

**Presentation to the  
FDA Science Board  
December 3, 2007**

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# **FDA Science and Mission at Risk**

Report of the  
Subcommittee on Science  
and Technology

Prepared For  
FDA Science Board

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# Overview of Process, Findings, and Recommendations

**Gail H. Cassell, Ph.D.**

Vice President, Scientific Affairs and  
Distinguished Lilly Research Scholar  
for Infectious Diseases  
Eli Lilly and Company

## Charge to Science Board

Appoint a Subcommittee to assess  
whether science and technology at FDA  
can support current and future core  
regulatory functions and decision-making

## Subcommittee Tasks

Identify....

1. Scientific gaps
2. Mechanisms for maximizing effectiveness of S&T capacity and priority-setting
3. Mechanisms for leveraging scientific capacity in public and private sectors

## Missing from the Charge

The Subcommittee was **not** asked to assess or make recommendations about resources.

## Uniqueness of this Review

- Unprecedented scientific advances to reduce regulatory uncertainty
- Increasingly complex product reviews based upon scientific advances and globalization
- Increased scrutiny of Agency by all stakeholders
- Unprecedented opportunities to leverage expertise and resource needs with external partners
- Decline in funding in real dollars
- Only the second time Agency has been reviewed as a whole entity
- Committee composition
- 100<sup>th</sup> Anniversary of FDA

## Science and Technology Subcommittee

- Gail Cassell (chair)\*
- David Altshuler
- Barbara Alving
- Les Benet
- Bruce Burlington
- Robert Califf
- Thomas Caskey
- Joan Chesney
- David DeMets
- Susan Desmond-Hellman
- Susan Ellenberg
- Garret Fitzgerald
- Robert Goldstein
- Alfred Gilman
- Lee Hood
- Peter Hutt
- Evan Kharasch
- Sang Kim
- Cato Laurencin
- Julia Lane
- Jeff Leiden
- Barbara McNeil\*
- Glen Morris
- Phillip Needleman
- Robert Nerem
- Dale Nordenberg
- Marc Overhage
- Jim Riviere
- Allen Roses\*
- Eve Slater
- John Thomas
- Roy Vagelos
- Cathy Woteki

## Process

- FDA self assessment
- Subcommittee assessment by Working groups
  - CBER
  - CDER
  - CFSAN
  - CDRH
  - CVM
  - NCTR
  - Genomics
  - Surveillance/Biostatistics
  - Information Technology
- Did not review individual scientists and laboratories but rather programs and processes

## Structure of the Report

- Executive summary
- Major Findings and Recommendations Involving Cross-Cutting Issues
- Detailed reports by Center and/or cross-cutting area (Appendices A-L)

## Subcommittee Conclusion

Science at the FDA is in a precarious position: the Agency suffers from serious scientific deficiencies and is not positioned to meet current or emerging regulatory responsibilities

Demands of FDA have soared.  
Resources have not!

## Demands Have Soared

- Extraordinary advance of scientific discoveries
- Complexity of new products and claims submitted to FDA for premarket review and approval
- Emergence of challenging safety problems
- Globalization of industries FDA regulates

Impact of deficiency profound precisely because science is at the heart of everything FDA does

