DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

STATEMENT

OF

JANET WOODCOCK, M.D.

DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH

FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

SUBCOMMITTEE ON HEALTH

COMMITTEE ON ENERGY AND COMMERCE

U.S. HOUSE OF REPRESENTATIVES

"21st-Century Cures: Modernizing Clinical Trials and Incorporating the Patient Perspective**"**

July 11, 2014

RELEASE ONLY UPON DELIVERY

INTRODUCTION

Mr. Chairman, Ranking Member Pallone, and Members of the Subcommittee, I am Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to be here today to discuss modernizing clinical trials, incorporating the patient perspective, and several FDA activities intended to promote pharmaceutical innovation.

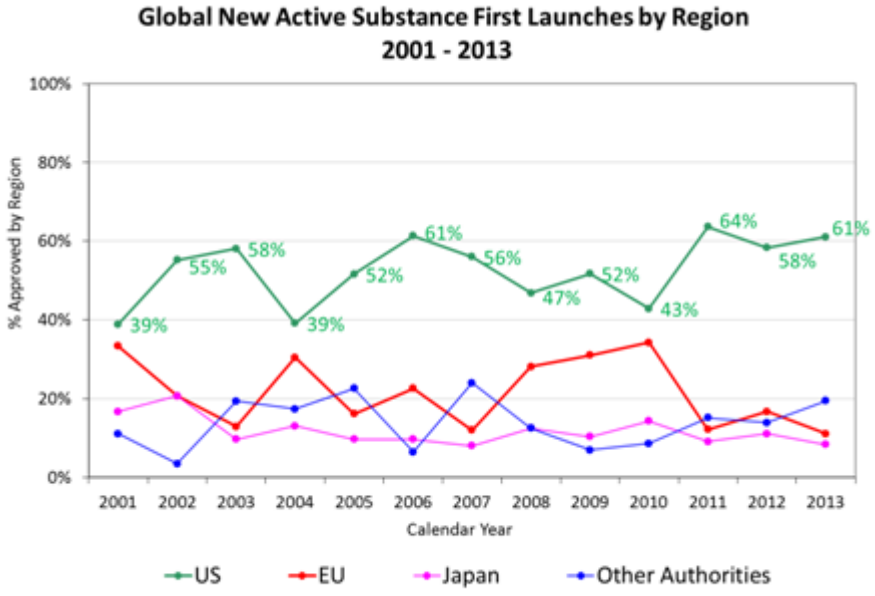
In recent years, there have been important advances to help ensure that therapies for serious conditions are approved and available to patients as soon as there are sufficient data to show that the therapies' benefits outweigh their risks. Despite this progress, there is much more work to be done. Many scientific discoveries still need to be translated into treatments for patients in need of new lifesaving therapies.

FDA is committed to doing our part to help bridge this gap. We have been actively scrutinizing, strengthening, and streamlining our regulatory processes at various steps along the path from drug discovery to drug approval, including the clinical development phase—the longest and most expensive period of drug development. As part of this effort, we have developed and successfully used a number of flexible and innovative approaches to expedite the development and review of drugs to the benefit of millions of Americans. FDA routinely works closely with drug sponsors to apply flexibility, including use of biomarkers, surrogate endpoints, non-traditional trial designs, and other available tools to expedite the development of products to treat

both common and rare diseases. Particularly for drugs intended to treat life-threatening and severely debilitating illnesses, FDA exercises the broadest flexibility in applying its statutory standards. We also have initiated and participated in many efforts to address the underlying scientific and clinical trial infrastructure challenges that affect the cost and timeliness of drug development. Some of these challenges need to be addressed by those outside of FDA; but we continue to look for ways to streamline the clinical development phase, where possible and within our purview.

Statement of the problem

FDA's approval process is now faster than anywhere else in the world (see figure below). Just last year, three-quarters of the new drugs FDA approved were approved in the United States before the European Union (EU) and Japan. Currently 90 percent of drugs that represent an advance over existing treatment are reviewed and decided on in 180 days, some in considerably fewer days.



Source: *Scrip Magazine* (2001 - 2006), *Pharmaprojects/Citeline* **Pharma R&D Annual Review** (2007 - 2014)

Despite the growing success and speed of the approval process and revolutionary advances in genomics more than a decade ago, FDA was among the first to underscore that the science necessary to translate these discoveries into treatments—development of biomarkers, genomic data, modernized clinical trial designs, computer modeling, and advanced imaging technology—was not keeping pace. As a result, the process of drug development leading up to submission of a marketing application is often inefficient, costly, and slow.

