

**EXAMINING PATIENT ACCESS TO
INVESTIGATIONAL DRUGS**

HEARING
BEFORE THE
SUBCOMMITTEE ON HEALTH
OF THE
COMMITTEE ON ENERGY AND
COMMERCE
HOUSE OF REPRESENTATIVES
ONE HUNDRED FIFTEENTH CONGRESS

FIRST SESSION

OCTOBER 3, 2017

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EXAMINING PATIENT ACCESS TO INVESTIGATIONAL DRUGS

TUESDAY, OCTOBER 3, 2017

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HEALTH,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 10:30 a.m., in Room 2322, Rayburn House Office Building, Hon. Michael C. Burgess (chairman of the subcommittee) presiding.

Members present: Representatives Burgess, Guthrie, Barton, Shimkus, Murphy, Blackburn, Lance, Griffith, Bilirakis, Bucshon, Brooks, Mullin, Hudson, Collins, Carter, Walden (ex officio), Green, Engel, Sarbanes, Schrader, Eshoo, DeGette, and Pallone (ex officio).

Staff present: Ray Baum, Staff Director; Adam Buckalew, Professional Staff Member, Health; Kelly Collins, Staff Assistant; Zack Dareshori, Staff Assistant; Paul Edattel, Chief Counsel, Health; Adam Fromm, Director of Outreach and Coalitions; Jay Gulshen, Legislative Clerk, Health; Jennifer Sherman, Press Secretary; Hamlin Wade, Special Advisor for External Affairs; Jeff Carroll, Minority Staff Director; Tiffany Guarascio, Minority Deputy Staff Director and Chief Health Advisor; Samantha Satchell, Minority Policy Analyst; Andrew Souvall, Minority Director of Communications, Member Services, and Outreach; Kimberlee Trzeciak, Minority Senior Health Policy Advisor; and C.J. Young, Minority Press Secretary.

Mr. BURGESS. The Subcommittee on Health will come to order, and I recognize myself for 5 minutes for the purpose of an opening statement.

OPENING STATEMENT OF HON. MICHAEL C. BURGESS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

I want to thank everyone for joining us this morning. We are here to explore an issue that is very personal to many patients, to their families across this country who are suffering from serious life-threatening conditions or terminal illnesses, and that is the availability to access investigational drugs and devices.

Currently, the United States Food and Drug Administration conducts an expanded access program aimed at helping these patients who do not qualify for clinical trials to help them gain access to therapies that are unapproved by the FDA.

I understand the feelings and the passions of individuals who believe these therapies have the potential to save their life or offer them a chance to alter the course of their illness.

I also recognize that the Food and Drug Administration must strike the right balance between ensuring public safety and granting access to new treatments.

Today, we will convene four panels of witnesses. I first want to welcome Representatives Brian Fitzpatrick and Andy Biggs to our subcommittee. We look forward to hearing your statements this morning on the actions that you both have taken.

Of course, we are pleased to welcome Dr. Scott Gottlieb. Dr. Gottlieb, no stranger to this subcommittee, but I believe this is your first opportunity to come before us as the Commissioner of the Food and Drug Administration. So we, certainly, welcome your appointment to that post and welcome you to the committee. It's nice to have you here.

Afterwards, we welcome Mr. John Dicken, the director of healthcare at the United States Government Accountability Office, and then, finally, we will hear from other stakeholders who are deeply engaged on this issue.

Our Nation has experienced an unprecedented amount of innovation and scientific breakthrough over the last decade from researchers in our finest academic institutions and from those working in the pharmaceutical and medical device companies.

However, I hear from patients with serious life-threatening conditions, constituents in north Texas, being frustrated with what they see as a regulatory barrier from trying and experimenting with new therapies when all others have failed them.

It seems we are at a crossroads when lifesaving treatments, while not yet approved, exist but patient cannot have access.

Since 2014, 37 States, including Texas, have passed a version of Right to Try laws through strong grassroots movements.

With that in mind, it is my hope that this hearing will start a constructive discussion on this important issue. The subcommittee will also examine several pieces of Federal legislation—S. 204, the Trickett Wendler Right to Try Act of 2017 authored by Senator Ron Johnson of Wisconsin; Representatives Biggs' and Fitzpatrick's House companion bills; and H.R. 1020, the Compassionate Freedom of Choice Act of 2017, introduced by our fellow Health Subcommittee member, Morgan Griffith of Virginia.

Members of this subcommittee have many questions and are looking forward to hearing from all of the witnesses. We want to learn the Food and Drug Administration's steps to streamline and communicate the expanded access program.

We want to dive in to what the Government Accountability Office found recently regarding this expanded access program, and we want to hear from our patient advocates and thought leaders on this topic.

There are strong view and I am confident that what comes out of this hearing will lead to a productive discussion and all of us getting closer to meeting the needs of our constituents and solving problems tomorrow that seem insoluble today.

[The prepared statement of Mr. Burgess follows:]

PREPARED STATEMENT OF HON. MICHAEL C. BURGESS

The subcommittee will come to order.
The Chair will recognize himself for an opening statement.

We are here today to explore an issue that is very personal to many patients, and their families, across the United States who are suffering from serious, life-threatening conditions or terminal illnesses—the availability to access investigational drugs and devices. Currently, the U.S. Food and Drug Administration conducts an expanded access program aimed at helping these patients who do not qualify for clinical trials gain access to therapies unapproved by the agency. I understand the feelings and passions of individuals who believe these therapies have the potential to save their life or to offer them a chance to alter the course of their illness. I also recognize that the Food and Drug Administration must strike the right balance between ensuring public safety and granting access to new treatments.

Today we will convene four panels of witnesses. First, I want to welcome Representatives Brian Fitzpatrick and Andy Biggs to our subcommittee. We look forward to hearing your statement this morning on actions you both have taken. Next, I want to welcome Dr. Scott Gottlieb. Dr. Gottlieb, I believe today's hearing is your first opportunity to come before our subcommittee—it is nice to have you here. Afterwards, we welcome Mr. John Dicken, Director of Health Care at the U.S. Government Accountability Office. Later, we will hear from other stakeholders who are deeply engaged on this issue.

Our Nation has experienced an unprecedented amount of innovation and scientific breakthroughs over the last decade from researchers in our finest academic institutions and those working in the pharmaceutical and medical device companies. However, I hear from patients with serious, life-threatening conditions—my constituents from North Texas—being frustrated with what they see as regulatory barrier from trying and experimenting with new therapies when all others have failed. It seems we are at a crossroad when life-saving treatments, while not yet approved, exist but patients cannot access. Since 2014, 37 States, including my State of Texas, have passed a version of Right to Try laws, through a strong grassroots movement. With that in mind, it is my hope this hearing will start a constructive discussion on this important issue.

The subcommittee will also examine several pieces of Federal legislation: S. 204, the Trickett Wendler Right to Try Act of 2017, authored by Senator Ron Johnson of Wisconsin, Representatives Biggs and Fitzpatrick's House companion bills, and H.R. 1020, the Compassionate Freedom of Choice Act of 2017, introduced by our fellow Health Subcommittee member, Representative Griffith.

Members of this subcommittee have many questions and are looking forward to hearing from all of our witnesses. We want to learn the Food and Drug Administration's steps to streamline the expanded access program. We want to dive into what the Government Accountability Office found recently regarding the expanded access program. We will hear from patient advocates and thought leaders on this topic. There are strong views but I am confident what comes out of this hearing will lead to a productive discussions and all of us getting closer to meeting the needs of all of our citizens.

I again want to welcome all of our witnesses and thank you for being here today. I look forward to your testimony.

I would like to yield the balance of my time to Ms. Blackburn of Tennessee for a statement.

Mr. BURGESS. I want to thank all our witnesses for being here today, and I will not yield the balance of my time, Mrs. Blackburn, but will be happy to recognize any Member on the Republican side who would like a minute and 12 seconds.

Seeing none, I will yield back my time and recognize the gentleman from Texas, Mr. Green, 5 minutes for an opening statement, please.

**OPENING STATEMENT OF HON. GENE GREEN, A
REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS**

Mr. GREEN. Thank you, Mr. Chairman, and I would also like to thank our administrator, Dr. Gottlieb, for being here and our two colleagues.

Mr. Chairman, expanding access, also known as compassionate use, allows patients to gain access to unapproved treatments that are on some stage of investigation outside a clinical trial.

The FDA has a long history of facilitating access to investigational therapies for terminally ill patients who are out of approved options and are ineligible for a clinical trial.

The 1997 FDA Modernization Act made amendments to allow patients to access investigational products under certain safety conditions.

In 2009, the agency revised its regulations to establish new categories of expanded access and streamlined the regulatory process for its program.

Last year, the FDA released guidance for industry about expanded access so that companies would better understand the rules of the road and avoid denying requests based on uncertainty.

It also streamlined the application, significantly reducing the time it takes to complete to, roughly, 45 minutes.

The FDA responds to individual patient access requests quickly and emergency requests are often granted immediately over the phone, something I know firsthand.

Today, we are examining two legislative proposals that are commonly referred to Right to Try bills. I am confident that we all strongly support helping patients with serious and life-threatening illnesses get the care they need and exercise their right to make their own decisions about the risk they are willing to take.

Families with a loved one face terminal illness out of the FDA-approved options can and do have the right to seek out treatments that are in the early stages of investigation.

Unfortunately, the bills they are considering today are well meaning but based on inaccurate premise. These proposals would simply take the FDA out of the equation when the FDA authorizes more than 99 percent of all expanded access requests.

There are very legitimate frustrations with the current system and this committee, through the 21 Century Cures Act and the FDA Reauthorization Act, has worked to address some of them, but more can be done.

There is a widespread lack of knowledge about the FDA's expanded access program. We need to fill this education gap by partnership with doctors and nurses and patients organizations and local advocates so patients in need know what their options are.

The FDA has made its Web site more user friendly, streamlined the application process, and has a turnaround time of days, not weeks or months, and less than 24 hours in certain emergency situations—again, something I have witnessed firsthand.

But the agency is correctly working to do more to clarify some myths and uncertainty that lead a manufacturer to deny a request.

There is a rampant misunderstanding about compassionate use that also must be addressed. The FDA does not have the authority to force a company to make investigational products available.

From October 2015 to September 2016, the FDA received 1,554 requests for expanded access, investigational new drugs and protocols and ultimately allowed 1,545 of those requests to proceed.

This is an approval rating of 99.4 percent. Of course, there is some requests for investigational products that companies deny and we can do a better job of ensuring that doesn't happen in inappropriate reasons including a lack of clarity about how adverse events would be treated.

Ultimately, the best way to speed access to drugs and development is through a clinical trial process. We have worked to do a better job on making clinical trials available on an equitable basis for all patients.

But expanding clinical trial access we can reduce the number of patients seeking access to investigational drugs outside of the trials and ultimately help even more patients by getting drugs approved and widely available.

I believe we can and should do more to advance policies that genuinely increase access to promising investigational therapies for patients in need.

However, removing the FDA from the process of assessing a therapy outside a clinical trial is not likely to facilitate any increased access to drugs in early trial stages.

Instead, we should be looking to examine principal reasons by patients interested in experimental therapies are unable to attain them through clinical trials or the existing expanded access and provide solutions to these real barriers.

We also must continue strong oversight of the implementation of requirements within the 21 Century Cures and have greater clarity from FDA on the use of adverse event data.

I appreciate our witnesses and, Mr. Chairman, I would like to ask unanimous consent to place a number of items into the record: the patient organization letter opposing Right to Try, American Cancer Society, Cancer Action Network, Friends of Cancer Research, the Leukemia Lymphoma Society and 18 other organizations, a letter to Congress regarding S. 204 submitted by Public Citizen and 17 other organizations. Do you want me to read this whole list, or can I just submit it?

Mr. BURGESS. Without objection, so ordered.

[The information appears at the conclusion of the hearing.]

Mr. GREEN. Thank you.

Mr. BURGESS. Does the gentleman yield back his time?

Mr. GREEN. I yield back my time.

Mr. BURGESS. Gentleman yields back his time.

Not seeing the chairman of the full committee having arrived yet, the Chair is prepared to yield to the ranking member of the full committee, Mr. Pallone of New Jersey, 5 minutes for an opening statement, please.

OPENING STATEMENT OF HON. FRANK PALLONE, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Mr. PALLONE. Thank you, Mr. Chairman.

Today's discussion is of great importance for so many patients and families who are facing diseases with no other treatment options and when someone has exhausted all of the available treatment options they will sometimes explore the possibility of trying unproven experimental therapies.

It is this desire that has led to calls for Federal legislation that would grant patients the right to try investigational products.

It is understandable that someone suffering from a disease that has no more options would want to try anything that could help them fight their disease.

Fortunately, both the FDA and Congress have taken some actions that provide some hope. Through the FDA's expanded access program, patients are able to get access to investigational products.

This FDA program approves 99 percent of all requests for investigational drugs or biologics that it receives. Last year, FDA received more than 1,500 requests and only nine were not approved.

And despite this high approval rate, supporters of Right to Try laws have argued that the process is too slow and burdensome. But I have not seen evidence that this is the case.

In fact, FDA often grants emergency requests for expanded access immediately over the phone and nonemergency requests are processed in an average of four days.

Despite these quick turnarounds, FDA responded to these criticisms. Last year, the agency streamlined their current process even further so that filling out an application now takes less than an hour.

FDA also released additional guidance to industry outlining the expanded access program's requirements and addressing common questions related to the different programs and submissions process, and all this was done to alleviate any confusion that may have existed in the past and I want to commend the agency for its commitment to improving expanded access and for its responsiveness to the concerns it heard from doctors and patients.

Now, this committee has also led efforts to facilitate greater access to investigational products for patients who are looking for additional options.

