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Tinamarie Hanson

Balancing Individualized Needs of Terminal Patients with Broader Societal Interests

Introduction

In September 2011, Nick Auden was faced with news that no one – especially a middle aged man with a wife and young children – wants to hear: he was diagnosed with melanoma and given a death sentence within a year.¹ Determined to fight his illness, Nick enrolled in a clinical trial for a promising new, investigational drug designed to treat his form of melanoma.² The drug was a ray of hope for Nick, with New York’s Memorial Sloan-Kettering Cancer Center oncologist Jedd Wolchok even stating that the drug could benefit patients “for months or years.”³ For an individual such as Nick, in the prime of his life and with young children, even a small amount of added time with his family would be a godsend.

Unfortunately, almost immediately after qualifying for the clinical trial, Nick was disqualified when he fell ill with a perforated intestine.⁴ Still determined to obtain the drug, he applied for a compassionate use exception, meaning he would be able to obtain the drug outside of the clinical trials process and prior to it being approved to go on the market.⁵ However, he was denied his request.⁶ Even after obtaining 500,000 signatures on change.org, and after garnering more than 31,000 followers on his facebook page, Nick was unable to motivate the

¹ Claire Martin. “Nick Auden, who lobbied to use experimental skin cancer drug, has died.” The Denver Post. (Nov. 29, 2013). Available at: http://www.denverpost.com/breakingnews/ci_24625182/nick-auden-who-lobbied-use-experimental-skin-cancer

² *Id.*

³ *Id.*

⁴ *Id.*

⁵ *Id.*

⁶ *Id.*

drug company, Merck, to budge and allow his compassionate use request.⁷ Sadly, Nick passed away in November 2013, leaving behind his wife and three young children – aged 7, 5, and 1.⁸

This paper will analyze the issues that arise when terminal patients, such as Nick Auden, who have tried all other forms of treatment, seek to obtain an investigational drug with the hopes that it may treat or mitigate their condition. While these patients have a strong interest in obtaining these drugs as quickly as possible - this is usually their last hope for a possible cure after all conventional forms of treatment have failed - drug companies and their stakeholders have several reasons for denying early use, such as liability concerns that come along with giving drugs out prior to approval, as well as the chance that the clinical trials process will be adversely affected. This paper will analyze the balance between the terminal patient's interests and the drug company's interest, and conclude with a discussion of the best possible outcome for all involved.

The paper will start out with a discussion of the history of the FDA, which tightly regulates drug production, and why this regulation is necessary. The paper will then go on to discuss the typical process of clinical trials and approval of a new drug. Next, the paper will discuss current ways in which individuals obtain drugs earlier than the typical market approval rate, chiefly expedited approval and compassionate use. The paper will then go on to discuss the more controversial way in which individuals obtain drugs prior to approval - through compassionate use exceptions - and why this is often frowned upon by drug companies. Then, the paper will discuss some of the pushback created by terminal patients and their supporters in an attempt to get drugs to patients more quickly: first the judicial avenue that has been taken,

⁷ *Id.*

⁸ *Id.*

and then the legislative attempts. Next, this paper will elaborate on 2009 changes in FDA regulation intended to help improve the current process. Finally, the paper will discuss more recent changes in 2014 which have helped improve the drug approval process, and how these changes, mainly expediting of the drug approval process, paired with a proper balancing of compassionate use allowances, hold the most promise for striking a balance between the needs of terminal patients and the needs of drug companies to properly test their drugs before allowing those drugs to be given to the public or to individuals outside of the clinical trial setting.

FDA History

If you were an ill patient prior to the 1900s, there were few government imposed hurdles that would impede your efforts to obtain a potentially life-saving drug. However, starting in the 1900's the United States government began to steadily increase its regulatory power over drug manufacturer's, which in turn affected consumers' ability to obtain drugs.

In 1906, the government responded to journalists' widespread reporting on improper conditions in both food processing and marketing patent medicine by passing the Pure Food and Drugs Act of 1906.⁹ This law put no hurdles in front of a product prior to its marketing, but it did specify conditions under which foods and drugs would be considered adulterated or misbranded.¹⁰ This was significant in that it required food and drug manufacturers to make sure that their products were manufactured under sanitary conditions and labeled properly.¹¹ This law had an only minimal effect on industry and was followed by increasingly strict legislation.

⁹ David G. Adams et. al, FOOD AND DRUG LAW AND REGULATION SECOND EDITION (Food and Drug Law Institute 2011), at 3.

¹⁰ *Id.* at 3.

¹¹ *Id.* at 3.

In 1938, over one hundred individuals died from consuming an antibiotic, Elixir Sulfanilamide, which contained antifreeze.¹² This prompted the passage of the Food, Drug, and Cosmetic Act of 1938, which delegated authority to the FDA to monitor food and drugs.¹³ Specifically, in regard to drugs, it authorized the FDA to ensure that drugs placed on the market were considered safe.¹⁴ While a manufacturer was not required to gain explicit FDA approval prior to marketing its drug, it was required to at the very least to conduct tests to establish whether or not the drug was safe, and to submit the drug to the FDA for an independent review.¹⁵ The drug would automatically be approved for commercial distribution unless the FDA later determined it not to be safe.¹⁶ The law in 1938 was particularly significant since, for the first time, the government imposed some sort of safety standards upon drug manufacturers.