What is needed to reduce the cost and length of drug development? Although no simple set of initiatives will quickly produce a flood of new treatments, much can be done to improve drug development, both in the short and long term. Today I want to talk about FDA's efforts to increase the speed and efficiency in several areas in the clinical trial phase of drug development. These include:

- Accepting flexible clinical development designs; such flexible programs may use surrogate endpoints, or have fewer than the two traditional randomized, controlled trials of efficacy, or have other non-traditional elements.
- Meeting frequently and working closely with industry sponsors throughout the development process to plan efficient clinical trial programs and agree on needed data, a process that has been shown to shorten drug development by up to several years.
- Helping create clinical trial networks and "master protocols," where appropriate, to greatly reduce the cost of conducting clinical trials and reduce the time needed to carry them out.
- Using surrogate endpoints, both in accelerated approvals (approvals based on an unvalidated surrogate endpoint that is reasonably likely to predict clinical benefit) and traditional approvals (i.e., approvals not requiring confirmatory evidence of efficacy post-

market). Surrogate endpoints have been the basis for 60 percent of rare-disease approvals.

- Listening carefully to patients and organizations that represent them to learn more about how they perceive benefits, risks, and unmet needs.
- When appropriate, encouraging the use of "adaptive" trial designs that allow design modifications as information about drug response accumulates, leading to more efficient studies.
- When appropriate, encouraging "enrichment" strategies to enroll patients more likely to respond to drugs under study, thereby reducing trial size and helping to direct drugs to patients who will benefit from them.
- Allowing the use of a wide range of study designs, including single-arm studies, when patient populations are extremely small, as in some orphan diseases, and the natural history of the disease is well-characterized and the drug's beneficial effects are large.
- Collaborating with scientists in industry and academia on biomarker development; and
- Identifying opportunities for streamlining regulatory processes.

I also want to point out some hurdles to efficient drug development, which require support for outside research and collaboration with other key stakeholders, including the National Institutes of Health (NIH), industry, and patient groups, to translate discoveries into treatments. These include basic research into a range of important diseases, such as Alzheimer's disease, whose causes are still poorly understood and for which drug development has proven particularly challenging.

Flexible Trial Design

People with serious or life-threatening illnesses, particularly those who lack good alternatives, have told us repeatedly that they are willing to accept greater risks in order to gain access to new approved treatments.

FDA has long taken a flexible, rather than one-size-fits-all, approach to clinical trial design, urging that trials be designed as efficiently as possible to determine whether new drugs under investigation are safe and effective for their intended use, taking into account the severity and rarity of the disease and unmet need. A new study published in the *Journal of the American Medical Association* found that more than a third of 188 novel therapeutic drugs for 208 indications (uses) between 2005 and 2012 were approved on the basis of a single pivotal clinical trial, and in many cases, trials involved relatively small groups of patients for shorter durations.[1] All of this is possible, of course, when the drugs demonstrate strong beneficial effects.

Over 60 percent of drugs for rare diseases are approved on the basis of a single pivotal study, often because the cause of the disease is well understood and the pivotal study is supported by evidence of pertinent pharmacological effects, and because the natural history of untreated disease for many orphan conditions is well-characterized. All patients in such trials are given the new treatment, and the results are compared with the well-characterized natural history.[2] Thus, for example, last year, FDA approved Imbruvica (ibrutinib), a treatment for mantle cell lymphoma, based on an "open-label, single-arm trial," which means that every patient received the treatment and the trial was unblinded; i.e., both patients and researchers knew they were receiving the orphan drug under study. The results were compared to how well the 111 participating patients had responded to previous treatment for their disease. These designs are

[1] Downing NS, Aminawung JA, Shah ND, Krumholz HM, Ross JS. Clinical Trial Evidence Supporting FDA Approval of Novel Therapeutic Agents, 2005-2012. *JAMA*, 2014; 311(4): 368-377.
[2] Sasinowski FJ. Quantum of effectiveness evidence in FDA's approval of orphan drugs. Drug Information J. 2012; 46:238-63.

appropriate where there are objective responses (tumor shrinkage and recurrence, survival) where observational bias is limited, and where the natural history is clearly different from what treated patients experienced (tumors do not shrink spontaneously; survival is greatly increased).

