Industry Perspective

Where Are We Now and How We Got Here?

Publication, Transparency, Drug Safety, and the Relationship Between Pharmaceutical Science and the Public (It's all very complicated…)

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Disclaimer: Views expressed do not represent those of my employer, "industry", government, or anyone except myself.

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Agenda

- Objective - Make us think. Incite controversy. Improve debate.
- Tour - The public: Baycol, and SSRIs, and Vioxx….oh, my!
  - Fear, doubt, concern….public debate
- Question - Why debate? This is easy! Those "bad people" should just disclose everything! Wait…maybe its not just reporting - they can't be trusted to do research….the feds should do it all!
  - Are those things really good?
  - What exactly are we debating?
- Beginning a Framework

Baycol, then SSRIs, then Vioxx…

- Baycol "superstatin" ('98-'01)
  - [Associated with rhabdomyolysis, esp. with a fibrate]
  - Did Bayer know in '99? (label was changed…)
  - Did the FDA know? (all PV reports go to FDA…)
  - "Just one example of a pharmaceutical company keeping quiet" – Bruce Psaty, U. Washington (JAMA Dec. '04)
  - "…a scientific riddle that takes time to solve" -"…a clear example of how the system should work" - Brian Strom, U Penn.
  - "System needs reform", because postapproval monitoring is "almost strictly in the hands of the pharmaceutical companies" – Catherine DeAngelis, editor-in-chief JAMA

The Public Has Doubts About the Pharmaceutical Industry's Willingness to Publish Safety Information about Their Drugs in a Timely Manner Recent reports of potentially dangerous side effects of certain drugs have led many patients to reevaluate their treatment options or change their behavior

PR Newswire Date: January 18, 2005

In the wake of the publicity surrounding the potentially harmful side effects of a variety of pain medications, the American public is skeptical about the willingness of drug companies to publish data about their products in a timely manner causing many patients to worry about the dangers of taking medication and to change or reconsider their treatment options.

Three in five (60%) U.S. adults are not very confident or not at all confident that drug companies will publish any information they have about the side effects of any of their drugs as soon as they have that information.

Britain to Publish Drug-Safety Data On the Internet

The Wall Street Journal Europe January 18, 2005

In the wake of several drug-safety scandals on both sides of the Atlantic, Britain's health minister said British regulators will begin collecting and publishing online patient reports of drug side effects.

Medical regulators world-wide have long solicited patient feedback on medicines in the marketplace but the information isn't usually published in an open forum.

The British program, to be overseen by the Medicines and Healthcare products Regulatory Agency appears to be the first effort to publish side-effect data on the Internet.

Scrutiny of drug safety has intensified during recent months after widely used medicines have been tied to dangerous side effects.

Baycol, then SSRIs, then Vioxx….

- "Inappropriate use can upset the scales of safety…can adversely affect the users who most need the medication…recalling a drug that has substantial side effects spares some people from injury, but it may deprive others of a powerful tool that would probably have done them more good than harm" - Ben Harder, Science News, Feb '05 Cover Article

- "roughly 20 million people were taking it, and it might have been the best drug for, say, 1 million of them" – (speaking of Vioxx) - Catherine DeAngelis

- "If Bayer had been able to eliminate use of Baycol with Fibrates, Baycol would probably still be on the market" – Brian Strom

- "Regulatory action may yet kill other effective medications that, used more discerningly, could genuinely benefit…patients" – Ben Harder

Baycol, then SSRIs, then Vioxx….

- "…trends in the pharm business have accelerated the approval of new drugs in the U.S., thereby putting them in widespread use before long-term safety data have accumulated" - Ben Harder, Science News, Feb '05 Cover Article

- EMEA director Thomas Lonngren has called for a radical shake-up in drug safety…Mr Lonngren added: "From a safety viewpoint, we are keen to have a slower release (of new drugs)." - Financial Times; January 28, '05, front page

Baycol, then SSRIs, then Vioxx….

- FDA's speed on Vioxx…"has raised major concerns about the undue control of industry over postmarketing safety data" – P. Juni et al: Lancet, Dec. 4 2004
- User fees generate a conflict of interest…because FDA is now partially funded by the companies it regulates – Sidney Wolfe, Public Citizen
- Withdrawals 2.0% of drugs approved '89-'92….3.5% of approvals '93-2000 : "To me, that's a red flag" - DeAngelis
- FDA commissions external audit…takes steps to improve monitoring and communication
  - "…initial steps are insufficient to dispel undue influence" – DeAngelis et al
- "We need independent Office of Drug Safety" – Pstay et al
  - Recalls discouraged because FDA must admit it made a mistake
- Carefully selected academic centers should get government funds to formulate and publicize drug prescribing guidelines – Brian Strom
- Academics, associations, agencies, all 'mired' in industry ties – Jerome Kassirer, former Editor-in-Chief, NEJM
  - E.g. NIH panel in July 2004 recommends statins; 9 of 10 have financial ties