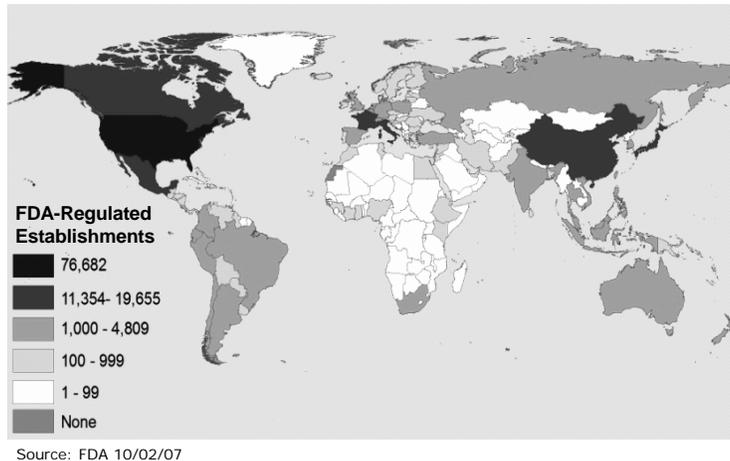
## FDA Regulatory Responsibilities

- Extends from stipulation of preclinical safety requirements through entire medical product lifecycle
- Ensures that 75% of the food consumed in the U.S. is safe, secure, sanitary, wholesome, and properly labeled
- Surveillance of all marketed regulated products for quality problems or for consumer/patient harm
- Detection/deterrence of criminal activity—counterfeits, drug diversion, tampering, illegal importation, health fraud, illegal or shortcuts, lying to the government
- Counter-terrorism activities: both facilitating development of countermeasures and protecting regulated products

## FDA Regulatory Activities

- Each of these activities has important public health, and individual health, implications
- Each activity has strong advocates who believe FDA should be doing more (or doing something different) in the given area
- Highest quality decision-making (and legally sustaining our decisions) in every area requires that the Agency is informed by the best available science

## The Breadth of FDA Responsibilities by Number of Establishments



## FDA Impact

- Touches lives, health and wellbeing of all Americans
- Integral to national economy and security
- Regulates \$1trillion in consumer products or 25 cents of every consumer \$ expended annually in this country
- Appropriated budget for 2007=\$1.6 billion
- Each American currently pays ~1 ½ ¢/day

## Major Findings Science

- FDA cannot fulfill its mission because its scientific base has eroded and its scientific organizational structure is weak
- Fire-fighting regulatory posture instead of pursuing a culture of proactive regulatory science, especially related to food safety
- FDA cannot adequately monitor development of food and medical products because it is unable to keep up with scientific advances (systems biology, wireless healthcare devices, nanotechnology, medical imaging, robotics, cell- and tissue-based products, regenerative medicine, and combination products).
- FDA cannot fulfill its surveillance mission because of inadequate staff and IT resources to implement cutting-edge approaches to modeling, risk assessment and data analysis.
- FDA lacks a coherent scientific structure and vision as a result of weak organizational infrastructure and a lack of consistent and rigorous external peer review

## Evidence of positive trends at the FDA but critical gaps persist

- Development of the Critical Path Initiative
- Request for IOM to review drug safety system
- Consolidation of laboratories and personnel at the White Oak Facility
- Proactive steps to establish Reagan-Udall Foundation
- Establishment of the position of Deputy Commissioner/Chief Medical Officer
- Request for Science Board to establish this Subcommittee to review current status of science and technology at the Agency

## **Recommendations Science**

- Provide significant and sustainable resources
- Rebuild CFSAN and CVM scientific base and their related inspection and enforcement functions to a level that is commensurate with their regulatory responsibilities
- Develop a program to manage “new science” that will ensure that the FDA can support innovation across regulated industries
  - Establish the Incubator for Innovation in Regulatory and Information Science (IIRIS)
- Immediately implement the IOM recommendations for improving drug safety, as well as those made by the Subcommittee working group on Surveillance/Biostatistics

## **Recommendations (con't) Science**

- Institute a new scientific organization (Deputy Commissioner, CSO, Deputy Director for Science in each center, Director of Extramural Collaborations and Training, establish an External Board of Scientific Counselors
- Other (Scientific program review, ORA, NCTR, more in depth review of research programs)
- Science Board should continue to play an active role in peer review of Centers and in development of a comprehensive implementation plan for timely and effective implementation of the recommendations by this Subcommittee

**FDA cannot fulfill its mission because its scientific workforce does not have sufficient capacity and capability**

- Capacity
- Recruitment and retention challenges
- Insufficient performance metrics for scientific staff
- Insufficient investment in professional development
- Does not have sufficiently extensive collaborations

