Drug Safety: What Should Companies Do Now?

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Agenda

- What Is “Now”?
- What Are Companies Being Asked to Do by Health Authorities?
- What Is FDA Doing that Impacts Companies?
- What Is Industry Doing?
- What Does Industry Need to Do?
- What About the Future?
- Solutions….

What is "Now"? A New Reality

- The pendulum has swung
  - "Questions don't change, answers do"
- Question of risk – and how much?
- Bar has been raised – greater expectations
- Trust by public has been eroded

What Has Changed?

- Risks- actual risks haven't, but perception about risk has
- Medical Practice – evolving from art to science: expert consensus evolves to evidence based science
- Benefit Risk Assessments will have to be more formal
- Trust in FDA and Industry has eroded – must be regained

What Are Companies Being Asked to Do?

- FDA Risk Management Guidances – March 2005
- ICH E2E – Pharmacovigilance Planning Guidances

- FDA says "not mandatory" – although in reality many drugs will need and many companies are doing as routine - but EU will require Pharmacovigilance Plan +/ Risk Minimization Plan (RiskMAP)

What Is FDA Doing?

- Critical Path Initiative
- Aims to bring more efficiency to drug development
- Will also play a major role in addressing safety concerns
  - Help prevent AEs by avoiding treatment of individuals at high risk of event
  - Better tools to monitor emerging toxicities
- Goal to create additional tools and biomarkers
  - Increase predictability in drug dev process
  - Improved decision-making by physicians (right drug at right dose to right patient)

What is FDA Doing? (2)

- Drug Safety Oversight Board (DSB)
- Independent oversight and advice to CDER Director
- Will identify, track and oversee the management of important drug safety issues and will provide emerging information to HCP and patients about risks and benefits of medicines
  - Enhance the independence of internal deliberations
  - Members of FDA, other government agencies =/- outside consultants

What Is FDA Doing? (3)

- "Drug Watch" Web Page:

  Information on the Web about drugs FDA is actively evaluating to determine the meaning and potential consequences of early safety signals
- Expands the existing communication channels to provide drug safety information to the public
  - Emerging information available in easily accessible form
  - Draft guidance was issued on May 10; comments to be submitted by Aug 8

What Is Industry Doing/Planning?

- Healthcare Provider Training Initiative
- Quality of spontaneous reports needs to be improved
- PhRMA is going to work in partnership with AMA, APhA, AAMC, others to develop/fund training programs (role of HCP in identifying and reporting ADRs)
- Issue of quality vs. quantity

What Is Industry Doing/Planning? (2)

- New Approaches to Pharmacovigilance
- New PV methods and tools are needed
- PhRMA will work with CERTS (Centers for Education & Research on Therapeutics) to develop opportunities related to proactive surveillance and other PV methods

What Is Industry Doing/Planning? (3)

- Patient Focused Risk Communication
- Better outreach is needed so patients have better understanding and expectations of the drugs they are being prescribed
- PhRMA will work with external stakeholders to better understand tools, roles, and messages in communicating benefit-risk to patients (done in concert with CERTS)

What Is Industry Doing/Planning? (4)

- Improving the Communication of Evolving Safety Profiles of Drugs to Physicians and Other Health Care Providers
- Communication to the HCP of important new safety information needs improvement; also need to be able to decrease time to effect change to drug labels
  - PhRMA will develop criteria for defining types of safety signals appropriate for streamlined notification procedure
  - Focus on decreasing time for label changes; also other ways to communicate if label change not appropriate

What Is Industry Doing/Planning? (5)

- Evidenced Based Medicines Approach
  - Developing principles via PhRMA
  - Focus on need to improve healthcare and patients' outcomes

EBM can help establish values of medicines

What Is Industry Doing/Planning? (6)

- PhRMA/sponsors with policies on supplying information to Web databases on clinical trials
  - Clinical Trials Database – located on US government's website
    - Registration of new and ongoing hypothesis-testing clinical trials on drugs marketed in US or intended for marketing in US, so medical community and patients can have direct link to information

What is Industry Doing/Planning? (7)

- Providing Reports/Data on Completed Trials:

  September 2004 – Clinical Study Results Database to provide centralized repository

  - Disclose results (positive or negative) of hypothesis-testing trials for US-marketed pharmaceuticals

  Must balance the "need to know" with proprietary/intellectual property issues

What Does Industry Need to Do?

