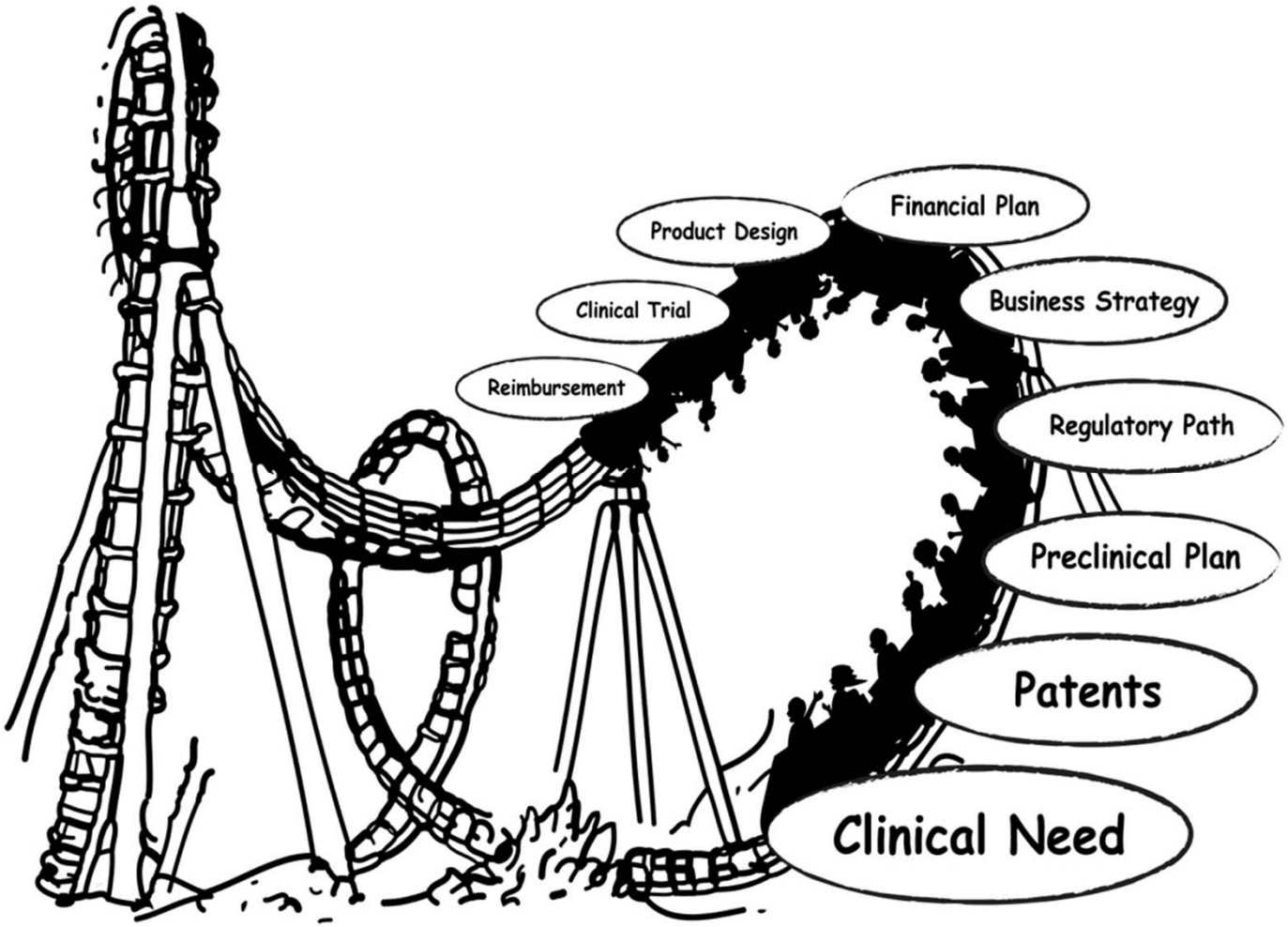
Translational Medicine Symposium 2013:
The Roller Coaster Ride to the Clinic



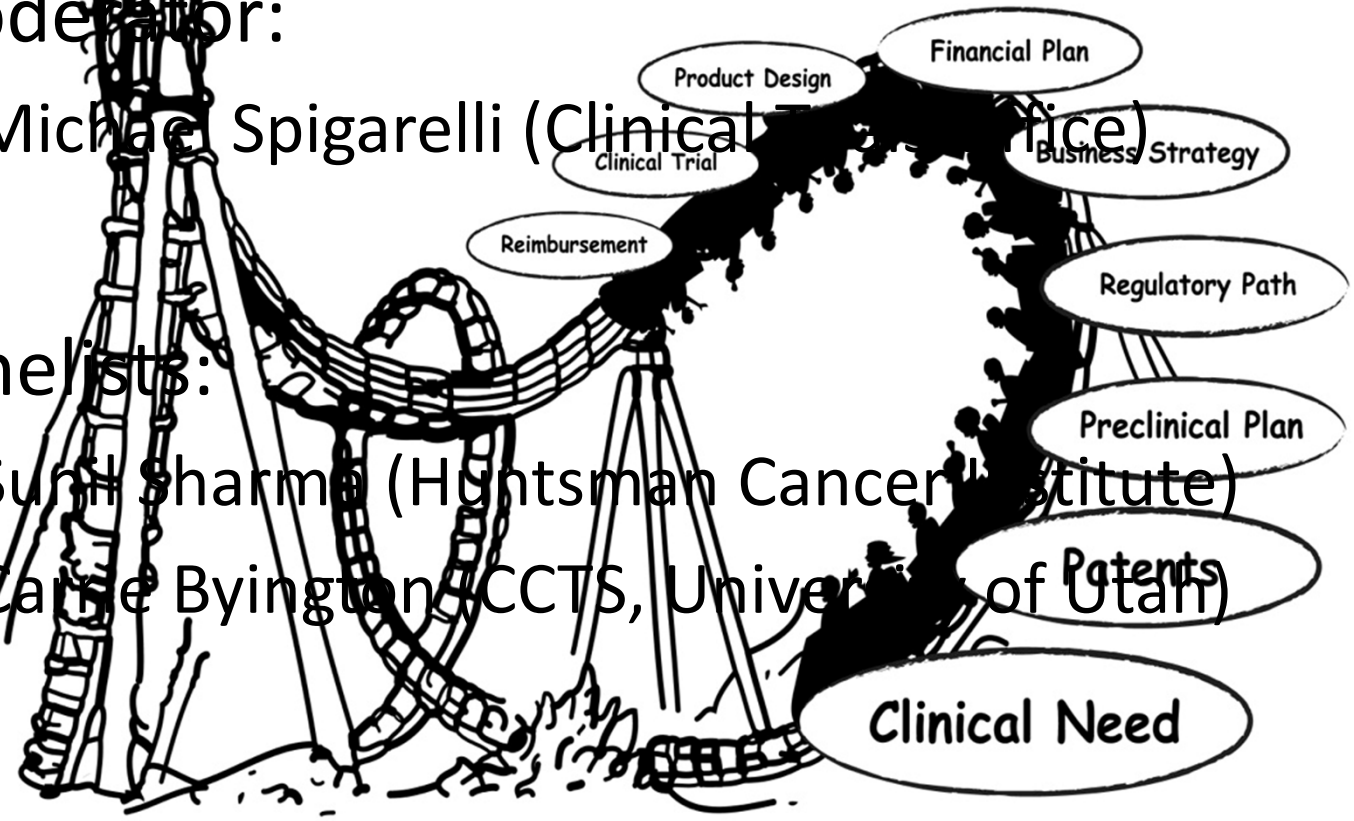
TRANSLATIONAL MEDICINE SYMPOSIUM 2013

CLINICAL DEVELOPMENT AND TRIALS

Bench to Business to Bedside:
The Roller Coaster Ride to the Clinic

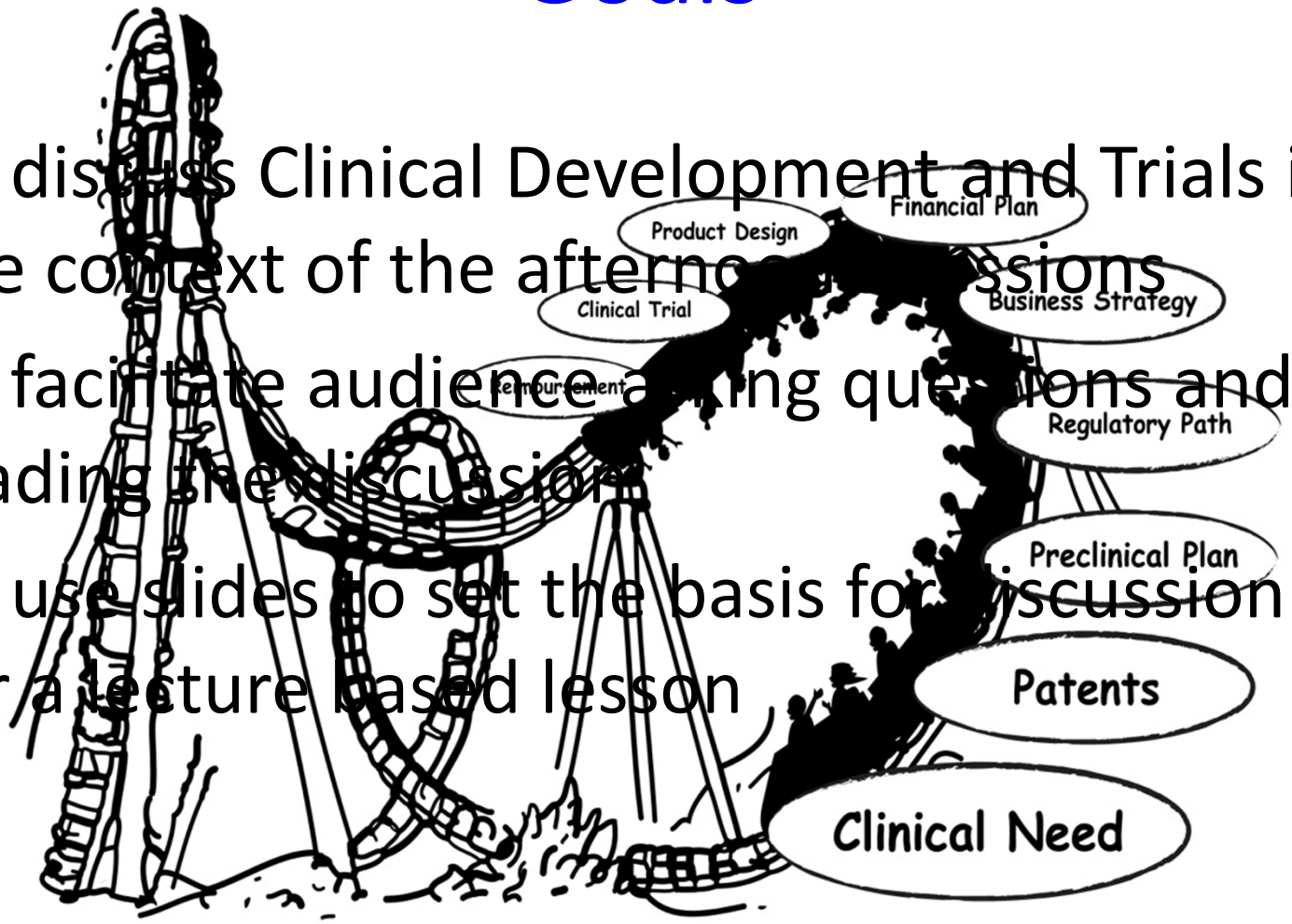
Introductions

- Moderator:
  - Michael Spigarelli (Clinical Translational Office)
- Panelists:
  - Sunil Sharma (Huntsman Cancer Institute)
  - Carrie Byington (CCTS, University of Utah)



