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Do Desperate Times Really Call for Desperate Measures? The Ethical Dilemma Behind the Regulation and Use of Experimental Drugs

Lauren Kuehn
lkuehn@alumni.nd.edu

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**DO DESPERATE TIMES REALLY CALL FOR DESPERATE
MEASURES? THE ETHICAL DILEMMA BEHIND THE REGULATION
AND USE OF EXPERIMENTAL DRUGS**

LAUREN KUEHN *

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INTRODUCTION

Throughout the decades, public health crises have shaped the regulation of drug approvals and public access to newly invented drug treatments.¹ In 1962, for instance, the Food and Drug Administration (FDA) introduced stringent testing and approval procedures in response to serious birth defects from the use of thalidomide by pregnant females without sufficient safety testing.² The FDA was prompted yet again to implement new strategies in approving drugs as a result of the AIDS crisis. New policies and regulations were proposed and implemented, including features of European systems, which accelerated access to new experimental drugs for life-threatening illnesses.³ The reality of the situation at the apex of the AIDS crisis showed the inadequacy of FDA processes

* Candidate for Juris Doctor, University of Notre Dame Law School, 2017; B.A. with Honors in Political Science and German, College of the Holy Cross, 2013. I would like to thank my adviser Professor Alford along with the many mentors I have been fortunate to have during my time at Notre Dame. A special thank you to my family, especially my parents and fiancé, for their constant support and their unconditional love throughout my entire academic career.

¹ See Harvey Teff, *Drug Approval in England and the United States*, 33 AM. J. COMP. L. 567, 573 (1985).

² 21 ROBERT JOHN KANE & LAWRENCE E. SINGER, *THE LAW OF MEDICAL PRACTICE IN ILLINOIS* 15 (3d ed. 2015).

³ See generally Julie C. Relihan, *Expediting FDA Approval of AIDS Drugs: An International Approach*, 13 B.U. INT'L L. J. 229, 238 (1995).

from the perspective of terminally ill, frustrated patients. Not only did a true drug lag exist between foreign countries and the United States (U.S.), it was argued that there was also no adequate existing treatment available in the first instance.⁴ As Wells commented,

The problem that the AIDS crisis presents is quite different than those resulting from other diseases. As of this writing, no clearly effective treatment exists. Additionally, the disease appears to be inevitably fatal. Desperate AIDS sufferers are crying out for access to treatment drugs which they know are still experimental and unproven. Arguably, under these special circumstances, such individuals should be allowed to make that choice.⁵

This debate over the access to experimental and investigational treatments for life-threatening illnesses has not ceased to exist. Quite to the contrary, the push for better and faster access to experimental treatment has only gotten stronger. In a contested court case, *Abigail Alliance v. Eschenbach*, terminally ill patients advocated in the U.S. for a fundamental right “to try” experimental treatments.⁶ Ultimately, the Court of Appeals for the District of Columbia Circuit held that patients had no fundamental right, protected under due process, to have access to investigational drugs.⁷

The importance of the debate over access to experimental treatment is still very much alive and well, as seen from the events surrounding the 2014 Ebola crisis and what many deem to be a wholly inadequate and inefficient response to the Ebola outbreak.⁸ The outbreak called for the ultimate ethical conundrum as the World Health Organization (WHO) proceeded to allow the use of drug treatments—that were entirely unapproved and only tested on animals—on patients suffering from the life-threatening diseases.⁹ Generally, the use of experimental treatments in the Ebola outbreak showed that “[m]uch more ethical work needs to be done to create a sound infrastructure for compassionate use in humanitarian emergencies.”¹⁰ Ebola prompted a dialogue about the ethical and legal ramifications of expediting access to pharmaceutical products that have not

⁴ See generally Anne E. Wells, Comment, *Regulating Experimental AIDS Drugs: A Comparison of the United States and France*, 12 LOY. L.A. INT'L & COMP. L.J. 393 (1990).

⁵ *Id.* at 410–11.

⁶ *Abigail Alliance for Better Access to Developmental Drugs v. Von Eschenbach*, 495 F.3d 695, 707 (D.C. Cir. 2007), *cert. denied*, 552 U.S. 1159 (2008).

⁷ See generally *id.*; see also Allison J. Goodman, Comment, *Abigail Alliance v. Von Eschenbach: Restricting Access to Potentially Lifesaving Drugs Since 2007*, 25 J. CONTEMP. HEALTH L. & POL'Y 107, 125 (2009).

⁸ See James G. Hodge et al., *Global Emergency Legal Responses to the 2014 Ebola Outbreak*, 42 J.L. MED. & ETHICS 595 (2014); see also James G. Hodge, Jr., *Legal Myths of Ebola Preparedness and Response*, 29 NOTRE DAME J.L. ETHICS & PUB. POL'Y 355, 356 (2015); see also Alexandra Sifferlin, *WHO Vows Reform After Ebola Outbreak Mistakes*, TIME (May 18, 2015), <http://time.com/3882556/who-reform-ebola-outbreak-mistakes/>.

⁹ See Kai Kupferschmidt, *Using Experimental Drugs and Vaccines Against Ebola is Ethical, WHO Panel Says*, SCIENCE MAG. (Aug. 12, 2014), <http://www.sciencemag.org/news/2014/08/using-experimental-drugs-and-vaccines-against-ebola-ethical-who-panel-says>.

¹⁰ *Id.*

gone through adequate testing and approval procedures. The questionable ethical atmosphere in which experimental treatments are afforded persists in global health dialogue, even after the release of successful results related to a new, promising Ebola vaccine.¹¹

It has also spurred an entire movement throughout the U.S., which has resulted in over twenty states introducing “Right to Try” bills since early 2014.¹² The FDA has been the subject of allegations regarding its perceived different behavior in times of crisis as compared to times in which terminally ill patients domestically seek outlets to retrieve experimental treatments. As Furchtgott-Roth criticizes, “[i]f [the] FDA applied the same sense of urgency to Ebola vaccines in the past or to other drugs in its pipeline, millions of people would be better off. Instead, it stalls until a crisis arises, resulting in more deaths and untold suffering.”¹³ How the FDA imagines its role in protecting the public health and upholding safety and efficacy in the regulation of pharmaceutical products in light of this legislative and politically charged movement remains to be seen. Regardless, the most recent Ebola crisis and the “Right to Try” movement help illuminate an age-old debate in a new period of time. The ethical, legal, and regulatory interests at stake shape the role of the FDA as well as the role drug regulation plays internationally both in times of public health crises and in their aftermath. If anything, the legal issues in the pharmaceutical industry have become more “complex and politicized because of the increase in global trade.”¹⁴

The regulation of pharmaceutical products generally requires a balance of various factors, most importantly public access to accurate information on medicines, continued confidence in health systems and professionals, and assurance that the manufacture, trade, and use of medicines is under appropriate and efficient regulation.¹⁵ In many respects, the regulation of drugs is quite different from other industries in that it concerns the population as a whole as well as serious consequences, including injury and death.¹⁶ What many frustrated patients neglect in conversations on pharmaceutical legislation and policy is that “[t]rying to achieve too much, too quickly, can be tempting[,]” but “[i]t took more than a hundred years for pharmaceutical policies and laws to evolve to current levels in the industrialized world.”¹⁷

This Note will explore the regulations and exceptions to the traditional drug approval process created by the FDA in order to respond to public health crises as well as the wishes and needs of terminally ill patients who have advocated for expanded access. Part I will highlight the regulatory framework in existence, exploring the traditional drug approval process, and detailing the various exceptions and expanded access and compassionate use programs. Subsection A

¹¹ See generally Annette Rid & Franklin G. Miller, *Ethical Rationale for the Ebola “Ring Vaccination” Trial Design*, 106 AM. J. PUB. HEALTH 432 (2016).

¹² Alexander Gaffney, “Right to Try” Legislation Tracker, REG. AFF. PROF’L SOC’Y, (June 25, 2015) <http://www.raps.org/Regulatory-Focus/News/Right-to-Try/> (last visited Mar. 9, 2017).

¹³ Diane Furchtgott-Roth, *The FDA Should Be in Ebola-Mode All the Time*, ECONOMICS 21 (Sept. 23, 2014), <https://economics21.org/html/fda-should-be-ebola-mode-all-time-1098.html>.

¹⁴ MGMT. SCI. FOR HEALTH, MANAGING ACCESS TO MEDICINES AND HEALTH TECHNOLOGIES, 101 (2012), <https://www.msh.org/sites/msh.org/files/mds3-jan2014.pdf>.

¹⁵ *Id.*

¹⁶ *Id.*

¹⁷ *Id.* at 102.

will explain the regulatory framework present in the U.S. established by the FDA, while Subsection B will explain the regulatory framework in the European Union (EU) made through the European Medicines Agency (EMA), and will specifically provide examples from Germany and the United Kingdom (U.K.). Part II will highlight the main points in the debate over the use of experimental drugs in the context of the AIDS crisis and Ebola crisis. Part III delves into further detail in the specific context of the Ebola crisis and exemplifies how the debate on experimental drugs can be seen through the eyes of those addressing ethical questions over drug regulation in the most recent public health crisis. Lastly, Part IV seeks to demonstrate the importance of this issue in light of the Ebola crisis and describes what has been unfolding in its wake, in particular the “Right to Try” movement. Part IV emphasizes the potential risks and harms that will come about should the goals of the “Right to Try” movement be realized.

Ultimately this Note will argue that, unlike what many patients believe, the FDA plays an invaluable and imperative role in seeking the efficacy and safety of new treatment options and drugs. The balance of interests between those who are terminally ill, who wish to see increased access to unapproved medicines; the general public, who has an interest in preserving the drug approval process; and the FDA, who has been mandated by law to safeguard the safety of the general public, creates a tension that will continue to go unresolved. Thus, the patients who continue to advocate for routes outside of the FDA regulatory process—threatening to diminish the strength of the FDA’s presence and to remove many new, unapproved drugs from the FDA’s jurisdiction—place the future of drug development and regulation in peril. The FDA’s role should not be eradicated, but instead it should be bolstered and preserved. Public health crises prove not that drug regulation is overly cumbersome, unnecessary, and a death sentence for patients, but rather that there has never been more of a reason to preserve the role the FDA has received by law.

I. EXPANDED ACCESS AND THE DRUG APPROVAL PROCESS

Generally, in order to be approved for sale, drugs must satisfy four standards: efficacy, safety, quality, and clinical use information. The medication must be effective for the indications claimed, it cannot display risks that outweigh its potential benefits, it should be well made, and all clinical information regarding its use—precautions, adverse effects, and so on—must be provided.¹⁸ Regulations are present in national legislation and regulatory frameworks as well as in international guidelines presented by various conferences and organizations, including, among others, the WHO, the International Conference on Harmonisation, and the International Conference on Drug Regulatory Authorities.¹⁹

¹⁸ *Id.* at 177.

¹⁹ *Id.* at 3–4, 18.

A. *The Drug Approval Process: The U.S.*

The FDA in the U.S. is enabled for the regulation of pharmaceutical products under the Federal Food, Drug, and Cosmetic Act (the Act).²⁰ From the Act's inception, the central focus has been ensuring that the requirement of adequate testing before use is enforced.²¹ Under current federal law, a drug is required to be the "subject of an approved marketing application before it is transported and distributed across state lines."²² The FDA requires that there be substantial evidence that a "drug is safe and effective for its intended use," and thus the pharmaceutical industry is the subject of "rigorous statistical testing procedures."²³ After a drug has been tested on animals, the manufacturer must complete a "Notice of Claimed Investigational Exemption for a New Drug" in order for the drug to be safely given to human volunteers.²⁴ After a drug receives "investigational new drug" (IND) status, clinical studies are divided into three phases using ever-increasing populations of human patients. The molecule to be tested on humans changes in legal status at this point under the Act and is therefore subject to specific requirements under the regulatory system at that time.²⁵ Phase I trials allow the drug to be given to a small group of individuals and Phase II expands the number of patients who can receive the drug.²⁶ While these earlier stages of clinical trials focus on toxicity and efficacy, Phase III trials focus on the safety and effectiveness in long-term use, observing side effects and interactions with other drugs.²⁷ A "New Drug Application" (NDA), or a request for marketing approval, will then be filed and awaits final approval depending on a showing of "'substantial evidence' that the drug is safe and effective, and that it satisfies the [FDA's requirements] as to the contents of the 'package insert.'"²⁸ FDA review of NDAs is statutorily prescribed at 180 days, but in reality can take as long as thirty months.²⁹

Despite having procedures that are generally similar to those of foreign countries, the FDA has been criticized for its "drug lag" and has responded to criticism by enabling quicker clinical trial progress and quicker access to experimental and investigational drugs that have not completed the entire approval process.³⁰ There are multiple ways for a patient to bypass normal FDA

²⁰ See Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 (1938); see also Teff, *supra* note 1, at 573.

²¹ See Teff, *supra* note 1, at 573.

²² *Investigational New Drug (IND) Application*, U.S. FOOD & DRUG ADMIN. (Aug. 1, 2016), <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm> (last visited Apr. 25, 2017).