In some cases, of course, small trials will not do the job. Some trials require large numbers of patients to demonstrate drug effects. This is often the case in studies of cardiovascular disease, where study endpoints, such as heart attack or stroke, while important, are not common.

Adaptive Trial Designs

FDA is also actively involved in developing adaptive trial designs, including designs with Bayesian adaptations based on interim assessments of biomarkers. Using this approach we try to find ways to adapt a clinical trial to the circumstances of the specific questions being asked in a way that is as efficient as possible but still gives us confidence in the results. The goal of these designs is to reduce trial duration and trial size. Importantly, these adaptations are performed with close attention to statistical rigor.

FDA is also conducting an internal research project to evaluate the amount and type of safety data required for new indications for cancer drugs. The goal is to identify ways to reduce the burden on sponsors, when submitting supplemental applications as well as regulatory review time, while ensuring patient safety. This research will be completed in November 2014.

Clinical Trial Enrichment

You also expressed interest in new tools to lower the cost of clinical trials. FDA issued guidance in December 2012 that explained how those developing drugs can use potentially powerful

strategies to demonstrate a drug's effectiveness using clinical trial data.[3] Appropriate use of what we call clinical trial enrichment strategies could result in smaller studies, shortened drug development times, and lower development costs.

Working Closely with Drug Sponsors

As part of goals within the prescription drug user fee agreements included in the Food and Drug Administration Safety and Innovation Act (FDASIA), FDA works closely with sponsors of new drugs to design a development and review pathway for each drug that best reflects the disease and patients it is intended to treat, the drug itself, and other treatment options. Sponsors who avail themselves of the opportunity to meet with FDA early in development have substantially reduced the time from the start of human testing—when FDA first becomes involved—until marketing approval. For the 181 new drugs approved from 2008 - 2013 (for which a clinical development time could be calculated), the sponsors of the 67 applications who met with FDA before submitting their Investigational New Drug (IND) applications had a median development time of only 6.6 years, compared to 8.0 years for applications for which such a meeting did not occur (a mean reduction of 1.4 years). The median drug development time for applications for which a meeting with FDA was held at the end of the Phase 1 (EOP1) milestone was 1.1 years shorter than for applications for which an EOP1 meeting did not take place. For orphan drugs, drug development was a median of 2.1 years shorter.

In April 2014, we approved Zykadia (ceritinib), a new drug for patients with a certain type of late stage, non-small-cell lung cancer (NSCLC). It is one of four targeted therapies for lung cancer that have been approved since 2011—therapies that are the result of a new and forward-thinking approach to understanding the disease and its causes. FDA granted breakthrough

[3] Guidance for Industry: Enrichment Strategies for Clinical Trials to Support Approval of Human Drugs and Biological Products.

designation to this drug, streamlining the development and review process with an "all hands on deck" approach. In fact, due to the enhanced understanding of how drugs like Zykadia work (by blocking anaplastic lymphoma kinase (ALK) and inhibiting the growth of lung cancer) and the frequent interactions between FDA and the drug's sponsor, it took less than four years—versus the roughly 10 years it used to take—from the initial study of the drug to FDA approval. This approval process exemplifies the strength of the collaborative process between FDA, industry, health advocacy organizations, and other stakeholders, while ensuring that FDA maintains its independent role in ensuring safety and efficiency of the product. And it illustrates the dedication and enthusiasm of FDA reviewers who carefully, but quickly, analyzed complex study results to allow for earlier approval and patient access to this new drug.

Surrogate Endpoints

The Accelerated Approval pathway allows for the use of surrogate endpoints, reasonably likely to predict a clinical benefit to get certain drugs for serious conditions more rapidly to patients. But many observers are not aware that FDA has also commonly used well-established surrogate endpoints for traditional approvals. Indeed, for the 94 new drugs approved by FDA between 2010 and 2012, 45 percent were approved on the basis of a surrogate endpoint. Once a surrogate is well established to predict clinical benefit, it can be used in traditional approvals and accelerated approval is no longer required. This saves time and the cost of the follow-up, confirmatory, clinical trial data collection required under accelerated approval.

