

New Trends Affecting Pharmaceutical and Medical Device Life Cycle Risk Management



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New Trends Affecting Pharmaceutical and Medical Device Life Cycle Risk Management – Overview

- Regulatory and economic environment for pharma/device firms will change substantially over the next few years
 - Will require focus on new mechanisms to effectively manage risk throughout the product life cycle
 - New trends include:
 - Enhanced regulatory enforcement and investigation
 - Widening scope of use and requirements of FDA REMS authority
 - Continuing shift to Asia of clinical testing/manufacturing outsourcing
 - Funding and development of health information technology
 - Funding and development of comparative effectiveness research

New Trends Affecting Pharmaceutical and Medical Device Life Cycle Risk Management – Overview

(cont'd)

- Expansion of use of new social media in marketing
- Expansion of scope of use of home testing and monitoring
- Expansion of scope of use of personalized medicine
- Changes from potential healthcare reform legislation
- Potential creation of a regulatory approval pathway for biosimilars
- All of these trends will have significant consequences for life cycle risk management

Managing Risk Across the Life Cycle – Enhanced Regulatory Enforcement and Investigation

- Enhanced reviews of NDAs, BLAs, PMAs, and 510(k)s for safety data
- Enhanced focus by FDA on safety labeling and updates of labeling
- Enhanced focus on clinical significance of study results (not only statistical significance)
- Enhanced focus on post-marketing (Phase IV) studies
- Enhanced reviews of DTC and other advertising
- Increase in early risk communication, untitled and Warning Letters, and consent settlements

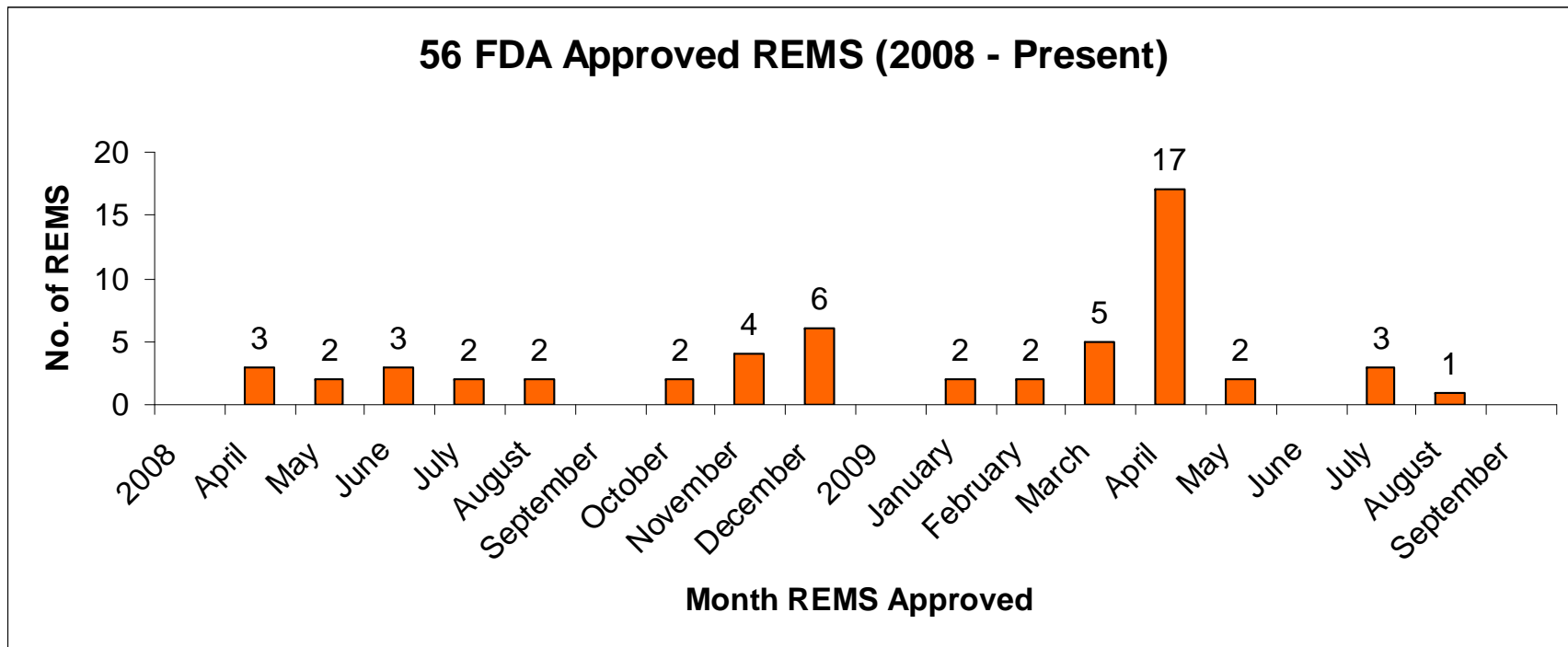
Managing Risk Across the Life Cycle – Enhanced Regulatory Enforcement and Investigation (cont'd)