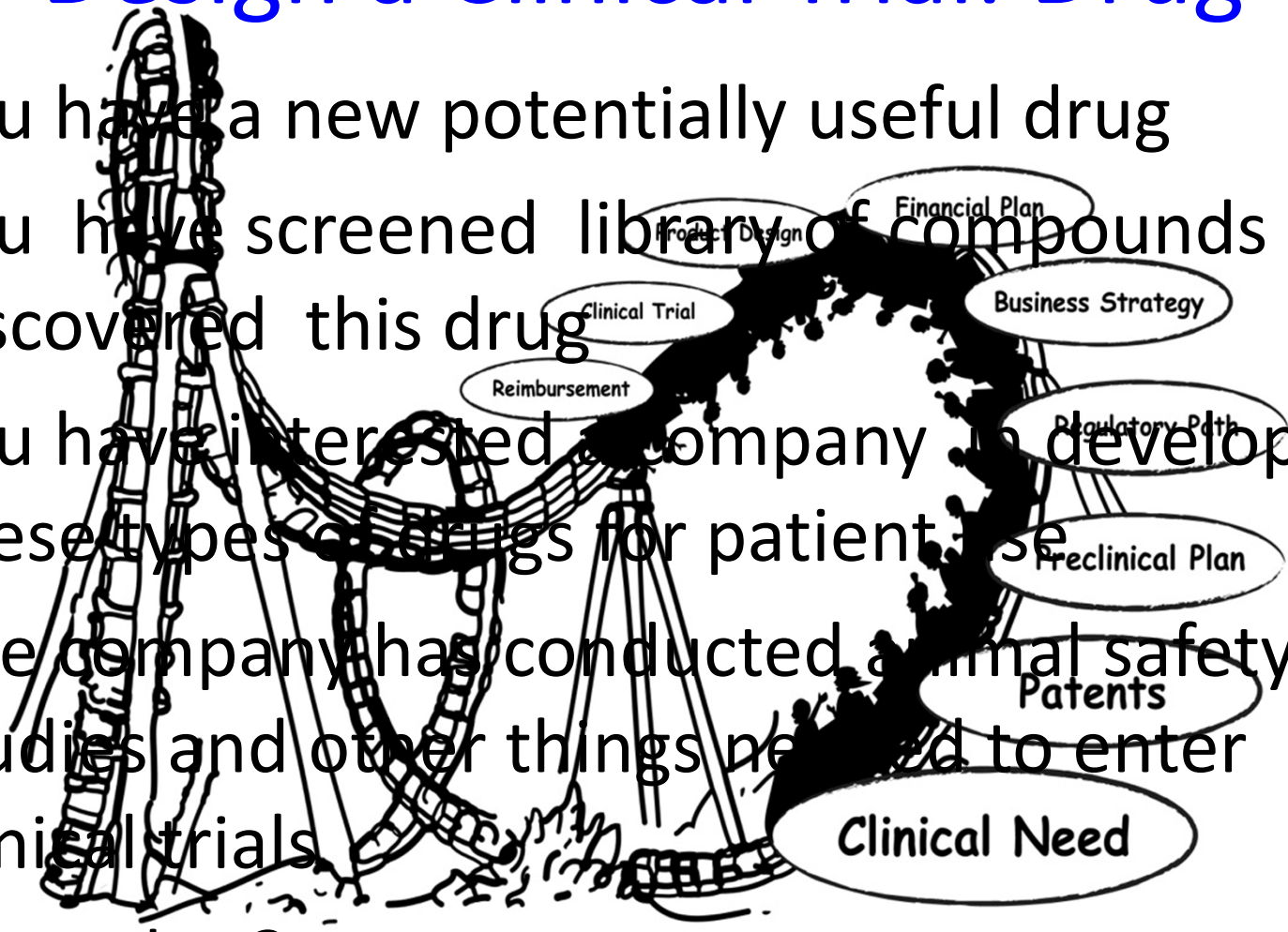
Goals

- To discuss Clinical Development and Trials in the context of the afternoon sessions
- To facilitate audience asking questions and leading the discussion
- To use slides to set the basis for discussion not for a lecture based lesson



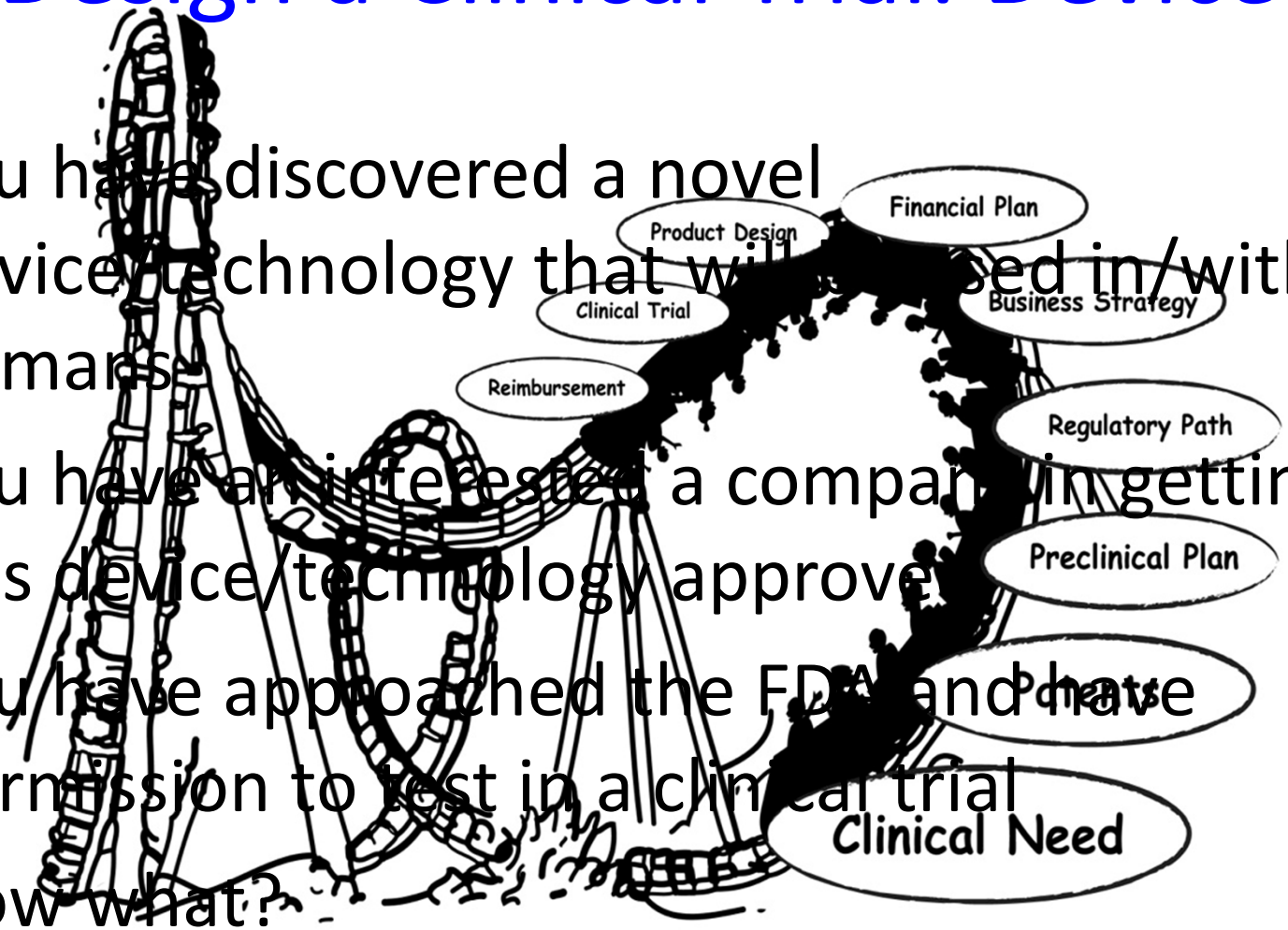
Design a Clinical Trial: Drug

- You have a new potentially useful drug
- You have screened library of compounds and discovered this drug
- You have interested company in developing these types of drugs for patient use
- The company has conducted animal safety studies and other things needed to enter clinical trials
- Now what?



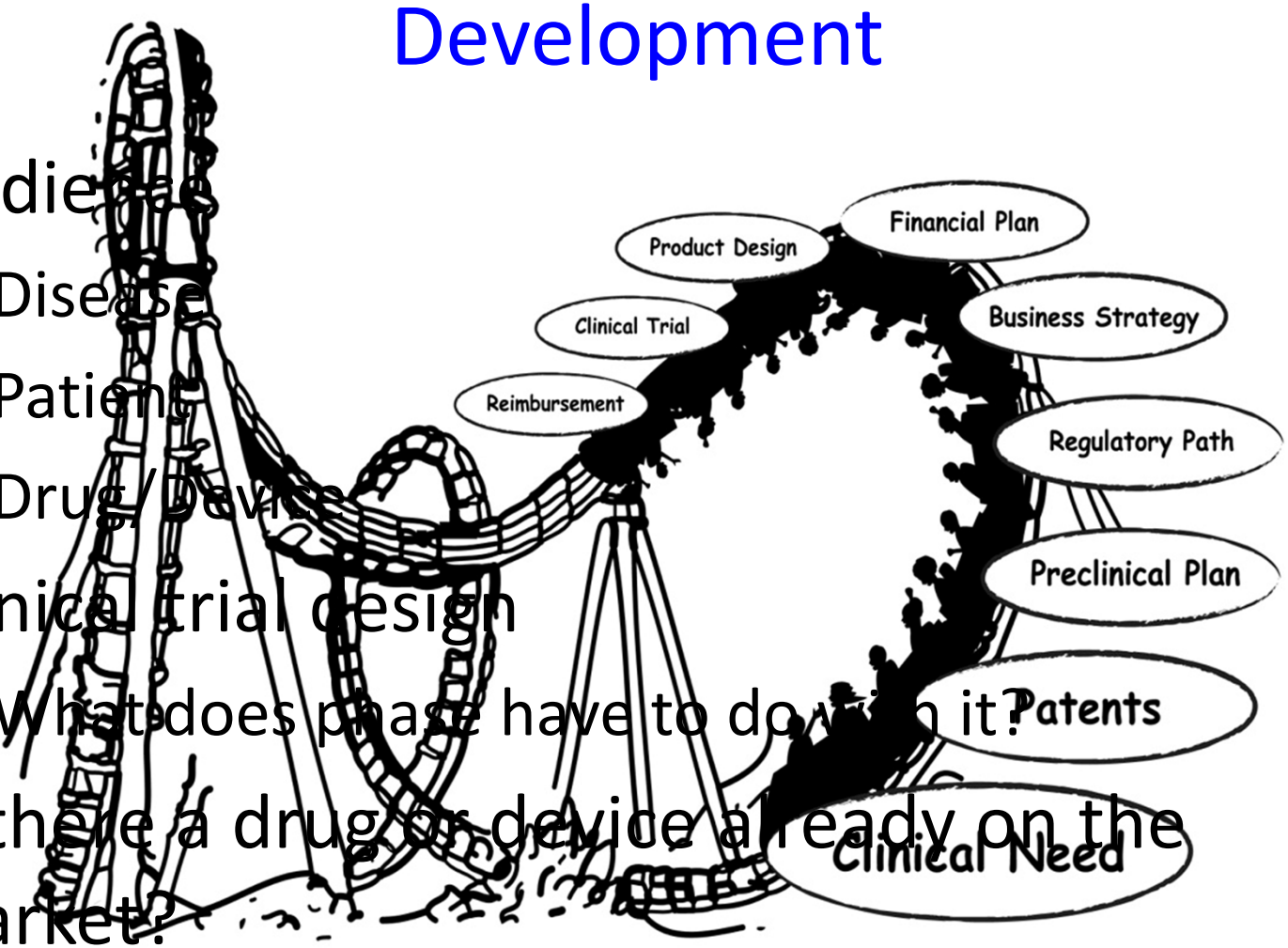
Design a Clinical Trial: Device

- You have discovered a novel device/technology that will be used in/with humans
- You have an interested a company in getting this device/technology approved
- You have approached the FDA and have permission to test in a clinical trial
- Now what?



