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FDA Science and Mission at Risk

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and Technology

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Table of Contents

FDA Mission Statement.....	iii
1.0 Executive Summary.....	1
1.1 Overview	1
1.2 Major Findings	3
1.2.1 The FDA cannot fulfill its mission because its scientific base has eroded and its scientific organizational structure is weak.	3
1.2.2 The FDA cannot fulfill its mission because its scientific workforce does not have sufficient capacity and capability.....	4
1.2.3 The FDA cannot fulfill its mission because its information technology (IT) infrastructure is inadequate.	5
1.3 Summary Statement and Recommendations.....	6
1.4 The Structure of This Report	8
2.0 Context: The Changing FDA Environment	9
2.1 Growing Disparity between Responsibilities and Resources	9
2.2 The Criticality of Science.....	12
2.3 The Changing Nature of Science	16
3.0 Discussion of Key Findings and Recommendations.....	20
3.1 Science: Capability, Capacity and Organization.....	20
3.1.1 Finding: FDA does not have the capacity to ensure the safety of food for the nation.	21
3.1.2 Finding: The development of medical products based on “new science” cannot be adequately regulated by the FDA.	24
3.1.3 Finding: There is insufficient capacity in modeling, risk assessment and analysis.	30
3.1.4 Finding: The FDA science agenda lacks a coherent structure and vision, as well as effective coordination and prioritization.	33
3.2 Workforce: Securing Critical Scientific Capability and Capacity.....	38
3.2.1 Finding: The FDA has substantial recruitment and retention challenges.	40
3.2.2 Finding: The FDA has an inadequate and ineffective program for scientist performance.	42
3.2.3 Finding: The FDA has inadequate funding for professional development.....	42
3.2.4 Finding: The FDA has not taken sufficient advantage of external and internal collaborations.....	43
3.3 Information Infrastructure	45
3.3.1 Finding: The Subcommittee believes that there is evidence of important, but slow, progress to improve information sciences and technology at the FDA over the past few years, yet significant gaps remain.	46
3.3.2 Finding: The FDA lacks the information science capability and information infrastructure to fulfill its regulatory mandate.	47
3.3.3 Finding: The FDA cannot provide the information infrastructure support to regulate products based on new science.	49

3.3.4	Finding: The FDA IT infrastructure is obsolete, unstable, and lacks sufficient controls to ensure continuity of operations or to provide effective disaster recovery services.	50
3.3.5	Finding: The IT workforce is insufficient and suboptimally organized.	51
4.0	Overarching Findings of this FDA Review	53
4.1.1	Finding: The FDA has experienced decreasing resources in the face of increasing responsibilities.....	53
4.1.2	Finding: Recommendations of excellent FDA reviews are seldom followed.	56

List of Appendices

A.	Subcommittee to the FDA Science Board	A-1
B.	The State of Science at the Food and Drug Administration	B-1
C.	Center for Food Safety and Applied Nutrition (CFSAN)	C-1
D.	Center for Veterinary Medicine (CVM)	D-1
E.	Center for Drug Evaluation and Research (CDER).....	E-1
F.	Center for Biologics Evaluation and Research (CBER)	F-1
G.	National Center for Toxicological Research (NCTR)	G-1
H.	Center for Devices and Radiological Health (CDRH)	H-1
I.	Genomics.....	I-1
J.	Surveillance/Statistics	J-1
K.	Information Technology (IT).....	K-1
L.	Task 1: Outline of Core FDA Regulatory Functions.....	L-1
M.	Task 2: Identify Limitations of Today's Regulatory Science, Mapped to Regulatory Functions	M-1

FDA Mission Statement

"The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health."

1**Executive Summary****1.1 Overview**

A strong Food and Drug Administration (FDA) is crucial for the health of our country. The benefits of a robust, progressive Agency are enormous; the risks of a debilitated, under-performing organization are incalculable.

The FDA constitutes a critical component of our nation's healthcare delivery and public health system. The FDA, as much as any public or private sector institution in this country, touches the lives, health and wellbeing of all Americans and is integral to the nation's economy and its security.

