FasterCures
The Center for Accelerating Medical Solutions

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Division of Dockets Management (HFA-305)
Food and Drug Administration (FDA)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Submitter: Greg Simon
Organization: *FasterCures / The Center for Accelerating Medical Solutions*

Re: Docket No. 2007N-0005 Notice of Public Meeting Prescription Drug User Fee Act (PDUFA)

Dear Madam/Sir:

FasterCures welcomes the opportunity to offer comment on the proposed recommendations for the reauthorization of PDUFA IV and on efforts at the FDA to enhance its drug safety activities. *FasterCures* is independent and non-partisan. We do not accept funding from companies that develop pharmaceuticals, biotechnology drugs, or therapeutic medical devices. Our primary mission is to improve the lives of patients by improving the research environment, research resources, and research organizations.

We would like to begin by thanking the dedicated public servants at the FDA for the work they do each day on behalf of the American public. The FDA's process through which medical therapies are approved for marketing in the United States is central to the translation of ideas into medical breakthroughs. However, we believe that the drug safety system in the American biomedical research enterprise needs improvement. We believe there must be a balance in getting patients access to new medications quickly and identifying adverse events and communicating them clearly, so that patients and physicians can make more informed treatment decisions.

At *FasterCures*, we believe in a broad set of principles that should guide any effort to strengthen the FDA so that the agency can continue to play a vital role in advancing 21st Century cures.

These principles are as follows:

1. The FDA needs to be able to assess a drug's impact post-approval, weigh both benefits and risks and take appropriate action to inform and protect the public;
2. To do that the FDA needs to convey any post-marketing information gathered to the public and to the medical community in a timely and efficient manner;

3. To do those things the FDA needs increased appropriations from Congress and should be able to use industry user fees for post-approval activities without limits on timeframe; and
4. And for all of this to work, the FDA needs a better understanding of how to communicate its scientific findings to the public to make them better informed participants in our health care system.

PDUFA IV AGREEMENT

We encourage the timely reauthorization of PDUFA IV. PDUFA has achieved the goal of getting needed resources to the FDA and thereby increasing patient access to new drugs and biologics. It has enabled the agency to virtually double the staff dedicated to reviewing new drug applications since 1992.

In an ideal world, the agency would not have to rely on industry to pay such fees and would be able to access new appropriated dollars. We believe it is important to note that continued reliance and expansion of user fees to cover new FDA initiatives and requirements will continue to give ammunition to skeptics who question the agency's independence.

We call on Congress to increase FDA appropriations. We are a member of both the FDA Alliance (Margaret Anderson, *FasterCures* Chief Operating Officer is on the FDA Alliance Board) and the Coalition for a Stronger FDA, two groups with a diverse array of members dedicated to increasing the resources FDA has to achieve its ever-expanding mission. There is simply no defending the fact that the FDA budget for providing 300 million Americans a safe food supply and safe and effective medical treatments is the same in real dollars as it was in 1996. The Superintendent of Schools for Montgomery County, Maryland has a budget equal to that of the FDA. This speaks well of Montgomery County's commitment to education but calls in question our national commitment to food and drug safety and the approval of new cures for diseases.

While PDUFA IV offers significant new resources that will help fund important new initiatives, we know that each year, the FDA receives minimal new appropriated dollars. Yet its costs increase, missions evolve, the scope of science expands, and inflation erodes the budget. The budget is holding the FDA back and preventing the agency from maximizing the benefits of these historical advances in science for the American public. The FDA staff are dedicated public servants who are ready to tackle these problems, yet we believe they are being held back by the overall lack of adequate resources.

Enhancing Premarket Review. We support the proposed enhancements to expedite drug development, particularly in the areas of clinical trial design. Clinical trials play a key role in scientific advances. Yet recruiting patients into clinical trials, and keeping them in trials once they have signed on, is a huge challenge that many in the industry view as daunting—and perhaps incurable. If the FDA can help the industry streamline its efforts on useful and productive trials, everyone benefits.

As part of our *Patients Helping Doctors (PHD) Program* which highlights and promotes the role of patients in the medical research process, *FasterCures* convened a conference in September 2006 titled

"Best Practices and Promising Approaches in Clinical Trial Recruitment and Retention" to offer solutions to these challenges. Leading up the conference, we conducted an environmental scan to assess activity in the field, in-depth interviews with experts, and in-depth interviews and focus groups with community physicians. We will release a report summarizing our work in this area in April 2007 and it will be available on our website at www.fastercures.org.