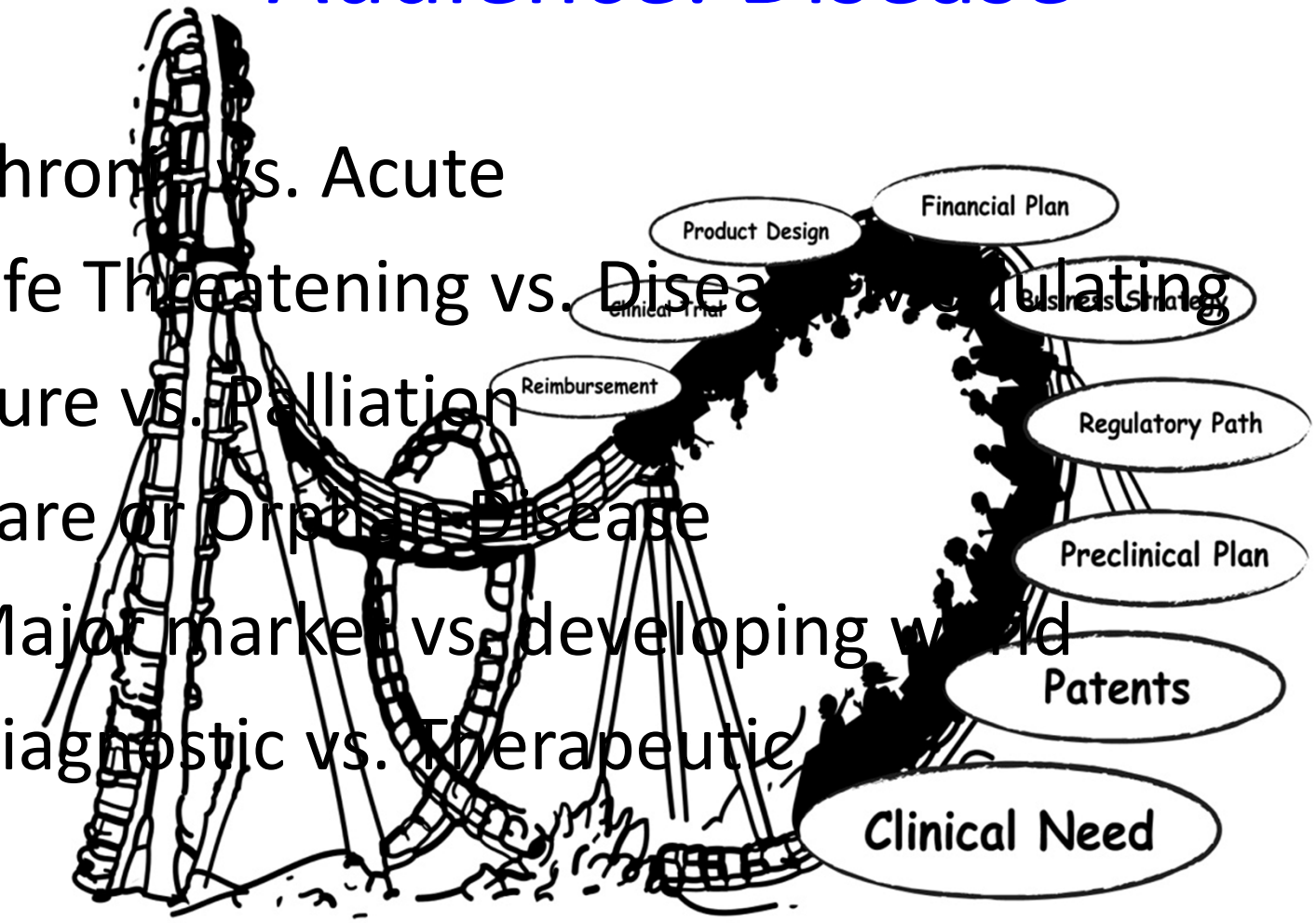
Considerations in Clinical Trial Development

- Audience
  - Disease
  - Patient
  - Drug/Device
- Clinical trial design
  - What does phase have to do with it?
- Is there a drug or device already on the market?



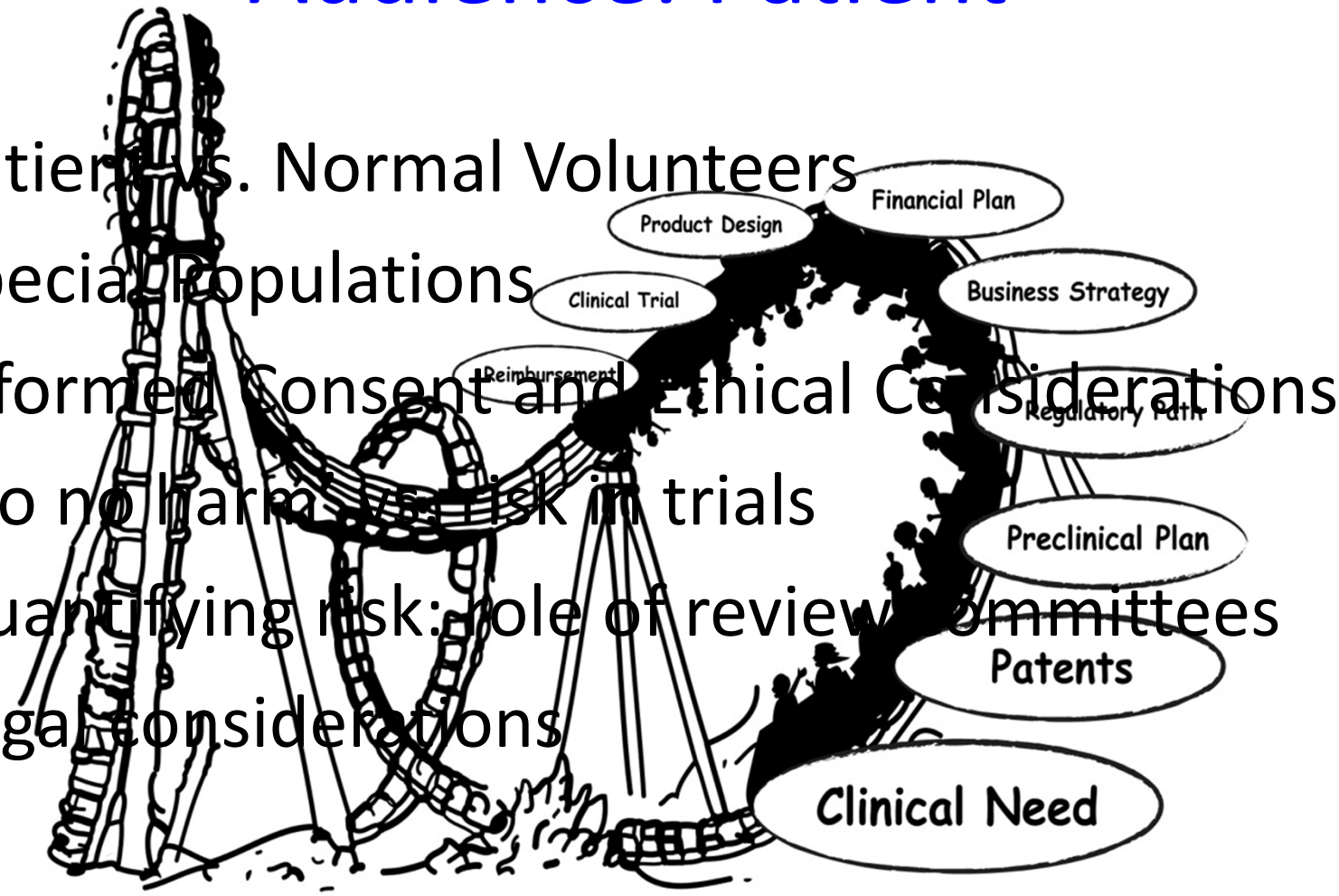
Audience: Disease

- Chronic vs. Acute
- Life Threatening vs. Disease Modulating
- Cure vs. Palliation
- Rare or Orphan Disease
- Major market vs. developing world
- Diagnostic vs. Therapeutic



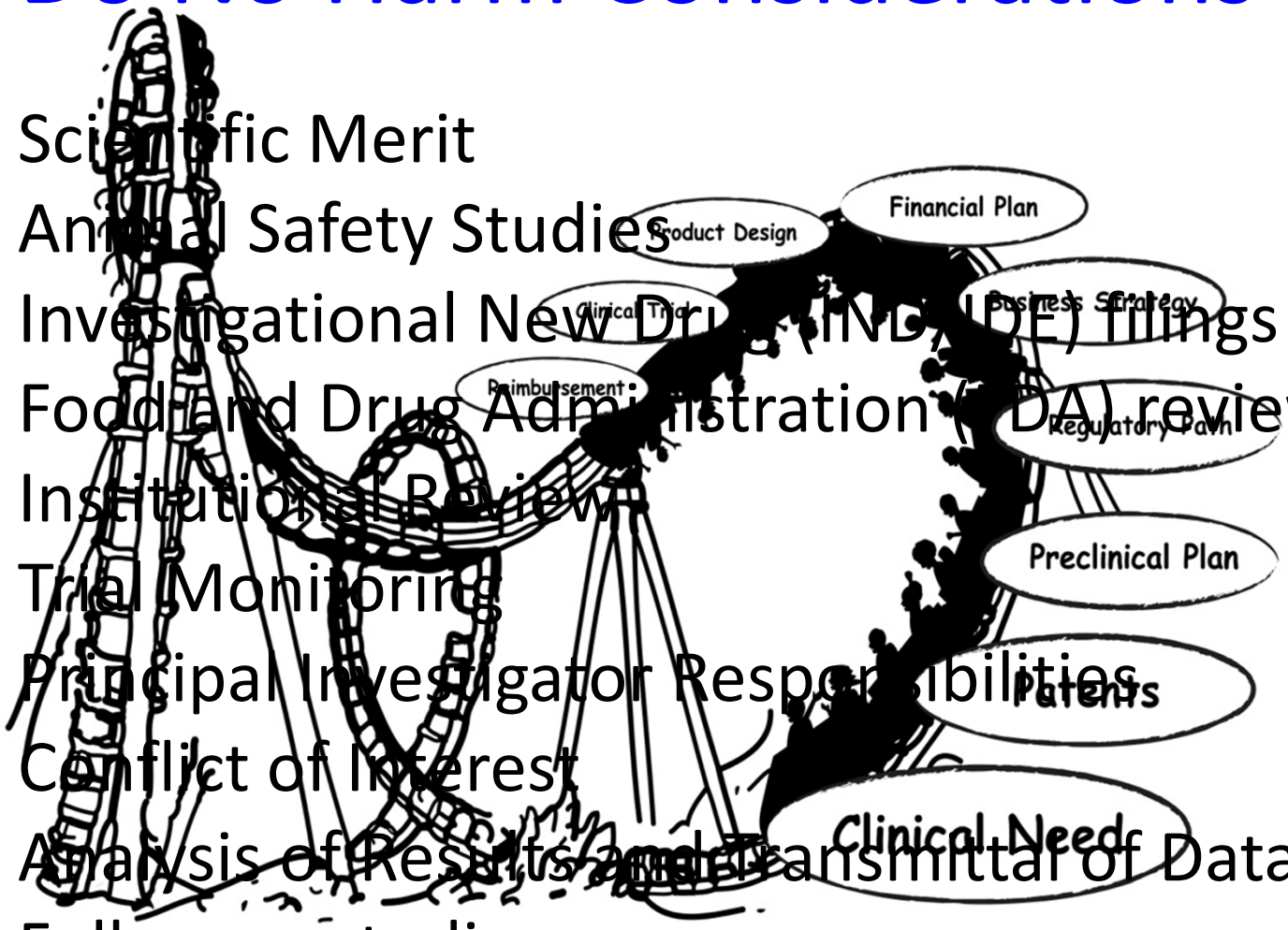
Audience: Patient

- Patient vs. Normal Volunteers
- Special Populations
- Informed Consent and Ethical Considerations
- ‘Do no harm’ vs. risk in trials
- Quantifying risk: role of review committees
- Legal considerations