For example, FDA regularly relies on a surrogate endpoint for approval of new therapies for diabetes, including several major new therapies in recent years, greatly expanding the physician's armamentarium for treating this disease. All were based on a well-established

December 2012 http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM332181.pdf.

laboratory test (the HbA1C test, a measurement of hemoglobin with attached sugar in the blood that reflects the extent and persistence of elevated blood sugar) as a surrogate for clinical improvement, rather than requiring the sponsor to conduct decades-long studies to demonstrate an effect on long-term health. Moreover, it is critical that these endpoints are supported by sound science. As science evolves, we may discover that some of these endpoints are not accurate predictors and such discoveries are likewise critical.

Biomarkers and Targeted Drug Development

One of the most promising areas for advances in drug development is in predicting which patient populations will best respond to a new drug therapy, thereby enabling drug development to focus on the "subpopulation" most likely to benefit. This "targeted" approach is believed to be one of the keys to lowering drug development costs and expediting approval, at least for the population for which the drug can be quickly and effectively identified as a successful therapy. For example, within the last decade, the high-quality data submitted in applications and our collective understanding of the genetic and molecular underpinnings of lung cancer have enabled us to move from classifying the disease by what can be seen under a microscope to looking at the patient's molecular profile and classifying and treating the cancer by specific subtype. Scientists can now identify "driver oncogenes," which cause a normal cell to become cancerous and promote the growth of a patient's tumor. They can develop targeted therapies aimed at shutting down these aberrant genes and pathways—an example of an approach called personalized medicine. A targeted treatment is directed to the patients who will respond, while sparing others the potential for toxicity and delay in receiving other potentially effective treatments.

In the early 1990s, only 5 percent of FDA's new drug approvals were for targeted therapies. Twenty years later, that number had risen to a quarter of new approvals, and in 2013, 45 percent

of FDA's approvals were for targeted therapies. Examples include several recently approved and important treatments for cancer, such as Mekinist, Tafinlar, Imbruvica, and Zykadia. The use of targeted therapies is expanding rapidly. Indeed, approximately 80 percent of new compounds FDA has designated as "breakthrough" therapies are targeted. Furthermore, accumulating evidence reveals that total development times for targeted therapies are up to two years less than for drugs aimed at broader treatment populations.

It is critical to understand, however, that our ability to use genomic data or to identify useful biomarkers depends on how well scientists understand the molecular and genetic causes and pathways of disease. The level of their understanding, in turn, depends on the strength of the foundational research into given diseases.

In some disease areas, we have made tremendous progress in our understanding of the causes of the disease and interventions that can treat or cure it. For example, decades of research on cancer and HIV/AIDS have given us critical insights into the pathways through which these (and related) diseases can be attacked, leading to discovery of biomarkers that predict disease progression as well as drug activity. Predicting likely progression allows selection of patients who will have many or earlier study endpoints, and thus use of fewer patients; predicting likelihood of response to treatment also allows for smaller studies and directs treatment to those who can benefit. FDA has been an active partner in developing and bringing therapies to market in these areas. This has resulted in important breakthroughs, rapid drug development, and a robust pipeline of new therapies.

However, the scientific community still lacks a complete understanding of the biology underlying disease such as Alzheimer's disease. As a result, many rational and well-intentioned

approaches to develop disease biomarkers or surrogates for clinical endpoints have encountered unanticipated obstacles. While progress has been made on developing biomarkers for disease progression, these obstacles have made the development of biomarkers to assess drug activity difficult, and the treatment options for Alzheimer's disease remain extremely limited.

Scientific understanding of diseases varies widely and is likely to remain the most important limiting factor for developing targeted therapies and personalized medicine. When we do not understand the disease pathways, biomarkers appearing to be linked to disease progression often fail because they are not, in fact, in the causal pathway for the disease. The surprising Phase III failure of torcetrapib—Pfizer's would-be blockbuster to prevent heart attacks by raising HDL (the "good" cholesterol)—illustrates the risks of relying on an unvalidated, albeit seemingly reasonable, biomarker that turns out not to predict treatment outcomes.

