Creating A 21st Century Food & Drug Administration (FDA)

A White Paper issued by the
Center for Health Transformation (CHT)
and its FDA Modernization Project

Released:
February 2012

Creating a 21st Century Food & Drug Administration (FDA)

Overview & Background

The U.S. Food and Drug Administration (FDA) is the world's "gold standard" in the regulation of food, medicines and even cosmetics. Today, the FDA regulates products which account for about 25 cents of every dollar spent by American consumers each year — products that touch the lives of every American every day.[i]

However, the astounding progress in science and technology, coupled with the impact of globalization, has increasingly placed stress on the FDA's ability to rapidly and reliably assure the safety and quality of regulated products — especially the medicines and food necessary for our well-being. Despite the best efforts of past and present FDA leadership, the mission of the FDA to promote and protect the health of the American people in the 21st century is now at risk. This has resulted in an urgency to create a 21st century FDA that will promote and protect the health of the American people while helping to advance American innovation. Creating the 21st century FDA will provide rapid and reliable availability of solutions to complex medical conditions and encourage investments in the US biotechnology and biomedical economies.

In late 2009, the Center for Health Transformation (CHT) created a two-year project which focused on examining public policy solutions which could ensure that the FDA remains the "gold standard." CHT brought together nationally recognized thought leaders and stakeholders to discuss and deliberate strategies that are necessary to create a 21st century FDA that would advance patient care and encourage innovative medical breakthroughs.

CHT's FDA Modernization Project looked at how successful transformation of other sectors of our economy could be applied to improve the clinical trials process, advance regulatory science, and accelerate innovation. Creating a 21st century FDA will require public policy changes which can be established by Congress as part of their reauthorization of FDA in 2012. Proposing structural and functional changes that could be achieved by the reauthorization legislation of 2012 became the primary focus of our project.

In this process CHT assembled thought leaders, healthcare experts, patient advocates, industry leaders and public policy experts under the banner of the FDA Modernization Project. Two working groups were established: the Steering Committee which deliberated the specific areas within FDA in which changes could have the greatest impact on performance; and, the Implementation Task Force which provided specific recommendations for those changes that should be made. Members of the working groups are listed on page 18 of this document.

The goal of the Project was to confine our policy recommendations to a few practical and strategic changes that could be rapidly implemented, have the greatest impact, and assure the success of the FDA in achieving its mission to promote and protect the health of the American people.

Supported by various CHT staff members, the Steering Committee and Implementation Task Force met regularly over the two-year period. In the interim, consultations and discussions were conducted with many other organizations that routinely engage with FDA. It was recognized at the outset that additional resources are essential for improvement in the performance of the Agency. Our efforts, however, are focused on policy changes that would modernize the regulatory process for medical products and overall operation of the FDA. We note that such changes, in some cases, would also enhance FDA's regulatory oversight of food and other aspects of its portfolio of responsibilities.

As a science-based global regulatory agency, the FDA needs a transformation which supports innovation and development of new medical breakthroughs. Rather than assuming the role as a passive "gatekeeper" determining the flow between discovery of new medical products and their delivery to patients, the FDA must transform into the role of a "facilitator" by playing an active role in the creation of new medical breakthroughs while at the same time assuring both the safety and effectiveness of these products.

In order to accomplish this vision, a modernized, science-based FDA must be created that either possesses or has access to the scientific expertise that can understand the complexity and the performance of the regulated product, as well as the human impact of the disease it is intended to treat. This foundation of regulatory science would assure greater precision in product regulation and enable essential improvements to the development process.

A 21st Century FDA is critical to fulfill the potential of our nation's investment in biomedical research and ensure that the United States maintains its current position as the global epicenter of innovation and medical breakthroughs. To achieve these goals, this report describes the following recommendations:

- *Create a Modernized FDA through Process Reengineering*
- *Establish an External Advisory Board*
- *Designate FDA as an Independent Agency*
- *Develop a "Total Life Cycle" Regulatory Approach*
- *Establish a Conditional Approval Process & Adaptive Clinical Trial Process to Improve Patient Care*
- *Support Improvements in Regulatory Science*

Creating a 21st Century Food & Drug Administration (FDA)

Introduction

The intent of the CHT FDA Modernization Project is clear: To develop policy recommendations that would support FDA's mission of promoting and protecting public health.

