Expanding Access to 21st Century Cures: Reforming Compassionate Use

Across the United States, patients with life-threatening conditions are desperate for treatments that hold the potential to save and prolong their lives. In some extreme cases, experimental drugs or devices may be a patient's only hope when no other traditional treatments approved by the Food and Drug Administration (FDA) are effective and when patients are unable to enroll in a clinical trial. Fortunately, the FDA permits patients, on a case-by-case basis, to access treatments still in the development process and outside of the clinical trial setting when certain criteria are met. This process is known as individual patient expanded access, or "compassionate use".

FDA's expanded access program may best be described as a symptom of an antiquated drug development regime in need of modernization. In the 1970s, the average cost for drug makers to bring a new treatment to the marketplace was $140 million. Today, it costs $1 to $2 billion and takes 10 to 15 years.[1] There are numerous barriers to drug development, including the increasingly complex, time consuming, and expensive process of conducting clinical trials for new drugs and devices. While the goal of this paper is to offer policy reform proposals regarding the expanded access program, such reforms should be coupled with broader efforts to improve the entire process of discovering, developing, and delivering new FDA-approved treatments to patients.

Individual patient expanded access requests to the FDA have increased from an average of approximately 659 submissions annually from 1997 to 2005[2] to more than 1,200 in 2012.[3] According to the FDA, the agency approves more than 99 percent of all expanded access requests.[4] However, this statistic does not reflect the full universe of expanded access requests because it excludes the number of appeals made directly to biopharmaceutical companies, which must be granted by the company before being reviewed by the FDA for final approval. The total number of requests for expanded access (typically submitted by a licensed physician on behalf of a patient) is unknown because biopharmaceutical companies do not track and report instances in which they receive or deny such requests.

The recent uptick in requests for individual patient expanded access to the FDA can be attributed to a number of likely factors. In 2009, the FDA predicted an increase after it finalized its expanded access regulations. The final regulation provided patients, physicians, biopharmaceutical companies, and other interested parties with more information and greater clarity about the expanded access program. Another contribution to the increase in expanded access requests may be that more information about drugs in

---

[1] Pharmaceutical Research and Manufacturers of America, 2014 Biopharmaceutical Research Industry Profile. Washington, DC: PhRMA, April 2014.

[2] Code of Federal Regulations, Expanded Access to Investigational Drugs for Treatment Use, Title 21, Sec. 312 and 316.

[3] Gaffney, Alexander. "Regulatory Explainer: FDA's Expanded Access (Compassionate Use) Program." Regulatory Affairs Professional Society. March 27, 2014.

[4] Silverman, Ed. "The FDA Says It's More Compassionate Than You Think." *Wall Street Journal*, May 5, 2014.

clinical development is now made publicly available on the Internet. This has motivated smaller biopharmaceutical companies, in particular, to aggressively publicize promising new investigational treatments in an effort to attract investment. This also has the effect of attracting the attention and hopes of prospective patients, including those who are unable to access such treatments in the clinical trial setting.

Indeed, most Americans know about "compassionate use" from social media. Many patients who are denied access to investigational new drugs (IND) often attempt to put public pressure on the IND sponsor to reverse its decision not to grant access. Using websites like Facebook and Twitter, patients who have nothing left to lose can become overnight social causes with the support of tens of thousands of online activists. This phenomenon puts biopharmaceutical companies in a difficult ethical dilemma. Companies that resist calls to furnish their drug may experience extraordinarily brutal publicity. Conversely, those who grant access to their treatment may be concerned that doing so will result in a flood of additional requests that the company may not be able to handle. Moreover, when safety and efficacy have not been firmly established, companies can – and should – be particularly reluctant to grant access to new treatments for fear of an adverse event. CNBC reporter Meg Tirrell observes that:

> *Compassionate use can be a complicated area for pharmaceutical companies, which cite issues including limited supply of experimental medicines and lack of data on their safety and efficacy in rejecting patients' requests. Their focus is on completing clinical trials to get drugs to market as quickly as possible; manufacturing enough medicine for the hundreds of compassionate use requests that may come in could be prohibitively expensive, and they argue that diverting resources outside of trials could slow the process down. There are also fears a bad outcome could derail an entire clinical program—or that making a drug available outside studies could deter patients from enrolling, and risk getting a placebo.*[5]

Recently, there have been several high profile cases of patients who sought expanded access using sophisticated media strategies with mixed outcomes.

