

The Statutory Limits of Compassion: Can Treatment INDs Provide Meaningful Access to Investigational Drugs for the Terminally Ill?

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INTRODUCTION

For thirty-four people suffering from the degenerative effects of Parkinson's disease, the drug sponsor Amgen held an alternative and hopefully miraculous treatment: glial cell line-derived neutropic factor ("GDNF").¹ Before GDNF could be made available to the public, however, the Food and Drug Administration ("FDA") required Amgen to conduct clinical trials to investigate the drug's safety and effectiveness.² All thirty-four Parkinson's patients qualified for the clinical investigation, and, in order to participate, underwent surgeries to implant medical devices that would facilitate the release of the drug.³ For the first six months of the

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¹ *Abney v. Amgen*, 443 F.3d 540, 543-44 (6th Cir. 2006); *Suthers v. Amgen*, 441 F. Supp. 2d 478, 481 (S.D.N.Y. 2006).

² *Id.*

³ Compl. and Jury Trial Demand at 6, ¶ 30, *Suthers v. Amgen*, 441 F. Supp. 2d 478 (S.D.N.Y. 2006) (No. 05CV04158) [hereinafter *Suthers* Complaint]. The surgery involved implanting a pump into the abdomen and "threading" a catheter under the skin to the brain, where holes were drilled in the skull to facilitate the injection of the drug. *Id.*

investigation, which took the form of a control group, some of these research subjects received only a placebo.⁴ In April 2004, however, Amgen converted the investigation to an open label study,⁵ during which the conditions of the patients who originally received the placebo substantially improved.⁶ For example, Robert Suthers, experienced physical, cognitive, and emotional improvements and, furthermore, was able to walk up to two miles per day while receiving GDNF.⁷

But in August 2004, Amgen noted that its continued animal testing revealed that the human research subjects may have been at risk for brain lesions or an acceleration in the disease's progression and concluded that the human studies should be terminated.⁸ The FDA agreed and Amgen stopped providing the participants with GDNF.⁹ The thirty-four clinical trial participants attempted to continue their access to the unapproved drug through a exception in the normal drug approval process popularly known as "compassionate use."¹⁰ In order to benefit from "compassionate use" and use an experimental drug, a patient must first receive permission from the FDA.¹¹ The FDA has promulgated several exceptions¹² for patients suffering from serious and life-threatening diseases that allow them to access *unapproved* experimental drugs prior to the official grant of marketing approval.¹³ These exceptions permit a patient to use an investigational new drug for treatment, rather than research, purposes before it has been approved for marketing by the FDA.¹⁴

Unfortunately, this exception allows patients only to "request" investigational drugs and does not compel the drug sponsor¹⁵ to provide the drug.¹⁶ Thus, a sponsor

⁴ *Id.* at 6, ¶ 33. The patients receiving the placebo during this time period did not report any benefit to their condition. *Id.*

⁵ In contrast to a clinical trial which uses placebos for a "control group," an open label study provides all patients with the experimental drug. *Abney*, 443 F.3d at 543. Counsel for Robert Suthers and his co-plaintiff Niwana Martin asserted that the effect of the drug during the open-label period was not the result of the placebo effect. *Suthers Complaint*, *supra* note 3, at 6, ¶ 34.

⁶ *Suthers Complaint*, *supra* note 3, at 7, ¶ 40-41.

⁷ *Id.* at 7, ¶ 39-40.

⁸ *See id.* at 8, ¶ 48-49 (explaining that the Principle Investigators recorded cerebellum damage in monkeys who received the GDNF resulting in Amgen's termination of the human clinical trials).

⁹ *Abney*, 443 F.3d at 544-45; *Suthers*, 441 F. Supp. 2d at 480.

¹⁰ *See Abney*, 443 F.3d at 545 ("FDA stated that it would permit compassionate use of GDNF but left the decision up to Amgen."); *see also* Peter M. Currie, *Restricting Access to Unapproved Drugs: A Compelling Government Interest?*, 20 J.L. & HEALTH 309, 314 n.37 (2007) (acknowledging the case-by-case review available for individuals who seek to invoke compassionate use). This exemption is also called the "expanded access protocol," 21 U.S.C. § 360bbb (2006), and "treatment IND," 21 C.F.R. § 312.34 (2007).

¹¹ 21 C.F.R. § 212.34.

¹² For a discussion of the exceptions to the normal approval process, *see* Part II.A.

¹³ *Id.* FDA derives its authority to control marketing approval of drugs, from the Food, Drug, and Cosmetic Act. 21 U.S.C. § 393 (2006). In 1997, Congress amended this Act to allow patients with "life-threatening" or "seriously debilitating" diseases to request unapproved experimental drugs from the drug sponsor prior to the issuance of the FDA approval. Mary Ann Liebert, *Expanded Access to Investigational Drugs for Treatment Use: Proposed Rule*, 26 BIOTECHNOLOGY L. REP. 40, 41 (2007) (quoting Joint Explanatory Statement of the Committee of Conference in House Report 105-399, November 9, 1997, p. 100.).

¹⁴ 21 C.F.R. § 312.34.

¹⁵ A sponsor is the individual or entity that "takes responsibility for and initiates a clinical investigation" and may take the form of a "pharmaceutical company, governmental agency, academic institution, private organization, or other organization." 21 C.F.R. § 312.3 (2007).

has no legal obligation to grant a terminally-ill patient, even if the patient has obtained FDA permission, access to its experimental drug.¹⁷ In the aforementioned example, Amgen denied “compassionate use” to the former clinical trial participants and refused to provide the drug.¹⁸ In order to resume treatment, the patients sued, asserting several claims including breach of contract.¹⁹

The foregoing, however, is merely an illustration of the alternative claims that patients must raise when federal regulations fail to provide a meaningful method of accessing experimental treatments. This comment investigates why “compassionate use” is not a meaningful exception for the terminally and seriously-ill by examining the interests of drug sponsors and, additionally, seeks to discover whether those interests can be resolved to serve both patient and sponsor. Part II outlines the FDA’s current regulations for the drug approval process as well as a specific exception known as treatment use of an investigational new drug (“treatment IND”). In concluding that treatment INDs are not meaningful channels for obtaining experimental drugs, Part II examines the language of treatment IND and the claims that plaintiffs have raised after this exception failed to grant access to an experimental drug.

Part III, with an eye towards the question of whether the FDA should have the authority to mandate the sale of a drug, examines the concerns of drug sponsors in making the decision to grant or deny a patient’s application for treatment IND. These concerns include the achievement of marketing approval, civil liability, and cost recovery in light of the sponsor’s prevailing interest in achieving FDA marketing approval for the investigational new drug. Part III argues that, although compassionate use is essentially meaningless to a terminally ill patient, the current law should not be amended to compel drug sponsors to grant access to patients who meet the criteria for this exemption. Part III, however, concludes by proposing more effective solutions that ultimately encourage drug sponsors to appropriately balance their concerns with the needs of individual patients who have exhausted approved treatment options.

