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## HSP/IRB Organizational & Administration

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### **1. Human Subjects Protection Program –**

- a. What is it (USC P&P Chapter 1)?
- b. Why is it needed (Amdur, 1-3)?
- c. What/who are the components?
- d. Who Reports to whom?

### **2. IRB Organization**

- a. Limits of IRB authority (Amdur, 1-7)
- b. Federal Oversight of IRBs (Amdur 1-6)
- c. IRB reporting structure (Amdur, 2-1)
- d. Functions of IRB office (Amdur, 2-4)
- e. The IRB Chair (Amdur, 3-2)
- f. Committee Size, Alternate Members, Consultants (Amdur, 3-5)
- g. Member Recruitment and Education (Amdur, 8-10)
- h. Investigator Training
- i. Policies and Procedures
- j. IRB Authority – approve, disapprove, modify, suspend, terminate
- k. Quorum requirements
- l. Other committee reviews (e.g. biosafety)
- m. expedited /exempt actions to all in minutes
- n. IT issues

### **3. Responsibilities and Authorities: Staff, Chair, Director**

- a. Minute taking
- b. what staff does/ is authorized to do
- d. what can staff approve ?eg a contingency?
- e. IRB Director/Chair/Staff responsibilities and authority
- f. IRB/ Staff/chair Education
- g . FWA/CIP
- h. privacy borad/hipaa/coi

# Concise Summary of Drug and Device Regulations

## IND Applications (21 CFR 312)

- IND allows a drug to be shipped from a sponsor to a site for the purpose of conducting clinical investigations (note: reference to shipping e.g. allows shipping across state lines)
  - New (unapproved) drug
  - Approved drug with new indication, new population, new route of administration
  - IND submitted by a sponsor or sponsor/investigator to FDA.
- **Treatment use** of an investigational new drug (21 CFR 312.34)
- makes promising new drugs available to very ill people before the drug is approved
  - 4 criteria must be met:
    - i. Intended to treat serious or immediately life-threatening disease
    - ii. No comparable alternative available
    - iii. The drug is covered by an IND
    - iv. The sponsor is pursuing approval of the drug
  - Sponsor or licensed practitioner submits protocol to FDA and must comply with all IND regulations
- **Emergency use exemption**
- Sometimes called “compassionate use” but that term is not defined or used in FDA or DHHS regulations
  - No IRB approval required, but must tell IRB within 5 days of use
  - Two required components:
    - i. Life-threatening situation in which no standard acceptable treatment is available
    - ii. No time for IRB to review
  - IRB acknowledges the emergency use only – NOT IRB “APPROVAL”
  - Single use only – subsequent uses must have prior IRB review and approval

- Must obtain informed consent (template usually supplied by sponsor)
- No equivalent regulation in Common Rule
- DHHS does not allow data to be used, FDA does allow data to be used for IND application

■ **Orphan Drug** (similar to HUD)

- To be discussed

**Investigational Device Exemptions\* (IDE) (21 CFR 812)**

\*exemption means ok to ship across state lines, otherwise shipping across state lines is prohibited for a new device

Categories of device investigations:

- Investigational Device Exemption (Significant Risk IDE)
- Abbreviated IDE (Nonsignificant Risk)
- Exemption from an IDE
- Treatment Use of an Investigational Device / Emergency Exception

1. Investigational Device Exemption (Significant Risk IDE)

- Device is used to diagnose, cure, mitigate, or treat disease, and has the potential for serious risk to subjects
- SR devices must have approved IDE from FDA before IRB can approve
- IDE submitted by sponsor
- Sponsor makes determination of SR, FDA must concur

2. Abbreviated IDE (Nonsignificant risk)

- Any device that doesn't meet SR criteria
- IRB approval required before use
- IRB confirms NSR determination
- No prior FDA approval needed for study (but marketing?)

3. Exemption from an IDE:

- Must meet requirements of one of the FDA exemption categories

- Must obtain IRB approval, (is FDA involved at all?)
4. Treatment Use of an Investigational Device / Emergency Exception
- Can be used for serious or life threatening condition, where no appropriate alternative exists
  - Most IRB's use their policy for emergency use/treatment use of investigational drugs to review emergency exception for devices (regs provide little guidance). (Darcy is this the same as the "treatment use" IND? Is this the same as "early expanded access involving a cohort or single subject?)

**Emergency Setting (this not the same as IND "emergency use exemption" see above**

(Emergency setting regulations/protocols can be for drugs or devices.)

- Criteria:
  - Subjects are in a life-threatening situation
  - Exception from Informed Consent because:
    - Subject's condition
    - LAR unavailable, person will die before LAR can sign
    - individual subjects can't consent – protocol defines subject population
  - Prospect of direct benefit to subjects
  - Research can't be done unless IC waived
  - Investigational plan defines the length of time PI can wait for LAR to consent
  - IRB approval and waiver of informed consent is required
  - Other protections:
    - Consultation with local community
    - Prior public disclosure to community
    - Disclosure of results to community afterward
    - Independent Data Monitoring Committee
  - IRB must ensure procedures are in place to notify subject/LAR ASAP

## ROUTES TO MARKETING: Drugs/Devices

(Note: this is NOT FDA approval for drug/ device testing which was required prior to this stage.)

Before a Drug or Device can be shipped across state lines, it must be cleared for marketing by the FDA. Devices can be cleared by the FDA in different ways, which are easier and less expensive than the IND process (IND to NDA). Note: FDA approvals to *market* (i.e. ship across state lines) are not approvals to test/treat subjects with the device (or drug).

### Routes to Marketing:

- ✓ New Drug Application (NDA): The NDA application is the FDA process for drug sponsors to formally propose that FDA approve a new pharmaceutical for sale and marketing in the U.S.
- ✓ Premarket Approval (PMA): Equivalent to the New Drug Application (NDA) process, a PMA is the FDA process for reviewing and evaluating the safety and effectiveness of Class III medical devices. PMA applications are submitted to the FDA after clinical trials have been completed. The FDA reviews the PMA application, and approves the device for marketing if the clinical trial data shows safety and efficacy.
- ✓ Substantial Equivalence “510k”: Sponsor claims that the device is substantially equivalent to an existing legally marketed device. If FDA agrees, sponsor can sell device, without any clinical testing. If FDA doesn’t agree, sponsor must conduct research in compliance with IDE regulations
- ✓ Exempt from “510K”: The FDA has a list of devices that are exempt from 510K. If the device is on the list, it can go to market without requesting FDA clearance (e.g. Class I devices).
- ✓ Extension of a Product Line: If the device company extends its product line (e.g. makes different sizes of the device), the company can add it to their catalog. But, they must include this new device in their annual report to the FDA.
- ✓ Reclassification: When a new device is constructed and is unlike any other existing device, it is automatically considered a class III. The sponsor can put in a request for the FDA to reclassify it as a class II device by submitting sufficient safety and efficacy data to the FDA.
- ✓ Humanitarian Use Device (HUD) – To qualify as a HUD, the device must be intended to benefit patients with conditions that affect fewer than 4,000 in US (similar to orphan drug). A Humanitarian Device Exemption (HDE) application

must be submitted to the FDA and approved. To market a HUD, it must receive a HUD designation, and the HDE must be approved by the FDA. HUD's allow local physicians to use the device at their institution. The use of a HUD is Not Research - it is treatment. IRB review is required even though it is not research. There is little guidance for IRBs for reviewing HUD protocols.