**Recommendations to address workforce issues**

- Create a distinctive and exciting regulatory science culture
- Enhance fellowship and visiting scientists programs
- Enhance the program to monitor performance metrics and put the appropriate IT infrastructure in place to track the evolution of those metrics.
- Develop and support strong ongoing professional development program
- Establish an EIS-like program to address emerging acute problems

## Information Technology Major Findings

- Positive trends but critical gaps remain
- Information sharing networks are not adequate to fully support regulatory mandate
- Inadequate capability and capacity to electronically collect, analyze, and provision data/information
- Technology infrastructure is not sufficiently robust
- Emerging sciences pose particulate challenge from both an information science and technology perspective
  - Workforce challenges
  - Technology challenges

## Information Technology Recommendations

- Accelerate efforts to establish a robust and reliable technology infrastructure
- Support extramural collaborations and activities to promote health information exchanges for safety and efficacy activities
- Invest in increased capacity for data storage, modeling, analytics, and sharing
- Ensure development of an IT component for the proposed incubator for innovation (IIRIS)
  - Information sciences
  - Technology-based medical devices
- Establish regulatory informatics training programs

# Science Organization

**Eve Slater, M.D., F.A.C.C.**

Senior Vice

President-Worldwide Policy, Pfizer, Inc.

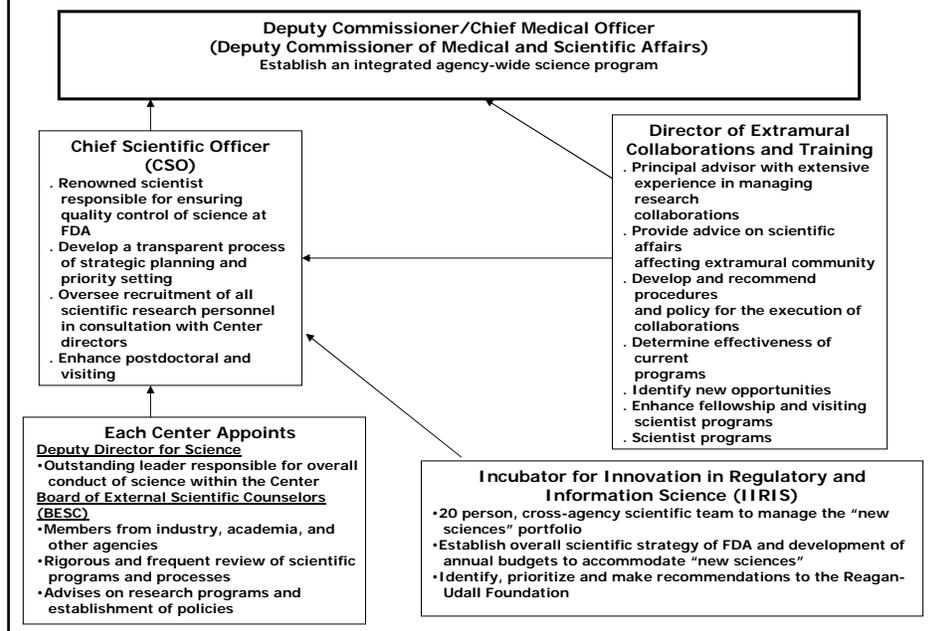
Former Assistant Secretary for Health,

US Department of Health and Human Services

Former Sr. Vice President of Merck Research Labs

for Clinical and Regulatory Development

## A New Scientific Organization Strengthening the Scientific Infrastructure at FDA



## The Orphan Centers:

Center for Veterinary Medicine  
Center for Food Safety and Applied  
Nutrition

**Catherine E. Woteki, Ph.D.**

Global Director of Scientific Affairs Mars, Inc.  
Former Undersecretary for Food Safety in the  
U.S. Department of Agriculture and  
Dean, Iowa State University College of Agriculture

