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Mitigating Potential Liability Risks From New Technologies



Setting The Stage – What We Will Cover

- Triggers For Potential Liability
- Risk Management and Labeling
- Anticipating And Minimizing Litigation Exposure
- Case Studies – Emerging Technologies
 - Innovation at the product level – Hypothetical of prescription drug and associated label
 - Innovation at the fundamental level – Employing nanotechnology to create new products




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Triggers For Potential Liability



- Liability Risks Ordinarily Presume Something Has Gone “Wrong”
 - Technology Fails To Work As Intended, Causes Injury or Harm, Provokes Unforeseen Reaction From Public Or Stakeholders
 - If Nothing Goes “Wrong” – Mitigation Irrelevant
- By Definition, New Technologies May Produce Unanticipated Developments


How Regulatory Professionals Can Manage These Risks

- Accept That Risk Of Product Failure, Adverse Effects, Etc., Are Unavoidable
- Goal: Anticipate And Mitigate Potential Liability From Regulators And Lawsuits Should Risks Materialize
- Challenges For Effective Mitigation Strategies:
 - Risks Frequently Materialize In Wholly Unexpected Ways
 - Effective Mitigation Must Begin Before Risks Actually Materialize
 - [Unstated] Expectation/Hope Of Zero Risk Of Failure




Risk Management and the Label Basic Principles, Risk MAPs and REMS

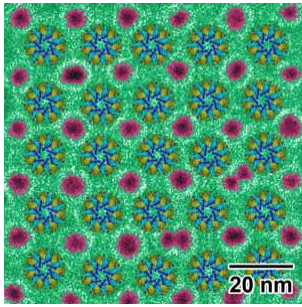


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Innovation





Ref: bellecitysoapworks.com




Ref: medgadget.com



Ref: xigris.com



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PDUFA History

- PDUFA I: FY93-FY97
 - Primary focus –decreased review times
- PDUFA II: FY98-FY02
 - Re-authorized in 1997 as part of FDAMA
 - Primary focus -decreased review times and shortened development times
- PDUFA III: FY03-FY07
 - Re-authorized in June 2002 as part of Bioterrorism Preparedness and Response Act
 - Focus: Expanded interaction and communication during 1st cycle review and support for post-market risk management for first 2-3 yrs post-approval

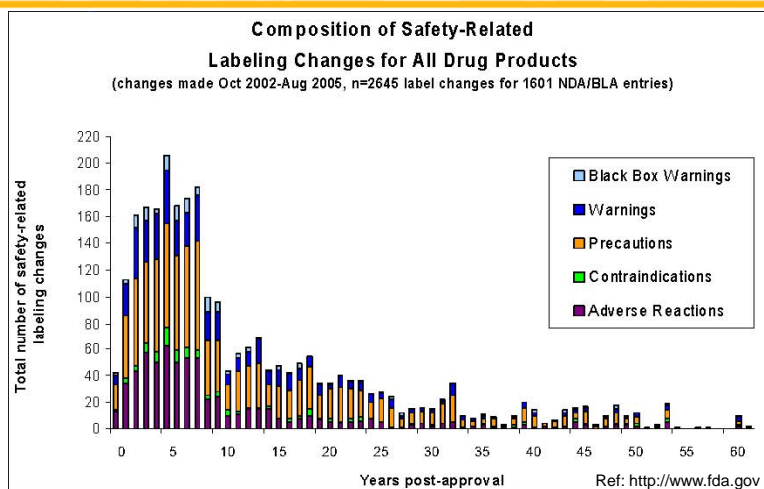
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Safety Lives as Long as the Drug/Device is in Market



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FDA Amendments Act 2007

- System to monitor data of 100 million lives
- Utilization and safety
- Additional tools
- Risk Evaluation and Mitigation Strategy

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Risk Evaluation and Mitigation Strategy

- FDA approved labeling
 - Timetable for periodic assessment
- +
- Assess, communicate, manage risks

Compliance:

- Civil money penalties

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Definition of Risk Management

Enterprise risk management:

- Processes and behaviors by which an organization identifies, assesses, controls and monitors [enterprise-wide] business risks to achieve its strategic goals and objectives

Risk Map

- “A strategic safety program designed to meet specific goals and objectives in minimizing known risks of a product while preserving its benefits. A RiskMAP targets one or more safety-related health outcomes or goals and uses one or more tools to achieve those goals”¹

Ref: ¹Guidance for Industry, Development and Use of Risk Minimization Action Plans. FDA, March 2005.
http://www.fda.gov/cder/guidance/6358fnl.htm#_Toc67721187

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Determining When a REMS/RiskMAP Should Be Considered - FDA

- Nature and rate of known risks versus benefits
- Preventability of adverse effects
- Probability of benefit

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Risk Management

Governance

Assessment

Quantification

Monitoring

Optimization

Delivering the
RIGHT drug/device
to the
RIGHT patient
at the
RIGHT time
and at the
RIGHT price