²³ See Teff, *supra* note 1, at 573–74.

²⁴ *Id.* at 576.

²⁵ See *Investigational New Drug (IND) Application*, *supra* note 22.

²⁶ See Teff, *supra* note 1, at 576.

²⁷ See *id.*

²⁸ *Id.* at 577.

²⁹ See Alison R. McCabe, Note, *A Precarious Balancing Act—The Role of the FDA as Protector of Public Health and Industry Wealth*, 36 SUFFOLK U. L. REV. 787, 791 (2003).

³⁰ See KANE & SINGER, *supra* note 2, at 15 ("[C]ommentators claim that because of this 'drug lag,' the FDA drug approval process requirements have caused more deaths and suffering than they have prevented."); see also 21 C.F.R. § 312.305; see also Expanded Access to Investigational Drugs for Treatment Use, 74 Fed. Reg. 40,900 (Aug. 13, 2009) (to be codified at 21 C.F.R. pts. 312 and 316) ("The final rule is intended to improve access to investigational drugs for patients with serious or immediately

regulatory procedure in order to gain access to a new drug. Patients can gain quicker access to unapproved drugs through compassionate use and expanded access programs. The FDA provides for several quicker routes to access and clinical testing that include emergency use or treatment INDs, emergency investigational new drug applications (EINDs), fast-track designations to speed up the traditional approval process, and emergency use authorizations (EUAs) preserved for the most extreme circumstances.

If a patient is not eligible to participate in a clinical trial, a drug developer and physician may submit an application, reviewed by the FDA on a case-by-case basis, in order for the patient to receive a “compassionate exemption.” The exemption will be granted on a showing that: (a) the patient has given informed consent, (b) there is no satisfactory alternative treatment, and (c) the drug is likely effective and free of unreasonable risks.³¹ INDs may also be expedited to meet a patient’s need. An emergency-use IND allows the FDA, for instance, to authorize use of an experimental drug in a situation that does not permit enough time for submission of a typical IND. In addition, treatment INDs allow use of experimental drugs, which show promise in clinical testing for serious, or immediately life-threatening conditions. The use can take place while the final clinical work and FDA review is completed.³² The FDA grants these exemptions but with the intention of scrutinizing requests and allowing for exceptions only in true emergencies.³³ Lastly, physicians may wish to pursue an EIND. To qualify, a physician must show that they consider the product may be urgently needed for the patient’s serious or life-threatening condition, no satisfactory alternative therapy is available, and the patient cannot receive the product through any existing clinical trials or expanded access protocols.³⁴

There are also ways to speed up the testing and review processes, such as “fast track” and “priority review” programs, that are specifically designed for a drug that has been “designated as a qualified infectious disease product.”³⁵ “Fast track” designation is intended to bring the drug to market expeditiously and is set forth in Section 506(b) of the Act.³⁶ The designation applies *only* for the specific use for which it is studied and the circumstances must satisfy the definition of “serious condition” laid out in Section III.A. in the Guidance. Furthermore there must be an unmet medical need or a “condition whose treatment or diagnosis is not addressed adequately by available therapy”—for instance, a condition which

life-threatening diseases or conditions who lack other therapeutic options and who may benefit from such therapies.”).

³¹ KANE & SINGER, *supra* note 2, § 39:15.

³² *Investigational New Drug (IND) Application*, *supra* note 22.

³³ U.S. FOOD & DRUG ADMIN., EXPANDED ACCESS TO INVESTIGATIONAL DRUGS FOR TREATMENT USE 13 (2016), <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351261.pdf>.

³⁴ *Investigational New Drug (IND) Application*, *supra* note 22.

³⁵ See U.S. FOOD & DRUG ADMIN., GUIDANCE FOR THE INDUSTRY: EXPEDITED PROGRAMS FOR SERIOUS CONDITIONS-DRUGS AND BIOLOGICS 7 (2014), <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm358301.pdf>.

³⁶ *Id.* at 9 (Section 506(b) provides for the designation of “fast track product . . . if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition.”).

has no or limited available treatment.³⁷ The “fast track” designation allows for frequent interaction with the FDA review board in order to assess the drug pre-IND—at the end of Phase I, at the end of Phase II, and so on—to discuss not only the extent of safety and concerns but also other critical issues and points related to the study design.³⁸ In addition, the product may at some point establish its ability to receive priority review and consideration of its marketing application before the sponsor of the drug—a company, research institution, or other organization that is responsible for developing the drug—has even submitted the complete application.³⁹

Priority review requires the FDA to take action on the marketing application within six months, as opposed to the usual ten months in standard review.⁴⁰ The drug must be one that treats a serious condition and would provide “a significant improvement in safety and effectiveness” of the treatment, prevention, or diagnosis of a serious condition—as defined by the Guidance.⁴¹ Sponsors may use scientific data—other than data from clinical trials—to compare a marketed product with the investigational drug. They may show: superiority relating to either safety or effectiveness; the drug’s ability to effectively treat patients who are unable to tolerate, or whose disease failed to respond to, available therapy; or that the drug can be used effectively with other critical agents that cannot be combined with available therapy.

Generally, “[c]ommunication with the [FDA] is a critical aspect of expedited programs”.⁴² Expedited programs, while arguably in the public interest, do put the onus on sponsors, requiring sponsors to prepare a commercial manufacturing program that can accommodate the demonstrated need and consumer demand so that the drug will be available—and be a quality product—at the time of approval. It is important to note as well that expedited programs do not immunize sponsors from performing the necessary clinical trials and being subject to clinical trial inspections by the FDA.⁴³

In a circumstance like the Ebola outbreak, the FDA is equipped with yet another exception. According to Section 564 of the Act, the “FDA Commissioner may allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by certain threat agents when there are no adequate, approved, and available alternatives.”⁴⁴ The FDA Commissioner is

³⁷ *Id.* at 4.

³⁸ *Id.* at 9.

³⁹ *Id.*

⁴⁰ *Id.* at 25.

⁴¹ *Id.* at 24.

⁴² *Id.* at 25.

⁴³ *Id.* at 25–26.

⁴⁴ See *Emergency Use Authorization*, U.S. FOOD & DRUG ADMIN. (Jan. 26, 2017), <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm>; see, e.g., Notice of Emergency Use Authorizations, 80 Fed. Reg. 32,140 (Jun. 5, 2015). The recent FDA guidance letter explains that “medical products that may be considered for an EUA are those that ‘may be effective,’” and it explicitly notes that “the ‘may be effective’ standard for EUAs provides for a lower level of evidence than the ‘effectiveness’ standard that FDA uses for product approvals.” U.S. FOOD & DRUG ADMIN., EMERGENCY USE AUTHORIZATION OF MEDICAL PRODUCTS AND RELATED AUTHORITIES: GUIDANCE FOR INDUSTRY AND OTHER STAKEHOLDERS 7–8 (2017), <https://www.fda.gov/downloads/Emergency>

only permitted to authorize an EUA during a declared emergency, which requires declarations from Secretary of Homeland Security, Secretary of Defense, or Secretary of Health and Human Services that there is a “heightened risk of attack” with chemical, biological, radiological, or nuclear agents.⁴⁵ In satisfying the requirements of Section 564, the Commissioner and the FDA are required to assess the medical product’s potential effectiveness as well as the risks and benefits of allowing its use. In doing so, the FDA can only make an assessment based on the information known at the time and the current state of scientific knowledge.⁴⁶ The FDA evaluates not only domestic, but also foreign clinical trial data as well as animal trial data. Furthermore, the FDA allows clinical experience *other than* that present in controlled trials to be considered “if the circumstances warrant.”⁴⁷ When establishing a lack of adequate, approved, and available alternatives, a potentially successful alternative product may be deemed “unavailable” by the FDA if the available supply of the product is unable to meet the full demands of the emergency need.⁴⁸ This is by far the most liberal way to gain access to experimental and unapproved drugs. It is a significant departure from normal drug-approval procedures. The FDA is essentially statutorily allowed to consider very little clinical information, and in doing so, it considers foreign clinical data that is not part of any normal review process conducted by the FDA. These EUAs have been issued not only for Ebola, but also for other widespread diseases such as Middle East Respiratory Syndrome (MERS), Anthrax, and Avian Flu.⁴⁹

B. The Drug Approval Process Abroad: The EU

Access to experimental treatment and investigational drugs is subject to regulation in the EU as well. Similar to the act enabling the FDA, Directive 2001/83/EC of the European Parliament requires that rules governing the production, distribution, and use of medicinal products must safeguard the public health while also promoting the development of the pharmaceutical industry and trade of medicinal products in the EU.⁵⁰

As for the regulation of pharmaceutical products in Europe, the EU has taken a more invested role in harmonizing drug regulations across Europe. Directive 65/65/EEC⁵¹ is the earliest measure taken by the EU to harmonize the safety and efficacy standards for medicinal products, requiring the Member States to enact laws prohibiting medicinal products from being marketed on their territories

Preparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/UCM493627.pdf [hereinafter FDA 2017 GUIDANCE LETTER] (emphasis added)

⁴⁵ FDA 2017 GUIDANCE LETTER, *supra* note 44, at 5–6.

⁴⁶ *Id.* (“FDA expects to interpret safety information in light of the seriousness of the clinical condition, alternative therapies (if any), and the specific circumstances of the emergency.”).

⁴⁷ *Id.*

⁴⁸ *Id.*

⁴⁹ *Emergency Use Authorization*, *supra* note 44.

⁵⁰ Directive 2001/83 of the European Parliament and of the Council of 6 November 2001 on the Community Code Relating to Medicinal Products for Human Use, 2001 O.J. (L 311) 67.

⁵¹ Council Directive 65/65 of 26 January 1965 on the Approximation of Provisions Laid Down by Law, Regulation or Administrative Action Relating to Medicinal Products, 1965 O.J. (L 22) 369.

without approval.⁵² Despite ever-increasing harmonization, approval of new pharmaceutical products is largely left up to national authorities.⁵³ The EMA is an agency of the EU responsible for what is called the “centralized procedure” for drug authorization in the EU.⁵⁴ The centralized procedure, which provides EU approval of most newly developed drugs given their “high-technology,” allows product access to several markets simultaneously and provides for time constraints on administrative structures that speed up the time it takes these products to go to market.⁵⁵

Exemptions from normal authorization or approval procedures are also available in the EU. For products that are eligible for authorization under the centralized procedure, Article 83 of Regulation 726/2004 provides a legal framework for compassionate use in the EU.⁵⁶ As the Article states, “by way of exemption from Article 6 of Directive 2001/83/EC, Member States may make a medicinal product for human use belonging to the categories referred to in Article 3(1) and 3(2) of this Regulation available for compassionate use.”⁵⁷ Under a compassionate use program implemented by a Member State, a medicinal product may be available to “patients with a chronically or seriously debilitating disease or whose disease is considered to be life threatening disease, and who cannot be treated satisfactorily by an authorized medicinal product.”⁵⁸ The medicinal product must either be the subject of a marketing authorization application or undergoing clinical trials.⁵⁹ There are two major types of compassionate use programs: named patient compassionate use programs and cohort compassionate use programs.⁶⁰ Whereas named patient programs are initiated by physicians on behalf of individual patients, the manufacturer predefines the cohort programs to allow a group of patients to access an unauthorized product.⁶¹ At the same time, it should be remembered that compassionate use, as the EMA emphasizes, is not a substitute for properly conducted trials.⁶²

Compassionate use programs are coordinated and established through national legislation of member states who decide how and when to open these programs.⁶³ Physicians who wish to obtain unauthorized products that seem promising for the treatment of their patients must contact the national authorities

⁵² See TAMARA K. HERVEY & JEAN V. MCHALE, HEALTH LAW AND THE EUROPEAN UNION 285 (William Twining & Christopher McGrudden eds., 2004).

⁵³ *Id.* at 289.

⁵⁴ *Id.* at 294.

⁵⁵ *Id.*

⁵⁶ Regulation 726/2004 of the European Parliament and of the Council of 31 March 2004 on the Laying Down Community Procedures for the Authorization and Supervision of Medicinal Product for Human and Veterinary Use and Establishing a European Medicines Agency, 2004 O.J. (L 135) 1.

⁵⁷ *Id.* at 65; see EUR. MEDS. AGENCY, GUIDELINE ON COMPASSIONATE USE OF MEDICINAL PRODUCTS, PURSUANT TO ARTICLE 83 OF REGULATION (EC) NO 726/2004, 3 (2006), http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004075.pdf.

⁵⁸ Regulation 726/2004, *supra* note 56, at 65.

⁵⁹ *Id.*; see EUR. MEDS. AGENCY, *supra* note 57, at 4.

⁶⁰ See *id.* at 3.

⁶¹ *Id.* at 4.

