

Physician-Initiated Device Studies

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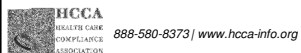
Special Investigations Branch

Division of Bioresearch Monitoring

Office of Compliance

Center for Devices and Radiological Health

Food and Drug Administration



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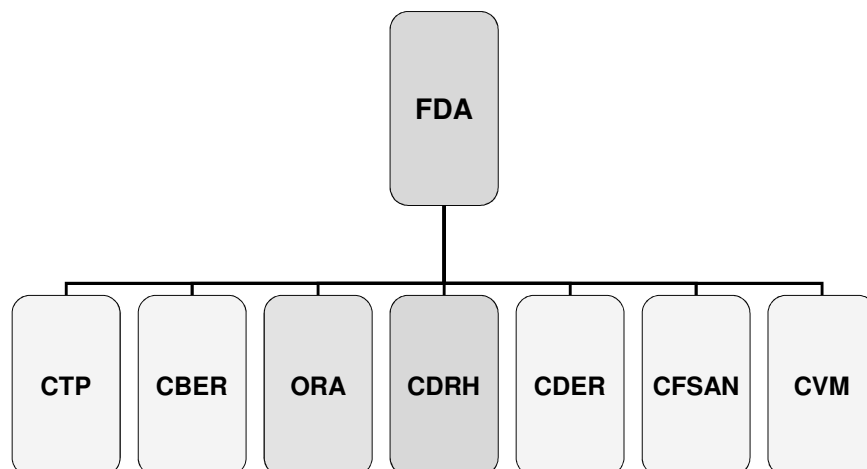
FDA Steps Up Enforcement!

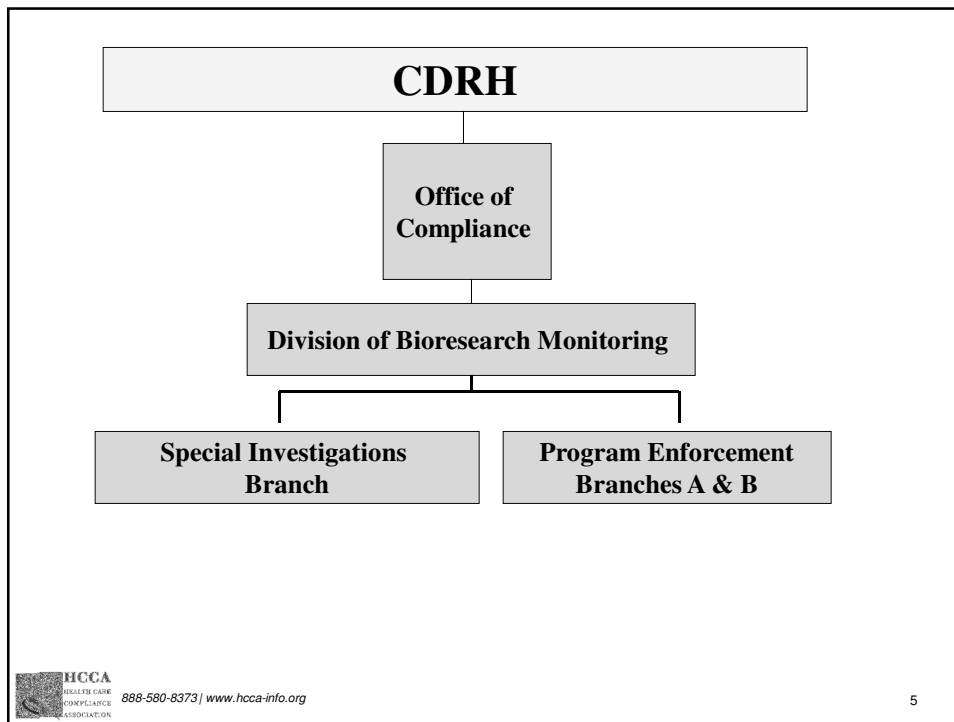


TOPICS

- FDA, CDRH & Bioresearch Monitoring
- Physician-Sponsored Research
- Doing Quality Research
- Ace University Hospital Case Study

