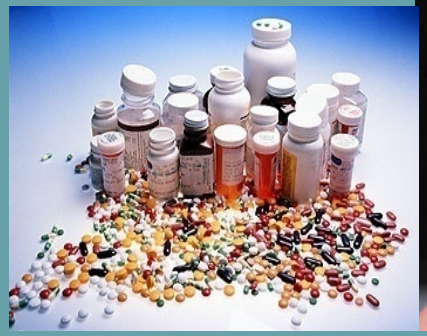
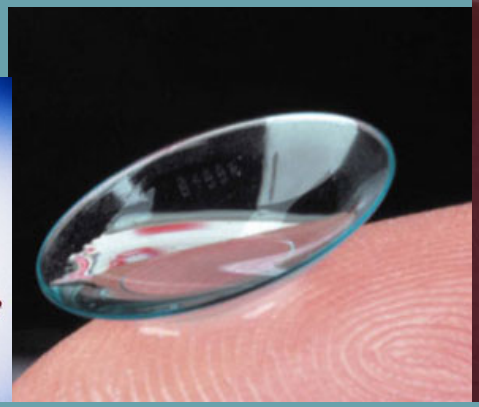
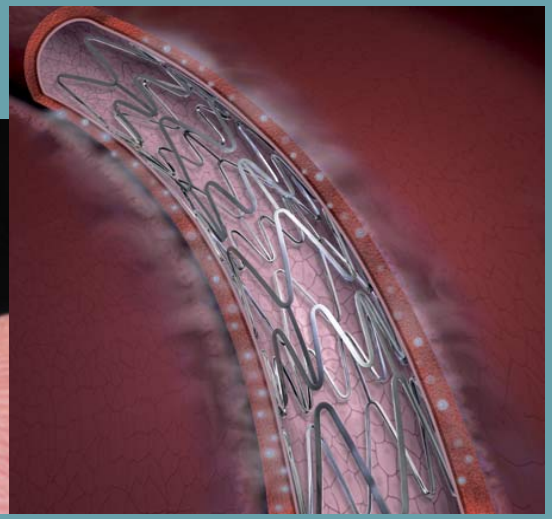
INVESTIGATIONAL DEVICES & DRUGS

What is an IRB to do?







What is a medical device?

- An instrument, apparatus, implement, machine, contrivance, implant, or *in vitro* diagnostic reagent
  - Recognized in the official National Formulary or the US Pharmacopoeia,
  - **Intended to:** diagnose, cure, mitigate, treat, or prevent disease,

    OR
  - **Intended to:** affect the structure or function of the body

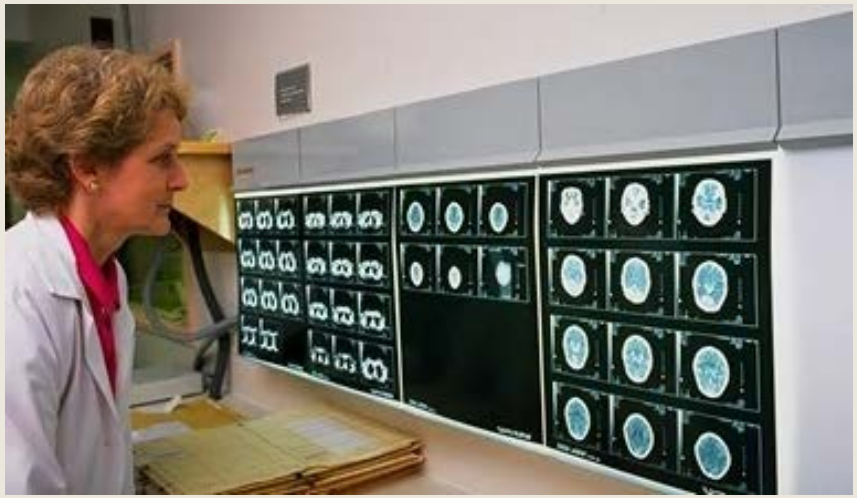
  AND
- Does not achieve primary purpose through chemical action (in the body);
- Is not dependent upon being metabolized (for its primary purpose)

Classes of Marketed Medical Devices

Device Classes	Class I	Class II	Class III
Risk	Low	Moderate	Highest
Marketing	510K Exempt or Clearance	510K Exempt or Clearance	Approval
Examples	Band-Aids, dental floss, tongue depressor	BP cuffs, sutures, catheters	Pacemakers, vascular stents

What is an investigational device?