PART II: AN OVERVIEW OF FDA REGULATIONS FOR INVESTIGATIONAL NEW DRUGS

The FDA’s overriding purpose is to protect public health by assuring the “safety, efficacy, and security” of consumer products.²⁰ Pursuant to the Food, Drug, and Cosmetic Act,²¹ the FDA has two specific functions: to review and approve new products that may improve public health and to protect the public from unsafe or ineffective products.²² The FDA, accordingly, has promulgated regulations that

¹⁶ 21 U.S.C. § 360bbb(b).

¹⁷ *See id.* (requiring patients to gain FDA approval prior to seeking an investigational drug for treatment use).

¹⁸ *Abney*, 443 F.3d at 545.

¹⁹ *Id.*

²⁰ U.S. Food and Drug Administration, FDA’s Mission Statement, <http://www.fda.gov/opacom/morechoices/mission.html> (last visited Mar. 26, 2008). *See Food and Drug Admin. v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133-34 (2000) (stating that the “essential purpose” pervading the Food, Drug, and Cosmetic Act “is to ensure that any product regulated by the FDA is ‘safe’ and ‘effective’ for its intended use”) (quoting 21 U.S.C. § 393(b)(2) (2007)).

²¹ 21 U.S.C. § 393.

²² Accountability Act of 1997, S. Rep. No 105-43, at 2, 105th Cong. § 1056 (1997).

prevent unsafe or ineffective drugs from being approved for marketing and distribution in the United States.²³

Both criticized and praised as the most stringent and comprehensive regulatory procedures in the world,²⁴ the FDA's drug approval process specifies how a new drug achieves marketing approval and disallows any drug to be sold for medical treatment without this approval.²⁵ The regular approval process, however, includes several exceptions that facilitate the faster provision of investigational drugs for treatment use; these exceptions fall into one of two categories – “expedited review”²⁶ or “expanded access.”²⁷ Within “expanded access,”²⁸ there is an exception called the treatment IND.²⁹ This section provides an overview of the current regulations for a new drug approval process and the treatment IND.

A. Achieving Approval: The Investigational New Drug Application

In order for a drug to be sold in the United States, the FDA must have reviewed and approved the drug for marketing and distribution.³⁰ To obtain marketing approval for an experimental drug, a sponsor must submit an Investigational New Drug Application (“IND application”) to the FDA.³¹ This application contains preclinical³² or clinical³³ data indicating that the drug is reasonably safe for human

²³ See generally 21 C.F.R. § 314.2 (2007) (stating that the overarching purpose of FDA's drug approval process is to efficiently and thoroughly “[f]acilitate the approval of new drugs shown to be safe and effective” and “ensure the disapproval of drugs not shown to be safe and effective”).

²⁴ HENRY I. MILLER, TO AMERICA'S HEALTH: A PROPOSAL TO REFORM THE FOOD AND DRUG ADMINISTRATION 25 (2000).

²⁵ 21 C.F.R. § 314.2.

²⁶ One type of expedited review is the “fast track” program which is a treatment designed for rarer or specific types of diseases and medical conditions for which there is an “unmet need.” FRAN HAWTHORNE, INSIDE THE FDA: THE BUSINESS AND POLITICS BEHIND THE DRUGS WE TAKE AND FOOD WE EAT 93 (2005). Because the need for this type of treatment is greater than other types of developing pharmaceuticals, the drug sponsor can petition the FDA for an expedited review of the drug to provide it more quickly to the intended patient population. *Id.*

²⁷ Currie, *supra* note 10, at 313-14. An example of one form of expanded access is 21 C.F.R. § 312.36 which provides instructions for patients who qualify for the emergency use of an investigational drug. This provision further authorizes the FDA to grant a “compassionate use” application on a case-by-case basis. Currie, *supra* note 10, at 314 n. 37.

²⁸ “Expanded access” is sometimes used synonymously with “compassionate use.” See Abigail Alliance for Better Access to Investigational Drugs v. Von Eschenbach, 495 F.3d 694, 697 (D.C. Cir. 2007) (*en banc*) (noting that appellants were seeking “expanded access” to investigational drugs that had not been approved).

²⁹ 21 C.F.R. § 312.34. Prior to “treatment IND” which was promulgated in 1987, the FDA provided a “compassionate use” program that allowed patients to access drugs prior to the grant of marketing approval. Lisa Terrizzi, *The Need for Improved Access to Experimental Drug Therapy: AIDS Activists Call For a Parallel Track Policy*, 4 ADMIN. L. J. 589, 601 n.62 (1991). Unfortunately, “compassionate use” was rather limited in scope, depended on the “benevolence” of the drug manufacturer, and was generally provided to patients only when the drug manufacturer was almost certain of receiving FDA approval. *Id.* Today, however, the term “compassionate use” is still more commonly used than “treatment IND.” See Steve Dunn, *Cancer Guide: Off-Protocol: Getting New Treatments Outside a Clinical Trial*, CANCERGUIDE, Dec. 2, 2002, <http://cancerguide.org/offprotocol.html> (explaining formal “compassionate use” programs).

³⁰ Areta L. Kupchik & Josephine M. Torrente, *R&D 101: Legal Issues During Research and Development*, in PHARMACEUTICAL LAW 2006: ACROSS THE PRODUCT LIFE CYCLE, at 10, 18-20 (PLI Patents, Copyrights, and Literary Prop., Course Handbook Series No. 9046, 2006).

³¹ 21 C.F.R. § 312.1 (2007).

³² Preclinical data include in vitro research or animal testing. Kupchik & Torrente, *supra* note 30, at 18.

testing through clinical trials.³⁴ Additionally, the IND application includes manufacturing information ensuring that the drug can be produced in the quantities necessary to support clinical trials and a protocol specifying the selection criteria for the trial participants.³⁵ Selection criteria, especially for the early stages of clinical trials, tend to limit who qualifies.³⁶ If the FDA does not issue an objection within thirty days, the sponsor may proceed with Phase One of the clinical trial process.³⁷

The clinical trial process includes at least three stages of testing.³⁸ During these trials, the goal of investigators is to assess the effectiveness of the drug in treating the disease and also to determine the short-term side effects and possible risks of the drug.³⁹ Phase One introduces the new drug into the human system and is designed to determine the drug's effect on humans, the side effects associated with specific doses, and whether there is any evidence of effectiveness.⁴⁰ Phase Two evaluates "the effectiveness of the drug for a particular indication or indications in patients with the disease . . . under study" and further establishes the drug's short-term side effects and other risks.⁴¹ The first two phases of clinical trials are generally limited in size: the number of Phase One participants ranges from twenty to eighty but the number of Phase Two participants usually is within a few hundred.⁴²

In contrast to Phases One and Two, Phase Three clinical trials may require up to several thousand participants to assess the overall "effectiveness and safety" of the experimental drug.⁴³ Investigators further "evaluate the overall risk-benefit relationship of the drug" for the purpose of establishing an "adequate basis for physician labeling."⁴⁴

B. Treatment Use of an Investigational New Drug

An IND application restricts the use of an experimental drug to clinical trial research; a treatment IND, however, allows individuals to use the drug for personal medical therapy.⁴⁵ Patients who seek the treatment IND usually do not qualify for the clinical trial.⁴⁶ The treatment IND represents a grant of FDA permission that allows patients who are not enrolled in the current clinical trial to approach the drug

³³ Clinical data include preliminary, small-scale human studies. *Id.*

³⁴ *Id.* at 19.