FDA Organization Chart





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

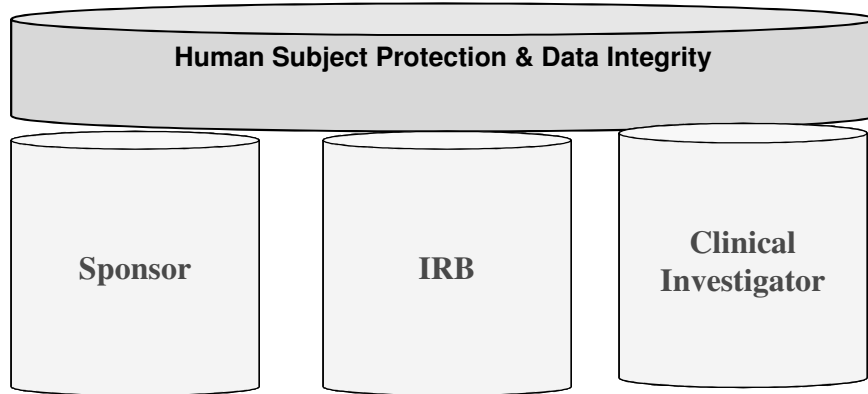
- “For Cause” Inspections
- Inspectional findings - HSP & Data Integrity
- Expert advice to other FDA components
- Complaints
- Allegations of Research Misconduct

FDA Probe Finds Violations in Study Of Heart Device

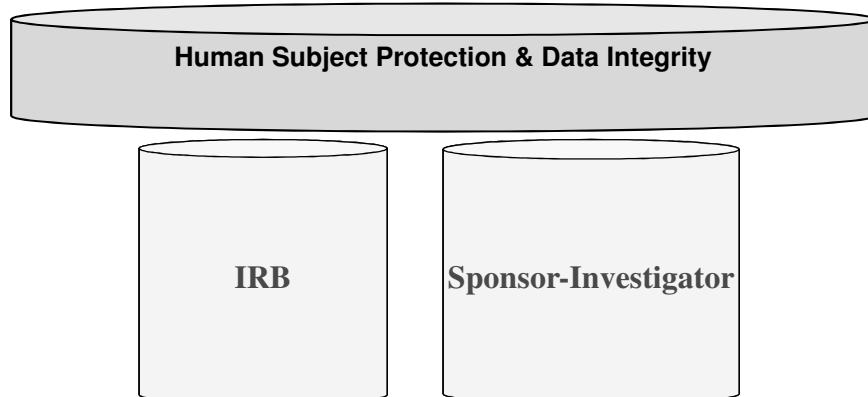


Physician-Sponsored Research

Typical FDA-Regulated Research



Physician-Sponsored Research



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

Doctor Pressed on Ties to Device Makers



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

By ROB STEIN
Washington Post Staff Writer

The next time the boss finds you snoozing at your desk, take heart. A large new study has found that people who regularly took a siesta were significantly less likely to die of heart disease.

"Taking a nap could turn out to be an important weapon in the fight against coronary mortality," said Dimitrios Trichopoulos of the Harvard School of Public Health in Boston, who led the study published yesterday in the Archives of Internal Medicine.

The study of more than 23,000 Greek adults — the biggest and best examination of the subject to date — found that those who regularly took a midday siesta were more than 30 percent less likely to die of heart disease.

Other experts said the results are intriguing. Heart disease kills more than 650,000 Americans each year, making it the nation's No. 1 cause of death.

"It's interesting. A little siesta, a little snooze may be beneficial," said Gerald Fletcher, a cardiologist at the Mayo Clinic in Jacksonville, Fla., speaking on behalf of the American Heart Association. "It's simple, but it has a lot of promise."

While more research is needed to confirm and explore the findings, there are several ways napping could reduce the risk of heart

physical activity, diet and other illnesses.

"This study has a number of advantages," Trichopoulos said.

He and colleagues at the University of Athens examined 23,681 Greek men and women ages 20 to 86 who had no history of heart disease or any other serious health problem when they enrolled in the study between 1994 and 1999. The researchers asked the participants whether they took midday naps and, if so, how often and for how long. They also asked detailed questions about their health and lifestyles, such as whether they had any illnesses that might make them sleep more, how much exercise they got and what they ate.

After an average of more than six years of follow-up, 732 of the study subjects died, including 133 who died of heart disease. Of that group, 94 were nappers. After the researchers accounted for factors that could confuse the issue, they found that those who took naps frequently were 34 percent less likely to die of heart disease than those who did not. The biggest nappers — 79 people who took a siesta for 30 minutes or more at least three times a week — had a 37 percent lower risk.

Naps appeared to offer the most protection to working men: Those who took midday siestas either occasionally or systematically had a 64 percent lower risk of death from

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 rxns 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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