Andrea Sloan

In 2013, Andrea Sloan, a 45-year-old lawyer in Austin, Texas, was told by her physician at MD Anderson Cancer Center that she had exhausted all traditional FDA-approved treatment options in her seven-year battle with Stage III ovarian cancer. Determined to pursue every possible avenue to extend her life, Ms. Sloan turned to a biopharmaceutical company for expanded access to an experimental PARP inhibitor recommended by her physician team. In spite of the fact that the company touted the drug's safety and efficacy to investors, the company rejected Ms. Sloan's request for expanded access because they told her that it was unsafe. The company tried to steer her toward clinical trials as an alternative, though she was ineligible for any open trials. After this, Ms. Sloan and her supporters from across the country turned to social media and television

---

[5] Tirrell, Meg. "When unapproved drugs are the only hope." *CNBC,* accessed August 5, 2014, http://www.cnbc.com/id/101860676.

news, and made an impassioned plea to the company to reverse its decision. Ultimately, the company stuck to its position despite the bad publicity. After months of pleading – a time during which her health vastly deteriorated – Ms. Sloan was eventually able to access a similar drug in development from another company, though she died from complications from pneumonia shortly after beginning the treatment.

Josh Hardy

In 2014, Josh Hardy, a seven-year-old pediatric cancer patient, underwent a bone marrow transplant that resulted in a potentially fatal infection. Told by his physicians at St. Jude Children's Research Hospital that only one specific experimental treatment would save his life, Josh's family appealed to a small biopharmaceutical company for expanded access. Their request was denied as a matter of company policy. The company, which had made the same drug available to over 400 patients, made a decision to discontinue its expanded access program for the drug and focus instead on getting final FDA regulatory approval to market the treatment. Using the hashtag #SaveJosh, the Hardy family solicited the assistance of social media users to pressure the company. After numerous stories aired on news stations across the country, 30,000 "Likes" on Facebook, and 20,000 signatures on Change.org, the FDA worked with the company to form a small open-label Phase III trial in place within one week. Josh Hardy, who was included in the trial, made a miraculous recovery as a result of the experimental treatment.

Ebola

The recent outbreak of Ebola in West Africa has prompted international interest in expanded access. While no drug has been developed and approved for marketing to treat or cure this deadly and highly infectious disease, several patients have reacted positively to unproven drugs that were approved for individual patient use by the World Health Organization in 2014. One of the unapproved drugs used to treat an Ebola patient in the U.S. was the same drug used by Josh Hardy. When news broke that the drug was being used by Thomas Eric Duncan, a Liberian man who tested positive for Ebola in Dallas, TX, the drug sponsor's stock prices climbed five per cent in one afternoon. Following Mr. Duncan's death a few days later, the company's stock prices dropped twelve points in spite of the fact that there was no scientifically conclusive evidence to indicate the treatment contributed in any way to his death.[6] This illustrates the intense pressure companies are under when considering the possible impact that expanding access to an unapproved therapy could have on their business.

Right to Try

Frustrated with the federal expanded access process, which critics say is too complicated and allows the FDA to stand between "patients and the treatments that may alleviate their symptoms or provide a cure"[7], several states across the country have adopted "Right to Try" laws designed to allow terminally ill patients to access experimental drugs directly

---

[6] Caulderwood, Kathleen. "Experimental Ebola Drug-Maker Chimerix Stock Falls After Dallas Ebola Patient Dies." *International Business Times*, October 8, 2014.

[7] Corieri, Christina. "Everyone Deserves the Right to Try: Empowering the Terminally Ill to Take Control of Their Treatment." Goldwater Institute. February 11, 2014.

from biopharmaceutical companies without final FDA approval. While well intended, these laws take a fragmented and piecemeal approach to a problem that deserves comprehensive federal attention. "Right to Try" represents an understandable dissatisfaction with the expanded access program in general; so too does the growing phenomenon of patients using social media to shame companies into providing them access to unapproved drugs. Taken together, these trends should compel lawmakers in Congress to reform the federal expanded access program.

Reforming Expanded Access

While the expanded access program is not new, public interest in the program and its flaws has grown more acute since Andrea Sloan's passing on January 1, 2014. Patient groups, the biopharmaceutical industry, state legislators, think tanks, and bioethicists, have proposed various solutions to the complex challenges associated with expanded access. These solutions run the spectrum from the "creation of a national 'Expanded Access Institutional Review Board,'"[8] to "providing patients the right to start compassionate access requests through a point of contact at the FDA".[9] Wholesale reform, such as taking away from companies the authority to make decisions whether or not to grant requests for expanded access, is unlikely. There are too many variables to consider for Congress to be able to legislate such a sensitive and complex issue.