A 21st century FDA would be responsive to public health by advancing innovative medical breakthroughs. However, creating a 21st century FDA will take appropriate resources and an efficient approach to using those resources. FDA Commissioner Margaret A. Hamburg, M.D., recently said, "Today, FDA is relying on 20th century regulatory science to evaluate 21st century medical products. Regulatory science is needed to provide better tools, standards, and pathways to evaluate products under development. It also serves to create efficiencies in the development process, and improve product safety, quality and manufacturing."[ii]

Many experts have previously agreed with Commissioner Hamburg in believing that the FDA does not currently have capacity or capability to carry out its science-based mission. In 2007, a report entitled "FDA: Science and Mission at Risk" concluded that FDA is unable to fulfill its mission, in part because it lacks modern scientific expertise. The lack of core scientific capacities for new and emerging technologies has hampered regulatory review at FDA, delayed the development of promising new therapies, and handicapped FDA's ability to promote and preserve public health.[iii]

Delays due to the lack of scientific and technology-based solutions are not only slowing access to innovative medical products; there is also significant economic impact. It is estimated that the cost to develop an approved medication rose from approximately $800 million in 2000 to over $1.2 billion in 2005.[iv] While the growing costs of successful R&D is not solely attributed to the FDA, a modernized Agency will have access to advanced information technology and scientific methods to ultimately help researchers and industry bring the best products forward into the clinical review and approval process.

Over the years, Congress has expanded the core mission of FDA. Unfortunately, the budget of the Agency has not kept up with the FDA's enhanced role in homeland security, ensuring food and drug safety and advancing medical innovation. Congress should provide the FDA with adequate resources to allow the Agency to be more efficient, more transparent, more predictable, more evidence-based, and more responsive in approving medical products for the American people. However, simply providing additional funding is not the entire solution. Vital additional resources must be spent strategically to transform the Agency into an efficient bridge rather than a cumbersome barrier to better health. This white paper is intended to address some of the strategic changes in the structure and function of the Agency that would lead to an efficient regulatory pathway without sacrifice of any of the safeguards that protect the public.

The state of health in the United States and around the world will cripple the future if it is not addressed now. Advancing biomedical research and developing the new medicine to combat this growing challenge is not the responsibility of the FDA, nor is the agency the cause of the current environment. However, the agency is a critical partner in the efforts of the biomedical research enterprise to improve human health.

More than half of the US population has at least one chronic disease.[v] Discovering, developing and bringing new, innovative treatment options to market to treat chronic disease such as heart disease, diabetes and cancer is necessary for the well-being of future generations. A recent study of the impact of Alzheimer's disease, which is just one of the many chronic diseases causing human suffering and burdening our society, indicates that Medicare and Medicaid will have spent an estimated $130 billion in 2011 on people with Alzheimer's and other forms of dementia. That figure is projected to increase to $805 billion in 2050 (before inflation). The rapid development and market deployment of innovative therapies capable of delaying the onset of Alzheimer's disease by just five years could save Medicare $50 billion annually.[vi]

Similarly, the national cost of diabetes in the U.S. in 2007 exceeded $174 billion. This estimate consists of $116 billion in excess medical expenditures attributed to diabetes, as well as $58 billion in reduced national productivity. Approximately one in ten healthcare dollars can be attributed to diabetes.[vii] Improved treatments and potential cures for patients with diabetes would help to reduce the unsustainable health expenditures in this country.

A worldwide survey describes how the increases in incidence of chronic diseases are contributing to failing economies. The Centers for Disease Control and Prevention (CDC) indicates that, "The United States cannot effectively address escalating health care costs without addressing the problem of chronic diseases."[viii] The Partnership for Chronic Disease indicates that chronic diseases kill more than 1.7 million Americans per year, are responsible for 7 of 10 deaths and the leading cause of death in America, and account for 75 percent of the nation's health care spending.[ix].

In addition, there is a need to advance the care and treatment of patients with acute disease including the threat of infectious diseases, like pandemic influenza, and the resurgence of tuberculosis and malaria. Influenza and its complications account for 10,000 to 40,000 excess deaths annually in the United States, of which more than 80 percent occur among the elderly.[x]

These challenges can be addressed by collaboration within the biomedical research community. For example, there are currently more than 1.2 million people living with HIV in the US due to the advancements made available by the commitment to research.[xi] While more can be done to improve the lives of people infected with HIV, it was not long ago that there were few durable treatment options for this disease.

A modernized FDA is an essential component to partnerships between the public and private sector. This collaboration will help to successfully translate the current revolution in science to new medicines that will help every American.

Creating a 21st Century Food & Drug Administration (FDA)

Policy Recommendations:

Recommendation 1: Create a Modernized FDA through Process Reengineering

The CHT FDA Modernization Project recommends that the FDA undergo a comprehensive, Agency-wide regulatory process reengineering and improvement initiative. This effort should be conducted by an external resource that is expert in developing new decision analysis tools, process mapping and continuous quality improvement procedures.

Regulation is in itself a "decision making" process that involves discrete steps that are expected to ultimately lead to approval or rejection of a product application. The length of time this process requires is a function not only of the actual review of the application but all of the separate steps involved in the discovery and development of that drug or medical device. Prior analysis of that process demonstrate the important role that FDA plays in influencing and determining the steps that sponsors must take in product development. From the standards that FDA sets for manufacturing to the advice it provides in design of a clinical trial the FDA defines the pathway to medical product approval. Delays and setbacks in the process involve enormous costs of millions of dollars to the developer of the product being reviewed. Most importantly, preventable delays result in the unnecessary loss of life to patients who suffer from diseases like cancer who are waiting on the development of new therapies.