## The Orphan Centers:

Center for Veterinary Medicine  
Center for Food Safety and Applied Nutrition

- Neglect and erosion of their resource needs over decades now means that
  - Nothing beyond the top priorities can be accomplished
  - Major issues of public health concern are not being addressed (cosmetic safety, nutrition)

## Context for the review

- Time frame: Winter to Spring, 2007
- Backdrop: cascading product recalls involving CFSAN and CVM
  - E. coli 0157:H7 in fresh spinach
  - Salmonella in peanut butter
  - Melamine-contaminated pet food
    - 18,000 phone calls
    - 2 people work full time on pet food issues

Finding: FDA does not have the capacity to ensure the safety of food for the nation.

- Basic functions--inspection, enforcement and rulemaking-- are severely eroded.
  - 78% reduction in inspections over 35 years
  - Food establishments inspected once every 10 years
  - CVM workforce 375 FTE, 4% of FDA total, but unique and diverse species and human health orientation
  - Since 2003, CFSAN workforce declined from 950 FTE to 771 FTE
  - Cosmetics safety has less than 20 FTE
  - CFSAN no longer generates the science needed in human nutrition

Finding: FDA does not have the capacity to ensure the safety of food for the nation.

- Why has this happened?
  - Dramatic increase and diversification of responsibilities
    - Since 2003, FDAMA-food contact substances, Bioterrorism Act, FALCPA-food allergen labeling, trans fat labeling, egg safety food cGMP, pandemic flu planning, minor use and minor species health
  - Increasing complexity of the tasks
  - Increased scientific demands
  - Inadequate funding

## This was predicted...

“There are deep concerns about the viability of the foods program and the lack of Agency priority for food issues. Decline in resources and program initiatives during the past 10-15 years indicate a lack of Agency management attention and interest in this area, although public interest in, and concern for, an effective food program remain high.”

Report of the Advisory Committee on the Food and Drug Administration to the Secretary of HHS

May, 1991

## The food regulatory area is complex and responsibilities are shared

- FDA/DHHS
  - Center for Food Safety and Applied Nutrition (CFSAN)
  - Center for Veterinary Medicine (CVM)
  - ORA
- Food Safety and Inspection Service/USDA
- Department of Homeland Security
- Centers for Disease Control and Prevention -
- State health and agriculture agencies
- Research: NIH/DHHS, ARS and CSREES/USDA

## Center for Veterinary Medicine

- Regulatory issues requiring high levels of science:
  - Methods to identify residues (synthetic and natural chemicals) and emerging infectious diseases
  - Antimicrobial resistance monitoring (science and informatics base of NARMS)
  - Biotechnology (genetic engineering, cloning, use of phages, biopharma)
  - New technologies in drug manufacturing and delivery (nanotech, genetics, biomarkers, new approaches to characterizing microbial resistance)

## Center for Veterinary Medicine

- Key Stressors
  - Convergence of massive data volume and complexity with newly developed products from the “omics revolution”
  - unique databases with respect to species, endpoints, human health
  - Under staffing (375 FTE), vacancies in key scientific positions, lack of funds (>80% of budget in salary)

## Center for Veterinary Medicine

- Recommendations:
  - Bolster in-house scientific capability in emerging areas relevant to veterinary medicine
  - Bolster IT capability, and integrate within FDA and with CVM partners (CDC, USDA), eliminate paper storage
  - Foster integration with cutting edge science activities across FDA and with external partners; expand the FDA Fellow Program

## Center for Food Safety and Applied Nutrition

- Regulatory issues requiring high levels of science:
  - Food production sciences; risk mitigation at the source
  - Consumer understanding of nutrition and food safety information; better labeling for public health
  - Implementation of the Food Allergen Labeling and Consumer Protection Act and effective interventions
  - Detection of foodborne viruses
  - Prevention of foodborne viral diseases
  - Safety of cosmetics
  - Adverse event reporting and analysis