- See FDA's Strategic Plan for Risk Communication (Fall 2009) (released Sept. 30, 2009)
- Six steps FDA will be undertaking to enhance enforcement:
 1. **Post-inspection deadlines.** The FDA will give no more than 15 days to firms to respond to significant inspection findings.
 2. **Speed of the Warning Letter process.** The FDA will streamline the Warning Letter process by limiting review of Warning Letters by the Office of Chief Counsel to those that present significant legal issues.
 3. **Coordination with regulatory partners.** When public health is at risk, the Agency will coordinate with state, local, and international regulatory partners to take rapid action.
 4. **Prioritize follow-up on Warning Letters and other enforcement actions.** The FDA will work quickly to assess and follow up on corrective action taken by industry after a Warning Letter is issued or major product recall occurs.
 5. **Take immediate action in response to public health risks.** FDA will act more quickly to deal with significant public health concerns and violations. The Agency has said such actions may occur before a formal Warning Letter is issued.
 6. **Issue "close-out" letter.** FDA will issue an official "close-out" letter that will be posted on its website when it has determined that a firm has fully corrected violations raised in a previous Warning Letter.

Managing Risk Across the Life Cycle – Risk Evaluation & Mitigation Strategies (REMS)

- FDA has authority to require one or more of the following elements in a REMS:
 - a Medication Guide or Patient Package Insert (“PPI”)
 - a risk communication plan; and
 - use and/or distribution restrictions
- Every REMS must include a timeline for submission of assessments
- Substantial civil penalties for REMS violations
- Use of REMS by FDA increasing

Managing Risk Across the Life Cycle – Risk Evaluation & Mitigation Strategies (REMS) (cont'd)



Managing Risk Across the Life Cycle – Risk Evaluation & Mitigation Strategies (REMS) (cont'd)

- Consequences for life cycle risk management:
 - Interpretation of new guidance on the format and content of REMS
 - FDA Draft Guidance, “Format and Content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS Assessments, and Proposed REMS Modifications” (Sept. 30, 2009)
 - Difficult to ensure consistency in REMS requirements and across product classes
 - Basis for REMS requirement varies greatly
 - Potential for products liability challenges based on REMS scope and operation

Managing Risk Across the Life Cycle –Outsourcing of Clinical Testing and Manufacturing

- Outsourcing to Asia of clinical testing and contract manufacturing already substantial and likely to increase
- Consequences for life cycle risk management
 - **Manufacturing quality control concerns**
 - e.g., Baxter International's marketing of heparin manufactured with contaminated ingredients from China
 - **Oversight of testing protocols**
 - **Data integrity concerns**
 - e.g., earlier this year, FDA suspended review of all pending drug applications from Ranbaxy that included data generated from an Indian plant because of allegations that some data had been falsified
 - **Potential product liability challenges regarding outsourced products/components**

Managing Risk Across the Life Cycle – Health Information Technology

- Health Information Technology for Economic and Clinical Health (“HITECH”) Act, part of the American Recovery and Reinvestment Act of 2009
 - Provides \$1.2 billion to support initial building of nationwide health IT infrastructure and electronic health records
- Consequences for life cycle risk management:
 - Substantial increase in electronic health data
 - Potential for use of expanded data for marketing purposes
 - Potential for increased privacy law concerns and potential additional data for products liability challenges

Managing Risk Across the Life Cycle – Comparative Effectiveness Research (“CER”)

