PD233: Design of Biomedical Devices and Systems

(Lecture-15 Clinical Trials)

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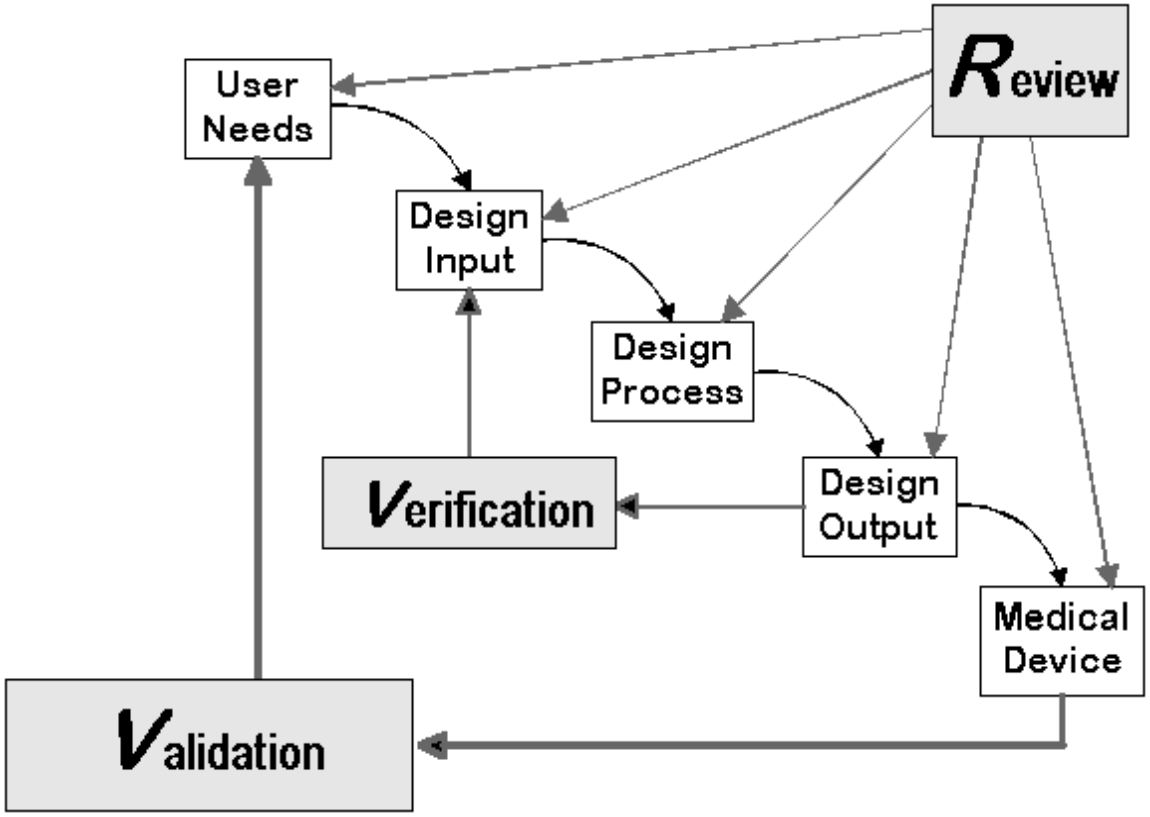
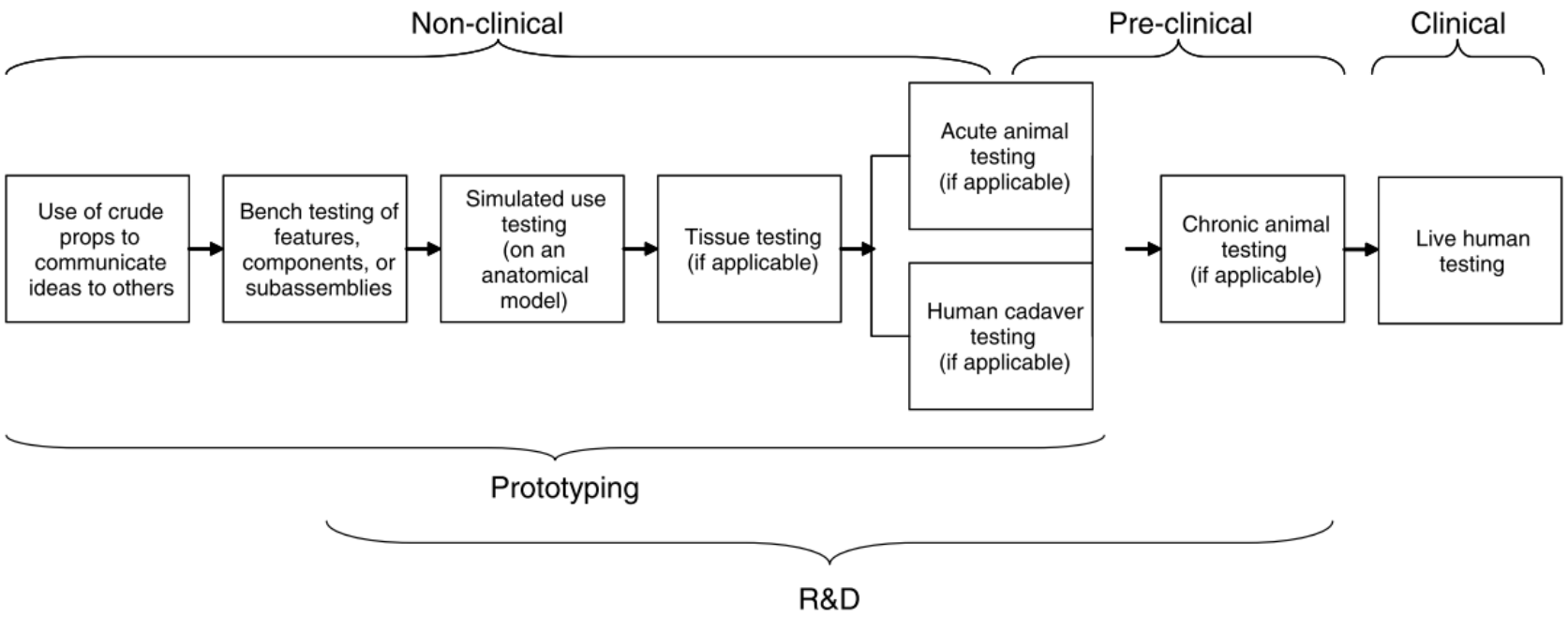
Course Website:
http://cpdm.iisc.ac.in/utsaah/courses/

