



PDUFA V: Medical Innovation, Jobs, and Patients

Energy and Commerce Subcommittee on Health

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Testimony of Ellen V. Sigal, PhD

Good morning, Chairman Pitts, Ranking Member Pallone, and Members of the committee. I am Dr. Ellen Sigal, Chair and Founder 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 has worked tirelessly in putting together this hearing. It is an honor to testify before you today on the important role that the Food and Drug Administration (FDA) plays in getting life-saving treatments to patients.

I started Friends of Cancer Research over 15 years ago after having lost a sister to breast cancer, my father to prostate cancer, and mother to pancreatic cancer. This is as personal for me, as it is for you Mr. Chairman, and likely everyone in this room who have been deeply affected by illness.

My testimony is intended to give perspective on the urgency of getting new lifesaving treatments to patients in the safest and quickest way possible, the importance of maintaining our global competitiveness, and to realize the full potential of biomedical research. None of these things can be accomplished without a fully resourced and rigorous Food and Drug Administration that has the necessary scientific capacity to continue to evaluate new approaches to treating different diseases.

While compelling progress has been made within the field of oncology, there is much more to be done to alleviate the burden of cancer. It is estimated that, in 2011, nearly 1.6 million Americans will have been diagnosed with some form of cancer. As a result, our healthcare system will be strained an additional \$228 billion.¹ Most importantly, this disease will claim the lives of 571,950 mothers, fathers, grandparents, sisters, brothers, and friends, this year.²

Advancements in basic science do not always translate to new medication as rapidly as many would desire. In fact, recent estimates indicate that it could take upwards of 12 years and over \$1 billion to

¹ The American Cancer Society: http://www.cancer.org/docroot/MIT/content/MIT_3_2X_Costs_of_Cancer.asp
Accessed 6/30/11

² <http://www.cancer.org/acs/groups/content/@epidemiologysurveillance/documents/document/acspc-029819.pdf>
Accessed 6/30/11

develop a new drug.³ While there are many factors that make development of new drugs complex and increasingly expensive, assessments of the process often focus on the Food and Drug Administration (FDA).

For many years the U.S. FDA has been portrayed by many critics as slow and inefficient compared to other countries. Anecdotally, some critics have 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 released in *Health Affairs* on June 16th that revealed the FDA is approving anti-cancer drugs in a more timely fashion than its overseas counterpart, the European Medicines Agency (EMA).

STUDY:

Our study shows that between 2003 and 2010 the FDA has approved 32 new cancer drugs versus only 26 by the EMA.⁴ FDA not only approved more cancer drugs, but they did so at a significantly faster rate; FDA approval averaged 182 days while EMA averaged 350 days. Access to new medicines five and a half months sooner has undoubtedly improved the lives of many of the 1.5 million Americans diagnosed with cancer each year.

The intent of this study 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 information about current trends in oncology drug review. It should also be noted that the review period prior to approval is only one component of a multi-step process to develop new medicine. In order to truly accelerate the pace in which patients are able to utilize innovative medicines, the entire drug development process will need to be examined.

While the FDA should be praised for their contribution to ensure efficient access to new medicine, the responsibility to ensure that this continues extends beyond the agency. Unquestionably, FDA should maintain its high evidentiary standards and rapidly evolve to include new scientific advancements, however, strong public support and additional Congressional appropriations are necessary for the FDA to be able to continue this trend and strengthen its scientific foundation.

As Congress begins to examine priorities that would support the FDA through the reauthorization of Prescription Drug User Fee Act (PDUFA), we believe that three areas in particular would strengthen the agency's role as a vital component in medical innovation. These areas include advancement in regulatory science, innovative approaches to drug development and approval, and novel mechanisms for FDA to obtain external input.

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

⁴ Roberts, S., Allen, J., and Sigal, E. *Health Affairs* 30, No. 7 (2011) Published online: June 16, 2011

Advancement in Regulatory Science

With great advances in molecular research, the field of drug development is becoming increasingly complex. In order to capitalize on the promise of new discoveries, the FDA, and its global counterparts, must keep pace with scientific advancement and be a catalyst to medical innovation for patients in need.

As recently as 2007 the FDA's own Science Board declared the agency's "mission at risk" due to its eroded scientific foundation.⁵ In response to this stark assessment, the FDA's 'Regulatory Science Initiative' has outlined areas for additional research and the development of new tools to support regulatory decision making for the scientific challenges of the future. Advanced scientific methods to evaluate both safety and efficacy will ultimately help the new products reach the right patients in the timeliest manner. This is increasingly important as new medicines continue to employ advanced approaches - such as the ability for new drugs to be designed for a select population based on genetic characteristics – which may require novel designs of the clinical trials to demonstrate safety and efficacy.

Each year billions of dollars are invested in biomedical research, through the federal government, philanthropic foundations and private sector industry. This investment has and continues to create tens of thousands of jobs, and generate incredible new understanding of how to battle diseases like cancer.

However, that research, and the promise and hope it brings to patients, will not be able to be translated into medical solutions at a fast enough rate if the resources and science at the FDA cannot keep pace with discovery. **Congress should ensure that FDA is provided with additional resources, particularly those that can support regulatory science programs.**

A weakened and underfunded FDA will cause companies to take their research overseas, creating a loss in jobs and investment, and threaten our standing as the global leader of science and innovation. Most importantly, an under resourced agency will mean delays in getting potentially life-saving treatments to patients battling disease and illness.