A formal external review by experts in process engineering could also identify opportunities for the FDA to isolate critical steps in the regulatory decision making process and implement an ongoing process improvement methodology.

The FDA regulatory process involves far more than simply reviewing the sponsor's application for approval. Yet, surprisingly, only the length of time of the review cycle itself has been a topic of intense focus by the industry and Congress as the subject of the Prescription Drug User Fee Act (PDUFA) and Medical Device User Fee Act (MDUFA). There has never been a systematic review of the entire regulatory process for the purpose of identifying, quantifying and monitoring the impact of strategic changes designed to improve the process. This review would need to take into consideration regulatory components beyond the core clinical investigations to demonstrate safety and efficacy, and include multi-disciplinary review of processes such as those used in dose determination or toxicology investigations. An all-encompassing review could help identify areas that could be improved upon over time, or where new tools would be particularly useful. Such efforts of continuous quality improvement

have long been adopted in the practice of medicine and in manufacturing processes especially based on the principles of process improvement fostered by Edwards Deming.[xii]

Such a reengineering and improvement effort should specifically focus on how to make the regulation of food and medical products a more predictable, efficient and effective process.

The individual centers at FDA have engaged in some efforts to a varying levels but the FDA should conduct a comprehensive Agency-wide regulatory process reengineering and improvement initiative. In addition to process improvement, the Agency must also adapt and align its regulatory functions with the emerging reality that medical products are increasingly made up of the complex integration of components. According to Centers for Drugs, Biologics, Medical Devices and Food, divisions of labor in the Agency is now being increasingly challenged by the integration of these components into a single product. At present, the combination of a diagnostic (device) with a therapeutic (drug or biologic) is challenging the Agency to work across traditional Center boundaries. In the future, the complexity of products emanating from the field of regenerative medicine or the multifunctional performance of nanotechnologies will paralyze the regulatory process without a modernization of the internal regulatory decision making process

Going forward, there will increasingly be the need for improved data management and information aggregation as well as data analysis processes that could be applied across all the FDA Centers. For example, there is a current need to integrate the regulation of companion diagnostics (within the Center for Devices and Radiological Health [CDRH]) and targeted therapeutics (within the Center for Drug Evaluation and Research [CDER] and Center for Biologics Evaluation and Research [CBER]). Currently there is no well-defined, Agency-wide process for multi-center regulation of a product or an established mechanism for tracking performance of a collaborative process.

As science and technology spur the development of integrated products, it is essential that there be a clear, predictable regulatory pathway that facilitates — rather than impedes — efficient and reliable regulation. This cannot be accomplished without a process and the tools to monitor that process.

Such an effort would not only increase the internal efficiencies of product review but would substantially increase the confidence and trust of stakeholders in the rigor, discipline, reliability, predictability, and transparency of FDA's decision making. A comprehensive Agency-wide regulatory process reengineering and improvement initiative would empower the Commissioner to help transform the FDA.

Recommendation 2: Establish an External Advisory Board

To create a 21st century FDA, the CHT FDA Modernization Project recommends the creation of an external Agency-wide Advisory Board comprised of recognized leaders from academia, healthcare professionals, industry, investors, business and patient advocates to serve as a resource for the Commissioner and senior leadership of the Agency. This Advisory Board would serve multiple functions such as providing management advice as FDA initiates new programs, such as continuous quality improvement of the regulatory pathway, reduction of the time required for application review in accordance with statutory user fee requirements, reorganize, reprioritize and redistribute internal resources including personnel to meet emerging new challenges and opportunities such as the impact of globalization of the supply chain of food and medical products.

The FDA is a large and complex agency with multiple Centers and several missions. Having an Advisory Board for the FDA would provide the Commissioner with available asset of informed experts representing all aspects of the discovery, development and delivery of the products that FDA regulates.

The Advisory Board could also serve as a mechanism for ongoing progress review or resolution of problems associated with internal modernization initiatives. This could include large-scale projects such as the implementation of a modern electronic data management system, the creation of a bioinformatics platform for post market surveillance of product performance, and implementing information systems for monitoring and analysis of food and medical product imports destined for the U.S. markets. The Advisory Board should meet regularly but no less than quarterly for a full day to engage in a review of FDA management issues. The Advisory Board could also serve the Administration and Congress in an objective assessment of FDA's resource needs.

Several other federal agencies have external advisory boards such as the National Cancer Advisory Board of the National Cancer Institute that provides ongoing and consistent consultation regarding the programmatic initiatives of the organization.

The FDA is a large and complex agency with multiple Centers and several missions. Having an Advisory Board for the FDA would provide the Commissioner with an available body of informed experts representing all aspects of the discovery, development and delivery of the products that FDA regulates.