Master Protocols and Clinical Trial Networks

One of the most serious limiting factors in drug development is the time and expenses required to design and conduct the Phase 3 clinical trials needed to demonstrate drug safety and effectiveness. As the President's Council of Advisors on Science and Technology (PCAST) observed in their 2012 report on drug innovation:

> *Clinical trials constitute the largest single component of the R&D budget of the biopharmaceutical industry, at approximately $31.3 billion, representing nearly 40 percent of the R&D budget of major companies. Unfortunately, there is broad agreement that our current clinical trials system is inefficient. Currently, each clinical trial to test a new drug candidate is typically organized de novo, requiring substantial effort, cost, and time. . . . .Navigating all of these requirements is challenging even for large pharmaceutical companies, and can be daunting for small biotechnology firms. Even in*

the best cases, the complexities add considerable time to trials—subtracting time from a successful drug's eventual time on the market without competition.[4]

Drug development need not necessarily be done in this way. There are often much better alternatives to reinventing the wheel every time a new clinical trial begins, including, where appropriate, the development of clinical trial networks and master protocols. The recently initiated Lung Cancer Master Protocol (Lung-MAP) is an excellent example of a new, less-costly paradigm for developing drugs, one that benefits both drug companies and patients. A master protocol creates a single clinical trial infrastructure that can test many drugs at the same time. Development of such a protocol requires close coordination with CDER reviewers, scientists in academia, NIH, and possibly other organizations, and the protocols themselves typically go through a peer review process. In the case of Lung-MAP, patients are assigned to one of five different drugs being simultaneously tested, based in part on their genetic profiles and their likelihood of responding to the study drug, and additional drugs can be added, while others are dropped, over time. The goal is to increase efficiencies through the use of a common biomarker screening platform, a common algorithm for assigning patients to multiple protocols ongoing concurrently, and the potential for sharing control patients across protocols for a given biomarker profile, all of which are possible because of the infrastructure established for the master protocol. FDA is highly supportive of master protocols.

Public-Private Partnerships and Stakeholder Engagement

Just like the September 2012 "Report on Propelling Innovation in Drug Discovery, Development, and Evaluation," from PCAST, FDA believes that bridging the gap between drug discovery and development can only be achieved through creative collaborations. Public-private partnerships enable stakeholders to leverage expertise and resources for the conduct of mutually

[4] "Report to the President on Propelling Innovation in Drug Discovery, Development and Evaluation," President's Council of

beneficial research activities in the pre-competitive domain. And indeed, CDER is involved in at least 22 unique science-driven, public-private partnerships that promote development of research tools, platforms, clinical databases and predictive models to advance knowledge of disease and safety profiles of drugs. The recent approval of Zykadia, as mentioned earlier, for patients with a certain type of late-stage (metastatic) non-small-cell lung cancer, benefited from FDA's collaborative efforts with industry, health advocacy organizations, and others to identify the molecular underpinnings of cancer that would make it possible to classify and treat cancer by specific subtype.

FDA is also a partner in the Clinical Trials Transformation Initiative (CTTI)—a public-private partnership whose mission is to identify and promote practices that will increase the quality and efficiency of clinical trials. CTTI now comprises more than 60 organizations from across the clinical trial enterprise. Members include representatives of government agencies, industry representatives (pharmaceutical, biotech, device, and clinical research organizations), patient advocacy groups, professional societies, investigator groups, academic institutions, and other interested parties. CTTI is actively pursuing many new initiatives to reduce the time and cost of clinical trial programs, such as development of streamlined protocols and data collection recommendations for clinical trials of hospital-acquired bacterial pneumonia. Another example of a CTTI project with the potential to affect the clinical trial enterprise is its collaboration with FDA's Sentinel Initiative (Sentinel is FDA's active surveillance system that uses pre-existing electronic health care data from 18 data partners, capturing information on more than 150 million patient lives). A working group comprised of CTTI and Sentinel investigators is elucidating current barriers and identifying appropriate processes for the use of such electronic health care data to facilitate the conduct of clinical trials.

Advisors on Science and Technology, The White House, Washington, D.C., September, 2012, p. 20

FDA also is partnering closely with many public-private initiatives, advocacy groups, and consortia. As one example, the Agency is a member of the recently announced NIH-led Accelerating Medicines Partnership (AMP), which is attempting to identify biological targets most likely to respond to new therapies and uncover biomarkers that may help predict clinical benefit in drug development in Alzhemier's disease, among others. FDA is working closely with the NIH's National Center for Advancing Translational Sciences (NCATS) to accelerate research on rare disease through NCATS' Innovative Therapeutics for Rare and Neglected Diseases program. We are also working with the Coalition Against Major Diseases (CAMD) to identify new tools and methods that can be applied to increase the efficiency of the development process of new treatments for Alzheimer's and Parkinson's diseases. The Agency's Drug Development Tool Qualification process also provides a mechanism to evaluate and qualify novel drug development tools (biomarkers, clinical outcome assessments, animal models under the Animal Rule) for an appropriate context of use. Recently, we deemed a "fit-for-purposed" drug development tool for Alzheimer's disease that CAMD has developed. These represent just a few of our many collaborations. See more at *http://blogs.fda.gov/fdavoice/index.php/page/5/#sthash.bWxzFv0M.dpuf*.

