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The Small Company Clinical Study Sponsor

Roles & Duties Vis-à-vis Liability

Outsourcing in Clinical Trials: Southern California
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- These slides are intended to provide general educational information and are not intended to convey legal advice.

Agenda

- **Considering your role and responsibility with regards to liability when you are a small company**
  - Clarifying exactly what you are responsible for and what you made be held accountable for
  - Analyzing degrees of liability between bigger and smaller companies
  - Ensuring that you are enforcing compliance from your outsourcing partners to avoid repercussions on yourselves
  - Determining aspects of your trial management that you should retain in-house as a minimum so as to avoid liability issues
  - Explaining to funders why quality and risk-assessments are a necessary expenditure above the cheapest options.

Sponsor Roles – Size Does Not Matter

- **You are still responsible to ensure the study is conducted according to GCP, HIPAA and other national, federal, state, and local laws**
- **Know and execute your responsibilities:**
  - Develop Protocol and Investigational Plan
  - Select Qualified Investigators
  - Provide investigator with Investigator Brochure (Update as necessary)
  - Maintain Effective IND
    - **1572 – delegation must be explicit; if not, it is yours**
  - Monitor Investigations to assure compliance with protocol, investigational plan, and FDA reqs.

Sponsor Roles – Size Does Not Matter …

- **Know and execute your responsibilities:**
  - Data Review for safety and efficacy
  - Notify FDA and Investigators about significant new adverse effects or risks
  - Maintain required records
  - Study Drug control documentation
  - Investigator financial interest –

    * rare problem, but does occur – e.g., Gelsinger
  - File required reports with FDA:

    -Annual Report

    -IND Safety Reports

FDA Violations – Where Sponsors Fail

FDA Warning Letter Citations to Sponsors – 1/10 to 9/12 [n = 6]	Number of WL's w/Citation
Started Study without an IND or IDE	6
Failure to Supply Investigators with the Investigational Plan	3
Failure to Monitor	3
Bar on Advertising an Investigational Device as Safe and Effective	3
Failed to Test Tissue Specimen for Infection	3
Product Disposition Records	3
Inadequate Informed Consent	2
Failure to Get Investigator Agreement	2
Failure To Maintain Correspondence	2
Failure to Ensure Investigational Plan Followed	1
Failure to Submit An Accurate Investigational Plan In an IDE application	1
Failure to Get FDA Approval to Charge for IND Drug	1
Started Study without a Protocol Amendment	1
Violated Clinical Hold	1
Failure to Get Investigator Compliance	1
Failure to Get Investigator Contracts with Sufficient Financial Disclosure Info	1
Tissue Donor Screening Violation	1
Failure to Notify FDA of Termination of Investigation	1
Failure to Include All Reports of Prior Device Testing	1
TOTAL	37

Table Source

"***FDA Enforcement in the Clinical Research Setting.***" Swit, Michael. Drug Information Association (DIA) Audio Conference. July 24, 2014.

Slides accessible at:

http://www.fdacounsel.com/files/Swit_--_FDA_GCP_Enforcement_--_--_DIA_Audio_Conf_--_20140721.pdf

Measures to Increase Compliant Clinicals and Decrease Liability from Vendors

1. **Assure Detailed and Complete:**
   - **Agreement --** use to regulate the relationship
     - if you want to make sure it gets done, put it in
     - investigators, contract mfrs., etc.
   - **Protocol –** both initial and amendments – ensure amendments are communicated effectively and, if needed, with training
   - **Investigator's Brochure**

Measures to Increase Compliant Clinicals and Decrease Liability from Vendors ...

2. **Require Investigator Training (even non-naïve investigators)**

   ** GCP

   ** Product – especially important for devices

3. **Require Standard Operating Procedures at the Sites**

   ** investigational sites

   ** other vendors (e.g., analytical labs, contract mfrs.)

Measures to Increase Compliant Clinicals and Decrease Liability from Vendors …

4. **Conduct Investigator/Contractor Due Diligence:**
   - Check FDA databases for disqualified and debarred investigators
   - Check FDA's NIDPOE database
   - Check FDA Warning Letter database
   - Check HHS Office of Research Integrity's database for Research Misconduct Cases
   - Check/PHS Actions/Debarment Actions database
   - FOIA FDA inspection documents on investigators
   - Check State Licensing Board to verify current Medical License
   - Google!!!