⁶² See *id.*

⁶³ EUR. MEDS. AGENCY, QUESTIONS AND ANSWERS ON THE COMPASSIONATE USE OF MEDICINES IN THE EUROPEAN UNION 2 (2010), http://www.ema.europa.eu/docs/en_GB/document_library/Other/2010/01/WC500069898.pdf.

and follow the requisite procedures.⁶⁴ The EMA is responsible for providing recommendations that neither replace national legislation nor provide a legal framework but help to provide ways to administer, distribute, and use certain medicines for compassionate use with the overall goal of standardizing compassionate use programs throughout Europe.⁶⁵ A limited number of compassionate use programs are actually endorsed by the EMA.⁶⁶

Expanded Access Programs allow physicians and patients to have access to medicines that are either unauthorized—approved by the EMA but not yet commercially available in Europe—or that are approved outside of the European Economic Area.⁶⁷ Other alternatives to compassionate use programs under Article 83—and Articles 3(1) and 3(2)—of Regulation 726/2004 include “named-patient basis” and “expanded access programs.” Named-patient basis programs are similar to treatment INDs in the U.S. Physicians contact the drug manufacturer directly for a medicinal product, which will be given to a patient under their direct care.⁶⁸ “‘Named-patient basis’ . . . should not be confused with compassionate use [programs].”⁶⁹ Under Article 5 of Directive 2001/83, a legal basis is set forth for pre-launched medicines.⁷⁰ It provides an exception to the general rule that medicines must be approved before use or must be used during an approved clinical trial. Although Article 5 does not detail the conditions for authorization, the Article is intended to give the Member States the authority to allow exceptions to the general rule. Treatment on a named-patient basis involves physicians obtaining medicines for their patients directly from the drug manufacturer.⁷¹ Therefore, it requires that physicians bear the sole responsibility for the treatment of their patients. Expanded access programs provide another avenue to early access to medicines directly from the drug manufacturer.⁷² Patients who have received a medicine during a clinical trial and have benefitted from the treatment may continue treatment through an expanded access program authorized by the national authority.⁷³ “It should be recognised that all medicines whether supplied via compassionate use or expanded access [programs] or as a ‘named patient’ supply are unlicensed medicines, and therefore information on their safety and efficacy may in some cases be limited to early phase clinical trials.”⁷⁴

Throughout Europe generally, individual member states have nationalized their own regulations regarding the use and availability of unauthorized

⁶⁴ *Id.*

⁶⁵ *Id.*

⁶⁶ See generally NHS GREATER GLASGOW & CLYDE, POLICIES RELATING TO THE MANAGEMENT OF MEDICINES, 1–27 (2010), http://ggcprescribing.org.uk/media/uploads/policies/section_9/9.1_ulm_policy_-_1105.pdf.

⁶⁷ See D. URBINATI ET AL., EARLY ACCESS PROGRAMMES (EAPs): REVIEW OF EUROPEAN SYSTEM (Nov. 3–7, 2012), http://www.creativ-ceutical.com/sites/default/files/Early%20Access%20Programmes_EU%20countries.pdf.

⁶⁸ EUR. MEDS. AGENCY, *supra* note 63, at 2.

⁶⁹ *Id.* at 2–3.

⁷⁰ Directive 2001/83, *supra* note 50, at 18.

⁷¹ EUR. MEDS. AGENCY, *supra* note 63, at 3.

⁷² *Id.*

⁷³ *Id.*

⁷⁴ NHS GREATER GLASGOW & CLYDE, *supra* note 66.

medicines.⁷⁵ Despite harmonized regulations such as Regulation 726/2004/EC, “regulations differ widely among analyzed countries, due to differences in national medical practices, resources available, product funding, hospital structures and national insurance systems.”⁷⁶ National regulations will differ based on the eligibility requirements, procedural elements, and review times.⁷⁷ Furthermore, there are many member states that have not put an expanded access program in place and have instead relied on compassionate use programs alone. Germany, for example, implements a “Hardship Case Program” through which a group of patients are able to gain access to medicines that have not yet been approved.⁷⁸

Compassionate use programs were introduced in Germany as part of an amendment to the German Medicines Act in 2009⁷⁹—an example of another legal exception to the traditional approval process. Generally, medicines are governed by the Bundesinstitut für Arzneimittel Medizinprodukte [the Federal Institute for Drugs and Medical Devices].⁸⁰ The German Medicines Act dictates that medicinal products are exempt from marketing authorization if they are meant for treatment of diseases that are life-threatening or result in severe disabilities, and cannot be treated satisfactorily with any approved product.⁸¹ Prior to 2009, German law authorized the use of unapproved medicinal products only to the extent it qualified as a “justifiable emergencies” under the criminal code.⁸² This changed with the Fifteenth Amendment to the German Medicines Act that outlined additional requirements, including patient informed consent and securing approval from the proficient authority.⁸³ According to Drug Hardship Ordinance of 2010, a compassionate use program will allow unauthorized medicinal products to be accessible to a group of patients *if* sufficient indications of efficacy and safety of the product exist and if a clinical trial is being conducted or an application for marketing authorization has been submitted to the EMA.⁸⁴ Again, only patients suffering from diseases which result in death or severe disability are eligible to participate and only if other authorized products do not provide

⁷⁵ URBINATI ET AL., *supra* note 67.

⁷⁶ *Id.*

⁷⁷ EUR. MEDS. AGENCY, *supra* note 63, at 2.

⁷⁸ URBINATI ET AL., *supra* note 67.

⁷⁹ Arzneimittelgesetz [AMG] [Medicines Act], Aug. 24, 1976 BUNDESGESETZBLATT, TEIL I [BGBl I] at 2445, as amended by Gesetz [G], July 17, 2009 BGBl I at 1990, art. 1 (Ger.).

⁸⁰ Kate Whitfield et al., *Compassionate Use of Interventions: Results of a European Clinical Research Infrastructures Network (ECRIN) Survey of Ten European Countries*, 11 TRIALS, no. 104, 2010, at 1, 4, http://download.springer.com/static/pdf/166/art%253A10.1186%252F1745-6215-11-104.pdf?originUrl=http%3A%2F%2Ftrialsjournal.biomedcentral.com%2Farticle%2F10.1186%2F1745-6215-11-104&token2=exp=1489181104~acl=%2Fstatic%2Fpdf%2F166%2Fart%25253A10.1186%25252F1745-6215-11-104.pdf*~hmac=38ed40f50d56b802b685883322670e5bcfa686295d32f0e9891efbe6212b9a1f.

⁸¹ AMG BGBl I at 2445, § 21, no. 2, *English translation available at* http://www.pei.de/SharedDocs/Downloads/EN/111013-amg-en.pdf?__blob=publicationFile&v=1; see Whitfield et al., *supra* note 80, at 5.

⁸² See *Lichtblick für Ausstherapierte Patienten [Bright Spot for Out-Therapied Patients]*, PHARMA FAKTEN [PHARMA FACTS], <https://www.pharma-fakten.de/fakten-hintergruende/innovationen-erfolge/compassionate-use/> (last visited April 25, 2017).

⁸³ Gesetz zur Änderung Arzneimittelrechtlicher und Anderer Vorschriften [Law on Amendments to Pharmaceutical and Other Provisions], July 17, 2009, BGBl I at 1990, art. 1 (Ger.); see Whitfield et al., *supra* note 80, at 5.

⁸⁴ Verordnung Über das Inverkehrbringen von Arzneimitteln ohne Genehmigung oder ohne Zulassung in Hartefallen [AMHV] [Drug Hardship Ordinance], July 14, 2010 BGBl. I at 935, ¶ 1 (Ger.).

satisfactory treatment for the disease.⁸⁵ The Drug Hardship Ordinance also provides that the federal authority may object to patients' participation in the program if the prerequisites for the implementation of the compassionate use program are not fulfilled or there are indications that the information submitted is incorrect or that the safe use of the medicinal product is not guaranteed.⁸⁶

Unlike in Germany, the use of unlicensed medicines on a "named patient basis" is a widely used practice in the U.K.⁸⁷

[B]ecause of the continually evolving area of oncology medicine, clinicians want to be able to prescribe outside this product license on a named patient basis—either an unlicensed drug or drugs unlicensed for specific indications if, in their professional opinion, they consider this to be the best option for a patient.⁸⁸

The responsible regulatory body, the Medicines and Healthcare Products Regulatory Agency, requires generally, under the Medicines Act of 1968, that all medicines have a marketing authorization or product license if they are manufactured or marketed in the U.K.⁸⁹ The U.K. provides another example of a European regulatory regime. There are three instances in the U.K. in which an unlicensed medicine may be prescribed. The unlicensed medicine may be prescribed (1) for uses that are outside the license scope of the prescribed diseases or conditions, (2) if the product is one which has been specially mixed for an individual patient because that patient's needs cannot be met by a licensed product, or (3) if the unlicensed product is either licensed in another country or is undergoing clinical trials.⁹⁰

Even unlicensed products appear to be highly controlled in their use. Hospital Pharmacy Quality Assurance departments assess any unlicensed medication before it is released and maintain any necessary recorded information.⁹¹ In addition, most unlicensed products are subject to approval by Drugs and Therapeutics Committees prior to when they are introduced on the hospital formulary.⁹² The U.K. provides compassionate use programs and expanded access programs as well. Special need programs allow physicians to provide patients who suffer from severe conditions a medicinal product without market approval in the U.K.⁹³ In addition, the Earlier Access to Medicine Scheme provides access to medicines that are particularly promising and have a clearly positive risk-benefit balance.⁹⁴ This scheme typically provides access

⁸⁵ *Id.* § 2.

⁸⁶ *Id.* § 4.

⁸⁷ See generally Siobhan Andrews, *Named Patient Medicines: A Pharmacist's Perspective*, 1 ONCOLOGY NEWS Issue 3, 10 (2006).

⁸⁸ *Id.* at 10.

⁸⁹ *Id.*

⁹⁰ *Id.* at 10–11.

⁹¹ *Id.* at 11.

⁹² *Id.*

⁹³ URBINATI ET AL., *supra* note 67.

⁹⁴ Off. of Life Sci., *Early Access to Medicine Schemes (EAMS): Task Group and Principles*, GOV.UK (May 10, 2016), <https://www.gov.uk/government/publications/early-access-to-medicines-scheme-eams->

between the end of phase III trials and licensing.⁹⁵ A regional division of the U.K. National Health Service provides guidelines for providing access to unlicensed products outside of clinical trials. These guidelines require prescribers to believe the product will be favorable for the patient, obtain the patient's consent before treatment, and explain to patients that the medicine is unlicensed.⁹⁶ The U.K. provides for the ethical review of compassionate use by the clinical ethics committee as well.⁹⁷ In addition, treatment in clinical trials will be extended to the patient at the trial's conclusion if the participant is benefitting from the device or product under expanded access.⁹⁸

As the spread of a life-threatening disease like Ebola becomes a world-wide public health crisis, the EMA as well as the WHO, like the FDA, have emergency use procedures in place to accelerate access to unauthorized medical products.⁹⁹ The EMA provides for conditional approval of products, despite limited data, in emergencies.¹⁰⁰ Under Decision 2119/98/EC of the European Parliament, member states are also urged in public health emergencies to provide rapid communication with the Commission and "exchange relevant data and information immediately via the Community network," thereby allowing more coordination than may otherwise exist between nations.¹⁰¹ The EMA is also equipped to accelerate the availability and use of high-quality medicines by their rapid scientific advice protocol. The Agency will provide the drug manufacturers advice on appropriate tests and studies to use in developing a medicine. This prevents objections from popping up later when the drug is evaluated for marketing authorization.¹⁰² In the case of a rare disease, protocol assistance allows the EMA to answer questions specific to a designated orphan medicine. Orphan designation is a tool used by the EMA to incentivize the development of drugs for those diseases that are more rare, affect a smaller population, and that

how-the-scheme-works/early-access-to-medicines-scheme-eams-task-group-and-principles (last visited Apr. 25, 2017).

⁹⁵ URBINATI ET AL., *supra* note 67.

⁹⁶ See Whitfield et al., *supra* note 80, at 5; THE KENT & MEDWAY AREA PRESCRIBING COMM., ACCESS TO UNLICENSED INVESTIGATIONAL DRUGS OUTSIDE OF CLINICAL TRIALS VIA EXPANDED ACCESS OR COMPASSIONATE USE PROGRAMMES 2 (Tim Root ed.), <http://www.southeastcsu.nhs.uk/Meds%20Management%20resource%20docs/01%20-%20Access%20to%20Unlicensed%20Investigational%20Drugs%20outside%20of%20Clinical%20Trials.pdf>.

⁹⁷ Whitfield et al., *supra* note 80, at 5.

⁹⁸ *Id.*

⁹⁹ See Michael Mezher, *An Argument for Emergency Authorization During Public Health Crises*, REG. AFF. PROF'LS SOC'Y, (Mar. 9, 2015), <http://www.raps.org/Regulatory-Focus/News/2015/03/09/21675/An-Argument-for-Emergency-Authorization-during-Public-Health-Crises/>; Ebola, EUR. MEDS. AGENCY (2017), http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000624.jsp&mid=WC0b01ac0580841e30 (last visited Apr. 25, 2017) (explaining that in the wake of the Ebola crisis, the EMA provided drug manufacturers with the option to receive "orphan drug designation" in order to accelerate and incentivize the creation and production of treatments intended to help diagnose, prevent, and treat the Ebola virus).