A public health crisis again led to tighter regulations in 1962. After thousands of European women who had taken the morning sickness drug Thalidomide gave birth to children with severe birth defects, Congress passed the Kefauver-Harris Amendments of 1962.¹⁷ Although this health crisis had happened in Europe, the FDA realized that greater protections would be necessary to prevent a similar crisis from possibly occurring at some point in the United States. These Amendments put a much higher burden on drug manufacturers, requiring them to submit “substantial evidence” of a drug’s efficacy prior to putting it on the market.¹⁸ The substantial evidence standard required a drug company to perform clinical trials and submit

¹² Robert M. Harper, *A Matter of Life and Death: Affording Terminally-Ill Patients Access to Post-Phase I Investigational New Drugs*, 12 MICH. ST. J. MED. & LAW, 265 (2008), at 268.

¹³ *Id.* at 268.

¹⁴ *Id.* at 268-269.

¹⁵ Harper, *supra* at 269.

¹⁶ *Id.* at 269.

¹⁷ *Id.* at 269.

¹⁸ *Id.* at 269-270.

a great deal of evidence as to a drug's efficacy to the FDA, prior to being permitted to market the drug.¹⁹ The drug approval process now takes on average seven years.²⁰

In 1997, in an attempt to offset this lengthy process, the FDA passed the FDA Modernization Act of 1997.²¹ This Act authorized the Secretary of Health and Human Services to accelerate the development and approval of a drug that was to be used for terminally ill patients with no other viable options.²² The Modernization Act basically set the foundation for expedited review processes in certain situations, in order to get life-saving drugs to market more quickly.²³

Drug Approval Process

As a result of this increasing regulation, there are several steps a drug company must walk through in order to gain approval as a new drug. Before even beginning clinical trials on humans, a drug company must submit an Investigational New Drug Application (IND) to the FDA, including detailed information on the drug as well as information on the proposed clinical investigation.²⁴ Prior to submitting the IND, a drug company must do animal testing in order to establish at least some baseline for safety before moving on to human clinical trials.²⁵

Once a drug company is permitted to move on to human clinical trials, it generally has to go through several phases of testing before gaining new drug approval. Phase I testing is done on a very small number of healthy subjects, usually 20-80 individuals, primarily to determine

¹⁹ Rachel E. Sherman et. al., *Expediting Drug Development – The FDA's New “Breakthrough Therapy” Designation*, New England Journal of Medicine, Nov. 2013, at 1877.

²⁰ Harper, *supra* at 270.

²¹ *Id.* at 270.

²² *Id.* at 270.

²³ Harper, *supra* at 270.

²⁴ Adams, *supra* at 364.

²⁵ *Id.* at 364.

safety related information such as “the metabolism and pharmacologic actions of the drug in humans, [and] the side effects associated with increasing doses.”²⁶ Additionally, the researchers sometimes will gain early evidence of effectiveness.²⁷

In the next stage, phase II studies expand the group of research participants up to several hundred individuals and include individuals afflicted with the disease being studied.²⁸ Phase II studies focus more heavily on the drug’s effectiveness as well as optimal dosage ranges, while still looking at any risks or side effects associated with the drug.²⁹

Finally, Phase III studies are the most detailed, including thousands or participants and often taking place at multiple locations.³⁰ These studies are focused on obtaining “substantial evidence” to meet the FDA’s standards for proof of “safety and efficacy” needed to obtain new drug approval.³¹

After completing phase III studies, a drug company will submit its new drug application to the FDA and hope for a timely approval.³² Sometimes, the FDA will ask for more information and the approval process can still linger on for some time.³³ Overall, it takes an average of seven years for a new drug to be approved.³⁴

For terminally ill individuals, waiting for a potentially life-saving drug to be approved under this lengthy process is not usually a viable option. While these individuals can attempt to enroll in clinical trials to obtain the drug, they are sometimes excluded as not meeting the

²⁶ *Id.* at 364.

²⁷ *Id.* at 364.

²⁸ *Id.* at 364.

²⁹ Adams, *supra* at 364.

³⁰ *Id.* at 364.

³¹ *Id.* at 364.

³² *Id.* at 364.

³³ *Id.* at 364.