³⁵ Kupchuk & Torrente, *supra* note 30, at 18. At this point, the new drug sponsor must also establish an Institutional Review Board ("IRB"). *Id.* The IRB is designed to ensure the fulfillment of the treatment protocol and monitor the safety of the participants, and, to do so, must include at least five experts and laypersons. *Id.* at 18-19.

³⁶ Complaint at 6, ¶ 15, *Abigail Alliance for Better Access to Developmental Drugs v. McClellan*, No. 03-1601, 2004 WL 3777340 (D.D.C. 2004) (No. 1:03CV01601) [hereinafter *Abigail* Complaint].

³⁷ *Id.*

³⁸ 21 C.F.R. § 312.21 (2007). A fourth phase of clinical trials is sometimes used after FDA marketing approval to continue to study dosage and side effects and explore other possible uses. Terrizzi, *supra* note 29, at 560.

³⁹ 21 C.F.R. § 312.21.

⁴⁰ 21 C.F.R. § 312.21(a).

⁴¹ 21 C.F.R. § 312.21(b).

⁴² 21 C.F.R. § 312.21(a) - (b).

⁴³ 21 C.F.R. § 312.21(c).

⁴⁴ *Id.*

⁴⁵ 21 C.F.R. § 312.34.

⁴⁶ See *Abigail* Complaint, *supra* note 36, at 6, ¶ 15.

sponsor and request the drug.⁴⁷ As the language of 21 U.S.C. § 360bbb indicates, the requested experimental drug is always the patient's last resort after approved treatments have failed.⁴⁸ In promulgating the regulations for treatment IND pursuant to 21 U.S.C. § 360bbb, the FDA had two explicit purposes: first, "to facilitate the availability of promising new drugs to desperately ill patients as early in the drug development process as possible," and also "to obtain additional data on the drug's safety and effectiveness."⁴⁹ In determining whether a seriously or terminally-ill patient qualifies for treatment use of an IND, the FDA considers four criteria.⁵⁰ First, the drug must be intended to treat either a serious or life-threatening disease.⁵¹ Second, the patient must have exhausted all other treatments, both conventional and alternative.⁵² Third, the new drug must be in the process of being studied in a clinical trial.⁵³ Finally, the sponsor of the new drug must be actively pursuing, with due diligence, marketing approval from the FDA.⁵⁴

21 C.F.R. § 312.34 further distinguishes "serious" diseases from "immediately life-threatening" diseases and lays out separate guidelines for both types.⁵⁵ The difference between "serious" and "life-threatening"⁵⁶ classifications is significant. For example, a patient suffering from a "serious disease" may receive a drug in Phase Three clinical trials but must show the presence of "appropriate circumstances" to receive a drug in Phase Two clinical trials.⁵⁷ A patient suffering from an "immediately life-threatening disease," however, may receive an investigational drug in Phases Three or Two without an additional showing of

⁴⁷ 21 C.F.R. § 312.34. The FDA derives the authority to promulgate this exception from 21 U.S.C. § 360bbb (2007), which permits the Secretary to allow patients suffering from "serious" or "life-threatening" disease or illness to request "emergency access" to an investigational new drug directly from the drug sponsor.

⁴⁸ 21 U.S.C. § 360bbb.

⁴⁹ 21 C.F.R. § 312.34(a). Providing seriously and terminally-ill patients with access to the potential benefits of investigational drugs has received "broad public acceptance and earnest support." Investigational New Drug, Antibiotic, and Biological Drug Product Regulations; Treatment Use and Sale, 52 Fed. Reg. 19,466, 19,466 (May 22, 1987) (to be codified at 21 C.F.R. pt. 312). After re-proposing an expanded access protocol, FDA received over 300 positive comments "representing virtually every affected constituency. These included consumers, consumer group leaders, health professionals and health care providers, representatives of specific disease and orphan drug organizations, State and local health departments, clinical investigators and research institutions, institutional review boards, pharmaceutical manufacturers, and former FDA officials." *Id.*

⁵⁰ 21 C.F.R. § 312.34(b)(1) (2007).

⁵¹ 21 C.F.R. § 312.34(b)(1)(i).

⁵² 21 C.F.R. § 312.34(b)(1)(ii).

⁵³ 21 C.F.R. § 312.34(b)(1)(iii).

⁵⁴ 21 C.F.R. § 312.34(b)(1)(iv).

⁵⁵ *Id.* In promulgating these regulations, the FDA further provided a list of diseases illustrating serious and life-threatening diseases. Investigational New Drug, Antibiotic, and Biological Drug Product Regulations; Treatment Use and Sale, 52 Fed. Reg. at 19,467. Serious diseases included advanced Parkinson's disease, Alzheimer's disease, advanced multiple sclerosis, active lupus, certain forms of epilepsy, and others. *Id.* Life-threatening diseases include advanced AIDS, "most advanced metastatic cancers," "advanced congestive heart failure," "severe combined immunodeficiency syndrome," and "far advanced emphysema." *Id.* The FDA emphasized that these lists were merely illustrative and not exhaustive. *Id.*

⁵⁶ The FDA has further defined "life-threatening" as "a stage of disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment." 21 C.F.R. § 312.34(b)(3)(ii).

⁵⁷ 21 C.F.R. § 312.34(a).

“appropriate circumstances.”⁵⁸ Furthermore, the FDA requires sufficient data supporting the “safety and effectiveness” of the drug for a serious disease⁵⁹ and, in contrast for a life-threatening illness, requires only a “reasonable basis” to conclude that the drug “may be effective” and that the drug would not pose an “unreasonable or significant risk of injury.”⁶⁰ Thus, in considering whether to grant a treatment IND application, the FDA recognizes the necessity of providing terminal patients investigational treatments by accepting a lesser showing of effectiveness.

C. Problems with Treatment IND

Although the treatment IND has been accorded broad public support,⁶¹ patients, their families, and their advocates have criticized this exemption, arguing that the treatment IND is limited in its capacity to provide a patient with an investigational drug.⁶² Indeed, the treatment IND exception is merely a grant of FDA permission to seek an experimental drug for treatment use.⁶³ To begin treatment after receiving this permission, the patient and physician, who originally recommended the experimental drug for treatment, must now *request* the drug from the drug sponsor.⁶⁴ Thus, patients who meet the relevant statutory requirements may “request” the drug from the sponsor but are not guaranteed the drug from FDA permission alone. The drug sponsor has no legal obligation to provide a patient with a drug for which it holds the exclusive rights.⁶⁵

Furthermore, the FDA does not have any authority to mandate the provision of an experimental drug for treatment use.⁶⁶ In 2006, the FDA stated that “under its existing authority, FDA cannot compel a drug manufacturer to provide access to an investigational drug for treatment use.”⁶⁷ Thus, a patient with FDA approval for a treatment IND will be unable to access the drug if the sponsor refuses. The problematic nature of a drug sponsor’s absolute right to refuse access has been illustrated in recent judicial opinions where patients, unable to avail themselves of

⁵⁸ *Id.* Furthermore, the language of this section does not allow seriously-ill patients to receive drugs in Phase One clinical trials but recognizes that patients with life-threatening illnesses may, in limited circumstances, receive Phase One drugs. *Id.*

⁵⁹ 21 C.F.R. § 312.34(b)(2).