¹⁰⁰ Ebola, *supra* note 99.

¹⁰¹ See Decision No. 2119/98/EC of the European Parliament and of the Council of 24 September 1998 setting up a network for the epidemiological surveillance and control of communicable diseases in the Community, 1998 O.J. (L 268) 1.

¹⁰² *Scientific Advice and Protocol Assistance*, EUR. MEDS. AGENCY (2017), http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000049.jsp&mid=WC0b01ac05800229b9 (last visited Apr. 25, 2017).

often is not financially “worth it” for drug companies to produce medicines for.¹⁰³ Similarly, WHO reviews three criteria before allowing the use of unapproved products in an emergency:

1. Review of technical documentation relating to safety and performance (for example, analytical and clinical evidence, stability data);
2. Review of the documentation relating to the manufacture of the product and the manufacturer’s quality management system (QMS);
3. An independent laboratory evaluation coordinated by WHO of the product’s performance and operational characteristics.¹⁰⁴

It seems by the language of these procedures that both the emergency procedure in place at the EMA and the procedure put in place by the WHO provide for more information about the sponsor of the drug and the drug itself than the emergency exception given to the FDA by law. The EMA emergency protocols focus on coordination and more of a priority review type action as compared to the FDA, which by law is granted the ability to “bend” all of its existing rules and procedures.

II. THE DEBATE

The essential issue, and the reason why this debate might never have a conclusion, is that our humanitarian instinct and the autonomy of patients as individuals to maximize their ability to thrive and seek health are at odds with, for instance, the ultimate mission of regulatory bodies such as the FDA which is mandated to promote the common good in public health. “Currently, the U.S. has the safest, most effective vaccine supply in its history” and that is certainly not something the country achieved alone.¹⁰⁵ The FDA holds as its mission the promotion and protection of public health. “The safety of the U.S. drug supply contributes to the nation’s health, and FDA is the agency responsible for ensuring this safety.”¹⁰⁶ Among its obligations in accomplishing its mission, the FDA

¹⁰³ See *Orphan Designation*, EUR. MEDS. AGENCY, http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000029.jsp&mid=WC0b01ac05800240ce (last visited Apr. 25, 2017) (defining orphan designation: “A status assigned to a medicine intended for use against a rare condition. The medicine must fulfill certain criteria for designation as an orphan medicine so that it can benefit from incentives such as protection from competition once on the market.” To qualify for orphan designation, a medicine must meet a number of criteria: it must be intended for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating; the prevalence of the condition in the EU must not be more than 5 in 10,000 or it must be unlikely that marketing of the medicine would generate sufficient returns to justify the investment needed for its development; no satisfactory method of diagnosis, prevention or treatment of the condition concerned can be authorized, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.).

¹⁰⁴ Mezher, *supra* note 99; see also *Emergency Use Assessment and Listing (EUAL) Procedure for Ebola Virus Disease (IVDs)*, WHO, http://www.who.int/diagnostics_laboratory/procurement/purchasing/en/ (last visited Apr. 25, 2017).

¹⁰⁵ CTR. FOR DISEASE CONTROL & PREVENTION, ENSURING THE SAFETY OF VACCINES IN THE UNITED STATES (2011).

¹⁰⁶ COMMITTEE ON ETHICAL & SCI. ISSUES IN STUDYING THE SAFETY OF APPROVED DRUGS, ETHICAL ISSUES IN STUDYING THE SAFETY OF APPROVED DRUGS: A LETTER REPORT 2 (2010).

focuses on three key aspects to promote and protect public health: assuring the safety and effectiveness of vaccines and other biological products, helping to be a catalyst for product innovations, and giving the public accurate and science-based information so that they use medicines to improve health.¹⁰⁷

On the other hand, a prominent ethical argument in favor of expanded access, for example, promotes the idea that “patients should have a right to mitigate extreme suffering and to enhance self-preservation. . . . [A]s rational actors, patients are presumed to be capable of making well-informed treatment decisions in consultation with their physicians.”¹⁰⁸ Without regard to the long-term negative effects of increased expanded access—such as delays in drug development, approval, and participation in preapproved clinical trials—patients at risk of terminal illnesses often advocate for the right to be able to utilize their own risk-benefit calculus and make their own treatment decisions that they deem appropriate. Many critics have issues with such a stance, since studies showing that informational asymmetries lead to patient vulnerability along with the public’s risk comprehension being low.¹⁰⁹ And these two shortcomings demonstrate just a couple of the risks in increasing expanded access.

Despite the established existence of exceptions to the normal drug approval process that clearly exist—not just in the U.S., but also around the world—the practice is not blindly accepted. The debate over experimental drugs and the efficacy of the FDA’s new drug approval process is not a new one. In fact, much of the tension and concerns in the context of recent public health crises like Ebola were raised in the context of AIDS treatment and cancer treatment over the last twenty to thirty years as well. It comes down to what has been described as a “utilitarian calculus” or “an attempt to balance competing social interests.”¹¹⁰ There is a tension between “new drug development hold[ing] out the promise of innovative treatments for debilitating disease, for extending the human life span, and for relief of suffering . . .” and “[o]n the other hand, the introduction of inadequately tested new drugs creat[ing] the risk of iatrogenic injuries through toxic side effects, carcinogenicity, et cetera.”¹¹¹ Tension exists between the push for improved access to new treatments and the FDA’s responsibility to ensure and maintain the safety and effectiveness of new drugs.¹¹² Activists continue to confront the inevitable conundrum of wanting both safe and effective drugs while also criticizing the regulation of an industry that cannot possibly satisfy all competing interests at once. Even when the FDA is more willing to risk making new drugs available even if they later prove ineffective or unsafe, activists still claim that the FDA has not gone far enough.¹¹³

The adequate balance of interests, risks, and benefits becomes all too complicated in the context of public health crises like AIDS. Similar to the Ebola

¹⁰⁷ *Id.* at 2–3.

¹⁰⁸ Jonathan J. Darrow et al., *Practical, Legal, and Ethical Issues in Expanded Access to Investigational Drugs*, 3 N. ENGL. J. MED. 279, 283 (2015).

¹⁰⁹ *Id.* at 284.

¹¹⁰ See, e.g., Relihan, *supra* note 3; see also Michael D. Greenberg, *AIDS, Experimental Drug Approval, and the FDA New Drug Screening Process*, 3 N.Y.U.J. LEGIS & PUB. POL’Y 295, 297 (2000).

¹¹¹ See Greenberg, *supra* note 110, at 297.

¹¹² See Relihan, *supra* note 3, at 232.

¹¹³ *Id.* at 238.

crisis of 2014, the AIDS crisis erupted in the context of what many believe was conservative regulation over new drugs absent any existing approved treatment in the U.S.¹¹⁴ Criticism soared as frustrated, terminally ill patients saw those same treatments rejected in the U.S. but approved in several countries abroad.¹¹⁵ As Anne Wells wrote,

AIDS constitutes a worldwide epidemic of an entirely new, infectious, and as of today, inevitably fatal disease unlike any faced in modern history. Because of the unique nature of the challenge that AIDS presents, the current “business as usual” approach taken by the federal government and the FDA is inadequate. FDA administrative regulations have overdeveloped to the point where they actually harm those that they were designed to protect.¹¹⁶

Critics, especially terminally ill patients suffering from fatal diseases like AIDS, consider the FDA’s process as a means of “sacrific[ing] today’s AIDS patients in order to save tomorrow’s patients.”¹¹⁷ Of course to a patient with no other alternative other than an unapproved, experimental alternative, the choice is simple. The risks involved behind clinical trials using placebos and needing supporting evidence to show that the treatment is in fact safe and effective simply become irrelevant.¹¹⁸ Instead, the FDA’s gatekeeping measures and precautionary, protective responses are simply a “death sentence.”¹¹⁹

The problem, however, is that terminally ill patients come to quite a different risk-benefit calculation than the general public.¹²⁰ “[T]he issue becomes whether it is ethical for the FDA to place greater emphasis on its long term regulatory needs than on the immediate needs of individual patients.”¹²¹ The court in recent years implicitly spoke to this issue when it ruled in *Abigail Alliance v. Von Eschenbach* that there is in fact no fundamental right to try experimental drugs,¹²² effectively preventing terminally ill patients from constitutionally overriding the place of the FDA. In a suit against the FDA Commissioner and the Secretary of the Department of Health and Human Services, patients sought to enjoin the FDA from preventing the distribution of drugs that had passed Phase I of the approval process to terminally ill patients.¹²³ The Court of Appeals for the District of Columbia Circuit ruled against *Abigail Alliance*, holding that terminally ill patients do not have a constitutional right to unapproved drugs and that it was not a fundamental right protected by the Due Process Clause.¹²⁴ Since the Supreme

¹¹⁴ See Wells, *supra* note 4.

¹¹⁵ *Id.* at 394.

¹¹⁶ *Id.* at 423–24.

¹¹⁷ See *id.* at 395.

¹¹⁸ See Greenberg, *supra* note 110, at 296.

¹¹⁹ *Id.*

¹²⁰ See *id.* at 298.

¹²¹ See Wells, *supra* note 4, at 414.

¹²² *Abigail Alliance for Better Access to Developmental Drugs v. Von Eschenbach*, 495 F.3d 695 (D.C. Cir. 2007), *cert. denied*, 552 U.S. 1159 (2008).

¹²³ See Goodman, *supra* note 7, at 123.

¹²⁴ *Id.* at 125.

Court denied certiorari in 2008, the constitutional answer to the ethical question of whether the FDA may place greater emphasis on its long-term regulatory needs than on the immediate needs of individual patients ethical question is a resounding “yes.”

Much of the criticism of the FDA is based off of observations regarding drug approval processes in European countries. Concerns have been raised throughout history with regard to the prevalent “American drug lag,” pressuring the FDA to change its regulations to look more like its European counterparts and to incorporate foreign clinical data in order to speed up the FDA’s approval process.¹²⁵ All of the criticism and pressure continues today despite the fact that the EU considers the FDA to be the “gold standard approval body.”¹²⁶

Yet the situation is far too complex for patients to comprehend, and it seems that criticism of the FDA is somewhat unfounded. Several scholars have questioned the ability of critics to even compare the FDA’s approval process to its European counterpart.¹²⁷ In a recent study, oncology journals attempted to compare FDA and EMA approval efficacies and did not come away with any answers as to why these agencies are capable of arriving at different approval outcomes for the same drug, with the same data and clinical trials.¹²⁸ If anything, the European drug approval process has become more legalistic and seems to many, over time, to be more cumbersome than the FDA process since it involves both a central agency and individual member states.¹²⁹ Furthermore, the FDA and EMA simply have a different focus in their respective approval processes. “The FDA continues to place its focus on the manufacturing facilities—much more so than do the European authorities. The EU instead places its focus on process control analysis.”¹³⁰

In a recent study of the differences in approval outcomes concerning the exact same drugs, it was clear that “[m]ost if not all of the differences in authori[zations] . . . are not about drugs with clear efficacy benefits compared with risk, but concern agents where there is highly complex detail about narrow therapeutic margins between benefit and harm.”¹³¹ In the end, drug approval is a matter of different value judgments and interpretations—of the proper level of risk and benefit—by human beings from different cultures and in the context of not only the interests of patients, but of political pressures and moral conclusions.¹³² Overall, it is not a blanket conclusion that European drug approvals take significantly less time than those in the U.S., nor can it be said that FDA approval requirements are more inflexible and leave struggling patients with less access to experimental treatment than existing European requirements. As Beishon iterates, “[d]ifferences can also arise because of timing and the options

¹²⁵ See Greenberg, *supra* note 110, at 343.

¹²⁶ Marc Beishon, *Approval Rating: How Do the EMA and FDA Compare?*, CANCERWORLD 12 (2014), http://www.cancerworld.org/pdf/9944_pagina_12_17_Cutting_Edge.pdf.

¹²⁷ See Martine Kraus, *A Comparison of Drug Approval at the FDA and the EMEA/CPMP*, 33 CAL. W.L. REV. 101, 105 (1996); see also Gaffney, *supra* note 12.

¹²⁸ See Beishon, *supra* note 126, at 12.

¹²⁹ See Kraus, *supra* note 127, at 105.

¹³⁰ *Id.* at 102.

¹³¹ See Beishon, *supra* note 126, at 13.

¹³² See Wells, *supra* note 4, at 414.

open to the regulator, in particular the FDA, which is often the first to receive an application for a drug, and also tends to implement more fast-track and conditional procedures than the EMA.”¹³³ RAPS also points out that in 2013 alone the FDA surpassed the EMA in approving new molecular entities,¹³⁴ or “first in-world approvals.”¹³⁵

In the end, it must be recognized that because the FDA’s mission is to promote and protect public health, the FDA and the U.S. generally play a role in developing new vaccines which has been recognized as among the many global public goods. Americans do, and should, care about global development in the arena of health because in recent times the U.S. has been at the forefront of research and development in efforts to eradicate disease and epidemics, despite criticism. Its efforts with global partners have spurred much of the important progress in vaccine development.