- American Recovery and Reinvestment Act of 2009 (economic stimulus bill)
 - provides \$1.1 billion to compare drugs, medical devices, surgery, and other ways of treating medical conditions
 - creates 15-member Federal Coordinating Council for Comparative Effectiveness Research
- Increasing development of comparative effectiveness data
 - e.g., emphasis by Johnson & Johnson on outcomes-based drug development to build the value proposition of a product. (Pink Sheet, July 27, 2009).
 - e.g., focus by Amgen on development of data to support adoption and reimbursement coverage by CMS for osteoporosis drug Prolia. (Pink Sheet, Sept. 21, 2009)
 - e.g., new study by Tufts University Center for the Study of Drug Development revealed that nearly 80% of third-party payer plans “ascribe a role in off-label use reimbursement decisions, with almost one-fifth saying cost-effectiveness data play ‘a very important role.’” (Pink Sheet, March 23, 2009)

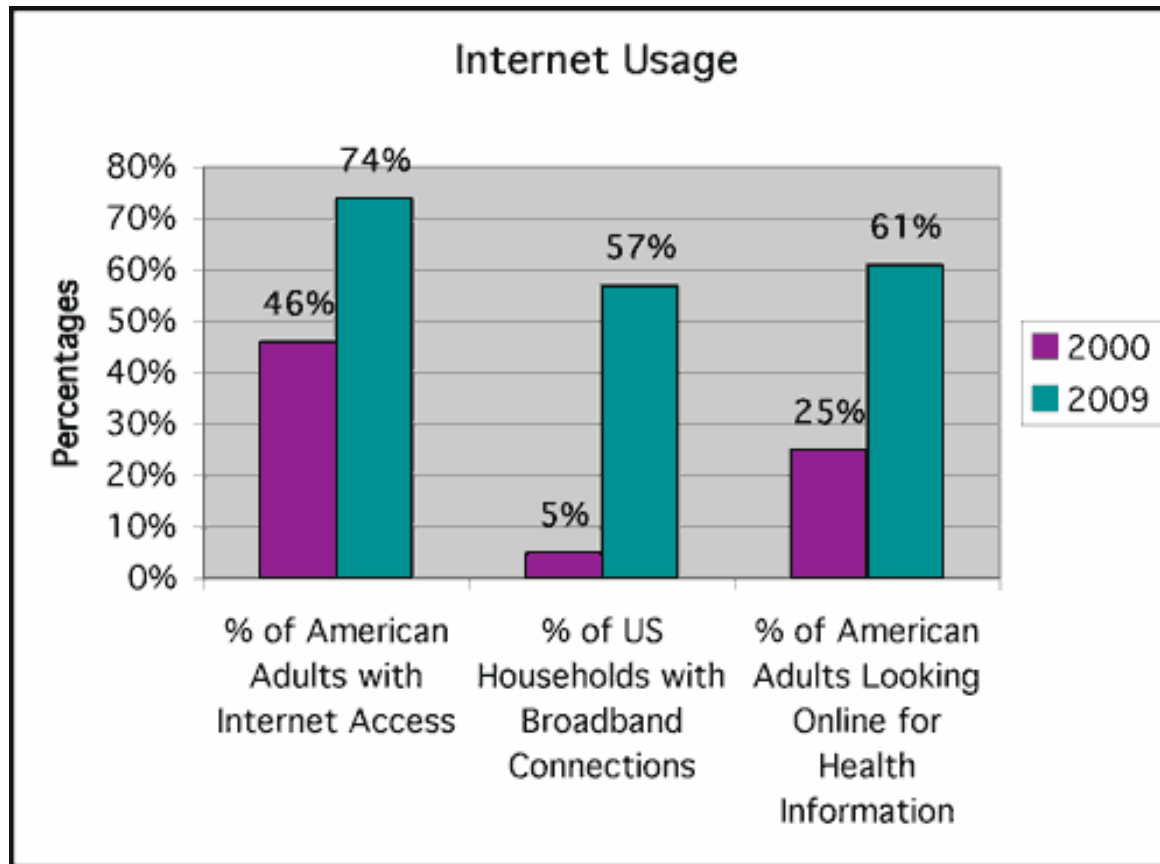
Managing Risk Across the Life Cycle – Comparative Effectiveness Research (“CER”)

- Consequences for life cycle risk management:
 - Effect on scope and type of clinical trials from focus on comparative effectiveness
 - Effects on possibility and scope of CMS and third-party payer reimbursement of drugs and devices
 - Effects on restrictions on availability for prescription or purchase of drugs and devices
 - Potential effects on products liability challenges from generation of comparative effectiveness/outcomes research data