Last year, we passed the 21st Century Cures Act, which provides greater transparency to expanded access programs by requiring manufacturers or distributors of investigational drugs to make publicly available their expanded access policies for the first time.

And then this summer we passed the FDA Reauthorization Act, which works to improve access to clinical trials for patients. The law does this by requiring FDA to conduct a public meeting on clinical trial criteria, report on barriers to patients participating in clinical trials, and offer potential solutions to include additional populations of patients.

The FDA Reauthorization Act also requires FDA to issue additional guidance to manufacturers regarding how clinical trials can be expanded to include broader populations and improve access to treatment for patients who may not qualify for these trials.

These are all meaningful steps that I believe will help to address some of the criticisms we will hear today. Now, our discussion today is important because I am concerned that the legislation being considered could expose seriously ill patients to greater harm instead of the greater access that they are looking for.

The Senate legislation would lower the bar for safety and effectiveness by allowing access to investigational drugs that have only completed a Phase 1 clinical trial, and that's an extremely small trial that does not determine the effectiveness of potential side effects of the drug.

There is also no assurance in the Senate bill that a manufacturer will provide patients with an investigational treatment under this pathway.

Today, pharmaceutical companies can choose to deny patient access to an experimental treatment because there is not enough of the drug available or because they are concerned about dangerous side effects.

The Senate legislation also erodes important patient safeguards. It limits FDA's ability to use clinical outcomes associated with the use of investigational product when reviewing a product for approval.

It also prevents any entity from being held liable for use of the treatment. Now, while I appreciate the intent of the Senate legislation, I have a hard time supporting it in its current form and I guess what I am hoping is that we will hear today about alternative solutions that may provide more meaningful access to investigational products without undermining FDA's ability to protect patients from this harm because the last thing I want to do is give patients false hope and to have Congress pass legislation that will not in fact help someone access investigational treatments.

So, hopefully, we will hear more about, you know, ways that we could make some changes that don't sacrifice safety, and I look forward to what I hope will be a thoughtful discussion about a path forward.

I yield back, Mr. Chairman.

[The prepared statement of Mr. Pallone follows:]

PREPARED STATEMENT OF HON. FRANK PALLONE, JR.

Thank you, Mr. Chairman. Today's discussion is of great importance to so many patients and families who are facing diseases with no other treatment options. And when someone has exhausted all of the available treatment options, they will sometimes explore the possibility of trying unproven experimental therapies. It is this desire that has led to calls for Federal legislation that would grant patients the right to try investigational products.

It is understandable that someone suffering from a disease that has no more options would want to try anything that could help them fight their disease. Fortunately, both the Food and Drug Administration (FDA) and Congress have taken action that provides some hope.

Through the FDA's expanded access program, patients are able to get access to investigational products. This FDA program approves 99 percent of all requests for investigational drugs or biologics that it receives. Last year, FDA received more than fifteen hundred requests, and only nine were not approved.

Despite this high approval rate, supporters of Right to Try laws have argued that the process is too slow and burdensome. But I have not seen evidence that this is the case. In fact, FDA often grants emergency requests for expanded access immediately over the phone, and nonemergency requests are processed in an average of four days.

Despite these quick turnarounds, FDA responded to these criticisms. Last year, the agency streamlined the current process even further so that filling out an application now takes less than an hour. FDA also released additional guidance to industry outlining the expanded access program's requirements, and addressing common questions related to the different programs and submission process. All of this was done to alleviate any confusion that may have existed in the past. I commend the agency for its commitment to improving expanded access and for its responsiveness to the concerns it heard from doctors and patients.

This committee has also led efforts to facilitate greater access to investigational products for patients who are looking for additional options. Last year, we passed the 21st Century Cures Act which provides greater transparency to expanded access programs by requiring manufacturers or distributors of investigational drugs to make publicly available their expanded access policies for the first time.

And then this summer, we passed the FDA Reauthorization Act, which works to improve access to clinical trials for patients. The law does this by requiring FDA to conduct a public meeting on clinical trial criteria, report on barriers to patients participating in clinical trials, and offer potential solutions to include additional populations of patients. The FDA Reauthorization Act also requires FDA to issue

additional guidance to manufacturers regarding how clinical trials can be expanded to include broader populations and improve access to treatments for patients who may not qualify for these trials. These are meaningful steps that I believe will help to address some of the criticisms we will hear today.

Our discussion today is also important because I am concerned that the legislation being considered could expose seriously ill patients to greater harm instead of the greater access that they are looking for. The Senate legislation would lower the bar for safety and effectiveness by allowing access to investigational drugs that have only completed a Phase 1 clinical trial. That is an extremely small trial that does not determine the effectiveness or potential side effects of a drug.

There is also no assurance in the Senate bill that a manufacturer will provide patients with an investigational treatment under this pathway. Today, pharmaceutical companies can choose to deny a patient access to an experimental treatment because there is not enough of the drug available or because they are concerned about dangerous side effects.

The Senate legislation also erodes important patient safeguards. It limits FDA's ability to use clinical outcomes associated with the use of an investigational product when reviewing a product for approval. And it also prevents any entity from being held liable for use of the treatment.

While I appreciate the intent of the legislation, I cannot support it in its current form. I hope that today's discussion will offer alternative solutions that may provide more meaningful access to investigational products without undermining FDA's ability to protect patients from harm. The last thing I want to do is give patients false hope, and to have Congress pass legislation that will not in fact help someone access investigational treatments.

I want to thank the witnesses for being here today, and look forward to what I hope will be a thoughtful discussion about a path forward.

Mr. BURGESS. Chair thanks the gentleman. The gentleman yields back.

The Chair now recognizes the gentlelady from Tennessee, Mrs. Blackburn, 5 minutes for an opening statement.

OPENING STATEMENT OF HON. MARSHA BLACKBURN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TENNESSEE

Mrs. BLACKBURN. Thank you, Mr. Chairman, and I am not going to take that full 5 minutes and will submit my full opening statement for the record.

I do want to welcome our colleagues here to the committee. I want to welcome Dr. Gottlieb. We are just so pleased that we are going to be able to take up what is, I think, a really important issue for us to address when we look at healthcare, and that is the right to try.

And we want to commend the FDA for going through the process and taking some efforts to simplify and expedite request. We do think that it is important for Congress to do something legislatively to ensure patient access to promising treatments but do it with the appropriate disclosure requirements and the liability protections.

So we welcome all of you that are here today. We appreciate the time and effort that has gone into this and the fact that we are going to have the multiple panels so we can kind of drill down and do a good solid look at this from the patient perspective, from the legislative perspective, from the regulatory perspective.

So to each of you, welcome, and thank you and I yield back.

Mr. BURGESS. Chair thanks the gentlelady. The gentlelady yields back. This concludes member opening statements. The Chair would remind Members, pursuant to committee rules all Members' opening statements will be made part of the record.

The gentlelady from Tennessee is quite correct. We have a total of four panels of witnesses testifying before the subcommittee today.

To start us off, we are going to hear from two of our House colleagues—Congressman Brian Fitzpatrick of Pennsylvania and Congressman Andy Biggs of Arizona.

We appreciate both of you being here with us this morning. Congressman Fitzpatrick, you're recognized for 5 minutes for your statement.

STATEMENTS OF HON. BRIAN K. FITZPATRICK, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA, AND HON. ANDY BIGGS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF ARIZONA

STATEMENT OF HON. BRIAN K. FITZPATRICK

Mr. FITZPATRICK. Thank you, Mr. Chairman.

Good morning. I want to start by thanking Chairman Burgess, Ranking Member Green, Vice Chairman Guthrie, and all members of this subcommittee for holding this hearing. It's a very important hearing on the right to try, and I also want to thank my colleague and friend, Andy Biggs, for your partnership on this issue.

Fellow colleagues, each year thousands of Americans receive the devastating news of a terminal diagnosis. Even with the amazing work done in American medical research and development, for far too many families access to these potentially lifesaving treatments will come too late or not at all.

Thousands of terminally ill patients suffer needlessly while waiting final approval for drugs, therapies, and other medical technologies, and while the Food and Drug Administration carries out its three-phase approval process, which can take years and cost billions of dollars, many patients simply want a chance to try treatments that are already demonstrated to be safe.

Mr. Chairman, it is my hope that we can come together with Federal regulators and industry leaders to clear the path forward to care for those who are fighting just for a shot at living.

A bill that was unanimously passed by the Senate—unanimously passed by the Senate—will offer them a chance to extend their lives.

The Right to Try Act would ensure that terminally ill patients, together with their physicians and pharmaceutical manufacturers, can administer investigational treatments where no alternative exists.

In fact, this bipartisan idea is already the law in 37 States in our Nation. A Federal Right to Try law would prevent the Government from blocking access to potentially lifesaving medications.

It would require patients who are unable to participate in clinical trials to first try all other available treatments.

Mr. Chairman, I want to note that these provisions only apply to terminally ill patients. It does not undo the FDA approval process but, rather, provides a potential lifeline to those who simply cannot wait.

It requires a physician to certify that all other options were exhausted or unavailable. This maintains the incentives for patients to seek out and join clinical trials.

This bill requires that a product meet demonstrated levels of safety by obtaining FDA Phase 1 approval. We have worked with the drug companies to ensure that adverse outcomes are not used against any ongoing application for approval.

Additionally, patients, doctors, and manufacturers do not assume any additional liability under this act. For those patients caught in between traditional drug approval delays, clinical trial process for which they do not qualify and limited time, this Right to Try legislation simply establishes the freedom for patients and their doctors to try therapies where the benefits far outweigh the risks.

It gives them the option of trying to save their life. Whether it is a father courageously battling ALS or a brave child living with Duchene muscular dystrophy, my colleagues, they deserve the right to try.

I want to sincerely thank the committee for your time and consideration and as your colleague I ask that you work with us to get this done on behalf of all terminally ill patients across America.

All that we ask—all that we ask is that this bill be put—be put on the floor of the House and allow each one of us to cast our vote and go home and answer for that vote.

Mr. Chairman, I yield back.

[The prepared statement of Mr. Fitzpatrick follows:]

STATEMENT OF
REPRESENTATIVE BRIAN FITZPATRICK OF PENNSYLVANIA'S EIGHTH DISTRICT
BEFORE THE SUBCOMMITTEE ON HEALTH
COMMITTEE ON ENERGY AND COMMERCE
UNITED STATES HOUSE OF REPRESENTATIVES
OCTOBER 3, 2017

I want to start by thanking Chairman Burgess, Ranking Member Green, Vice-Chairman Guthrie and other members of the Energy and Commerce Subcommittee on Health for holding this hearing on Right to Try. Thank you to my colleague, Rep. Biggs, for your steadfast leadership on this issue.

Each year more Americans receive the devastating news of a terminal diagnosis. Even with the amazing work done in American medical research and development, for too many families, access to these potentially lifesaving treatments will come too late, or not at all.

Thousands of terminally ill patients suffer needlessly while awaiting final approval for drugs, therapies, and other medical technologies. While the Food and Drug Administration carries out its three-phase approval process – which can take years and cost billions of dollars – many patients simply want the chance to try treatments that are already demonstrated to be safe.

Mr. Chairman, it is my hope to come together with federal regulators and industry leaders to clear the path forward to care for those who are fighting just for a shot at living. A bill unanimously passed by the Senate will offer them a chance to extend their lives.

The *Right to Try Act* would ensure that terminally ill patients - together with their physicians, and pharmaceutical manufacturers - can administer investigational treatments where no alternative exists. In fact, this bipartisan idea is already law in 37 states. A federal Right-to-Try would prevent the government from blocking access to potentially lifesaving medications. It would require patients to first try all other available treatments and be unable to participate in clinical trials.

Mr. Chairman, I want to note that these provisions only apply to terminally-ill patients. It does not undo the FDA approval process, but provides a potential lifeline for those who cannot wait. It requires physician certification that other options to be exhausted or unavailable. This maintains the incentive for patients to seek out and join clinical trials. This bill requires that a product meet a demonstrated level of safety by attaining FDA Phase I approval. We've worked with drug companies to ensure adverse outcomes are not used against the ongoing application for approval. Additionally, patients, doctors, and manufacturers do not assume any additional liability under this act.

For those patients caught between the traditional drug approval delays, a clinical trial process for which they do not qualify, and limited time, Right to Try simply establishes the freedom for patients and their doctors to try therapies where the benefits far outweigh the risks. It gives them the option of trying to save their life.

Whether it's a father courageously battling ALS or a brave child living with Duchene Muscular Dystrophy, they deserve the right to try.

Thank you all for your time and consideration. I look forward to working with you.

Mr. BURGESS. Chair thanks the gentleman. The gentleman yields back.

Chair recognizes the gentleman from Arizona, Mr. Biggs, 5 minutes, please, for your statement.

STATEMENT OF HON. ANDY BIGGS

Mr. BIGGS. Thank you. Thank you, Mr. Chairman.

I, first, also thank Chairman Burgess, Ranking Member Green, and all the members of the committee for allowing me to address you today.

I am here with my friend and colleague, Representative Brian Fitzpatrick, to fight for passage for the Right to Try Act.

This bill that I introduced with Mr. Fitzpatrick in February now has dozens of bipartisan co-sponsors including members in this very room today.

I am particularly pleased that Senator Ron Johnson's bill will be considered today as well. As the committee may know, Senator Johnson's bill passed the Senate by unanimous consent.

Anyone who understands the arcane procedures of that chamber can attest that this is no mean feat. I am strongly supportive of Mr. Johnson's efforts. He has been a tireless advocate of Right to Try for years.

I won't take up a great deal of this committee's time elaborating on the virtues of the bill Representative Fitzpatrick and I introduced because, frankly, very little explanation is necessary and Mr. Fitzpatrick has done a great job explaining it.

