Subject Selection and Recruitment

Subject Selection – The Regs

Criteria for Approval: Equitable Subject Selection

- Consider the purposes of the research
- Consider the setting in which the research will be conducted
- Consider special problems when involving vulnerable populations
  - Children, prisoners, pregnant women, handicapped, or mentally disabled persons, economically or educationally disadvantaged persons

See 21 CFR 56.111(a)(3) / 45 CFR 46 46.111(a)(3)

- The goal of this criteria is to fairly distribute research risks and benefits among the populations that stand to benefit from it.

  No group or individual should be categorically excluded from research without a good scientific reason to do so.

Subject Selection – Reg Guidance

FDA Guidance for IRBs and Clinical Investigators:
Evaluation of Gender Differences in Clinical Investigations

3 points for IRBs to consider in drug *and* device trials:

1. FDA lifted restrictions on participation by most WOCBP in Phase I and early Phase II trials
   - Protocol should include pregnancy monitoring/testing
   - Protocol should address pregnancy prevention
   - Contraceptive counseling required for subjects

Subject Selection – Reg Guidance

2. FDA requirements for Sponsors
   - Collect gender-related data during R&D and analyze it for gender effects
   - Include fair representation of both genders to detect clinically significant gender-related differences
3. Pharmacokinetics (PK)issues to consider
   - Effect of menstrual cycle
   - Effect of hormonal therapy on product
     - Including oral contraceptives
   - Effect of product on oral contraceptives

Subject Selection – FDA Reg Guidance for Drugs/ Devices

FDA Guidance for Industry:

Collection of Race and Ethnicity Data in Clinical Trials

- IND holders must include #of enrollees by age, race, and gender in annual reports
- NDA sponsors must include effectiveness/safety data for demographic subgroups, including age, gender and race
  - Also must provide analysis of dosage or dose interval modifications needed for subgroups
- Device regs have no comparable requirements
  - But where race/ethnicity data is relevant to device safety/effectiveness, FDA encourages similar data collection

Subject Selection – Not the Regs

ICH Guideline: Ethnic Factors in the Acceptability of Foreign Clinical Data (E5)

- For global development, studies should include populations representative of the regions where the drug is to be registered
- Compare compounds sensitive v. insensitive to ethnic factors
  - Identified early in development process
- "Bridging Studies" allow extrapolation of foreign clinical data to a new region

Subject Selection – Not the Regs

- The Belmont Report
  - Principle = Justice
    - Who receives research benefits
    - Who bears research burdens
  - Application = Selection of Subjects
    - Fair procedures and outcomes in subject selection
      - Individual level (requires fair researchers)
      - Social level (requires fair study design)

Recruitment – Reg Guidance

FDA Guidance for IRBs and Clinical Investigators - Recruiting Study Subjects

- Addresses direct advertising for subjects
- Does not address
  - Doc-to-doc letters
  - News stories
  - Publicity for other audiences (i.e. investors)
- FDA considers direct ads for subject to be the start of the informed consent and subject selection process

Recruitment – The Regs

General requirements for informed consent

- Circumstances of seeking consent must:
  - Provide subject sufficient opportunity to consider whether to participate
  - Minimize possibility of coercion/undue influence
- Information provided must be in understandable language
- No exculpatory language
  - Subject is made to waive their legal rights
  - Subject releases investigator/site from liability for negligence

See 21 CFR 50.20 / 45 CFR 46.116

Recruitment – Not the Regs

AAHRPP Evaluation Instrument for Accreditation

- Recruitment methods and payment may adversely affect equitable subject selection
  - Example: targeting economically disadvantaged subjects
    - Recruitment method (mode)
    - Advertisement content
    - Payment arrangement

Recruitment – Not the Regs

ICH Guideline: Good Clinical Practice (E6)

- IRB should review amount/method of payment
  - Assure no coercion/undue influence
  - Prorate payments
  - No payments wholly contingent on study completion

Submission/IRB Requirements

- Initial Submission form (L. SUBJECT IDENTIFICATION AND RECRUITMENT) prompt investigators to describe recruitment plans.
- All recruitment fliers, posters, brochures, or phone scripts must be submitted to the IRB for review.
- Reviewer sheets cover all elements of subject selection and recruitment.
- Protocol Guidelines suggests including recruitment methods in the Summary (VI> Informed Consent Process)


RECRUITING CHILDREN
JOIN OUR STUDY
KID'S WANTED
FREE CANDY
IT'S FUN!
Don Mayne