⁶⁰ 21 C.F.R. § 312.34(b)(3)(A)-(B).

⁶¹ Investigational New Drug, Antibiotic, and Biological Drug Product Regulations; Treatment Use and Sale, 52 Fed. Reg. at 19,466.

⁶² *E.g.*, *Abigail* Complaint, *supra* note 36, at 6, ¶ 15 (noting that plaintiffs did not attempt to avail themselves of “compassionate use” on the basis that the manufacturer had no incentive to grant access); *Abney v. Amgen*, 443 F.3d 540, 545-46 (6th Cir. 2006) (holding that clinical trial sponsors who canceled a clinical trial were not required to continue providing the drug to participants based on breach of contract, promissory estoppel, or breach of fiduciary duty); *Suthers v. Amgen*, 441 F. Supp. 2d 480, 485-89 (S.D.N.Y. 2006) (holding that clinical trial sponsors who canceled a clinical trial were not required to continue providing the drug to participants based on “breach of contract, breach of the implied covenant of good faith, promissory estoppel, breach of fiduciary duty, negligence and violation of [state law]”).

⁶³ 21 C.F.R. § 312.34.

⁶⁴ *Id.* Additionally, 21 U.S.C. § 360bbb(b) (2007) provides that “[a]ny person . . . may *request* from a manufacturer or distributor, . . . after complying with the provisions of [21 U.S.C. § 360bbb], an investigational drug or investigational device for the diagnosis, monitoring, or treatment of a serious disease or condition . . .” *Id.* (emphasis added).

⁶⁵ 21 C.F.R. § 312.34; 21 U.S.C. § 360bbb.

⁶⁶ Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75,147, 75,150 (Dec. 14, 2006) (to be codified at 21 C.F.R. pt. 312).

⁶⁷ *Id.*

treatment IND, have instead resorted to alternative causes of action including constitutional challenges to the FDA's existing regulations and claims based in contract, promissory estoppel, violation of rights pursuant to state law, and breach of fiduciary duty.⁶⁸

For example, the *Amgen* litigation⁶⁹ arose when the clinical trials were stopped after many of the plaintiffs claimed to have begun benefiting from GDNF, and the defendant, Amgen, refused to continue providing GDNF.⁷⁰ Amgen argued that, based on its animal studies, the patients were in danger of developing brain lesions.⁷¹ Plaintiffs argued that (1) the animals received much higher doses than would be used in humans, (2) the abrupt withdrawal of GDNF caused the brain lesions, and (3) the short shelf life and difficulty in manufacturing the drug, both of which would lead to higher costs for the defendant, were the true reasons behind the cancellation of the study.⁷² Although the FDA "stated that it would permit compassionate use of GDNF," Amgen declined to provide the drug and plaintiffs were unable to continue the GDNF treatment.⁷³ In response, the plaintiffs unsuccessfully asserted a breach of contract claim, in addition to several others, based on their signing of an informed consent form at the beginning of the study.⁷⁴ The District Court in *Suthers* reasoned that the informed consent did not present the "meeting of the minds" necessary for the formation of the contract; thus, the patients did not have a contractual right to continue the GDNF treatment.⁷⁵

Similarly, in *Abigail Alliance for Better Access to Experimental Drugs v. Von Eschenbach*, the D.C. Circuit sitting en banc held that there is no fundamental right to investigational drugs that have not cleared Phase One of clinical trials.⁷⁶ Petitioner Abigail Alliance for Better Access to Experimental Drugs ("Abigail Alliance"), named for the founders' daughter, a young woman who passed away while fighting for access to the experimental cancer treatments Erbitux and Iressa,⁷⁷ argued that the FDA's stringent regulations for experimental drugs were unconstitutional pursuant to the Due Process Clause.⁷⁸ In rejecting this claim, the D.C. Circuit reasoned that the right to refuse potentially life-saving treatment was not a corollary to the right to access potentially life-saving *investigational* treatment.⁷⁹

The foregoing examples are merely illustrative of federal regulations that are

⁶⁸ *Abigail Alliance*, 495 F.3d at 701 (considering whether terminally-ill patients have a constitutional right through the Due Process Clause to access investigational drugs that have cleared Phase One clinical trials); *Abney*, 443 F.3d at 545; *Suthers*, 441 F. Supp. 2d at 480.

⁶⁹ See *supra* text accompanying notes 1-10 for a discussion of the clinical investigation of GDNF that gave rise to lawsuits against Amgen.

⁷⁰ *Abney*, 441 F.3d at 544-45.

⁷¹ *Id.* In its petition to the FDA for the termination of the study, Amgen noted that the brain lesions indicated that GDNF was not safe for humans, and the FDA agreed. *Id.*

⁷² *Id.* at 544-45.

⁷³ *Id.* at 545. In reaching its decision not to provide GDNF, Amgen consulted with "eight external experts (three bioethicists and five Parkinson's disease experts), seven of whom advised Amgen to terminate the use of the drug." *Id.*

⁷⁴ *Id.* at 543; *Suthers*, 441 F. Supp. 2d at 482.

⁷⁵ *Suthers*, 441 F. Supp. 2d at 488.

⁷⁶ 495 F.3d 694, 696 (D.C. Cir. 2007) (en banc).

⁷⁷ The Abigail Story, <http://www.abigail-alliance.org/story.htm> (last visited April 6, 2008).

⁷⁸ *Abigail Alliance*, 495 F.3d at 700.

⁷⁹ *Id.* at 713.

without meaning to terminally and seriously-ill patients where the drug sponsor refuses to grant the treatment IND. Although the language in 21 U.S.C. § 360bbb⁸⁰ and 21 C.F.R. § 312.34⁸¹ recognize the need to provide the terminally ill with alternative experimental therapies, neither the statute nor the federal regulations provide a meaningful method of access to these drugs.

PART III: BALANCING THE NEEDS OF THE TERMINALLY ILL WITH THE NEED FOR SAFE AND EFFECTIVE DRUGS

If patients who face imminent death or who experience a diminished quality of life are willing to accept the risks of unproven therapies, it appears that the law should shift in their favor by compelling drug sponsors to grant patients access to experimental drugs. But setting aside the question of whether denying a terminal patient access to a drug of last resort is *morally* correct,⁸² granting patients access to an experimental drug defeats the original purpose of the FDA, in ensuring the safety and efficacy of drugs, and ultimately detracts from the quality and variety of medical treatments available to society as a whole.⁸³

Although there are proposed amendments that would make obtaining FDA approval for the use of an investigational treatment easier for patients, these proposed regulations do not strike at the heart of the problem.⁸⁴ Congress wisely has not given the FDA the statutory authority to mandate the sale of a pharmaceutical by an unwilling drug sponsor.⁸⁵ Indeed, doing so would violate the Patent Act.⁸⁶ More problematically, however, there are no regulations that encourage sponsors to institute programs that furnish experimental drugs for treatment use.

⁸⁰ 21 U.S.C. § 360bbb (2006).