Fundamentally, our legislation allows terminally ill patients who have no further options—I repeat, no further options—the opportunity to try experimental drugs that could save their own lives.

Yes, there are also provisions in our bill to protect both the patients themselves and the pharmaceutical companies who want to participate.

But those provisions are secondary to its primary purpose. The primary purpose of our Right to Try Act is to give brave patients across this country some choice over their own destinies when all other avenues are closed.

We should all share the same goal of doing everything we can for patients fighting to save their lives and I have no doubt that the intentions of everyone in this room are good.

So what are we waiting for? Why isn't this committee doing everything possible to get Right to Try passed out of Congress and onto President Trump's desk? That's really the next step. We need to get this out of the House.

The status quo is not the answer. We will hear claims today from the FDA and other agency officials that their own expanded access program is working and continues to improve.

There may be some truth to that and I am sure that Commissioner Gottlieb works tirelessly to help as many terminal patients as he can.

But that program is simply not enough. Frankly, that program was not put into high gear without Federal legislation looming.

I know that the program is simply not enough because I have talked to dozens and dozens of patients, family members and advocates, who tell me it is not enough.

They come to my office. They call me on the phone. They write me impassioned letters. These same advocates have ensured that Right to Try has become law in 37 States.

Think about that for a moment. In half of those 37 States, Right to Try laws passed with unanimous support—bipartisan support—and in my home State of Arizona, voters approved this initiative with nearly 80 percent of the popular vote and I am convinced that the other 20 percent were just the folks that always vote no.

At a time when pundits are claiming that our politics are broken—Republicans and Democrats can't come together on anything—here is a cause—here is the cause that Americans of all political stripes believe in.

I was first introduced to Right to Try while serving in the Arizona State Legislature with fellow legislator and friend, Laura Knaperek. By 2014, she was no longer a legislator but she was an advocate, suffering in the fight of her life against ovarian cancer.

Her mission became to see Right to Try passed into law. In the end, her efforts for this cause succeeded beyond everyone's wildest expectations. Unfortunately, Laura is no longer with us. She lost her brave battle with cancer but her legacy as a tireless patient advocate lives on.

I will continue to carry on Laura's fight, not just for her but for all those brave patients across this country who are battling against the odds every day.

I fight for Bertrand Might, for Jordan McLinn, for Matt Bellina, who is testifying today, and I fight for the countless other patients who deserve a right to try. I urge you to join in that fight. We must act further without delay.

Thank you again, Mr. Chairman, and Ranking Member Green and members of the committee. I yield back.

[The prepared statement of Mr. Biggs follows:]

Testimony of Representative Andy Biggs (Member of Congress)

October 3, 2017

Hearing: Examining Patient Access to Investigational Drugs

House Energy and Commerce Subcommittee on Health

Chairman Burgess, Ranking Member Green, and other members of the Committee: thank you for allowing me the opportunity to address you today.

I am here this morning along with my friend and colleague, Representative Brian Fitzpatrick, to fight for passage of the Right to Try Act. While I had come to this hearing expecting our legislation to be front-and-center in this discussion on expanded access to medications, I am disappointed to see that this is not the case. In fact, the bill I introduced with Mr. Fitzpatrick in February—which now has dozens of bipartisan cosponsors, including Members in this room today—is cited as an afterthought on the roster of hearing documents. I am, however, pleased that Senator Ron Johnson’s bill will be discussed. As the Committee may know, Senator Johnson’s bill passed the Senate by unanimous consent. Anyone who understands the arcane procedures of that chamber can attest that this is no mean feat. I am strongly supportive of Mr. Johnson’s efforts: he has been a tireless advocate of Right to Try for years.

I won’t take up a great deal of this Committee’s time elaborating on the virtues of the bill Representative Fitzpatrick and I introduced, because, frankly, very little explanation is necessary. Fundamentally, our legislation allows terminally ill patients who have no further options left—I

repeat that: no further options left—the opportunity to try experimental drugs that could save their own lives.

Yes, there are also provisions in our bill to protect both the patients themselves and the pharmaceutical companies who want to participate, but those provisions are secondary to its primary purpose. The primary purpose of our Right to Try Act is to give brave patients across this country some choice over their own destinies when all other avenues are gone.

We should all share the same goal of doing everything we can for patients fighting to save their lives. I have no doubt that the intentions of everyone in this room are good. So what are we waiting for? Why isn't this Committee doing everything possible to get Right to Try passed out of Congress and on to President Trump's desk?

Certainly the status quo isn't the answer. We will hear claims today from the FDA and other agency officials that their own Expanded Access program is working and continues to improve. There may be some truth to that, and I am sure that Commissioner Gottlieb works tirelessly to help as many terminal patients as he can. But that program is simply not enough.

I know this, because I have talked to dozens and dozens of patients, family members, and advocates who tell me it is not enough. They come to my office, they call me on the phone, they write me impassioned letters.

These same advocates have ensured that Right to Try has become law in 37 states. Think about that for a moment. With one more state you could ratify a constitutional amendment.

In half of these 37 states, Right to Try laws passed with unanimous support, and in my home state of the Arizona, voters approved this initiative with nearly 80 percent of the popular vote. At a time when pundits are claiming that our politics are broken, that Republicans and Democrats can't come together on anything, here's a cause that Americans of all political stripes believe in.

I myself was first introduced to Right to Try while serving in the Arizona State Legislature. It was back then that I got to know Laura Knaperek. Laura was also serving in the Legislature when I first met her, but by 2014 she was no longer a legislator; she was an advocate. That year, Laura was in the fight of her life against ovarian cancer, and her mission was to see Right to Try passed into law. In the end, her efforts for this cause succeeded beyond everyone's wildest expectations. Unfortunately, Laura is no longer with us—she lost her brave battle with cancer last year—but her legacy as a tireless patient advocate lives on.

I will continue to carry on the fight not just for Laura Knaperek, but for all those brave patients across this country who are battling against the odds every day. I fight for Bertrand Might, I fight for Jordan McLinn, I fight for Matt Bellina—who is testifying today—and I fight for the countless other patients who deserve a right to try. We must act without further delay.

Thank you again for the opportunity to testify today.

Mr. BURGESS. And the gentleman yields back, and the Chair thanks the gentlemen.

The Chair thanks both gentlemen for being here, taking time to share with us your stories and your passion and taking the time to testify before the subcommittee. It is helpful to us in our deliberations.

Again, I want to stress that there are four panels today so we are going to move smartly to the next panel. As is customary, there will not be questions for the Members from the Members, but following each of the other panels there will be opportunities for questions from Members.

Our second panel we are very, very pleased to have Dr. Scott Gottlieb, Commissioner of the United States Food and Drug Administration.

Doctor, we certainly sincerely appreciate you being here today, and you are now recognized for 5 minutes for your opening statement, please.

STATEMENT OF SCOTT GOTTLIEB, COMMISSIONER, FOOD AND DRUG ADMINISTRATION

Dr. GOTTLIEB. Good morning, Mr. Chairman, Mr. Ranking Member, and members of the subcommittee.

I want to thank you for the opportunity to testify this morning. This is my first time testifying before the Energy and Commerce Committee, and I'd like to take a moment to thank you for your strong support of FDA and its public health mission.

I know this committee and this subcommittee in particular worked hard to enact the 21st Century Cures legislation and FDARA, and I also want to acknowledge your continued efforts to modernize the review and approval of OTC products through user fee legislation and I look forward to working with you closely on all of our shared goals.

Throughout my career I've worked to advance policies to enable terminally ill patients to obtain earlier access to promising new drugs and this includes preapproval access to experimental medicines.

As a cancer survivor who used an approved drug in an off-label fashion in the treatment of my own cancer, I've grappled with some of these issues first-hand.

While my cancer was very curable, I know that many patients with serious illness face long odds, and their best chance at gaining an advantage in those odds is with something unproven and experimental, and we need to make sure that we serve these patients.

Before I discuss these goals and the issues related to Right to Try legislation, I'd like to take a moment first to acknowledge the tragedy in Las Vegas and then to expand on another tragedy unfolding in the south, the crisis facing Puerto Rico.

I want to just brief the committee on some steps that are going on right now with respect to that crisis at FDA.

I was grateful for the opportunity to accompany the Secretary of the Department of Homeland Security on her trip to Puerto Rico on Friday.

I visited with my FDA team stationed in San Juan where we have about a hundred full time staff. Our large staff is a reflection

of the significant medical product manufacturing capacity on that island.

We are now engaged in a sweeping effort to cross the entire agency to provide direct assistance to our staff and fellow citizens on the island and this includes efforts to get food and medical products onto the island and get hospitals back into full operation.

But the devastation in Puerto Rico presents a broader challenge to the FDA because it is home to a very large medical product manufacturing base for both drugs and devices.

Some of these facilities make products that could be in shortage if production is sharply diminished or pushed offline. This is particularly concerning because some of these products are critical to Americans.

A loss of access to these drugs and devices could have significant public health consequences. This includes products for the treatment of cancer and a lot of other unmet medical needs.

Getting these facilities back online is a public health priority. It's also a priority of Puerto Rico's recovery. I've discussed this matter directly with the Governor of Puerto Rico and his staff.

These sites directly employ about 90,000 residents of Puerto Rico and represent 30 percent of the island's GDP. Puerto Rico is home to an excellent high-quality manufacturing for sophisticated medical products including many injectable drugs and complex devices.

A highly skilled, highly dedicated, highly productive Puerto Rican workforce enables the success of this industry.

If we don't get these facilities back online in a timely way and they decide to relocate after this disaster, it would jeopardize the island's economic future. For many reasons, not least our concern for the people of Puerto Rico, we need to work to help to restore this manufacturing base.

I can tell you the leadership of FDA is committed to all these efforts. We stand with the people of Puerto Rico. I have been personally engaged in troubleshooting these issues, working directly with my colleagues at HHS and DHS and the staff of the Governor of Puerto Rico, and I am available to brief this committee directly on these efforts.

On the topic we are here to discuss today, I want to share some insight into some of the recent steps FDA took to improve our expanded access program and continue to facilitate access to promising drugs targeted to unmet needs prior to approval for patients with serious or immediately life-threatening illnesses who don't have other alternatives.

I have announced some new policy actions that we are taking today and we intend to take additional steps in the near future.

Critics of these efforts may look at our actions individually and say that none of these measures will materially change the current balance.

But this effort cannot be solved in one step. We need to look across the totality of what we are doing to measure the impact of our endeavors.

My goal is to establish a framework that preserves our current approval process while making sure that there are efficient achievable avenues for patients to access promising drugs targeted to unmet needs.

We need to serve all the interests of patients facing serious illness who lack good options. This includes their interest in trying unproven drugs.

I am committed to this goal. I believe in this right. I support this idea. I look forward to answering questions.

Thanks a lot.

[The prepared statement of Dr. Gottlieb follows:]



TESTIMONY OF
SCOTT GOTTLIEB, M.D.
COMMISSIONER

U.S. FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE
SUBCOMMITTEE ON HEALTH
COMMITTEE ON ENERGY AND COMMERCE
U.S. HOUSE OF REPRESENTATIVES

EXAMINING PATIENT ACCESS TO INVESTIGATIONAL DRUGS

OCTOBER 3, 2017

RELEASE ONLY UPON DELIVERY

INTRODUCTION

Mr. Chairman and Members of the Subcommittee, I am Dr. Scott Gottlieb, Commissioner of Food and Drugs at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to testify today on efforts to expand access to investigational drugs and biologics for terminally ill patients.

Access to investigational products for patients facing serious or immediately life-threatening diseases is not an abstract issue to me. As a cancer survivor who used a commercially-available combination therapy in an off-label manner, I understand, on a very personal level, that patients who are fighting serious or life-threatening diseases want the flexibility to try new therapeutic approaches, including access to investigational medical products, particularly when there is no other FDA-approved treatment option.

As a physician and the Commissioner of Food and Drugs, I also take very seriously the responsibility entrusted to FDA by Congress to ensure the safety and efficacy of the medicines on which our Nation's patients and their doctors depend. FDA works closely with industry sponsors to promote rigorous clinical trials for testing investigational products and accelerating access to safe and effective new treatments. The Agency has also long recognized that investigational products may serve as the only lifeline to patients with serious or immediately life-threatening diseases or conditions, who are unable to participate in clinical trials – and has sought to assist these vulnerable patients and their caregivers. Therefore, I am pleased to be here today to talk about our work in this critical area and new steps that we are undertaking that I

sincerely believe will better serve patients, physicians, and their caregivers in their fight against terminal diseases.

FDA's Expanded Access Program

FDA has a long history of supporting patient access to investigational new treatments. This includes working with drug companies through the clinical trial process that may lead to FDA approval of treatment, and through our expanded access program.

For over two decades, the Agency has had in place this expanded access pathway to help many patients gain access to investigational products. Since the late 1980s, FDA has facilitated access to investigational medical products for the treatment of certain seriously ill patients. In 2009, following amendments to the Federal Food, Drug, and Cosmetic Act (FD&C Act), FDA revised its regulations to consolidate and expand the various provisions regarding the use of investigational drugs and biological products for expanded access use.

In recent years, FDA has received over 1,000 applications annually for expanded access to treat patients with investigational drugs and biologics. FDA authorizes 99 percent of these requests. Emergency requests for individual patients are usually granted immediately over the phone and non-emergency requests are generally processed within a few days.