- Transparency
- Objectivity
- Collaborate with FDA/NIH/Academics – all need to rebuild trust in clinical trial process/investigators as unbiased
- Follow through on any commitments

We must work to regain the trust of patients!

What Does Industry* Need to Do?
*Yes, Your Company!

- Share information on studies
- Be responsible about DTC – we must self-regulate
- Improve electronic infrastructure and technology – need a robust IT system
- Don't do "bad" things – ALWAYS do the right thing
- PUT PATIENTS FIRST!

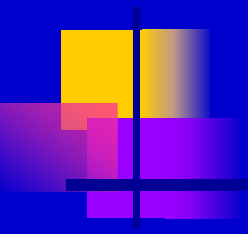
What About the Future?

Hard to predict – why things are so difficult to plan for, BUT

- Communication – over Internet
- Pharmacogenomics- not clear what extent
- Clinical Trials – smaller, electronic
- Sales Reps – dinosaurs? (lessons of Encyclopedia Britannica)

Solutions

- Need to regain trust – really put patients first
- Need to come together to show patients we want to help them, then can build on this
- Provide *value* to patients
- Make sure our *values* are patient-oriented



The End*

*but only the beginning

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Compliance Perspective

- Recent examples of what NOT to do
- Assessment of corporate risk in the safety continuum
- Recommended Actions

Recent examples (1):Vioxx

- WSJ reported that Merck head of R&D sent an e-mail in 2000 stating that cardiovascular problems related to Vioxx are “clearly there” but that the sales force should be instructed to “dodge the issue” when speaking to physicians.
- NYTimes reported that a senior Merck scientist urged a researcher by e-mail to change his views that a patient’s cause of death was due to an MI "so that we don't raise concerns."

Recent examples (2): Paxil

- GSK officials admitted failing to publish studies with negative results about antidepressant use in children
- Elliott Spitzer sued GSK for violation of NY consumer protection laws

Assessment of risk in the safety continuum

- Information relevant to drug safety comes from every area of the business
  - *Positive* business value: **Safety DOES Sell!**
- Companies must establish processes in ALL areas of the business to ensure that safety information is recognized, collected, and analyzed in a timely manner
  - *"Forewarned is forearmed"*

Questions to ask

- What did we know?
- When did we know it?
- What did we do about it?
- Was what we did about it consistent with our duty to protect patients?
- Most importantly – would the public *agree* that we did the "right" thing?
  - Gap between regulatory/legal requirements and moral/ethical responsibilities, as well as public expectations

Actions to take:

- Evaluate existing policies and processes
  - Global *and* local
  - Identify gaps, conflicts, and where updates are needed
  - When in doubt – be conservative!
- Eliminate deviations and exceptions
  - Inconsistency increases compliance risk
  - Get rid of the *"But We're Special"* mentality
- Evaluate existing documentation
  - E-mail
  - Slide presentations

Actions to take:

- Train, train, train
  - Global *and* local
  - Educate on consequences of non-compliance
  - What NOT to do as well as what to do
- Document, document, document
  - First – establish strong rules on good documentation practices
- Audit, audit, audit
  - Evaluate effectiveness of training
  - "What we said we'd do" versus "what we really did"
  - Find evidence of non-compliance ASAP

Actions to take:

- Respond to non-compliance
  - Response should be consistent
    - Need to have a policy regarding repeat offenders
  - Response should be documented
    - Should include documentation of why action was NOT taken
  - Response should always include actions taken to prevent recurrence

Remember……

- There is no “end” to our responsibility to protect patients.