

# Virtual Mentor

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## HEALTH LAW

### The Terminally Ill, Access to Investigational Drugs, and FDA Rules

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Abigail Burroughs was in her late teens when she was diagnosed with head and neck cancer. A year into her treatment, her doctors had exhausted all standard therapies but Abigail's condition had not improved [1]. Abigail's oncologist believed she might benefit from an experimental cancer drug that targeted the same receptors as her cancer but that was only being studied in patients with colon cancer. Another cancer trial would not enroll her and, when she was finally accepted to a clinical trial several months later, she was by then too ill to travel. She died a month later at the age of 21 [1].

To honor his daughter, Abigail's father formed the Abigail Alliance, a patient rights group that advocates for expanded access to experimental drugs for terminally ill cancer patients [2]. The group sued the Food and Drug Administration for broadened access, critiquing FDA's existing compassionate use regulations (discussed in greater detail later). The suit launched a legal battle over two questions: is there a fundamental constitutional right to experimental therapies, and should the terminally ill be permitted to expose themselves to unusually great research risks for a small chance of benefit? This paper explores relevant legal cases and the FDA's response to this evolving area of law.

#### *U.S. v Rutherford (1979)*

Before the Abigail Alliance suits (and before the FDA had introduced specific rules allowing compassionate use of experimental therapies), terminally ill cancer patients and their spouses brought suit against the FDA to enjoin it from interfering in the marketing and distribution of Laetrile [3]. Laetrile was an extract of apricot pits and almonds, available outside the U.S. and widely believed to be an effective cancer treatment. Parties to the suit believed Laetrile was their last and only option [3, 4]. The FDA had blocked approval for marketing of the drug and was waiting for greater clinical research data on efficacy and safety [3, 4].

Recognizing the limited options that terminal cancer patients faced, the U.S. Supreme Court in *Rutherford* stood by the FDA actions and concluded that the right to access unproven therapies did not exist in this case [3]. Acknowledging that there is a clear protected right to refuse life-saving treatment, the Court distinguished this from a positive right to access a particular treatment or medication. It argued that a drug is as unsafe for the terminally ill as for anyone else if its prospects of death and physical injury are not outweighed by its potential for benefit, and the FDA had not yet found evidence that Laetrile was safe and effective [3]. Furthermore, the Court

asserted, the government (specifically the FDA) has an interest in regulating unsafe drugs and protecting the public's health [3]. The Court believed that if patients were to have expanded access to Laetrile, the question would more appropriately be handled by the FDA or the legislature than by the judiciary [3].

### ***Abigail I (2006)***

Almost three decades later, the U.S. Court of Appeals for the District of Columbia heard *Abigail Alliance for Better Access to Developmental Drugs v. Von Eschenbach* and was asked to address the same fundamental question raised in *Rutherford* [5]. While the FDA by then had special procedures in place that gave some individuals access to developing drugs, the alliance rejected these procedures as “effectively inoperative” and called for greater rights for the terminally ill [6].

A three-judge panel held in favor of the alliance and a right to access experimental therapies [5]. They framed the question as one of whether terminally ill patients have a fundamental right to make informed decisions that may prolong their lives, specifically access to experimental therapies that have completed phase I testing [5]. They saw this right as arising from due process clause, the part of the Fifth Amendment to the Constitution that guarantees that no person shall be deprived of life, liberty, or property without due process [5]. The due process clause protects rights and traditions that are deeply rooted in our nation's history and are implicit in the concept of liberty [5]. The three-judge panel pointed to a longstanding tradition in America of protecting a right to control one's body, demonstrated in the right to self-defense and self-preservation (including an exception to violate some laws in order to preserve one's life, for example to damage another's property). And while there is no long-standing general duty to rescue or save another's life, there is long-standing liability for interfering with an individual's ability to save him- or herself [5].

In contrast with these age-old traditions in the law, the regulation of drugs by the government is fairly new, not undertaken until 1906 [5]. Drug safety did not become a significant regulatory issue until 1938, and drug efficacy only became a requirement for FDA approval in 1962 [5]. Thus, for half of American history, patients could obtain drugs without any government interference, and important aspects of patient access still remain unregulated, for example the provision of off-label prescriptions [5]. Relating this to *Cruzan* (the renowned 1990 Supreme Court case affirming a fundamental due process-derived right to *withdraw* life-saving medical care) [7], the finding in favor of the alliance was based not on a positive right to access something, but on a negative right to be free from governmental intrusion [5].

### ***Abigail II (2007)***

The FDA appealed the three-judge panel's determination and sought an *en banc* review (meaning a larger pool of Appellate Court judges to hear the case). In a landmark decision, the *en banc* review overturned the appeals court's decision in *Abigail I* and agreed with the FDA that there is no fundamental right to access

experimental therapies for anyone, including the terminally ill. [8]. This time, the court “reframed the issue not as a personal autonomy right to control one’s body but as a right to access something that is presently inaccessible: drugs that FDA has not yet approved for marketing and use by the public” [9]. Moreover, the court in *Abigail I* had not recognized a strong argument about the government’s interest in regulating drug *safety* [8]. Here, the *Abigail II* court found a long-standing regulatory history. At the state level, regulation of dangerous drugs had begun as early as 1736, with a Virginia law limiting the dispensing of drugs to amounts that were necessary but not harmful [8]. By the 1850s at least 25 states had some regulation related to adulterated and unsafe drugs [8]. Therefore, FDA prohibitions on the sale of drugs were seen by the court as “entirely consistent with our historical tradition” [8].

