The RPM Report

REGULATION | POLICY | MARKET ACCESS

FDA Drug Safety Changes

Impact On Pharma

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Editor-in-Chief

The RPM Report

November 8, 2007

Key Takeaways

- **New Drug Safety Law: A Positive Turning Point for Pharma**
- **Significant *Evolutionary* Increase in Regulation**
  - **Active Surveillance**
  - **REMS**
- **Stresses and Adjustments for Pharma and Pharma Service Companies**
  - **Spending**
    - More for surveillance/pharmacovigilance, monitoring MDs and patients
  - **Structures**
    - Changing roles for sales, medical affairs, marketing

Three Reasons to Love FDAAA

1. Something Had to Change
2. The Climate Began Improving Sept. 27
3. The Alternative Was Worse

FDAAA=FDA Amendments Act

2007: A Year to Forget

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Zelnorm

Trasylol

Avandia

Zimulti

EPO

Bifeprunox

Pristiq

Arcoxia

Prexige

Galvus

Safety: One Piece of FDAAA

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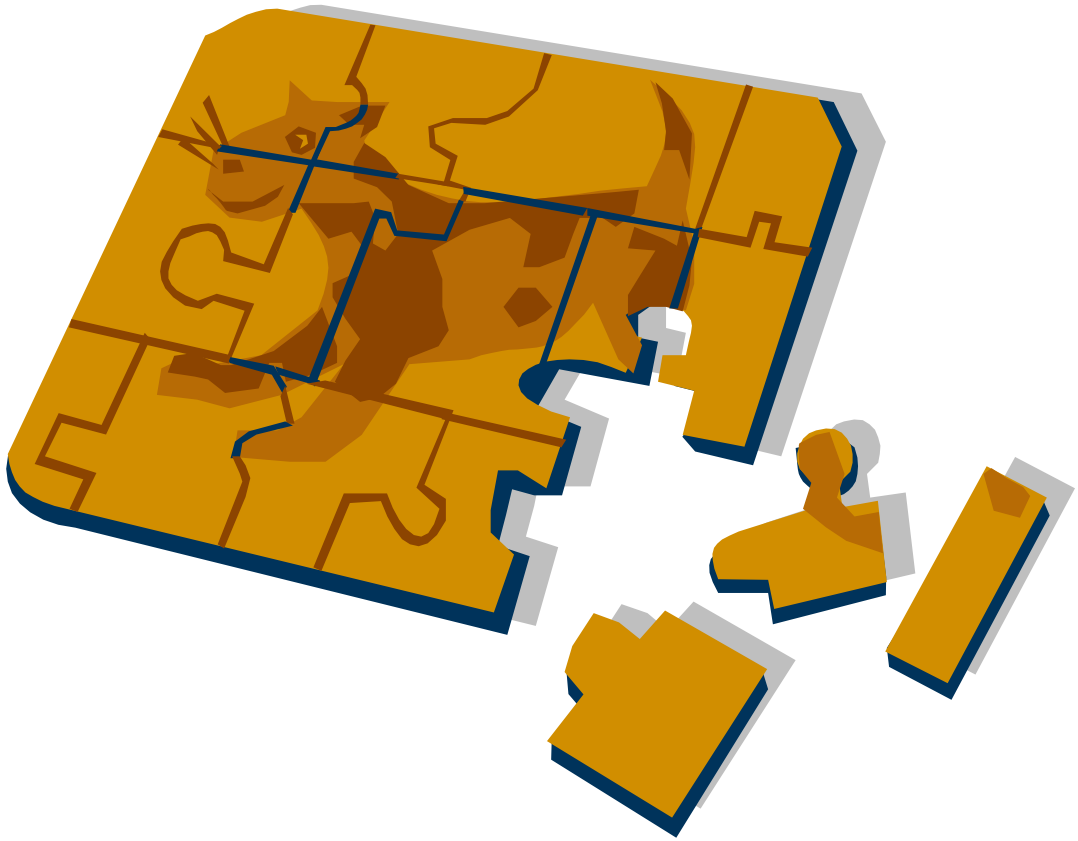
- User Fee Reauthorization
- Clinical Trial Registries
- Advisory Committee Conflicts of Interest
- Critical Path
- Tropical Disease Incentives
- Medical Device Fees
- Pediatric Exclusivity for Drugs and Devices
- Food Safety
- Rx Imports



Key Drug Safety Provisions

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- Active Surveillance
- Risk Evaluation and Mitigation Strategies (REMS)
- Mandatory Phase IVs
- Transparency (Public Registries)
- Direct-to-Consumer (DTC) Advertising

