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CAN A 21ST CENTURY FDA ACCELERATE BIOTECH INNOVATION TO CURE DISEASE AND SAVE LIVES?

James C. Greenwood
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James C. Greenwood, President and CEO, Biotechnology Industry Organization (BIO)

I. INTRODUCTION

Biotechnology innovation offers some of the most promising opportunities for achieving the important national goals of improving healthcare and reducing the human and financial burden of chronic disease on society.

But regulatory review processes are not keeping up with rapidly advancing science and are making the environment for developing new treatments and preventions for deadly and debilitating diseases more difficult. Unleashing the promise of biotechnology requires a comprehensive national strategy that fine-tunes some policies and overhauls others.

That strategy should include a U.S. Food and Drug Administration (FDA) that recognizes its national role in advancing innovation by reviewing innovative products in a timely manner and promoting a consistent and science-based decision-making process that is reflective of patient needs. By creating a 21st century FDA and a more patient-centric clinical research and development process, we can establish a clear and effective pathway for turning hope into cures.

FDA should incorporate the latest advances in regulatory science into its operations and should have transparent review processes and requirements that are understood by patients, physicians, industry, investors and policymakers. Also, the agency must find better, more collaborative ways to incorporate the views of patients when evaluating the health products it regulates.

The Biotechnology Industry Organization (BIO) worked with other stakeholders to develop policy proposals designed to accomplish these ends. These are specific legislative and administrative changes to the structure, mission and processes of FDA.

II. BACKGROUND

Biotechnology provides breakthrough therapies to treat, prevent and diagnose disease. The biotech industry has produced more than 260 FDA-approved therapies and vaccines for serious diseases, including cancer, HIV, diabetes, stroke and cardiovascular disease, asthma, Alzheimer's disease and many other conditions. Biotechnology companies have discovered and developed the majority of scientifically novel and orphan disease drugs.[1]

But the pace of biotech innovation—and, more specifically, the pace at which new biologic treatments reach patients who need them—is not keeping up with our nation's healthcare needs. The average time between treatment discovery and availability to sick and suffering patients is between 10 to 15 years. That is much too long.

POLICY RECOMMENDATIONS

Congress and FDA should enact measures to:

- Elevate FDA and empower operational excellence.
- Advance regulatory science and innovation.
- Enable modernized patient-centric clinical development.

The American population is growing older. This year, the 72 million Baby Boomers began reaching retirement age and are becoming eligible for Medicare coverage in record numbers. In fact, ten thousand people a day will turn 65 every day for the next 20 years.

Unfortunately, a growing number of Americans suffer from chronic disease. As of 2009 about 45 percent of the population had at least one chronic disease such as heart disease, cancer or diabetes.[2] By 2025 an estimated 164 million Americans will be affected.[3]

Chronic disease causes much human suffering and is also the main driver of rising healthcare costs. About 75 cents of every dollar that the U.S. spends on medical care is directed toward the care of people with chronic diseases.[4]

Biotechnology innovation can save lives and save dollars. Advances in biotechnology medicines offer real solutions to our most pressing healthcare needs: curing disease, reducing costs, increasing quality, and ensuring that people enjoy not only longer lives, but better and more productive lives. By developing new therapies to help better detect, prevent and cure disease we will have fewer sick people, less suffering and significant healthcare savings.

For example, in 2005 Medicare spent $91 billion caring for people with Alzheimer's and other dementias.[5] Delaying the onset of Alzheimer's disease by just five years could save the Medicare program $50 billion per year.[6] There are 79 research and development projects for treatment of Alzheimer's, along with hundreds of potential therapies in development for other dementias, cancer, diabetes, heart disease and other chronic conditions. But the current new drug development and approval process is uncertain, lengthy and expensive.

Again, it can take 10 to 15 years to develop an approved new drug product available for use by patients. The cost of developing an approved drug has been estimated between $800 million and $1.2 billion.[7]

The present regulatory environment contributes to both the high cost and slow pace of developing new drugs. Between 1999 and 2005, the average length of clinical trials grew by 70 percent,[8] while the number of unique procedures per clinical trial protocol increased by 46 percent.[9] FDA approval of new medicines with truly novel chemical compounds was significantly lower during 2005-2008, with only an average of 19, compared with the 1990-1999 period average of 31.[10]

Regulatory review processes are not keeping up with rapidly advancing science and are making it a more difficult environment to develop new treatments and products. The status quo at FDA is at odds with our nation's desire to maintain global leadership in biotech innovation, to cure disease, and to make the U.S. healthcare system more affordable, more efficient, and of higher quality.

