FDA’s Global Reach: Actions & Industry Reactions

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Topics

- Drivers for Global FDA
- Actions by FDA
- Reactions by Industry
- Considerations for Industry
Drivers of FDA’s Global Approach

Public has challenged FDA about

- Product and food contamination
- Counterfeiting and raw material substitution
- Increased outsourcing
- Product recalls
- Product withdrawals
Topics

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- **Actions by FDA**
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New Commissioner to bring change

- “Prevent harm to the American people through swift, aggressive, and effective enforcement of FDA laws and regulations,” Commissioner Hamburg, FDLI, 6 August 2009

- “Hamburg sees and activist role for the US FDA,” Scrip, 26 June 2009

- “FDA to Double Foreign GMP Inspections this Year,” Drug Daily Bulletin, 28 August 2009
FDA is increasing its inspection cadre

- Hiring new inspectors
- Time to train and field
- Permanent foreign assignments
- Hair Trigger enforcement seen as FDA sends in U.S. Marshals and negotiates consent decrees in cases without even first issuing warning letters.

The Gold Sheet, August 2009
FDA will inspect and act quickly

- Industry can expect to see FDA
  - Work closely with regulatory partners
  - Take immediate action where needed
  - Set post-inspection deadlines
  - Speed the warning letter process
  - Promptly reinspect
  - Implement a warning letter close-out process

FDA goes international

- FDA seeks membership in PIC/S
  - Pharmaceutical Inspection Convention and Pharmaceutical Inspection Cooperation Scheme
- Participating in Global Harmonization Task Force for Devices
- Anecdotal confirmation of joint and parallel inspections
- Establishing international offices

Legislation may bring more global requirements

While the impact of sweeping healthcare reform unknown, legislation to specifically increase FDA’s role has been circulating

- FDA Globalization Act of 2009 (pending)
  - Subpoena, seizure and recall powers
  - Annual registration of domestic and foreign firms
  - Requires affirmative verification of identity and purity
  - Achieve parity in foreign and domestic inspections
  - Country of Origin labeling required for APIs
  - Denies entry for products whose facilities limit FDA inspections

Enforcement Actions are increasing

- Double the rate of enforcement actions
  - 18 drug warning letters in 1H09 (2X 08 or 07)
  - Some with little to no notice
  - Many drug recalls and seizures
  - 2 drug manufacturer Consent decrees signed

“... Next week you will be reading about how FDA has placed a company on import alert only seven business days after the conclusion of a foreign inspection”

Edwin Rivera-Martinez, CDER International Compliance Branch
FDA’s Global Reach …

- FDA adapts to a new world
  - More resources, new inspectors
    - More foreign Inspections
    - Harsher Enforcement
  - Harmonization and interaction with ROW
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Global Companies (G), Importers to the US (I), and Contractors (C), are equally affected, however they will develop specific strategies.
Redesign the network of factories so that each site is under limited regulatory jurisdiction (G, I, C)

Companies are narrowing site scope to supply fewer regions

- Often, authorities create conflicting expectations and results
- Sites require mastery of several requirements
- Transparency between regulators compounds severity
Several global companies that have a global network and outsourced over the last decade have decided to consolidate all global products in a few US based factories

- Will maximize control, at the highest standards
- Can no longer rely on distant regional or third party networks with many decision points and little control
- Will require major regulatory supplements but expect to be cost positive
- Drive to better utilize existing factories
License-holder responsible for contractor & supplier production (G)

Global companies have created new organizations to manage & control the quality for global sourcing
- Expand QA organization
- New policies & standards
- Enforce Quality Agreements
- Comprehensive inspections
- Central single complaint systems
- Strict governance, communication, and escalation
Compliance knowledge of suppliers & contractors will be shared (G,I,C)

Industry has established consortiums with standards and programs to exchange or share reporting
- Now driven by compliance in addition to cost
- IPEC – International Pharmaceutical Excipients Council
- Rx360 – International Pharmaceutical Supply Chain Consortium
- There is mixed acceptance by industry and regulators ...
  many issues to be resolved
Global pharmaceutical companies actively supported development of ICH Q8, 9, 10

- Goal was to create clarity in approaches to satisfy regulators
- Could ease the creation of joint ventures and shared manufacturing facilities
- (G) Global companies have set the standards and have a competitive advantage
- (I,C) – Most contractors and companies that export to US need to upgrade to achieve the same standard; expect major investment in the near future
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Considerations for Industry
Companies may not understand FDA initiatives

Understand the FDA “hot button” issues

- **Management Controls** – Active engagement of the organization towards compliance
- **State of Control** – new interpretations of validation
- **Quality Systems** – Prevent field alerts and recalls
- **Supply Chain Management** – Compliance of vendors, contractors, & suppliers
Regulators do not separate Quality from Compliance

State of compliance is defined by the observations from regulators and not by internal quality indicators and the necessary state of control

- **Compliance** – Regulatory observations, etc.
- **Quality** – RFT, Yields, Cost of Quality, etc.
- **State of Control** – Knowledge of products, processes, infrastructure necessary to maintain and improve, and support decision making
Companies have been blinded by “positive” inspections

Company leaders in many cases wonder why they are being targeted by agencies after a history of “good” relations and inspections with a “few” observations

- Blame the regulator, miss the message
- Failures must be evaluated against Quality System robustness
- Do not evaluate the impact to other sites & corporate
Rely on corporate auditors for “certification” of compliance

Auditors can only discover few deficiencies, compared with those known to operators

- Audit Results
  - We knew 80%
  - Only 10% are of value
  - 10% are misinformed
- The opportunity is to create a total disclosure process with incentives
Recognize that compliance is perishable

Management often does not maintain adequate investments, allowing capabilities to degrade, and resulting in surprising compliance failures

- Ongoing investment is needed to maintain compliance
The right governance supports sustainable compliance

Governance is a process to evaluate the capabilities to sustain a desired state of quality and compliance

- Requires the capabilities to define leading indicators to perform a sustainability risk analysis
- Does not rely on lagging indicators only
Questions?

Thank you,

Claudio & Owen