Ethics of regulation and Legal Implications

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Miscellaneous FDA Activities

• **MedWatch** -- FDA provides safety information on drugs and other FDA-regulated products, and allows for adverse event reporting.

• **Recalls** -- FDA posts significant product actions of the last 60 days.

• **Inspections** - FDA inspects processing plants and other agency-regulated facilities.

• **Advisory Committees** - FDA convenes public meetings with outside experts for advice on making key public health decisions.
FDA Monitoring

What we’ll talk about today

1. Evaluating new products before they are marketed
2. Collecting and monitoring adverse effects from marketed products and investigations
3. Taking action when necessary to prevent injury or death
The FDA has several examples of effective monitoring to prevent loss of life

- Pacemaker found during clinical studies to have microprocessing design flaws
  - One in every few hundred paced at 200 beats per minute
  - Redesigned to be marketed

- New stent – smaller and more flexible
  - Marketed in Europe
  - FDA engineers identified design feature led to fatigue and breakage
    - Redesigned before clinical studies
Case Study 1
Case Study

• "Margaret Anderson" is an active 64-year-old mother of two children who are attending college.
• Hip pain for over 20 years from arthritis
• Pain in her hip became so severe that her doctor referred her to an orthopedist, Dr. W.
• After several office visits, x-rays, diagnostic tests, and much discussion with family and friends, she decided to have her hip joint replaced with an artificial one.
• After careful rehabilitation she resumed her normal activities.

Adapted from: But Doctor, It's My Hip!: The Fate of Failed Medical Devices, John H. Fielder and Jonathan Black
Case Study

• Last Wednesday, three years after her surgery, as she rose from the breakfast table, she and her husband heard a loud snap.

• She experienced some pain and was unable to get out of her chair.

• She was taken to the hospital where Dr. W examined her and reported that her artificial hip joint had broken.

• Surgery to replace the joint was quickly scheduled.
Case Study 2
**VIOXX® FACTS**

- Annual Sales - $2.55 billion
- One of the 30-most prescribed drugs in the US (2003).
- Since its approval, over 100 million prescriptions have been written for Vioxx in the United States.
- Sales struggled after FDA study warned of risk of heart attack from high doses of Vioxx.
- Competing drug: Pfizer's Celebrex.
MERCK’S $27 BILLION HEART ATTACK

“Total Recall”
Four Corners reports on the Vioxx controversy - the biggest drug recall in history.
Arachidonic Acid

COX-1 (Constitutive)

- PGs
  - Stomach
  - Intestine
  - Kidney
  - Platelet

COX-2 (Inducible)

- PGs
  - Disease targets: Arthritis, Pain, Cancer
  - COX-2 Inhibitor

Non-specific NSAIDs
VIGOR (Vioxx Gastrointestinal Outcomes Research)
“The difference was so wide that Dr. [Edward] Scolnick, the Merck research chief, appeared to recognize it couldn’t come solely from naproxen’s protective effect but must involve some sort of risk inherent to Vioxx. “

“To explain a 5-fold difference, naproxen would have had to be one of the most potent and effective cardio-protectants known,”
Final Findings

“From 1999 to 2003, there were an estimated 92,791,000 prescriptions for rofecoxib [the medical name for Vioxx], of which 17.6% were high-dose. Combine this with data on mean prescription length, we estimate that the increased rofecoxib risk observed in this study would yield an excess of 27,785 cases of AMI [acute myocardial infarction or heart attacks] and SCD [sudden cardiac death] in the US over the years 1999-2003.”

The fatality rate from these incidents is approximately 27 percent. This would indicate that Vioxx use was responsible for an estimated 7,500 deaths between 1999 and 2004. Since Graham found that the increased risk of heart attacks was not general to all COX-2 inhibitors, but specific to Vioxx, his study suggests that all of these deaths could have been prevented through the use of any other NSAID, including Celebrex.

Vioxx use results in a 90 percent increase in hospitalization rate for gastrointestinal bleeding compared to Celebrex. If this is true, than it means that there are no important health benefits associated with Vioxx use relative to other drugs on the market.
Patients have the right to expect that any treatment they receive, including implantable medical devices, will be "of acceptable risk"
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