Measures to Increase Compliant Clinical and Decrease Liability from Vendors …

5. **Employ an Effective Monitoring and Auditing Program**

**** Clinical Studies**

- Pre-Study Visit
- Study Initiation Visit
- Periodic and Closeout Visits
- Follow up on deficient monitoring visits
- Audit your sites – use independent auditors
- Audit your CRO if you have one

**** Clinical Supply, and other Vendors**

What to Hold and What to Discard

- **Key variable – your human resources**
  - "Perfect" small company – has been there before with the same team or similar types of players and understands what needs to be done
    - CEO
    - CFO
    - Chief Medical Officer
    - Head of R&D
    - Regulatory
    - Clinical Operations
    - CMC expertise
    - Mfg. expertise

What to Hold and What to Discard …

- **Further you get away from "perfect" small company model, more you need to outsource … and harder to do**
  - ***Catch-22*** -- If your company get too far away from perfect, your expertise to manage the CROs and vendors degrades
    - May lead to need for a "Construction Manager" to ride herd on the CRO (e.g., via a savvy independent consulting firm)
  - But, be careful about putting all your eggs in one CRO basket as there is not check on the CRO's views on study size, etc.
- **The more duties you keep, the greater potential that liability will attach to you directly; although buck comes back**

Funders Need to Understand Quality Matters

- **Clinical research is a highly regulated activity –** essential to do right, especially relative to:
  - Study design
    - vet the protocol aggressively before going to FDA
  - Data integrity
    - experienced investigators with strong GCP pedigrees
    - monitoring and site selection

DON'T END UP LIKE J&J – see 2009 Warning Letter at:

http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm177398.htm

Led to a complete response letter requiring more studies – see:

http://www.basilea.com/News-and-Media/FDA-issues-ceftobiprole-Complete-Response-Letter/317

Funders Need to Understand Quality Matters…

- FDA strategic "validation" -- essential
  - overall regulatory strategy
  - protocol

Final Sermons

- ***Don't Bury Your Head To Problems –*** investigate, fix and, if needed, disclose promptly
- ***Don't Fall Madly In Love With Your Technology***
  - **You Have To *Prove* Safety And Effectiveness –**
  - ***"I just know it works" --*** not the standard in the Federal Food, Drug, and Cosmetic Act –

… your baby may have warts

Be prepared to un-adopt your baby – but data should drive.

Questions?

- ***Call, e-mail or fax:***

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About Your Speaker

***Michael A. Swit, Esq.*, is a Special Counsel in the San Diego office of the international law firm, Duane Morris, LLP, where he focuses his practice on solving FDA legal challenges faced by highly-regulated pharmaceutical and medical device companies. Before joining Duane Morris in March 2012, Swit served for seven years as a vice president at The Weinberg Group Inc., a preeminent scientific and regulatory consulting firm in the Life Sciences. His expertise includes product development, compliance and enforcement, recalls and crisis management, submissions and related traditional FDA regulatory activities, labeling and advertising, and clinical research efforts for all types of life sciences companies, with a particular emphasis on drugs, biologics and therapeutic biotech products. Mr. Swit has been addressing vital FDA legal and regulatory issues since 1984, both in private practice with McKenna & Cuneo and Heller Ehrman, and as vice president, general counsel and secretary of Par Pharmaceutical, a top public generic and specialty drug firm. He also was, from 1994 to 1998, CEO of *FDANews.com,* a premier publisher of regulatory newsletters and other specialty information products for FDA-regulated firms. He has taught and written on many topics relating to FDA regulation and associated commercial activities and is a past member of the *Food & Drug Law Journal* Editorial Board. He earned his A.B., *magna cum laude*, with high honors in history, at Bowdoin College, and his law degree at Emory University.**