Lastly, FDA is engaged with TransCelerate Biopharma, Inc. (TCB), a non-profit organization established to facilitate pre-competitive collaboration among biopharma companies with the goal of accelerating the development of new medicines by identifying ways to make the clinical trial process more efficient. FDA is engaged in TCB's efforts to improve the conduct and efficiency of clinical trial sponsor oversight of clinical sites, clinical site qualification, and development of a common protocol template.

Regulatory Science

The 21st century has seen rapid advances in biomedical research. New cutting-edge technologies have led to thousands of new drug candidates including: the sequencing of the human genome; combinatorial chemistry, a new method of chemical synthesis that makes it possible to prepare thousands of compounds in a single process; biosynthesis, which enables scientists to synthesize complex chemicals in living cells; and high throughput screening, which allows researchers to quickly conduct millions of genetic, chemical, or pharmacological tests. In addition, cutting-edge electronics and materials science have the power to transform medical devices, and research on nanotechnology-based materials will provide a better understanding of the safety of the use of nanomaterials in over-the-counter drugs. FDA's regulatory science research agenda is critical to help translate new technologies and basic science discoveries into safe and effective real-world diagnostics, treatments, and cures and to reduce the time, complexity, and cost of product development.

There can be no doubt that further modernizing and streamlining the science of how products are developed and evaluated is a complex challenge requiring new models and approaches that stress cross-sector and cross-disciplinary research. Advancing regulatory science has been one of FDA Commissioner Hamburg's key initiatives. New biomedical innovations may be enhanced by partnerships such as the Biomarkers Consortium, which promotes the development and qualification (or regulatory acceptance) of biomarkers (of which surrogate endpoints are a subset), using new and existing technologies.

Consideration of Additional Approval Pathways

PCAST also recommended the creation of a drug approval pathway under which sponsors could propose, early in the development process, to study a new drug for initial approval that would be

reserved for use in a specific subgroup of patients that would allow a narrower development program than required for traditional approvals. While FDA has existing authority to approve products for subpopulations, in practice, drug development protocols generally evaluate drugs in a broader population, resulting in larger, lengthier trials. PCAST notes that a more clearly defined Special Medical Use or Limited Population pathway could encourage novel development programs for limited, well-defined subpopulations and complement FDA's existing efforts to get drugs to small, in-need populations faster. Such a pathway needs to consider the implications of market entry of a product for limited use. For example, an important consideration is how to encourage appropriate prescribing with the approved limited use for a specific population. Legislation focused on a pathway for drugs for serious or life-threatening bacterial and fungal infections in patients with unmet medical need—a particular area of unmet medical need highlighted in the PCAST report—has been introduced to address this issue, and we welcome the opportunity for continued discussions with stakeholders.

Having multiple approval pathways is important because they give drug sponsors options to help get therapies to patients needing them faster. Different pathways may also prove better for different products. In June 2013, less than one year after the enactment of the Food and Drug Administration Safety and Innovation Act (FDASIA), FDA issued draft guidance to bring more clarity to the accelerated approval program and other expedited programs for drugs and biologics that target serious conditions, so as to further encourage the use of these programs, *http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf*. That guidance was finalized in May 2014. Although FDA has been able to speed the availability of drugs and biologics for serious conditions that provide a meaningful therapeutic benefit to patients over existing treatments under the accelerated approval program since 1992, FDASIA clarified that authority in legislation and emphasized FDA's ability to

consider epidemiologic, pharmacologic, or other evidence developed using biomarkers or other scientific methods or tools in determining whether an endpoint can support accelerated approval.

Accelerated approval for drugs and biologics has been used primarily in settings in which the disease course is long and an extended period of time would be required to measure the intended clinical benefit of a drug or vaccine.