V&V processes



Non-clinical, preclinical, clinical testing



Chapter 5, Zenios *et al*., Biodesign

Clinical Trials

Why?

- Regulatory approval
- Market acceptance
- Reimbursement

The main objective of clinical trials is to demonstrate that new device offers ***measurable, clinically important*** benefits to patients in terms of its ***effectiveness and safety***

Clinical Study Gaols

- Regulatory Approval:
  - What results are needed to support regulatory approval?
- Reimbursement:
  - Are economic outcomes important to support reimbursement decisions?
- Market Adoption:
  - What results would KOLs need to making their recommendations?
  - Will data be necessary to help market the device to physicians and/or patients?

Clinical study may be carried out to address one or more of the above

FDA regulatory pathway

Pathway	Description
Device exemption	These are devices for which the risk is so low that they are exempt from regulatory clearance. Most class I devices take this pathway.
510(k)	This is the largest category of medical device applications, in which clearance is based on a device being similar to existing devices in clinical use. Some class I devices and most class II devices take this pathway.
Premarket approval (PMA)	This is the most stringent pathway, used for devices that are significantly different from existing technologies and/or represent the highest risk to patients. The vast majority of class III devices take the PMA pathway, although a few remain eligible for 510(k) clearance.

Pilot Clinical Investigation

- **First-in-human studies**
- Small scale, preliminary human studies
- Primary objective is establishing safety
  - Though investigators observe if the device performs as indented
- 10-100 cases performed in real world setting as **Registry of cases or Observational studies**
- Learn enough about device to design a definitive trial of the device
- **Case Controlled studies** allow statistical comparison of group of patient treated with new device or procedure to a matched group with no treatment or standard treatment.

Prospective, randomized controlled (blinded) trials

- Gold Standard of medical device testing
- Have statistical ‘power’ to discriminate whether or not the outcome and safety profile of the new device indeed superior **to the control group**.
- In ‘double blind’ trials both the patients and the physician are blind to the treatment
- Also know as **pivotal trial**

Post-market studies

- After commercial approval of the device
- Maybe required as part of Pre-market approval (PMA)
- But also useful as part of overall strategy e.g. for getting reimbursement etc.

Clinical trial cost:

- The **cost of the device(s)** being used in the trial.
- The **cost of performing the procedure**, including physician costs and hospitalizations, if needed.
- The **costs of follow-up clinical visits** and/or tests to evaluate the safety and efficacy of the medical device.
- The **cost of paying investigators and institution study coordinators** to perform the clinical studies.
- The cost of conducting the trial, including training, monitoring, and data management.
- Patient recruitment costs, including advertising and potential payment to patients.
- In-house management and personnel costs.
- The cost of trial support and other resources provided by contract research organizations (CROs).
- Institutional review board (IRB) costs.
- Consulting expenses for **data safety monitoring boards, physician advisory boards, and core laboratories** to independently evaluate trial results.

2000 – 100,000 USD per patient depending on complexity in US

Cost in India substantially lower but significant

Institute Review Board (IRB) approval

- For any study on non-approved medical device approval of IRB is required to assess safety of patients during the trail
- IRB is responsible for protecting the rights, safety, and welfare of research subjects
  - monitoring complications
  - screening point for issues of conflict of interest
- IRB may include statistical experts and ‘lay’ person
- Lead investigator is responsible for designing the study protocol

Investigative Device exemption (IDE)

- Devices with significant risk require IDE as part of PMA process
- Needed to before clinical trail in human can being
  - Obtained from ‘Competent Authority’
  - Purpose to assess that risk outweighed by potential benefit to subjects and knowledge gained and investigation is scientifically sound.
- Once IDE approval is obtained ‘investigational device’ can be legally used for clinical trials.

Funding sources for individual innovators and startups:

- Fellowship:
  - Entrepreneur in Residence Schemes e.g. DesIC
  - SPARSH fellowship - BIRAC
  - Social Alpha
  - Biodesign fellowship (International School of BioDesign)
  - CHFE
- Idea to PoC grant schemes
  - Biotechnology Ignition Grant (BIG) - BIRAC
  - Elevate- 100 Government of Karnataka
  - Grand Challenges Explorations (BMGF)
- Incubator/ Accelerator
  - TBI-CPDM
  - C-CAMP
  - IKP Eden