Evolution, Not Revolution…

Active Surveillance

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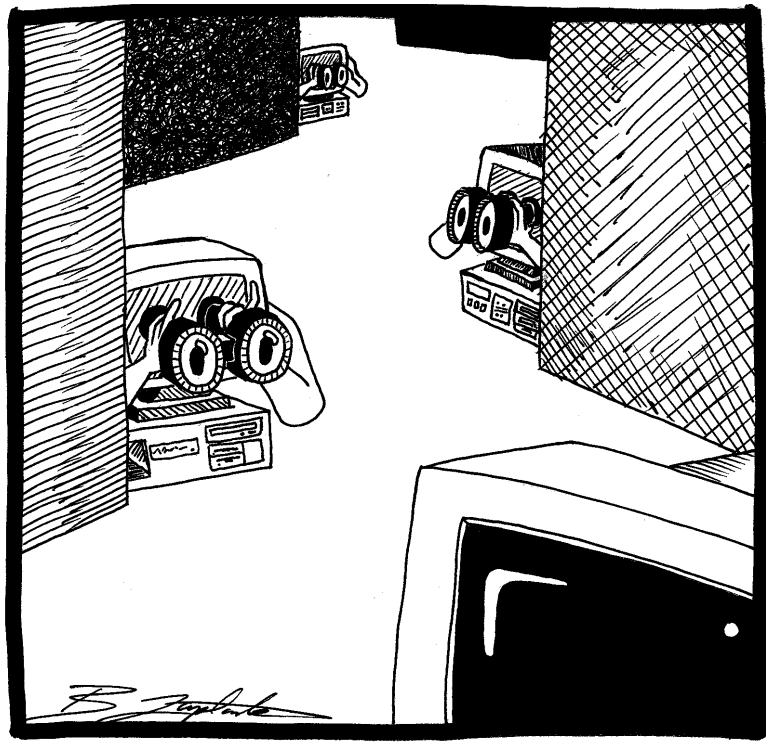
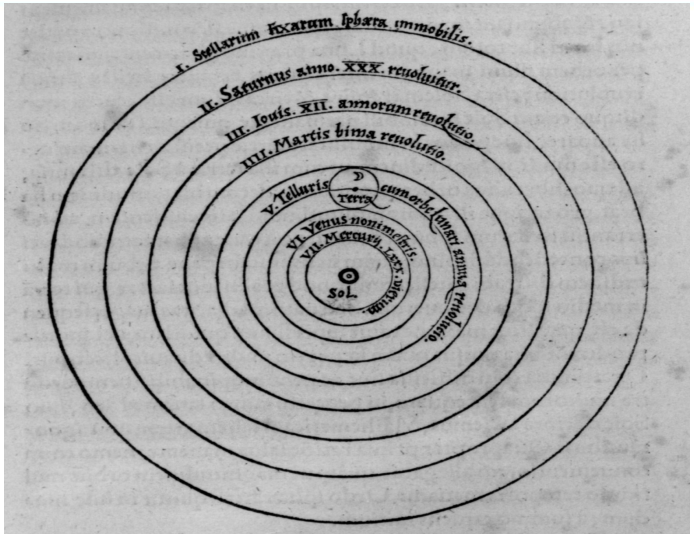
- **Boost for an Old Idea**
  - $25 Million in Funding Per Year
  - Two Years to Create “Public Private Partnerships”
- **Implementation is Key**
  - Goals of Government Will Define Role of Industry
  - Private Partner(s) Will Be Critical
  - Former FDA/CMS Head McClellan Likely Involved



Post-Market Challenge



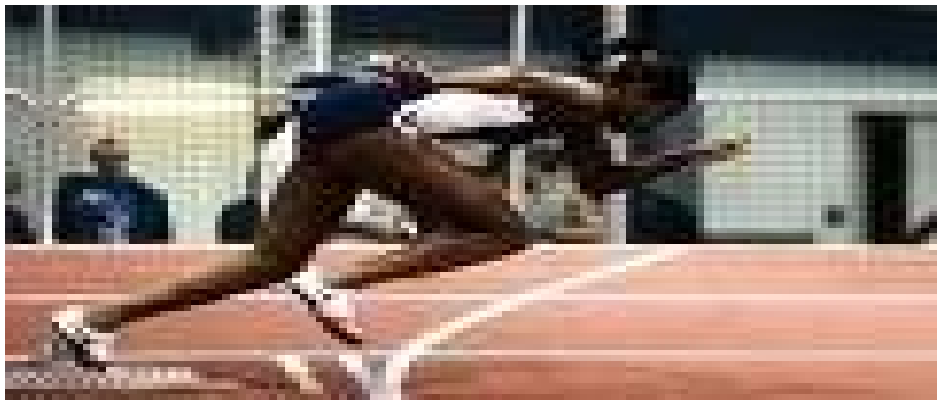
- Pharma sponsors will no longer control the flow of information about medicines
- Payors, providers, consumers will interact directly with the regulator and its surrogates

The other stakeholders will enter the field of post-marketing research in a significant fashion.