Such a Board should be prohibited from any knowledge or influence over the regulatory decision-making process regarding a specific product as that must always remain within the confidential confines of the FDA. No regulatory decision regarding a specific product would ever be permitted to be a subject of review or discussion by this advisory board. However, the board should be constituted in a manner that its members could provide valuable insights with regard to the future strategic opportunities and daunting challenges posed by the explosive progress in scientific research and technology development likely to create future regulatory challenges for the Agency and could provide independent, informed and trusted advice regarding programmatic initiatives under consideration by the Agency's leadership. The external Advisory Board's recommendations would have the sole purpose of assisting the Commissioner in improving the FDA's ability to fulfill its mission.

Recommendation 3: Designate FDA as an Independent Agency

The CHT FDA Modernization Project encourages the Administration and Congress to designate the FDA as an independent Agency. The FDA currently regulates nearly a quarter of the goods which are supplied to and consumed by Americans including most food and agricultural products, pharmaceuticals and biologics, and medical devices. In exercising its regulatory responsibility, the actions and policies of the FDA have direct, and at times, dramatic implications for almost all federal Agencies which are characterized as "Cabinet Status."

There are many Independent Agencies which operate within the U.S. federal government including the Environmental Protection Agency (EPA), the Federal Communication Commission (FCC), Federal Reserve Board, U.S. Securities and Exchange Commission (SEC), the National Labor Relations Board (NLRB) and the Federal Trade Commission (FTC).[xiii] Because of the similar role of the FDA in this greater federal regulatory environment and the broad scope of regulatory authority, the FDA should be designated as an Independent Agency.

Other thought leaders support congressional action to elevate the FDA to independent Agency status. Former Congressman Jim Greenwood, chief executive officer of the US Biotechnology Industry Organization, has indicated that the FDA deserves to be elevated to independent Agency status.

Since the FDA interacts with so many federal agencies, regulatory overlap occurs frequently. Because the FDA is not an independent federal Agency, when discrepancies occur, the FDA is at a significant disadvantage. According to an author familiar with Federal regulation, "It [FDA] is not a Cabinet department like Agriculture. It is not an independent agency like the EPA. It is not headed by someone with a direct mandate from the voters, like a city. So when it collides with another agency and loses, the public health issue at stake might be decided by the other agency's rules—whether tougher or weaker."[xiv]

Other thought leaders support congressional action to elevate the FDA to independent Agency status. Former Congressman Jim Greenwood, chief executive officer of the US Biotechnology Industry Organization (BIO), has indicated that the FDA deserves to be elevated to independent Agency status.[xv]

The CHT FDA Modernization Project participants determined that granting independent Agency status to the FDA would address two very specific needs:

1) The Agency must be able to rapidly engage in dialogue directly with other Agencies directly affected by its timely regulatory action. The relationship of FDA to other Agencies within the Department of Health and Human Services (HHS) such as NIH, CDC, CMS are relevant but much more important are the direct interactions with USDA, Homeland Security, Commerce, State, Defense, Trade, Veterans Affairs, EPA and OMB. These issues are best exemplified by the example of urgent regulatory actions on an agricultural (USDA) or medical product (HHS) that is imported (Commerce/Trade) through one of the nation's numerous ports of entry (Homeland Security) from a foreign country (State Department) or the regulation of products that are considered of urgent importance to our protection from a terrorist threat (DOD).

2) Independent Agency status also helps to rationalize the current appropriations dilemma where the Administration and OMB consider the FDA as a budgetary component of HHS. However, when the FDA appropriation is decided by the Congress, the FDA budget is considered by the Appropriations Subcommittee for Agriculture.[xvi] Though not a complete solution, the independent agency status would permit the agency to submit its budget proposal to OMB directly and allow FDA to represent its budget to Congress separately from HHS where it competes with FDA, CDC, CMS, and other health agencies for resources.

Recommendation 4: Develop a "Total Life Cycle" Regulatory Approach

Creating a 21st Century FDA is also predicated on dramatically and dynamically changing the manner in which FDA reviewers and investigators interact with the product(s) they are assigned. CHT recommends that the FDA foster a "total life cycle" approach to product development. This initiative would engage FDA staff reviewers and investigators during the entire "life cycle" of the product — from the earliest pre-clinical stages of product discovery through post-approval.

Our FDA Modernization Project participants recognized that the most important issues center on the FDA's regulatory approval process. The approval process begins long before an application is submitted and must continue long after the application is approved. The focus of user fees is the time it takes to review an application, but the success of approval and the promotion and protection of the public involves much more.

The capacity for "total life cycle" will require additional resources that will enable the Agency to be more involved during product development, whether it is the creation of a new vaccine by a biotech company or an innovative new medical device. Pre-submission engagement would help assure that the investments and decisions being made during early-stage research are consistent with regulatory expectations and policy. Similarly, by enhancing FDA's role in post market surveillance there could be more rapid identification of unanticipated adverse events. Additional post market research may also help to identify the patients most likely to benefit from a particular treatment.