⁸¹ 21 C.F.R. § 312.34 (2007).

⁸² Interestingly, international guidelines governing the treatment of human research subjects indicate that access, or at least continued access, to a medical treatment should not be denied. *E.g.*, International Ethical Guidelines for Biomedical Research Involving Human Subjects, Guidelines 10, 21, Council for International Organizations of Medical Sciences (CIOMS) (Geneva, 2002) (indicating that sponsors have an ethical obligation to make any product developed or any knowledge gained from experimentation with human research subjects reasonably available to the subjects' communities); World Medical Association, Ethical Principles for Medical Research Involving Human Subjects, Declaration of Helsinki, article 29 (affirming the requirement that all study participants should be assured access to the "prophylactic, diagnostics and therapeutic procedures" after the conclusion of the study in a manner that allows for evaluation by an ethical review committee). Pursuant to these international ethical guidelines, the plaintiffs in *Suthers v. Amgen* and *Abney v. Amgen* would have been allowed to continue the GDNF treatment despite the lack of a *legal* obligation of a drug sponsor to provide the treatment.

⁸³ See sources cited *supra* note 20 (explaining the original purpose of the FDA).

⁸⁴ See, *e.g.*, National Cancer Act of 2007, S. Rep. No 1056, 109th Cong. § 1056 (2007) (endeavoring to provide better access to cancer treatments); Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75,147, 75,150 (Dec 14, 2006) (to be codified at 21 C.F.R. pt. 312) (addressing "expanded access" programs for investigational drugs).

⁸⁵ Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. at 75,151. The grant of authority to mandate the sale of an investigational drug would vest greater discretionary power in FDA without *necessarily* assuring that more patients will ultimately receive an experimental treatment. Indeed, if FDA suspects a drug is neither safe nor effective, the agency likely will not grant a treatment IND application and force a drug sponsor to provide the IND.

⁸⁶ See 35 U.S.C. § 271 (2006) ("[W]hoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefore, infringes the patent.").

Drug sponsors, like other companies, are motivated by profit.⁸⁷ Unlike other industries, however, drug manufacturers are subject to the most stringent and complicated regulatory scheme in the world.⁸⁸ The costs of research, development, and compliance with FDA regulatory guidelines are multi-million dollar investments.⁸⁹ Furthermore, unless the FDA grants marketing approval, the drug sponsor cannot sell the drug and cannot recover any of the research and development costs.⁹⁰ If a drug is deemed ineffective, unsafe, or both and marketing approval is denied, the drug sponsor loses the time and money put into developing the unsafe or ineffective drug and must rely instead on other products to support its company.⁹¹

Consider again the example of the *Amgen* litigation.⁹² Although Amgen argued that patient safety was the reason for terminating the study, the patients maintain that the cost of the drug was the true reason for terminating the investigation.⁹³ But regardless of the “true” reason for the termination of the clinical trials, the high cost of bringing a drug to market presents a valid reason for halting the a clinical investigation. For example, Amgen originally acquired the GDNF license for \$240 million and spent substantially more in researching, developing, and providing the implantation surgeries for each clinical study participant, and also in furnishing adequate supplies of GDNF.⁹⁴ These costs, coupled with animal research that indicated GDNF was not safe and human research that suggested the drug was not effective, signified that to continue the study would (1) not increase the likelihood of obtaining marketing approval, (2) endanger the human subjects, and (3) cause the drug to have a prohibitively high cost at market.

As a result of the tremendous risk and financial investment associated with a new drug, sponsors tend to view anything with the potential to jeopardize FDA marketing approval unfavorably and suspiciously.⁹⁵ Accordingly, sponsors have myriad concerns in assessing the legal and financial issues accompanying the provision of an unapproved drug for treatment use. First, drug sponsors must consider the

⁸⁷ Joel Lexchin, *The Pharmaceutical Industry and the Pursuit of Profit*, in *THE POWER OF PILLS: SOCIAL, ETHICAL AND LEGAL ISSUES IN DRUG DEVELOPMENT, MARKETING AND PRICING 1* (Jillian Clare Cohen, Patricia Illingworth, and Udo Schuklenk, eds., 2006).

⁸⁸ MILLER, *supra* note 24, at 19.

⁸⁹ *Id.* at 21 (estimating that the cost of bringing a drug to market in 1998 to be \$313 to \$432 million and opining that these costs are “unquestionably much higher now”); *see generally* Neal J. Meropol & Kevin A. Schulman, *Cost of Cancer Care: Implications and Issues*, 26 *J. OF CLINICAL ONCOLOGY* 180, 180 (2007) (calculating the total cost of cancer care in the United States in 2005 to be \$209.9 billion dollars with patient care, pharmaceuticals, and medical devices accounting for \$74 billion).

⁹⁰ *See* 21 C.F.R. § 312.7 (2007) (outlining the few and very specific instances where a drug manufacturer may recover any of the cost for an investigational drug).

⁹¹ *See* MILLER, *supra* note 24, at 21 (“[B]ecause of the high cost and high risk of drug research, companies must rely on a limited number of highly successful products to finance their continuing research and development.”).

⁹² *See supra* notes 1-10 and accompanying text (explaining the clinical investigation that gave rise to the litigation); *see also* *Abney v. Amgen*, 443 F.3d 540, 540 (6th Cir. 2006) (providing a more detailed discussion of Amgen’s arguments).

⁹³ Backgrounder on GDNF, http://www.grassrootsconnection.com/splash_packet/backgrounder_on_gdnf.htm (last visited Jan 18, 2008).

⁹⁴ Indeed, the investigational drug does not have to be deadly; any showing of “less safe” or “less effective” can be grounds for the FDA to withhold marketing approval. Lexchin, *supra* note 87, at 13.

⁹⁵ *See also id.* at 13-14 (noting the high-pressure to produce favorable results with a low risk of adverse effects which poses fewer financial risks to drug companies).

integrity of the pharmaceutical research during clinical trials.⁹⁶ Second, drug sponsors open themselves, their clinical trial sponsor, the members of their Institutional Review Board, the hospitals where the studies are conducted, and many other entities to potential liability.⁹⁷ Third, drug sponsors are extremely limited in the economic costs that they are allowed to recover from a treatment IND patient; in such a scenario, the sponsor may recover only the cost of the components of the investigational drug.⁹⁸

A. Problems with Maintaining the Integrity of the Clinical Research

In reviewing an IND application, the FDA scrutinizes the “scientific quality” of the clinical trials.⁹⁹ Moreover, in Phases Two and Three of a clinical investigation, the FDA’s concern for “scientific quality” takes priority over its concern for the safety of research subjects.¹⁰⁰ The favored “gold standard” for investigating an experimental drug is the control group, double-blind study where neither the clinical trial participant nor the administering doctor knows whether the actual drug or a placebo is being used.¹⁰¹ In these studies, the first group, the control group, receives a placebo; the second group, the experimental group, receives the drug under investigation.¹⁰² Without the proper controls to measure the effectiveness of the drug, the scientific value is questionable and the FDA may reject the IND application.¹⁰³ Consider the specific example of Erbitux,¹⁰⁴ for which the FDA denied marketing approval.¹⁰⁵ The agency cited, among other reasons, the failure of the drug sponsor, ImClone, to compare in Phase Three clinical trials the effectiveness of (1) chemotherapy alone with (2) Erbitux alone with (3)

⁹⁶ E.g., MILLER, *supra* note 24, at 23-24. (noting that even the undetermined cause of death of clinical trial patient was sufficient to terminate the sponsoring university’s gene therapy program, attribute fraud and misconduct to the investigators, and halt clinical trials involving a *similar* drug).