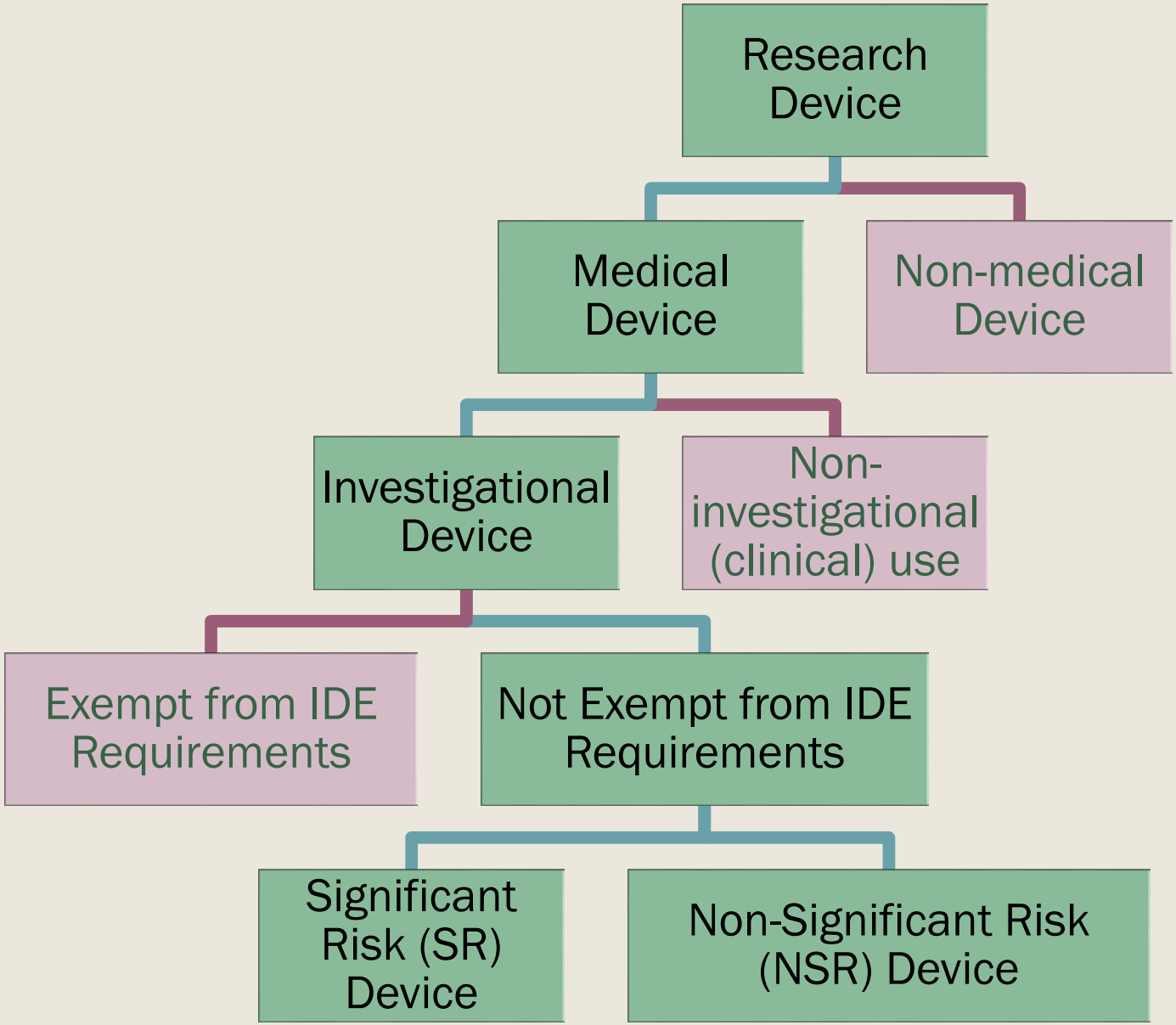
- Research to determine the **safety and/or effectiveness** of a device. In essence, the device is the subject of the investigation
- Examples:
  - *New device that is not FDA approved/cleared, OR*
  - *An established device used in an investigational manner (off label)*