BIO represents more than 1,100 biotechnology companies. Most of its members are small, investor-funded, research-intensive companies. The typical biotech firm has fewer than 50 employees, has up to five therapy products in development, and is three or more years away from having product revenue.[11] When the product review process is lengthy and the criteria for approval often opaque, the ability of these companies to successfully develop new cures and solutions to address our nation's most pressing healthcare needs is at risk.

As FDA Commissioner Dr. Margaret Hamburg correctly observed, "Regulatory science is an essential part of the overall scientific enterprise, yet it has been under-appreciated and under-funded. Because of this, we have been unable to apply the best possible science and technology to the tasks before us. And we are left relying on 20th century approaches for the review, approval and oversight of the treatments and cures of the 21st century."[12] She also notes that, "Without advances in regulatory science, promising therapies may be discarded during development because we lack the tools to recognize their potential and because outdated, inefficient review methods unnecessarily delay the approval of critical treatments."[13]

Working with other stakeholders in a rigorous, year-long process, BIO developed a set of policy proposals, ***Unleashing the Promise of Biotechnology***, which it believes will better align the regulatory environment for biotech innovation with our nation's priorities.[14] The proposals discussed in more detail below are intended to make FDA an agency that recognizes its

national role in advancing innovation, maintains the ability to effectively review innovative products in a timely manner, and promotes a consistent and science-based decision-making process that is reflective of patient needs.

III. ISSUES IN DISPUTE

To accelerate biotech innovation, Congress should take steps to elevate the role of FDA within the executive branch and empower this critical agency to achieve greater operational excellence. As the key regulator of several innovation-driven industries FDA should strive to remain at the cutting edge of science. And because the health, well-being, and even lives of millions of patients depends on FDA's regulatory decisions, the agency should do more to integrate the patient perspective into its operations and enable modernized patient-centric clinical development.

A. Elevate FDA and empower operational excellence.

1. FDA's mission should be updated for the 21st century.

FDA's mission, as amended by the Food and Drug Administration Modernization Act of 1997 and set forth in section 903 of the Federal Food, Drug, and Cosmetic Act (FDCA), is to promote and protect the public health. However, the FDA mission statement does not reflect the agency's critical role in incorporating modern scientific advances into review practices to ensure that innovative treatments and therapies are made available to the patients who need them.

The pathway for such long-sought health technology advances as personalized medicine, health applications of nanotechnology, and other cutting-edge developments to reach patients and to improve healthcare in the United States goes through FDA. The agency has a critical role in facilitating healthcare innovation, but this fact is not formally and forcefully recognized in FDA's legislative mandate.

2. FDA needs greater operational independence.

FDA is a large, complex organization that regulates nearly a quarter of the consumer goods supplied to the American public. However, the agency's status within the executive branch of the federal government does not reflect FDA's impact on public policy and the economy.

FDA is housed within the Department of Health and Human Services (HHS) and is therefore subject to the management, budgetary restrictions and oversight of the larger department and must inevitably compete with other departmental components for budget and resources. Other high-impact regulatory agencies with powers to supervise certain sectors of the economy, such as the Environmental Protection Agency (EPA) and the Federal Communications Commission, have been granted status as independent agencies.

FDA should have greater operational independence and be empowered to speak with its own voice within the executive branch and in its communications with Congress over appropriations, responsibilities and other legislative matters.

3. FDA needs new approaches to effectively manage the agency's many responsibilities.

The substantial size of FDA presents a challenge to agency leadership. FDA employs more than 11,500 full-time equivalent staff across the world. The agency is responsible for regulating more than $2 trillion in food, drugs, medical devices, cosmetics, dietary supplements and other consumer goods—nearly a quarter of the U.S. consumer goods supply.

Since the passage of the 1906 Pure Food and Drugs Act, new statutory requirements have significantly expanded FDA responsibilities. The Food and Drug Administration Amendments Act of 2007 (FDAAA) imposed substantial new requirements on FDA in a range of areas, including medical product safety, advisory committee membership and

recruitment, risk evaluation and mitigation strategies, and clinical trial registries. More recently, FDA was granted authority to regulate tobacco products, directed to establish a pathway for approval of biosimilar biological products, and provided with new tools to improve the agency's ability to prevent contamination in the food supply.