FDA believes that difficult decisions about individual treatment are best made by patients with the support and guidance of their treating physicians – and the expanded access program is

predicated on this belief. To qualify for the program, the patient's treating physician has to determine that the probable risk to the person from the investigational drug is not greater than the probable risk from the patient's disease or condition. Once the physician makes this determination and together the patient and physician decide that it is appropriate to pursue this treatment option, the physician approaches the pharmaceutical company to obtain agreement from the sponsor/company that it will provide the drug being sought. If the company agrees, the physician then submits the request to FDA. Key protections are included for patients receiving experimental treatments through the expanded access program. These protections include specific labeling requirements, prohibitions on promoting or commercializing investigational drugs by sponsors and investigators, and limits on the costs charged to patients for investigational drugs.

While the Agency permits almost all expanded access applications to proceed, it makes meaningful changes in approximately 10 percent of these cases to enhance patient safety. For example, modifications may be made to adjust dosing amounts, increase safety monitoring, and bolster informed consent. The changes are based on the scientific and medical expertise of our staff, and informed by confidential information provided to FDA by product sponsors during the course of development. This information is often unavailable to the treating physician – and the larger medical community – and becomes available only after a drug is approved.

It is important to note that access to investigational products requires the active cooperation of the treating physician, industry, and FDA in order to be successful. The most common obstacle to access to the investigational product is the willingness or ability of companies to provide it.

Neither FDA nor physicians or patients can compel a company to make a product available – and companies may decline requests for a variety of reasons. For example, they may have produced only a limited quantity of the product (companies ramp up manufacturing after marketing approval), have minimal resources to administer expanded access requests, or have concerns that granting requests for expanded access may exacerbate the challenge of recruiting clinical trial participants – and delay product development.

Once FDA permits treatment to proceed, the treating physician is responsible for obtaining informed consent from the patient and approval from an ethics committee, known as an Institutional Review Board (IRB), before administering the drug.

Recent Efforts to Streamline Expanded Access and Increase Transparency

Since its inception, FDA has continually worked to improve the expanded access program to better serve patients and physicians. Many of these changes have been made in response to feedback the Agency received from stakeholders. The Agency has a dedicated staff to assist physicians and patients to navigate the expanded access process and expedited telephone process for daytime and after-hours emergency requests. We are committed to helping patients and physicians.

Last year, FDA implemented significant changes to streamline the process for requesting expanded access for individual patients and promote greater transparency. We took a comprehensive and thorough look at the information requested by the Agency -- and slashed the

number of required fields and attachments to streamline this process. It now takes about 45 minutes to complete a single patient application form and requires just one attachment (compared with up to eight attachments previously required). The new form is accompanied by step-by-step instructions on how to complete it.

We also released guidance that explains what expanded access is, when and how to submit a request, and what type of information should be included in requests. We clarified when and how patients may be charged for investigational drugs, notably that the sponsor may generally recover only its direct costs of making the drug available to the patient. Simultaneously, FDA revamped its expanded access website and produced Fact Sheets for physicians, patients, and industry.

FDA and the National Institutes of Health/National Library of Medicine (NIH), working with patient advocacy groups, industry and others, have taken a number of steps to provide more information about the availability of clinical trials and how to obtain investigational products through expanded access. A final HHS rule, administered by NIH and FDA, which became effective earlier this year, expands the legal requirements for submission of information to *ClinicalTrials.gov* about the availability of expanded access for drugs being studied in applicable drug clinical trials and how to obtain information about such access for persons who do not qualify to participate in the clinical trial. Clinical trial sponsors who manufacture the drug product and are required to submit information to *ClinicalTrials.gov* must indicate in the registration record whether expanded access is available. If available, those sponsors must submit specific information to *ClinicalTrials.gov* that enables patients and healthcare providers

to obtain further information about access to the product. Information on the availability of expanded access must be updated when changes occur. FDA and NIH continue to provide information to assist clinical trial sponsors and investigators to help them understand their responsibilities under the final rule.

In July, we collaborated with the Reagan-Udall Foundation, patient advocacy groups, the pharmaceutical industry, and other federal agencies to launch a new online tool called the Expanded Access Navigator (Navigator). The Navigator was created to serve as a comprehensive online resource for information on obtaining investigational therapies to treat patients with serious or life-threatening illnesses who lack therapeutic alternatives. It collects for the first time, in one centralized online location, links to drug manufacturers' expanded access policies, procedures, and points of contact. The Navigator also includes additional information to help guide patients and physicians through the steps to obtain such treatments.

The Navigator offers a valuable resource for information on available investigational therapies including clinical trials. The patient and caregiver section provides links to resources on clinical trial participation, their physician's role in helping them obtain an investigational drug, and contact information for FDA's Office of Health and Constituent Affairs' Expanded Access Team. Physicians can use the tool to identify investigational treatment options, learn about important factors to discuss with patients when considering expanded access, and get contact information for FDA's Division of Drug Information for assistance with their expanded access application.

Today, FDA announced additional improvements including changes required by the recently enacted FDA Reauthorization Act of 2017 (FDARA) and the 21st Century Cures Act. Current regulations require physicians to obtain approval for expanded access requests by a full IRB in order to treat a patient with an investigational drug. IRB review is an important step to protect the rights, safety, and well-being of human subjects in clinical research – but practical delays in convening the full review board can impede prompt decision-making and vital treatment. As required by FDARA and as part of a plan to simplify the process for single patient expanded access, we just announced FDA’s plan to streamline IRB review for expanded access protocols for individual patients. At the request of the physician, just one IRB member – the chair or another appropriate person – can concur with the treatment use. I believe a simplified IRB process will facilitate access while still protecting patients.

The Agency also recognizes companies’ concerns identified in the Government Accountability Office (GAO)’s recent report regarding expanded access-related adverse events data – and is taking action to address them. Patients receiving treatment through expanded access may have more advanced disease than clinical trial participants, have multiple diseases, and/or be receiving other drugs at the same time. These factors make it more difficult to be certain about the cause of an adverse event. FDA is updating its guidance entitled, “Expanded Access to Investigational Drugs for Treatment Use: Questions and Answers” today to explain the reason for FDA’s review, to better explain our expectations with respect to adverse event reporting, and to clarify the context in which FDA reviews this information for industry.

I am confident these changes will help to address recent issues raised; however, FDA acknowledges that we can seek to continually evaluate our expanded access program for areas of

improvement. We recently awarded a five-year Blanket Purchase Agreement (BPA) to a strategic consulting firm to assist FDA with modernizing regulatory science and advancing medical products development. An evaluation of the Expanded Access program will be the first Task Order awarded under this BPA. We welcome suggestions for additional improvements.

S. 204, Right to Try Act

FDA appreciates the strong desire on the part of patients and families facing life-threatening illnesses to access experimental treatments, and how right to try policies could be limited but important avenues for these patients in some situations. Supporting patients facing such difficult situations by helping to facilitate their access to investigational therapies is a high priority for the administration. FDA appreciates the opportunity to work with Congress on right to try legislation. Right to try policies are rooted in a strong desire to help patients facing desperate situations access experimental therapies with the hope that they will help them. As noted above, this administration has supported expanding access to experimental therapies — FDA has continued to refine our Expanded Access program, authorizing over 99% of all such requests. The administration looks forward to working with Congress to help patients and their families explore available treatment options in a responsible and ethical manner, including through right to try legislation.

HHS and FDA provided technical assistance to the Senate sponsors of S. 204, the “Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017,” on earlier versions of the legislation passed by the Senate. We appreciate the changes included in

the bill so far and look forward to continuing to work with Congress and this Committee to further refine this legislation as it advances.

Technical Suggestions

The President and Vice President generally support policies that would broaden access to unapproved products to patients facing terminal illness. In order to provide greater consistency with the intent of most supporters of such policies, we recommend narrowing the eligibility in S. 204 from patients who face a “life-threatening disease or condition” to “terminal illness.” Many chronic conditions are life-threatening, but medical and behavioral interventions make them manageable without recourse to unapproved therapies.

In addition, the term used in the bill for “terminal illness” would benefit from a clear definition. We recommend defining it as “a stage of disease in which there is a reasonable likelihood that death will occur within a matter of months.”

Aligning Accountability Measures

The FD&C Act and FDA’s implementing regulations include several key protections for patients, such as provisions that ensure that unapproved products are not marketed to patients as if they are approved, and that companies are restricted in what they can charge for investigational products. These include requirements to label investigational products as such, restrictions on promoting and commercializing investigational drugs, and limits on the amount a patient may be charged. The exemption language included in S. 204 appears to bind only sponsors and

investigators to these requirements, which are found in FDA's regulations at 21 CFR sections 312.6, 312.7, and 312.8. However, it does not appear to bind others covered by the bill, which includes "**any person** who manufactures, distributes, prescribes, dispenses, introduces or delivers for introduction into interstate commerce, or provides to an eligible patient an eligible investigational drug," to these requirements. We recommend revisions clarifying that the applicable regulatory requirements would, in fact, apply to all persons listed in the bill.

Similarly, we believe that the liability effect of S. 204 may be different from what Congress intended, and suggest adjustments. If enacted without changes, sponsors and other persons providing eligible investigational drugs to eligible patients under the specified conditions of the bill would not be subject to a number of sections of the FD&C Act and FDA regulations related to clinical trials, premarket approval, and labeling. The current language in S. 204 may therefore preclude FDA from taking enforcement actions based on those provisions. However, we believe that the Senate intended FDA to retain authority to address violations of other sections of the FD&C Act, for example, those pertaining to good manufacturing practices, intentional adulteration, and truthful and not misleading labeling, and suggest edits to clarify this. We also suggest language to clarify that the Agency would not be liable under the Federal Tort Claims Act (FTCA) for actions or omissions related to the provision of eligible investigational drugs to eligible patients, as we do not believe that the Senate intended to create a cause of action under the FTCA.

CONCLUSION

Patients are at the forefront of FDA's mission to protect and promote the public health and we look forward to continuing to engage with Congress as the Agency fulfills its public health mission on behalf of patients.

The clinical trial process is crucial to the development of innovative new medical products that can improve or save patients' lives. Adequate policies and processes must be in place to appropriately balance individual patients' needs for access to investigational therapies while recognizing the importance of maintaining a rigorous clinical trial paradigm for testing investigational products to demonstrate safety and efficacy.

FDA is proud of its efforts to serve patients through its expanded access program who are unable to participate in trials and are in the difficult, heart-wrenching position of having no other therapeutic options. We look forward to making additional changes to enhance our efforts and working with you on these important issues.

I am happy to answer any questions you may have.

Mr. BURGESS. The Chair thanks the gentleman for his statement and I am in agreement with the Commissioner about the need for our intention upon helping the citizens—United States citizens in Puerto Rico and their recovery and I think you'll see some of our efforts in the children's health insurance bill that we mark up tomorrow.

Already beginning some effort to—with some help that is—that is going to be available there. But it by no means completes that task and this committee—this Congress will have a significant ahead of it in recovering from the—from the storms of September.

I am going to recognize myself for 5 minutes for questions, and we will alternate between Republicans and Democrats.

Commissioner, I guess my first question is, you know, when I arrived in the United States Congress, I don't think I had prior knowledge, as a practising physician for 25 years—I don't think I knew about clinicaltrials.gov and so as a follow-on to that, how are we communicating, yes, clinicaltrials.gov and making sure people are aware that there are clinical trials that are available but then, moreover, the availability of these expanded use programs? So what do you see as a communication strategy coming from the agency in that regard?

Dr. GOTTLIEB. Well, Mr. Chairman, in answer to your question, I think the short answer is until recent years we probably didn't communicate very well and that's why patients face more obstacles getting access to experimental drugs than perhaps they should have.

With the help of this committee we have taken new steps to try to make information about the availability of drugs through expanded access programs more available, easier to find.

There's provisions in 21 Century Cures Act that requires sponsors to post notification of the availability of drugs through expanded access programs on their Web site.

We are starting to work with sponsors to gain compliance with that. There's also provisions that they need to post information about clinical trials to clinicaltrials.gov and we are working with sponsors to broaden the compliance with that as well.

But we are not just relying on those measures, as potent and as important as they are. We are also working with the private sector and patient group interests to create some new tools and one of those tools is something I am talking about—I talked about today in my written testimony for the record, something called the Navigator, which we developed with the Reagan-Udall Foundation, which is going to create a one-stop portal for access to information about expanded use programs.

Right now that tool is targeted to drugs for oncology, for cancer. We announced today that we are going to broaden it for drugs targeted to rare diseases and we look to broaden this even further.

I think that this could become a consolidated web portal, if you will, for access to this kind of information so patients have one place to go and we've been working closely with sponsors to get them to report to this—to this new tool.

Mr. BURGESS. I thank you for that answer. In our next panel we are going to hear from the Government Accountability Office and

their recommendation for action that they give at the conclusion of the GAO report.

So their recommendation—let me just read it here—“the Commissioner of the Food and Drug Administration should clearly communicate how the agency will use adverse event data from expanded access use when reviewing drugs and biologics for approval and marketing in the United States.”

So we are going to hear testimony in the next panel that this recommendation has been given to the FDA and can you kind of brief us as to the status of that recommendation?

Is this something of which you were aware? Is this accurate?

Dr. GOTTLIEB. Well, I hate to short circuit the testimony of my colleague at the GAO, but we've taken their advice and we've announced that today.

And so we've doubled down on a proposition that we have long held that this information typically isn't used in the consideration of a product and a product's approval and we've clarified in a new guidance document that we are posting today that the circumstances under which this information would and wouldn't be used and the bottom line is that information gleaned from an expanded access program is exceedingly unlikely to be incorporated into a consideration of the approvability of a product.

We are saying today in the guidance document that we must consider the circumstances in which the product is being used as a component of whether we'll consider whether or not an adverse event recognized in the use of that product is attributable to the drug.

And in the setting of an expanded access program when you—when you have a patient with a terminal illness who is oftentimes on a lot of other therapy, it is very hard to make a determination that any one drug was responsible for any one observation in that setting and so we are exceedingly unlikely to use that information.