## Center for Food Safety and Applied Nutrition

- Key Stressors:
  - Lack of resources (950 FTE in 2003 vs. 771 FTE in 2007; new mandates; elimination of research programs)
  - Globalization of the food supply
  - New food processing technology
  - New threats to public health
  - Ongoing response to emergencies
  - Outmoded IT systems and laboratory instruments
  - Addressing only the highest priorities

## Center for Food Safety and Applied Nutrition

- Recommendations:
  - Additional resources to attract, retain and leverage scientific expertise and regulatory research in the 7 priority areas
    - CFSAN does a commendable job setting priorities, developing innovative ways to leverage what they have
  - Provide leverage for regulatory research collaboration with NCTR, USDA (ARS, CSREES), NIH

## Priorities

- Immediately correct the lack of support for staff and infrastructure - that means funding!
- Invest in 21st century regulatory science that could anticipate future food safety issues and develop a cadre of professionals capable of applying the new science to emerging challenges.

## In addition,

- Leverage research programs sponsored by NCTR, ARS, CSREES, CDC, NIH and DHS
  - For this, CFSAN and CVM need resources they can bring to the partnership to be used to fund joint RFP's managed through granting agencies
- Conduct this activity with the Chief Scientific Officer

While building veterinary and food safety capacity, don't neglect nutrition and cosmetics

- Dietary supplements industry has >\$20 billion in annual sales
- Cosmetics industry has >\$60 billion in annual sales

# Genomics

## **C Thomas Caskey, M.D., FACP**

Chief Operating Officer and CEO/Director Elect  
The Brown Foundation  
Institute of Molecular Medicine,  
Executive Vice President  
Molecular Medicine & Genetics  
The University of Texas Health Science Center at  
Houston

## Historical Milestones in Genomic Science

1. Plethora of Disease Gene Discoveries (1989 to Present)
2. NIH/DOE 1990 Commitment
3. Forensic Science Transformation
  - Triplet Repeat Discovery
  - 1B to FBI - 1995
4. Formation of NHGRI
  - \$480 Million/annum – Year 1992
5. Complete Microbial Sequence – Year 1995
6. Human Genome Framework – Year 2001/2003
7. Stanford Expression Technology – Year 1996
8. HAP Map Access – Year 2005
9. Individual Genome Sequence – 2007

## DRUG DISCOVERY RELEVANCE

1. Industrial Shift to Gene Specific
  - Drug development
2. Target Validation b
  - Mouse KO
  - RNAi
  - Expression Chips
3. Preclinical Safety
  - Expression Chips
  - Cell Based HTS Pathway Analysis
  - P450 Alleles
  - Mass Spectroscopy
4. Clinical Trial Sectoring (Selection)
  - Cancer
5. Biomarker Usage
  - HIV
6. Post Launch Gene Tox
  - HIV

## FDA ADAPTATIONS

1. Critical Path Initiative – 2004
  - Biomarker Emphasis
2. Expression Data Sharing
3. DNA Outsourcing in Infection Diseases
4. Formation of Genomics Working Group

## **REVIEW FINDINGS**

1. Critical path initiative was visionary but underpowered.
2. Genomics leadership was small, predominantly add on to other responsibilities and worked very much in an ad-hoc manner.
3. The focused genomic leadership has only recently been enhanced but felt to be still inadequate.
4. The technology base is now limited off the shelf instruments and not forward looking for state of art.

## **Summary of Findings and Recommendations**

### **Recommendation 1:**

It is necessary to formalize the organization of a genomics Program.

## Summary of Findings and Recommendations

### Recommendation 2:

Mechanisms for recruitment, training, and retention of high quality scientific staff with multi-disciplinary training and skilled in bioinformatics are needed to support the highly developed and labor-intensive efforts required for genomics analyses.