The size and complexity of FDA, increasing statutory responsibilities, and globalization of FDA-regulated industries have placed significant demands on FDA and may have hampered its ability to develop forward-thinking strategies. FDA's already extensive portfolio of responsibilities will no doubt continue to expand in the future. Merely keeping up with the day-to-day demands of running such a large enterprise is enough to occupy the agency's leadership. Attempts to get ahead of the curve with strategic planning and to incorporate new management perspectives often founder amid the agency's huge workload. FDA needs a formal mechanism for reviewing its own processes and injecting strategic management perspectives and improvements into its operations.

B. Advance regulatory science and innovation.

1. The Reagan-Udall Foundation for regulatory science is a neglected resource that should be fully utilized.

Under the FDAAA, Congress established the Reagan-Udall Foundation for the Food and Drug Administration, an independent non-profit organization intended to support public-private partnerships for the purpose of advancing the mission of FDA to "modernize medical [and other] product development, accelerate innovation, and enhance product safety."[15] The Foundation could, for example, form collaborations to advance the use of biomarkers, surrogate markers, and new trial designs to improve and speed clinical development. However, Congressional appropriations bills for the agency have subsequently restricted FDA's ability to transfer federal funding to the Foundation. These funding restrictions should be lifted so that the Reagan-Udall Foundation can fulfill its promise.

2. FDA must have more effective institutional means of staying at the forefront of promising new scientific and regulatory approaches.

FDA has developed several initiatives to advance regulatory science. These include the FDA/NIH Joint Leadership Council,[16] the academic Centers of Excellence in Regulatory Science and FDA's Critical Path Initiative.

The current Office of Regulatory Science and Innovation is theoretically charged with, among other things, supporting core scientific capacity and infrastructure within FDA, and fostering development and use of innovative technologies in product development and evaluation. This Office, however, lacks the statutory mandate to respond to external and internal recommendations by establishing specific pilot programs, and to implement successful programs into FDA's everyday regulatory decision-making process.

To fully incorporate modern science into its regulatory processes, FDA needs an internal entity with unified responsibility for systematically analyzing the findings and recommendations from internal and external sources of scientific advice, and with clear authority to pilot promising scientific and regulatory approaches.

3. FDA should create systems to enhance its access to external scientific and medical expertise.

The FDCA establishes FDA as the preeminent agency charged with evaluating cutting-edge science as it is applied to products for the prevention, diagnosis and treatment of human disease. FDA has also been perceived by many as the global standard bearer for regulatory review of drug and biologic applications.

However, scientific and medical knowledge, techniques and technology are advancing at a more rapid pace today than at any other time, and FDA's capacity to access information about these advances has not kept pace. FDA should improve existing systems and develop new organizational mechanisms to enhance its access to scientific and medical advice.

C. Enable modernized patient-centric clinical development.

1. FDA should increase access to innovative treatments and therapies through a progressive approval mechanism.

Federal law generally prohibits the distribution and marketing of new drugs prior to FDA approval. Patients suffering from life-threatening or serious medical conditions have long sought access to drugs earlier in the drug development and approval process. Advocacy by HIV/AIDS patients in the 1980s led to the accelerated approval scheme, and advocacy by terminally ill patients in the 1990s led to improvements in compassionate use programs that can provide access to investigational drugs. However, since these pathways are limited, a new mechanism is needed to provide patients, particularly those with illnesses for which no adequate therapy exists, earlier access to promising new therapies.

2. Leverage electronic health records to facilitate clinical research.

Every new drug's sponsor spends years designing and conducting clinical trials to show the drug is safe and effective. Using health information technology (IT) such as electronic health records (EHRs) in clinical research will improve and speed up the drug development process, and decrease costs.

To develop a new therapy for use by patients, companies spend the majority of the drug development phase conducting clinical trials to demonstrate that the drug is safe and effective. This process can take six to seven years. EHRs can be used to improve how clinical research is conducted.

Specifically, EHRs can help companies more effectively identify, recruit and enroll patients for clinical trials. Companies often face challenges recruiting subjects to participate in clinical trials studying drugs for a rare disease or for trials that require a large number of patients. But EHRs can be used to notify a physician if a patient is eligible for a clinical trial.