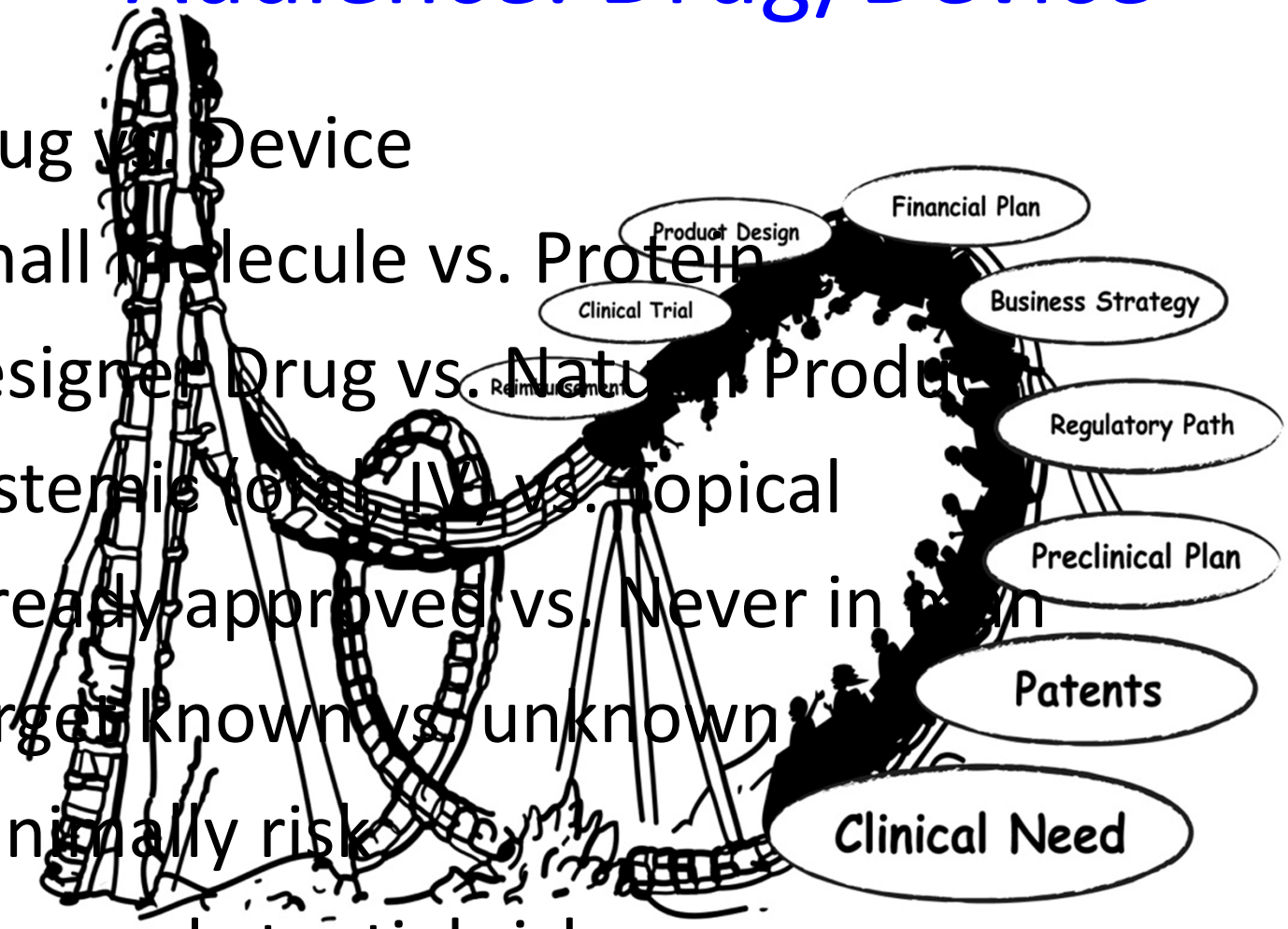
Do No Harm Considerations

- Scientific Merit
- Animal Safety Studies
- Investigational New Drug (IND, IDE) filings
- Food and Drug Administration (FDA) review
- Institutional Review
- Trial Monitoring
- Principal Investigator Responsibilities
- Conflict of Interest
- Analysis of Results and Transmittal of Data
- Follow up studies

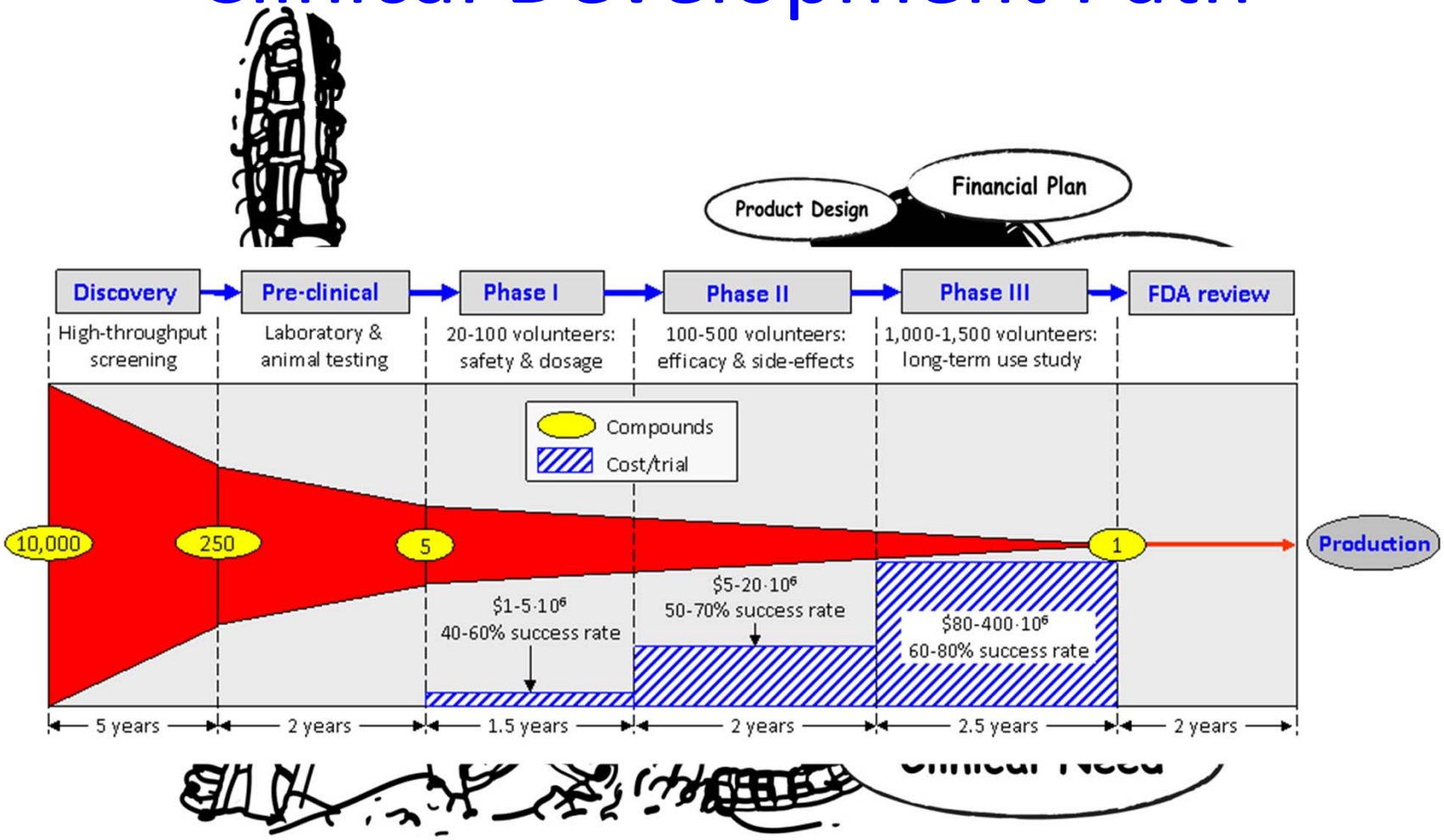


Audience: Drug/Device

- Drug vs. Device
- Small molecule vs. Protein
- Designer Drug vs. Natural Product
- Systemic (oral, IV) vs. Topical
- Already approved vs. Never in man
- Target known vs. unknown
- Minimally risky
- More substantial risk



Clinical Development Path



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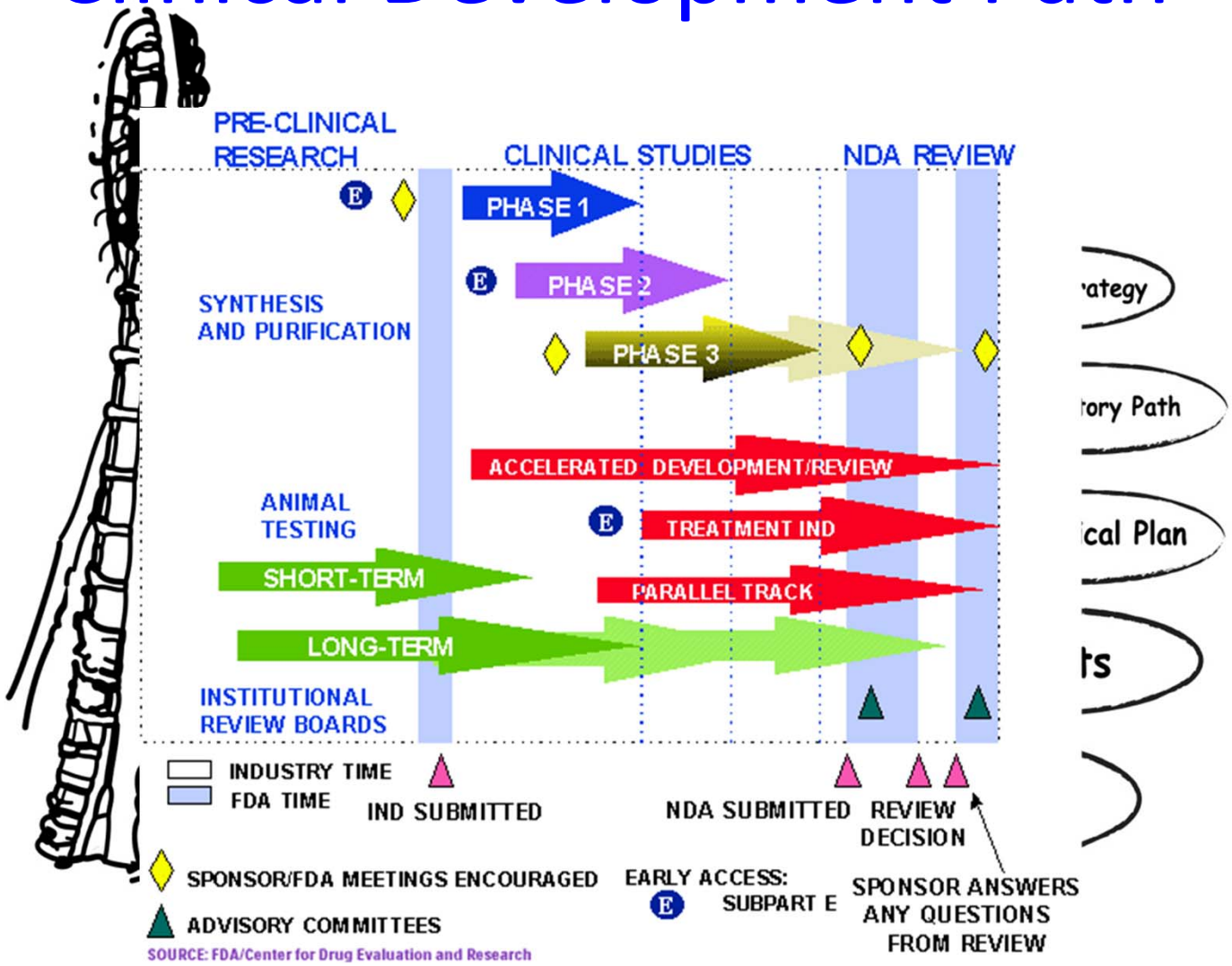
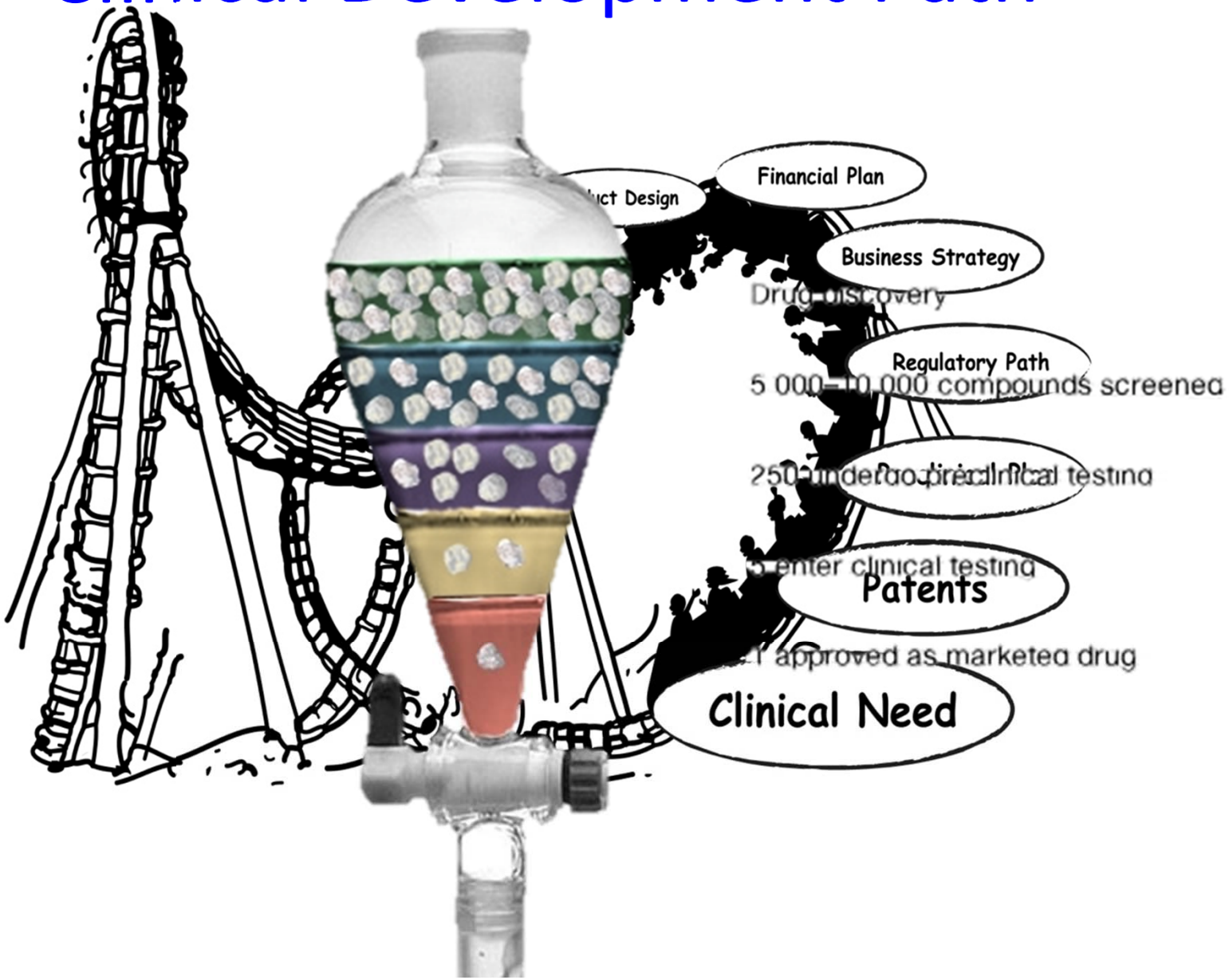
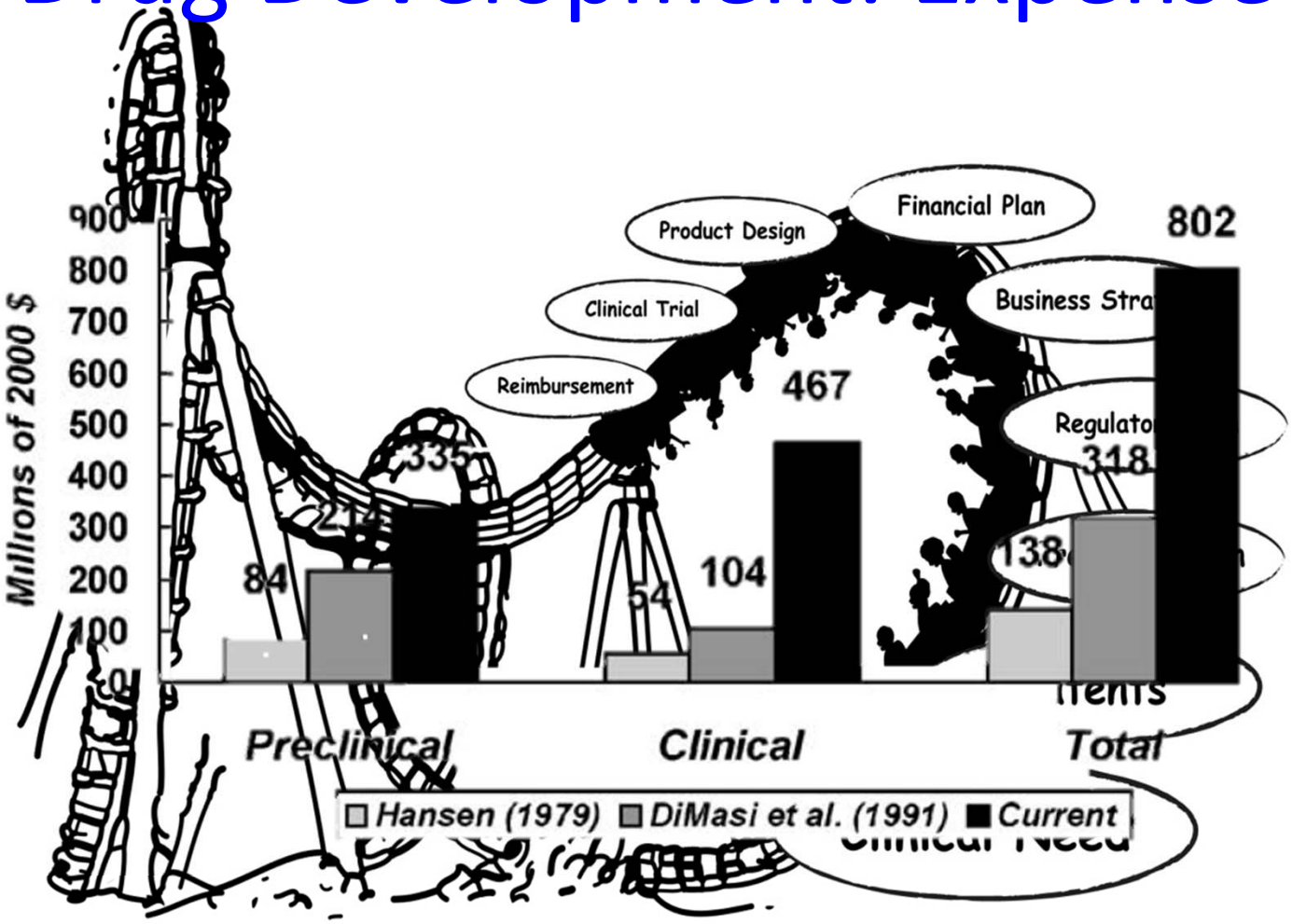