By engaging with the FDA prior to the submission of an investigational new drug application (IND), the sponsor will better understand the expectations of their development plan, and the Agency scientists will gain deeper understanding of the underlying science, such as the mechanism of action of the drug and the rationale for clinical consideration. An improved understanding of the development and regulation of a medical product or the processes involved in the production of food can only enhance the confidence of the Agency, the consistency of the industry, and trust by the public in a regulatory decision.

Recommendation 5: Establish a Conditional Approval Process & Adaptive Clinical Trial Process to Improve Patient Care

In order to improve the drug evaluation and approval process, CHT FDA Modernization Project participants recommend that the Congress create a conditional approval process. Conditional approval may help bring potentially promising new medical therapies to the patients most in need as rapidly as possible.

Additionally, CHT recommends that the Agency embrace and deploy new policies and practices for the widespread use of "enriched" clinical trials and "observational" studies rather than complete reliance on randomized placebo controlled studies. Using modern tools such as genomics or other biomarkers, researchers for investigational new drugs (INDs) would select and test new therapies on patients ideally suited for the proposed mechanism of action of the drug rather than in a general population where the true benefit might be obscured.

Conditional Approval: Several thought leaders have suggested that routine drug development would be improved by adopting an approval strategy similar to the Progressive Approval mechanism made available by the European Commission. This type of pathway would allow the FDA to approve a drug that has clinically demonstrated a favorable benefit-risk profile in a specific subset of seriously ill patients prior to full testing in other populations that may one day use the drug. This approval would remain valid on the condition that post-market studies confirm the benefit of the drug and test it in the broader population.

The Agency has already taken steps in this direction but the FDA should be empowered by Congress to accelerate and more broadly apply mechanisms for earlier approval. To do so would also require greater compliance and cooperation by sponsors and providers to create a stronger mechanism for post market surveillance so that product performance can be adequately monitored once it is widely available outside of the limits of a pre-approval clinical trial.

Progress in validating biomarkers to select patients will help researcher design smaller and faster trials to get promising new drugs to the patients most in need. Since the conditional approval pathway should focus exclusively on unmet medical needs and serious conditions, patients suffering from life-threatening diseases would be able to receive personalized treatments to alleviate, mitigate or eliminate their disease well in advance of the current approval process.

Advances in health information technology (health IT) will allow FDA reviewers and research scientists to more carefully monitor patient populations thereby enhancing patient safety. Because the approval is conditional upon future research, the FDA can uphold their ongoing commitment to patient safety and product effectiveness when approving a new drug as well as after it is on the market. A conditional new

drug approval pathway will allow physicians to treat patients with the most serious forms of an illness, for which there are no existing adequate therapies, earlier than current mechanisms may allow.

Currently, FDA has several mechanisms for helping drugs move faster through the approval process, but only one pathway that might be said to be an alternative pathway.[xvii] FDA describes it as follows:

> ACCELERATED APPROVAL: [I]n 1992, [the] FDA instituted the *Accelerated Approval* regulation, allowing earlier approval of drugs to treat serious diseases, and that fill an unmet medical need based on a surrogate endpoint….For example…FDA might now approve a drug based on evidence that the drug shrinks tumors because tumor shrinkage is considered *reasonably likely to predict* a real clinical benefit [e.g. prolonged survival].

In an October 2011 report entitled, "Driving Biomedical Innovation: Initiatives to Improve Products for Patients," the FDA outlines a new expedited drug development pathway. In the report, the FDA indicated:

> "Sometimes during the development of a new drug to treat a serious or life-threatening disease that has few therapeutic options, the new treatment performs much better than standard-of-care in the early trials. While there is general agreement that such a drug should be developed quickly, there is not a common understanding of how to appropriately speed up development while simultaneously gathering adequate evidence about the performance of the product." [xviii]

In a separate report, the President's Council on Jobs and Competitiveness also recently weighed in on this issue. In an interim report entitled, "Taking Action, Building Confidence: Five Common-Sense Initiatives to Boost Jobs and Competitiveness," the Council endorsed the creation of a new conditional approval pathway in order to increase employment, expand investments in and by biomedical and biotechnology firms, and advance our economic competitiveness. The report recommends that:

> "While continuing to focus on patient safety, the FDA should also improve the Accelerated Approval pathway into a so-called progressive approval system. Rolling out new drugs, diagnostics, or medical devices to specific subpopulations of the public with significant unmet medical needs (with appropriate safeguards) will allow for additional data and learning to inform the full approval decision and provide patients with earlier access to innovative medicines.[xix]

Therefore, to facilitate the improvement of the drug approval process, CHT recommends that the FDA create an accelerated, patient-centric,

conditional approval mechanism. This would allow the FDA flexibility to approve products shown to successfully treat diseases or conditions in specific subpopulations prior to testing in larger, more representative population.