³⁴ Sherman, *supra* at 1877.

criteria; if they are accepted, they run the risk of being placed into a placebo group and not gaining access to the drug at all.³⁵ Thus, over time policies have been implemented that allow for an expedited review process for particularly promising drugs.³⁶ Additionally, compassionate use policies have been established which allow certain terminally ill patients a chance to gain access to drugs that have not yet completed all phases of clinical testing.³⁷

Expedited Approval

The FDA has established ways in which a drug may be approved much more quickly than the average 7 year timeline. The primary way in which this occurs is through a drug's designation to the "Fast Track" program.³⁸ A drug designated for the fast track approval process must be intended to treat a life threatening or very serious condition.³⁹ The drug must also be intended to address an unmet medical need; an unmet medical need can be as straightforward as there being no other therapy available, or it can mean that the drug has "improved efficacy over existing therapies; efficacy for serious elements of a condition that are not treated by existing therapies; efficacy in patients who do not respond to or cannot tolerate existing therapy; or reduction in serious toxicity of existing therapies, or avoiding other toxicities that cause discontinuation of treatment with other therapies."⁴⁰

For a drug that qualifies for fast track designation, the FDA takes on a more active and collaborative role throughout the drug development process, in order to help expedite the

³⁵ Ashley Ochs, Comment, *A Study in Futility: Abigail Alliance for Better Access to Developmental Drugs Will Not Expand Access to Experimental Drugs for the Terminally Ill*, 39 SETON HALL L. REV. 559 (2009), at 586.

³⁶ Adams, *supra* at 384-386.

³⁷ Adams, *supra* at 368.

³⁸ *Id.* at 384-385.

³⁹ *Id.* at 384-385.

⁴⁰ *Id.* at 385.

development and review of the drug.⁴¹ This hands on and more active role can make a significant difference in getting a drug to market much more quickly than the usual lengthy timeline. For example, AZT, the first drug approved for treating the AIDS virus, had a total drug approval time of only two years.⁴² This is significantly lower than the average seven year process for drug approval. Undoubtedly, many lives were saved by the expedited approval of this life saving drug, for many individuals were able to gain access to it years before it would have hit the market under the usual drug approval process. Thus, expedited review plays a pivotal role in helping certain drugs become accessible to the general public much more quickly.

Compassionate Use

Shortening approval time by several years may be very helpful to some patients, but for others who may only have weeks to months to live, this might not be enough. Thus, the FDA has also established compassionate use policies that allow some individuals to gain access to drugs which have not yet been approved.⁴³ The FDA's compassionate use programs cater to both individuals and intermediate size patient populations who have a "serious or immediately life-threatening disease or condition...[with] no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition."⁴⁴ For a drug to be approved for compassionate use, the potential benefit to the person or groups being treated must outweigh the potential risks to the person or group of individuals.⁴⁵ Additionally, making the drug available through compassionate use to the person or individuals must not interfere with the clinical trials

⁴¹ *Id.* at 385.

⁴² Ochs, *supra* at 573.

⁴³ Adams, *supra* at 369.

⁴⁴ *Id.* at 369.

⁴⁵ *Id.* at 369.

process.⁴⁶ In rare instances, compassionate use will allow an individual to gain access to a drug as early as post phase I testing, but generally it will only allow an individual access after the drug has entered or completed phase II testing.⁴⁷

For many terminal individuals who cannot get approved to participate in clinical trials, and for whom all existing treatment is not working, the opportunity to gain access to a drug through compassionate use is a last hope. Yet, drug companies sometimes deny compassionate use requests, due to several valid concerns.

Lack of Adequate Informed Consent

Prior to any medical procedure, an individual is required to be given informed consent. This is no different in the case of an ill individual seeking to gain early access to an investigational drug. Before a drug company will allow an individual to receive a drug through a compassionate use policy, it will first need to provide that individual with informed consent.⁴⁸ Informed consent requires that the individual understand the risks of taking the drug, as well as the potential benefits.⁴⁹ However, compassionate use by nature involves obtaining a drug before the manufacturer has had a chance to complete all of its testing for both safety and efficacy. Thus, the drug manufacturer has only a very limited ability to delineate to an individual all of the risks that may be involved in taking an experimental drug. Although a drug manufacturer can inform the patient that there may be a multitude of possible adverse side effects that are yet unknown, the adequacy of this type of informed consent is questionable. Even more, the efficacy and thus the benefits that may come from taking the drug are uncertain as well. Thus,

⁴⁶ *Id.* at 369.

⁴⁷ Adams, *supra* at 369.

⁴⁸ Ochs, *supra* at 582-583.

⁴⁹ *Id.* at 582-583.

the informed consent document may be very limited in the amount of information it can convey to the individual.

This lack of a thorough and comprehensive informed consent process can set the stage for significant litigation against the drug manufacturer, if the individual were to fall even more ill after taking the drug. Drug companies may be unwilling to subject themselves to this type of liability – providing an already very ill patient with a drug that may or may not be effective, and may indeed cause further harm to the patient. The limited informed consent document and process may do very little to mitigate any litigation that may ensue from an adverse event.

Numerous legal claims have been raised against researchers and drug companies who have caused injury to participants during clinical trials. Many of these claims are started based upon inadequate informed consent processes.

