Reflections of a Former FDA Chief Counsel: Creative Compliance Strategies

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Overview

- Current Environment
- What to Watch Out For
- Some Suggested Strategies
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The Situation Before 2004

- Healthy appreciation for risk/benefit
- All drugs have risks
- FDA as a risk management agency
- Lessons of the AIDS experience
- Bayesian statistics discussion
- Focus on post-marketing systems
- Role of PDUFA
2004

- Preemption
- Importation
- Flu Vaccine
- SSRIs
- Vioxx

The last three all involve substantial compliance issues!
Key Development – Introduction of other “regulators”

- US Attorneys\DOJ
- State Attorneys General
- Plaintiffs’ Lawyers\State Juries
- NGO’s\Medical Journals

Most of whom are NOT scientific!
Others to worry about

- Congress
- Media
- Public Citizen and other so-called consumer groups
- EU and other countries’ authorities
- Physicians
- Patients!
U.S. Legal Landscape

- Federal Food, Drug and Cosmetic Act Concerns Transmogrified Into Fraud and Abuse Offenses
  - Drug Safety Failures Implicate Both The Federal Food, Drug and Cosmetic Act (GMPs, GCPs, Adulterated Drugs) and The Health Care False Claims Act and Anti-Kickback Law
  - Huge Penalties/Exclusion Even Where Underlying FFDCA Issue Not Clearly a Violation
    - Corporate Healthcare Settlements Up to Almost $1 Billion
    - Debarment From Working in the Pharmaceutical Industry if plea or conviction
    - Criminal Exposure: Jail And Large Fines
      - Felony -- Imprisonment and penalties for individuals: up to $250,000
      - Misdemeanor - up to 1 year and penalties for individuals: up to $100,000
    - Civil Penalties for Individuals: Up to Tens of Millions
    - Injunctions Naming Companies and Individuals
- State Consumer Fraud, Product Liability, and Securities Class Actions Now Follow
  - Paying Many Times for the Same Allegation
Impact of the Preemption Preamble

• In the Physician Labeling Rule, FDA declared that state law challenges to the label are, in its view, preempted

• In response, plaintiffs lawyers and state AGs are increasingly focusing on company activity outside the label

• Next major focus of lawsuits – failure to comply with GMPs, GCPs, GLPs?

• Almost every 483\WL leads to lawsuits, bad press, and competitive\reputational harms
EU Enforcement Trend

- Increased Pharmacovigilance Enforcement Focus
  - EU Requiring Member States to Impose “Effective and Dissuasive Penalties”
    - Numerous Criminal Investigations Under Way
    - Product Liability-Type Actions Being Pursued
    - May Serve as Predicates for Private Lawsuits

- Commission Guidelines Leave Companies With Open Compliance Issues and Difficult Legal Counseling Decisions

*Maurits Lugard, Sidley Austin Brussels*
Global Regulatory Trends

- While FDA Has Moved Toward A Risk-based Approach, Emphasizing Internal Controls And A GMP-type Regime, Congress Is Pushing The Other Way
- EU Authorities Have Ramped Up Enforcement Machine
- Criminal Enforcement Being Utilized To Create Industry “Poster Children”
  - Companies In U.S.; Individuals In EU; Countries On Other Continents Are Investigating As Well
- Product Liability “Export” To Europe
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Issues Raised in Regulatory Actions

- Validation
- Lack of Sterility Assurance
- Failure to Sterility Test
- Inadequate investigation of failure to meet specifications or unexplained discrepancies
- Cross Contamination
- Adequacy of Mix – Blending
- Packaging and Labeling Issues including product mix-ups

Source: Joe Famulare
Some Current FDA Pharmacovigilance Concerns

- Failure to Trend Obvious Data Points
  - Leads to Failure to Report Safety Issues
- Failure to Report Signals Where Appropriate – Including From Foreign Sites
- Inadequate Safety Data Collation In Clinical Trial Stage
- Software Validation
- Bottom Line: FDA Dislikes Surprise -- Wants to be Advised in a Timely Fashion
Promotional Issues

- Watch out for cumulative effect
- MSLs
  - Avoid suggestions of ROI
- Consider regular audits to ensure compliance with plan
- CME\Meeting Sponsorships
  - Minimize influence; independence is key
- WLF leave-behinds
- Direct mail to physicians\unsolicited requests
- Medical writing support
- P & T committees\PE data
- Advisory boards
Regulatory Significance of Final Labeling

- New legislation
  - Will approved labeling continue to be the centerpiece of risk management for drugs?
  - Will all new drugs require risk management plans that reduce emphasis on labeling?
  - How does this implicate FDA’s assertion that labeling in the new format would prevent medical errors and yield other public health benefits?
  - Will MedGuides be required for all products?
  - How does the new authority affect preemption?
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FDA: What Can Industry Do?

