Physician-Initiated Device Studies

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FDA Steps Up Enforcement!
TOPICS

• FDA, CDRH & Bioresearch Monitoring
• Physician-Sponsored Research
• Doing Quality Research
• Ace University Hospital Case Study
Device Bioresearch Monitoring (BIMO)

- Protection of human subjects in clinical research
- Quality and integrity of data FDA relies on in its decisions
DBM-Program Enforcement Branches

- Pre-Submission meetings
- PMA filing and 100 day meetings
- Routine inspections assignments for PMAs & IDEs
- Inspectional findings - HSP and data quality

DBM-Special Investigations Branch

- “For Cause” Inspections
- Inspectional findings - HSP & Data Integrity
- Expert advice to other FDA components
- Complaints
- Allegations of Research Misconduct
FDA Probe Finds Violations in Study Of Heart Device

Physician-Sponsored Research
Typical FDA-Regulated Research

Human Subject Protection & Data Integrity

Sponsor
IRB
Clinical Investigator

Physician-Sponsored Research

Human Subject Protection & Data Integrity

IRB
Sponsor-Investigator
### Sponsor-Investigator Responsibilities

**Sponsor**
- IRB Approval
- IDE, when required
- IDE Supplements
- 5-day Notices
- Study Records
- Device Disposition
- Selecting & Monitoring other investigators, when applicable
- Prohibitions

**Investigator**
- Informed Consent
- Subject Records
- Device Accountability
- Protocol
- Adverse Events
- Progress Reports
- Financial Disclosure
- Prohibitions

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### Doctor Pressed on Ties to Device Makers

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Doing Quality Research

Quality Device Research – 1

- Know whether an IDE application is required

- Know when an IDE Supplement is required*
  - changes that require prior approval

- Know when a 5 day notice is required*
  - changes that do not require prior approval

*See handout for FDA guidance, regulations, and contact information
Quality Device Research - 2

When is an IDE needed?

IDE Application Required
- Significant Risk (SR) Device*

Abbreviated Requirements Only
- Nonsignificant Risk (NSR) Device*

Exempt from IDE requirements
- Legally marketed device used on label
- Certain unapproved diagnostics, with limitations*

*See handout for FDA guidance, regulations, and contact information

Quality Device Research – 3

- IRB approval – no lapses
- IRB’s conditions of approval
- Informed Consent documents
  - correct version
  - basic elements
  - risks
Quality Device Research – 4

• Report Adverse Events
• Monitor (multi-site studies)
• Follow the Investigational Plan & FDA regulations

Compliance Tools

• Untitled or Warning Letter
• 3rd Party Audit
• Exclude Data, Revoke IDE
• Application Integrity Policy
• Civil Money Penalties
• Formal Administrative Hearing
• Disqualification
  – Investigator, IRB, or Non-Clinical Lab
Sponsor-Investigator Lessons Learned

- 42% significant or egregious conditions or practices (OAI) in FY08-09
- 35% Warning Letters
- 15 working days to respond
- Redacted copy is PUBLIC!
- Response = Time and $$$

Midday Naps Found to Help Fend Off Heart Disease

L. Ron Stevens
9:45 am - Post-Mortem Water Cafe

The power of the snooze button may be something you take for granted. A new study finds that taking a nap — even a brief one — can help fend off heart disease.

“Taking a nap could turn out to be an important weapon in the fight against heart disease,” said Dr. Thomas W. Evans, a researcher at the University of Michigan in Ann Arbor, who led the study.

The study, published in the Journal of the American Medical Association, found that those who took naps during the day were less likely to develop heart disease than those who did not.

The researchers analyzed data from more than 3,000 people who were monitored for an average of 10 years. They found that those who napped at least three times a week had a 33% lower risk of developing heart disease than those who did not.

The study also found that napping was more effective than exercise or diet in reducing the risk of heart disease.

But the researchers admit that their study was limited by the fact that it was observational, not experimental. They say more research is needed to confirm their findings.

Still, the results are encouraging, especially for those who are unable to exercise regularly due to physical limitations.

“Naps are easy to do and require no special equipment,” said Dr. Evans. “They are a simple way to improve heart health.”
Ace University Hospital Case Study

Dr. Pat & Dr. Ella Patella Repair Study

Gumum is FDA approved for metatarsal repair (SF)
Dr. P wants to study Gumum for patellar repair (TF)
Dr. E agrees to also be a clinical investigator
Dr. P offers Dr. E $30K bonus if 15 subjects complete 12 mo. follow up
Dr. P gives protocol and informed consent to Dr. E
Staff from both offices train via webcast video produced by Dr. P
Dr. P orders & ships Gumem to Dr. E’s
Dr. P submits protocol and informed consent for IRB approval
At Dr. Ella’s site -- 1

Dr. E is so excited, she implants 4 subjects right away
Dr. E consents subjects 1-5 with forms from Dr. P
Dr. P sends the IRB approved informed consent documents to Dr. E
Pipe burst at Dr. E’s, Gumem labels damaged, lot numbers illegible
Dr. E enrolls subjects 6-15 with approved informed consent
Subjects 4 and 5, who have latex allergies, develop rxs at surgical site
Dr. E assumes gloves were the cause & treats with meds

At Dr. Ella’s site -- 2

At 12 mo, subjects 2, 5, 6 & 8 failed to return for follow up
Dr. E asked her secretary to call, after numerous calls, 2 & 5 came in
Subject 5 refused x-ray, Dr. E believes she can assess by palpation
Dr. P pays Dr. E $28K bonus for 14/15 subjects completing trial
Dr. Ella’s Issues?  -- 1

Video training?
Consent after surgery?
Version of the informed consent document?
Adverse Events reported?
Protocol deviation (subject 5, 12 month visit) documented?

Dr. Ella’s Issues?  -- 2

Conducted trial according to
- investigator agreement?
- protocol?
- FDA regulations?
Devices accounted for?
Financial interest disclosed?
At Dr. Patella’s site

Dr. P saw no reason to watch her own training video
Dr. P only did the surgeries
Nurse T conducted f/u visits & signed off as Dr. P, as instructed by Dr. P
Protocol excluded subjects taking Vit D or aspirin
Dr. P enrolled one subject taking Vit D, one subject taking aspirin

Dr. Patella’s Sponsor Issues?

Was an IDE required?
IRB approval?
Provide unapproved protocol and informed consent to Dr. E?
Obtain a Signed Investigator Agreement from Dr. E?
Monitor Dr. E’s site?
Dr. Patella’s Investigator Issues?

- Fail to watch her own video?
- Delegate follow up visits to Nurse?
- Instruct Nurse to sign off follow up visit forms for Dr. P?
- Enroll subjects excluded (Vit D & aspirin) by protocol?

Will Doing Poor Quality Research BREAK Your Bank?
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