Sponsors can also use health IT to better inform clinical study design, more efficiently collect study data, and allow investigators to protect subjects enrolled in a clinical trial by more effectively monitoring for adverse events.

However, there are significant barriers preventing widespread use of health IT in clinical research, including slow adoption by providers and lack of standards development. FDA and Congress should help remove those barriers.

IV. RESEARCH AND RESPONSE

A. Elevate the FDA and empower operational excellence.

1. Update the FDA mission statement.

FDA needs a clear mandate to encourage the development of innovative products. In addition, FDA must have the capacity and commitment to incorporate the latest scientific advances into its decision making so that regulatory processes can keep pace with the tremendous potential of companies' leading-edge science. Congress can help by updating FDA's statutory mission to underscore the need for FDA to advance medical innovation by incorporating modern scientific tools, standards and approaches into the agency's work, so that innovative products can be made available to those who need them and in a timely manner.

FDA's mission should reflect the importance of a modern agency that is equipped to respond to advances in science that can benefit the public health. Amending the FDCA to update FDA's mission will keep FDA focused on, and accountable to, this important principle.

2. Grant FDA status as an independent agency.

FDA should have the same authorities to make budget, management and operational decisions as afforded other independent agencies such as EPA. This would empower the agency to work more effectively with the President and Congress to carry out its mission to promote and protect the public health. Creating an independent agency would also enhance the agency's ability to obtain quality and consistent leadership. Congress should establish FDA as a free-standing independent agency outside of the departments of the executive branch, as defined under §104, Title 5 of the United States Code.

As an independent agency, FDA would have a stronger position and profile within the executive branch, which would correspondingly increase the profile of the Commissioner of Food and Drugs, also enhancing FDA's ability to supervise its sector. In addition, FDA would have more freedom in its budget request since it would no longer be required to go through the department budget process, which often requires agencies to curtail their overall budget requests. It is critical that if FDA were to become an independent agency, it continue to coordinate appropriately with other HHS operating divisions such as the National Institutes of Health, the Centers for Disease Control and Prevention, the Centers for Medicare & Medicaid Services, and the Agency for Healthcare Research and Quality.

3. Establish an external Management Review Board for FDA.

FDA is a large, complex organization. To fulfill its responsibilities effectively, it must be well organized and well managed. It is critical that the agency's organization and management capabilities be periodically analyzed, and that the Commissioner of Food and Drugs be provided with fresh, visionary and independent thinking on how to improve the ability of the agency and its Centers to promote and protect the public health, as well as the support necessary to implement recommendations. An external advisory board composed of individuals with experience in organizational management could help the agency address operational challenges. Current law should be amended to establish a Management Review Board (MRB) to conduct periodic reviews of FDA's management and organizational structure, and to provide recommendations to the Commissioner about ways to improve FDA operations.

The establishment of an external MRB could help identify deficiencies in FDA's management and organizational structures that threaten the agency's ability to meet its numerous regulatory responsibilities. The success of the MRB will be highly dependent on the personal and committed involvement of FDA senior leadership, including the Commissioner of Food and Drugs, in recruiting highly qualified, visionary and independent thinkers to serve on the MRB; alternatively, an outside body might be charged with recruiting members and/or convening the board.

B. Advance regulatory science and innovation.

1. Congress should support regulatory science public-private partnerships by restoring funding for the Reagan-Udall Foundation.

The FDAAA provides detailed information on the composition and activities of the Reagan-Udall Foundation, including its duties, Board membership, governance, funding and requirements for assuring accountability.[17] The FDAAA legislative history indicates that Congress envisioned the Foundation as helping to foster the development of new research tools to aid in the evaluation of the safety and effectiveness of drugs, biologics and medical devices.[18]

The duties of the Foundation include the identification of unmet needs for the development, manufacture, and evaluation of drugs, biologics, and devices (including diagnostics), and establishing goals and priorities to meet these needs. They also include providing "objective clinical and scientific information to the [FDA] 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.

Unfortunately, the Foundation has yet to receive any Congressional appropriations. This is in large part due to concerns regarding accountability, including allegations that industry would have too much influence over the Foundation's activities. However, FDAAA required the Foundation to establish policies on conflicts of interest (and many other standards). The Foundation's Board of Directors[19] has adopted bylaws[20] which were published for comment and which include several provisions that meet not only the FDAAA requirements but put in place further protections to protect the integrity of the Foundation's work.