And while expanded access to experimental therapies might be akin to self-defense, such a right can always be limited by the legislature [8]. For example, a group arguing for access to medical marijuana was denied it because the drug had already been forbidden under the Controlled Substances Act [8, 10]. Similarly, the FDA (through the legislature) has already acted to limit access to unsafe drugs [8, 11]. While the *Abigail I* court agreed with a long-standing history of forbidding interference with a person’s ability to save or rescue him- or herself, the *Abigail II* court disagreed that the FDA was preventing the terminally ill from rescuing themselves [8]. Instead, clear science and medical communities were protecting the terminally ill from unsafe drugs that had not been approved for marketing [8]. The court suggested that the law could someday strike a balance between access to experimental drugs and appropriate risk taking, but the specific question before this court was whether the Constitution itself demands that terminally ill people have access to nonapproved drugs [8]. Like the *Rutherford* court, the *Abigail II* decision insinuated that this was an issue perhaps better handled by the legislature, nodding to recent efforts by the FDA to expand access [8].

### **FDA Regulations**

In bringing *Abigail I* and *II* to court, the Abigail Alliance for Better Access to Developmental Drugs did not pay much attention to the existing FDA regulations that allow some expanded access for terminally ill patients to experimental drugs. Perhaps this is because it was trying to win the much larger battle of establishing a recognized Constitutional right and, additionally, found the FDA expanded-access rules too limiting and ineffective to warrant greater attention.

To date, there are several channels that patients like Abigail Burroughs might consider. The FDA updated the policies in 2009 (and as recently as May 2013 provided draft guidance on their implementation [12]). There are currently three possible channels for expanded access for patients. (1) The FDA allows expanded access on a case-by-case basis for individual patients if the probable risk of ill effects from the drug is not greater than the probable risk posed by the disease and if the patient cannot gain access to the drug in other ways. A drug sponsor or physician must file the paperwork to open this channel [13]. (2) Small groups of patients can gain access to experimental therapies if they do not qualify for an experimental trial

and there is sufficient evidence of experimental therapy's safety and efficacy [14]. (3) Lastly, larger groups may gain access to the drug once it has passed phase III (or rarely, with strong evidence of safety and effectiveness, phase II) and the sponsor is seeking marketing approval [15]. These channels have been critiqued as slow and burdensome for patients. The FDA sometimes defers decisions on these requests until there is greater knowledge of the safety and effectiveness of drugs, which can be too slow a process for some patients [4, 9]. In 2011, approximately 1,200 patients received some form of early access under FDA's compassionate use channels [16].

This issue, despite prior legislation and the ongoing development of FDA rules, continues to be presented before the courts. There was, for example, a 2008 case in the Third Circuit Court of Appeals in which a pharmaceutical company was held not to have an obligation to provide a promising treatment in phase II studies to a patient with Duchenne muscular dystrophy [17]. Ongoing innovation and development in medicine is bound to increase the tension over how early to provide access to non-FDA-approved drugs to patients who have no other treatment options available.

## References

1. Plionis NJ. The right to access experimental drugs: why the FDA should not deprive the terminally ill of a chance to live. *William & Mary Bill of Rights J.* 2008;16(3):901-933.
2. Abigail Alliance for Better Access to Developmental Drugs web site. <http://www.abigail-alliance.org/>. Accessed June 10, 2013.
3. *US v Rutherford*, 442 US 544 (1979).
4. Romano LV, Jacobson PD. Patient access to unapproved therapies: the leading edge of medicine and law. *J Health Life Sci Law.* 2009;2(2):46-72.
5. *Abigail Alliance for Better Access to Developmental Drugs v Von Eschenbach*, 445 F3d 470 (2006).
6. *Abigail Alliance for Better Access to Developmental Drugs v Von Eschenbach*, 469 F3d 129 (2006).
7. *Cruzan v Director, Missouri Department of Health*, 497 US 261 (1990).
8. *Abigail Alliance for Better Access to Developmental Drugs v Von Eschenbach*, 495 F3d 695 (2007).
9. Leonard EW. Right to experimental treatment: FDA new drug approval, constitutional rights, and the public's health. *J Law Med Ethics.* 2009;37(2):269-279.
10. *US v Oakland Cannabis Buyers' Cooperative*, 532 US 483 (2001).
11. New drugs, 21 USC section 355 (a).
12. Food and Drug Administration Center for Biologics Evaluation and Research. Guidance for industry: expanded access to investigational drugs for treatment use—Q&As. <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM351261.pdf>. Accessed June 10, 2013.
13. Individual patients, including for emergency use, 21 CFR 312.310.
14. Intermediate-size patient populations, 21 CFR 312.315.
15. Treatment IND or treatment protocol, 21 CFR 312.320.

16. Dooren JC. Connecting patients with experimental drugs. *Wall Street Journal*. October 22, 2012.  
<http://online.wsj.com/article/SB10000872396390444592704578062640104322714.html>. Accessed June 10, 2013.
17. *Gunvalson v PTC Therapeutics*, 303 Fed Appx 128 (3rd Cir 2008).

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