FDA guidance on topics such as adaptive and enriched trial design is needed. Additionally, we believe that given current trends toward personalized medicine and smaller markets, the FDA should bring disease researchers together to achieve consensus regarding which biomarkers and surrogate endpoints are the most promising to pursue.

We believe that these areas will not only positively affect the time and cost of clinical trials but also will ultimately benefit patients. Given the demands that clinical trial participation imposes on patients, not to mention the difficulty and expense of finding enough patients to enroll in clinical trials, and the ultimate impact this has on slowing down research, particular focus should be given to maximizing the return on every patient's participation in a clinical trial.

Additionally, we know that traditionally nonprofit disease foundations have focused on funding basic research and stayed away from issues related to clinical trials and drug development. More and more however, as the gap between basic discovery and later stage development widens, such organizations are focusing on efforts to fill that gap. Although there has been some success in this regard, most groups are operating with little or no information on how to pursue translational research effectively. Developing an outreach effort to provide groups with better access to information and expertise relevant to the critical path process across disease types is one way that the FDA could enhance ongoing foundation efforts in Critical Path initiatives. If even a small portion of the $3 Billion currently invested by the nonprofit sector in biomedical research efforts were strategically directed into targeted Critical Path initiatives, this could significantly accelerate therapeutic development efforts.

Within each patient lies the key to a cure; yet a very low percentage of patients are actively engaged in supporting the research process. As the FDA moves forward with all of these efforts to streamline and improve the clinical trials process, we would welcome the opportunity to work with the agency to both expand patient participation and ensure that this precious resource is used as effectively and efficiently as possible.

Improving Information Technology (IT) Infrastructure. We applaud the FDA's efforts to speed progress toward a fully automated human drug review by building an FDA Electronic Gateway and certainly concur that this will increase the efficiency of the review process. While we recognize the enormity of the task in both financial and human resources, it would be prudent to move this along even more quickly if resources become available. (See additional comments below under post-marketing surveillance and access to data.)

MODERNIZING AND TRANSFORMING THE POSTMARKET DRUG SAFETY SYSTEM

We support efforts at FDA to enhance the drug safety program and concur that the language that limits the spending of user fees outside the specified timeframe should be changed, since safety issues can arise even after eight or more years. All drugs present risks, but without taking those risks we cannot develop cures for diseases. Our goal should be to facilitate the identification and management of those risks through collaboration among the government, the drug manufacturers, patients, and physicians. Through such collaboration we can avoid time-consuming confrontations and conflict, expedite the flow of drug safety information, and move more quickly to protect patients from harm.

The FDA needs to heed the concerns of the Institute of Medicine (IOM) Committee with a thoughtful plan that balances safety with efficacy. As the IOM pointed out in the *Future of Drug Safety—Promoting the Health of the Public* report, it is impossible to think about safety independent of efficacy, and the two must be considered together throughout the lifecycle of a drug. The report went on to cite an imbalance in the regulatory attention and resources available before and after a drug's approval. The challenge for the FDA as it moves forward is how to improve the drug safety side of the equation, without causing unnecessary and unwanted delays or slowdowns on the approval side. Like it or not, the Vioxx withdrawal and other drug safety concerns have heightened the public's concern about FDA's performance.

In order for the FDA to continue as the "gold standard" for consumer protection and regulatory science, the agency will need to address the credibility issues both in the public and in Congress. We support the FDA's plan to better integrate the pre-and post-market staff and ultimately improve communication and coordination. By addressing drug safety as part of the lifecycle of drug development, significant advances in credibility can be re-established and patients can benefit. We look forward to learning more specifics about new scientific approaches and efforts to determine the best way to maximize the benefits associated with adverse event reporting.

Patients cannot wait for treatments and therapies, and research has shown that someone's risk-benefit threshold is dependent on their own situation. If you are facing a life-threatening disease without many therapeutic options, you want the FDA to move things through the process as quickly as is possible. We support FDA efforts to improve the benefit-risk communication dynamic between providers and patients so that better health decisions can be made. The FDA needs to communicate with the patient advocacy community as this drug safety plan is created, so that any concerns about a slowdown in approvals can be addressed and remedied.

