



**FDA User Fees 2012: Hearing on Issues Related to Accelerated  
Approval, Medical Gas, Antibiotic Development and Downstream  
Pharmaceutical Supply Chain**

**Testimony Before  
Committee on Energy and Commerce  
Subcommittee on Health  
United States House of Representatives**

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## **FDA User Fees 2012: Hearing on Issues Related to Accelerated Approval, Medical Gas, Antibiotic Development and Downstream Pharmaceutical Supply Chain**

Testimony of Jeff Allen, PhD, Executive Director, Friends of Cancer Research

Good morning, Chairman Pitts, Ranking Member Pallone, and Members of the sub-committee. I am Dr. Jeff Allen, Executive Director of Friends of Cancer Research, a cancer research think tank and advocacy organization based here in Washington. I would like to thank the staff of this committee who have worked very hard in putting together this important hearing. It is an honor to testify before you today and provide our perspective on several vital mechanisms that the U.S. Food and Drug Administration (FDA) uses to get a new drug or biological products to patients.

While compelling progress has been made within the field of oncology, there is much more to be done to alleviate the current cancer epidemic and profound suffering it causes. It is estimated that, in 2012, over 1.6 million Americans will be diagnosed with some form of cancer. As a result, our healthcare system will be strained an additional \$226 billion.<sup>1</sup> Yet tragically, cancer will claim the lives of 571,950 mothers, fathers, grandparents, sisters, brothers, and friends, this year. This, Mr. Chairman, is roughly the equivalent of every citizen in your home county of Lancaster, Pennsylvania.<sup>2</sup>

With such startling statistics and profound toll on human health, improved ways to combat cancer are needed as quickly as possible. Unfortunately, advancements in basic science do not always translate into new treatment as rapidly as many would desire. In fact, recent estimates indicate that it could take upwards of 12 years and over \$1 billion to develop a new cancer drug.<sup>3</sup> While there are many factors that make development of new drugs complex and increasingly expensive, assessments of the process often focus on the U.S. Food and Drug Administration (FDA).

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<sup>1</sup> The American Cancer Society: <http://www.cancer.org/Cancer/CancerBasics/economic-impact-of-cancer> Accessed 3/1/12

<sup>2</sup> <http://www.cancer.org/acs/groups/content/@epidemiologysurveillance/documents/document/acspc-029819.pdf> Accessed 3/1/12

<sup>3</sup> Adams, C. P. and Brantner, V. V. Health Economics, 19 (2010), 130–141. doi: 10.1002/hec.1454

Today, I would like to describe some of the current standards and mechanisms employed by the FDA for new drug review and approval, explore how these tools have been used to date, and propose a new tool to ensure that the most promising new medicines reach the market as quickly and safely as possible.

### **Standards to Protect and Promote Health**

The role of the FDA is to protect and promote the health of the American public by ensuring the safety, effectiveness, and security of medical products, devices, food, and cosmetics.<sup>4</sup> The authority and tools to fulfill this responsibility has evolved over time. For example, in 1962 President Kennedy signed the Kefauver-Harris Amendments into law amending the Federal Food, Drug and Cosmetic Act to require that new drugs demonstrate not only their safety but also efficacy in order to be approved for marketing.<sup>5</sup> Without this requirement, American patients would have continued to have been given medicines that actually provided no improvement to their health and gave them false hope. **As this committee seeks to optimize and improve FDA practices in reviewing new treatments, the requirement to demonstrate both safety and efficacy must be upheld.** While the need for new treatments is immense, and the challenges significant, the solution is not to arbitrarily lower this important standard that has been in place for 50 years, saved countless lives, and improved the health of so many Americans.

Thirty years after establishing these requirements, Congress again took an important step to help the FDA's fulfill its role by giving the agency the authority to collect user fees to support the review functions of the agency. The 1992 passage of the Prescription Drug User Fee Act (PDUFA) has provided essential resources to the agency to alleviate a backlog of new drug applications, and support efficient review of applications --ultimately allow Americans access to potentially life-saving new medicine.<sup>6</sup>

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<sup>4</sup> About FDA: <http://www.fda.gov/AboutFDA/Transparency/Basics/ucm192695.htm> Accessed 3/1/12

<sup>5</sup> Kefauver-Harris amendments to the 1938 Food, Drug, and Cosmetic (FD&C) Act [PL 87-781; 76 Stat. 788-89]

<sup>6</sup> ER Berndt, AHB Gottschalk, TJ Philipson. *Industry funding of the FDA: effects of PDUFA on approval times and withdrawal rates*. Nature Reviews Drug Discovery 4:7 (July 2005) 545-554.