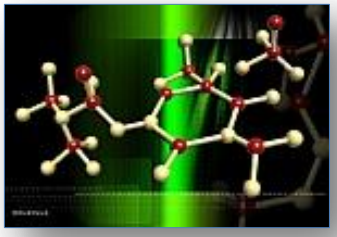
Adaptive Trial Design: Adaptive trial design refers to a clinical study design that ‘‘uses accumulating data to decide how to modify aspects of the study as it continues, without undermining the validity and integrity of the trial.”[xx] The goal of adaptive designs is to learn from the accumulating information and to apply what is learned as quickly as possible. In such trials, changes are made intentionally and by design. Therefore, adaptation is an inherent *design feature* which enhances the trial as opposed to a remedy for inadequate planning.

Increased flexibility within the adaptive design framework can result in better treatment of patients within trials (possibly including the use of fewer patients), more efficient drug development, and better use of available resources. Adaptive designs require rapid data collection to create efficient and effective clinical trials. Therefore the utilization of electronic platforms to collect and manage data in real time, or as close to real times as possible is important.

Adaptive designs also allow gains in efficiency in terms of time and investment. Additionally, adaptive trial designs make it more feasible to explore dose response earlier in the course of clinical drug development. This will enable better patient care by developing improved, data-driven decisions.[xxi] Innovative trial designs may help ineffective therapies be discontinued earlier and with greater confidence. This is a major challenge to drug developers as current estimates indicate that only 45% of drugs that enter Phase III ultimately get approved.[xxii] This high level of late-stage failure would be improved by screening out unsuccessful compounds earlier. It also may be reduced by facilitating the correct dose or doses being taken forward in pivotal trials. Better understanding of the dose response could also yield important dosing information for clinicians and patients at the time of launch.

Therefore, the Center for Health Transformation recommends that the Agency help researchers develop innovative adaptive trial designs for the approval of new medical products.

Recommendation 6: Support Improvements in Regulatory Science



In order to advance patient care, CHT recommends that Congress continues to support the Reagan-Udall Foundation. According to the Food and Drug Administration Amendments Act of 2007, the purpose of the Foundation is to "advance the mission of the Food and Drug Administration to modernize medical, veterinary, food, food ingredient, and cosmetic product development, accelerate innovation, and enhance product safety."[xxiii]

The statute also establishes and enumerates the duties of the Foundation which include:

> (1) taking into consideration the Critical Path reports and priorities published by the Food and Drug Administration, identify unmet needs in the development, manufacture, and evaluation of the safety and effectiveness, including post-approval, of devices, including diagnostics, biologics, and drugs, and the safety of food, food ingredients, and cosmetics, and including the incorporation of more sensitive and predictive tools and devices to measure safety;
>
> (2) establish goals and priorities in order to meet the unmet needs identified in paragraph (1);
>
> (3) in consultation with the Secretary, identify existing and proposed Federal intramural and extramural research and development programs relating to the goals and priorities established under paragraph (2), coordinate Foundation activities with such programs, and minimize Foundation duplication of existing efforts;
>
> (4) award grants to, or enter into contracts, memoranda of understanding, or cooperative agreements with, scientists and entities, which may include the Food and Drug Administration, university consortia, public-private partnerships, institutions of higher education, entities described in section 501(c)(3) of the Internal Revenue Code … and industry, to efficiently and effectively advance the goals and priorities established under paragraph (2);
>
> (5) recruit meeting participants and hold or sponsor (in whole or in part) meetings as appropriate to further the goals and priorities established under paragraph (2);
>
> (6) release and publish information and data and, to the extent practicable, license, distribute, and release material, reagents, and techniques to maximize, promote, and coordinate the availability of such material, reagents, and techniques for use by the Food and Drug Administration, nonprofit organizations, and academic and industrial researchers to further the goals and priorities established under paragraph (2);
>
> (7) ensure that--(a) action is taken as necessary to obtain patents for inventions developed by the Foundation or with funds from the Foundation; (b) action is taken as necessary to enable the licensing of inventions developed by the Foundation or with funds from the Foundation; and (c) executed licenses, memoranda of understanding, material transfer agreements, contracts, and other such instruments, promote, to the maximum extent practicable, the broadest conversion to commercial and noncommercial applications of licensed and patented inventions of the Foundation to further the goals and priorities established under paragraph (2);

(8) provide objective clinical and scientific information to the Food and Drug Administration and, upon request, to other Federal agencies to assist in agency determinations of how to ensure that regulatory policy accommodates scientific advances and meets the agency's public health mission;

(9) conduct annual assessments of the unmet needs identified in paragraph (1); and

(10) carry out such other activities consistent with the purposes of the Foundation as the Board determines appropriate.