--Former FDA Commissioner

Mark McClellan

Sprint to PDUFA V



October 2007

October 2012

12 months: Election

14 months: New FDA

36 months: PDUFA V Warm-up

59 months: PDUFA V

Political milestones

New Congress

PMS Phase-in

25 million people

100 million people

24 months: Locate surveillance data sources: convene expert meeting on safety research methods

42 months: Contract with entities for PMS

36 months: Standardize ADRs, Collect data from Federal sources; trend and pattern systems

REMS: The Sleeper in FDAAA

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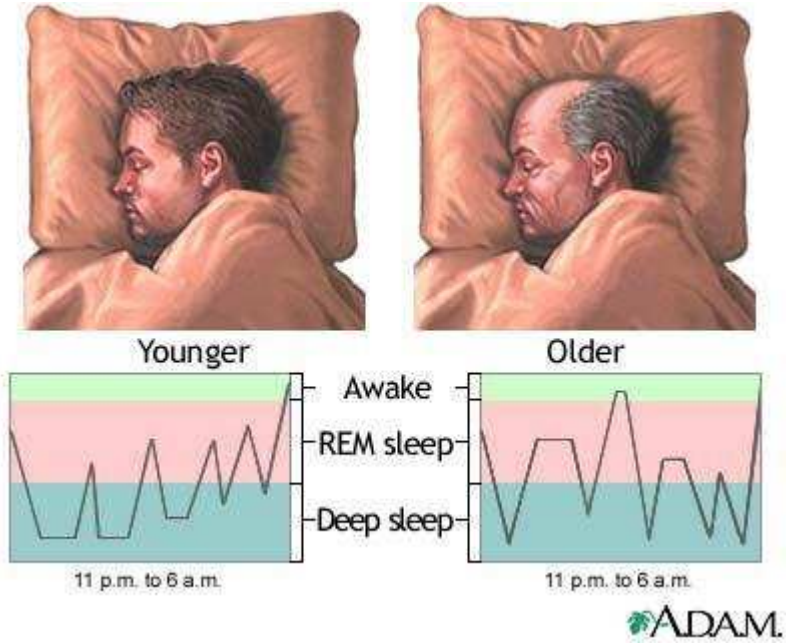
- Not a new concept
- Requires closer contact/ monitoring of doctors and patients
- Will dominate how pharma firms think about markets, marketing and NDAs



Game-changer in the model of "adequate and well controlled clinical trial" from 1962 Efficacy Amendments

Acronym Is New

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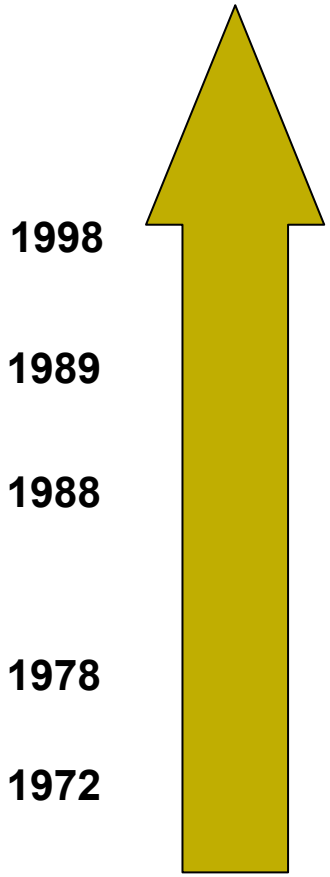
Risk Evaluation & Mitigation Strategies



FDA has been experimenting with risk minimization programs for 35 years

Thalomid – STEPS, registered MDs only, one-month supply, pregnancy tests

Clozaril – "no blood, no drug," registered pharmacies, National Registry

Accutane – Pregnancy Prevention Program, monthly tests, one-month supply, pateint and MD surveys

Atromid-S – too many Rxs

Methadone – special clinics

Already the Standard

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- **Elaborate risk minimization plans are not new**
  - **130 RiskMAP plans submitted to FDA between Oct. 2002 – Dec. 2006**
  - **30 drugs already have RiskMAPs**
- **New NDAs include risk minimization programs**
  - **Pfizer's *Selzentry:* safety registry and labeling**
  - **Acambis *ACAM2000* smallpox vaccine**
  - ***Tysabri* for Crohn's Disease: modified TOUCH**

Data for REMS

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Patients	Estimated size of patient population
Disease description	Seriousness of disease or condition
Benefit	Expected benefit of drug with respect to disease or condition
Length of treatment	Expected or actual duration of drug treatment
Adverse effects	Seriousness of known or potential adverse events related to drug; background incidence of events in patient population
Novelty	Is drug a new molecular entity?