And just to reinforce that, we looked across a decade of experience with expanded access, 322 products that were approved over that period of time, 28 percent of which had expanded access opportunities associated with the products, and we could find no instance where information gleaned from an expanded access program was used to deny approval of the drug.

We found one instance where information gleaned from the expanded access program was incorporated into drug labeling, and we actually found one instance where the data gleaned from the expanded access program actually informed our consideration of the effectiveness of that product and helped lead to its approval.

Mr. BURGESS. I thank you for the answer.

I will yield back and recognize the gentleman from Texas, 5 minutes for questions, please.

Mr. GREEN. Thank you, Mr. Chairman, and again, Dr. Gottlieb, thank you for being here.

The legislation we are considering today offered by Senator Johnson proposes to offer terminally ill patients a new pathway to investigational products without FDA review or approval.

One of my concerns with this legislation how broadly it would apply. For example, under the Senate legislation, an eligible pa-

tient is defined as a patient diagnosed with a life-threatening disease or condition.

My first question, Commissioner, as I understood, S. 204 would provide eligibility to a much broader range of patients than those with terminal illness and even under State Right to Try laws.

Would you discuss further when a patient population is eligible for FDA's expanded access program currently and what patient population would be eligible under S. 204?

Dr. GOTTLIEB. I appreciate the question, Congressman.

I think your statement embedded in the question is correct. Right now, our expanded access program is generally available for patients facing life-threatening conditions and terminal illness.

We provide for both emergency and nonemergency situations. As part of the technical assistance that we provided to Congress in their consideration of this bill, one of the comments that we made is with respect to the definition of a terminally ill patient.

If you look across the State laws and States that have passed Right to Try laws, the language typically speaks about a patient being terminally ill to qualify for consideration under the Right to Try provisions.

Congress, in consideration of some of this legislation—and there's various bills that have been considered by this body—but in some of these legislative measures have broadened that to include life-threatening diseases or diseases that could be life threatening—excuse me, diseases that are—that are either terminal or life threatening, and this, in our estimation, could also potentially include chronic illnesses like diabetes or other diseases that while not—don't set a patient on a terminal course in an immediate way, certainly are life-threatening diseases.

And so one of the suggestions that we've had in our technical assistance, and it is also a component in my written testimony, is to consider more carefully the definition and maybe map it more closely to what some of the States have done in their consideration of this measure.

Mr. GREEN. OK. So the two issues would be terminal or life threatening?

Dr. GOTTLIEB. That's right, Congressman. As part of our technical assistance, we urge Congress to consider that language and consider whether or not it should be defined as a patient who is terminally ill, similar to what the State laws have done.

The component of a life-threatening disease is a broader definition and, as Dr. Burgess would probably agree, there's a lot of chronic illnesses that are certainly life threatening but not immediately terminal.

Mr. GREEN. My understanding from supporters of the Senate legislation and from those supporting the State Right to Try laws is that the intent is to help support increased access to investigational products for terminally ill patients.

If we are to consider legislation moving forward regarding this goal, it is my hope that we would all agree that we should align any legislation with that targeting population we are discussing in terminally ill patients and that way to make most terminally ill patients access to the drug is to have drug approval by conducting clinical trials.

I am not convinced that the FDA is a barrier to investigational treatments and I continue to have concern about this legislation. But I appreciate your testimony on this today. Yes?

Dr. GOTTLIEB. I just want to—if I may follow up, with your—with your indulgence, Congressman.

The reason—the reason why I think it might be important to consider how we define terminal illness here and not—and make sure we are not too expansive if we do move forward with this legislation is so as not to broaden it in a way that it might undermine its intended purpose.

I think the more we broaden this measure and the more it is opened up to a broader set of conditions, the more we risk undermining the central purpose of the legislation and that would be—that would be the policy reason for considering how we define that.

Mr. GREEN. Thank you, Mr. Chairman. I am almost out of time and I don't think you have time to answer the question.

One of my concerns it requires doctors and distributors to report adverse events. We need to make sure that's—if the legislation moves forward we need to make sure that's defined correctly, Mr. Chairman, and I yield back my time.

Mr. BURGESS. Gentleman yields back. The Chair thanks the gentleman.

Chair recognizes the gentleman from Oregon, Mr. Walden, chairman of the full committee, 5 minutes for questions, please.

Mr. WALDEN. I thank the gentleman and I appreciate the indulgence of the committee. We have been down with another hearing on Equifax and the little data breach issue that only affected 145.5 million Americans. So I have been done at that hearing.

Dr. Gottlieb, first of all, delighted to have you before the committee. We are delighted you're at the FDA. We appreciate the reforms that you're bringing to that agency and we look forward to a long continued interaction with you and this committee in the work that you're doing.

The FDA recently took action to simplify the expanded access process, specifically the new form for physicians as 11 elements compared to the previous 26 elements, and there is now a partnership with the Reagan-Udall Foundation to help patients and physicians navigate the process.

I know it may be a bit premature, but are you able to share any statistics on the impact of these two modernizations to the expanded access program?

Dr. GOTTLIEB. Congressman, it is too early for us to really draw any conclusions about, you know, the direct impact that it has had. We hope it will be very impactful.

Mr. WALDEN. And I appreciate your testimony and that of our colleagues, certainly, Mr. Fitzpatrick and Mr. Biggs, and I know your own personal experience.

And, you know, having lost loved ones to really tough diseases, especially cancer, and I think we all sort of grasp isn't there something else out there I can try, and it is that balance in public policy of patient safety versus trying to help people with terminal illnesses get access to something that could help them.

And so when you look at this legislation—I know you talk about better definition on the terminal illness piece—could you speak more to that and what—why that clarification might be necessary?

Because I have been told by at least one of the Senate sponsors of this bill that they are not looking for the House to make any changes out of fear it may fail if it goes back with changes. And so I am concerned about that.

Dr. GOTTLIEB. Well, I mean, the bottom line is that the definition, if it were to incorporate life-threatening diseases is broad and as a clinician I can certainly contemplate a lot of diseases that are life threatening but not immediately life threatening, and the way it is written I think the agency would have to, as a matter of legal policy, have to interpret that potentially expansively.

So it could—it could sweep in a whole range of conditions for which we didn't intend. And I would just be mindful that if the goal is to make sure that we are serving the interests of patients who are facing terminal illnesses, the more we broaden this provision and the more we potentially sweep in conditions for which we might be exposing people to unwanted side effects from experimental therapies, the more we risk undermining the whole venture that we are trying to engage in here, which is to narrowly tailor something to people who really don't have good options from available therapy.

Mr. WALDEN. And do you think the way this is currently written could hurt people then?

Dr. GOTTLIEB. Well, I think the way this—

Mr. WALDEN. The process?

Dr. GOTTLIEB. I think the way this is currently written it could undermine some of the goals of the policy and we've been consistent in providing that technical assistance all the way through.

And so I am representing the agency's point of view. In terms of hurting people, to the—to the extent that we are trying to strike a balance between taking potentially some significant risk in a setting of a terminal illness and allowing patients to take that risk and make that informed judgment and then opening up that same risk to patients who don't necessarily face the same circumstances, we are certainly going to be exposing patients with potentially less severe conditions to a risk that we might think as a matter of public policy is only appropriate if we are being good stewards of the public health is only appropriate in a setting of a terminal illness.

And so I think we need to be just cognizant of that. We are willing to allow patients to take certain risks in one setting. We think it is their right.

The question is do we think it is appropriate for patients who are in a much different setting to contemplate those same risks outside of a regulatory process that we've carefully constructed. That makes careful balances.

Mr. WALDEN. So help me understand this, if you can, the term life-threatening disease or condition. What—in real people speak, what does that mean? Who would be—what sort of conditions?

Dr. GOTTLIEB. Well, as a physician who used to treat until recently hospitalized patients, I would consider advanced diabetes a life-threatening disease. I would consider class two heart failure a life-threatening disease.

There's a lot of Americans with those conditions. They're not immediately life threatening. A lot of those patients will go on to live many years, but they face a chronic illness that is life-threatening, certainly. They might eventually succumb to their illness. That is a broad category of patients.

So, with that language, we potentially open it up to a very broad category of patients, and I can tell you through discussions that I've had with attorneys at FDA I think we'd have to interpret that broadly.

I don't think that we'd be able to, as a matter of our own interpretation of the law, further narrow that. I think, if anything, we would have to interpret that fairly expansively.

Mr. WALDEN. All right. My time has expired. Thank you very much.

Mr. BURGESS. Chair thanks the gentleman. The gentleman yields back. The Chair recognizes the gentleman from Oregon, Dr. Schrader, 5 minutes for questions, please.

Mr. SCHRADER. Thank you, Mr. Chairman. Appreciate that.

Somewhat along, I guess, the same lines of the question that's been going on here, I guess, Mr. Gottlieb, seems like there are a lot of provider groups that are not enthusiastic about the need for this legislative change. Would you comment on that?

Dr. GOTTLIEB. Well, we've heard from a lot of provider groups, certainly, and some groups that represent patients about concerns related to this legislation and I think the general concern is about the risk of undermining a regulatory process that has been carefully crafted over many years to strike a very careful balance.

I think people do worry about upsetting that balance, given all the thought that has gone into how we've created that framework.

Mr. SCHRADER. Was the—you have indicated that you already made some changes based on the GAO report. Was the report overall favorable or unfavorable to the current program?

Dr. GOTTLIEB. I felt that—I can only speak for my own interpretation of the report—I felt the report was overall favorable—a favorable view of what FDA was doing with some targeted recommendations about improvements that we can make.

Mr. SCHRADER. And, you know, again, it has been mentioned that 99 percent of the expanded use or compassionate use applications are approved.

How does it get much better than that with this new legislation? How would this new legislation affect that approval rate?

Dr. GOTTLIEB. Well, the legislation is certainly not going to affect—you know, affect an approval rate that, to your point, is 99 percent and actually getting better than 99 percent is a sweep of over a decade, and, when you look in the more recent years, I think the agency has gotten even more vigilant at trying to move these things through the agency in an efficient fashion and approve these.

I think there is a perception, and I can't speak to the perception, that there are certain companies and products that aren't necessarily being offered under the current construct and the Right to Try legislation might provide more of an incentive and an opportunity.

Probably an opportunity incentive would be the wrong word—an opportunity for companies to offer products in a different setting.

I don't necessarily see that same opportunity, because I think that the biggest obstacle to offering drugs through expanded access is the supply constraints.

I think we ought to think about how we address that separately. It think there might be ways to address that through incentives.

But from my perception where I sit—and I've been on the other side of this—I've worked in—with small biotech companies before I came to the agency, as the committee knows—the biggest obstacle I see is the availability of supply for patients who want to get access to unproven therapies.

Mr. SCHRADER. Given the fact that there are all these States that are passing or have passed Right to Try legislation, why would they be doing that if the program seems to be working so well by, you know, your testimony—would indicate working so well at this time?

Why are States doing that? Are we seeing a big upsurge or uptick in new drugs, new medical devices being approved in these Right to Try States we wouldn't through your process?

Dr. GOTTLIEB. It is hard to tell. We don't have data yet, Congressman.

I mentioned that I used a drug experimentally in my—in the treatment of my own cancer at the outset. I had a very curable cancer. I was told that I had an over 90 percent chance of curing my cancer.

What I was looking for was how do I get 90 percent to 91 and 92 percent, and the way I was going to do that was to look for pristine clinical data that could help inform me how to use available therapy in a better fashion to slightly improve my odds.

That's very different from a patient who's told that they have a 10 or 20 percent chance of surviving their illness and they are looking for something very different.

They're not looking necessarily for a study that's going to tell them how to get 20 percent to 25 percent. They are looking for something unproven—a silver bullet—something that could dramatically change their odds, and invariably that's going to be something experimental, and if it wasn't then they wouldn't be told that they only have a 20 percent chance of surviving.

I think we need to make sure we serve both patients. I am not sure that we always do. I am committed to doing that. That's why we are working on the reforms that we are doing.

I think that there's a broad perception out there that we don't always serve both patient communities well and that's been the impetus for these Right to Try laws.

I think that there are things we can do. We'll certainly work with Congress on this legislation. If Congress passes it, we will certainly implement it in a robust fashion.

I still think that there is a lot that I can do as the FDA Commissioner to try to improve programs for patients who are told that your chances of surviving your illness are 20 percent.

Mr. SCHRADER. Very good. Thank you. I yield back.

Mr. BURGESS. Chair thanks the gentleman. The gentleman yields back.

The Chair recognizes the gentleman from Texas, Mr. Barton, the vice chairman of the full committee, 5 minutes for questions, please.

Mr. BARTON. Well, thank you, Mr. Chairman. Thank you for holding this hearing.

Doctor, we appreciate you being here. I really just have one basic question and that is if we—if we believe in the doctor-patient relationship, which I do, if your doctor comes to the decision that all reasonable conventional therapeutic efforts have been exhausted in trying to protect your life and is willing to state that, and if the patient is willing to forego any legal lawsuit claims against some of these new therapies, why wouldn't the FDA approve that?

And I am told at the staff level that the FDA has been extremely responsive the last 3 or 4 years in approving requests for new treatments when the patient has exhausted all of their options.

But, you know, I listened to your answer to Chairman Walden and it sure does seem to me that even with the best of intentions the FDA still thinks they know better than the—than the doctor who's treating the patient.

Dr. GOTTLIEB. Well, Congressman, I appreciate the questions. I am not sure that I agree with the conclusion.

We do approve it. The bottom line is we do approve it and, you know, data has been quoted here that in more than 99 percent of cases that we have a request even on an emergency basis or a non-emergency basis we do approve it, and in 10,000 encounters, requests for expanded access in a nonemergency setting where we—where we denied about 25 of them, in about half of those denials it was because the drug just wasn't available and in other cases it is because we know that the drug is on a clinical hold for a significant safety reason but the public doesn't know that because the existence of the clinical hold is confidential information.