⁹⁷ See Michelle M. Mello, David M. Studdert, Troyen A. Brennan, *The Rise of Litigation in Human Research Subjects*, 139 ANNALS INTERNAL MED. 40, 41 (2003) (explaining the increasing number of creative actions that plaintiffs bring against drug manufacturers for unexpected effects of pharmaceuticals); see also MILLER, *supra* note 24, at 30-34 (explaining the chilling effects that civil litigation has on research and development in the pharmaceutical industry).

⁹⁸ 21 C.F.R. § 312.7 (requiring any sponsor to request from the FDA, in writing, permission to charge the patient).

⁹⁹ 21 C.F.R. § 312.22 (2007).

¹⁰⁰ *Id.*

¹⁰¹ Sharona Hoffman, *The Use of Placebos in Clinical Trials: Responsible Research of Unethical Practice*, 33 CONN. L. REV. 449, 454 (2001) (quoting Kenneth J. Rothman & Kevin B. Michaels, *The Continuing Unethical Use of Placebo Controls*, 331 NEW ENG. J. MED. 394, 395 (1994)).

¹⁰² PETER GRAY, PSYCHOLOGY 46 (Worth Publishers 2002). Robert Suthers and Niwana Martin were originally in the control group. *Suthers*, 441 F. Supp. 2d at 481. Before Amgen converted the investigation to an open label study, neither Mr. Suthers nor Ms. Martin reported any improvement. *Suthers* Complaint *supra* note 3 at 4, 5, ¶¶ 21, 26. Indeed, Mr. Suthers's daughter reported that his condition improved during using the reporting a open label study. Robert Pollack, *Patients in Test Won't Get Drug, Amgen Decides*, N.Y. Times, Feb. 12, 2005, http://www.nytimes.com/2005/02/12/business/12amgen.html?pagewanted=1&_r=1&oref=slogin.

¹⁰³ See Hoffman, *supra*, note 101, at 454-55 (noting that both the FDA and the American Medical Association advocate the continuing use of placebo-controlled studies).

¹⁰⁴ Erbitux was granted “fast track” approval status by the FDA, and was designed to shrink cancerous tumors. HAWTHORNE, *supra* note 26, at 224.

¹⁰⁵ *Id.* at 224-25.

chemotherapy and Erbitux together.¹⁰⁶

The concerns for drug sponsors are twofold. First, if a patient is given the options of receiving a placebo or receiving the drug, the patient likely opt for the drug.¹⁰⁷ In enrolling for a clinical trial, patients, regardless of whether they are terminally ill or seeking an alternative treatment, will not risk receiving the placebo, and will instead resort to treatment IND options.¹⁰⁸ Thus, drug manufacturers fear that if treatment INDs or other expanded access options are too readily available to patients, the clinical trial will lose a control which is essential to the validity of a study.¹⁰⁹

The second concern for drug sponsors is the lack of guidance as to the effect a treatment IND patient may have on the overall results of a trial. No authority indicates whether a terminally ill patient can receive an experimental drug as a “last-ditch” attempt to live without skewing the clinical trial results.¹¹⁰ The Conference Report accompanying the Food and Drug Administration Modernization Act of 1997 explicated fears about the reluctance of drug manufacturers to allow seriously-ill patients to use an investigational drug.¹¹¹ Conferees indicated that drug sponsors feared specifically that the inclusion of research gained from a seriously-ill patient would “jeopardize” marketing approval by “conflicting” with or being “inconsistent” with the data obtained in clinical trials.¹¹² The conferees requested that the FDA address this problem, “particularly for terminal patients who have failed existing therapies.”¹¹³ This fear stems from the idea that a patient who has exhausted all other conventional and approved medical options will not likely benefit from an experimental treatment in the same manner as a patient with an early-stage of the disease.¹¹⁴

B. Liability Problems

Drug manufacturers, sponsors, Institutional Review Board members, clinical investigators, sponsoring hospitals, and any other entity involved in the investigation of an experimental drug may be subject to lawsuit.¹¹⁵ Claims are increasing in variety and creativity but, moreover, plaintiffs are beginning to sue any person or entity involved in the study.¹¹⁶ As a result, the time and expense necessary for

¹⁰⁶ *Id.*

¹⁰⁷ Indeed, instituting a system where individuals are given a choice between the placebo and the therapy would likely put an end to the more effective double-blind studies; thereafter, open label studies would likely become the standard type of clinical investigation.

¹⁰⁸ See Hoffman, *supra* note 101, at 454 (noting that all patients are informed of “blinding” and must consent to the possibility of blinding to enroll).

¹⁰⁹ *Id.*

¹¹⁰ See Lexchin, *supra* note 87, at 13-14 (noting that too much variation in either the control or experimental group can skew the results which can either favor or disfavor the approval of the new drug).

¹¹¹ H.R. Conf. Rep. 105-399, at 100 (1997), reprinted in 1997 U.S.C.C.A.N. 2880, 2890. The Food and Drug Administration Modernization Act provided “statutory direction” to expand expanded access protocols for the purpose allowing more people suffering from “life-threatening” or “seriously debilitating diseases” the opportunity to access potentially improved treatments. *Id.*

¹¹² *Id.* at 2890-2891.

¹¹³ *Id.* at 2891.

¹¹⁴ See 21 C.F.R. § 312.34(b) (providing the criteria that a patient must meet for the submission of a treatment IND to the FDA).

¹¹⁵ Mello, Studdern, & Brennan, *supra* note 97, at 40.

¹¹⁶ MILLER, *supra* note 24, at 23-24.

defending these claims increases and finding willing investigators, clinical trial sites, and investigational review board members for the clinical testing becomes more difficult.¹¹⁷

A proper informed consent form was at one time sufficient to prevent a lawsuit by clinical trial subjects.¹¹⁸ Nearly all of the claims brought against drug manufacturers or clinical trial sponsors were based on a lack of informed consent.¹¹⁹ Furthermore, lack of informed consent claims were usually raised by then-expectant mothers whose children suffered birth defects as a result of the experimental treatment.¹²⁰ Problematically, what constitutes “informed consent” varies across jurisdictions and is not consistently enforced.¹²¹ Because many drug sponsors are national or multi-national entities, drawing up the correct documents can be difficult.¹²² Furthermore, experimental therapies can trigger unexpected or adverse results – in these situations, the FDA has placed the onus squarely on the Institutional Review Board or the clinical investigator to monitor the subjects closely and also to terminate immediately the study in the presence of any adverse effect.¹²³ Upon discovery of a “life-threatening adverse drug experience,” a “serious adverse drug experience,” or an “unexpected adverse drug experience,” the sponsor must immediately notify the FDA.¹²⁴ Additionally, clinical trial sponsors must report any new information not within the scope of the clinical protocol, treatment IND, or safety reports.¹²⁵ If any of this new information was “unexpected,” “adverse,” or “life-threatening” *and* went unreported, a sponsor or manufacturer could leave himself open to be liability.¹²⁶ Finally, although currently there are no drug product liability cases where a manufacturer or sponsor was held liable when all warnings and informed consent were sufficient,¹²⁷ sponsors, by the nature of their products, which can heal or kill, are prime targets for litigation.¹²⁸

C. Problems with Recovering the Cost of the Pharmaceutical

There are limited circumstances where a manufacturer may charge for an investigational drug. 21 C.F.R. § 312.7(d)(2) provides that a drug sponsor or investigator may charge for a treatment IND if (1) there is sufficient enrollment in an ongoing clinical trial; (2) the “charging does not constitute commercial marketing”; (3) the drug is not being advertised or promoted; and (4) marketing approval for the drug is being pursued “with due diligence.”¹²⁹ This regulation further defines “commercialization” as charging a price that is greater than the “cost of manufacture,

¹¹⁷ *Id.* at 33.