The FDA's responsibilities for protecting the health of Americans are far-reaching. The FDA protects our nation's food supply through regulatory activities designed to cover 80 percent of the food consumed in this country. The FDA also regulates all drugs, human vaccines, and medical devices, and hence plays a critical role in ensuring the appropriate safety and efficacy of rapidly emerging medical products. Indeed, countries around the world have historically looked to the FDA for guidance on sound, science-based regulation, and have looked to its product approval decisions as accurate determinations of new product safety.

The FDA is also central to the economic health of the nation, regulating approximately \$1 trillion in consumer products or 25 cents of every consumer dollar expended in this country annually. The industries that FDA regulates are among the most successful and innovative in our society, and are among the few that contribute to a positive balance of trade with other countries.

The importance of the FDA in the nation's security is similarly profound. The FDA plays a central role in protecting the nation from the potential effects of terrorist attacks¹, such as anthrax, smallpox, attacks on the food supply, nerve agent attacks and radioactive contamination, as well as from naturally occurring threats, such as SARS, West Nile virus and avian influenza.

¹ http://www.fda.gov/fdac/features/2004/104_terror.html

Thus, the nation is at risk if FDA science is at risk. In recognition of this threat, in December 2006, FDA Commissioner Andrew von Eschenbach, MD requested that the Science Board, which is the Advisory Board to the Commissioner, form a Subcommittee to assess whether science² and technology at the FDA can support current and future regulatory needs. Specifically, the Subcommittee's charge was to identify the broad categories of scientific and technologic capacities that FDA needs to fully support its core regulatory functions and decision making throughout the product life cycle, today and during the next decade. The Science and Technology Subcommittee of the FDA Science Board (hereafter called the Subcommittee) was composed of three members of the Science Board and other experts representing industry, academia and other government agencies, and included individuals with extensive knowledge of cutting-edge research. Most importantly, these experts possess a deep understanding of regulatory science and the core mission of the Agency³. This report is the product of that assessment.

The Subcommittee concluded that 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.

The Subcommittee found that the deficiency has two sources:

- The demands on the FDA have soared due to the extraordinary advance of scientific discoveries, the complexity of the new products and claims submitted to FDA for pre-market review and approval, the emergence of challenging safety problems, and the globalization of the industries that FDA regulates.
- The resources have not increased in proportion to the demands. The result is that the scientific demands on the Agency far exceed its capacity to respond. This imbalance is imposing a significant risk to the integrity of the food, drug, cosmetic and device regulatory system, and hence the safety of the public.

The Subcommittee further noted that the impact of the deficiency is profound precisely because science is at the heart of everything FDA does. The Agency will flounder and ultimately fail without a strong scientific foundation. That foundation rests on three pillars. The first pillar is strong selective scientific research programs that are appropriately mission-supportive, in all areas of FDA responsibility. This research is critical because it is not conducted by other public or private entities, but is fundamental to the discharge of FDA's statutory responsibilities to protect and promote the public health. The second pillar is excellent staff with cutting-edge scientific expertise appropriate to the mission. This expertise includes the ability to access, understand

² For the purpose of this report, the Subcommittee elected to use the term "science" broadly to encompass all of the disciplines and activities within the FDA that have a scientific basis, e.g., research, review of submitted applications and petitions, development of scientific policy, guidelines and procedures, and the analytical and inspection responsibilities of the office of regulatory affairs.

³ See Appendix A, *Subcommittee to the FDA Science Board*.

and evaluate science; effectively apply this science to the regulatory process; and communicate the implications of its findings for product safety and efficacy to the public. The third pillar is an information infrastructure and processing capability that ensures the FDA has access to the best data and information necessary to support the regulatory science required to fulfill FDA's mission

1.2 Major Findings

The Subcommittee found substantial weaknesses across the Agency, with the possible exception of some drug and medical device review functions funded by industry user fees. There are several areas of greatest concern, however, which form the basis for this report's most significant findings.

1.2.1 The FDA cannot fulfill its mission because its scientific base has eroded and its scientific organizational structure is weak.