Despite these efforts and protections, Congress continues to block funding for the Foundation. The FY 2011 appropriation for FDA contained a prohibition against implementing the statutory provision that is the funding mechanism.[21] Without the federal funds (and support) necessary to build an infrastructure, the Foundation will never become an operational organization. Congress should remove restrictions on FDA's ability to transfer federal funding to the Foundation as allowed by statute.

2. Create an FDA "Experimental Space," led by a Chief Innovation Officer, to pilot promising new scientific and regulatory approaches.

An FDA "Experimental Space," led by a new Chief Innovation Officer, should be established with the responsibility and authority to ensure that promising new approaches are integrated into agency operations at all levels.

Currently, FDA's Office of the Chief Scientist is charged with coordinating internal and external outreach to identify critical regulatory science and innovation needs and developing a strategic plan for science at FDA. FDA has also established a high-level advisory board, the Science and Innovation Strategic Advisory Council, comprising the Chief Scientist and representatives from the Office of the Commissioner, the various Centers, and the FDA Office of Regulatory Affairs. The Advisory Council meets twice a year to identify and communicate key scientific priorities from each Center, to set and discuss major cross-cutting scientific priorities for the agency, and to propose and evaluate major programs and partnerships.

FDA also has an FDA Science Board that provides advice to the Commissioner, the Chief Scientist and the Centers on complex scientific and technical issues within the agency, industry and academia. The Board reviews the Science and Innovation Strategic Advisory Council's scientific plan and regulatory science priorities.

Within the Office of the Chief Scientific Officer is the Office of Regulatory Science and Innovation, which provides strategic leadership, coordination, infrastructure and support for innovation in FDA science that is intended to advance the agency's ability to meet its mission to protect and promote public health. As noted previously, however, this Office lacks the statutory mandate to establish specific pilot programs and to implement successful programs into FDA's everyday regulatory decision-making process.

The FDCA should be amended to establish an FDA "Experimental Space," led by a new Chief Innovation Officer, with the responsibility and authority to identify promising new scientific and regulatory approaches, with input from stakeholders inside and outside the agency, and ensure that these approaches are integrated into agency operations and harmonized with the approaches of other mature regulatory agencies.

Examples of such approaches might include the qualification of a particular biomarker, the acceptance of novel clinical trial design methodologies, incorporation of EHR technologies, alignment and rationalization of regulatory pathways for the approval of drugs/biologics and companion diagnostics, or adoption of novel methods in predictive toxicology.

Among the Chief Innovation Officer's duties should be the systematic analysis of the recommendations of all internal and external entities involved in advancing regulatory science, such as the FDA Science and Innovation Strategic Advisory Council, the FDA Science Board, the National Center for Toxicology Research, the FDA/NIH Joint Leadership Council, the Reagan-Udall Foundation, and key public-private partnerships such as the academic Centers of Excellence in Regulatory

Science, the Biomarkers Consortium, the Patient Reported Outcomes Consortium (PROC) and the Predictive Safety Testing Consortium (PSTC).

The Chief Innovation Officer's responsibilities should include the development of implementation plans for pilot programs to incorporate recommendations from governmental, public/private organizations and academic regulatory science initiatives into agency regulatory decision making. Implementation plans should be published for public comment for at least 60 days prior to initiation of any pilot program.

Most importantly, the Chief Innovation Officer should have the authority to establish and oversee the implementation of pilot programs within the Centers, and ensure participation by cross-disciplinary pilot teams.

3. Enhance FDA's access to external scientific and medical expertise.

FDA's access to scientific and medical advice should be enhanced by improving the operations of FDA Advisory Committees, establishing Chief Medical Policy Officers in the immediate offices of the Center Directors, and providing FDA staff with additional avenues for accessing external scientific and medical expertise.

FDA regularly looks to outside experts to provide the agency with independent opinions and recommendations on a variety of complex medical and scientific issues, typically through the use of Advisory Committees.

In recent times, FDA has found it more difficult to populate Advisory Committees with qualified members. This is in part due to the establishment of new conflict of interest requirements under the FDAAA (Title VII), and FDA's interpretation of that statute. Over time, the new requirements progressively limit FDA's ability to grant waivers permitting individuals with essential expertise, but who also have a conflict of interest, to participate with respect to a particular matter before the committee.