For example, in *Gelsinger v University of Pennsylvania*, the parents of now deceased Jesse Gelsinger, who died during a phase I clinical trial, sued the drug company claiming that the informed consent process failed to disclose that previous subjects in the protocol had died.⁵⁰ It is no stretch to say that in cases of compassionate use, an individual harmed may have a similar claim if the drug companies fail to disclose any adverse events, even an event that had occurred as early as in the animal and in vitro studies. Even if a drug seems to be safe after it has completed phase I testing and entered into phase II testing, it is doubtful that there have been no negative side effects from it. Drug companies may attempt to disclose these events to the individual, but the possibility of neglecting to mention a tangential adverse event and this leading to significant liability may cause hesitance for the drug company to want to make its drug

⁵⁰ Michelle M. Mello et al. The Rise of Litigation in Human Subjects Research, 139 ANN. INT. MED. 40 (2003).

available for compassionate use. Granted, failure to disclose deaths, as in the Gelsinger case, is an extreme failure to disclose, it does open the door for one to wonder exactly where the line would be drawn in relation to information that needs to be disclosed.

The Gelsinger's also made a products liability and fraud claim against the drug company.⁵¹ Again, drug companies who have not finished all stages of testing may be concerned that, if harm should ensue after allowing their drug to be used for a compassionate use, they may face a products liability claim, too.

Furthermore, the fraud claim in the Gelsinger case claimed that the principal investigator had financial ties to the sponsoring company.⁵² This was not disclosed during the informed consent process, and thus the Gelsinger's claimed that fraud had occurred.⁵³ Yet again, drug companies may be concerned that if they do not disclose every single financial incentive they have, they too may be susceptible to a fraud claim. For drug companies who have received a request for compassionate use, millions of dollars are oftentimes invested into their research. They have a financial stake in seeing their drug succeed, and at times the researcher does as well. If all of this is not disclosed to the individual seeking compassionate use, the drug companies may set themselves up to be vulnerable to a fraud claim. Even for a drug company that is "on the up and up" and wants to do things properly, the fear of forgetting or failing to disclose some tangential, possibly relevant information may make them quite hesitant to set themselves up for the liability that may ensue, all simply for compassionate use, not even to further their own research.

⁵¹ Mello, *supra*.

⁵² *Id.*

⁵³ *Id.*

Ultimately, drug companies are well aware that they themselves are balancing risks versus benefits when they run clinical trials. Many of the above mentioned risks also apply to clinical trials. However, in clinical trials the benefits are huge – that they may be able to successfully put a drug on market that can treat a serious illness. The risks, though, are huge as well – harm may come to the research participants, and significant liability may ensue – even if the company did do all in its power to try to ensure an adequate informed consent process. As rational actors, many drug companies weigh the benefits versus risks and continue on with their clinical trials.

However, for compassionate use situations, the benefits to the drug company are markedly small. The individuals seeking compassionate use are generally not going to be participants contributing to the research. However, the risks are high for the drug company. An adverse event may lead to substantial liability, under a whole host of possible claims. Many drug companies are thus, understandably, reluctant to allow their drugs to be used for compassionate use.

Significant Harm to the Research Process

Not only can adverse events that occur from compassionate use lead to financial liability for the drug company, but it can also stymie the research process. Any adverse events – even those occurring outside of a clinical trial – need to be reported to the FDA.⁵⁴ A serious adverse event has the potential to halt the clinical trials, or slow down the overall process.⁵⁵ Since many individuals seeking compassionate use are already very ill as is, the odds that they may experience an adverse event after taking the drug are substantial. Whether or not the adverse

⁵⁴ Ochs, *supra* at 587.

⁵⁵ *Id.* at 587.

event is related to the drug may be hard to determine, and thus even if the adverse event had nothing to do with the drug, the drug company may be forced to halt its research trials or change its protocol. Furthermore, an adverse event such as death would need to be reported to all future research participants in order for informed consent to be adequate; the risk of death (in the eyes of the participants) may in turn lead to a reduction in the amount of participants who are willing to partake in the research.

Just as the adverse events that may occur would need to be reported and could reduce the amount of willing future research participants, so too could the compassionate use allowance reduce the amount of research participants. If individuals know that they are likely to be granted the drug through the compassionate use program, they will be much less likely to enroll in clinical trials. Clinical trials at times run with both placebo and non-placebo groups, so individuals enrolled in the trial are not necessarily guaranteed to be given the potentially beneficial drug.⁵⁶ Why enroll in a research study with a 50/50 chance of gaining the drug, when you can just apply for compassionate use and guarantee yourself the drug? Furthermore, many research trials can be inconvenient for ill patients. Some trials require significant travel to other locations or other inconvenience.⁵⁷ Again, why be burdened with all of that, when you can just get the drug dispensed to you directly through your treating physician? Thus, drug companies are hesitant to allow many compassionate use exceptions for their drugs, since this can severely limit the amount of research participants willing to partake in the clinical trials. Without enough participants for clinical trials, the research process cannot be adequately completed, and this can lead to significant delays in getting the drug to market. This hurts not only the drug companies

⁵⁶ *Id.* at 586.