U.S. resources and research and technical capacity committed to health are unparalleled. Total U.S. public spending on medical research and development equals that of all other nations combined. Over many decades, a good proportion of this spending has gone toward the prevention and control of diseases most prevalent in developing countries. Scientists at the publicly funded National Institutes of Health (NIH) helped develop antiretroviral drugs to treat HIV/AIDS and to prevent mother-to-child transmission during birth, saving lives at home and across the developing world. The NIH’s Vaccine Research Center is at the forefront of developing new vaccines for some of the most dangerous diseases, such as swine flu and Ebola. The Center for Disease Control and Prevention (CDC) leads efforts to monitor, isolate, and treat infectious diseases, protecting the health of Americans as well as people around the globe.¹³⁶

Furthermore, while it is difficult to accept, patients must understand that the proper balance—between government regulation and personal autonomy, between regulation of new drugs and the degree of accepted experimentation, and between satisfying the needs of pharmaceutical companies with the means to control the development of new treatments and the safety of consumers—is a balance that may never be perfectly struck regardless of changes to existing regulation.¹³⁷ As Michael Greenberg explains in the context of the AIDS crisis,

On the one hand, for people confronting sickness and death from

¹³³ See Beishon, *supra* note 126, at 13.

¹³⁴ See Gaffney, *supra* note 12. An NME is an active substance that has never been used for a given purpose and therefore is a substance that requires new evidence of safety and efficacy. According to the Regulatory Affairs Professionals Society (RAPS), it is the best indication of a regulator’s efficiency.

¹³⁵ *Id.*

¹³⁶ NANCY BIRDSALL & ANNA DIOFASI, GLOBAL PUBLIC GOODS THAT MATTER FOR DEVELOPMENT: A PATH FOR US LEADERS 3 (2016).

¹³⁷ See Greenberg, *supra* note 110, at 329.

AIDS-related illnesses that remain refractory to treatment with current medications, the pace of new drug development is still too slow, even given FDA efforts to cut years from the development time in the new drug pipeline. On the other hand, even some AIDS activists have questioned whether the FDA has gone too far in abbreviating the new drug development process, and whether the FDA has compromised traditional safety and efficacy standards in the effort to make experimental drugs more widely and more rapidly available.¹³⁸

The solutions may very well have nothing to do with increased rights and access to experimental medicines and treatments. Over time, there has been a consistent request for additional funding for the FDA. There is a prominent complaint that the FDA is being asked to produce a number of approvals and results that are simply impossible to fulfill at an understaffed, underfunded government regulatory body.¹³⁹

Notably, this debate deals not only with the rights of patients—as tends to be the main focus—but also ties directly to the rationale behind clinical trials and related ethical questions, as well as residual effects that may not be apparent at the onset.¹⁴⁰ For instance, many critics—such as Dr. Krim of the American Foundation for AIDS research—argue that the use of placebos in clinical testing to be “inhumane”; especially when such a fatal disease leaves patients without an opportunity to live if not given treatment.¹⁴¹ Yet, there are plenty of experimental treatments that, without proper clinical trials, will remain ineffective. For example, placebo-control and randomization are indispensable for research and the furthering of future treatments that could actually eradicate grave illnesses.¹⁴²

In addition, the push for earlier and increased access to experimental medicines outside of clinical trials has not only led to truncations of the trial process, but has also led to the postponement of research that would otherwise have been done in the absence of increased access. These changes risk degrading the quality of information-gathering as well as “sabotaging” the process itself.¹⁴³ Additionally, changing regulations to be more accommodating to the terminally ill patients will predictably do more than simply affect access to medicines.¹⁴⁴ Only prioritizing the interests of terminally ill patients at the expense of clinical research and the proper, safe development of new treatments and medicines “may lead to an equilibrium in which everyone is worse-off. If formal clinical trials genuinely do develop information that is otherwise impossible to obtain, then efforts to improve individual welfare by degrading the research process may

¹³⁸ *Id.* at 328.

¹³⁹ *Id.* at 342; *see also* Relihan, *supra* note 3, at 244; *see also* Wells, *supra* note 4, at 394.

¹⁴⁰ *See* Greenberg, *supra* note 110, at 331–32.

¹⁴¹ *See* Wells, *supra* note 4, at 414.

¹⁴² *See* Greenberg, *supra* note 110, at 332.

¹⁴³ *Id.* at 333.

¹⁴⁴ *Id.* at 332 (“[T]o the extent that demonstrably effective new drugs are vital to the welfare of PWAs, an argument may be made that the clinical trial process is integral, rather than detrimental, to that interest.”).

ultimately prove to be self-defeating gestures.”¹⁴⁵ It is the unfortunate reality that the effects of drugs cannot be discovered or known beforehand.

It is all too easy to forget the astounding negative and extensive effects that could ensue in either of two extreme circumstances: a world with complete patient autonomy and ability to access experimental treatments without regulatory interference, or a world—as once existed before the FDA expanded the options for earlier access to unapproved medicines—where no medicine could be accessed without FDA approval and full clinical testing. A world with complete patient autonomy, like the one advocated for by AIDS activists where patients would choose for themselves what risks were worth taking and the regulatory bureaucracy, is not the answer but rather potentially the fastest route in the race to the bottom:

[The] extreme of a completely unregulated market has potentially negative consequences for commercial development, despite the prospect of superficial autonomy enhancement in a world free from FDA interference. Exactly how manufacturers would respond to an unregulated marketplace is unclear; but, given the costs of advertising compared to clinical trial research, it seems plausible that competition might favor reduced research and increased directed marketing, especially in the absence of any government imposed standards for proof of new drug safety and efficacy.¹⁴⁶

Nevertheless, we continue to be confronted in the wake of the Ebola crisis with the same cycle that has been responsible for increased flexibility in the FDA’s regulation of new drugs and a complete change in approach the FDA has fostered in recent years: a disease without an existing treatment; a significant portion of the globe’s population becoming infected with the disease; proof of the disease’s tragic fatality rate; an ensuing public health crisis; increased patient frustration and political activism; and the resulting liberalization of access to new, experimental drugs and treatments that continues to move the FDA away from protecting consumers from the effects of unapproved treatments at too early a stage and toward a regulatory world that bows to the demands of patients. The FDA, in response to the AIDS crisis and criticism from innumerable AIDS patients, created many of the exceptions that now exist, including: expanded access; parallel tracking; fast tracking; and treatment and compassionate use exemptions, among others. That is now the world post-Ebola as well.

We are left with the ultimate questions: is *over-regulation* of drug approval and the use of experimental drugs actually possible? Or has the FDA gone too far in compromising safety and efficacy standards but continuously creating loopholes to the access of unapproved treatments? Does this age-old debate really leave us without any alternative but to dwindle down FDA regulation and the agency’s mission to nothing, to satisfy the interests of patients? If the FDA

¹⁴⁵ *Id.* at 333.

¹⁴⁶ *Id.* at 337.

does stay its course, does this really mean that thousands upon thousands of terminally ill patients are “*sentenced to death*?”

III. EBOLA: A HEALTH CRISIS OF INTERNATIONAL CONCERN

For the third time since 2007, our world was faced with a public health emergency. Officially declaring an emergency of international concern on August 8, 2014, the WHO changed the legal ramifications of doctors' and countries' activities and sparked debates of infinite proportions.¹⁴⁷ When emergency laws are set in place, they provide legal powers, options, and flexibility; but without guidance, clarity, or set ways to utilize this flexibility to provide the best legal response for the particular situation.¹⁴⁸ This was the legal environment in which doctors and regulatory bodies decided to bypass regulatory normalcy and engage in the use of experimental drugs as well as the review of drugs in the regulatory process without sufficient scientific information.

The FDA worked to use all of its authorities and response mechanisms to deal with the world's first Ebola *epidemic* by facilitating access to products.¹⁴⁹ It created an Ebola Task Force across the various divisions of the FDA, worked with global entities to exchange information and provide orphan designation to certain medicinal products, and used its power under the Emergency Use Authorization to make products available that were not on the traditional regulatory track.¹⁵⁰ The agency worked, and continues to work as we see from the announcement of a new Ebola vaccine,¹⁵¹ with medical product sponsors and other U.S. government agencies to clarify regulatory requirements, provide risk-benefit assessments, gather scientific data, and develop agreements for “further development and availability of medical countermeasures.”¹⁵²

Beginning in September 2014, international regulators agreed to work together cooperatively in the fight against Ebola.¹⁵³ The EMA worked in parallel with the WHO to efficiently and expediently help to bring drugs to market that would provide treatment to the thousands of emerging Ebola cases. Specifically, the EMA's efforts consisted of assigning “orphan designation”¹⁵⁴ to certain

¹⁴⁷ See James G. Hodge, Jr., Commentary, *Global and Domestic Legal Preparedness and Response: 2014 Ebola Outbreak*, 9 DISASTER MED. & PUB. HEALTH PREPAREDNESS 47 (2014), https://www.cambridge.org/core/services/aop-cambridge-core/content/view/D8F0EA6CAEDE747DBCD79EA155DD3F07/S1935789314000962a.pdf/global_and_domestic_legal_preparedness_and_response_2014 Ebola_outbreak.pdf.

¹⁴⁸ *Id.* at 2.

¹⁴⁹ U.S. Dep't of Health & Human Serv., *Ebola Preparedness in the U.S.—One Year Later*, YOUTUBE (Oct. 6, 2015), <https://www.youtube.com/watch?v=Ctp-C1bkEjw>.

¹⁵⁰ *Ebola Response Updates from FDA*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm410308.htm> (last visited Apr. 25, 2017).

¹⁵¹ See, e.g., *All Things Considered: Scientists Announce Ebola Vaccine*, NAT'L PUB. RADIO (Dec. 23, 2016), <http://www.npr.org/2016/12/22/506727690/scientists-announce-ebola-vaccine>.

¹⁵² *Id.*

¹⁵³ See *Ebola*, *supra* note 99.

¹⁵⁴ *Id.* The orphan designation, as defined on the EMA website, is: “A status assigned to a medicine intended for use against a rare condition. The medicine must fulfill certain criteria for designation as an orphan medicine so that it can benefit from incentives such as protection from competition once on the

medications and providing “rapid scientific advice”¹⁵⁵ to certain companies, such as GlaxoSmithKline.¹⁵⁶ Both the EMA and FDA often work to exchange information regarding applications they had received as well as the assessment of the respective applications.¹⁵⁷ Additionally, the EMA—on its own and in collaboration with the European pharmaceutical industry and the EU generally—launched a multi-million euro program to collaborate with experts and regulators to confront the unique challenges of Ebola and related disease research.¹⁵⁸

In addition to the individual responses of the FDA and the EMA, the WHO and its ethics panel—made up of researchers, ethicists, and patient safety advocates—came to unanimous agreement that in the “special circumstances of this Ebola outbreak it is ethical to offer unregistered treatments.”¹⁵⁹ In other words, the WHO decided that offering unregistered treatments is ethical, despite the unknown efficacy of such drugs or the unknown adverse effects of these medications, to use such treatments to cure or prevent the disease in victims.¹⁶⁰ It may be hard to argue against such a declaration since multiple sources call the outbreak in 2014 the largest Ebola outbreak on record.¹⁶¹ Depending on the country reporting, the death rate varied between 28–61%.¹⁶² At one point, the WHO reported an overall death rate of 41%.¹⁶³ The epidemic was responsible for the death of over 11,000 people and the infection of 30,000 people.¹⁶⁴ “Crisis mode” amped up when President Obama announced his intention in September 2014 to deploy three thousand military personnel and contribute 750 million dollars to the effort to eradicate the disease.¹⁶⁵ To most people, it seemed like desperate times called for desperate measures. The flexibility provided by the emergency legal regime, prompted by the WHO’s and President Obama’s declaration of an international health emergency, aided the FDA and WHO in facilitating the use of drugs that would otherwise have still been under FDA review.

market.” *Glossary: O*, EUR. MEDS. AGENCY (2017), http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/glossary.jsp&mid=&startLetter=O (last visited Apr. 25, 2017).

¹⁵⁵ *Id.* Scientific advice entails: “the provision of advice to a company by the European Medicines Agency on the appropriate tests and studies required in the development of a medicine or on the quality of a medicine.” *Glossary: S*, EUR. MEDS. AGENCY (2017), http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/glossary.jsp&mid=&startLetter=S (last visited Apr. 25, 2017). Developers can request information such as details regarding clinical trial design and so on.

¹⁵⁶ *See Ebola*, *supra* note 99.

¹⁵⁷ *Id.*

¹⁵⁸ *Id.*

¹⁵⁹ Kupferschmidt, *supra* note 9.

¹⁶⁰ *Id.*

¹⁶¹ *Id.*

¹⁶² Dennis M. Sullivan, Commentary, *Ebola: Ethical and Legal Ramifications of Using Experimental Drugs*, 30 WESTLAW J. PHARM. 2, 1 (2014).