You know, we are committed to continuing to push on this and to make it easier for patients to access it. I think the issue isn't do we approve it do we not approve it.

The bottom line is in the vast, vast majority of cases we do approve it. The issue is, is it always available and do patients always know about it. And I think on the question of do patients always know that they can pursue these options, we can make that easier.

We can make that information more readily available with the help of Congress and the provisions in the 21 Century Cures.

On the question of whether or not it is always available, the answer is, unfortunately, it is not. Unfortunately, these products are supply constrained because of manufacturing constraints.

I think there, too, there are things that we can do through how we design clinical trials that potentially could make more product available in the setting—in the preapproval setting.

Mr. BARTON. Then why not just empower the FDA to say that we approve it but you may not be able to get the drug—you may not be able to get the therapy because it is not available.

Or, if you tell them no, say because this stuff is most of the time not working—we put a hold on it because it is not helping anybody, I mean, I am with you on that.

But my brother died of liver cancer and they tried all the conventional therapies in the world on him and it just wasn't working,

and we got him into a clinical trial that was helping 90 percent of the liver cancer patients but the 10 percent it didn't help it expedited the disease and he was, unfortunately, one of the—in the 10 percent group that it accelerated his cancer as opposed to terminated it.

But we knew what we were doing. We took that chance. He and his wife and his—myself and my mother, we all—and his pastor, we—we said we are going to give this a shot because if it works it will really help, and it didn't.

But we didn't—we didn't then go back and say, oh, jump on the FDA for doing it. We knew up front what the risk was and I don't—I just don't see—I mean, Mr. Griffith has a bill before this committee right now, and there are others, let's err on the side of the doctor/patient knows more.

And I am not being negative on the FDA but you're trying to protect the broad public health, which is commendable. But I would—I would say in this case let's pass some law that makes it easier to get this stuff—agreeing that in most cases you folks have been very positive about giving them the chance.

With that, Mr. Chairman, I yield back.

Mr. GUTHRIE [presiding]. Thank you. The gentleman yields back. I recognize Ms. Eshoo for 5 minutes for questions.

Ms. ESHOO. Thank you, Mr. Chairman, and welcome, Dr. Gottlieb. It's wonderful to have you here, and congratulations on heading up the FDA.

In listening to everyone, I am reminded that we are all a diagnosis away from something and I admire how you not only handled your own challenge.

But it is a source of comfort to me that—not to you probably but that you had this challenge and that you can view so many of these issues through that lens and I think that that is very important and it has really added a lot to, I think, to your testimony today.

What I am struggling to figure out what is broken here. The FDA has very good figures. I have read the GAO report and, overall, I agree with your description of it and they do add some things that the FDA can do.

But what do you think is broken here? It is my understanding that if a patient—it starts with the patient. Patient goes to the doctor and says, I have either read out or I have heard about or whatever such and such a experimental drug and I want it.

The doctor then has to request that of the manufacturer? Is there something broken down that breaks down in that process? Because we have bills before us that suggest that it is larger than what the numbers—what the data suggests.

So can you identify what you think is broken?

Dr. GOTTLIEB. Well, I would like to just start, Congresswoman—I appreciate the opportunity to answer your question.

I am—in response to the last question, I am in favor of giving patients—sick patients options and in the setting of a patient who's suffering—in the setting of most patients that's the safe and approved option that's been reviewed by the FDA.

Ms. ESHOO. Right.

Dr. GOTTLIEB. But sometimes that's an unproven option and sometimes the risk of nothing is worse than the risk of something

experimental and we need to consider that and we do consider that through our expanded access program.

But this is a complicated issue, and to your point, there are things that aren't working that are frustrating the ability of patients even who have a physician who's willing to work with them, even who I have identified a drug that they think can help their illness, even with an FDA that is devoting a lot of new resources to trying to facilitate access to these products.

Even with all of that, patients still have trouble getting access to products that they think can help save their life.

Ms. ESHOO. But why are they having trouble getting access to it?

Dr. GOTTLIEB. The supply—the biggest reason is supply.

Ms. ESHOO. It is the supply?

Dr. GOTTLIEB. The biggest reason is that when we do clinical trials—when companies do clinical trials, they don't have continuous manufacturing.

They don't have large facilities online pumping out endless supplies of a drug. They will do what they—what they call discontinuous batches.

They'll do—they'll do runs just to create batches of drug supply and API—active pharmaceutical ingredients—sufficient for the clinical trial and that supply doesn't go through the good manufacturing standards that a supply of drug goes through that's commercially available.

Ms. ESHOO. On this supply issue, do either one of the bills address any of this?

Dr. GOTTLIEB. No. We would have to think of different ways to provide incentives or perhaps a different clinical trial framework to try to get at that issue.

Ms. ESHOO. Uh-huh. Now, one of the bills before us today would allow patients to access the investigational drugs while the other would allow patients to access investigational drugs and devices. That's a—that's a whole another very important area.

Now, if patients are granted access to unapproved medical devices that a physician isn't trained to use, there could be, I think, some bad outcomes.

Now, I understand that medical device companies already face many challenges to enrolling patients in clinical trials. The Right to Try proposals that include devices could divert patients from otherwise—I think from participating in a clinical trial.

So give us your thoughts on Right to Try legislation including medical devices in addition to drugs.

Dr. GOTTLIEB. Well, I think your statement is correct. I agree with it. Medical devices are tools in the hands of physicians. Physicians often have to undergo very rigorous training on devices, even after they are newly approved.

And so there's a different set of considerations and potential risks associated with making devices available in a setting where you don't have the normal structure—regulatory structure in place.

But setting that aside, we believe that the compassionate use framework on the medical device side of our house is working quite well, has a very quick turnaround time.

We don't necessarily see the same considerations in that setting that we see in the setting of new drugs nor are we likely to see

the availability of the devices to be used in a preapproval way like we might have.

At least in certain circumstances, you have drug supply preapproval that could be lotteried out in many cases to patients who want to get access to it on an expanded access basis. In the medical device setting, you typically would not have excess medical device supply.

Ms. ESHOO. I don't understand your answer. [Laughter.]

Do you—are you saying that you don't think it is necessary to include devices to drugs?

Dr. GOTTLIEB. We don't—we don't see the same—I don't see the same concerns in part because the compassionate use program on the medical device side—of the house is working well and I also would say I don't see the same opportunity for patients because to the extent that I've said that the supply of the drugs is constrained preapproval the supply of devices preapproval is even more constrained.

Ms. ESHOO. Thank you very much.

Thank you, Mr. Chairman.

Mr. BURGESS [presiding]. Gentlelady yields back.

The Chair recognizes the gentleman from Kentucky, Mr. Guthrie, 5 minutes for questions, please.

Mr. GUTHRIE. Thank you very much, and I will ask a question, Dr. Gottlieb. Thanks for coming. I appreciate you being here.

Kind of the scenario that my friend from Texas, Mr. Barton, gave when he said that his brother or people get to the point where the doctor said everything conventionally has been done for you—there's nothing else we can do for you and then you have the right to try, and that's a traumatic time. I know it is a traumatic thing and people are looking at opportunities and that's what's available for them.

So they choose to go to the experimental side—the unproven side—and agree to pay for that treatment. So but what's unclear in the legislation is what if—and I quote, you said that you could get unwanted side effects.

So what if the unwanted side effects creates a whole series of health—puts them back in the hospital? And so instead of agreeing to pay what—an X amount for some kind of treatment all of a sudden there's new hospital bills that could be astronomical that's not looked at in the legislation.

So my question, do you have any insight or opinion on how to best examine or solve this type of issue?

Dr. GOTTLIEB. Well, I think it is one of the unknowns associated with using, you know, any product that hasn't gone through a full evaluation where we don't know the scope of the effectiveness of the product, you know, and we don't know—we certainly don't know the full scope of the side effects.

A product that has gone through a Phase 1 clinical trial—we call a Phase 1 trial a safety trial, but it is a trial for determining safety—to answer the question on whether or not the drug can proceed into the next phases of clinical trials doesn't fully establish the safety profile of the product.

We are continuously learning about the safety of a product all through the three phases of a clinical study, and, in fact, a lot of

what we learn about the safety of products is in the post-market setting.

So there are a lot of unknowns in this setting and we need to be cognizant of that and, you know, patients who use these products through an expanded access program we make sure that they are cognizant of it.

Mr. GUTHRIE. But my question gets into if they agree to pay for this and then it leads into further medical costs outside of just the experiment that puts them back in the hospital and so forth, which I guess would be part of it, do you have any opinion how that should be addressed?

Dr. GOTTLIEB. The system—I would—I would put that question to my colleague, Seema Verma, at CMS. I mean, this is going to be an issue for the broader health system and for the payers to have to contemplate because the cost would be—would be born back on the—on the payer system.

Mr. GUTHRIE. OK. Thanks for that.

And I do want to mention just a comment to you while you're here. I do want to mention one more issue regarding the potential threat of glass fragment contamination.

As you may know, the FDA issued an advisory regarding glass fragment contamination for injectable drugs in 2011. I ask that you look into and fully consider updating the advisory to reflect recent discoveries. So no reason for that.

And for my final couple of minutes, I understand—and there's an Equifax hearing going on downstairs, so I was there earlier and I understand you talked about your trip to Puerto Rico.

I just ran into my colleague on the way up here from the Virgin Islands and, you know, it is very dramatic or very—very drastic situation and dramatic as well and that's going on there.

And would you just kind of update us on what you're doing to combat potential drug shortages and access to issues that may come as a result of damages. I know your trip to Puerto Rico and also the Virgin Islands.

Dr. GOTTLIEB. As I mentioned, we have a list of about 40 drugs that we are very concerned about. It reflects maybe about 10 different first. These are drugs—13 of them are sole-sourced drugs.

They're only manufactured in Puerto Rico to supply the entire U.S. market and these are—these are important medicines. These are drugs—these are HIV medications and chemotherapeutics and injectable drugs that are hard to manufacture.

There's biologics. There's very sophisticated medical devices manufactured down there. The biggest issue right now—well, there's a lot of issues.

One is getting gasoline and basic sustenance to employees so they can return to work. People are living in very difficult circumstances there and I met a lot of—a lot of local resident who work for FDA. But the longer-term issue that we are grappling with and worried about is power supply.

The grid is probably going to be stood back up. They'll create some micro grids. They won't stand up the whole electrical grid. They'll create micro grids.

But the challenge for the manufacturers is that they need stable power and typically they need dual feeds coming in because of the

equipment that they use. And we know that the grid is going to be unstable for a long period of time.

In fact the power company would like to reconnect the manufacturing facilities because as they bring up the power system they need load balance and the manufacturers are regular users of power. But manufacturers want to stay off the grid right now.

And so they are going to be operating for long periods of time, potentially, on their generators—generators that were never meant to operate for months and months on end.

So they don't have necessarily the fuel. Thanks to do it and they might not have generators that are up to that challenge.

And so we are trying to trouble shoot that with them on an individual basis now and trying to put in place contingencies if things do go wrong and backups if we need them.

We've been doing that manufacturer by manufacturer, working very closely with DHS and the staff of the Governor of Puerto Rico, who we are now in personal contact with who understands the implications and the importance of this manufacturing base not just for all of the United States but for the island of Puerto Rico as well.

Mr. GUTHRIE. Thank you very much. I appreciate your efforts.

Mr. BURGESS. Chair thanks the gentleman. The gentleman yields back.

The Chair recognizes the gentleman from Maryland, Mr. Sarbanes, 5 minutes for questions, please.

Mr. SARBANES. Thank you, Mr. Chairman.

Thank you, Dr. Gottlieb, for your testimony here today. I am sort of picking up on the line of questioning from Congresswoman Eshoo in terms of trying to understand what the piece of this process that you would view—that one would view as broken when you've got over a 99 percent rate of responding to these requests for approval.

And, obviously, there is a constituency out there that feels that notwithstanding what the FDA is doing in its efforts to respond to these inquiries and requests that there's still something more than can be done in terms of accessing expanded treatment options.

So maybe—could you give me the 30-second caution that FDA—sort of a digest of a lot of what you've been saying—the caution you would give us as we are examining and reviewing and debating the pieces of legislation that kind of stimulated the hearing today and that we got some testimony about at the outset?

From your perspective, what would you just say to us—here's what I would look out for, be cautious about as you're examining the kind of Right to Try legislation that's being proposed?

Dr. GOTTLIEB. Well, I would just say, you know, you asked about the—and I know I am limited to 30 seconds. You asked about the obstacles.

You know, one of the obstacles is are patients informed and we are trying to do all we can to make sure they are informed of these opportunities.

The other obstacle I talked about was—which is just the supply. That's harder to fix. I think there's a perception that this legislation will create more pressure on companies to offer the drug so

that might create more pressure on the companies to have a supply available.

I think that's an open question. I think that's something Congress should contemplate.

But in terms of the question of the caution, you know, in addition to the technical assistance we've provided that is more detailed about legislative language, I just would be mindful that we don't create a process and a policy framework where the only people who take advantage of the avenue are people who have the least promising products.

I think what we want to—what we want to do is create a framework where the most promising products are being made available to patients and this doesn't become sort of an opportunity for those sponsors or maybe even individual clinicians who want to do some advanced marketing of a product to use this vehicle.

And I am not saying that this legislation will do that. I am just saying if I was providing feedback to Congress of what to be mindful of, that's something that I would caution Congress around.