The FDA is not without its critics. Recently, the FDA has been portrayed as slow and inefficient compared to other countries. Some critics have anecdotally indicated that the pathway to market approval for new medicines is more collaborative, consistent, and transparent in Europe compared to the U.S. This criticism is particularly concerning in the field of cancer, where severely ill patients have few effective treatment options. In order to explore such claims, Friends of Cancer Research conducted a study published in *Health Affairs* last summer that revealed the FDA is actually approving anti-cancer drugs in a more timely fashion than its overseas counterpart, the European Medicines Agency (EMA).<sup>7</sup> In fact, since 2003 to date, FDA has approved 42 new cancer medicines and EMA has approved 32. Of the 28 common approvals, all 28 were available to U.S patients first.

The intent of this research is not to conclude that one regulatory agency is approaching drug review in the best possible manner and the other is not. It is simply to provide reliable information about current trends in oncology drug review and is an example of the positive impact of the PDUFA program. In order to continue this efficient review trend, **Congress should ensure the swift passage of the PDUFA V reauthorization.**

### **Drug Review Authorities of the Food and Drug Administration**

It should be noted that the review period prior to approval is only one component, and a relatively short one, of a multi-step process to develop new medicine. In acknowledgement of intense public health need, and due in part to new scientific methods reasonably likely to predict clinical benefit, regulations were developed to establish the Accelerated Approval mechanism for the FDA. These regulations allow for the approval of new drugs that show improvement over existing therapies to treat serious and life-threatening illnesses based upon the measure of a surrogate endpoint.<sup>8,9</sup> Such approvals include the requirement for additional studies to confirm the benefit predicted by the surrogate endpoint positively

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<sup>7</sup> Roberts S, Allen J, Sigal E. *Despite Criticism of the FDA Review Process, New Cancer Drugs Reach Patients Sooner in the United States than in Europe.* Health Affairs 30:7 (July 2011) 1375-81.

<sup>8</sup> 21 Code of Federal Regulations, Part 314.510

<sup>9</sup> 21 Code of Federal Regulations, Part 601.41

measured in the initial trials. Accelerated Approval has shown to be an important tool used by the FDA to uphold the rigorous scientific standards while facilitating access to life-saving drugs as quickly as possible. In oncology, for example, accelerated approval has been used in over a third of new cancer drug approvals since 1999 (18/53).<sup>10</sup>

When examining the annual trends of the recent accelerated approvals, it is noted that since 2007, the empirical number and percent of oncology drugs approved through this mechanism are less than in the period from 1999-2006, despite the overall number of new cancer drugs remaining relatively similar.

The reasons for this are not fully known, and may be reflective of a variety of issues relating to the sponsors as well as the FDA.

In order to optimize this tool as a means to provide rapid access, while upholding the essential standards of FDA, **Congress should enhance Accelerated Approval to ensure that it is applied consistently, efficiently, and effectively across all therapeutic areas.** This is not to suggest in any way that the previously described standards of safety and efficacy should be adjusted or compromised, but rather to examine additional opportunities in which Accelerated Approval is the optimal approach to promote patient health based up a demonstrated improvement to a clinical endpoint.

Another mechanism that was created in the original PDUFA is Priority Review. Drugs applications that are granted Priority Review have a goal application review time that is four months shorter than the standard review goal time. For new cancer drugs since 1999, Priority Review has been granted in the vast majority of cases (77%, 41/53).<sup>10</sup> Of these Priority Review drugs the reduced review time goal has been met 56% of the time (23/41).

In 1997, the Food and Drug Administration Modernization Act (FDAMA) was passed and again amended Federal Food Drug and Cosmetic Act to include a new designation of Fast Track Products.<sup>11</sup> This

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<sup>10</sup> Hematology/Oncology (Cancer) Approvals & Safety Notifications:

<http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm> Accessed 3/2/12

<sup>11</sup> Food and Drug Administration Modernization Act of 2007 (P.L. 105-115); Section 506 (21 U.S.C. 356)

mechanism is also designed to make new promising new products available to patients without compromising existing standards of safety and efficacy. The Fast Track program is available to products intended to treat a serious and life-threatening illness, and conveys advantages such as additional meetings with FDA following designation as a Fast Track product, as well as the ability to submit clinical trial data that is part of the new drug application as it is developed, also referred to as "rolling submissions." Fast Track designation has been given to 64% (34/53) of new cancer drugs since 1999.<sup>10</sup>

While each of these three mechanisms have, in many cases, improved new drug review and approvals, there still remains a need to do better. While the FDA is certainly not the cause of this, additional tools could help the agency be part of the solution.