¹⁶³ Thomas M. Burton, *Disputes Emerge on African Ebola Drug Trials*, WALL ST. J., May 13, 2015, <http://www.wsj.com/articles/disputes-emerge-on-african-ebola-drug-trials-1431471041>.

¹⁶⁴ *Final Trial Results Confirm Ebola Vaccine Provides High Protection Against Disease*, WORLD HEALTH ORG. (Dec. 23, 2016), <http://www.who.int/mediacentre/news/releases/2016/ebola-vaccine-results/en>; Michaelen, *First Ebola Vaccine Likely to Stop the Next Outbreak*, NAT’L PUB. RADIO (Dec. 23, 2016), <http://www.npr.org/sections/goatsandsoda/2016/12/22/506600875/first-ebola-vaccine-likely-to-stop-the-next-outbreak>.

¹⁶⁵ Laurie Garrett, *Ebola’s Lessons: How the WHO Mishandled the Crisis*, FOREIGN AFF., (Sept./Oct. 2015), <https://www.foreignaffairs.com/articles/west-africa/2015-08-18/ebolas-lessons>.

A. *Ethical Considerations Revisited*

Again, it is important to pause and observe the environment in which these “life or death decisions” were made. In a climate of fear and desperation, decisions were made, experimental drugs were provided, and ethical and legal debates—and their consequences—ensued, continuing to trouble ethics and scientific experts today, even after the announcement of an efficacious Ebola vaccine in the making. As Acting Chief Scientist at the FDA, Luciana Borio explained that in times of public health emergencies and crises

we humans have a very difficult time with the idea that when we are faced with a serious illness that we may not get a test drug that could potentially help . . . often not considering the potential harm. . . . Fear tends to prevail over logic but this very understandable human reaction is not in our best individual or common interest and that’s because most drugs that enter human clinical trials are not proven safe and effective¹⁶⁶

Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases, testified before the Committee on Foreign Affairs of the House of Representatives that ZMapp was administered to several Ebola patients for the first time as an experimental treatment—even though it was impossible to determine at the time whether the treatment was safe or effective.¹⁶⁷ Additionally, he referenced the work being done *at that time*—not in advance of using the experimental treatment—to advance testing to determine whether the medication was in fact safe or effective.¹⁶⁸ Chief Scientist Luciana Borio also availed the lack of credible scientific information for these experimental treatments when she too testified in front of the Committee, noting above all that

[t]he investigational vaccines and treatments for Ebola are in the earliest stages of development and have not been tested for safety or effectiveness in humans. Currently, there are only small amounts of some experimental products that have been manufactured for testing. This constrains our options for both properly assessing safety and efficacy of these investigational products in and making material available for therapeutic use outside of, a clinical trial (also known as expanded access) to respond to the epidemic.¹⁶⁹

What may seem simply like a desperate measure for a desperate time sparked the

¹⁶⁶ *You May Hold the Cure*, TEDx UTAH ST. UNIV., <http://tedx.usu.edu/portfolio-items/luciana-borio/> (last visited Apr. 25, 2017).

¹⁶⁷ *Global Efforts to Fight Ebola: Hearing Before the Subcomm. on Afr., Global Health, Global Hum. Rts., & Int’l Orgs. and H. Comm on Foreign Aff.*, 113th Cong., 32 (2014) (statement of Anthony Fauci, Dir. of the Nat’l Inst. of Allergy and Infectious Diseases).

¹⁶⁸ *Id.*

¹⁶⁹ *Id.* (statement of Luciana Borio, Dir., Office of Counterterrorism and Emerging Threats, Office of the Chief Scientist, U.S. Food & Drug Admin., U.S. Dep’t of Health & Human Servs.).

ethical and scientific debate that has ensued since the crisis about the appropriate use of experimental drugs. As Hodge reminded the regulatory community, “[u]nleashing a harmful experimental drug (or vaccine) on populations facing the threat of Ebola may result in a legal and ethical firestorm, even if such harms were unperceived or unintended.”¹⁷⁰

Ethical considerations in this kind of public health crisis are two-fold. First, there is the continuing question even in times of normalcy as to whether experimental treatments should be given outside of clinical trials. Second, there is the question of whether it is feasible to allow humans to receive experimental treatments when clinical trials are beyond difficult to develop and lack of a controlled method of delivering the treatment could lead to disaster. These two questions incorporate the same balance of interests that have plagued the criticism of the FDA throughout the past thirty years. It is hard to argue against those who advocated to provide ZMapp and other experimental drugs to those dying from the Ebola virus—despite the lack of scientific information and knowledge of the risks. It is a natural human reaction to save those who are facing death rather than to allow their health to diminish. It, however, is still imperative that physicians and health care workers do so responsibly and with the help of regulation.

It is not the idea of conducting clinical trials or providing care to those facing an epidemic—or even curbing rules in times of emergency—with which scholars of all backgrounds take issue. The FDA’s Committee on Ethical and Scientific Issues in Studying the Safety of Approved Drugs noted,

[a] trial in which the risks to participants are not outweighed by the prospect of direct medical benefits to participants may be justifiable if a question of pressing public health importance cannot be properly answered without the conduct of the trial and if other conditions intended to safeguard the rights and interests of participants are satisfied.¹⁷¹

Clearly the FDA has rationalized instances in which trials are necessarily conducted if the public health importance requires it. Rather, it is the extent to which those rules are curbed and the abandonment of law’s delegation in times of emergency that unnerves those who have been part of the academic dialogue. As explained in Section I, the FDA has empowered itself in times of health crises to make decisions based on extremely little information. The FDA has been pressured time and time again to loosen its regulatory grip on the drug approval process. The FDA has been bullied into continuing to offer more increased access to medicines in times when the FDA would normally take years to adequately assess the drug’s safety and effectiveness, as mandated by law. When will patients be satisfied with the FDA’s role in controlling access to medicine? There will come a time where exceptions will outgrow the rules, when the FDA’s role is moot and no longer provides what it has been mandated to do by law:

¹⁷⁰ See Hodge, Jr., *supra* note 147, at 48.

¹⁷¹ COMMITTEE ON ETHICAL & SCI. ISSUES IN STUDYING THE SAFETY OF APPROVED DRUGS, ETHICAL ISSUES IN STUDYING THE SAFETY OF APPROVED DRUGS: A LETTER REPORT 11 (2010).

develop safe and effective new medicines. This trend is not only detrimental in normal times but it is also threatening in times of public health emergency as demonstrated by points made throughout the debate on compassionate use during the Ebola outbreak.

As the director of the National Institute of Allergy and Infectious Diseases testified before Congress, “[i]t is important to balance the urgency to deploy investigational medical countermeasures in an emergency such as the current Ebola outbreak with the need to ensure the maximal safety and to determine the efficacy of candidate drugs and vaccines for Ebola.”¹⁷² Yet, experimental drugs were employed impulsively with very little information on their safety and effectiveness, without any protocol to determine in such an emergency which scientific factors health officials were required to consider before use and which factors could wait to be discovered, and without any information as to side effects or pain.¹⁷³ Moreover, critics pushed the FDA to review drug applications in a matter of days rather than in a matter of months or even years.¹⁷⁴ The FDA has admitted to “bending” its rules in order to deal with the crisis, leaving some critics to wonder how safe their decisions actually were.¹⁷⁵ It begs the question of whether the FDA would have been able to pursue the same course of action if the crisis had happened in the U.S.¹⁷⁶

The issues with using experimental treatment in emergency situations such as Ebola continue to compound. Aside from the issues within the regulatory body’s decision making, there is simply a lack of information on the ground to best evaluate risks and benefits to patients.

Triage in scarce, established treatments is often possible when the natural history of the disease, medication effects, and status of the patient are taken into account. Yet, with experimental treatments, few of these factors can be determined vis-à-vis the effect of the drug—one loses the ability to discern the patients likely to benefit. With this inability to properly triage, the consequences of misuse may be 3-fold: poorer outcomes for the “treated” severely ill population, missed opportunities for realistically treatable patients, and a possible induction of resistance that bears worse outcomes for future patients.¹⁷⁷

The drug-testing regulations put forth by the FDA are meant to define the safety

¹⁷² *Global Efforts to Fight Ebola: Hearing Before the Subcomm. on Afr., Global Health, Global Hum. Rts., & Int’l Orgs. and H. Comm on Foreign Aff.*, 113th Cong., 36 (2014) (statement of Anthony Fauci, Dir. of the Nat’l Inst. of Allergy and Infectious Diseases).

¹⁷³ Marina Koren, *Ebola Has the FDA Working Overtime on Reviewing Experimental Drugs*, NAT’L J., (Oct. 16, 2014), <https://www.nationaljournal.com/health-care/2014/10/16/ebola-has-fda-working-overtime-reviewing-experimental-drugs>.

¹⁷⁴ *Id.* (emphasis added).

¹⁷⁵ See Koren, *supra* note 173 (“The FDA has had to bend the rules in its review of applications for new drugs, too. Most of the drugs that the FDA has approved for emergency use against Ebola have not even reached clinical trials yet.”).

¹⁷⁶ *Id.* (“But in the mean-time, Borio said, if a patient is dying of Ebola in the U.S., the FDA has to change its rules.”).

¹⁷⁷ Andrew Hantel & Christopher Olusola Olopade, *Drug and Vaccine Access in the Ebola Epidemic: Advising Caution in Compassionate Use*, 162 ANNALS OF INTERNAL MED. 141 (2015).

of new drugs' use while also developing an adequate understanding of their nature before the average consumer may use them. Yet, using experimental drugs bypasses these requirements; therefore, there is no evidence to support the drug's use before human beings receive it. It may be one thing to allow this practice in a controlled situation with physician approval, a complete evaluation of the patient's illness and prognosis, and a discussion of available options—as takes place under normal compassionate use or expanded access procedures. Imagine employing such a practice on a widespread scale in the middle of an epidemic.¹⁷⁸ Patients do not get the information they need nor are they able to evaluate their situation properly to understand the risks and benefits to them and the society using these experimental treatments.

The concerns go beyond those of actually risking a patient's health, however. There is agreement across the board that the gold standard in drug development is randomized and controlled clinical trials. No expert would dispute the fact that to properly encourage safe and effective drug development, the drug approval process involving stages of clinical trials must be utilized. In the case of Ebola, no existing treatment existed and the only alternatives were experimental drugs that had not yet gone through the drug approval process. Regulators were only left with the choice to conduct clinical trials in the midst of the crisis in order to at least obtain information that could lead to drug approval and mitigation of the ongoing epidemic in the future.

Even when a clinical trial is set up in the middle of an epidemic, there are practical issues that act as deterrents in certain circumstances from setting up clinical trials in a time of crisis. As *Foreign Affairs* reports, “[r]outine health care had collapsed in all three affected countries, and even minor medical complications, in childbirth, car accidents, and simple falls, were proving lethal.”¹⁷⁹ Advanced healthcare did not exist in the countries in which the disease was spreading and this will not be unique to the Ebola outbreak. Additionally, the volunteer physicians were dealing with a population of patients with an entirely different culture and understanding of health-related concepts. Issues with adequately informing patients about the disease and the experimental nature of the treatment ensue. “[P]hysicians’ ability to meaningfully inform vulnerable populations is overestimated. The belief that informed consent is understood by patients naive to advanced health care, especially in an epidemic, is cavalier.”¹⁸⁰

As a result, there is essentially no such thing as meaningful informed consent—the most important legal and ethical component of using experimental drugs. First, a patient suffering from Ebola cannot possibly be able to rationally assess the benefits and risks associated with receiving the unapproved drug. Second, physicians operated, and operate in other outbreaks, in countries with very little resources where hundreds of cases erupt each day. Imagine the chaos ensuing as physicians attempt to treat as quickly as possible, and the lack of

¹⁷⁸ Nancy Kass, *Ebola, Ethics, and Public Health: What Next?*, 161 ANNALS OF INTERNAL MED. 744 (2014) (“The threshold for determining that an individual patient receive access to a highly experimental drug on a compassionate-use basis does, and *should*, differ from the threshold for rolling out a treatment program to an entire community, even one facing a life-threatening epidemic.”).

¹⁷⁹ See Garrett, *supra* note 165.

¹⁸⁰ See Hantel & Olopade, *supra* note 177, at 141.

understanding and trust a patient must have in this dire situation. Using experimental drugs is technically ethical, but that presupposes the ability to obtain informed consent and perform an evaluation of the risks and benefits to the patient, both of which could not adequately come to fruition in the Ebola epidemic and likely will not come to fruition in a future outbreak.¹⁸¹ Comparing this situation in the Ebola crisis to the four ultimate goals and requirements of the law enabling the FDA, there is no question that medical authorities were asked to do more than slightly “bend” the rules.