- Continue to innovate and develop products that advance public health
- Demonstrate a corporate philosophy of compliance
- Pay attention to signals
- Be forthright and proactive

Source: David Elder
HHS Guidance to Pharma Companies (Healthcare)

- "At a minimum, a comprehensive compliance program should include ...(5) The use of audits and/or other risk evaluation techniques to monitor compliance, identify problem areas, and assist in the reduction of identified problems"

- “F. Auditing and Monitoring

- The extent and frequency of the compliance audits may vary depending on variables such as the pharmaceutical manufacturer’s available resources, prior history of noncompliance, and the risk factors particular to the company. The nature of the reviews may... include a prospective systemic review of the manufacturer’s processes, protocols, and practices...

- The reviews should also evaluate the company’s policies and procedures regarding other areas of concern identified by ... federal and state law enforcement agencies."
Audit To Ensure That the Reports Are Accurate

- A Key Factor In Investigations
- Puts Accepted Conclusions to the Test
  - Need to Drill Deeply in Selected Areas
- Keep Privileged to The Extent Possible
  - Try to Ensure A Valid Use of the Privilege
  - Confer with Legal Department

Source: Scott Bass
Importance of a good PV system

- Can be helpful in getting drugs approved
- Not just about compliance – an important tool in ensuring safe use
- Recent shift towards stricter enforcement of stricter EU rules
- New draft of “Volume 9” (EU Guideline on Pharmacovigilance)
Emails Become Permanent Evidence

- Write What You Mean To Say
- Avoid Mass Emails--Check Your Cc’s
- Use Privilege Where Appropriate
- Use Proper Company Compliance Reporting Procedures

- Do Not Over Characterize
  - “Worst I Have Seen”
  - “Rumor Has it”
  - “Can’t Believe I Told Her Once Before”
  - “I Hope Management Never Sees This”

- Let The Legal Department Determine The Law

Source: Scott Bass
Organizational Changes May Be Critical in Avoiding Governmental Pain

- As in GMP Compliance, Systems Approach by Authorities
- Critical To Avoid:
  - Decision-Making Voids (Common)
  - Conflicting Jurisdiction
  - Marketing or Sales Top Decision Authority
  - Failure to Fix Acknowledged Weakness
Competitor Complaints

- To complain or not to complain?
  - (At least) 2 views
- GC-to-GC resolution
- Be strategic
  - intended use example
- How-to
  - emphasize level playing field
  - agree steps with business
Data Quality Act Challenge

DQA imposes data quality standards on federal agencies and allows private parties to file information correction request (ICR) with agency after agency dissemination of information

Agency generally must respond to ICR within 90 days

– Possibility of judicial review upon denial of ICR

Case law so far not favorable

– Montana District Court held that DQA did not provide a private cause of action and that, since DQA did not provide any meaningful standards for review, agency action is committed to agency discretion. In re: Operation of Missouri River System Litigation, 03-MD-1555 (PAM), (6/21/04)

– 4th Circuit held that petitioners lacked standing to appeal agency denial of an ICR because DQA “does not create a legal right to access to information or to correctness.” Salt Institute v. Leavitt, No. 05-1097 (3/6/06)
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Drugs Team  
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Veterinary Medicine Team

Medical Devices Team

Foods Team
Points to Consider

- Is FDA acting within one of its core areas of expertise?
- What is at issue -- science or law/regulation?
- What are your best arguments? Do you have a public health case?
- Are you willing to devote time and resources to the dispute?
- Which venue/procedure is best?
Bottom-Line Advice

- Think strategically
- Think cooperatively
- Think globally
Thank you!

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