Is the use of the device exempt from an IDE?

- Legally marketed device when **used in accordance with its labeling;**
- Diagnostic device if it complies with the labeling requirements and if the testing:
  - *Is noninvasive;*
  - *Does not require an invasive sampling procedure that presents significant risk;*
  - *Does not by design or intention introduce energy into a subject; and*
  - *Is not used as a diagnostic procedure without confirmation by another medically established diagnostic product or procedure.*
- Consumer preference testing, testing of a modification, or testing of a combination of devices if:
  - *the testing is not for determining safety/effectiveness AND does not put the subjects at risk*

IDE Flow Chart



Is the use of the device in the study significant risk?

- An investigational device that presents a potential for serious risk to the health, safety or welfare of a subject due to its intended use **AND** is used:
  - *As an implant **OR***
  - *For supporting or sustaining human life **OR***
  - ***Of substantial importance** in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health **OR***
  - *Presents some other serious risk to patient's health, safety, or welfare*

- If yes, an IDE application to FDA is required
- If the above definition is not met, the use of the device is non-significant risk and abbreviated IDE requirements apply.

Examples

Non-significant risk

- Conventional hospital catheters
- Digital mammography
- Elastic Band-Aids
- Conventional GI or Urology endoscopes
- Ob/Gyn diagnostic ultrasound within FDA parameters
- MRI used within FDA parameters
- EEG devices
- Daily wear contact lenses

Significant Risk

- Cardiovascular catheters
- Intravascular stents
- Breast implants
- Absorbable adhesion barrier devices
- Sutures
- Contraceptive devices
- Computer guided robotic surgery
- Extended wear contact lenses

Who decides the risk of the device?