Created by Congress to help support and promote FDA's regulatory science priorities, the Reagan-Udall Foundation is independent of the FDA with its own 14-member Board of Directors.[xxiv] The Reagan-Udall Foundation should create public-private partnerships to advance research in regulatory science, enhance medical decision making, and promote innovation. It should aggressively advance regulatory science and help foster the growth of intellectual capital in regulatory science at the FDA through the FDA Commissioner's Fellowship Program and other training and educational programs. The Commissioner's Fellowship Program combines graduate-level training and a mentored regulatory science research project.[xxv] Advancing the fellowship program and other education/training programs would advance the regulatory science agenda necessary to create a modernized FDA.

Conclusion:

While assuring America's continued leadership in medical innovation and product development involves an ecosystem of discovery, development and delivery, FDA regulation remains a core and essential element. At the Center for Health Transformation, our FDA Modernization Project focused on those recommendations for modernizing the regulatory framework that could be implemented in the short term. If implemented, these recommendations will have a dramatic impact on the FDA and the American people. Congress, as it considers reauthorization of user fees, must now adopt the changes that will create a 21st century FDA which advances patient-centered models of care which reflect the art and science of today's medical care.

To specifically reiterate our recommendations, they are:

- Create a modernized FDA through a comprehensive Agency-wide regulatory process reengineering and improvement initiative;
- Establish an external Agency-wide Advisory Board comprised of recognized leaders from academia, consumers, industry, investors, business and patient advocates to serve as a resource for the Commissioner and senior leadership of the Agency;
- Designate the FDA as an independent federal Agency;
- Foster a "total life cycle" approach to medical product development;
- Advance patient care through a conditional approval process and an adaptive clinical trial process; and
- Improve regulatory science by supporting the Reagan-Udall Foundation

By adopting these recommendations, progress will be made toward a modernized, 21st century FDA which would be more efficient, more predictable, more transparent and more effective. Creating that 21st century FDA is vital for the future of the economy as well as for the health of all Americans. There has never been a more appropriate time to consider and implement these recommendations. At the Center for Health Transformation, we look forward to working with the broad biomedical community to create a 21st century Food and Drug Administration.

CHT FDA Modernization Project Leads

Wayne W. Oliver, JD Andrew C. von Eschenbach, MD

FDA Modernization Project Steering Committee:

David Acheson, Leavitt Partners, LLC
Catherine J. Arnold, Credit Suisse
Fred Hassan, Bausch & Lomb and Warburg Pincus
Michael Mentesana, PricewaterhouseCoopers (PwC)
Sudip S. Parikh, Battelle Health and Life Sciences
Jay Schnitzer, Boston Scientific and Defense Advanced Research Projects Agency (DARPA)
Stephen Sundlof, Virginia-Maryland Regional College of Veterinary Medicine

FDA Modernization Project Implementation Task Force:

(Individuals who participated or were invited to participate)

Justin Barnes, Greenway Medical Technologies
Hans Beinke, Siemens Healthcare
Tim Birdsall, Cancer Treatment Centers of America
Elizabeth "Liz" Blackwood, GE Healthcare
Donald Braun, CTCA
Karoom Brown, L-3 Health
Elizabeth "Liz" Whalley Buono, MWV Healthcare
Paul Burn, Sanford Health
Jason Colquitt, Greenway Medical Technologies
Cathy S. Fischer, Gundersen Lutheran Health System
Gregory Davault, Given Imaging
E. Cartier Esham, Biotechnology Industry Organization (BIO)
Ron Fitzwater, Missouri Pharmacy Association
Lara Henry, L-3 Health
Craig Kephart, Centric Health Resources
John Klimek, National Council of Prescription Drug Programs (NCPDP)
Tom Knox, Allergan
Tom Looby, Given Imaging
Linda Onnen, GE Intelligent Platforms
Gio Patterson, IBM
Gaile Renegar, GlaxoSmithKline
Alejandro Reti, Verisk Health
Sean Robinson, GE Intelligent Platforms
Mary Stranger, Synovus
Helen Thompson, True North
Kendall VanPool, BlueCross BlueShield Association
John W. Walsh, Alpha-1 Foundation

Project Notes: CHT members are bolded. Members of the Steering Committee and Implementation Task Force may or may not support all of the recommendations contained in this white paper.

Special Thanks

We want to thank several individuals who have made working on this two-year project much easier and more enjoyable. The members of the Steering Committee listed on the previous page were instrumental to creating the vision of the 21st Century FDA. The members of the Implementation Task Force also listed on the previous page were essential to developing our consensus-driven collaboration.

Several members of the CHT team also need recognition. Rynnie Ross Cotter helped provide organization and structure to the project in the early days. Bassem Mikhael helped to provide much needed research assistance for the Project. Elizabeth "Liz" Noelcke provided focus and project management skills for the Project. Lee Schalk helped with research and guided the project as we released this white paper.