⁵⁷ *Id.* at 586.

who are seeking to make a profit, but society as a whole, which may be eagerly awaiting a new life saving drug.

Clearly, drug companies lack many incentives to allow their drugs to be used for compassionate use. As such, individuals have sought to change the procedure for compassionate use, in order to help motivate drug companies to allow a higher number of sick individuals to obtain these drugs as soon as possible, as opposed to being forced to die waiting for the years it may take a drug to gain market approval. Although the desired drug may or may not be effective, for many people it is the last hope, and the last thing try, when all other forms of treatment have been exhausted and proven ineffective.

Judicial Avenue

The courts are one avenue which interested parties have utilized to attempt to make it easier to obtain drugs through compassionate use. Rather than worry about creating incentives for drug companies to expand their cases of compassionate use, these individuals have first focused on attempting to change certain FDA regulations that restrict compassionate use cases. The most stringent statutory provision, and the one litigated, has been the provision that prohibits the sale of post-phase I drugs, drugs which have not gotten too far in the clinical testing process.

Abigail Alliance generated a great deal of notoriety when it filed suit against the FDA, attempting to enjoin it from enforcing its policy restricting compassionate uses of drugs which have just completed phase I testing.⁵⁸ Alliance argued that this restriction was an infringement upon due process rights.⁵⁹

⁵⁸ Ochs, *supra* at 576.

⁵⁹ *Id.* at 576.

Initially, their claim was dismissed, with the lower court finding that there was no fundamental right to use investigational new drugs to save or extend one's life.⁶⁰ Two years later, the United States Court of Appeals for the District of Columbia reversed this decision, holding that competent, terminal patients with no other alternatives do indeed have a fundamental right to use investigational drugs to save or extend their lives.⁶¹

Finally, in August of 2007, the District of Columbia Circuit Court used rational basis review to determine that the government had a legitimate interest in ensuring that individuals were not subjected to unreasonable risks from investigational new drugs.⁶² Thus, FDA's policy limiting access to investigational drugs as early as post phase I was indeed constitutional.⁶³

The judicial route, even if it had been successful, would be unlikely to ameliorate the current issues – many terminal patients are not able to obtain potentially life-saving drugs when they need them. The FDA itself generally approves compassionate use requests. It is often times the drug companies themselves who decline the requests. Thus, even if the judiciary were to require the FDA to change its regulations and allow compassionate use requests for drugs post-phase I, this would not mean the individuals would necessarily be able to obtain these drugs that early in the clinical testing process. Drug companies would be even more unlikely to approve compassionate use requests so early in the testing process, when the possibility for adverse events and ensuing liability is even greater.

Thus, it does not seem that the judicial avenue is the best way to help remedy the current situation. The other avenues in which individuals have tried to affect change have been more

⁶⁰ *Id.* at 576-577.

⁶¹ *Id.* at 577.

⁶² *Id.* at 578.

⁶³ *Id.* at 578.

fruitful for, at the very least, they have generated many potential solutions to be placed on the table.

Legislative Proposal

One legislative proposal that gained a great deal of attention is Senator Brownback's 2008 ACCESS Act proposal. Although it ultimately did not pass, the bill advocated several ideas intended to increase the availability of investigational drugs to terminal patients more quickly than the current process.⁶⁴

For one, the bill built upon Alliance's attempt to allow terminal patients to access drugs as early as post Phase I. The bill set up provisions under which an investigational drug can essentially gain market approval after Phase I testing, provided that the drug company can present sufficient evidence to the FDA that the safety and efficacy of the drug will provide more benefit to the patient than the risk of morbidity or death from the condition or disease.⁶⁵ This threshold is actually relatively low, for even if there is some risk to a drug, the terminal patient is already facing death as a very real possibility. Thus, if the FDA were to perform a balancing assessment using that standard, it seems that they would almost always weigh in favor of approval of the post Phase I drug.

Yet, the great majority of drugs that pass Phase I testing end up failing for either safety or efficacy reasons.⁶⁶ Thus, one has to consider the implications of allowing terminal patients broad access to these drugs at such an early stage. Terminal patients might end up forgoing other conventional, more promising methods of treatment in lieu of trying a new drug, which is very

⁶⁴ Ochs, *supra* at 593-594.

⁶⁵ *Id.* at 594.

⁶⁶ Patricia J. Zettler, *The Implications of Post-Phase I and "Off-Label" Treatment Use of Experimental Drugs: How Expansive Should Expanded Access Be?*, 18 KAN. J.L. & PUB. POL'Y 135 (2009), at 165.

likely to end up proving ineffective. Additionally, the new drug may have adverse side effects that have not yet been discovered so early in the testing process. As a result, a terminal patient may end up choosing to forgo dying in a comfortable and dignified matter, and instead be subjected to numerous unnecessary discomforts and grievances at the end of his life.