## Summary of Findings and Recommendations

### Recommendation 3:

The committee strongly recommends increased collaboration with academic centers of excellence, other agencies, and the private sector.

## **Summary of Findings and Recommendations**

### **Recommendation 4:**

Public/private initiatives will be required for the continuing evaluation of the safety of approved drugs.

## **Summary of Findings and Recommendations**

### **Recommendation 5:**

Within the FDA, there should be a genomics central lab, with expertise in expression profiling, sequencing, informatics, proteomics, metabolomics, and systems biology.

## **Summary of Findings and Recommendations**

### **Recommendation 6:**

In order for the genomics core group to function effectively, it is critical to upgrade FDA's information technology infrastructure.

## **Emerging Science and Innovation in Regulatory and Information Science**

**Garret A. Fitzgerald, M.D.\***

Professor of Medicine and Professor and  
Chair of Pharmacology  
Department of Pharmacology  
University of Pennsylvania School of Medicine

## Emerging Science: Preparedness or Catch-Up

- Emerging sciences present an opportunity for the refinement of how we use drugs, specifically to enhance the likelihood that individuals will benefit safely from a given dose of a given drug
- FDA needs to be empowered to increase its critical mass with skills in and/or familiarity with these new technologies
- Unrealistic to think that they can muster in house sufficient human capital in any near term
- Academic sector represents a huge area of potential value to the FDA , presently unharvested
- FDA needs resources to align the interests of key programs in the academic sector with their regulatory mission to add value to its intramural efforts to build capacity

## Incubator for Innovation for Regulatory and Information Science (IIRIS)

- IIRIS will integrate intramural program with extramural centers with focus in emerging areas such as systems biology, translational therapeutics, metabonomics, proteomics, etc
- IIRIS can also serve as a device for training fda employees in new interdisciplinary ways to pursue regulatory science and can facilitate intramural exposure of extramural scientists to regulatory science at the fda
- The extramural loci of IIRIS can also serve as a site for pursuit of concepts related to the emerging science initiated by FDA scientists

# Information Technology

**Dale Nordenberg, M.D.**

Managing Director,  
Healthcare Industry Advisory  
PriceWaterhouseCoopers,  
Former Associate Director for Informatics  
and Chief Information Officer  
National Center for Infectious Diseases  
Centers for Disease Control and Prevention

## IT Arenas

- Science and regulatory program activities
  - Quality, safety and efficacy
  - New science
  - Food safety
- Technology infrastructure and practice considerations
  - Technology infrastructure
  - Best practices
  - Workforce
  - Legislative activity

# Information Technology

## Overview of scope

- All data and information assets, e.g. databases, reports
- Data and information collection, sharing initiatives and networks
- IT infrastructure including hardware, software and telecommunications
- Information and computer sciences and related disciplines
- All associated IT management activities
  - Security
  - Capital planning and investment control
  - Enterprise architecture
  - Technology, data, and information exchange standards
- Policy, guidelines, and legislative mandates for IT

# Information Technology

## Overview of key processes

- Electronic application processing, e.g. submissions and communications
- Safety and efficacy data sharing networks including clinical trials and pharmacovigilance
- Risk detection technology and methodology
- Data and information dependent devices
- Support and promote innovation in the domains of FDA regulated products

## Challenges

- Vast amounts of data
- Emerging science
- Information sciences
- Rapidly emerging technology
- Globalization
- Shared/overlapping areas of jurisdiction
- Large number of sites that require monitoring

## Positive Trends But critical gaps persist

- New CIO, COO, and CTO with strong track records at other government agencies
- Internal IT governance boards are operational with strong program/scientific support and participation
- IT activities are evolving into more efficient centralized administration
- Standards activities are in process with strong external collaboration
- Recognition of key challenges is consistent across large groups of internal FDA stakeholders
- Business process delineation in progressing well
- Strong collaborations with external partners
- The Office of the CIO is championing five critical initiatives

