How to Run Clinical Trials in Private Practice

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DISCLOSURE

Dr. Siler has received research grants from GlaxoSmithKline, Forest, Boehringer Ingelheim, Sunovion, Novartis, Daiichi, Elevation and participates in Boehringer Ingelheim, Novartis, and UCB speakers’ bureau, but these do not create a conflict related to the following presentation.
Disclosures

• Research Support
  – Pearl Therapeutics, Forest Research Institute, GSK, Novartis, Sunovion, Boehringer-Ingelheim, Daiichi-Sankyo

• Speakers Bureau
  – UCB, Novartis, Boehringer-Ingelheim
Question 1

What is the best basketball program in the NCAA?

1. Duke
2. Kansas
3. Kentucky
4. Syracuse
What is the best basketball program in the NCAA?

1. Duke
2. Kansas
3. Kentucky
4. Syracuse

33% 25% 25% 17%
Pay Heed, All Who Enter: BEWARE OF "THE PHOG"
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• Practice located in St. Charles, MO in St. Louis Metro area
• 2 Physicians and 4 Nurse Practitioners
• 5 full time research staff
  – 1 pharmacist, 1 RN, 1 medical assistant and 2 BA
  – All staff are certified by ACRP (CCRC)
  – Research staff is devoted to research only
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- First clinical trial done in 1994
- Have been involved in over 125 trials
- Last year had 193 subjects and 14 active trials
- Primarily COPD trials, have also done anticoagulation trials
- Have done Phase 2, 3 and 4 trials
- Initially did some inpatient trials, now only outpatient
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• Initially started with one NP working part time on one trial
• Quickly discovered that part time staff does not work well – difficult to keep up with all of the paperwork and scheduling required
• Moved quickly to hiring full time staff dedicated to research
• Research moved to separate area
Question 2

Do you do clinical trials?
A. Yes, in private practice
B. Yes, in academic practice
C. No, but have in past
D. No, have never done trials
Do you do clinical trials?

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C. No, but have in past
D. No, have never done trials

18% 25% 25% 33%
Factors to Consider

• 75% of investigators do one trial

• Need line of credit or other financial resources
  – Payment often occurs 3-6 months after services are performed
  – Need capital to pay staff and research subjects
  – Once site is up and running can make significant revenue if carefully managed

• Physician needs time to be involved in supervising trials – FDA requires oversight
Staff

- Dedicated staff that do not have non-research duties is ideal
- Background of my staff is broad – I have 1 pharmacist, 1 RN, 1 medical assistant and 2 staff with college degrees
- Finding staff with previous research experience is helpful especially when starting
- All staff is required to have GCP and human subject protection training including sub-investigators
Staff

• Clinical research coordinators are basic staff to collect research data
• My site has a director of research who negotiates contracts, does regulatory documents and manages staff
• Larger sites often have dedicated recruiters – one of my coordinators does recruiting half-time
Staff Certification

• All of my staff are Certified Clinical Research Coordinators (CCRC) offered by ACRP
  – Requires 3,000 hours of experience with college degree or RN, 4,500 hours without
  – Must pass written exam on GCP, CFR and conduct of clinical trials
  – Must have 24 research contact hours every 2 years

• Certification also offered by SOCRA (CCRPR)
Staff Training

• Each staff member attends a national research meeting at least every 2 years
• Staff also receives training on each protocol at investigator meetings
• As we do COPD trials, all staff has had extensive training in spirometry and lung volume testing. I have a full-time RPFT on my clinical staff to provide support
Facilities

• Our site is physically separate from the clinical practice and is located across the hall
• We have 6 exam/procedure rooms
• For COPD trials, some of which require 14 hour visits, a lounge area for subjects is essential
• Each coordinator also has a desk with computer to do paperwork and data entry
Facilities

• Need secure storage for investigational products (IP)
• Storage for records also needed. Although most sponsors are using electronic case reports forms, many source documents are still on paper
• Need space for study monitors to review records
Facilities

• Need refrigeration for some IP’s which also needs to be locked
• Trials doing pharmacokinetics often require samples to be stored a -70 C until shipped. We use a space in the hospital lab for this
• High speed wireless Internet access for monitors and transmitting data essential
• Analog phone lines also needed for modem transmission of data
Question 3

Which of the following are important factors in running a clinical trials practice?

1. Staff dedicated to clinical research that do not have other practice responsibilities.
2. Separate space.
3. Principal investigator involvement.
4. All of the above.
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4. All of the above.