Further, the Agency oversees other programs that expedite the availability of new drugs for patients with serious conditions. For example, as part of FDASIA in 2012, Congress gave FDA new authority to designate drugs as breakthrough therapies. Breakthrough therapy designation is a program designed to expedite the development and review of drugs that are intended to treat a serious condition and which preliminary clinical evidence indicates may demonstrate substantial improvement over available therapy on one or more clinically significant endpoints. The breakthrough therapy program has already been well-utilized. As of June 13, 2014, CDER has received 164 requests for breakthrough therapy designation. CDER has granted breakthrough therapy designations for 48 of those requests, denied 83 such requests, and approved six breakthrough therapy drugs. CBER has had 31 breakthrough therapy designation requests, four of which it has granted and 26 of which it has denied.

FDA Efforts on Patient Engagement

In accordance with our commitments in the Prescription Drug User Fee Act of 2012 (PDUFA V), FDA has initiated the Patient-Focused Drug Development (PFDD) program. The objective of this five-year effort is to more systematically obtain the patient's perspective on a disease and its impact on patients' daily lives, the types of treatment benefit that matter most to patients, and the adequacy of available therapies for the disease. As part of this commitment, FDA is holding

at least 20 public meetings over the course of PDUFA V; each of which will focus on a specific disease area. We have already held patient meetings on several major diseases.

After conducting a public process to nominate disease areas for Fiscal Years 2013-2015, FDA held the first PFDD meeting on April 25, 2013. This meeting focused on chronic fatigue syndrome (CFS) and myalgic encephalomyelitis (ME), sometimes called CFS-ME, a debilitating disease for which there are currently no FDA-approved treatments.

Here, we heard directly from patients, patient advocates, and caretakers about the symptoms that matter most to them, the impact the disease has on patients' daily lives, and the patient experience with currently available treatments. FDA staff, including members of FDA's Division of Pulmonary, Allergy, and Rheumatology Products, listened carefully to the personal accounts of this devastating condition.

After the meeting, we released a report titled *The Voice of the Patient: Chronic Fatigue Syndrome and Myalgic Encephalomyeliti*, a detailed summary of the meeting. In this report we documented, in the patients' own words, what disease impacts and treatment approaches mattered most to them. This summary included patient testimony at the meeting, perspectives shared in 230 docket comments, as well as unique views provided those joining the meeting via webcast. Moreover, on March 11, 2014, FDA also released draft guidance (found at *http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM388568.pdf)* for industry entitled "*Chronic Fatigue Syndrome/Myalgic Encephalomyelitis:*

Developing Drug Products for Treatment." The purpose of the guidance is to assist sponsors in developing drug products for the treatment of CFS-ME.

The PFDD reports, such as the one developed after the CFS-ME meeting, will serve an important function in communicating to both FDA review staff and the regulated industry what improvements patients would most like to see in their daily lives. These reports will strengthen the structured framework for benefit-risk assessment in the new drug process, which FDASIA (Sec. 905) requires and which is currently in development, that will be used to help communicate patients' values to the FDA review team during product review. FDA believes that the long-term impact of the PFDD program will be a better, more informed understanding of how the entire drug development community might find ways to develop new treatments for diseases.

Soon after the CFS and ME meeting, in June 2013, we conducted similar meetings on HIV and lung cancer, and the summary reports are now available on our website. The reports for our recent meetings on narcolepsy and sickle cell disease will be posted soon. We have also held meetings on fibromyalgia, pulmonary arterial hypertension, and metabolism.

By the end of FY 2015, we plan to have conducted at least 16 PFDD meetings to hear from patients suffering from and living with a wide range of conditions. These are currently identified on our webpage: *http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm347317.htm.* For the remaining two years in PDUFA V, we will conduct another public process to identify the diseases that will be addressed during that time.

We are gratified by the enthusiastic response within the patient community to PFDD, and we look forward to continued input from these meetings—and to the long-term benefit they can offer for drug development in important therapeutic areas.

In addition to these efforts, CDER established the Professional Affairs and Stakeholder Engagement program that will serve as a focal point and enhance two-way communications and collaboration with health professional organizations and patient advocacy and consumer groups about drug products.

CONCLUSION

FDA welcomes the opportunity to constructively engage and work with Congress and stakeholders in an effort to improve review efficiency and effectiveness while maintaining the high safety and efficacy standards for which FDA approval has become the global "gold standard."

Thank you for the opportunity to testify today. I am happy to answer any questions.