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Elements to Framework

Governance

Context, identification, assessment,
categorization

Assessment

Context, accountability, strategy

Quantification

Quantification, analysis

Monitoring

Reporting, monitoring, controls

Optimization

Improve performance

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Recommended Elements of a RiskMAP/REMS Submission to the FDA

- Background Context, identification, assessment, categorization
- Goals, Objectives Context, accountability, strategy
- Strategy and Tools Quantification, analysis
- Evaluation Plan Reporting, monitoring, controls
- Action Plan Improve performance

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What About Content? Progress Reporting

- Summary Context, governance
- Methodology Categorization
- Data Observations
- Results Reporting - Risk Profile, Monitoring
- Discussions and conclusions Action Plan

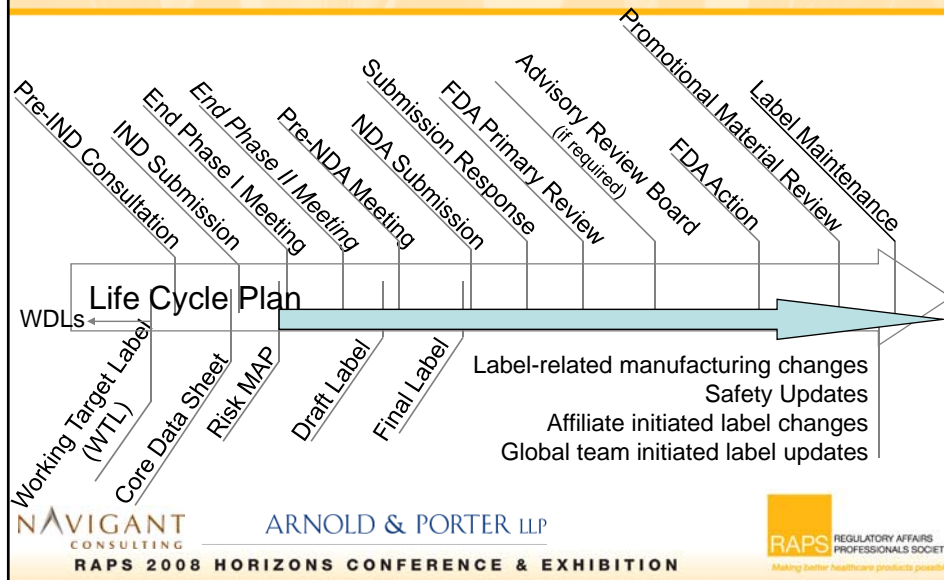
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Timing for RiskMAP/REMS Development



The Label

- Structured product labeling
- Federal marketing authorization
- January 2006: FDA published the final rule on “Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products” (21 CFR Parts 201, 314, and 601).

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Wyeth v. Levine

- Supreme Court hearing – March 2008
- Phenergan injection, gangrene, amputation
- FDA approved the use of injections to administer Wyeth's anti-nausea drugs and labeling included warnings against injecting it in an artery
- Preemption?

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Implications to Label

- Regulatory document
- Marketing opportunity
- Legal defense

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ANTICIPATING AND MINIMIZING LITIGATION EXPOSURE

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Special Considerations For Pharma/Medical Device Industries

“The manufacture of prescription drugs . . . has provided many of the 20th century’s greatest success stories and some of its worst tragedies. Because they cure disease, alleviate pain, and prolong life, prescription drugs have been a great benefit to society. But prescription drugs sometimes cause severe complications and side effects, inflicting great anguish as well as temporary and even permanent disability on some individuals.”

Carlin v. Superior Court, 13 Cal. 4th 1104, 1118-19 (1996)
(Kennard, J., concurring and dissenting).

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Recent Developments Appear To Favor “Strong” Preemption

- 2006 Final Rule is FDA’s assertion of its primacy in regulating labeling of prescription drugs
 - DOJ amicus briefs address particular cases
- In *Wyeth*, Supreme Court may address conflicting rulings on 2006 Final Rule
- February 2008 *Riegel* opinion adopts “strong” preemption for Class III medical devices

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On The Other Hand . . .

- Powerful legal and political considerations may weigh against too sweeping preemption regime
 - Long history of state-law tort litigation not questioned (and arguably accepted) by Congress
 - Possible legislative reaction against pro-preemption decisions deemed excessive
- Preemption doctrines often offer room for case-by-case application turning on specific facts

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Arguments Potentially Limiting Even “Strong” Preemption

- Specificity, timeliness of FDA’s focus on particular risk in question
 - Not-infrequent judicial skepticism about FDA’s adequacy of resources/carefulness
- Impact of allegations that FDA not provided full and complete information
- Argument that state lawsuits impose requirements that are “same” as FDA regulations

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Relevant Principles If Preemption Is Not Applied