The critical ethical dilemma that has been debated most often is: who should receive the experimental drug that is only available in limited supply? Critics took issue with the fact that two Americans received the doses as opposed to native African patients.¹⁸² There is not, and never will be, a right answer to this question. So how should doctors deal with this question in increased magnitude when a clinical trial is supposed to have a control group? “[H]ow can researchers justify a control group in the first place, given a mortality rate approaching 60 percent?”¹⁸³ Yet without such a controlled group and an actual clinical, randomized trial, patients who survive from the treatment do not actually tell us anything about the safety or efficacy of the medication.¹⁸⁴ It is the unfortunate reality that using experimental drugs in an epidemic and “[a]llowing considerations of rescue rather than scientific hypotheses to drive use of novel agents . . . risks compromising the acquisition of knowledge needed to clarify their role in the next epidemic and ultimately to maximize benefits for patients.”¹⁸⁵

B. *The Recent Results from the rVSV-ZEBOV Trial and the Lessons Learned*

The debate is no different after the release of a report in *The Lancet* that details the trial conducted by researchers on a new drug rVSV-ZEBOV at the latter half of the Ebola epidemic. The vaccine and the trials leading up to this point have been praised, not only for their efficacy but also for the ethical consideration that prompted the design of the trial as well as its success. A testament to the effectiveness of global collaboration, attention, and resources, the vaccine was tested using a ring vaccination strategy in “record time—just two years.”¹⁸⁶ Because of the results, the vaccine awaits official approval by the FDA and the WHO in 2018.¹⁸⁷ While the new vaccine presents an answer for future populations battling the horrific disease, many scientists are still hesitant to praise the work done during an epidemic. Scientists wrote in *The Lancet* report that “[a]

¹⁸¹ See George Annas, *Annas on Ebola Treatment: Ethical Issues at Heart of Debate over Experimental Drug Use*, BOSTON U. (Aug. 12, 2014), <http://www.bu.edu/sph/2014/08/12/annas-on-ebola-treatment-ethical-issues-at-heart-of-debate-over-experimental-drug-use/>; see also Kupferschmidt, *supra* note 9.

¹⁸² See Annas, *supra* note 181.

¹⁸³ Sullivan, *supra* note 162, at 2, 5.

¹⁸⁴ *Id.*

¹⁸⁵ *Id.*

¹⁸⁶ Michaelleen Doucleff, *First Ebola Vaccine Likely to Stop the Next Outbreak*, NAT'L PUB. RADIO (Dec. 23, 2016), <http://www.npr.org/sections/goatsandsoda/2016/12/22/506600875/first-ebola-vaccine-likely-to-stop-the-next-outbreak>.

¹⁸⁷ *Id.*

devastating outbreak of Ebola virus disease is clearly not the ideal situation for doing a vaccine trial.”¹⁸⁸

In designing clinical trials—and particularly in emergency situations such as these—the same ethical questions and trade-offs continue to arise:

Early scholars . . . clearly recognized that there was often an inherent trade-off between ethical requirements and scientific rigor. The means to resolving the trade-off came not necessarily through insisting on validity over ethics, but rather in reaching consensus on what is at stake. If a significant reduction in mortality might be gained from an experimental treatment, then health care providers need not be absolutely certain that it is highly effective before prescribing it In other situations, ethical and epistemic considerations may point in the same direction.¹⁸⁹

Scientists sought to responsibly wrestle with this trade-off when they designed the trial of rVSV-ZEBOV. They chose what is called the “ring vaccination strategy”—the type of trial used to eradicate smallpox. In so choosing, ethical considerations played an important role. Ring vaccination is defined as follows: an infection control measure that vaccinates clusters of individuals with the experimental treatment who are at high risk for disease infection based on their connection with a known case of a disease.¹⁹⁰ The ring vaccination strategy was thought to be ethically superior to other trial designs, specifically because it entailed all participants receiving a dose of the treatment as opposed to placebo-controlled trials, in which a random group of individuals received a placebo instead. The placebo approach is often ridiculed in a particular instance like an epidemic because it deprives a certain group of treatment. Oftentimes there is risk for bias in choosing groups, which receive treatment as well. Additionally, the ring vaccination strategy prioritized those candidates who were at the highest risk of contracting disease. Randomization was also involved, as certain individuals received the vaccine after twenty-one days and others immediately.¹⁹¹ The trial team carefully planned and executed ways to ensure that participants were monitored, educated, and had consented prior to participation. The study team gave infection prevention advice, created a

¹⁸⁸ Ana Maria Henao-Restrepo et al., *Efficacy and Effectiveness of an rVSV-vectorized Vaccine in Preventing Ebola Virus Disease: Final Results From the Guinea Ring Vaccination, Open-Label, Cluster-Randomised Trial (Ebola Ça Suffit!)*, THE LANCET 11 (Dec. 22, 2016), [http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(16\)32621-6.pdf](http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(16)32621-6.pdf).

¹⁸⁹ Ross Upshur & Jonathan Fuller, *Randomized Controlled Trials in the West African Ebola Virus Outbreak*, 13 CLINICAL TRIALS 10 (Jan. 14, 2016), <http://journals.sagepub.com/doi/pdf/10.1177/1740774515617754>.

¹⁹⁰ See Rid & Miller, *supra* note 11.

¹⁹¹ See *id.* at 433; see also Morenike Oluwatoyin Folayan et al., *Ebola Vaccine Development Plan: Ethics, Concerns, and Proposed Measures*, (Feb. 8, 2016), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4746804> (“A key feature of the *Ebola ça Suffit* design is that it did not have a placebo arm. Also, it prioritized access to the vaccine candidate for all people at highest risk. . . . The randomization to immediate vaccination compared with delayed vaccination, using carefully calibrated timing, meets the principle of distributive justice while still allowing experimental comparison between groups.”).

Guinean Ebola response team locally in the community, which was responsible for daily home visits, and conducted post-vaccination visits as well.¹⁹²

Some officials, however, continue to be hesitant:

The new vaccine is “a step in the right direction but not the ultimate solution” said Dr. Gary J. Nabel, chief scientific officer for global health research at the Sanofi pharmaceutical company A randomized clinical trial involving tens of thousands of subjects is the preferred way to test any vaccine, he noted.¹⁹³

It also still holds true that in communities like the one used for the trial, the sense of urgency that accompany any health crisis in addition to a lack of community education will increase risks of therapeutic misconceptions.¹⁹⁴ Annette Rid and Franklin G. Miller also raise ethical concerns about the process. They commented, “[t]he prevailing ethical confusion about the trial design raises concern that its broad acceptance rests on false beliefs and expectations.”¹⁹⁵ Aside from providing treatment that had only passed Phase I, and later Phase II, of clinical trials, Rid and Miller noted that though the study was praised for its alternative design from a placebo-controlled trial, the clusters which received delayed treatment were no better off than those that would have otherwise received a placebo.¹⁹⁶ “Sponsors, investigators, and commentators tended to portray the trial as an ethically preferable alternative to a placebo-controlled trial without clearly acknowledging or downplaying the fact that it, too, withheld the study vaccine for a period of time.”¹⁹⁷ Even scientists involved in the study admitted in *The Lancet* that “the healthcare system in Guinea was strained, potential trial participants were worried about a candidate vaccine made by foreign people, and the Ebola virus disease response teams were facing security issues.”¹⁹⁸

The takeaway from this experience is, namely, that despite safeguards, experimental treatment and public health crises pose reoccurring issues in the quest for effective and safe medication. There is a trade-off between scientific advancement and ethical perfection—between saving lives and ensuring an adequate clinical testing environment. What this latest study shows is that with the right community collaboration, the right emphasis on ethical considerations, and the prioritization of those most at risk, there may be some prayer of coming to a point of compromise.¹⁹⁹

¹⁹² See Rid & Miller, *supra* note 11, at 433.

¹⁹³ Donald G. McNeil, *New Ebola Vaccine Gives 100 Percent Protection*, N.Y. TIMES (Dec. 22, 2016), <https://www.nytimes.com/2016/12/22/health/ebola-vaccine.html>.

¹⁹⁴ See, e.g., Folyan, *supra* note 179.

¹⁹⁵ Rid & Miller, *supra* note 11, at 432.

¹⁹⁶ *Id.*, at 433.

¹⁹⁷ See *id.* at 434.

¹⁹⁸ See Henao-Restrepo, *supra* note 188, at 11.

¹⁹⁹ *Id.* Henao-Restrepo explains:

Therefore, we made a deliberate decision to tailor the logistical implementation of the trial to local conditions. The close collaboration with, and the support from, the Guinean National Authorities was a catalyzing factor in the successful implementation of the trial. In addition, we made efforts to ensure full ownership and understanding by national authorities and communities through active community

Observing a public health crisis like Ebola requires us to think back to those ultimate questions: does the regulatory process really give terminally ill patients a death sentence? Can we ever resolve the natural tension between the interests of terminally ill patients who see their death imminently awaiting—without a cure—and the general population who has a significant interest in seeing the FDA drug approval process work for the future of drug development? The Ebola outbreak shows the growing concerns with the use of experimental drugs and mandates the continuing presence of the FDA and a robust regulatory framework that demands safety and efficacy as well as increased information to patients, despite the costs.

IV. THE FUTURE OF DRUG REGULATION

Although the Ebola epidemic resulted in the loss of thousands of lives and led the world to scramble to respond to a crisis it was wholly unprepared to deal with—much like the AIDS crisis—it has positively impacted the role of government agencies. It has also shaped emergency preparedness and the ability of the U.S.—and the world—to adequately counter another public health emergency of its kind. The Ebola epidemic has also been a catalyst for change and medical innovation. “Ultimately, only the huge, explosive 2014 outbreak . . . provided the political and economic drive to make an effective vaccine.”²⁰⁰ Since the apex of the Ebola crisis, the FDA and its Commissioner, Luciana Borio, have also made an adamant push to provide more resources and information to advocate for clinical trials and the development of sufficient clinical trial designs. To this end, the FDA has been accepting input since December of 2015 on designing clinical trials in emerging infectious diseases.²⁰¹ In the summer of 2016, Merck announced its Breakthrough Therapy Designation from the FDA for the investigational Ebola Zaire Vaccine, which will expedite its development and review.²⁰² The FDA has also published additional and updated guidance geared towards dealing with another potential Ebola outbreak.²⁰³ The 2014 Ebola crisis has sparked the creation of multiple training programs and educational opportunities for our hospital system and health care workers so that they may have the proper understanding of how to respond to such an infectious disease.²⁰⁴ Additionally, protocols, including a single common clinical trial protocol, and other guidance materials have been created to streamline emergency responses

engagement and individual consent. Despite the challenges, our team was able to do the trial in compliance with good clinical practice and international standards.

Id.

²⁰⁰ Donald G. McNeil, Jr., *New Ebola Vaccine Gives 100 Percent Protection*, N.Y. TIMES (Dec. 22, 2016), https://www.nytimes.com/2016/12/22/health/ebola-vaccine.html?_r=0.

²⁰¹ *Ebola Response Updates from FDA*, *supra* note 150.

²⁰² *Merck Receives Breakthrough Therapy Designation from FDA and PRIME Status from EMA for Investigational Ebola Zaire Vaccine*, YAHOO (July 25, 2016), <http://finance.yahoo.com/news/merck-receives-breakthrough-therapy-designation-120000201.html>.

²⁰³ *Id.*

²⁰⁴ U.S. Dep’t of Health & Human Serv., *Ebola Preparedness in the U.S.—One Year Later*, YOUTUBE (Oct. 6, 2015), <https://www.youtube.com/watch?v=Ctp-C1bkEjw> (last visited Apr. 25, 2017).

and preparedness for the future.²⁰⁵ In February 2015, the FDA disclosed revisions to its process for compassionate use applications.²⁰⁶ The process will now only require one form and thirty days. FDA officials may even grant expanded access over the phone.²⁰⁷ Generally, between the efforts of the FDA, the U.S. Department of Health and Human Services, the Center for Disease Control and Prevention, and others, clinical trials have successfully been initiated and nearly completed, showing officially that with the help of these regulatory bodies, Ebola is in fact a survivable disease.²⁰⁸ The heads of these agencies have agreed that the U.S. is much safer and better prepared than it was before the crisis.²⁰⁹

Yet outside of the epidemic context and public health emergency context, terminally ill patients and other patients similarly situated criticize the FDA and advocate access to unproven medicines. Despite the FDA approving 5,816 of the 5,849 expanded access applications it has received in the last four years, critics argue that the FDA's process is overly cumbersome and slow.²¹⁰ Patients advocate for increased access to experimental drugs, despite the years of revisions to regulation and the increased number of exceptions and exemptions from the normal rules. The "Right to Try" debate has ensued, existing alongside the Ebola epidemic and persisting over the last year. In fact, the alarming fact is that in over twenty-four states in America, "Right to Try" legislation has been proposed, and in many instances passed by state legislatures, and which threaten to have innumerable and unknown consequences for the use of experimental drugs and the role of the FDA. Indeed, it seems to many experts that "Right to Try" advocates, having begun their plight for drug reform during and after the *Abigail Alliance* litigation, wish to get rid of FDA oversight as well as the FDA's role in providing earlier access to experimental treatment. "Access advocates criticize the FDA's substantive standards governing patient access, but what they really object to is the review requirement itself."²¹¹ The movement could result in the removal of powerful drugs, without any evidence of safety or efficacy, from FDA jurisdiction.²¹²

Most importantly, advocates claim that this legislative movement will increase the number of patients who will access investigational products.²¹³ Remember, this number is unknown and could certainly be immeasurable since in most instances the conversation for now has involved only the "terminally ill" patients. At the same time, patients who are not terminally ill but who suffer with no relief from existing treatments for their ailments—or face diseases without a

²⁰⁵ *Id.*

²⁰⁶ Peter Lurie, *A Big Step to Help the Patients the Most in Need*, FOOD & DRUG ADMIN. (Feb. 4, 2015), <https://blogs.fda.gov/fdavoices/index.php/2015/02/a-big-step-to-help-the-patients-most-in-need/>.