Dissecting and Naming the Issues

- A morass of ideas and issues clouds and confuses discussion
  - Disclosure of trials? Are drugs "safe"? Drugs approved too fast/slow? Conflict of interest (academics, industry, FDA/EMEA)? Too much freedom to prescribe by doctors? Public access to pharmacovigilance data? Is the current peer-review model of sharing science inadequate? How to achieve medical innovation - free enterprise vs. government monopoly? Fundamental issues of trust in scientists?
- What's the Issue We Wish to Discuss?
  - "The beginning of Wisdom is to call things by their right names" -Chinese Proverb
- Name five "distinct" issues for purpose of furthering debate

Dissecting and Naming Interlinked Issues

- #1 - Disclosure
  - Release all research results with/without peer review publication
  - What research and what risks?
    - Does a trial need to be human? Phase 2? Confirmatory?
    - Risk of circumventing “promotional” law/regulation?
    - Will people use inadequate trial reports to Rx patients?
    - Is chance of publication jeopardized?
    - What about negative trials? (“Publication Bias”)
    - Trials with investigational vs. marketed drugs?
    - Release of design/protocol vs. results
  - Where? How? Who can search it? Etc.

"In an unprecedented move, …major international pharmaceutical associations…agreed... The "Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases" demonstrates…industry's commitment to increasing the transparency of clinical trials….

The voluntary principles (excerpt):

_ describe the types of information that member companies should make available, at a minimum, in registries of clinical trials;

_ provide that member companies should include information on ongoing and new trials in a registry by September 13, 2005;

_ express member companies' commitments to post in an accessible clinical trial results database the results of clinical trials completed from today forward on all marketed products…

-EFPIA, IFPMA, JPMA, and PhRMA press release; Jan 6, 2005 (www.phrma.org)

Results of all clinical trials (except those that are considered "exploratory") on a drug approved for marketing and commercially available in at least one country should be posted on a publicly available website, "regardless of outcome," the paper says. The results should be posted within one year after the drug is commercially available. Trials completed after an initial approval should be posted within one year of completion, the paper says. Companies should use a "non-promotional" format and provide links to any peer-reviewed journal articles.

The Pink Sheet, January 7, 2005

"*Some legislators, physicians, editors of academic medical journals, and consumer groups said the snail's pace of voluntary disclosure is all the more reason* ***Congress this session should craft laws*** *to require that companies disclose all information to the public about potentially life-threatening side effects hidden in America's drug supply*."

Christopher Rowland: The Boston Globe, January 9, 2005

Dissecting and Naming Interlinked Issues

#2 - Protecting Patient Safety

- How is patient safety best achieved?
  - Simple - Just Don't Hide Data! (Especially safety data…)
- Is it really that easy?
  - **"Risk/Benefit"** : elusive and evanescent
    - Safety from the disease and from the drug…
    - Balancing risks of under- or over- treating
    - Risk perception, risk communication
  - Difficulty of understanding cause-effect
    - Hard for scientists – Requires public trust without understanding?
  - Confuscation by detail…are patient reports helpful?
  - Should government use "strong arm" to control use of drugs by prescribers and patients?
  - Can the "peer review" (non-public funded) publication model work?
  - Are safety and efficacy results equally about "patient safety"?
  - Linked to disclosure…linked to following issues…

Dissecting and Naming Interlinked Issues

#3 - Conflict of interest
- Funding for regulators? From industry?
- How about academics? Is disclosure a fix?
  - Is it wrong for a researcher to be paid for his ideas or inventions? In Medicine? Better alternatives?
- Role of academics in discovery and clinical research?
  - Who should pay for and incentivize medical discovery and research at Universities? Role in safety and standards?

#4 - Role of government in medicine and science
- To assure basic protection of public? (Access, claims, …)
- To regulate risk/benefit? Standards for use?
- Perform all discovery and clinical research?
- Role of free enterprise "for profit" model? Invisible hand?

#5 - Role of the Media
- Science reporting – peer review (uneven and unpaid)
- Lay press reporting of medical science – what's hot?
- Reporting of hypothesis generating vs. testing, context, controversy, risk perception, …

Conclusion

- Today's Topic: Publication of Study Results
  - Raises many issues – its not really just about transparency…
- Consider many inter-related issues. Start with:
  - Disclosure
  - Patient Safety (& Risk/Benefit)
  - Conflict of Interest
  - Role of Government
  - Role of the Media
- The issues are complex…
  - Sometimes issues of political philosophy intrude
- Next Step – nuanced debate of underlying issues…