Clinical Development Path



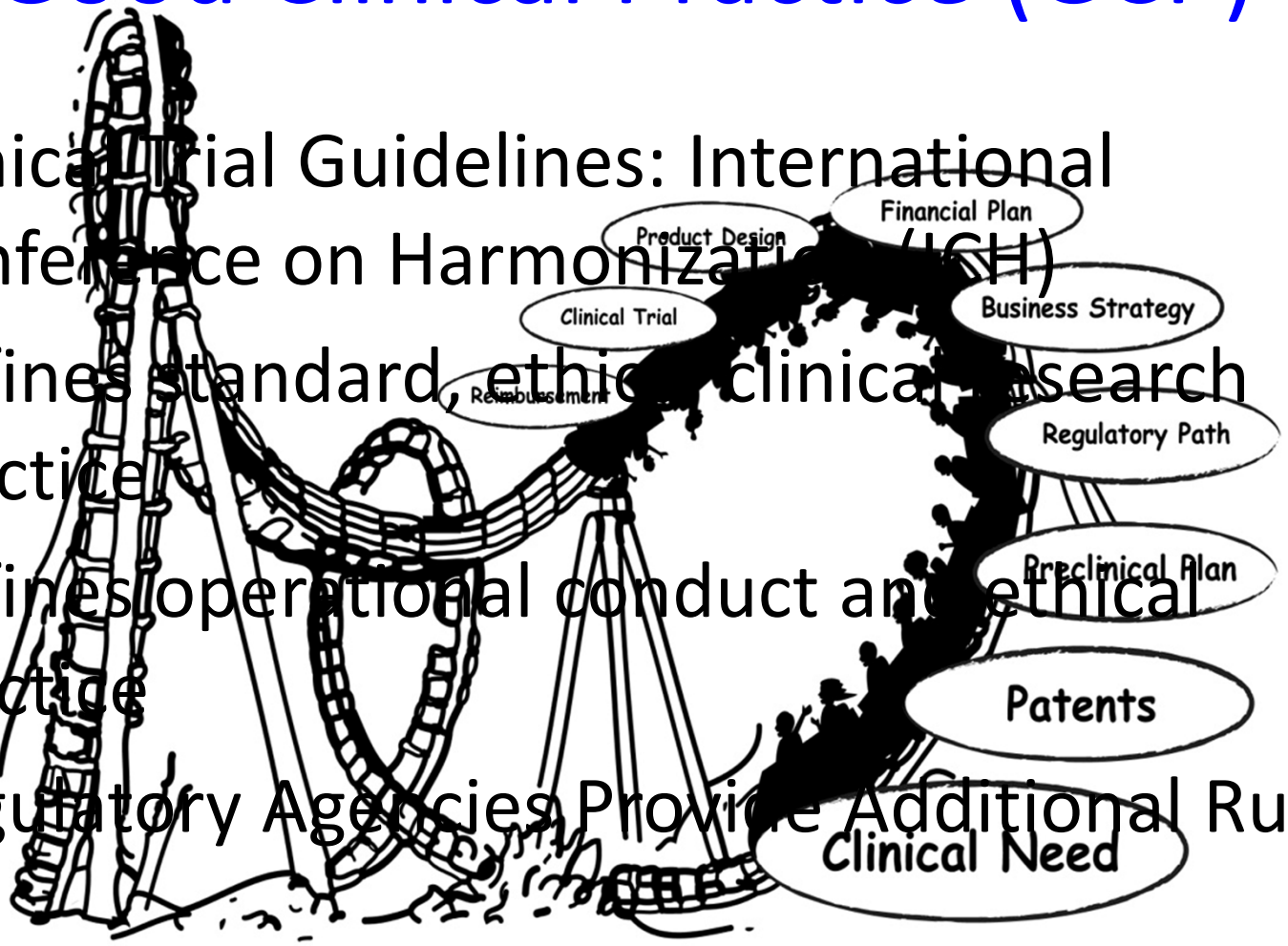
Drug Development: Expense



DiMassi et al 2003

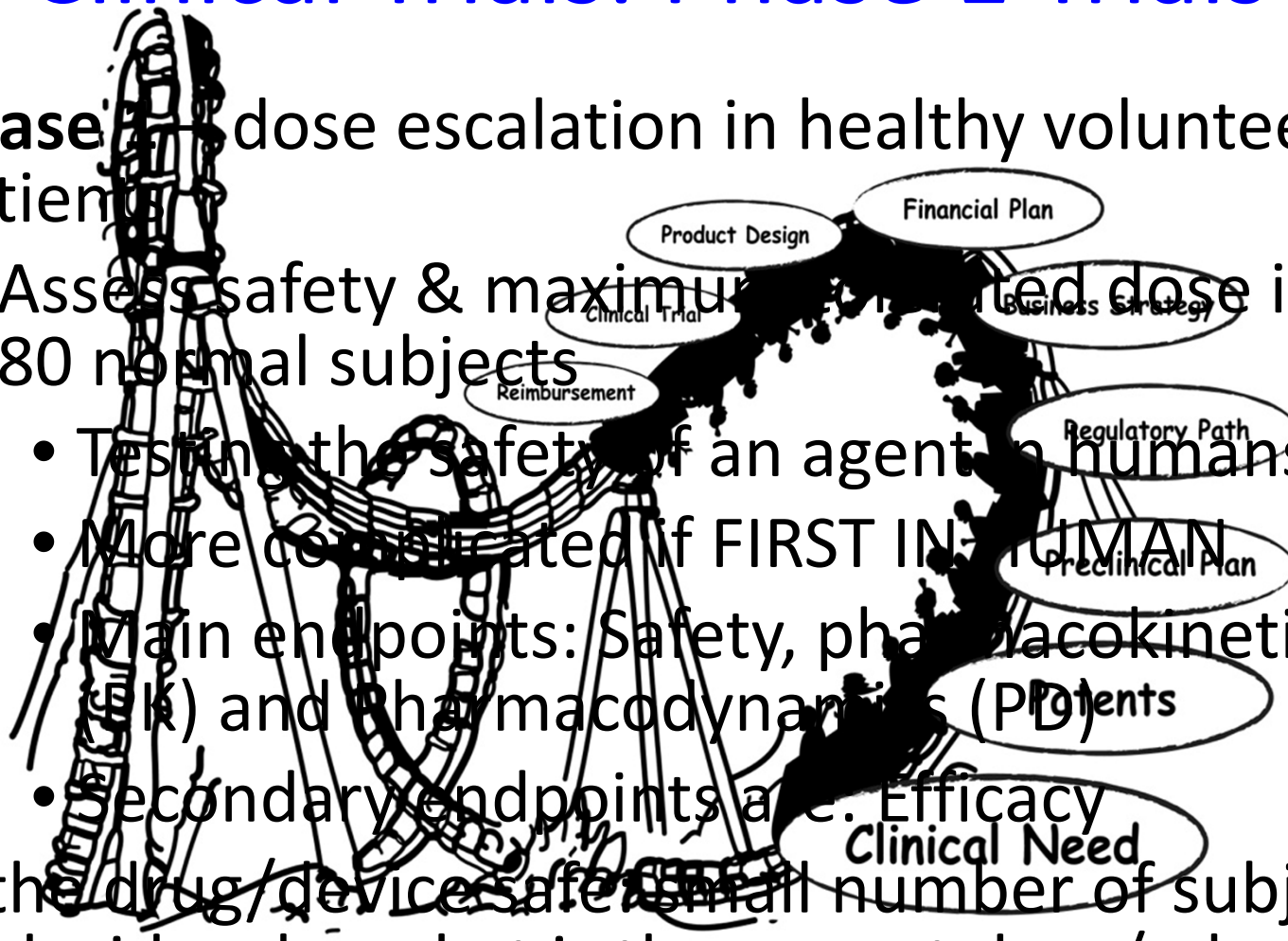
Good Clinical Practice (GCP)

