The Problem: Loss of Trust

Specific Concerns:
- FDA lacks authority and funding for adequate oversight of drug safety
- FDA organizational structure underweights safety considerations
- FDA not acting quickly or effectively enough on new evidence of safety risks
Underlying Issues

- Communication
  - Not fast enough
- Structure
  - Not clear enough
- Authority
  - Not strong enough
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Fixes: Communication

- Get emerging safety information out faster: DrugWatch (May 2005)
- Drugs for which FDA is “actively evaluating early safety signals”
  - Newly observed SAEs
  - New risk minimization measures
  - Significant emerging risks that may be avoided by proper countermeasures
DrugWatch: Concerns

- FDA imprimatur on unvalidated safety information
  - Potential for confusion, overreaction
  - Irreparable damage to drug’s reputation
  - No sponsor input
  - Undermines status of drug label as key source of safety information
FDA Response: New Guidance

- FDA puts DrugWatch on hold (Nov. 2005)
- New guidance on communicating drug safety information (March 2007)
  - Key concept: “emerging drug safety information” = information not yet fully analyzed or confirmed
  - “Period of uncertainty” while FDA evaluates new safety information; “tension” between need to inform & need to substantiate
  - May advise public of emerging issue
Advisory Committee

- FDA announces new Risk Communication Advisory Committee (July 2007)
- Implements IOM recommendation
- To advise agency on strategies and programs to communicate risks and benefits of products in order to facilitate optimal use
- Experts in social marketing, health literacy, cultural competency, journalism, bioethics, and risk communication
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Proposed Fixes: Structure

- Take drug safety function out of FDA altogether (NTSB model)
- Take drug safety office out of CDER, reporting directly to Commissioner
- Enhance role of FDA drug safety office in premarket reviews and postmarket safety deliberations
Fixes: Structure

- Drug Safety Oversight Board
  - Identify, track, and oversee important safety issues and establish policies
  - Adjudicate organizational disputes
  - Ensure that drug safety decisions receive input of experts not involved in primary review or pre-market evaluation
DSOB: Activities

- Meetings closed; brief written summaries posted to web
- Relate mostly to selection of drugs for patient or HCP information sheets or public health advisories
- FDARA will substantially expand role
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Authority: Issues

- IOM: FDA needs
  - increased enforcement authority and better enforcement tools
  - fines, injunctions, and withdrawal of drug approvals

- Labeling
  - authority to compel safety changes

- Postmarketing studies
  - authority to enforce commitments
  - authority to require new studies
Authority: Is there an issue?

- **Existing Authority Over Labeling**
  - Power to issue patient/HCP information sheets, public health advisories, Talk Papers, etc.
  - Authority to declare drug misbranded for omitting material safety information
  - Ability to withdraw approval over safety concern, suspend marketing if “imminent hazard”
  - Not always easy or practical to utilize
Authority Over Label: Proposed Fixes

- Basic idea: Give FDA power to order safety changes to drug label; avoid lengthy talks, sponsor foot-dragging
- Sanctions for non-compliance may include misbranding charge, civil money penalties
Post Marketing Study Commitments

- Key element of drug approval process: almost \( \frac{3}{4} \) of drugs approved since 1998 carried PMCs
- FDAMA, FDA regs require annual sponsor status reports
- Enforcement of existing PMCs: Is there a problem?
  - FDA: Four percent of confirmatory studies for accelerated approval drugs are delayed; one percent of all pending postmarket studies for drugs
Authority over PMCs: Proposed Fixes

- Little to no direct FDA authority over completion of PMCs
- Little to no direct FDA authority to impose new postmarketing study requirements
- Pending legislation would make failure to complete postmarketing studies a violation under FDCA, allow for civil money penalties
  - Would also give FDA limited authority to require new postmarketing studies
The New Safety Landscape

- Faster, more aggressive risk communication
- DSOb with expanding powers and mandate
- Enhanced role of safety experts in drug reviews
- New authorities over labeling, PMCs
The New Safety Landscape

- Active Surveillance
  - Expanded databases
  - Intensified data mining, meta-analyses
- Heightened Awareness of Safety Issues
- Diffusion of Control Over Safety Information
  - Away from sponsors
  - Toward FDA and outside parties
The Changing Communication Environment

- Greater Speed, Broader Spread in Communicating Risks
  - Few limits, filters
  - Sometimes sensationalized
- Less Room for Communicating Benefits
  - Crackdown on off-label communication
- Greater Scrutiny of Sponsor Safety Communication
  - Enforcement against sponsors for failing to disclose risk information
Net Result: Power Shift

- Less Sponsor Control
- More FDA Authority, but
- Less FDA Discretion
- Fundamental Shift in Patterns of Use?
  - Imbalance: risk over benefit?
  - More conservative approach – fewer AEs but more unmet need?
  - Overall impact on public health?