Rather, Congress should incentivize companies to provide patients with greater clarity and certainty about how they handle requests for expanded access. Because decisions about expanding access are left up to companies, there are a multitude of different internal processes and procedures that drug sponsors use to process requests and make determinations. Patients often have difficulty identifying who in the company to turn to when seeking access to an experimental drug. Even when a point of contact is identified, it is not always clear how a request is made and what considerations go into evaluating the request. Worst of all, many times when a request is denied, patients are given absolutely no reason – or even conflicting reasons – why their request was turned down. For a terminally ill patient, the only thing worse than being denied access is being denied access without any explanation.

Congress should also seek more information about the expanded access program to guide possible future efforts to reform and improve the existing program. Conflicting (and often inaccurate) reports about how much time it takes to complete an expanded access request, how many requests are approved and denied by companies and the FDA, reasons why patients are denied access, and which patients are most likely to seek access (i.e. cancer patients), could be clarified with more reporting and tracking. Currently very little of this information is collected and made publicly available.

Based on these considerations, Congress should do four things:

---

[8] Caplan, Arthur, and Kenneth Moch. "Rescue Me: The Challenge Of Compassionate Use In The Social Media Era." *Health Affairs*, August 27, 2014.

[9] Usdin, Steve. "Patching Compassionate Access." *Bio Century*, Week of September 29, 2014.

1. ***Incentivize biopharmaceutical companies developing innovative medical treatments and devices to have clear and publicly accessible expanded access policies.***

   Drug sponsors applying for Accelerated Approval, Breakthrough, Fast Track, and Priority Review designations should be required to develop and make publically available their expanded access policy for such treatments. For example, this information should be accessible on the company's website and easy to understand. At a minimum, the policy should include the following pieces of information:

   A. A single point of contact who receives and processes expanded access requests;
   B. Procedures for requesting expanded access;
   C. Minimum eligibility criteria for patient access to the unapproved treatment; and
   D. The amount of time a patient may expect to wait before the company makes a decision regarding their request for expanded access.

   Treatments eligible for these types of FDA review categories "might identify products that could have high potential for expanded access requests"[10] and therefore policies should be developed to communicate with patients how and under what conditions they may be eligible for expanded access. According to preliminary studies conducted by researchers and bioethicists at the NYU Working Group on Compassionate Use, only a small minority of biopharmaceutical companies have their policies for accessing unapproved drugs publicly accessible on their websites.[11]

2. ***Ensure that patients know why their request for expanded access is denied.***

   When a patient's request for expanded access is denied, the drug sponsor should notify the patient of their decision and explain why the request was denied.

3. ***Require requests for expanded access to be tracked and reported to the FDA.***

   As previously discussed in this paper, the total universe of expanded access requests is unknown because only requests approved by the drug sponsor are reported to the FDA. This is a limiting factor for policy makers who wish to better understand the FDA's expanded access program and how it can be improved in the future. Therefore, drug sponsors should be required to report to the FDA any time they deny a patient's request for expanded access, including information about the treatment such as the name of the investigational drug or device, the indication for use of such drug or device, the indication for which the patient is seeking access, and the reason why expanded access was denied. The FDA should aggregate this information and report the results to Congress while protecting the identity of the companies. For an outside perspective, the Governmental Accountability Office (GAO) should analyze the results and provide recommendations for policy makers to consider further.

---

[10] Sanghavi, Darshak, Meagan George, and Sara Bencic. "Health Policy Issue Brief: The Four A's of Expanding Access to Life-Saving Treatments and the Regulatory Implications." The Brookings Institution. July 31, 2014.

[11] Bateman-House, Alison. Email message to author, October 16, 2014.

4. ***Establish a stakeholder task force to make recommendations to further improve the expanded access program.***

With newly acquired data gained from implementing the third recommendation above, all parties impacted will have the capability to make better informed decisions about appropriateness, delivery and evaluation of expanded access cases. Accordingly, stakeholders from the patient community, biopharmaceutical industry, provider groups, and government should work together to explore additional options for reform. Special consideration should be given to:

A. Unique challenges faced by children with likely fatal diseases and no standard options for care;
B. Incentives for biopharmaceutical companies and providers to participate in expanded access programs;
C. How the FDA interprets and takes into consideration adverse event data collected as a result of expanded access;
D. Streamlining and standardizing the process for requesting expanded access; and
E. The costs incurred by biopharmaceutical companies for the time, effort and delivery of unapproved treatments to patients.[12]

[12] The University of Texas MD Anderson Cancer Center, "Compassionate Use – Draft Federal Legislation Comments," October 26, 2014.