- Clinical Trial Guidelines: International Conference on Harmonization (ICH)
- Defines standard, ethical, clinical research practice
- Defines operational conduct and ethical practice
- Regulatory Agencies Provide Additional Rules



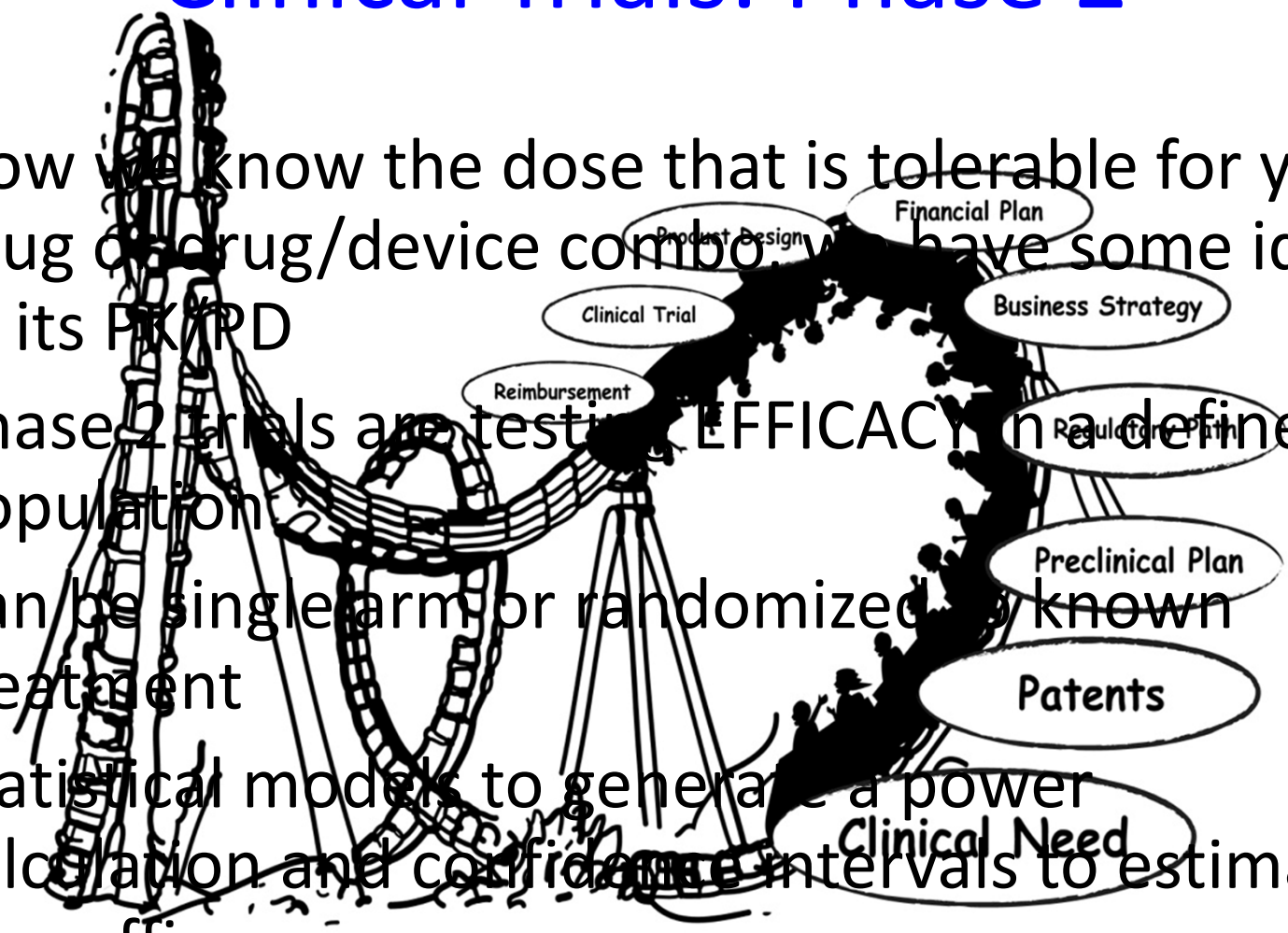
Clinical Trials: Phase 1 Trials

- **Phase I** – dose escalation in healthy volunteers or patients
  - Assess safety & maximum tolerated dose in 20-80 normal subjects
    - Testing the safety of an agent in humans
    - More complicated if FIRST IN HUMAN
    - Main endpoints: Safety, pharmacokinetics (PK) and Pharmacodynamics (PD)
    - Secondary endpoints are: Efficacy
- Is the drug/device safe in small number of subjects to decide, also what is the correct dose/schedule?



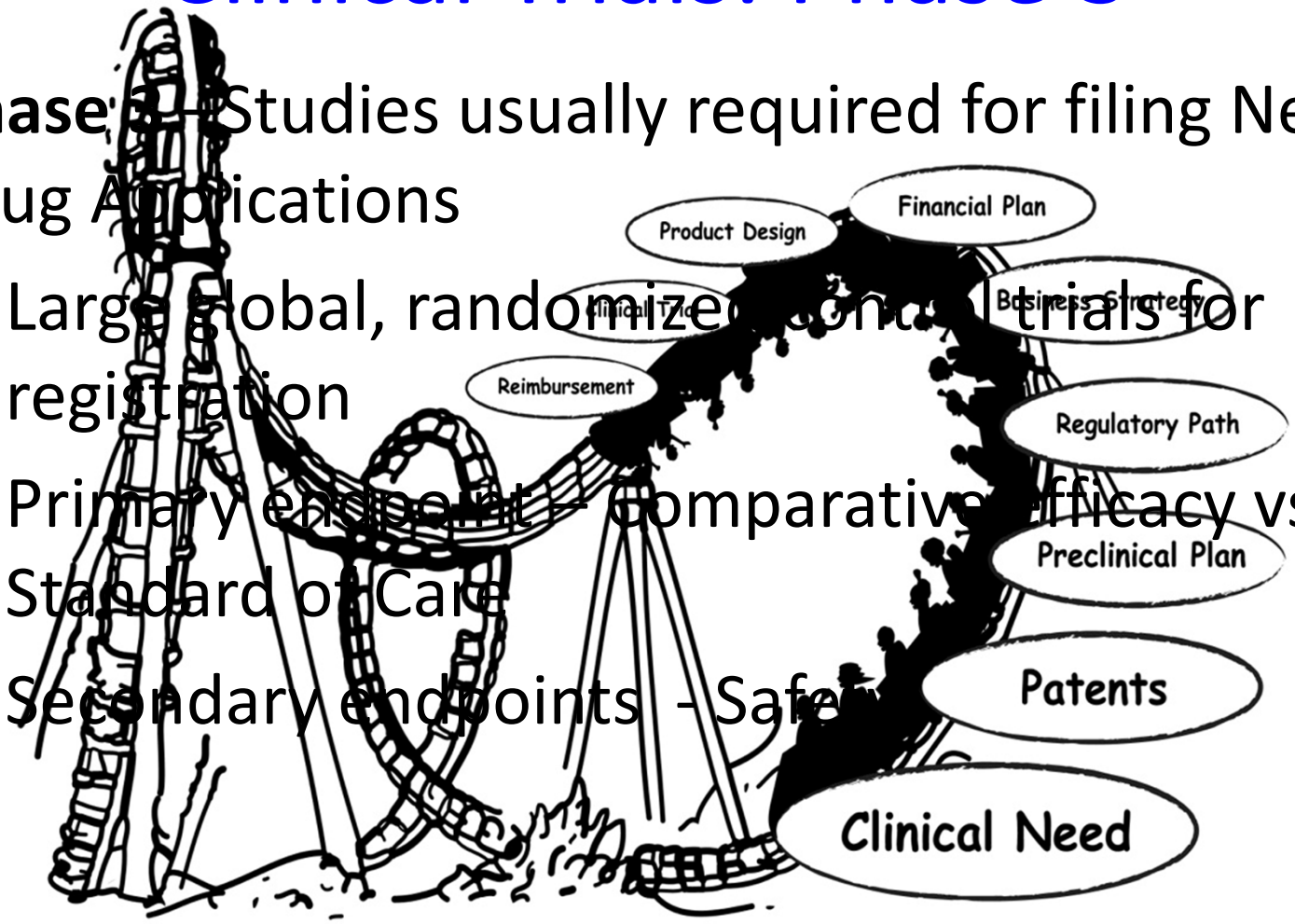
Clinical Trials: Phase 2

- Now we know the dose that is tolerable for your drug or drug/device combo, we have some idea of its PK/PD
- Phase 2 trials are testing EFFICACY in a defined population
- Can be single arm or randomized to known treatment
- Statistical models to generate a power calculation and confidence intervals to estimate true efficacy



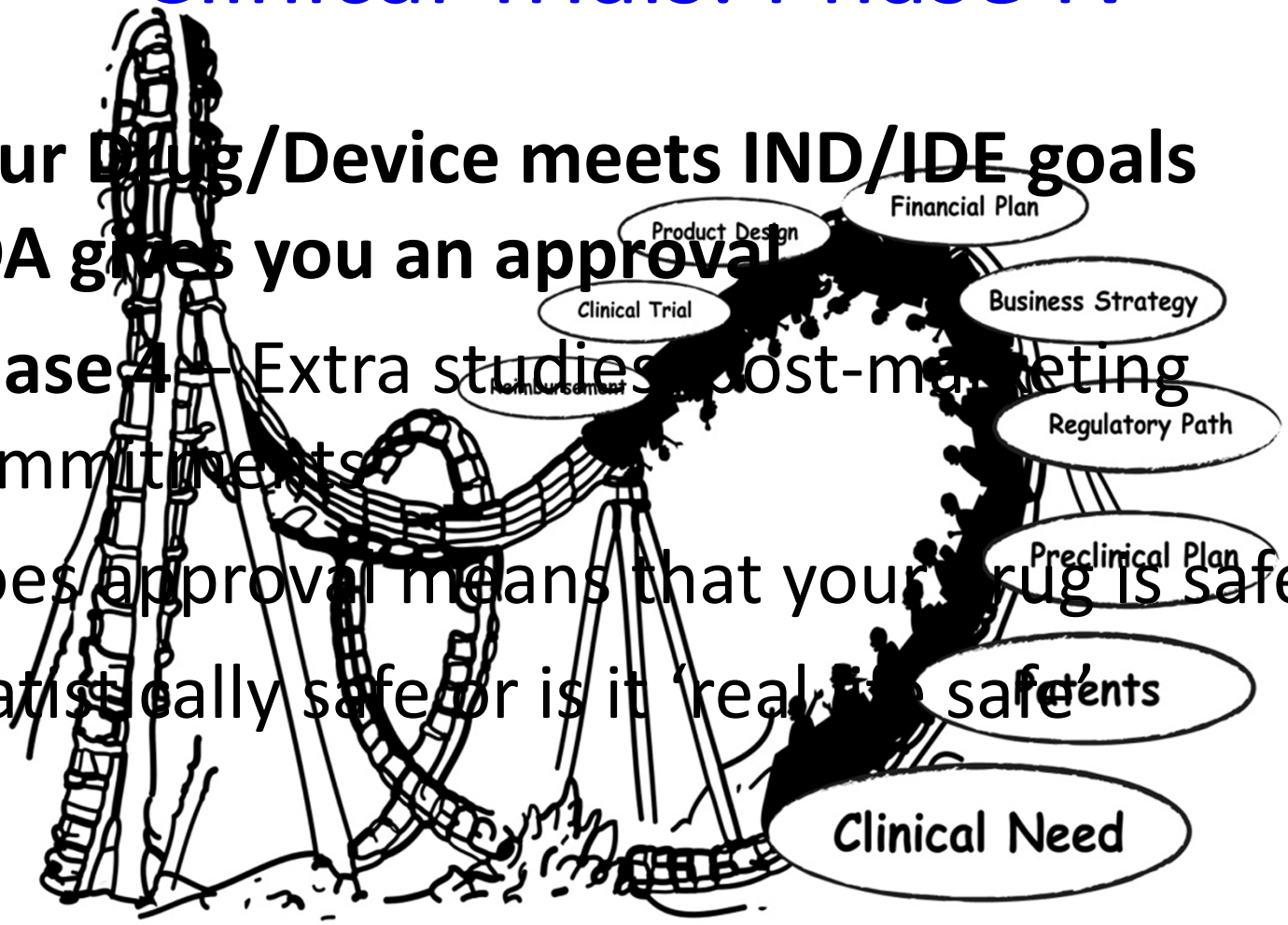
Clinical Trials: Phase 3

- **Phase 3** – Studies usually required for filing New Drug Applications
  - Large global, randomized controlled trials for registration
  - Primary endpoint – comparative efficacy vs Standard of Care
  - Secondary endpoints – Safe