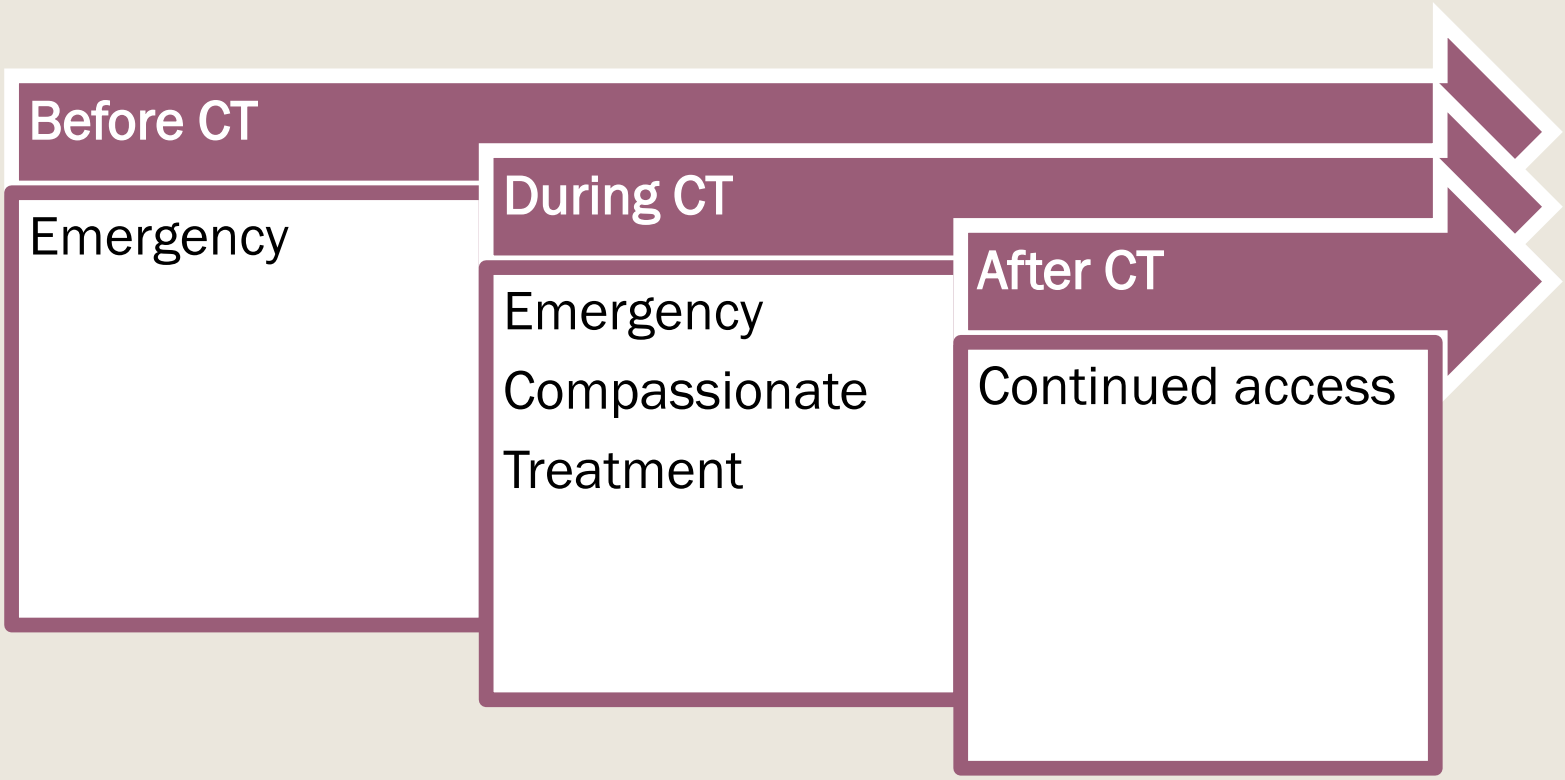
- Sponsor proposes an initial determination and rationale to the IRB
- Unless the FDA has made a SR/NSR risk determination, the IRB must review the sponsor's determination and agree or disagree with the sponsor's assessment at the time of initial review.
- The IRB is also responsible for documenting the findings in the IRB minutes and on the determination form.
- FDA is the final arbiter – when asked by the sponsor, investigator, or the IRB.

Tips for Risk Determinations

- Assess the overall risk of the study AND assess the risk of the device on the study.
  - *IRBs should not confuse their responsibility for making SR/NSR determinations with the concept of "minimal risk". The IRB has to make the SR/NSR determination and also look at the overall risk of the study.*
- Risk determination is based on the proposed use of a device in an investigation, not on the device. In essence, a device could be non significant risk on one protocol and significant risk on another protocol.
- If a device is marketed, how does FDA classify it (class I, II, or III)?
- If it is not marketed, is there another device on the market that is similar? If so, how is it classified by FDA?
- Review FDA guidance on risk determinations

Expanded Access of IDEs

- A health care provider may wish to use an unapproved device to save the life of a patient or to help a patient suffering from a serious disease or condition **for which there no other alternative therapy exists.**



Processes for IDE Expanded Access

Mechanism	Criteria	When? How many?	FDA approval?	Subject protections
Emergency use	Life threatening; no alternative; & no time for FDA approval	Before or after trial Limited to a few patients	No. Submit report after use	Independent assessment; IRB chair concurrence; informed consent
Compassionate use	Serious disease or condition & no alternative	During trial Individuals or small groups	Yes	Independent assessment; IRB chair concurrence; informed consent
Treatment IDE	Life threatening or serious; no alternative; controlled trial; & sponsor prusuing marketing approval	During trial. Wide access	Yes	IRB approval; informed consent
Continued access	Public health need or preliminary safety & effectiveness data	After trial Same rate as study.	Yes	IRB approval; Informed consent