Innovative Approaches to Drug Development and Approval

The Prescription Drug User Fee Act was originally enacted as a program to increase the efficiency of the FDA drug review process and ultimately provide patients access to new products sooner. It has been largely successful in accomplishing this goal. As a part of the original Act, the 'Accelerated Approval' pathway was established. Under this program new drugs and biologics that treat serious or life-

⁵ Report of the FDA Subcommittee on Science and Technology: FDA Mission at Risk. November, 2007: http://www.fda.gov/ohrms/dockets/AC/07/briefing/2007-4329b_02_01_FDA%20Report%20on%20Science%20and%20Technology.pdf Accessed 6/30/11

threatening illness and provide meaningful benefit over existing therapies can be made available based upon demonstrated improvement of a surrogate endpoint.⁶

Accelerated approval is accompanied by the requirement for post-market studies in order to confirm the long-term benefit that was initially indicated by the surrogate marker. This program has proven extremely valuable for patients, particularly those facing a situation in which they may have had no treatment options for their disease. Our research indicates that of the 32 new oncology drugs approved by the FDA from 2003-2010, 10 were approved by accelerated approval.

The FDA must continue to utilize this process and Congress should encourage FDA to explore novel regulatory paradigms and provide clarity on how existing frameworks can be applied to advanced science. In oncology, and several other genetically-driven diseases, new products are being developed for use in particular subclasses of patients based on the presence of a molecular marker. These “targeted therapies” may be highly effective (and less toxic than treatments that are unable to differentiate between normal and abnormal cells) in the molecularly identified patient set, yet ineffective in patients without the marker. In situations that a marker is known and characterized prior to approval of a new drug, a modified approach to the overall development program could be explored and expedited. In general, new drug research is currently conducted in a manner where a phase 1 study is performed and analyzed, followed by a phase 2 study, and culminating with large randomized phase 3 studies. However, for therapies that show a large-magnitude of clinical benefit in their target population early in the development process, the traditional multi-phase, sequential development approach may not be appropriate, particularly if current treatment options for those patients have limited efficacy.

An ‘Expedited Drug Development Program’ could be employed to abbreviate or combine traditional phases of development, thereby shortening the pathway to approval and avoid giving larger numbers of patients a potentially harmful or ineffective drug. In addition, a robust capacity for on-going post-market research to better collect and understand emerging evidence about a new product will allow increased use of an expedited drug development program and ensure that new medicines can be made available to patients without compromising their safety. There are historic examples where the traditional Phase 1-3 stepwise development has been modified. For example, Gleevec™ (imatinib mesylate) was approved in 2001 based upon Phase 2 data due to its early demonstrated clinical benefit;⁷ however such an expedited pathway is not fully defined as to when and how a similar approach that condenses different phases of development could be utilized. Establishment of an ‘Expedited Drug Development Program’ could help to provide guidelines applicable to the entire development process (not just the approval process) in order to facilitate the development of targeted therapies.

⁶ 21 CFR 314.500

⁷ Cohen, MH, Williams, G, et al. Clin Cancer Res. Vol. 8 (2002) 935-942

Novel Mechanisms for Input

To fulfill its mission to protect the public health, FDA needs to interact with stakeholder groups including patient advocacy organizations, disease specialty societies and others to obtain the information necessary to address difficult scientific and policy questions. Currently, as established by the Federal Advisory Committee Act, FDA uses its standing advisory committees as the primary source of scientific advice.⁸ While the advisory committee process has shown to be a valuable venue to aid scientific decision making, it should be just one way in which FDA can participate in discussions with scientific experts. FDA should have the ability to convene and actively interact with qualified subject-matter experts that are able to provide input on larger scientific and policy issues, rather than solely drug specific situations. Interactions could include participation in scientific conferences, task forces, and public meetings. This would provide FDA rapid access to multiple sources of high-quality, scientific expertise.

In addition to scientific input, appropriate channels should be created to facilitate input from patients with greater frequency. The decisions made by the FDA ultimately impact the people using medical products. Developing methods for interactions between medical reviewers and patients or care givers to discuss their direct experiences would improve the understanding of difficult to quantify metrics such as risk-tolerance, disease impact on quality of life, or symptomatic burden.

Congress should ensure that mechanisms are put into place to allow FDA rapid access to diverse scientific expertise and direct patient viewpoints. This type of input could increase transparency and greatly aid difficult decisions that may need to be made at all stages of the drug review process.

Conclusion

The role of the Food and Drug Administration as a component of medical innovation is critical. Our data indicate that the end-stage review is on average half the duration by the US FDA than the EMA. While this indeed translates to American cancer patients gaining access to new drugs sooner, it does not address the fundamental challenges to advancing health innovation that are currently facing our society. In order to begin to solve this larger problem, all of the sectors represented at this hearing today, and several of those that are not, must at times, set aside our individual interests and work toward the common goal of improving the health of the country, both economic and personal, through innovation. As patients, which we all have been or will be, we should demand it. The people we all work on behalf of deserve it.

I would conclude today by asking the members of this committee, and your colleagues on both sides of the aisle, to keep the best interest of patients in mind and support the agency that plays such a vital role in bringing new hope and potentially lifesaving treatments to them everyday.

⁸ 21 CFR Part 14, Subpart A