Post-marketing surveillance and access to data. We understand that a key challenge facing the FDA is how to weigh and assess the adverse event data reported each year. We support expanded access to other population databases at agencies such as the Veterans Health Administration and the Centers for Medicare and Medicaid Services which would help the FDA assess the increase in the number of serious adverse event reports that has occurred in the past years. Clearly the IT infrastructure at FDA, including the AERS system, is inadequate.

Since its inception, *FasterCures* has focused on making the benefits of 21st-century IT as available to medical researchers and patients as they are to stockbrokers and travel agents. We produced a white

paper *Think Research: Using Electronic Medical Records to Bridge Patient Care and Research* that examined the challenges of doing research using electronic health records (EHRs) and catalogued a number of the pioneers and innovators in this effort.

In May 2006, we hosted a forum on "Ensuring the Inclusion of Clinical Research in the Nationwide Health Information Network" to begin to distill exactly what are the best cases for research use of the NHIN. There was agreement that the ability to use the NHIN to conduct post-marketing surveillance (Phase 4) studies would provide a beneficial test case for other types of research. It would benefit both the pharmaceutical industry and patients using the products. Certainly the invaluable role that EHRs can play in post-marketing research was evidenced in Kaiser Permanente's use of their database to examine the role of NSAIDs in increased risk of heart attack. Additionally, meeting participants agreed that the infrastructure, policies, and procedures developed to accomplish post-marketing surveillance also could be used as a "stalking horse" for the larger agenda of enabling population-based research across a spectrum of exposures, outcomes, and interventions. Along with using EHRs to conduct population-based health surveillance, they could also enable the identification of potential subjects for clinical research.

We believe that as the FDA seeks to improve both the IT infrastructure and overall drug safety efforts, there needs to be full coordination and consideration of existing efforts both within government and in the private sector. One barrier to faster cures that cuts across all aspects of the medical research and drug development process is the lack of effective cooperation and coordination among the relevant federal agencies, researchers, research institutions, and industry. Successful large-scale scientific collaborations, such as the Human Genome Project, show how important collaboration is.
The pursuit of these recommended strategies is no small effort and goes well beyond the purview of the FDA. It would require concerted efforts to standardize the capture and storage of data, standardize definitions, protect confidentiality, and create interoperability and the capability to search across records. We look forward to working with the FDA as standards for clinical research and EHRs are developed.

CONCLUSIONS

In closing, *FasterCures* is supportive of the reauthorization of PDUFA IV. To summarize, we believe the following:

1. Congress should make increased appropriations for FDA a top priority.
2. We support the proposed enhancements to expedite premarket review, particularly in the areas of clinical trial design.
3. New FDA guidance on topics such as adaptive and enriched trial design is clearly needed.
4. We support FDA efforts to enhance drug safety efforts, and agree that limits on user fees outside the specified timeframe should be changed.
5. The FDA needs to heed the concerns outlined in the IOM *Future of Drug Safety* report with a thoughtful plan that balances safety with efficacy.
6. In order for the FDA to continue as the "gold standard" for consumer protection and regulatory science, the agency will need to address the credibility issues both in the public and in Congress.

7. We support FDA efforts to improve the benefit-risk communication dynamic between providers and patients so that better health decisions can be made.
8. We support expanded access to other population databases which would help the FDA assess the increase in the number of serious adverse event reports that has occurred in the past years.

All of the efforts in PDUFA IV have the potential to contribute to the goal of saving lives by saving time in making new therapies available for use sooner. We believe this potential will be realized only to the extent that the agency pursues this effort in a collaborative way that enlists all relevant stakeholders in defining problems and developing and implementing solutions.

FasterCures is committed to working with the FDA to realize the goals outlined in PDUFA IV. We would welcome the opportunity to work with the FDA in developing and implementing the steps necessary to overcome the obstacles hindering progress on the critical path to successful drug development. Our mission, to accelerate medical solutions, aligns closely with the new initiatives outlined in PDUFA IV and we look forward to collaborating with the FDA on many of these initiatives in the future.

We thank the FDA for the opportunity to provide comment.

Sincerely,

Gregory C. Simon, JD
President, *FasterCures / The Center for Accelerating Medical Solutions*