While it is true that many drugs that pass Phase I testing do indeed provide a cure or at least mitigate a serious disease or condition, the fact that so many drugs do end up failing provides a strong case for not allowing patients access to drugs this early in the testing process. Even for drugs that do offer a cure or mitigate a disease or condition, there are side effects that may not be known so early in the testing process; some of these effects might so severe that they do not outweigh the possibility of morbidity or death. For example, a severe stroke which leaves a person permanently and severely disabled may be worse than death, for some individuals. It is difficult for the FDA to truly weigh the risks and benefits of a drug as early as post Phase I, for many of the risks may not yet become known. Thus, although this part of the ACCESS Act's proposal is well intended, it seems that it could end up doing more harm than good to terminal patients.

The bill attempts to provide some safeguards rather than just broadly granting access for patients to approved post Phase I drugs.⁶⁷ The first safeguard is the requirement that a patient who wishes to obtain the drug must provide written informed consent.⁶⁸ As discussed earlier in this paper, attempting to provide informed consent before many of the risks are known causes one to question just how adequate this informed consent could be.

⁶⁷ Ochs, *supra* at 594.

⁶⁸ Ochs, *supra* at 594.

The second safeguard requires that a patient provide a written waiver of the right to sue the manufacturer (along with the sponsor, physician, or any institution) for any adverse events that may occur.⁶⁹ One possible issue with this provision is that a terminal patient, fearing death and feeling hopeless, may not even be competent to sign a waiver, thereby voiding the entire waiver. While this may or may not be true, it is definitely a claim a lawyer may bring in attempting to hold a drug company liable. Lawsuits could end up bankrupting a company or limiting the funds available to finish the research process' phase II and phase III testing.

The final safeguard for a patient wishing to obtain these drugs is that the patient must provide consent that the sponsor can obtain information on the drug's usage in the patient.⁷⁰ This provision is rational and initially seems helpful. The drug manufacturer will be able to obtain even more data. But, what if this data is negative? Many of the patients seeking these drugs may be close to death to begin with. If a death occurs while taking the drug, this may need to be reported as an adverse event. Too many deaths or adverse events may lead the FDA to compel the drug manufacturer to stop clinical trials with the drug, and thus may prevent a helpful drug from getting to market. One could argue that it is better to allow the drug to be tested in controlled, clinical trials, to ensure that any adverse events are a result of the drug, and thereby to allow the FDA to make a more valid assessment of the drug's safety and efficacy. Allowing individuals outside a controlled trial to easily gain access to these drugs may increase the amount of adverse events reported – which may or may not be tied to the drug. This could stymie the research process and ultimately prevent a good drug from getting to market. While it is possible that the drug may help terminal patients improve or even recover, thus creating a positive event which would be beneficial to the research process, the fact that patients requesting

⁶⁹ *Id.* at 594.

⁷⁰ *Id.* at 594.

compassionate use are knocking at death's door already makes it more likely that adverse events will be more frequent.

Thus, the portion of the ACCESS Act that attempts to allow post Phase I drugs to get to market is misguided, and the safeguards do little to make this allowance any better. Patients may end up worse off, and the public as a whole may end up worse off as well, for this type of access may ultimately impede the clinical research process and the ability of drugs to make it through all stages of the clinical trial process and reach the public as a whole.

Additionally, the ACCESS Act proposes a prohibition on placebo groups in clinical trials with “respect to any life-threatening condition or disease where reasonably effective approved alternative therapies exist for the specified indication.”⁷¹ This regulation presumably would prevent terminal individuals from being forced to make a choice between a known method of treatment, such as radiation for cancer, and participation in a study with a promising new drug, yet only a 50-50 chance of actually being given this drug. While this regulation is intended again to increase a chance of a patient gaining access to a promising new drug, it could ultimately hurt the research process, as clinical trials are at times more thorough when they have both a placebo and non-placebo group. Furthermore, there is no guarantee that the drugs in these trials will actually be effective in treating the specific disease or condition they are targeted against. Thus, an individual who forgoes a proven method of treatment, such as radiation, is essentially taking a gamble by participating in a clinical trial – even if they were to know they would be given the new drug. Since these individuals are taking a gamble by participating in a clinical trial regardless, and placebo groups are essential to thorough research, the provision to eliminate placebo groups is also a misguided attempt at remedying the limited access ill patients have at

⁷¹ Ochs, *supra* at 595.

obtaining investigational, promising new drugs.

The most positive and potentially beneficial proposal under the ACCESS Act is that of the creation of an Accelerated Approval Advisory Committee.⁷² This committee would be made up of independent professionals whose job would entail reviewing applications and issuing recommendations to the Secretary of Health and Human Services.⁷³ This committee would serve to expedite the approval process.⁷⁴ Expediting the approval process seems a great starting point for helping terminal patients obtain drugs more quickly.

