 - Exempt Studies
 - Significant Risk/Serious Risk
 - Intended as an implant, potential serious risk to the health and safety or welfare of subject
 - Supporting or sustaining life
 - Substantial importance in dx, curing, mitigation, or treatment of a disease, or preventing impairment of human health
 - Non-significant Risk
 - Does not meet the standard of significant risk

+ Applying IDE Regulations

Step 1: IDE Exempt Status

- ⦿ **Investigators/study staff** determine whether a device is Exempt or Non-Exempt from IDE regulations when applying for IRB review.
- ⦿ **IRB** verifies this determination.
- ⦿ **Exempt devices do not require an IDE.**
- ⦿ Studies with exempt devices may be eligible for expedited IRB review.

Exempt devices include:

- ⦿ **Approved devices for approved use**
- ⦿ Certain non-invasive diagnostics that are *not used as a diagnostic procedure without confirmation by another medically established diagnostic product or procedure*
- ⦿ Devices that are not studied for safety/effectiveness and do not put subjects at risk, and the focus is on:
 - Consumer preference testing
 - Testing a modification to an approved device
 - Testing a combination of two or more approved devices
- ⦿ Custom devices

+ Applying IDE Regulations

Step 2: SR vs. NSR

For **Non-Exempt** devices, if FDA has not made a determination already, IRB determines whether an investigational device is **Significant Risk (SR)** or **Non-Significant Risk (NSR)**.

- SR: Apply for IDE with FDA.
- NSR: No IDE application required.

An SR Device:

- ⦿ Presents a potential for serious risk to the health, safety, or welfare of a subject and is:
 - Intended as an implant;
 - Used in supporting or sustaining human life; or
 - 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.



Informed consent process

Important for device studies



- Ensure language understandable
- Ensure there is no exculpatory language
- **Ensure patient given opportunity to consider whether or not to participate**
- Ensure possibility of coercion or **undue influence** is minimized
- **Ensure patient is given adequate opportunity to read it before it is signed and dated**
- IRB: ask about the process at initial and continuing review

+ IRB Review and Informed Consent

FDA has no waiver of
informed consent
(except for emergency use)





Non-Significant Risk Device

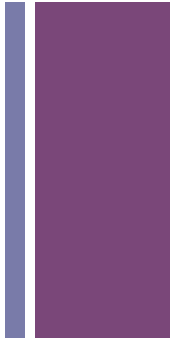


- FDA is not aware of NSR studies
- IRB is only oversight body for NSR studies
- Sponsor will make the initial NSR determination



IRB Review

Non-Significant Risk Device



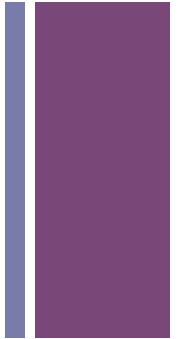
- IRB must determine whether the NSR device research is NSR or SR

- How we make the determination
 - Review the SR definition
 - Review Sponsor's brief explanation of why the device is not a SR
 - Review the proposed use of the device
 - Review the additional procedures - surgical
 - Ask FDA for assistance: 301-594-1190



IRB Review

Non-Significant Risk Device

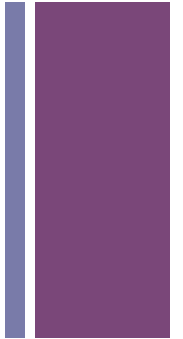


- IRB determination of whether the NSR device research is NSR or SR
 - If NSR, IRB may continue their review for implementation at the site. If approved, study is considered to have IDE; it may start; must follow abbreviated requirements at 812.
 - If SR, IRB reports its determination to the CI and where appropriate the sponsor and wait for the sponsor to obtain an IDE before approving the research study at the site.



21 CFR 812.2(b)

Non-significant risk device studies



- **Sponsor responsibilities [21CFR 812.2(b)]**
 - Label: “Caution-Investigational device limited by Federal law to investigational use.
 - **Ensure IRB approval after presenting the IRB with explanation of why device is NSR.**
 - Ensures Investigators obtain informed consent
 - **Monitoring**
 - Maintains records: name and use of device; explanation of NSR; name and address of CIs; name and address of each IRB; GMP statement, and adverse effects & complaints

+ Applying IDE Regulations

Step 2: SR vs. NSR (cont.)

■ Per FDA Guidance

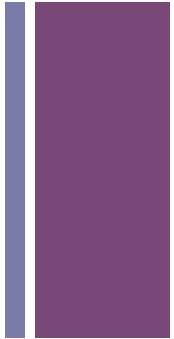
- IRB **has a** SOPs that explain how SR/NSR determination is made.
- IRB **makes** SR/NSR determination at a convened meeting.
- IRB **should** document determination in minutes.

■ Information to Collect:

- Sponsor's determination
- Information from investigator
- Device manual, instructions for use, etc.
- Relevant communications with FDA



What is a Sponsor-Investigator?



Study Sponsor

Initiates the investigation

Is responsible to obtain FDA approval of the IDE

Monitor the collection of quality data

Maintain specific records

File required reports

Control distribution of investigational devices

Investigator

Conducts the clinical investigation

- Obtain IRB approvals
- Follow the study protocol
- Maintain control of investigational devices
- Ensure quality records are complete
- File required reports, and
- Oversee the study team

Sponsor Investigator

Must meet the responsibilities of both the sponsor and the investigator to ensure the protection of human subjects participating in a medical device study.

+ Applying IDE Regulations

Expedited Studies

Relationship between category 1(b) and NSR devices:

- Two ways to interpret the “no IDE” requirement in expedited category 1(b)
 - No IDE application – NSR can qualify
 - No IDE at all – NSR does not qualify because of “abbreviated” IDE requirements
- No clear guidance from FDA
- NSR devices can be determined NSR at a board meeting and subsequently reviewed under expedited category 9.



Getting an IDE

- Significant risk device studies must have an IDE approved by the FDA, along with IRB approval, prior to the initiation of any research activity.
- **Even if you have no plans for marketing**, if you are conducting a significant risk device study, you need an IDE.
- Conditions of an IDE include:
 - Obtaining informed consent and IRB approval
 - Product labeling “for investigational use only”
 - Monitoring of the study
 - Submission of reports
 - Maintenance of records





Key Regulations and Guidance



- IDE Regulations: [21 CFR 812](#)
- IRB Regulations: [21 CFR 56](#)
- Informed Consent Regulations: [21 CFR 50](#)
- FDA [Device Advice Website](#)
- FDA Training <http://www.fda.gov/Training/CDRHLearn/ucm162015.htm>
 - Two modules are commended
 - Medical Devices overview
 - BIMO Part 2 Clinical Investigator Responsibilities
- [FAQ FDA Medical Devices](#)
- Relevant Guidance Documents:
 - [Significant Risk and Nonsignificant Risk](#)
 - [In Vitro Diagnostic FAQs](#)