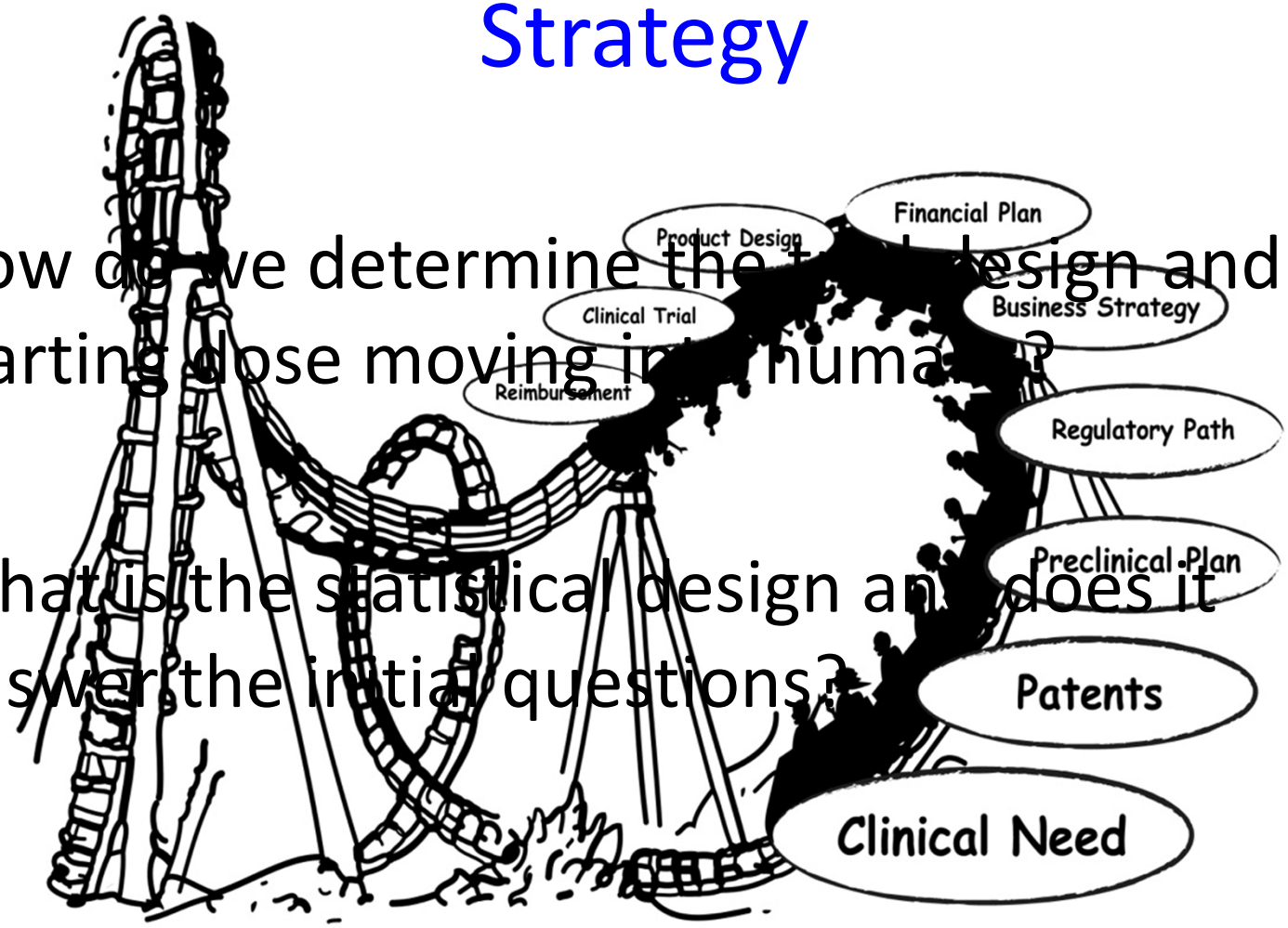
Clinical Trials: Phase IV

- **Your Drug/Device meets IND/IDE goals FDA gives you an approval**
- **Phase 4** – Extra studies post-marketing commitments
- Does approval means that your drug is safe?
- Statistically safe or is it 'real' safe



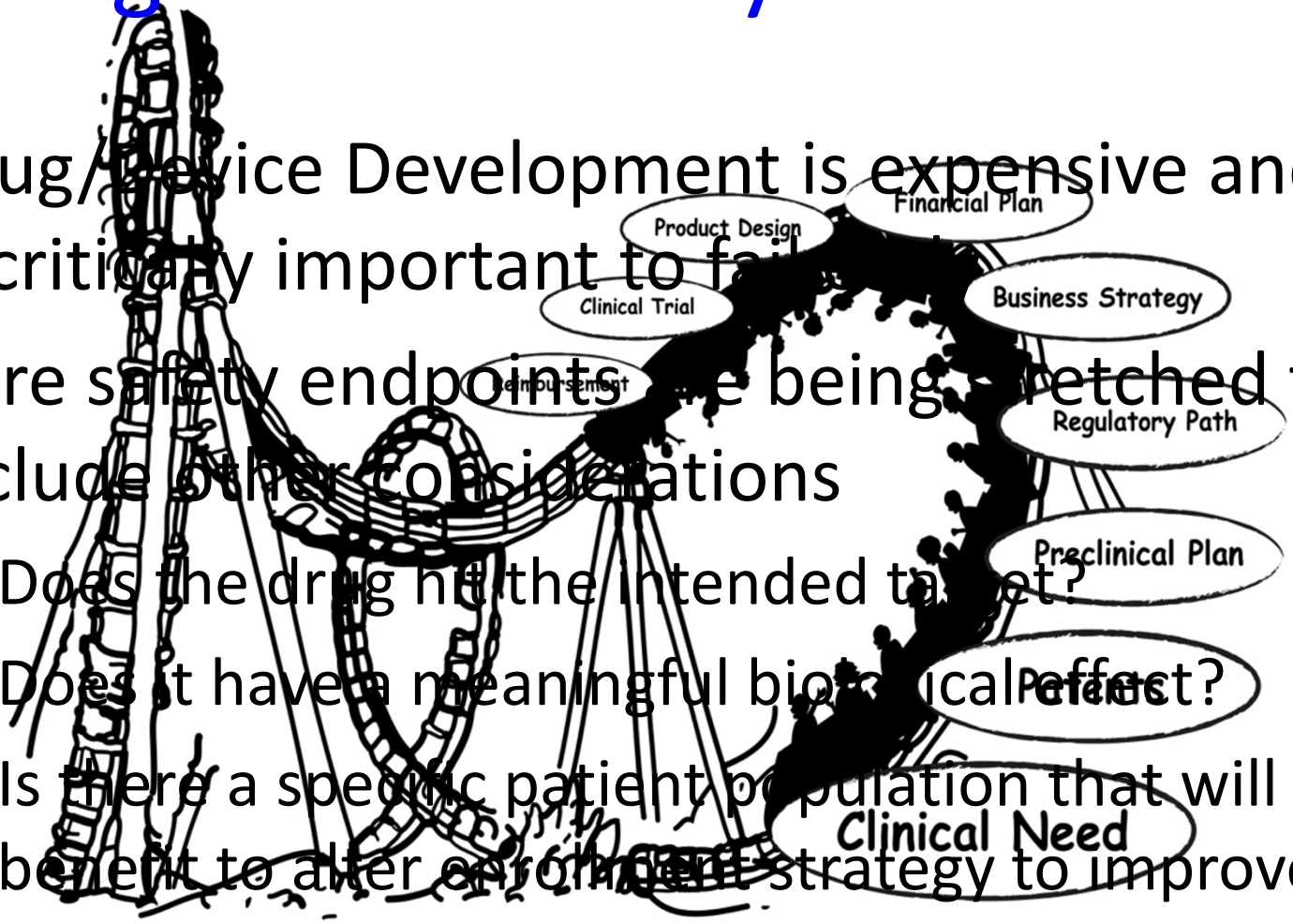
Determining the First in Human (FIH) Strategy

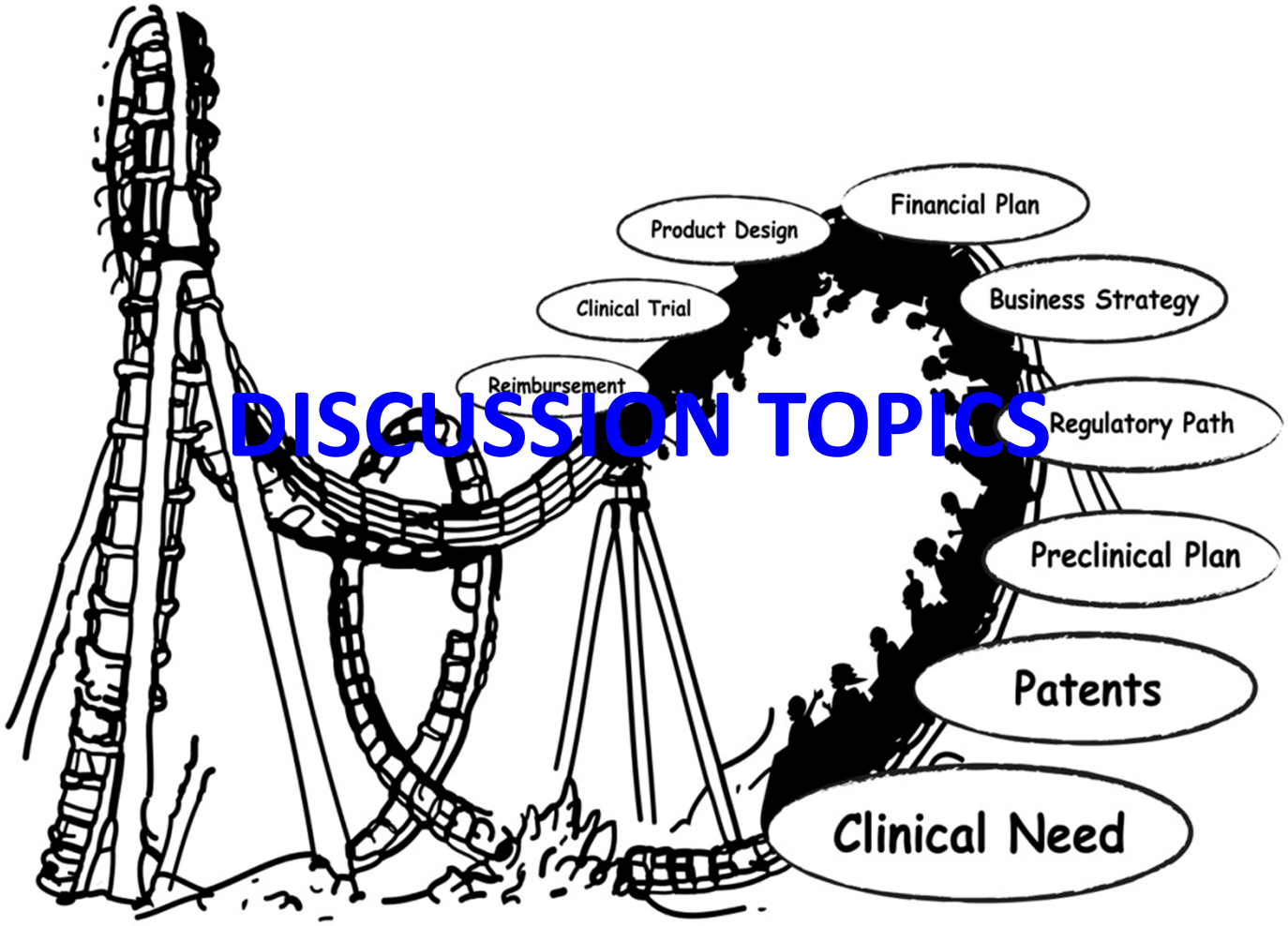
- How do we determine the trial design and starting dose moving into human?
- What is the statistical design and does it answer the initial questions?



