Key Compliance Risks in Clinical Trials

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Key Compliance Risks in Clinical Trials

- Areas of Compliance Focus for Sponsors of Clinical Trials:
  - OIG Guidance
  - Federal and State Fraud Investigations
  - State Health Care Provider Disclosure Laws
  - FDAA of 2007 - New Requirements in the Clinical Trials Area
    - Pediatric Trial Requirements
    - Registration of Clinical Trial Results
    - Enforcement of Phase IV Commitments

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- **OIG's Compliance Program Guidance**
  - Applies to wide range of activities – beyond traditional "marketing" programs
  - Specific Mention of Research Funding as an "Area of Concern" – this is becoming an increasing focus of regulatory/prosecutorial activity.
  - Particular Risks Noted:
    - Fair Market Value of incentives paid to investigators and patients
    - Placement of research studies with customers,
    - Post-Approval Studies – are they "seeding" trials?
    - Payment for Clinical Supplies

Key Compliance Risks in Clinical Trials

- Clinical Trials Issues in Fraud Investigations and Prosecutions
  - Kickbacks:
    - Placement of clinical trials with a Key Opinion Leader or Top Prescriber – a reward or inducement?
    - Reimbursement sought for clinical supplies?
    - Payments to Researchers/Recruiters/Study Subjects – Inconsistent with Fair Market Value of services?

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- Clinical Trials Issues in Fraud Investigations and Prosecutions
  - Does the clinical data support the off-label use?
    - Research and Development Plans for New (Off-Label) Indications or Populations - company documents can reflect:
      - change in strategy – lack of funding to pursue a new indication or a study in an expanded population;
      - or WORSE – that the indication was studied, but the trial failed to achieve safety/efficacy goals necessary for an approval (and no commensurate change in strategy)

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- State Disclosure Rules for Health Care Provider Payments
  - Currently - Maine, Minnesota, Vermont, West Virginia (other states considering similar enactments – New Jersey, etc.)
    - Require disclosure of all “consulting” payments made to health care professionals
    - Includes Clinical Trial Payments – do your systems capture payments to a particular physician regardless of the source? Integration of databases? Appropriate and timely filing of required information?

Key Compliance Risks in Clinical Trials

- **FDA Amendments Act of 2007**
  - **New Compliance Obligations**
    - Pediatric Adverse Event Reporting for Newly-Approved Drugs;
    - Clinical Trials Databases and Registry Requirements;
    - Increased Surveillance Requirements for Approved Drugs

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Clinical Trial Registries

- Previously - Companies under no regulatory or legal requirement to publicly disclose all clinical study results and registry requirements limited
- FDA not required to disclose data in its possession, except in the context of labeling changes, Advisory Committee meetings, etc.
- Registries mainly voluntary in the U.S., with a few exceptions (GSK and Forest settlements with New York Attorney General), NIH database of ongoing studies for serious and life-threatening illnesses

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- **FDA Amendments Act of 2007**
  - Expansion of Clinical Trials Databases and Registry requirements beyond trials for drugs intended to treat serious and life-threatening conditions.
  - *Required* registration of clinical studies in NIH Clinical Trials Registry
    - "Publicly Available and Searchable Information," about trials must be provided, including status of study; anticipated completion date; description of study; contact information
      - Information must be truthful and not misleading and updated at least annually (unless no changes)

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- **FDA Amendments Act of 2007**
  - Required submission of study *results* in the "registry and results data bank"
    - "Non-technical" summary of patient demographics and characteristics
    - Primary and secondary outcomes
    - Disclosure of agreements protecting privacy of study subjects
    - Submitted within one year after study is completed (unless certification is made to NIH that there is a pending application with FDA for a new drug or new use)

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- Clinical Trial Registries – Compliance & Risk Issues
  - What are “full disclosures?”
  - How to characterize the efficacy results
  - How are the safety issues described? Which adverse events are significant enough to be mentioned?
  - Can the data be mischaracterized or otherwise criticized?

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- **FDA Amendments Act of 2007**
  - Post-approval clinical studies may now be required rather than voluntary
    - FDA must be aware of “new safety information,” i.e., a signal or new and unexpected safety issue, and that post-marketing surveillance is insufficient to clarify the issue.
    - FDA Request and Timetable submitted by Sponsor
    - Penalties now provided for non-compliance
  - Safety Labeling Changes May be Required
    - FDA may require a labeling change if becomes aware of new safety information that it believes should be added to the label
    - Risk Evaluation and Mitigation Strategies (REMS) plan may be required as part of initial approval or subsequently.

Key Compliance Risks Regarding Clinical Trials

- **FDA Amendments Act of 2007 – Additional Noteworthy Provisions**
  - Additional User Fees for DTC television ads
  - Pediatric assessments required for *all* applications
  - Expedited reporting of all pediatric adverse events for one year following a pediatric-specific labeling change
  - Changes to pediatric exclusivity provisions

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