Mr. SARBANES. Well, actually I appreciate that because you've led—in your answer you've gone right to the place that I have some anxiety about, which is the potential to create something that may start small but would grow as a kind of unregulated space and that once established as a kind of alternative route, not just for patients that are genuinely seeking whatever option is available to them but for manufacturers as well, it becomes a kind of alternative space in which to operate and then it could be vulnerable to some unscrupulous activity, in a sense creating a place where the opportunity to experiment with experimental drugs is expanded and that's what makes me a little bit nervous.

So in the 1 minute that's left maybe you could speak to that.

Dr. GOTTLIEB. Well, I would build on it by saying—you used the word “manufacturer.” I would build on it by saying it is not just the manufacturer.

We recently took regulatory action against two clinics that were marketing unapproved products as regenerative medicine. In one case, we had U.S. marshals seize a product that we felt was creating certain public health concerns, and I won't get into the details of it today since it is an ongoing activity.

But there's also going to be individual providers who potentially could promulgate products under this—under this framework and one of the—one of the elements of feedback that we've given to Congress through our technical assistance is to make sure that the patient protections that Congress intended to be available under this legislation are also available to patients who are getting products directly from physicians or physician-operated clinics and not just manufacturer because the way Congress crafted the draft legislation it could be interpreted in certain settings as those patient protections only applying to products promulgated by manufacturers, by sponsors, and in fact under this legislation it will also be providers who are promulgating products.

Mr. SARBANES. OK. That's very helpful. Thank you.

Mr. BURGESS. Gentleman yields back. The Chair thanks the gentleman.

The Chair recognizes the gentleman from New Jersey, Mr. Lance, 5 minutes for questions, please.

Mr. LANCE. Thank you, Mr. Chairman.

Good morning to you, Dr. Gottlieb. The legislation passed unanimously in the Senate. Were you involved in that or was it a situation with your—with a predecessor?

Dr. GOTTLIEB. That happened on my predecessor's watch.

Mr. LANCE. And it is unusual—not unique but it is unusual when legislation passes unanimously in the Senate I think that would be fair to say and from your perspective, reviewing it, knowing that you were not then in charge, why do you think that this legislation passed unanimously in the Senate?

Dr. GOTTLIEB. Actually, I'll reopen the record to say I am not sure the date that it passed. It might have been on my watch but—

Mr. LANCE. Fair enough.

Dr. GOTTLIEB [continuing]. So we'll just—we'll leave it open.

Mr. LANCE. But you were new to your responsibilities. I understand that.

Dr. GOTTLIEB. But, look, I think as I've stated in my comments here today, this touches on a very important issue and it touches on an issue that I think is very visceral for most Americans.

We have all—most of us have seen loved ones, unfortunately, or friends succumb to serious illness and in certain situations we've seen them do that in a setting of feeling like they didn't have good options to try to beat back—beat back a serious illness.

And so, you know, the idea of being able to get access, we are seeing all this new technology, all these extremely promising drugs and development.

We are seeing the potential to fundamentally cure pediatric inherited disorders through things like gene therapy and regenerative medicine.

With all this technology coming online, I understand the desire of people who are—who are stricken with the disease now to want access to that. I think that this—I think this phenomenon is being driven in part by the opportunities we have available to us now.

Mr. LANCE. Thank you. As a matter of full disclosure, since you have kindly indicated you might technically have been in charge but certainly the bulk of the work in the Senate was before you were in charge, I have worked with Congressman Fitzpatrick.

The district that I am honored to represent borders his district although we are in different States, and I've worked with Mr. Worthington, who is in this room, on this very important issue.

The FDA may place a clinical hold on a drug. If, for example, human volunteers are being subject to unreasonable and significant risks of illness or injury, has the FDA placed a clinical hold on a drug as a result of an adverse event during an expanded access protocol?

Dr. GOTTLIEB. I don't know the answer to the question. I would tend to think not, just given the numbers of situations where we've recognized adverse events in the setting of an expanded access program that have led to any kind of regulatory decision.

You know, we've done some systematic looks back and found very few instances where something we observed in the setting of an ex-

panded access program has prompted us to take certain regulatory actions.

Certainly, the inverse case where we have—you know, I think I mentioned previously a large percentage of the very small number of cases where we might deny a patient a request for—to use a drug in an expanded access setting is predicated on the existence of a clinical hold that might not be known to the public because it is commercially confidential information.

Mr. LANCE. Thank you. If you would, at your convenience could you get back to us, to the subcommittee, on whether or not that has occurred? I would appreciate that.

Dr. GOTTLIEB. Sure.

Mr. LANCE. Thank you.

This is a very difficult issue and I certainly understand your point of view. I think there are many of us in Congress who are sympathetic to what occurred in the Senate and, certainly, sympathetic to the legislation of our colleagues who testified, to my immediate right, and we want to continue to work with you.

But, certainly, I believe there is merit to the legislation that's being considered.

Thank you for your testimony, Dr. Gottlieb.

Dr. GOTTLIEB. Thanks a lot, Congressman.

Mr. BURGESS. Chair thanks the gentleman. Gentleman yields back.

The Chair recognizes the gentleman from Virginia, Mr. Griffith, 5 minutes for questions, please.

Mr. GRIFFITH. Thank you very much, Mr. Chairman. Thank you, Dr. Gottlieb for being here with us today.

In testimony earlier today you were talking about the definition of terminal. I would note that neither House bill, neither Mr. Fitzpatrick and Mr. Biggs' or mine goes the step beyond terminal—that the Senate went and I can appreciate that. Then we got into, you know, what the definition of terminal ought to be.

I am happy to work with you all on that. I think, if I remember correctly, and you correct me if I am wrong, that you indicated somewhere around 20 percent survival odds was where you would probably put it. I'd probably push it a little higher.

Dr. GOTTLIEB. I wouldn't. I didn't—

Mr. GRIFFITH. I misunderstood—

Dr. GOTTLIEB [continuing]. Mean to suggest that there is an objective figure. I was just using the example of a patient who's given a very grim prognosis. I would certainly consider 20 percent odds of survival grim.

Mr. GRIFFITH. And I would, too, and I think that's where this is coming from. I might push that a little higher. Anything less than 50/50—you know, if it were me, I'd want to be able to find out what was out there.

Dr. GOTTLIEB. It was grim when I was told it was 90 percent odds of living 5 years. That felt pretty grim at the time, too, Congressman.

Mr. GRIFFITH. Yes, sir. I can appreciate that.

So I want to work with you on that, but I do think that we need to pass something, and we'll try to figure it out.

But I can see where you're concerned about chronic—you know, FDA was created in 1906 to protect Americans, not to get in the way of them taking treatment and I will—if it were to be me and I—right now, I am fine.

But as Ms. Eshoo said, we are all one diagnosis away from facing something. I would take the chance with the silver bullet or the Hail Mary, and we are going to hear testimony later today that the—some wealthy Americans are going to other countries to get treatments or to get drugs.

And so my question would be if it has already been approved somewhere else and you have a terminal diagnosis, why shouldn't you be able to get that in the United States?

Dr. GOTTLIEB. Well, I think you're touching on the issue of reciprocity, which is—which is some legislation that has been introduced in other—other settings, whether or not FDA should predicate approvals here in the U.S. on the basis of foreign approvals.

And we are certainly happy to work with Congress on those legislative ideas. The framework that we operate in right now is a requirement that we determine safety and efficacy based on our statute and clinical trials that we work with sponsors to conduct and evaluate.

You know, another element of this consideration is also relying more on foreign data, which we are doing as a matter of regulatory policy and that is something we can do without new legislative authority.

We can do that within the constructs of our current regulatory considerations and we are looking for ways to do that.

Mr. GRIFFITH. And I appreciate that and I appreciated your comments earlier about some of the new things that you're doing and that you're announcing today and I appreciate that as well.

You know, the GAO report found that when the FDA did not allow a request for expanded access to proceed one of the reasons listed was due to the requested drugs demonstrated a lack of efficacy for its intended use.

But what if data showed that the intended use—it may not have been the intended use but that it actually had benefits that were unexpected in another area and you're facing that terminal illness that it does have the benefit for. I am just curious how the FDA would deal with that in its current process.

Dr. GOTTLIEB. Well, most of the cases where we are authorizing or, you know, allowing drugs to be used, in 99 percent of the cases where we—where we allow patients to use drugs in the setting of expanded access it's in a setting that is not the intended use of the product—that they'd be used for which the drug itself is being studied.

So it's in an unstudied indication or an indication that might be being evaluated in very small clinical trials.

When we—when you—when the GAO says that it was something when we didn't allow it to be used and something unproven because of something we knew, typically it was something we knew because we get a lot of clinical data from a lot of different sponsors and we might know that a drug in a certain class doesn't work in that class because of other data that we are seeing.

And so then we might make a judgment that we shouldn't allow that drug to be made available in a setting of expanded access when we have objective proof that it's not going to provide any benefit.

I mean, bear in mind, we know that 70 percent of all drugs that are offered in an expanded access are never approved by FDA. So the vast majority of people who will use a drug through expanded access are using a drug that doesn't work.

Mr. GRIFFITH. And I appreciate that. I am running out of time so I am just going to make one last comment. I do think that the two House versions both have device in there.

I think we should keep that because, as you said, science is moving fairly quickly. That's one of the reasons that people want to try these things before you all have had a chance.

There's some wonderful things out there with science. Again, if I had a diagnosis with inoperable cancer and they had a new nanobot technology, I'd be finding out where I could get that, and that is considered a medical device and it may be very, very helpful.

Not ready yet, but if it were when I was ready or needed it, I'd want to be able to use it.

Thank you so much for your time, and I yield back.

Mr. BURGESS. Gentleman yields back. The Chair thanks the gentleman.

The Chair recognizes the gentleman from North Carolina, Mr. Hudson, 5 minutes for questions, please.

Mr. HUDSON. Thank you. Dr. Gottlieb, thank you for being here today with your testimony.

FDA categorizes expanded access and the four different types of requests, as you're aware, are single patient, single patient emergency, intermediate size, and treatment for widespread populations.

While the standard process seems to get a lot of attention, I'd like to ask more about the intermediate size and treatment for widespread populations.

How are these two types of requests separate and unique from the larger clinical trial?

Dr. GOTTLIEB. Congressman, we could get you more detailed information because there's a spectrum of opportunities.

It is the case that, for example, and I think you mentioned this—when a drug is—in the period of time when it's completed its clinical trials but is awaiting approval decisions, companies will open up large expanded access programs typically like simple large protocols and offer drugs on a protocol basis.

I think that these are—these are important opportunities because what we are talking about today, a one-off request for a drug—an individual patient and their doctor working with the agency to ask for a drug in a single situation.

I think what we'd like to see is more opportunities to offer products in things like simple large safety trials and certain simple protocols where patients aren't being randomized but some basic information is being collected that can help inform—inform what we know about that product but also provide for more wide scale access.

And this gets into a broader question around how do we embrace different clinical trial designs and if we can go down these routes we can come up with constructs I think can enable much broader access preapproval.

Mr. HUDSON. Makes sense. Are these patients incorporated into the broader clinical trial population for the purposes of data collection and efficacy?

Dr. GOTTLIEB. Sometimes. Sometimes we are collecting data from these kinds of protocols. Sometimes we are not.

I think to the extent that we can get into collecting more data and being able to make efficient use of that data it can help accelerate the development process.

So this is something, you know, that we are looking at when we talk about seamless clinical trials. You know, we talk about allowing the study of different indications within the confines of a single clinical trial.

These are all some of the new scientific frameworks that we are looking at to try to—try to evolve how we do clinical trials and I think can both allow us to get better information and make the development process itself more efficient but also enable larger, more access to drugs preapproval and in some kind of clinical trial where there is—where there is good protections being afforded to patients as well.

Mr. HUDSON. Have there been any cases where patients have been denied access to a clinical trial but received access through an intermediate size or treatments for widespread populations as a result of the expanded access program?

Dr. GOTTLIEB. Oh, I am sure there has, Congressman.

Mr. HUDSON. Is the expanded access program alone adequate to address the needs of patients and physicians who are seeking to obtain investigational drugs?

Dr. GOTTLIEB. Well, I don't think we'd be here today if there was a perception by Congress and the broader community that the existing system was adequate.

And I am not going to tell you that the existing system is perfect. That's why we announced a set of changes today and that is why, as part of that announcement, I committed to do additional things down the road that—some of which we are working on right now to help continue to improve that process.

Mr. HUDSON. Great. We look forward to working with you on that.

Dr. GOTTLIEB. Thanks a lot.

Mr. HUDSON. With that, Mr. Chairman, I will yield back.

Mr. BURGESS. Chair thanks the gentleman.

The Chair recognizes the gentleman from Georgia, Mr. Carter, 5 minutes for questions, please.

Mr. CARTER. Thank you, Dr. Gottlieb, for being here.

Help me understand, basically. We are talking about two different scenarios here. We are talking about drugs that have been approved already by the FDA for something but what they are wanting to be used for is not an indication so physicians are trying to use it off label, if you will.

And we are also talking about investigational drugs that have not been approved yet but are in the pipeline and is—am I right in that?

Dr. GOTTLIEB. Well, I think that you're right that those are two constructs that exist for patients to get access to unproven therapy.

I was a patient who used an approved product in an off-label fashion and that is actually typically what you see in these settings.

You'll see products used—especially oncology you'll see products used off-label. I think what we are focused on with respect to the legislation here, respectfully, is the second scenario that you offered, which is a product that hasn't yet been approved by the FDA but patients want to use it in an experimental or investigational way.

Mr. CARTER. OK. It's my understand the FDA—your responsibility is to protect the public from any side effects, any bad effects that a medication may have but also to make sure that it's available if it could benefit the public as well. Is that correct?

Dr. GOTTLIEB. Well, I think the scope of the FDA's mission is broader. I think the scope of our mission and our responsibility to patients is much broader in this context.