The nation's food supply is at risk. Crisis management in FDA's two food safety centers, Center for Food Safety and Applied Nutrition (CFSAN) and Center for Veterinary Medicine (CVM), has drawn attention and resources away from FDA's ability to develop the science base and infrastructure needed to efficiently support innovation in the food industry, provide effective routine surveillance, and conduct emergency outbreak investigation activities to protect the food supply.

FDA's inability to keep up with scientific advances means that American lives are at risk. While the world of drug discovery and development has undergone revolutionary change — shifting from cellular to molecular and gene-based approaches — FDA's evaluation methods have remained largely unchanged over the last half century. Likewise, evaluation methods have not kept pace with major advances in medical devices and use of products in combination.

The world looks to FDA as a leader — to integrate emerging understandings of biology with medicine, technology and computational mathematics in ways that will lead to successful disease therapies. Today, not only can the Agency not lead, it cannot even keep up with the advances in science.

Due to constrained resources and lack of adequate staff, FDA is engaged in reactive regulatory priority setting or a fire-fighting regulatory posture instead of pursuing a culture of proactive regulatory science. This is particularly true for CFSAN and CVM, which are in a state of crisis (Finding 3.1.1). The FDA cannot adequately monitor development of food and medical products because it is unable to keep up with scientific advances (Finding 3.1.2). The Subcommittee identified the following eight emerging science and technologies that are most challenging the FDA: systems biology (including genomics and other “omics”), wireless healthcare devices, nanotechnology, medical imaging, robotics, cell- and tissue-based products, regenerative medicine, and combination products. Each of these emerging areas is developing at an exponential rate and each generates novel scientific, analytic, laboratory and/or information requirements. The 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 (Finding 3.1.3). The FDA lacks a coherent scientific structure and vision as a result of weak organizational infrastructure (Finding 3.1.4). Strong scientific leadership is needed at all levels to develop a new vision to build a strong science base within the Agency, and in parallel, this leadership must establish optimal mechanisms to access the best scientific knowledge and expertise from throughout the government, academia and industry. Consistent and rigorous peer reviews of programs and processes, which are currently lacking, are critical for wise utilization of resources and for rebuilding the Agency’s ability to implement its science-based regulatory responsibilities effectively.

1.2.2 The FDA cannot fulfill its mission because its scientific workforce does not have sufficient capacity and capability.

The Subcommittee found that despite the significant increase in workload during the past two decades, in 2007 the number of appropriated personnel remained essentially the same — resulting in major gaps of scientific expertise in key areas⁴. More importantly, despite the critical need for a highly trained workforce to fulfill its mission, the FDA faces substantial recruitment and retention challenges. The turnover rate in FDA science staff in key scientific areas is twice that of other government agencies, *GAO-02-958 PDUFA User Fees* (Finding 3.2.1). There are insufficient programs of measurement to determine worker performance (Finding 3.2.2). There is insufficient investment in professional development, which means that the workforce does not keep up with scientific advances (Finding 3.2.3). Finally, for various reasons, the FDA does not have sufficiently extensive collaboration with external scientists, thus limiting infusion of new knowledge and missing opportunities to leverage resources (Finding 3.2.4).

⁴ See Appendix B, *The State of Science at the Food and Drug Administration*.

FDA's failure to retain and motivate its workforce puts FDA's mission at risk. Inadequately trained scientists are generally risk-averse, and tend to give no decision, a slow decision or, even worse, the wrong decision on regulatory approval or disapproval. During our encounters with staff and center leadership, we were struck by the near unanimity that the shortage of science staff (due to lack of resources to hire) and the inability to recruit and retain needed expertise are serious, longstanding challenges. Internal expertise and experience to provide the science capability and capacity needed in highly specialized and fast-evolving areas is disturbingly limited. The lack of a trained workforce means that the FDA is ineffective in responding to emerging fields that require individuals and work teams with multidisciplinary skills built on very complex, highly specialized, often esoteric bodies of knowledge.