Doing More in Early Clinical Trials

- Drug/Device Development is expensive and it is critically important to fail
- Pure safety endpoints are being stretched to include other considerations
  - Does the drug hit the intended target?
  - Does it have a meaningful biological effect?
  - Is there a specific patient population that will benefit to alter enrollment strategy to improve response rates in early trials?

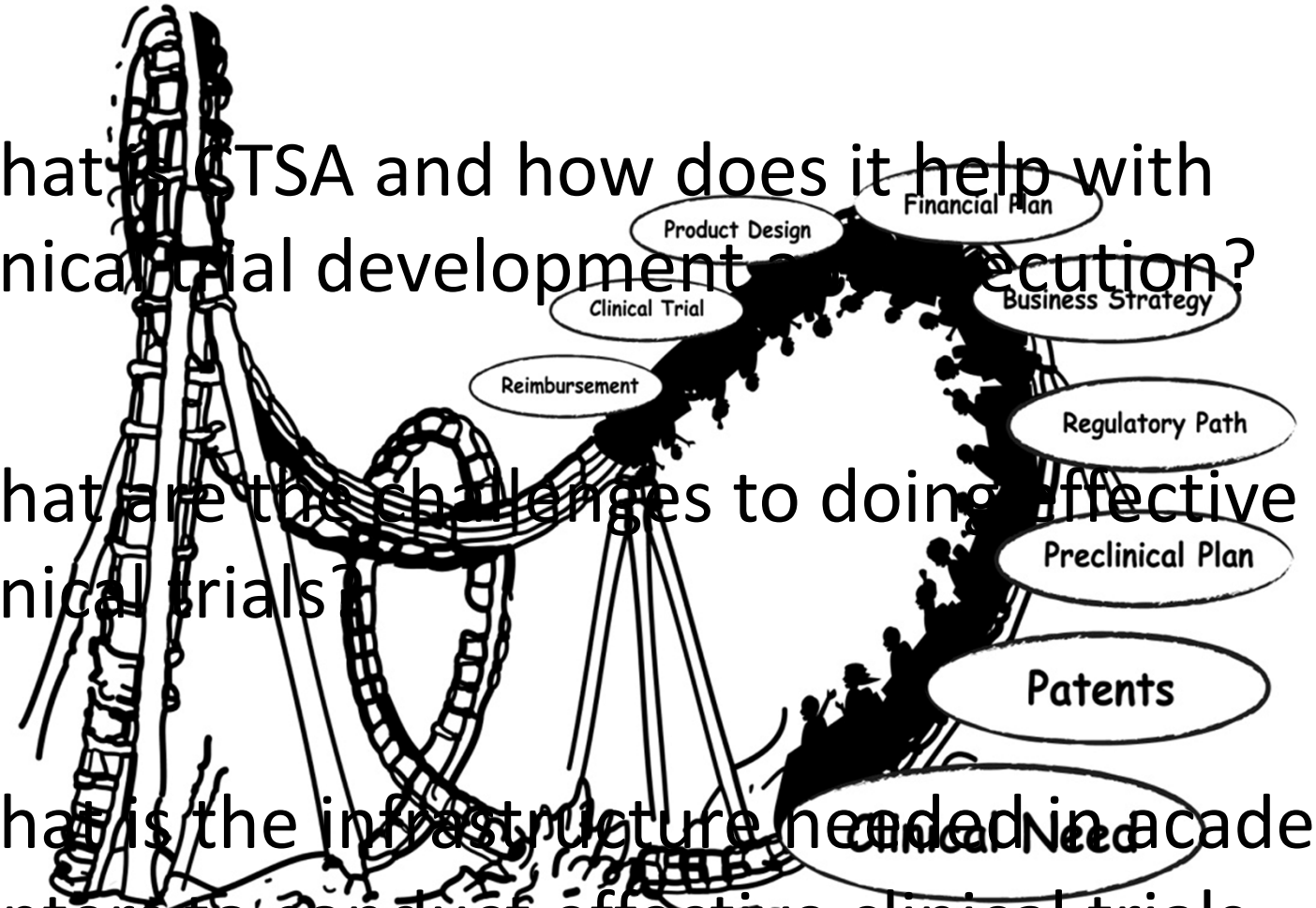




DISCUSSION TOPICS

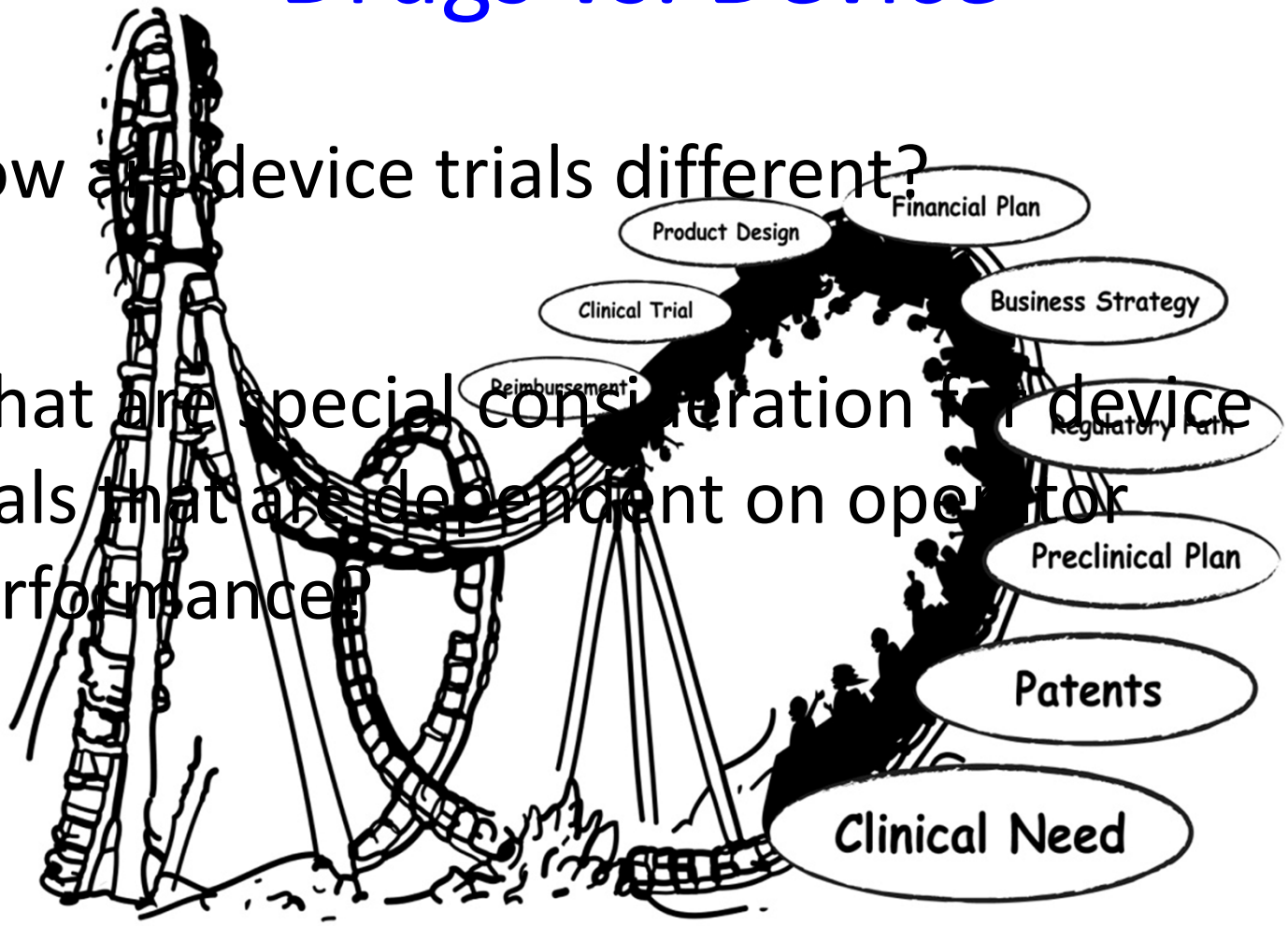
Role of Academic Institutions

- What is CTSA and how does it help with clinical trial development & execution?
- What are the challenges to doing effective clinical trials?
- What is the infrastructure needed in academic centers to conduct effective clinical trials



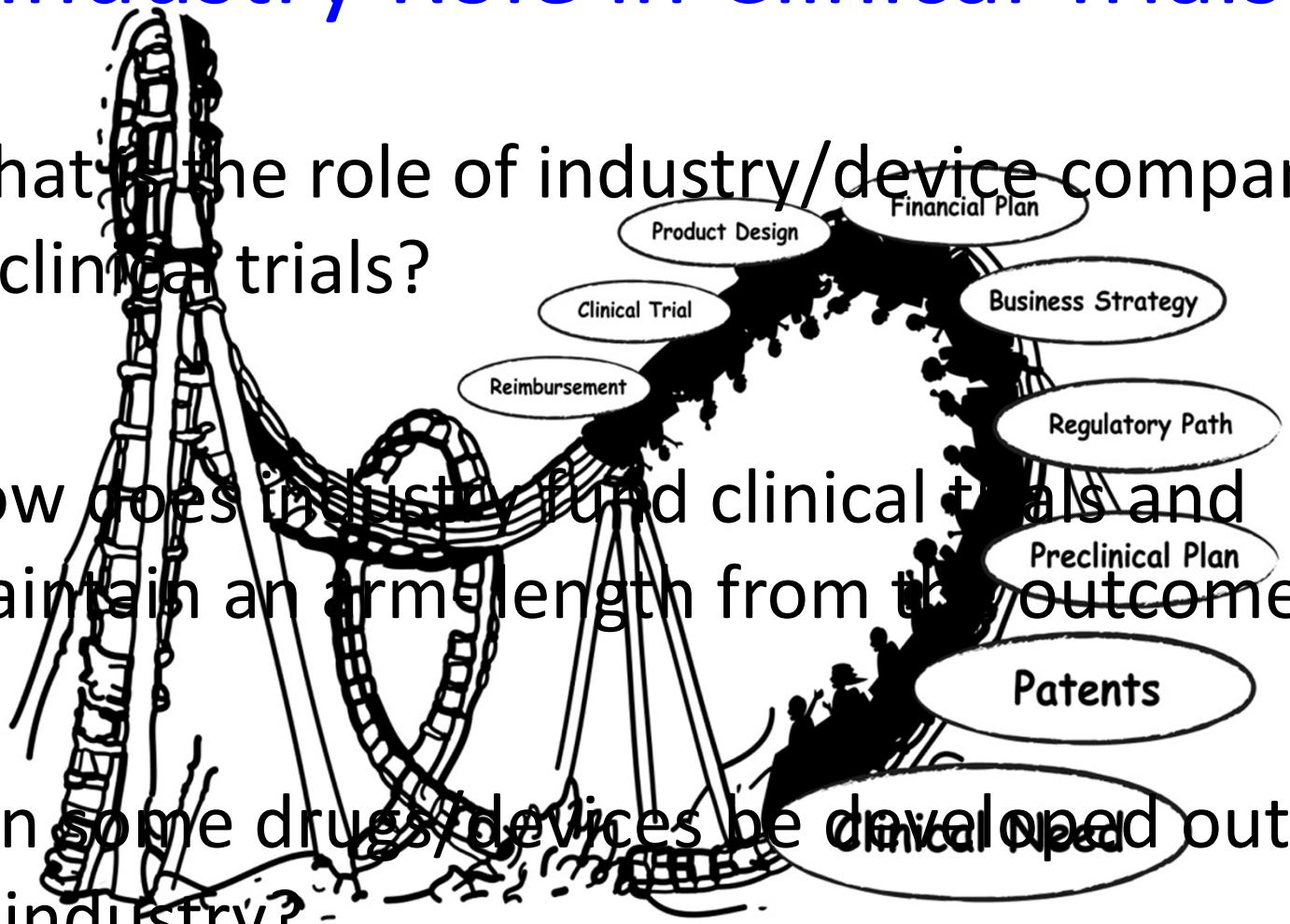
Drugs vs. Device

- How are device trials different?
- What are special consideration for device trials that are dependent on operator performance?



Industry Role in Clinical Trials

- What is the role of industry/device companies in clinical trials?
- How does industry fund clinical trials and maintain an arms length from the outcome?
- Can some drugs/devices be developed outside of industry?



General Issues in Clinical Trials

- Clinical Research as a viable career path
- Is it difficult to do clinical trials globally?
- How do patients find out about clinical trials?
- Is there patient benefit from clinical trials?