In the late 1980's another health epidemic was occurring in the form of HIV/AIDS. In 1992, due to new advancements in science and the ability to quantify and measure a surrogate endpoint, Congress gave FDA the tool to approve a drug using this scientifically advanced approach. Today, due to on-going advancements in science, the paradigm of new drug development is again beginning to shift. Much like FDA was given additional tools to address the changing scientific landscape in 1992 and 1997, an updated mechanism is needed to respond to the advancement of science today. This will continue to ensure that the most promising, novel drugs are able to reach the patients most in need.

### **Expedited Development of Breakthrough Products**

With the expansion of knowledge about the biological basis of complex disease, new therapies are being developed that are targeted to unique molecular changes known to "drive" a disease. These new, "targeted therapies" allow selection of patients highly likely to respond to the new treatment. For these new treatments (or combinations) that show major clinical activity and significant improvement over currently-available treatment early in the new drug's development, the traditional multi-phase, sequential development approach may not be appropriate, particularly if existing treatment options have limited efficacy.

Currently, there are no clear guidelines to expedite subsequent studies that would generate the needed evidence on safety and effectiveness as efficiently as possible, and minimize the number of patients who would need to be assigned to the standard of care control. Strategies to address this challenge were discussed as part of a multi-stakeholder conference, co-hosted by Friends of Cancer Research and the Engelberg Center for Health Care Reform at Brookings, which brought together leadership from FDA, NCI, industry and advocacy.

In order to address this issue, **Congress should enact legislation that would designate a new compound that shows substantial clinical activity in early phase trials as a Breakthrough Product.** Upon designation, the sponsor, working closely with FDA, would develop trial designs to abbreviate or combine traditional phases of development. This would shorten the pathway to approval and avoid giving larger numbers of patients a potentially harmful or ineffective drug as part of a control arm, while maintaining current safety and efficacy standards.

There are a number of expedited development paths that a breakthrough product could follow. First, for diseases or disease subgroups where the natural history or the underlying disease mechanism is well understood, and the early observed treatment effect appears to have a major effect on disease course, a single arm study can be rapidly expanded at the optimal phase 2 dose to improve confidence in the estimate of the treatment effect, and to evaluate safety. If a major treatment effect continues to be seen, and safety is acceptable, the drug could be approved under either accelerated or traditional approval, depending upon the type of endpoint used in the trials. This may require post-market confirmatory trials in order to minimize the number of patients on a control arm if the only method of post-market confirmation is determined to be a randomized study.

Another scenario would involve initiating a randomized controlled phase 2 trial (with the potential for cross-over available to patients with progressive disease on the standard arm) when a large treatment effect is seen in phase 1, with the intent of generating adequate data on safety and effectiveness for

drug approval at the trial conclusion. Such a trial would be smaller and the initial interim analysis should be performed relatively early in the accrual process. This could be an accelerated or traditional approval depending on the endpoints used.<sup>12</sup>

The establishment of this new designation would help FDA respond to highly innovative new medicine quickly and consistently across the agency, as well as to communicate and encourage drug developers to pursue trial designs that are able to show potential benefit early in development.

## **Conclusion**

Accelerated Approval, Fast Track, and Priority Review mechanisms play an important role in advancing new products and therapies and have shown, over time, to be an extremely important tools to get patients access to new medicine, all while upholding the essential and rigorous standards of the FDA. While this standard should not be compromised, the FDA should be given the ability to respond to cutting-edge science and the most promising new therapies. As part of the discussion regarding the reauthorization of PDUFA V congress should explore the prospect of new and/or enhanced tools to bolster FDA's ability to get drugs to market sooner and safer. An enhanced accelerated approval mechanism and the Breakthrough Product designation will allow FDA to take rapid and decisive action in these situations and optimize the path to approval for potentially life-saving new drugs and improve the medicines that are available to patients.

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<sup>12</sup> Friends of Cancer Research and Engelberg Center for Health Care Reform at Brookings 2011 Conference on Clinical Cancer Research: Conference Issue Brief: <http://www.focr.org/images/stories/pdf/panel4final11411.pdf>  
Accessed 3/3/12



## **About Friends of Cancer Research**

**Friends of Cancer Research** (*Friends*) is a cancer research think tank and advocacy organization based in Washington, DC. *Friends* is a leader in developing partnerships and advocating for policies that will get treatments and therapies to patients in the safest and quickest way possible. Working with federal health agencies, congressional leadership, academic research centers and private sector industry, *Friends* continues to create innovative educational, policy, and scientific approaches to improve health outcomes and cancer care. [www.focr.org](http://www.focr.org)

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