1.2.3 The FDA cannot fulfill its mission because its information technology (IT) infrastructure is inadequate.

The Subcommittee was extremely disturbed at the state of the FDA IT infrastructure. While some good progress is being made to improve information sciences and technology (Finding 3.3.1), the Subcommittee found that the FDA lacks the IT infrastructure necessary to meet its mandate (Finding 3.3.2). It also found that the FDA has insufficient access to data and cannot effectively regulate products based on new science due to lack of a supportive IT infrastructure (Finding 3.3.3). The Subcommittee noted that the FDA IT infrastructure is obsolete, unstable and lacks controls to execute effective disaster recovery protocols that ensure continuity of operations when systems are compromised (Finding 3.3.4). Finally, the IT workforce is insufficient (Finding 3.3.5).

The IT situation at FDA is problematic at best — and at worst it is dangerous. Many of the FDA systems reside on technology that has been in service beyond the usual life cycle. Systems fail frequently, and even email systems are unstable — most recently during an *E.coli* food contamination investigation. More importantly, reports of product dangers are not rapidly compared and analyzed, inspectors' reports are still hand written and slow to work their way through the compliance system, and the system for managing imported products cannot communicate with Customs and other government systems (and often miss significant product arrivals because the system cannot even distinguish, for example, between road salt and table salt).

There are inadequate emergency backup systems in place: recent system failures have resulted in loss of FDA data. Critical data reside in large warehouses sequestered in piles and piles of paper documents. There is no backup of these records, which include valuable clinical

trial data. The FDA has inadequate extramural funding programs and collaborations to accelerate the development of critical health information exchanges in order to support clinical trials and pharmacovigilance activities.

1.3 Summary Statement and Recommendations

Although this Subcommittee was asked to review gaps in scientific expertise and technology and not to assess available resources, it rapidly became apparent that the gaps were so intertwined with two decades of inadequate funding that it was impossible to assess technology without also assessing resources. This conclusion is based on an analysis of the reports of previous review committees⁵⁶⁷⁸⁹, each of which was given similar charges during the past 50 years. The themes raised by the previous committees, as well as the present Subcommittee, are very consistent: 1) the criticality of high-quality science to the regulatory mission; 2) the need for the science to be mission driven; 3) persistent expressions of dissatisfaction with the quality and credibility of the scientific programs; 4) consistent calls for major change in the organization and management of the Agency's scientific endeavors; and 5) consistent inability of the Agency to implement needed changes. Not all of the reasons for failure are apparent, but our analysis, as well as those of previous committees, revealed a very dangerous trend: the continual expansion of FDA responsibilities coupled with a dramatic decline in resources, particularly during the past two decades.

In contrast to previous reviews that warned crises would arise if funding issues were not addressed, recent events and our findings indicate that some of those crises are now realities and American lives are at risk.

⁵ Edwards Commission Report: Final Report of the Advisory Committee on the Food and Drug Administration, Advisory Committee on the Food and Drug Administration, U.S. Department of Health and Human Services, 1991

⁶ CBER Report: Review of Research Programs, Center for Biologics Evaluation and Research, Food and Drug Administration, Subcommittee for Review of CBER Research, Science Board to the Food and Drug Administration, *Final Report*, October 1998

⁷ CFSAN Report: Review of Research Programs, Center for Food Safety and Applied Nutrition, Food and Drug Administration, April 1999

⁸ CDRH Report: Science at Work at CDRH: A Report on the Role of Science in the Regulatory Process, Submitted by the External Review Committee, Center for Devices and Radiological Health, Final Report, November 2001

⁹ See for example, David Korn. FDA Under Siege: The Public at Risk, *Science* 276:1627, 1997 and <http://www.cfsan.fda.gov/~frf/sxsbra.html>.