¹¹⁸ Mello, Studdern, & Brennan, *supra* note 97, at 40.

¹¹⁹ HAWTHORNE, *supra* note 26, at 36.

¹²⁰ Kupchyk & Torrente, *supra* note 30, at 36-37.

¹²¹ *See id.* (“[W]hat is ‘adequate’ and what constitutes being ‘fully informed’ continues to be an unsettled and perplexing issue for researchers as well as for lawyers”).

¹²² *Id.*

¹²³ *See* 21 C.F.R. § 312.32 (describing the actions that the investigator or drug sponsor must take in the presence of an adverse, unexpected, or possibly life-threatening effect).

¹²⁴ *Id.*

¹²⁵ 21 C.F.R. § 312.31.

¹²⁶ *Id.*

¹²⁷ Kupchyk & Torrente, *supra* note 30, at 36.

¹²⁸ MILLER, *supra* note 24, at 31.

¹²⁹ 21 C.F.R. § 312.7(d)(2) (2007).

research, development, and handling of the investigational drug.”¹³⁰

Because there is high degree of uncertainty in whether a drug manufacturer is going to achieve marketing approval, fewer drug companies may be willing to take on additional patients, who did not qualify for the original clinical trials, and furthermore pay for the cost of treating those patients. The costs associated with providing the drug can be prohibitively high – for example, drugs often can be difficult to synthesize, store, transport, or even administer.¹³¹ Additionally, a patient may not be able to afford the cost of “manufactur[ing], research[ing], develop[ing], and handling of the investigational drug,” which complicates the issue of cost recovery.

D. Proposed Solutions

When a drug sponsor is faced with these problems that may jeopardize the ultimate goal of marketing approval, it has no incentive to grant access for treatment use.¹³² Indeed, the variety of claims raised by patients seeking a treatment IND indicate that this exception is not effective.¹³³

One possible solution that has been proposed by Congress is the National Cancer Act of 2007, which would amend 21 U.S.C. § 360bbb by adding the Oncologic Compassionate Access Program.¹³⁴ The purpose of this program is to make a “comprehensive federal effort” in providing cancer patients with more treatment options.¹³⁵ This new compassionate access program mandates the establishment of a program that provides additional opportunities to use unapproved therapies for cancer treatment.¹³⁶ In establishing this program, the FDA must distribute “written guidance” that (1) describes the compassionate access programs, (2) facilitates the provision of INDs “without reasonable delay,” and (3) “facilitates the contribution of safety and efficacy data of investigational treatments from participants in such compassionate access program.”¹³⁷

In comparison with the current language of 21 U.S.C. § 360bbb, this proposed language appears to make gaining access to drugs easier for patients, but at the same time, does not provide the FDA authority to compel the sale of an investigational drug.¹³⁸ Thus, the FDA has no power to mandate the provision of a treatment IND

¹³⁰ 21 C.F.R. § 312.7(d)(3).

¹³¹ See *supra* text accompanying note 95 (indicating the original cost of the license for GDNF and the cost of providing the surgeries to the clinical trial participants; see also *supra* note 3 and accompanying text (providing information about the surgeries in the *Amgen* litigation).

¹³² *Abigail Alliance for Better Access to Investigational Drugs v. Von Eschenbach*, 495 F.3d 694, 700 (D.C. Cir. 2007) (en banc) (considering argument that banning companies from charging profits discourages participation in treatment INDs).

¹³³ See, e.g., *id.* at 700 (examining plaintiff’s constitutional challenge); *Abney v. Amgen*, 443 F.3d 540, 540 (6th Cir. 2006) (considering claims based on contract, promissory estoppel, and breach of fiduciary duty); *Suthers v. Amgen*, 441 F. Supp. 2d 478, 481 (S.D.N.Y. 2006) (considering claims based on breaches of contract, implied covenant of good faith, fiduciary duty, and duty of care to continue supplying drug and violation of state law).

¹³⁴ National Cancer Act of 2007, S. Rep. No 1056, 109th Cong. § 1056 (2007).

¹³⁵ *Id.*

¹³⁶ *Id.*

¹³⁷ *Id.*

¹³⁸ This legislation is not Congress’s first attempt to address the needs of the terminally ill. Congress has previously proposed (and rejected) legislation that would improve a patient’s access to unapproved medical treatments. Access to Medical Treatment Act, H.R. 746, 109th Cong. § 2792 (1998). Relevant

and the drug sponsor still has no further incentive to provide the experimental drug.¹³⁹ The language does not address the issues of liability or cost recovery, nor does it give further indication of what ethical and legal considerations should guide the use of data gained from treatment IND patients. Given this lack of guidance, the proposed amendments do not come any closer to inducing a drug sponsor to grant access by providing protection from liability or direction as to the effect compassionate use data will have on the ultimate goal of marketing approval.

Additionally, the FDA has proposed new rules that affect 21 C.F.R. § 312.34 for the purpose of clarifying the existing regulations for the treatment IND and expand the situations where an experimental drug treatment is available to a terminally or seriously-ill patient.¹⁴⁰ In proposing these new rules, the FDA is attempting “to strike the appropriate balance between authorizing access to promising drugs for treatment use” and “ensuring the integrity of the drug approval process.”¹⁴¹ The FDA articulated three criteria to apply to all types of expanded access, one of which requires the agency to determine that providing the experimental drug “will not interfere with the . . . clinical investigations that could support the marketing approval” of that drug.¹⁴² The FDA predicts that individual patient submissions for expanded access will increase from the current average of 659 patients to between 923 and 1,054 in three years.¹⁴³ The FDA further notes, however, that “by establishing clear eligibility criteria and submission requirements, the proposed rule would ease administrative burdens . . . on sponsors *willing* to make promising unapproved therapies available for treatment use.”¹⁴⁴

In addressing concerns of the integrity of clinical investigations and ultimate goal of obtaining marketing approval, the proposed merely rule scratches the surface of the problems that discourage drug sponsors from utilizing the current treatment IND provisions. This rule addresses only whether the patient will affect the clinical investigation – indeed, if the patient will affect the clinical investigation, the patient may not qualify for expanded access. There is no guidance as to the effect a patient who dies during the experimental drug treatment should have on the clinical research. Conversely, there is no guidance as to whether a patient who successfully uses the drug and lives will positively impact the clinical research .