1. 2. 3. 4. 100%
Study Contracts

• Legal review of contracts recommended
  – Sponsors write contracts that favor them
  – Indemnification sections need to be carefully reviewed to insure adequate protection

• Contracts are usually made either directly with sponsors or with Contract Research Organizations (CRO)
  – With CRO contracts must insure protection in the event of CRO problems that payment to site is not effected
Site Management Organizations

- SMO’s provide access to contracts for a fee
- Fee is often based on contracted number of subjects so if a site under enrolls a study, fee can be a large part of the total reimbursement
- I have never used an SMO – I think it’s better to leave out the middleman and work directly with sponsors and CRO’s
Study Contracts

• Number of subjects
  – Most sponsors want sites to commit to a certain number of subjects
  – Be very careful to be realistic – if you commit to 10 subjects and enroll 3, a sponsor may not want to work with you again. It’s better to be conservative and then go back and ask to over enroll if you have reached your contracted number
Study Contracts

- Don’t be afraid to refuse studies that your site cannot meet enrollment or is outside of the expertise of your site. Sponsors respect sites that know their capabilities.
- Sponsors indicate many sites just sign contracts and never ask any questions or request revisions.
Budgets

• Probably the most important factor in financial success of a site
• Sponsors often low ball budgets and usually sites can negotiate higher payment
• We always ask for non-refundable study start up payment
  – Covers the cost of doing regulatory documentation, IRB communications and contract and budget review
Budgets

• Review each visit in protocol
  – We prepare a spreadsheet with each study procedure – informed consent, medical history, exams, vital signs, EKG’s, spirometry, blood draws, questionnaire administration and any other procedures in protocol
  – We have a standard charge for each procedure in spreadsheet

• We also ask for money for query resolution, record storage and SAE reporting.
Budgets

• Once analysis is done, it is much easier to go back to a sponsor or CRO and tell them that your analysis shows that the budget is too low

• If a sponsor will not increase the budget to a reasonable amount, we walk away
  – If you don’t get adequate compensation you put your practice at financial risk
  – We find that often, when they realize we are serious, they will come back with a better offer
Payments

• Be careful in reviewing payment milestones
  – Sponsors will often set payments based on monitoring milestones
  – Better to have payment based on visit completion and computer data entry by site, not monitor
  – Try and get payments made monthly or based on visits completed
  – Sponsors will often pay quarterly which may mean payments will be made 4-6 months after work done which can cause cash flow problems
Payments

• Must keep track of payments owed
• Hold sponsors and CRO’s to contracted payment schedules
• We have been forced to threaten to stop enrollment and in one case, threatened to stop patient visits in order to force payment
Institutional Review Boards

• Advantage of being in private practice for sponsors is the ability to use a Central IRB rather than a local IRB for protocol approval
  – This can significantly decrease start up time
  – Also makes reporting easier for site as the sponsor can transmit reports for multiple sites
  – Site is still responsible to submit information concerning subject safety directly to IRB
Recruiting

• **Recruit from practice**
  – We get about half of our subjects from our practice
  – Important to have all providers remember to offer research opportunities to appropriate subjects

• **Advertising**
  – We always try to get advertising money from sponsors in our contracts
  – We have used direct mailing, radio and TV
  – Some sponsors use national advertising
Recruiting

• Screening subjects
  – We pre-screen all subjects after they sign a generic screening consent form with spirometry and a medical history review
  – This avoids finding out a subject’s FEV1 is not appropriate for a study after reviewing a 25 page consent form with them
  – This also reduces our screen fail rate for studies which is important to sponsors
FDA Requirements

• Code of Federal Regulations Title 21 (CFR 21) contains the federal law governing the FDA’s oversight responsibilities for clinical trials

• International Conference on Harmonization (ICH) provides guidance for Good Clinical Practice (GCP)
  – ICH-E6 is current guidance
  – Guidance has origins with Declaration of Helsinki
FDA Requirements

• Form 1572 outlines requirements of principal investigator (PI)
• PI is responsible for all activities at site
• Procedures can be delegated to study staff members based on their credentials but PI is ultimately accountable
• FDA may inspect sites to insure compliance
• Our site has had one audit
FDA Requirements

• Audits
  – 3 findings – No action indicated (NAI), voluntary action indicated (VAI) or official action indicated (OAI)
  – VAI requires a response
  – OAI can result in civil and/or criminal penalties

• Our audit had VAI findings
Common FDA Audit Findings

- Failure to follow protocol
- Inadequate records
- Drug accountability
- Informed consent deficiencies
- IRB Communication
- Adverse event reporting
Who is responsible for conduct of a trial at a clinical site?

1. Sponsor
2. CRO
3. Principal Investigator
4. FDA
Who is responsible for conduct of a trial at a clinical site?

1. Sponsor
2. CRO
3. Principal Investigator
4. FDA

- Sponsor: 2%
- CRO: 0%
- Principal Investigator: 98%
- FDA: 0%