Managing Risk Across the Life Cycle – Use of New Social Media

- Use of new social media and other Internet communication tools increasing by drug and device companies
 - **Social media and Internet mechanisms include:**
 - emails to patients and physicians; sponsored links to company websites; Facebook; LinkedIn; Twitter; YouTube; MySpace; company blogs; “sponsored-post” blogs
 - e.g., companies using YouTube recently include Johnson & Johnson; Novartis; AstraZeneca; Teva; and Boehringer Ingelheim. Several have blogs, including Johnson & Johnson and GlaxoSmithKline.
 - **upcoming Google Wave might also be used**
 - A real-time communication platform that combines aspects of email, instant messaging, wikis, web chat, social networking, and project management

Managing Risk Across the Life Cycle – Use of New Social Media (cont'd)



Managing Risk Across the Life Cycle – Use of New Social Media (cont'd)

- Consequences for life cycle risk management
 - **FDA enforcement focus on promotional communication using Internet mechanisms**
 - e.g., DDMAC recently issued 14 Notices of Violation to drug companies in connection with sponsored links that are listed in response to key word queries on search engines such as Google, for allegedly failing to include all of the mandatory risk information on the face of the sponsored link.
 - **Lack of FDA/FTC guidance**
 - Neither FDA nor the FTC has provided guidance on the parameters of Internet drug and device advertising
 - FDA's draft *Guidance for Industry, Presenting Risk Information in Prescription Drug and Medical Device Promotion* (May 2009) silent on Internet advertising
 - FDA has announced a public meeting in Nov. 2009 to discuss how it should regulate use of the new social media. (FDA has itself begun to provide information through Twitter) (Inside Health Policy, Sept. 25, 2009)
 - **Potential for challenges regarding privacy concerns by reason of information obtained through social media mechanisms**
 - **Potential for product liability challenges based on information obtained through social media mechanisms**
 - **Potential for private challenges to use of social media mechanisms**
 - e.g., NAD/NARC review of tooth-whitening claims through sponsored-post blogs by eCommerce Solutions (Tan Sheet, Sept. 21, 2009).

Managing Risk Across the Life Cycle – Home Testing and Monitoring

- Likely increase in use of home testing and monitoring devices, in response to cost-containment concerns and consumer demand
- Consequences for life cycle risk management:
 - FDA regulatory approval issues concerning consumer education/IT linkages/test sensitivity and specificity
 - Potential for challenges regarding privacy issues from data collected through home testing devices
 - Potential for products liability challenges from data collected through home testing devices

Managing Risk Across the Life Cycle – Personalized Medicine

- Increased use of personalized medicine (pharmacogenomics)
 - uses genetic tests or other biomarker assessments to tailor products and treatments to sub-populations
 - genetic factors used to personalize use for, e.g., Marovirac; Plavix; Warfarin

Managing Risk Across the Life Cycle – Personalized Medicine (cont'd)

- Consequences for life cycle risk management
 - FDA regulatory approval issues as to scope and use of pharmacogenomic data and biomarkers
 - Potential for disputes concerning collaborations between drug and device manufacturers
 - Potential for privacy challenges based on collection of genetic information
 - Potential for products liability challenges based on inaccurate diagnoses

Managing Risk Across the Life Cycle – Healthcare Reform Legislation

- Potential healthcare reform legislation, with likely substantial expansion of healthcare coverage to millions of the currently uninsured, and with cost-containment mechanisms in view of substantial likely increased demand for healthcare products and services
- Consequences for life cycle risk management
 - Increased focus by government on cost-containment mechanisms
 - Increased focus by government on life cycle management mechanisms (e.g., “pay-for-delay” agreements; use of authorized generics; “evergreening”/product migration strategies)

Managing Risk Across the Life Cycle – Biosimilars

- Potential for creation of a FDA regulatory approval pathway for biosimilars, as part of healthcare reform legislation or separately
- Consequences for life cycle risk management
 - Potential effects on life cycle management for biologics (regulatory and litigation challenges to patent and FDA market exclusivity)
 - Potential effects on scope and degree of reimbursement for biologics
 - Effects on scope of regulatory due diligence for biologics and corporate valuation assessments for transactions involving biotechnology companies and biologic products
 - See FTC Report, “Emerging Health Care Issues: Follow-On Biologic Drug Competition” (June 2009)

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