The more effective way to improve access to drugs for terminally-ill patients is through reform that, without authorizing the FDA to mandate access to an experimental drug, provides a drug sponsor with significant protections. These protections should eliminate the disincentives, including liability, cost recovery, and risks to achieving marketing approval, that prevent drug sponsors from providing INDs for treatment use. This solution maintains the FDA’s original, overriding purpose of ensuring the safety and efficacy of drugs, but also encourages drug

to the lingering question of whether FDA should have the authority to compel the sale of an IND, however, the rejected legislation specifically states that the administration of a medicine shall not violate licensing laws. *Id.*

¹³⁹ Terrizzi, *supra* note 29, at 600 n.62.

¹⁴⁰ Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75,147, 75,150 (Dec 14, 2006) (to be codified at 21 C.F.R. pt. 312).

¹⁴¹ *Id.*

¹⁴² *Id.* at 75,151.

¹⁴³ *Id.* at 75,158

¹⁴⁴ *Id.* at 75,157 (emphasis added).

sponsors to allow a seriously or terminally-ill patient access to a drug of last resort.

Foremost in these concerns is whether granting access will jeopardize marketing approval. Tied into this question are the two issues of how a terminally-ill patient may alter the results of clinical research and how to maintain patient enrollment in clinical trials. The FDA should promulgate *specific* regulations as to the extent a treatment IND patient will effect the FDA's determination of the drug's safety and effectiveness in the decision to grant or deny marketing approval. Furthermore, the resistance of sponsors to granting more treatment INDs stems in part from the reliance on the clinical trial.¹⁴⁵ Without willing, fully-informed research subjects, the current method for reviewing IND applications will fail. Rather than continuing to loosen regulations regarding treatment IND and allowing more patients to seek experimental therapies, the focus should be on fast track programs and other forms of accelerated review,¹⁴⁶ with an eye towards instituting additional levels of postmarketing review.¹⁴⁷ This solution would allow more seriously and terminally-ill patients to access therapies sooner, if such a need exists, while remaining consistent with the original purpose of the FDA.

Furthermore, any patient who has failed all conventional therapies and who elects to use an experimental treatment as a last resort for survival should be formally precluded from later suing for adverse and even deadly effects.¹⁴⁸ Although a hypothetical patient (or the patient's family and advocates) may be ultimately unsuccessful in a liability claim, the drug sponsor must still defend against the claim, which adds to the mounting cost and time of drug development.¹⁴⁹ Other forms of legal remedies are insufficient to guarantee the protection of a drug manufacturer.¹⁵⁰ For example, even a contract signed by the research subjects and all of the entities involved in the clinical investigation may not provide the necessary legal protection due to the disparate bargaining power between a terminally-ill patient and the drug sponsor.¹⁵¹

Finally, the FDA must address the issue of cost recovery. The current guidelines regarding charging for treatment INDs allow the FDA enormous discretion in determining whether any cost recovery is permitted.¹⁵² Proposed solutions include mandating that health insurance companies help cover some of the cost of the treatment IND,¹⁵³ but Frank Burroughs, father of Abigail Burroughs and a co-

¹⁴⁵ See generally Hoffman, *supra* note 101, at 454 (explaining the FDA's reliance on the placebo control as the "gold standard" for clinical trials).

¹⁴⁶ HAWTHORNE, *supra* note 26, at 93.

¹⁴⁷ *Id.* FDA's proposed regulations appear to address this concern in allowing treatment protocols and treatment INDs for intermediate-sized patient populations. For example, if the FDA receives a number of requests from patients with similar diseases or conditions for the same experimental drug, the FDA may "ask a sponsor to consolidate expanded access" pursuant to proposed section 21 C.F.R. § 312.315. Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. at 75,167.

¹⁴⁸ This solution, however, is predicated upon the informed consent of a terminally or seriously-ill patient.

¹⁴⁹ MILLER, *supra* note 24, at 9.

¹⁵⁰ See, e.g., *Suthers*, 441 F. Supp. 2d at 480 (demonstrating the myriad of creative claims that plaintiffs can raise).

¹⁵¹ See *id.* at 481 (rejecting a contract claim based on an informed consent form signed at beginning of a clinical trial).

¹⁵² 21 C.F.R. § 312.7(d)(2) (2007).

¹⁵³ See generally Sharona Hoffman, *A Proposal for Federal Legislation to Address Health Insurance Coverage For Experimental and Investigational Treatments*, 78 OREGON L. REV. 203, 206-07 (1999)

founder of the Abigail Alliance, offered the following solution: “set up a foundation, or other vehicle, to raise money from private sources, from the giant pharmaceutical industry, and the U.S. Government to provide money to pay for more production of hopeful experimental cancer drugs to be distributed through compassionate use.”¹⁵⁴ Mr. Burroughs recognized that a prohibitively high cost may be associated with providing an experimental drug for a treatment IND.¹⁵⁵ A foundation, developed in conjunction with new FDA regulations would create another entity that could help subsidize the costs of a treatment IND. Thus, drug sponsors would be able to shift at least some of the cost of treatment INDs and provide more patients with additional treatment options.

PART IV: CONCLUSION

The FDA’s current regulations for treatment INDs fail to balance the competing interests of drug sponsors and patients suffering serious and life-threatening illnesses. The problem of allowing patients to seek an unapproved investigational drug when the drug manufacturer has no legal obligation to provide the drug will continue to grow as Congress and the FDA approve greater numbers of patients for treatment INDs.¹⁵⁶ As courts have had opportunities to consider this issue through *Abigail Alliance*,¹⁵⁷ *Suthers*,¹⁵⁸ and *Abney*,¹⁵⁹ judicial action is unlikely to benefit any patient who sues for access to an experimental drug. Indeed, the notion of a court ordering the provision of an unapproved drug implicates the same problems as the FDA having authority to mandate the provision of a drug. Until Congress more fully considers this problem in light of drug sponsors’ concerns and provides greater legal protections for those drug sponsors who would provide access for terminally and seriously-ill patients, any proposed amendments broadening the treatment use of an unapproved drug should not be passed. To do otherwise is inconsistent with FDA’s purpose of ensuring the safety and efficacy of new drugs for the society as a whole.

(arguing for the implementation of federal legislation that would require health insurance companies to provide at least some coverage for experimental medical treatments).

¹⁵⁴ *Experimental Drugs for the Terminally Ill: Hearing Before the Comm. on House Gov. Reform of H.R. 2448*, 109th Cong (2001) (statement of Frank Burroughs, Co-founder, Abigail Alliance for Better Access to Developmental Drugs).

¹⁵⁵ *Id.*

¹⁵⁶ Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75,147, 75,158 (Dec. 14, 2006) (to be codified at 21 C.F.R. pt. 312).

¹⁵⁷ 495 F.3d 694, 700 (D.C. Cir. 2007) (en banc).

¹⁵⁸ 441 F. Supp. 2d 478, 480 (S.D.N.Y. 2006).

¹⁵⁹ 443 F.3d 540, 544-45 (6th Cir. 2006).