We want to thank CHT founder Newt Gingrich for casting a strong vision of what a 21st Century FDA should be. And, for discussing what a 21st Century FDA can bring to patient-focused healthcare and to the advancement of science and technology. His vision helped our Project better understand that creative medical breakthroughs can significantly enhance life and expand the American economy in terms of investment in innovation and jobs.

Finally, we want to thank the members of the Center for Health Transformation for their support of and participation in CHT's FDA Modernization Project. The success of this project to create the 21st Century FDA is due in large part to the collaboration with and among CHT members.

Creating a 21st Century Food & Drug Administration (FDA)

End Notes

[i] Executive Summary: Strategic Plan for Regulatory Science, August 2011, www.fda.gov.

[ii] Statement of FDA Commissioner Margaret A. Hamburg, M.D. before the Subcommittee on Agriculture, Rural Development, Food and Drug Administration, and Related Agencies, U.S. House of Representatives, March 10, 2010.

[iii] Report of the Subcommittee on Science and Technology, prepared for the FDA Science Board, November 2007.

[iv] J. DiMasi and H. Grabowski. (2007). The Cost of Biopharmaceutical R&D: Is Biotech Different? Managerial and Decision Economics, 28, 4-5, 469-479.; and J. DiMasi, R. Hansen and H. Grabowski. (2003). The Price of Innovation: New Estimates of Drug Development Costs. Journal of Health Economics, 22,2, 151-185.

[v] De Vol R, Bedroussian A, et al. "An Unhealthy America: The Economic Burden of Chronic Disease -- Charting a New Course to Save Lives and Increase Productivity and Economic Growth." The Milken Institute. October 2007.

[vi] "Alzheimer's Disease Treatments = Savings for Medicare and Medicaid," Alzheimer's Association, March 2011.

[vii] American Diabetes Association, http://www.diabetes.org/advocate/resources/cost-of-diabetes.html.

[viii] Centers for Disease Control and Prevention. Chronic Disease Overview page. Available at: http://www.cdc.gov/nccdphp/overview.htm.

[ix] Centers for Disease Control and Prevention. Chronic Disease Overview page. Available at: http://www.cdc.gov/nccdphp/overview.htm

[x] Lui KJ, Kendal AP. Impact of influenza epidemics on mortality in the United States from October 1972 to May 1985. Am J Public Health 1987;77:712-716. Available at: http://www-ijr.ujf-grenoble.fr/docs/immuno_D1/1021.pdf

[xi] CDC "HIV Prevalence Estimates -- United States, 2006;" MMWR 57(39), October 3, 2008.

[xii] Lighter,DE., "Continuous Quality Improvement-What every physician leader needs to know;" Stahl,MJ., Dean,PJ., The Physician's Essential MBA; 1999.

[xiii] http://www.usa.gov/Agencies/Federal/Independent.shtml

[xiv] Hawthorne, Fran, "Inside the FDA: The Business and Politics Behind the Drugs We Take and the Food We Eat," pages 66-67; 2005.

[xv] PharmaTimes; "FDA 'must be made an independent agency,' says biotech," July 4, 2011

[xvi] Eye on FDA, "Food Safety Modernization Act – Passed but Not Funded – A Conversation with Congressman Jack Kingston of the House Appropriations Committee;" http://www.eyeonfda.com/eye_on_fda/2011/01/food-safety-modernization-act-passed-but-not-funded-a-conversation-with-congressman-jack-kingston-of-the-house-appropriations-committee.html January 20, 2011

[xvii] "Bold Discussions: Possible New Approval Pathways for Breakthrough Drugs;" FDA Matters, November 14, 2011.

[xviii] Driving Biomedical Innovation: Initiatives to Improve Products for Patients, US Food & Drug Administration, October 7, 2011; http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/ucm274333.htm

[xix] President's Council on Jobs and Competitiveness, *Taking Action, Building Confidence: Five Common-Sense Initiatives to Boost Jobs and Competitiveness* (Interim Report), November 2011, http://files.jobs-council.com/jobscouncil/files/2011/10/JobsCouncil_InterimReport_Oct11.pdf

[xx] Adaptive Design in Clinical Drug Development; Taylor & Francis Group, LLC; 2006. Available at : http://www.gemini-grp.com/Bayes/PhRMA.pdf

[xxi] Adaptive Design in Clinical Drug Development; Taylor & Francis Group, LLC; 2006. Available at : http://www.gemini-grp.com/Bayes/PhRMA.pdf

[xxii] Kola, I., Landis, J; "Can the pharmaceutical industry reduce attrition rates?;" Nature Reviews Drug Discovery. 3:711–716; 2004.

[xxiii] Food and Drug Administration Amendments Act of 2007. Available at: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110

[xxiv] "FDA Announces Board Members of Reagan-Udall Foundation," November 16, 2007. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm109029.htm;.

[xxv] http://www.fda.gov/AboutFDA/WorkingatFDA/FellowshipInternshipGraduateFacultyPrograms/CommissionersFellowshipProgram/default.htm