2009 Regulatory Changes

The FDA reacted to the ACCESS Act and public pushback by revising its regulations in 2009.⁷⁵ These regulations allows for expand compassionate use situations in both individuals as well as intermediate size populations that are eligible.⁷⁶ The criteria for granting access require that “the drug is intended to treat a ‘serious or immediately life-threatening disease or condition’ for which there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or conditions; that the potential patient benefit outweighs the potential risks; and that providing the drug for treatment uses will not interfere with the clinical investigations that could support marketing approval.”⁷⁷

This rule seems to help mitigate some of the concerns with compassionate use. For one, it ensures that patients are not forgoing a more reliable cure in favor of the new, investigational

⁷² Ochs, *supra* at 595.

⁷³ *Id.* at 595.

⁷⁴ *Id.* at 595.

⁷⁵ *Id.* at 595.

⁷⁶ Adams, *supra* at 369.

⁷⁷ Adams, *supra* at 369.

drug. The regulation specifically requires that there be no comparable or satisfactory alternative.⁷⁸

Furthermore, the regulation helps protect the integrity of the clinical trials process, by requiring, too, that the compassionate use will not interfere with clinical investigations.⁷⁹ While this theoretically may be hard to ensure – compassionate use exceptions may undoubtedly limit the amount of participants willing to participate in clinical trials when they can attempt to just obtain the drug directly – the regulation at least gives drug companies something to fall back on if they wish to deny a compassionate use request. In essence, drug companies will have a firm footing to deny compassionate use requests if need be. Rather than look like “the bad guy” for denying someone’s request, a drug company has a legitimate argument that the request must be denied if it will interfere with its research process.

In sum, these current regulations are the best possible outcome in terms of the delicate balancing act between allowing for compassionate use, and recognizing that there are a great deal of reasons not to allow for compassionate use. These regulations, with their stringent criteria for allowing for compassionate use, grant a great deal of latitude to drug companies. While a drug company would never be required to grant someone compassionate use, these regulations give drug companies several valid ways in which they can deny compassionate use requests without seeming to do so for no good reason. Denying compassionate use requests is oftentimes necessary in order to adequately complete the research process, and thus these regulations ensure that drug companies are able to do so more easily.

The Best Balance

⁷⁸ *Id.* at 369.

⁷⁹ *Id.* at 369.

What, then, is the best balance between the competing interests of terminal patients, who have an urgent need to obtain a potentially life-saving drug as quickly as possible, and drug companies, which have a plethora of valid reasons not to give drugs to patients too early in the clinical trials process?

First, the compassionate use procedure as it exists now is the best balance of these interests. The FDA has implemented strict oversight to insure that compassionate use exceptions are allowed for the individuals who need them. The burden falls on the drug companies to decide when to allow their drug to be given outside the clinical testing process. While some have continued to argue that the regulations should be less strict, this paper has shown that there are valid reasons to keep the regulations as they stand now.

However, keeping the policy as it stands will still allow for compassionate use exceptions in many cases. In 2013, for example, the FDA approved a total of 974 compassionate use cases.⁸⁰ Rather than attempt to make the regulations more relaxed, individuals have garnered success by turning to social media, in order to put pressure on drug companies to approve compassionate use requests.

For example, Merck expanded access to its investigational drug shortly after Nick Auden passed away in November 2013.⁸¹ Merck spokesman Ian McConnell stated, “We have been accelerating all aspects of the development program to bring this investigational medicine to as

⁸⁰ Catherine E. Shoichet & Elizabeth Cohen. “Drug Company Will Give Ailing 7 Year-Old Medicine That Could Save Him.” CNN. (March 12, 2014) Available at: <http://www.cnn.com/2014/03/11/health/josh-hardy-drug-study/index.html>

⁸¹ Brooks Hays. “Merck Expands Cancer Drug Access, but Too Late for Denver Dad Nick Auden.” UPI Health News. (March 18, 2014) Available at: http://www.upi.com/Health_News/2014/03/18/Merck-expands-cancer-drug-access-but-too-late-for-Denver-dad-Nick-Auden/1451395162356/

many people who might benefit from it as quickly and fairly as possible.”⁸² While the drug company has financial motives in moving along its clinical trials process as efficiently as possible, one could argue that the media pressure from Nick Auden’s situation increased their desire to get the drug to a point in which they felt confident that it would be safe and effective for compassionate use cases. McConnell stated, “Now that we have more safety and efficacy data in melanoma, and we have adequate supply we have started our planned [Expanded Access Program] in the U.S. for treatment of eligible patients with advanced melanoma.”⁸³ One could argue that societal pressure and the desire to maintain a positive reputation motivated Merck to work efficiently to get its drug to that point quickly. The pressure from the media helps keep a drug company balanced in that it has more motivation to approve compassionate use cases when it feels it can safely do so. A drug company that does not allow for any compassionate use with its drug may garner a negative public image that it does not want. However, a drug company that just blindly allows a drug to be used for compassionate use too early in the drug trials process may also garner significant negative attention if there are severe adverse side effects – such as death – from its drug. Thus, the current FDA regulations balanced with the role of societal pressure, particularly in the role of social media, help keep a healthy balance between approval and rejection of compassionate use requests.