FDA Advisory Committees have historically used the most knowledgeable and highly qualified individuals to obtain the best available information. This authority is critical for reviews of the cutting-edge science and next-generation innovation that is the bailiwick of biotechnology companies. In many cases, only a handful of qualified experts may exist to provide the agency with appropriate review of complex and technical issues surrounding new products. For example, for certain rare disease areas or product categories, the universe of highly knowledgeable and qualified individuals may be quite small. In some circumstances, virtually the only experts in an area are individuals who are involved as advisors or participants in the research and development leading to the innovation being reviewed by FDA.

Allowing such individuals to participate in an FDA Advisory Committee is vitally important because making decisions based on the best and most relevant science depends on the agency's ability to seek and use the advice of these experts. Flexibility in the issuance of waivers is crucial to achieving this goal.

FDA Advisory Committee policies should be revised to improve committee operations. The financial conflict of interest waiver caps should be repealed (while retaining appropriate disclosure requirements) to ensure that FDA has, and uses, significant discretion to grant financial conflicts of interest waivers on a case-by-case basis for potential Advisory Committee members whose expertise is essential.

Also, Congress should amend section 505 of the FDCA to include language requiring that committees considering the safety or effectiveness of drugs or biologics include at least one medical or scientific expert chosen by a patient group or research foundation whose interests are in the specific disease or diseases proposed to be treated by the drug or biologic under consideration. Such representatives would be in addition to any consumer representative already present on a given committee, and should be full voting members of that committee.

FDA should further enhance its access to medical expertise by creating Chief Medical Policy Officers within the immediate Offices of the Directors for the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research

and assigning them responsibility for identifying and addressing broad medical and scientific policy disputes, and ensuring that FDA staff have access to the external expertise necessary to resolve those disputes.

C. Enable modernized patient-centric clinical development.

1. Increase access to innovative treatments and therapies through progressive approval.

Expanding and improving the accelerated approval pathway into a progressive approval mechanism would help provide patients more timely access to needed therapies. This pathway would be limited to innovative products for unmet medical needs, significant advances to standard of care, targeted therapies, and those that have been approved by the European Medicines Agency or other mature regulatory agencies. This pathway also would ensure risk-benefit analysis that incorporates the safety and needs of patients in the real world.

Currently, FDA may grant accelerated approval to new drugs for serious or life-threatening diseases that represent a meaningful therapeutic benefit over existing treatment. The agency may approve such a drug on the basis of a surrogate endpoint "reasonably likely" to predict clinical benefit or another clinical endpoint other than survival or irreversible morbidity. The sponsor of a drug approved under the accelerated approval pathway must perform adequate and well-controlled clinical trials after approval, to verify the anticipated clinical benefit of the therapy.

Second, under its expanded access regulations, FDA permits the use of an investigational drug for treatment of patients with "immediately life-threatening" or "serious" medical conditions when there is no comparable or satisfactory alternative treatment as well as during an emergency. FDA grants expanded access for patient groups of varying sizes, depending on the state of the evidence on safety and effectiveness.

Accelerated approval and expanded access, while helpful, are narrow in their scope. In fact, most patients do not benefit from them. These pathways do not provide subpopulations of patients access to promising therapies that may help them. For example, cancer patients identified using a biomarker, for which targeted drug therapy has been shown effective, would not receive early access to the therapy under any existing program. Terminally ill patients do not always receive early access to promising therapies, despite the fact that the risks they face from the disease may far outweigh risks they face from taking the drug. Accelerated approval only applies to a subset of drugs that have the potential to treat serious diseases; thus, fewer drugs are made available via that pathway. Last, no existing program provides a method for companies to fund continued research of a promising drug. As a result, promising drugs may never be made available to patients because companies do not have the resources to continue developing the drug.

FDA should establish a mechanism for progressive approval available for a new drug intended to provide a meaningful advancement in the treatment of serious or life-threatening disease, which offers the promise of one or more of the following:

- first approved therapy for a condition or targeted subpopulation with the condition
- ability to treat patients unresponsive to, or intolerant of, existing approved therapies
- ability to treat rare diseases or disease subpopulations based on biomarkers or genetics (e.g., personalized medicine)
- ability to offer a significant improvement in outcomes for patients compared to existing approved therapies, either alone or in combination with existing approved therapies. Improvement in outcomes may reflect improved efficacy, improved safety, or an enhanced balance of efficacy and safety, compared to existing approved therapies and products that have been approved by the EU and other mature regulatory agencies

The relative risk/benefit profile of these drugs is different from other drugs, which justifies their earlier availability to patients (subject to appropriate controls and additional data gathering). For purposes of determining whether a new drug offers

the promise of a meaningful advance over existing approved therapies, only therapies with full FDA approval should be considered as existing approved therapies (e.g., drugs available under the Progressive Approval or Accelerated Approval pathways should not be considered as existing approved therapies).