²⁰⁷ Y. Tony Yang, "Right to Try" Legislation: Progress or Peril?, 33 J. CLINICAL ONCOLOGY 1 (2015).

²⁰⁸ See U.S. Dep't of Health & Human Serv., *supra* note 204.

²⁰⁹ *Id.*

²¹⁰ See Yang, *supra* note 207, at 1.

²¹¹ Rebecca Dresser, *The "Right to Try" Investigational Drugs: Science and Stories in the Access Debate*, 2 TEX. L. REV. 1632, 1642 (2015) (article within Symposium *Science Challenges for Law and Policy* (2015)) <http://ssrn.com/abstract=2628679>.

²¹² Jann Bellamy, *The Illusions of "Right to try" Laws*, SCIENCEBASEDMEDICINE.ORG (Mar. 6, 2014), <https://www.sciencebasedmedicine.org/the-illusions-of-right-to-try-laws/>.

²¹³ Alison Bateman-House et al., *Right-to-Try Laws: Hope, Hype, and Unintended Consequences*, 163 ANNALS OF INTERNAL MED. 796 (2015).

cure—will also be seeking to try experimental drugs.²¹⁴ In other words, this movement could have undefined negative consequences for patients in general. We are left with the ultimate question that we faced during the AIDS crisis and continue to face as regulators and citizens battle over the proper use and availability of unapproved drugs: “whether the gain in providing the terminally ill with a slim chance at prolonging life is worth endangering a process designed to ensure the public health and the development of safe, effective medicines.”²¹⁵ We may indeed never have an answer, but certainly ridding the issue of regulatory oversight and diminishing the power of the FDA’s jurisdiction and regulatory framework are not an answer.

The Ebola crisis and all that has been improved and created since the beginning of the public health crisis, as well as our experiences throughout the AIDS crisis should, instead of creating disdain and criticism against the idea of regulatory bodies in this space, highlight two important observations. It is clear from the testimonials of U.S. commissioners in the FDA and U.S. Department of Health and Human Services, among others, that the Ebola crisis showed the harm and ineffectiveness of not having these bodies involved from the beginning, the benefit of using such regulatory bodies and frameworks effectively in addition to the importance of international regulatory cooperation.

Let us use Ebola not as a ground for criticism of the FDA, its approval process and the regulation of using unapproved drugs, but rather as an instance to show how differently the crisis could have been handled with the efforts that were in place at the end, had they been present from the beginning. Indeed, let us see the Ebola outbreak as an instance to think about how differently the crisis would have been handled absent any regulatory body to ensure that human rights were abided by, patients were educated, and treatments were adequately administered. It can be argued that despite the legal and ethical issues that were present, the regulatory bodies at least attempted to safeguard patient rights, something that would have been wholly absent if the crisis was governed merely by the natural human reaction.

The bottom line is that criticism of “Right to Try” advocates is being misplaced. The reasons for clinical trials, the importance of oversight, and the jurisdiction of the FDA—if practiced wholly and effectively—is to prevent the ethical risks highlighted above in Part III, Section A and allow the use of experimental treatments to be somewhat tolerable.

As Dr. Arthur Caplan and Dr. Alison Bateman-House suggest, the “Right to Try” debate and the resulting legislation is simply an understandable “impulse to rescue individual patients facing dire diseases”²¹⁶ Even though the FDA is mandated in the U.S. to ensure the safety and efficacy of drugs that enter the market, healthcare providers have a duty not to harm patients and pharmaceutical companies insist that the FDA “plays a vital role in both drug development and patient protection.” The drug approval process is endangered at the behest of terminally ill patients and other advocates who demand to have FDA review of

²¹⁴ Arthur L. Caplan & Alison Bateman-House, Editorial, *Should Patients in Need be Given Access to Experimental Drugs?*, 16 EXPERT OPINION ON PHARMACOTHERAPY 1275, 1276 (2015).

²¹⁵ Yang, *supra* note 207, at 1.

²¹⁶ See Caplan & Bateman-House, *supra* note 214, at 1275.

requests for access to investigational drugs be dispensed with and wish to access unapproved drugs outside of clinical trials. Again we battle the unresolved balance: “an individual patient’s very understandable desire to try to extend his or her life versus the orderly and efficient functioning of a drug development and clinical trial system that benefits much larger numbers of patients.”²¹⁷ Except this time we threaten to dissolve the FDA’s jurisdiction and threaten the safety and health of those who, without understanding the risks involved, will choose to ignore the risks and receive experimental treatments unfit for human consumption.

To the advocates who ask, “What’s the harm?” in allowing unrestricted access, one expert responded, “If there’s anything worse than dying of a terminal illness, it’s dying of a terminal illness and suffering unnecessary complications or pain for no benefit and having to pay for the medications causing the complications yourself.”²¹⁸

The reforms these patients wish to enact are actually harmful on multiple levels: to the pharmaceutical industry, to patient well-being, and to drug development—not to mention many of the difficult points raised earlier in this Note. Generally speaking, the “Right to Try” laws that have been passed in states across the country permit terminally ill patients to request access to investigational drugs that have yet to be approved by the FDA.²¹⁹ These laws create issues with inequitable access, lack of appropriate oversight, and informed consent. Since the definition of the term “terminally ill” is unclear and can vary, it neglects to include patients who will not suffer from death but have nevertheless exhausted all existing treatment options. Moreover, patients hope to receive experimental treatments without truly appreciating the potential health risks they could suffer should the treatment be ineffective. “The overwhelming majority of drugs that are found to have manageable toxicity in phase I clinical trials do not subsequently receive FDA approval for marketing [In the end,] the terminally ill could potentially be shortening what little time they have left.”²²⁰ Additionally, there is a lack of oversight that occurs since there are no specified qualifications for the health care providers or physicians providing the assessments. Patients are not guaranteed an optimum evaluation of their condition or their likely benefit from the experimental treatment. No rules are in place “to stop the creation of research mills in which interventions with no scientific evidence are promoted as possible cures, which has happened in the field of stem-cell based treatments.”²²¹

Furthermore, these laws do not adequately provide for rules requiring informed consent nor do they realistically lead to a patient’s sufficient understanding of the best *and* the worst outcomes that could come from the use of

²¹⁷ *Id.*

²¹⁸ Dresser, *supra* note 211, at 1643.

²¹⁹ See Caplan & Bateman-House, *supra* note 214, at 1277.

²²⁰ See Yang, *supra* note 207, at 2.

²²¹ See Bateman-House et al., *supra* note 197, at 796.

the experimental drugs. The drugs used as a result of these laws are drugs that have only passed through Phase I testing. In other words, they have only been tested for toxicity and adequate doses, not for safety or efficacy.²²² The laws “are patently untruthful in stating that patients will be given a description of the ‘potentially best and worst outcomes of using the investigational drug’ and a ‘realistic description of the most likely outcomes.’”²²³ This may also lead patients to bypass opportunities for joining controlled clinical trials and instead be tempted to go with the falsehood of trying the “get-well-quick” option of receiving these unapproved drugs outside of a clinical trial with oversight.²²⁴ Over time, this could slow down the approval process and thus lead to slower development of new drugs.²²⁵

There are additional risks from which drug companies and the pharmaceutical industry could suffer. The biggest issue in the new “right to try” legislation is that it does not require drug manufacturers and sponsors to comply and grant access to medications that have only passed Phase I clinical trials. To most, the financial incentives will not be adequate enough for sponsors to allow expansive access to drugs in development that this new legislation seeks to provide.²²⁶ Adverse effects patients may suffer from such things as damaging toxicity levels could negatively impact a drug company’s ability to subsequently receive FDA approval.²²⁷ Such a problem will not be mitigated by the fact that doctors and drug companies are shielded from tort liability by “right to try legislation” legislation.²²⁸ If anything, drug companies would still be advised by legal professionals to go through the FDA approval process when given the choice.²²⁹ Thus, legislation that patients believe will grant them early access to drugs they would otherwise not receive will dissuade drug companies from making them available.

What patients truly call for is deregulation in this area. They want to gain access to medicines outside of the FDA’s jurisdiction, despite the mandates the FDA has received by law. Bureaucracy may be cumbersome, protocols may at times seem useless, but deregulation of the use of pharmaceutical products should be looked at differently. Overall, as case studies abroad have found, the deregulation of this industry has only led to unintended negative consequences.

[M]edicines deregulation triggered two effects: (i) it gave rise to some level of distrust towards cheaper alternatives to branded products, hence raised average medicines prices which in turn reduced access, and (ii) it reduced product surveillance, in turn leading to a lowering of the average quality of medicines. Therefore, we suggest that medicines deregulation can exert

²²² See Bellamy, *supra* note 212.

²²³ *Id.*

²²⁴ See *id.*

²²⁵ See Yang, *supra* note 207, at 2.

²²⁶ *Id.*

²²⁷ *Id.*

²²⁸ See Sam Adriance, *Fighting for the “Right to Try” Unapproved Drugs: Law as Persuasion*, 124 YALE L.J.F. 148, 150 (2014).

²²⁹ See *id.* at 154.

detrimental effects by eroding trust in the quality of local products to the benefit of international companies.²³⁰

CONCLUSION

Observing the debate over experimental drugs throughout the AIDS crisis, the Ebola outbreak, and the “Right to Try” movement, one comes to many of the same conclusions. The balance of interests between the terminally ill who wish to see increased access to unapproved medicines, the general public who has an interest in preserving the drug approval process, and the FDA who has been mandated by law to safeguard the safety of the general public creates tension that will continue to go unresolved. The use of unapproved drugs is in and of itself controversial but using them in the midst of a public health crisis involving populations without adequate health systems or understanding of healthcare is that much more risky. There is something about using drugs that have only been tested on monkeys that is disturbing, whether or not the patients are terminally ill. There is something legally unsound about “bending the rules” to create more exceptions to rules that preserve the safety of the public health. There is also something immensely frustrating about an ethical balance that will never be resolved or further justified, even in an epidemic.

Critics of the FDA have persisted for years, pointing to the sluggishness of the drug approval process and the rights they think they own as citizens to personal autonomy in healthcare decisions—including access to any treatment that may be in existence, even if untested. These criticisms, however, are in many instances without evidence. The same research process and drug development process that patients and physicians criticize as overly costly and cumbersome is the same process that cures cancer, finds cures to fatal diseases, and makes up a large amount of industry in the U.S. It is the same process that incentivizes drug developers to take risks to continue work and preserves the safety of the public health. To that end, criticism of the FDA is misplaced.

The lack of a cure or treatment options for certain diseases is not so much the fault of the FDA. Take Ebola, for example. If there is any criticism to be warranted, it should be pointed at the fact that the outbreak was resolved through the last minute scrambling of international organizations that should have had emergency protocols already in place and should have been cooperating on exchanges of information and drug development in times of normalcy. The FDA should receive the increased funding and manpower it deserves so that their existing framework can be carried out more effectively, not eradicated. Drug manufacturers should receive increased incentives to develop treatment options that, under normal circumstances, may not be the most lucrative to manufacture.

Throughout the past twenty to thirty years in particular, criticisms and public health events have changed the nature of the regulatory framework in response.

²³⁰ See Joan Costa Font, *Deregulation and Access to Medicines: the Peruvian Experience*, 28 J. INT'L DEV. 997, 998–99 (2016).

Out of the AIDS crisis, expanded access exceptions to the normal drug approval process were born numerous—that continue to persist today. Observing the ways in which the FDA has responded in past years to improve the efficacy of their review, and the ways in which the FDA collaborated with international institutions over the last three years, we see again the positive responses to a momentous public health event in our history. With the large number of exceptions to the normal drug approval process providing increased access, however, it is difficult to envision how the regulatory framework for the use of experimental drugs could possibly be liberalized any more. If the cycle continues as it has in the past after the AIDS crisis, however, we can expect criticisms and changes to occur nonetheless. The “Right to Try” movement provides the opportunity for change, though not for the best. Patients continue to advocate for routes outside of the FDA regulatory process and threaten to diminish the strength of the FDA’s presence and to remove many new, unapproved drugs from the FDA’s jurisdiction. This can only lead to irresponsible uses of untested drugs and decreased growth in drug development. This sounds less like a death sentence for the terminally ill and for the general public and their interest in sound medicine. It would truly be in the best interests of the public to continue to preserve the FDA’s regulatory role and mitigate any or all ethical risks associated with responding to terminal illness and infectious disease. It is imperative to separate our natural human reactions from what the rational and appropriate course of action necessitates. Desperate times should not always call for desperate measures.