This was also evidenced in the recent case of Josh Hardy, a 7 year old boy, who after fighting cancer for most of his life, was on death’s door as he fought against an adenovirus.⁸⁴ Josh’s family made a compassionate use request for the drug brincidofovir and was initially

⁸² *Id.*

⁸³ *Id.*

⁸⁴ Shoichet & Cohen, *supra*.

denied.⁸⁵ The drug had shown great promise in clinical research up to that point, and even Josh's doctors at St. Jude Children's Research Hospital put pressure upon the drug company to allow for this compassionate use.⁸⁶ The drug company's denial seemed to have little to do with safety, and more to do with a limited supply.⁸⁷ The company argued that if it opened the door for Josh it would open the door for several others who had requested compassionate use – in the past two years, over 80 people have requested a compassionate use for the drug.⁸⁸ In the clinical trials process supplies are limited, and drug companies do not have endless funds to invest in making more drugs which are not to be used in the research process.⁸⁹ This rationale did not deter Josh's family, who set up a Facebook page and went to the media – garnering nationwide sympathy and attention to the case.⁹⁰ The overwhelming public pressure resulted in the drug company changing its stance and allowing for compassionate use both for Josh, and several other individuals who had requested the drug.⁹¹ Thus, again, social media put pressure on the drug company to do the right thing given the circumstances.

There is no need to change regulations or the legal framework for compassionate use – as it stands, there is sufficient latitude for drug companies to allow for compassionate use in situations in which it is appropriate. While some may argue that there is little incentive for the drug companies to do so, it is evident that the desire to maintain a positive image and the power of social media are motivation enough.

⁸⁵ *Id.*

⁸⁶ *Id.*

⁸⁷ *Id.*

⁸⁸ *Id.*

⁸⁹ *Id.*

⁹⁰ *Id.*

⁹¹ *Id.*

Furthermore, allowing for more promising drugs to get to market more quickly and efficiency will help improve outcomes for both terminal patients and drug companies. The FDA Safety and Innovation Act of 2012 aims to do this, both by creating a new “breakthrough therapy” designation for promising investigational drugs, and by expanding situations in which accelerated approval can occur.⁹²

The breakthrough category is for drugs which are intended to treat a “serious or life-threatening disease or condition” and which have shown through early studies that they may demonstrate a substantial improvement over current therapies.⁹³ Drugs that fall into this category get on track to get approved more quickly, for the FDA commits to working closely with the drug company to ensure efficient tests for safety and efficacy, with goals to get the drug to market more quickly.⁹⁴

Ideally, all drugs that show significant promise will be able to be approved as either a breakthrough therapy or as qualified for accelerated approval. Going forward, the FDA should expand its resources to increase its staff and ensure that there are ample individuals to work one on one with each and every drug company that submits an INDA for a drug that has the potential to show significant promise in treating a serious disease or condition.

Approving a drug more quickly benefits both the patients and the drug companies. Patients will be able to obtain the drug more quickly with more guarantee of safety and efficacy than they may have if the drug were obtained through a compassionate use program. Drug companies will be able to give their drug to individuals and have a higher degree of confidence in its safety and efficacy; additionally, by getting the drug approved more quickly and efficiently,

⁹² Sherman, *supra* at 1877.

⁹³ *Id.* at 1878.

⁹⁴ *Id.* at 1878.

they will be able to market the drug and make a profit from all the money and time that were invested in their research. Profit is a necessary incentive for drug companies to attempt to create new drugs, and thus the ability to get their products to market quickly and efficiently will help incentivize drug innovation, which will result in even more promising treatment options for ill patients. It is a win-win situation.

Conclusion

While terminal patients' interests and drug companies' interests seem inherently different, they both have the same end desire – to end up with a drug that is safe and effective for use. Terminal patients want to obtain a potentially beneficial drug as quickly as possible, but drug companies have to weigh other concerns, such as liability issues that could arise from allowing for individuals to use the drug too early in the research process, as well as the effect that compassionate use exceptions could have on the research process.

The best balance to these competing concerns is, first and foremost, to continue to allow the compassionate use exception to stand as it stands now. The current regulations provide an appropriate balance between the competing interests of terminal patients and drug companies. While some may argue that drug companies lack any real motivation to provide drugs in compassionate use cases, recent situations in the media have shown that this is not true. The desire for a positive reputation and the power of social media will continue to help keep drug companies in check and motivated to allow for compassionate use when appropriate.

More promising are the increased opportunities for drug companies to get their drugs to market more quickly, be it through being designated as a breakthrough therapy or qualifying for some type of accelerated approval. Ideally, the FDA will invest heavily in more resources and

man power, so they can work closely with any and all drug companies which submit an INDA for a promising new drug. This will help shorten the normally cumbersome and lengthy drug review process and ideally lead to drugs getting to market much more quickly, but still showing the same promise of safety and efficacy that is normally established over an average seven year period. Thus, drug companies get their drugs to market more quickly and terminal patients receive a promising new treatment more quickly and with more assurance of both safety and efficacy.