The Purpose of REMS

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- **Inform**
  - Targeted Education & Outreach
- **Nag or Nudge**
  - Reminder Systems
- **Impose Limits**
  - Performance-Linked Access

New Launch Model

McClellan

Drug launches will be more like medical devices: quicker approval for targeted populations, with expanded uses in the future.

Tysabri: The Midas TOUCH

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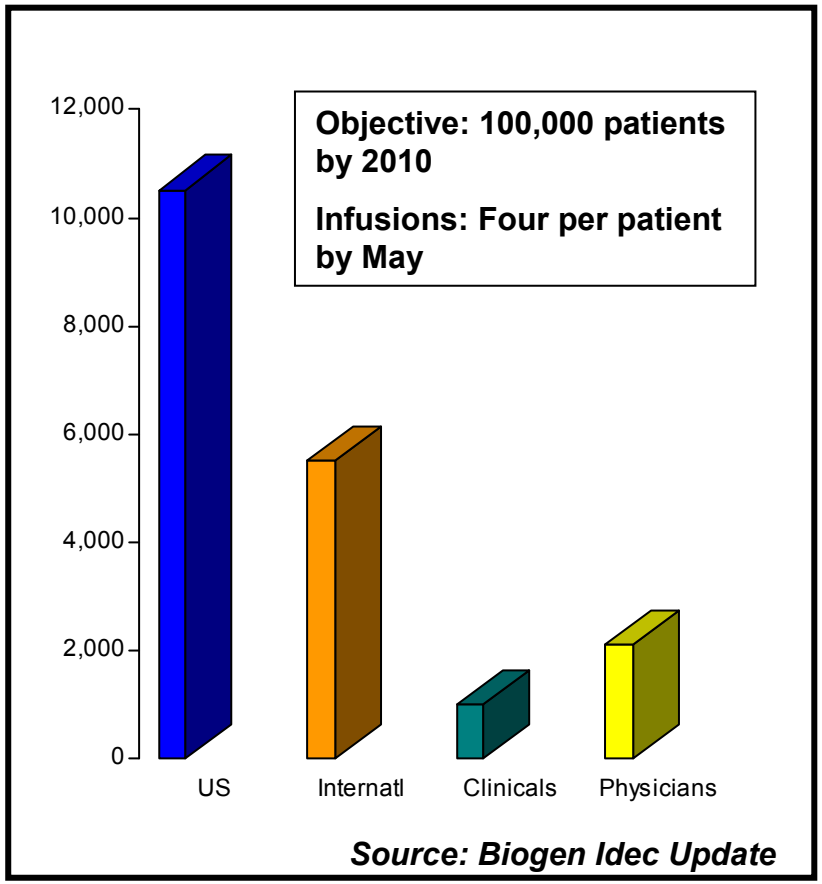
- **7,500 patients** during first aborted US marketing period (Nov. 2004-February 2005)
- **17,000 patients** in US during renewed marketing under TOUCH RiskMAP (June 2006 – Sept. 2007)
- **2,100 physicians** registered to use product (same number of infusions sites)