Humanitarian Use Devices (HUD)

- A device that is intended to benefit patients in the treatment or diagnosis of diseases or conditions that affect < 8,000 individuals in the US each year.
- Regulatory Pathway: Requires submission and approval of a humanitarian device exemption (HDE) application by FDA
  - *HDE application not required to contain scientifically valid effectiveness data*
  - *HDE application must contain sufficient information for the FDA to determine that the probable benefit outweighs the risks and that no comparable devices are available.*

What are the IRB responsibilities?

- FDA requires IRB review and monitoring even though the activity is not considered research.
- Initial review of IRB's HUD application and consent form
  - *Check FDA website to confirm that the HDE is approved.*
  - *Confirm that the HUD is not being used as part of a clinical investigation designed to collect data to support an FDA premarket approval application.*
- Continuing review at least annually

What are the IRB responsibilities? (Cont.)

- Review the IRB application including:
  - *Name of device, FDA HDE number, date of HUD designation, indications for use, description of device, contraindications, warnings, precautions for use, adverse effects, alternative practices or procedures, marketing history, summary of previous studies*
- Review the consent document.
  - *Ensure that the consent document conforms with Penn requirements*
  - *Research HIPAA authorization not required. Patient signs standard HIPAA form.*
  - *The activity is considered treatment. Do not refer to as "Research" and the "study"*

Investigational Drugs

- A new drug or biologic requires submission of IND application to FDA
- Investigational use of an approved drug or biologic requires an IND if:
  - *Results will be reported to FDA in support of a new indication for use OR to support significant labeling change;*
  - *It is intended to support a significant change in advertising;*
  - *Any of the following **significantly increase the risks** OR **decrease the acceptability of the risks***
- Route of administration,
- Dose,
- Use in a subject population, or
- Some other factor

What are the IRB's responsibilities?

- If the study is being conducted under an IND
  - *Document this and the IND number*
- If the study is not being conducted under an IND or this is unclear:
  - *Require a formal IND exemption determination from one of the following entities:*
- FDA,
- SOM Office of Clinical Research, Sponsor Support Unit
- SOM Abramson Cancer Center (CTSRMC) for cancer trials,
- Radioactive Drug Research Committee (RDRC) for any radio isotopes,

Processes for IND Expanded Access

Mechanism	Criteria	When?	FDA approval?	Subject protections
Emergency use	Life threatening; no alternative; & no time for traditional IND submission	One subject; one time use	Yes; emergency IND	IRB review required unless IRB cannot convene in time; informed consent required unless 4 conditions are met. Requires 5 day report to IRB.
Open label protocol or open label IND	Uncontrolled study to allow subjects to continue until marketing approval is obtained	After trial has ended	Yes	IRB review & informed consent
Treatment IND	Serious or life-threatening; no satisfactory alternative; sponsor pursuing approval	Drug under investigation or after trial	Yes	IRB approval; informed consent

Criteria for Emergency Use

- The PI and a physician not participating in the clinical trial certify in writing that:
  - *The subject is confronted with a life threatening situation necessitating the use of the test article;*
  - *Informed consent cannot be obtained because of the inability of the subject to communicate with or obtain legally effective consent;*
  - *Time is not sufficient to obtain consent from the subject's legal representative; and*
  - *No alternative method of approved or generally recognized therapy is available that provides an equal or greater clikelihood of saving the subject's life.*

References & Resources

- Devices
  - *Definition of a Medical Device*
  - *IDE Regulations: 21 CFR Part 812*
  - *FDA's Guidance: Significant Risk vs. Non Significant Risk*
  - *FDA's Guidance: Humanitarian Use Devices*
  - *FDA's webpage: Device Expanded Access*
- Drugs
  - *IND Regulations: 21 CFR 312*
  - *FDA's webpage: Drug Expanded Access Information*
  - *FDA's Guidance: IND Exemption Guidance*