- In itself, compliance with FDA/state rules and regulations not preclude liability, although helpful
- Most liability derives from failure to warn theories (hence importance of 2006 FDA Final Rule, *Wyeth*)
- Pharmaceutical or medical device “defective” only if
 - Improper manufacture or preparation, or
 - No net benefit to any class of patients

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Focusing On Failure To Warn

- Often said that “duty to warn runs *to the physician*, not to the patient.” *Carlin*, 13 Cal. 4th at 1116 (emphasis in original).
 - Exceptions exist
- Warnings judged against known *or scientifically knowable* risks
- Should act without delay if credible new information develops

First Precept: Priority Upon Avoiding Harm

- If nothing ever goes “wrong,” no liability
- All companies presumably invest great effort to identify, and correct, potential issues before a product reaches people
- But, particularly if technology is new or innovative, even the most careful testing and trials, scrutiny by outside scientific advisors, and review by regulators, will not catch all concerns

Litigation = Trial By Hindsight

- Discovery rules allow access to e-mails, drafts, personal notes, and virtually any other record of what occurred.
- Experts paid by plaintiffs may interpret questions, qualifications, unexpected test outcomes as proof that alleged risk was “scientifically knowable.”
- High stakes of product litigation make adversaries extremely well financed.

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E-Discovery: How This Changes Things

- 12/06 amendments to Federal Rules of Civil Procedure have focused attention of courts and lawyers on ESI (electronically stored information) and its production and use in litigation.
- Assumption that record retention policies can effectively manage what is kept – still valid?
- New stakes in managing records: spoliation claims.

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When Consideration Of Mitigating Potential Liability is Needed

- Short answer – at every stage.
- If potential issue arises, questions may be raised about:
 - Initial design and subsequent modifications
 - Testing and trials, at every stage
 - Interactions with regulators, scientific advisors, testing agencies
 - Reacting to unexpected test/trial results or reported instances of failure/injury
- Best to think of company as working in a transparent bubble

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Appropriate Action vs. Overreacting

- Actions taken need not always assume worst-case scenarios
- Often, best role is to raise questions, identify potential concerns, document why a decision was made
- Consider possible benefits from candid disclosures, seeking third party validation

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Importance Of Interactions With Regulators

- Very often, if litigation, most important facts are the company's interactions with FDA (and others in government, if relevant)
- Critical that information provided, and the timing of disclosures, satisfy trial by hindsight
- Affirmative support from regulators for company's challenged decisions can be crucial

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Tensions In Applying Liability Rules To New Or Emerging Technologies


- Precautionary principle, prevailing in Europe, urges presumption against introduction of new technologies if uncertainty as to possible harms
- In U.S., more "open" regulatory regime presents companies with both opportunities and risks
- Sound risk management is vital

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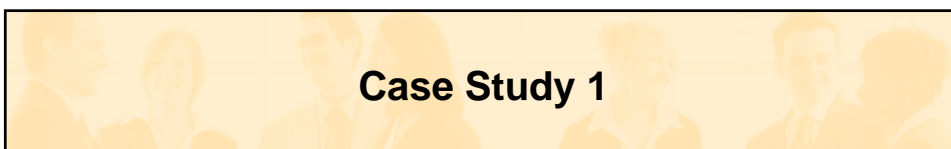
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Discussion Of Case Studies

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Case Study 1

- Drug X
- Label contains: “caution should be exercised when used in patients with a history of myocardial ischemia..... should be used with caution and introduced at the lowest recommended dose in patients with fluid retention, hypertension and heart failure”
- RiskMAP?

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Case Study 2: Employing Nanotechnology

- What is different about Nano?
 - “Materials made in the nanoscale size range can often have chemical or physical properties different from . . . their larger counterparts. . . . [B]ecause of . . . their special properties, they may pose different safety issues . . . “ 8/9/06 FDA Press Release re Nanotechnology Task Force
- Very wide range of potential applications
- Possibility of multiple, highly integrated functions in a single product – e.g., disease diagnosis, drug targeting, non-invasive imaging

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FDA Guidance re Nanotechnology

- Single guidance document so far –
Report of Nanotechnology Task Force,
approved by Commissioner (7/07)
 - Followed October 2006 public meeting
 - Similar documents issued by NIOSH and EPA
- Agency appears to be feeling its way cautiously, and welcoming collaboration by industry

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Numerous Open Issues For Science and Regulatory Policy

- Multiple issues that will require further, and often fundamental, science and policy work
 - Lack of generally accepted definitions, standards, testing methods for nano materials
 - Key properties may “change repeatedly as size” varies within nano range
 - Unknown how different material parameters produce biological interactions at nano sizes
 - Ability to track nanoparticle movements within the body
 - Need to apply “life cycle” analysis

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Key Take-aways

- Many questions, few specifics from FDA
- Decision to use nano material may “change the regulatory status/regulatory pathway” for a product
- Companies strongly encouraged to “communicate with agency” early in development process, particular for highly integrated combination products
- Where premarket approval authority exists, FDA believes that existing legal powers are adequate

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