## Critical Information Supply Chains

- Finding
  - Quality, safety and efficacy functions lack adequate information supply chains
- Recommendations:
  - Establish critical information supply chains including FDA submissions
  - Integrated premarket/postmarket information sharing networks
  - Development of sensing technologies to support FDA site monitoring/quality activities
  - Cross Agency collaborations to define clear business processes

## New Science and Emerging Risk

- Finding
  - The FDA's information infrastructure is not capable of responding to new and rapidly evolving requirements that are arising from 'new science' and new technologies
- Recommendation
  - Install information sciences representation on the FDA Science Advisory Board
  - Dedicate resources to the proposed incubator for innovation (IRISC)
    - Develop expertise in emerging sciences such as panomics, wireless healthcare devices, nanotechnology, medical imaging, robotics, cell- and tissue-based products, regenerative medicine, and combination products
    - Develop external partnerships

## Food Safety

- Finding
  - The food supply is at risk due to insufficient data/information sharing networks for surveillance and response
- Recommendation
  - Establish effective coordination of food safety activities across government agencies
  - Establish and/or participate in national repositories for molecular epidemiology
  - Invest in sensing technologies that can be deployed at sites that FDA regulates

## IT Network and Communications Infrastructure

- Finding
  - The FDA IT infrastructure is obsolete, unstable, and lacks sufficient controls to ensure continuity of operations
- Recommendation
  - As many as 80% of servers have exceeded recommended service life
  - Critical network components are not centralized and secured
  - Bolster data storage, search and analysis infrastructure
  - Assess and develop dedicated laboratory infrastructure
  - Invest in and develop IT best practices including capital planning and investment control and enterprise architecture
  - Continue to develop evolving IT governance activities

## Workforce Improvement

- Finding
  - The IT workforce is insufficient and suboptimally organized
- Recommendation
  - Establish a regulatory science informatics training program
  - Establish tight integration with IIRIS (incubator for innovation) to ensure information technology capability for new sciences evolves to support
  - Migrate to an enterprise (Agency-wide) model for IT management as rapidly as possible
  - Perform detailed assessment of Agency-wide staffing requirements based on enterprise model and taking into account complexity of FDA mission

## Legislative

- Finding
  - Legislative support for information technology is not being leveraged sufficiently to progress the quality, safety, and efficacy missions of the FDA
- Recommendation
  - Support the development of a legislative agenda that promotes the emergence of:
    - Health information exchanges to support efficacy and safety
    - Programs to support innovation in the area of remote sensing
    - Programs that support e-pedigree activities

## Rationale for Investment

- Critical gaps in ability of 'IT' to support regulatory mandate

But with....

- Evidence of commitment and progress
- Strong management

\*The subcommittee believes that the IT organization has the capability to leverage additional investment to effectively strengthen the FDA's information collection, processing and provisioning capability to fulfill its regulatory mandate

## Food Safety

**Peter Barton Hutt**

Former Chief Counsel FDA

Covington & Burling LLP

## Summary and Next Steps

**Gail H. Cassell, Ph.D.**

Vice President, Scientific Affairs and  
Distinguished Lilly Research Scholar  
for Infectious Diseases  
Eli Lilly and Company

## Summary Statement

- Without a significant and sustained increase in funding, the FDA cannot perform its mission
- Subcommittee not asked to assess resources but rather identify scientific gaps but impossible to do one without the other
- The current situation has developed over many years, the question is not why or how we got here but rather how do we strengthen FDA going forward
- FDA staff highly dedicated to protect the public's health but can no longer fulfill their mission without appropriate tools and personnel
- Composition of committee—government, academia, and industry
- Unanimous agreement upon findings and recommendations
- Findings not new!!!
- Situation is urgent. The Public's health is at risk!

## Recommendation

- Science Board accept the report of the Subcommittee
- Take steps to provide further review of in depth analysis of high priority scientific programs, role of NCTR, and scientific capacity and processes of ORA