Our Subcommittee, therefore, spent considerable effort garnering as much information as possible about the current roles and responsibilities of Agency staff, available resources, the current status of science within the Agency, and the implication of emerging science for the future of FDA and the public's health. We found that FDA's resource shortfalls have resulted in a plethora of inadequacies that threaten our society — including, but not limited to, inadequate inspections of manufacturers, a dearth of scientists who understand emerging new technologies, inability to speed the development of new therapies, an import system that is badly broken, a food supply that grows riskier each year, and an information infrastructure that was identified as a source of risk in every Center and program reviewed by the Subcommittee. We conclude that FDA can no longer fulfill its mission without substantial and sustained additional appropriations. Numerous reports by the National Academies of Science (including two recent reports by the Institute of Medicine [IOM] on drug safety)¹⁰, the Government Accountability Office (GAO), the Health and Human Services (HHS) Inspector General, Congressional committees, and other expert groups have come to the same conclusion. The opinion of these studies is unanimous — current gaps are due to chronic underfunding of the Agency, and if these gaps are not addressed immediately, FDA is in jeopardy of losing its remaining dedicated staff. The extraordinary efforts of these committed FDA staff members are the very reason further catastrophic food and drug events have been averted.

Although there is indeed great urgency to stem the tide of continued deterioration in the science that supports the regulatory decisions of the FDA, the magnitude of changes that are needed will require a phased approach based on a well-thought-out plan. Strategic plans must be developed within a strengthened science organization, as recommended in this report. Recruitment of outstanding talent with up-to-date skills will also take time. However, there must be an immediate commitment to make the needed investments in order to recruit the most outstanding talent. For example, during the time of our review, the directorship of two of the largest FDA centers, CFSAN and the Center for Drug Evaluation and Research (CDER), became vacant. It will be difficult, if not impossible, to recruit the best leaders unless there is assurance that adequate resources and staff will be available to address the challenges.

The magnitude of the resources required to restore scientific capability and capacity is substantial. The IOM has indicated the minimum immediate appropriation necessary to address urgent needs in drug safety is \$350 million. And the Grocery Manufacturers/Food Products Association has recommended a minimum of \$450 million over five

¹⁰ See IOM (Institute of Medicine) 2007. Challenges for the FDA: The Future of Drug Safety. Washington, DC: The National Academies Press
IOM (Institute of Medicine) 2007. The Future of Drug Safety: Promoting and Protecting the Health of the Public. Washington, DC: The National Academies Press.

years is needed to ensure food safety¹¹. Other groups, for example the Coalition for a Stronger FDA (co-chaired by the last three HHS Secretaries and endorsed by a number of former FDA Commissioners), have stated that a 15 percent increase in appropriations per year during the next five years will be required¹². The Subcommittee believes that these increases would still be an insufficient amount to allow the Agency to initiate and support all of the changes necessary to fulfill its mission. Thus, we strongly recommend that the most immediate increases be used to address those critical gaps identified in this report.

We recognize that adequate resources — human and financial — alone will not be sufficient to repair the deteriorating state of science at FDA, which is why we also recommend significant restructuring. But without a substantial increase in resources, the Agency is powerless to improve its performance, will fall further behind, and will be unable to meet either the mandates of Congress or the expectations of the American public. This will damage not only the health of the population of the US, but also the health of our economy. Currently each American pays about a penny and a half a day for the FDA; an increase to three cents daily would not, in our view, be a great price to pay for the assurance that our food and drug supply is, indeed, the best and safest in the world.

1.4 The Structure of This Report

The Subcommittee's report is structured as follows. It first provides the context within which the FDA operates. The subsequent section discusses key findings and recommendations, organized into three categories based on the three pillars deemed critical to the FDA's ability to fulfill its mission: Science, Workforce and Information Infrastructure. The final section provides a concluding statement about the study.

The Appendices include not only source material for the Subcommittee's findings and recommendations, but also, in Appendices C–K, detail on the gaps in science and technology for each of the FDA Centers and the cross-cutting issues reviewed by this Subcommittee (genomics, surveillance/biostatistics and information technology).

¹¹ <http://www.fpa-food.org/content/newsroom/article.asp?id=463>, Coalition for Stronger FDA (news release, September 25, 2006)

¹² <http://www.fdacoalition.org/news.php>, FDA Coalition Seeks Increases to Agency Budget (press release, February 6, 2007)