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Anticipating the FDA Regulatory Environment for Product Review

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Factors Affecting the FDA Environment

- Public and political confidence in FDA
- Financial resources available to FDA
- Employee morale
- Public attitudes toward the pharmaceutical industry
- Agency trust of pharmaceutical industry
- Competing priorities within FDA

These Factors Can Change Dramatically and Quickly

- New wave of product withdrawals and safety warnings
- Congressional hearings, whistleblower charges about FDA
- Media allegations of industry cover-ups
- Resource reductions and reallocations under PDUFA, overall budget
- Medical thought leaders' criticisms of FDA, industry

As Environment Changes, So Does Drug Approval Process

- Decision to approve a drug is inherently risky
  - Undetected safety issues
  - Off-label uses
  - Misinformation among physicians, consumers
- Public perception of degree of risk involved fluctuates
- FDA reacts to these perceptions
  - Thalidomide (1962) led to IND, informed consent, restrictions on drug testing in women
  - AIDS activists accelerated approval process

Importance of Recent Safety Experiences

- FDA has declining confidence in labeling changes
  - Published studies show that physician behavior not altered
  - Risk management programs require more effective interventions
- Post-approval ADE reports cannot detect many increased risks over background rates
  - Recent safety issues found in controlled studies

FDA Will Likely Be More Conservative

- Reject notion that FDA will simply stop approving drugs
- Accept idea that FDA wants to maintain public trust
  - More articulation of decisions (transparency)
  - Greater emphasis on internal consensus
  - Close attention to safety issues pre- and post-approval
  - More sensitive balancing of benefits and risks

Will FDA Radically Change the Drug Approval Process?

- FDA historically evolves cautiously
  - Builds on past practices
- The issue today is safety, not efficacy
  - How to discover all important drug risks quickly
- FDA believes that faster approvals require more rapid withdrawal mechanisms
  - 1992: A key element in Subpart H (accelerated approval) regulations -- but not part of PDUFA

FDA Is Constrained in What It Can Do

- Republican control of Congress will discourage any expansion of drug law
- Budget deficits and Bush agenda will prevent any radical increase in financial resources
- Industry R & D costs need to be reduced, not increased
- Major changes in regulation can have unintended consequences on industry incentives, behavior

How Might FDA Change the Process?

- Political demands for greater protection of public safety will continue
  - Focus will be on safety data and assessments
  - Long-term hope: new technologies
- Short-term options:
  - Review different drugs differently
  - Expand use of accelerated approval regulations
  - Create a peri-approval period for all drugs

Treat Different Drugs Differently

- "Life-saving" drugs vs. "life-style" drugs
  - Public perception that data requirements, time for testing and approval are always the same
  - Public skepticism that the public health benefits are similar
- FDA options: Explicitly vary data requirements, review times among candidates
  - Changes in PDUFA agreements, ICH guides needed?

Expand Use of Accelerated Approval Rule

- Subpart H not limited to drugs with surrogate endpoints; covers life-threatening or serious illnesses
- Subpart H permits FDA to --
  - Impose RiskMAP requirements (prevent off-label use? mandate ADE reporting by physicians?)
  - Require Phase 4 studies (controlled safety studies?)
  - Preclear promotional materials (delay DTC ads?)
  - Withdraw approval expeditiously

Create a Peri-Approval Period

- Essentially, apply Subpart H to all new drugs
- Premise: A new drug must either (1) be tested exhaustively preapproval or (2) be subject to intense post-approval monitoring, testing, and controlled use, before unrestricted general Rx marketing
- Would not delay approvals, but put all drugs on probation
- Would require new regulations (but possibly not new legislation)

Will FDA Take Any of These Options? What Should Industry Plan For?

- My speculation, not inside knowledge --
  - FDA will try all three in some form or other
- Industry should anticipate these changes
  - Revisit development, approval and launch strategies
  - Take potential safety issues as serious priorities
  - Work toward the longer term technological solutions

Questions and Discussion

The floor is open

If you have additional questions, feel free to contact me at:

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