***Tysabri* Vital Statistics:**

June 2006 – Sept. 2007



Towards Personalized Medicine

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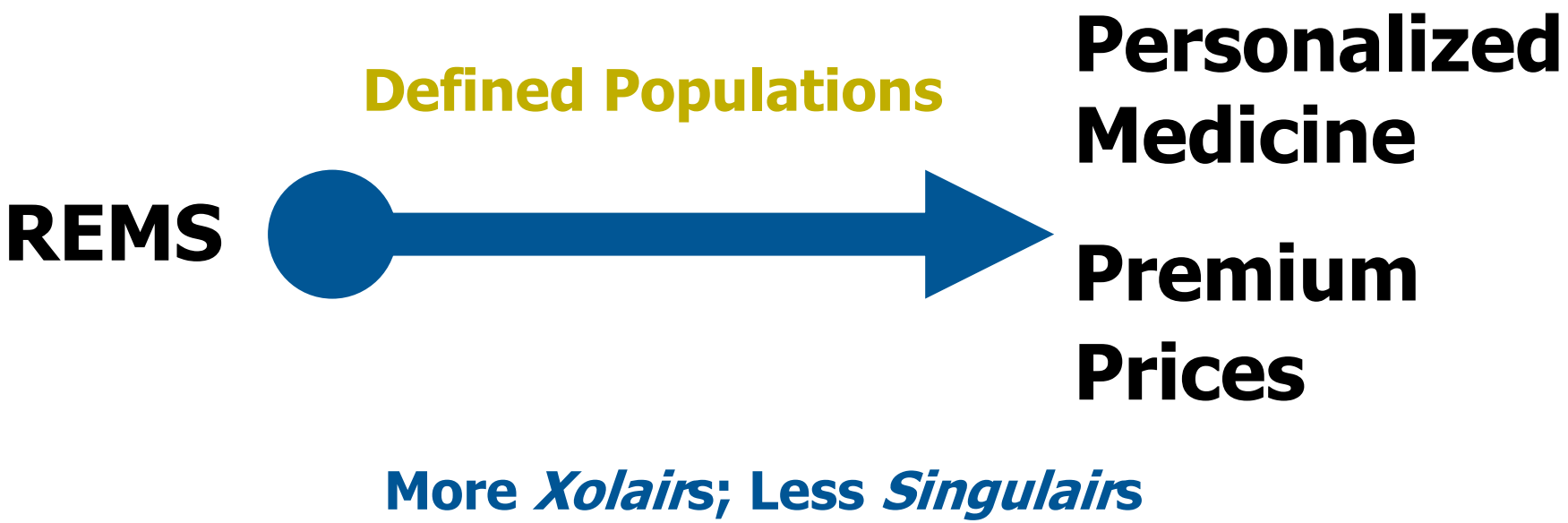

More *Xolairs*; Less *Singulairs*

RiskMAPs are a natural step towards personalized medicine.

Brian Strom, University of Pennsylvania

Specialty Drugs to the Fore

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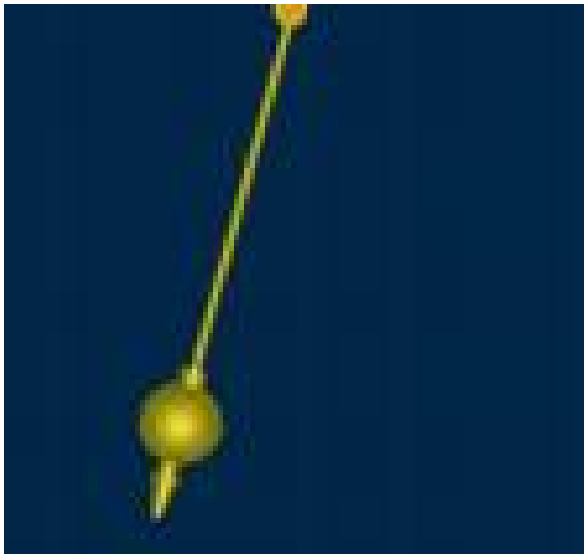
- **FDA's preference in words of senior pharma R&D exec**
  - FDA is still interested in primary care drugs
  - But agency recognizes that PCP products give them the greatest "heartburn."
  - FDA looking for products that will be well-controlled in post-market setting
- **Pharma is following suit**
  - R&D budgets and pipelines are shifting to specialty
  - 20-25% looks like the new standard
  - Risk plans de rigeur for all new products

Pendulum shift?

Permanent shift?



Marketing And REMS

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- **Expect questions on marketing plans (and advertising) during NDA process**
  - Part of the process of patient identification
  - FDA can justify the concern as a way to assure that marketing will not undercut REMS objectives
  - Will commitments made during NDA discussions increase the threat of off-label challenges?
- **An organizational challenge for pharma**
  - How will marketing plans be presented during NDAs?
  - Coordinating marketing and regulatory affairs; selecting one to present to FDA

REMS and Sales

- **Shift to patient/physician contact?**
  - **Sales resources to medical affairs?**
- **Another organizational issue:**
  - **How will these outreach efforts dovetail with sales force activities?**
  - **Separate: A firm line between sales and safety messages?**
  - **Complementary: RiskMAP plans exhibit opportunities for establishing stronger ties with MDs and patients**
- **Compensation for appropriate use, not more scripts**

REMS and R&D

- **Where will the money for expanded REMS programs and pharmacovigilance come from within pharma?**
- **Changes for Phase IV testing?**
  - **With transparency, firms are already experiencing the dangers of traditional strategic research.**
  - **"Marketing" studies are coming back to haunt companies with the aggressive outside analysis of data.**

Questions?

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