The sponsor could apply at, or any time after, a pre-investigational new drug meeting. Whether a drug should be considered for, or the subject of, progressive approval can be recommended by FDA, but should be the option of the sponsor. FDA should issue, upon request within 60 calendar days, a written determination explaining whether a drug and a proposed indication is, or is not, eligible for progressive approval.

Progressive approval should be granted, in general, at the earliest possible time when the available evidence suggests that the drug is more likely than not to provide a favorable benefit-risk tradeoff to its intended patient population. For example, progressive approval may typically be granted following completion of one Phase II trial, provided that the available evidence suggests a favorable benefit-risk evaluation.

Approval should be conditioned on written agreement between FDA and the sponsor regarding further development plans designed to lead to the submission of a supplement for full approval under section 505 of the FDCA, or 351 of the Public Health Service Act, within a period of time to be negotiated on a case-by-case basis. FDA should also have the authority to waive the requirement to obtain full approval, if it finds that the data necessary to satisfy the standard in question cannot be collected, for example due to ethical concerns or scientific limitations (referred to as "exceptional approval").

2. Leverage electronic health records to facilitate clinical research.

Despite the vast potential for improving clinical research through the use of health IT, significant barriers remain. Although Congress has provided funding to encourage the adoption of electronic health records, the use of EHRs in clinical practice remains relatively low at this time. Work must be done to ensure interoperable standards and the secure exchange of data. In addition, validation methods for clinical research health IT tools are needed. But most importantly, FDA must issue standards governing activity in this area. Companies are less likely to use different approaches to clinical trial research, even if those methods lead to more efficiency and better protections for clinical subjects, if FDA is unwilling, or unprepared, to apply data generated in clinical research using health IT in drug approval decisions.

The FDCA should be amended to provide that the Commissioner of Food and Drugs appoint, within the Office of the Commissioner, a Clinical Informatics Coordinator. The Clinical Informatics Coordinator should develop a process to validate the use of health IT in clinical research and encourage the use of new health information technologies in clinical research protocols. FDCA should also require that the Clinical Informatics Coordinator establish pilot projects to explore and evaluate the methods of incorporating emerging health IT to make the clinical research process more efficient.

After evaluating the pilot programs, FDA should issue guidance for the conduct of clinical trials incorporating health IT. The guidance should explain how FDA will evaluate such information when reviewing medical product applications.

V. IMPACT OF POLICY RECOMMENDATIONS

BIO developed the proposals discussed above as part of a long-term strategic agenda intended to unleash greater biotechnology innovation. It believes adopting these policies will help achieve important national goals such as curing disease, saving lives, improving the nation's healthcare system and fiscal circumstances, as well as maintaining U.S. global leadership in a critical industry.

FDA plays a central role in determining the success of biotechnology innovation. By incorporating innovation into FDA's mission, and elevating FDA to an independent status that reflects its impact on not only biotech, but a significant portion of the U.S. economy we will empower the agency to better perform its critical mission—and better advocate Congress for the resources it needs to do so.

A more empowered FDA will be able to constantly improve its own internal operations and do a better job of keeping current with advances in regulatory science and medical innovation. A more transparent and patient-centric FDA will, without compromising safety, develop greater ability to effectively review innovative products in a timely manner, and promotes a consistent and science-based decision-making process that is reflective of patient needs.

Creating such a 21st century FDA will accelerate biotech innovation to cure disease and save lives. Biotech companies will waste less time and money navigating the regulatory and review process when it is more transparent and predictable, better resourced, and up to date with the latest advances in technology. That will make it easier for the small biotech companies that comprise most of the industry to raise adequate capital and to invest their resources in developing new therapies. This will mean more projects in the pipeline and more treatments and cures reaching patients sooner. Unleashing the promise of biotechnology in this way will lead to less sickness, less suffering and significant overall savings in healthcare costs.

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