Pharmaceutical Regulatory and Compliance Congress

Compliance Issues and Strategies for Clinical Research

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Topics to Cover

- **PhRMA Principles, Clinical Trials and Communication of Results**
  (Effective October 1, 2002)

- **Kickbacks and Post-Marketing Studies**

PhRMA Principles: Clinical Trials

1. **Ensuring safety of research participants**
2. **Conduct of trials**
   - **Adherence to GCP world-wide, local laws and regulations**
   - **Ethical studies with scientific value and IRB/EC approval**
   - **Qualified and trained investigators**
   - **Documented informed consent**

PhRMA Principles: Clinical Trials

2. Conduct of trials (continued)
   - Monitoring GCP compliance
     - Reporting scientific misconduct
     - Reporting safety issues
   - Privacy
   - Studies in developing world - collaboration with investigators and local authorities

PhRMA Principles: Clinical Trials

3. Objectivity

- Independent data and safety monitoring board (no investigators, conflicts of interest)
- Payments to research participants - IRB review, reasonable, informed consent
- Investigators
  - Reasonable compensation, no stock/options
  - Written contract
  - Not tied to outcome
  - No direct ownership interest in drug

PhRMA Principles: Disclosure

4. Public disclosure of results

- Communication
  - Marketed/Approved products
  - "Meaningful results" of controlled clinical trials
  - Exploratory studies: proprietary vs. significant medical importance
  - Access to information: Investigators, Participants and Journals

PhRMA Principles: Disclosure

4. Public disclosure of results (continued)

- **Results: objective, accurate, complete, balanced**
- **Authorship:**
  - **–Substantial contribution in study design, data acquisition or data analysis;**
  - **–Writing/Revising manuscript; and**
  - **–Final approval before submission.**

PhRMA Principles: Clinical Trials and Communication of Results

4. Public disclosure of results (continued)

- **Sponsor review**
  - **Right to review pre-publication**
  - **No suppression or undue delay**
  - **Resolve differences through scientific debate**

Kickback Risks and Clinical Research

Anti-Kickback Statute, 42 USC § 1320a-7b(b)

- **Remuneration to induce/influence purchase, prescription or recommendation of any item for which payment may be made under Medicare, Medicaid, other Federal Health Care Program**

- **Statute violated if inducement is "one purpose," *U.S. v. Greber*, 760 f.2d 68 (3d Cir. 1985)**

Kickback Risks and Clinical Research

Anti-Kickback Statute, Personal Services Safe Harbor, 42 CFR § 1001.952

- **Commercially reasonable business purpose and necessary services**
- **Written agreement spelling out all services**
- **Fair market value - independent of business volume**
- **Term of not less than one year**

Kickback Risks and Clinical Research

Post-marketing and pre-launch clinical studies: Elevated kickback risks

- **Science for promotion: Is it genuine research or a sham?**
- **Practicing physicians as investigators: How are investigators selected and compensated?**

Genuine Research vs. Sham Research

- **Adequate and well controlled studies" 21 CFR § 314.126**
  - **Protocol : objectives and analyses**
  - **Control comparison**
  - **Subject selection and randomization**
  - **Minimize bias, i.e., blinding**
  - **Reliable methods of assessment**
  - **Analysis of study results to assess effects of the drug**
- **Planned publication in peer review journal**
- **Exploratory studies**

VS.

- **"Seeding" or "Experience" study**
  - **High numbers of investigators**
  - **Open label**
  - **Single arm**
  - **Minimal data collected**
  - **Excessive compensation**
  - **No publication**
- **"Switching" studies**

Investigators: Selection

- **Who Selects: research/operations or marketing?**
- **Criteria:**
  - **Qualified to do research, follow GCP**
  - **Expertise in the relevant field**
  - **Potential to recruit eligible participants**

VS.

  - **Key customers**
  - **"High Prescribers"**

Investigators: Compensation

- Written contract, spells out work to be performed
- Fair market value
- Payment for services performed (not volume of business)
- Extra payments where enrollment is difficult
  - In writing
  - Specify purpose (advertising, keeping clinic open longer)
  - No gift certificates, cash
  - Other risks - ineligible patients, informed consent
- Investigator meetings - reasonable expenses and location
- Free drug vs. marketing the spread

End Product - What Happens When the Study is Done?

Genuine Science:

- Data analyzed
- Results published in peer review journal
- Used in promotion
- Results from exploratory study used in future studies

Sham Research:

- No data analysis, study shoved in a drawer
- Investigator prescribing habits analyzed pre-post study (“ROIs”)
- No publication

Other Risks

- False Claims Act
- Exploratory studies in promotion - misbranding
- Other criminal statutes
  - 18 USC § 371, Conspiracy to Defraud the Government
  - 18 USC § 1035, False Statements (in connection with payment for health care services)
  - 18 USC § 1347, Health Care Fraud (applies to public and private health programs)
  - 18 USC § 1518, Obstruction of Criminal Investigation of Health Care Offenses
- State commercial bribery statutes and anti-kickback laws
- Damage to reputation for quality research

Questions???