I would—I would tweak it by saying I think our responsibility is to make sure that patients and providers are fully informed of both the risks and the benefits in these settings.

Mr. CARTER. OK. Having said that, can you explain to me why the FDA keeps putting their head in the sand when it comes to medical marijuana?

I am not—and I don't want to hear marijuana is a Schedule One drug for investigational use only. But here we have—I don't know how many States we are up to now—that have approved it.

Here we have all these States, and most of them with a different strength of what they've approved, and yet the FDA just continues to ignore that.

Isn't it your responsibility to address that?

Dr. GOTTLIEB. Well, I see people who are developing products based on marijuana, making all kinds of clinical claims on the market.

I see people who are developing products making claims that marijuana has antitumor effects in the setting of cancer, and I think reasonable people can ask reasonable questions about whether marijuana is a chemotherapeutic agent.

So, you know, it's a much broader question, Congressman, about where our responsibility is to step into this and start to ask questions about the claims that are being made.

Mr. CARTER. And that is my question. Where does your responsibility come in? It would appear to me, when you've got all these States that are approving it, it would appear that the FDA should be stepping in to give some kind of consistency here.

Dr. GOTTLIEB. Well, I think that we'll have some answers to this question very soon because I think we do bear a responsibility to start to address these questions.

Mr. CARTER. Let me ask you, the bills that we are considering today how will that change your approach? Will it change your approach at all? Will it change your role in the process at all?

Dr. GOTTLIEB. If these bills are passed, we look forward to working with Congress to make sure that they are faithfully implemented.

It will—it will open up a new vehicle for patients to potentially get access to certain therapies. I think the question that I outlined throughout my testimony today still remains about whether or not sponsors will offer these opportunities on any—on any greater basis and whether or not this legislation alone is enough to compel sponsors to have supply available to offer products more generously on an expanded access basis.

I think that those questions remain unanswered. I don't have an answer to those questions.

Mr. CARTER. OK. Two more things, real quick.

First of all, you've read over the legislation, I assume, that is being proposed?

Dr. GOTTLIEB. Certainly.

Mr. CARTER. Is there any part of it that you think that the FDA potentially could have trouble because what—understanding or implementing because what I don't want to happen is to have legislative intent interpreted by the agency when that is not what we were intending to do?

Dr. GOTTLIEB. Well, I mean, I've outlined some of the—some of the places—

Mr. CARTER. We've had that experience before in other areas.

Dr. GOTTLIEB. Right. Well, look, and legislation can be interpreted differently by different FDA Commissioners as well, as you're well aware.

I have outlined some of the areas where we think that there might be ambiguity in the current language right now where Congress might take closer consideration of how certain things are crafted and how certain things are worded to potentially tighten this up.

And we have tried to be constructive. We will continue to try to be constructive and work with Congress if this legislation does advance.

Mr. CARTER. OK. Once last question—I just—you know, and I go back to my question at the beginning—I am to understand your answer about medical marijuana is that FDA is going to be addressing that situation very soon?

Dr. GOTTLIEB. Congressman, you know, the question is should we be taking enforcement action against people who are making certain claims in the market? Because I don't necessarily understand your question. We don't have—we have 20—

Mr. CARTER. My question is simple: Why does the FDA continue to ignore medical marijuana when we have States who are approving it?

Dr. GOTTLIEB. Well, this—

Mr. CARTER. We have States who are actually taking on the responsibility of approving medications.

Dr. GOTTLIEB. We have two frameworks that we operate in.

One is sponsors who bring us applications requesting that we approve a product for a certain intended use. We have 20 INDs and active INDs in house right now that are for marijuana products.

They are typically for marijuana extracts because delivering an active pharmaceutical ingredient through inhalation isn't always the most efficient route.

The other question that gets to your question is whether or not there are certain claims being made in the market by people who are marketing marijuana in interstate commerce that are unapproved new drug claims and could potentially put people at risk. That's a separate question.

I think that we are addressing—we will address the sweep of these questions in time, including the questions put before us from sponsors that have 20 INDs.

Mr. CARTER. If you can — can I get some kind of idea of when you're going to address this?

Dr. GOTTLIEB. Well, we have 20 INDs in house and so we are addressing those as part of our review process.

Mr. CARTER. Do those 20 INDs have all these States approving them already?

Dr. GOTTLIEB. These are—these typically are sponsors who are putting products through—trying to put products through a scientific process and not just marketing it on a Web site.

Mr. BURGESS. And the Chair would advise there's likely to be a multiagency approach to this. It is not going to be exclusively through the Food and Drug Administration.

Mr. CARTER. And that is well understood. But, certainly, they have a role in it that I feel like they are ignoring.

Mr. BURGESS. And the gentleman's time is expired and the Chair will recognize the gentlelady from Colorado, Ms. DeGette, 5 minutes for questions, please.

Ms. DEGETTE. Thank you very much, Mr. Chairman. Tempting though it may be to follow up on this medical marijuana, being from Colorado, I want to talk to you—

[Laughter.]

Ms. DEGETTE [continuing]. Broadly about the current safeguards that are in place under the FDA's expanded access program to protect patients.

Can you please describe those for me?

Dr. GOTTLIEB. The safeguards that we have in place with respect to patients who get products through our current—

Ms. DEGETTE. Right.

Dr. GOTTLIEB. Well, the requests come into to FDA and we are asked to evaluate them, and we do go through the protocols and make certain assessments and in certain cases we provide feedback to the providers.

As has been stated here, we grant over 99 percent of the requests. But there are about 10 percent where we make certain modifications to protect patient safety and the most common modification that we'll make is to give feedback to adjust the dose and that will be on information that we might have about what the—what the most potentially beneficial dose of the product might be.

Another modification that we'll oftentimes make is on the informed consent. Sometimes the consent that is being provided to the patient might not be comprehensive. And so we'll ask for modifications to be made to the informed consent.

So that gives you a flavor of the kinds of protections that we think we are providing by being part of this process and part of the evaluation.

Ms. DEGETTE. You know, as you say in your testimony, the Senate Right to Try legislation tries to apply some of the protections to investigational product use under Right to Try, but it doesn't make clear that the requirements apply to all individuals who might provide a drug under Right to Try.

Can you explain how this loophole might be exploited?

Dr. GOTTLIEB. Well, I think you're referring to the—how the legislation currently tries to map to existing regulations in terms of importing some of the existing patient protections that exist in regulation to apply to patients in the setting in one version of the bill.

The way we interpret it there is the potential that as a matter of law you could interpret the regulations that exist as applying to sponsors, companies, and I think what we are likely to experience in the setting of Right to Try, if we look at some of the anecdotal experience in the States—and right now we only have anecdotal experience, because we don't have any data about the availability of drugs that have been provided through these Right to Try laws—but it is possible that it will be the case that some of the products that will be offered under the framework contemplated by this legislation will be offered by individual sponsors or small clinics that might not qualify as a sponsor for purposes of the way the regulation is currently crafted.

Ms. DEGETTE. Yes. Thanks.

Now, as I understand it, of the 99 percent of requests for expanded access that FDA has approved, the agency proposed changes in 10 percent of the applications to ensure patient safety either through dosing changes, informed consent, or safety monitoring.

Under the Senate-passed legislation, the FDA review of INDs would no longer be required. Can you talk to us a little bit further about how—about what you see the FDA's role in reviewing these INDs and whether it protects patients—whether under this new legislative paradigm some things could potentially be missed because the FDA is not reviewing it?

Dr. GOTTLIEB. Well, we certainly believe that we are helping to provide additional safeguards and protections to patients. I think we would state very strongly that we also think we are providing additional opportunities to patients because, you know, in terms of—you mentioned the issue of the dose adjustments.

Sometimes we will request dose adjustments because we might have information to suggest, based on other trials ongoing that we are looking at, that if there is a benefit to be derived it would have to be a higher dose or it might have to be a lower dose.

And so we are making adjustments to help maximize the opportunity for the patient to derive a benefit and not experience a side effect.

Ms. DEGETTE. So what I am hearing you say is, is the agency is really concerned about making sure these—that the dosages are correct and all of that.

You're not really trying to use this as a barrier to people getting much-needed medication for some of these diseases.

Dr. GOTTLIEB. Well, I think statistics speak louder than anecdote and if we are granting well over 99 percent of these requests, both the emergency and nonemergency requests, the agency—the agency's process once a patient walks up to the door and is able to walk through that process, that process where we are applying a level of review is not in and of itself a barrier.

I mean, the numbers demonstrate that. I mean, the question is are patients able to walk up to that door and that's where we are making reforms and trying to put in place new tools like the Navigator to get more patients into that door.

Ms. DEGETTE. And you're open to more requests like that?

Dr. GOTTLIEB. We absolutely are.

Ms. DEGETTE. Thank you. I yield back.

Mr. BURGESS. Chair thanks the gentlelady. The gentlelady yields back.

And recognizes the gentlelady from Indiana, Mrs. Brooks, 5 minutes for questions, please.

Mrs. BROOKS. Thank you, Mr. Chairman, and good to see you, Dr. Gottlieb.

I want to continue to discuss briefly about the expanded access program but then also I want to make sure we spend a little bit of time just talking about your recent trip to Puerto Rico.

But with respect to the expanded access and the FDA's desire to increase the requests and so forth, of the 99 percent of the requests made for expanded access and which are approved, I understand that only about 30 percent of those therapies actually make it through the full clinical trial process.

And so what are the steps a manufacturer has to then go through to proceed on with the clinical trial when they are including the expanded access?

Dr. GOTTLIEB. Well—

Mrs. BROOKS. How does it impact their clinical trials?

Dr. GOTTLIEB. We would say it doesn't impact the clinical trials and, you know, one of the questions has been does—could something observed in the setting of an expanded access program where you have drugs being provided in a more unstructured way, typically by physicians who might not be as familiar with the product itself—could something—could an observation made in that setting go on to help delay the development process and that's always been argued to be something that causes manufacturers' reluctance to offer these.

We would say no, and what I would say simply in response to your question is these two things can exist in parallel and they do exist in parallel.

Companies will offer drugs on an expanded access basis and they'll have an ongoing clinical development program. The question for the sponsor—and I mentioned earlier I have been on the other side of this working with small biotech companies before coming into this position—the question for the sponsor is just the ability to both service the expanded access program—these oftentimes are small companies—but also have the product available—also have the supply.

Mrs. BROOKS. And then does the process—how do the results from the expanded access—are they included in the data and the

findings in the clinical trials or are they in a little separate set of findings?

Dr. GOTTLIEB. Well, we don't sequester the information but what we've said today in the guidance that we promulgated and what we've observed when we've gone back and looked at this systematically is typically the information, if there is any information to be gleaned from the expanded access program, doesn't have an impact on the development program one way or the other.

We found very few situations—we looked at 321 regulatory approvals over a 10-year period. Twenty-eight percent of the drugs had expanded access.

We could find only two instances where something observed in the expanded access setting informed the drug approval.

In one case, it led to labeling around a certain safety issue and in one case it actually helped us approve the drug by helping to augment the information we had about the effectiveness of the product.

So it is atypical, very atypical, that information gleaned in this setting would impact the drug approval and the guidance we put out today is sort of doubling down on our assertion that it is atypical.

We are saying it is very, very atypical that we would consider something in that setting in part because these settings are very unstructured and the patients are very sick.

Mrs. BROOKS. Thank you. I would like to turn to Puerto Rico and thank you for making the trip to Puerto Rico and, obviously, manufacturing over 50 pharmaceutical facilities—as you said, thousands of employees producing treatments for cancer, HIV, immunosuppressants, and so forth.

Has the agency ever faced this kind of challenge before after a natural disaster and has FDA ever dealt with something with this much impact, with this many companies ever being impacted?

Dr. GOTTLIEB. I, certainly, have no recent memory. I've been around the agency for 15 years either as an observer on the outside doing policy work or working for three separate commissions.

I've never seen something on this scale where we've had a region that had so much important, concentrated manufacturing impacted in such a profound way.

I mean, our priority first and foremost is to the people of Puerto Rico, and we are doing a lot to provide them direct assistance. But this is an existential risk that we face as a nation if these facilities are permanently impacted.

And I will just state that the facilities themselves are intact.

Mrs. BROOKS. Right.

Dr. GOTTLIEB. The challenge is going to be the logistics of maintaining their operations and moving—getting their workers to work, maintaining their operations on what are right now generators and in moving product off the island.

The issue of moving the product off the island is improving. The getting the workers to work is starting to get better.

The companies themselves have done a lot to provide direct assistance to their employees. They are opening the cafeterias. They are offering three meals a day, providing gasoline to their employees. I've been on the phone with many of these CEOs.

My biggest long-term concern right now is the power and also the secondary supply chain—are they going to be able to get supplies from their local suppliers who we are not necessarily monitoring as closely and they might not be FDA-regulated facilities.

Mrs. BROOKS. My time has expired.

However, I did wonder, since we haven't dealt with this, might there be protocols to be put in place in the future in case anything like this were to happen, unless there are already protocols in place to work with these manufacturers to mitigate the shortfalls?

Dr. GOTTLIEB. There—there are, and these are hardened facilities that have substantial generators—I mean, 800,000 kilowatt generators on some of these facilities, bigger than that.

I don't think anyone anticipated something on this scale where a Category 4 hurricane went through the longitudinal access of the island and decimated the entire island.

Mrs. BROOKS. Thank you. I yield back.

Mr. BURGESS. Chair thanks the gentlelady. Gentlelady yields back.

Dr. Gottlieb, if I could, let me just ask you, on the guidance that you're going to be providing does it address the issue for someone who has been on—someone who's been on a critical trial, the drug is not approved, and yet the perception of the patient is this is the only thing that helped me, and so now that product is not going to be available? Would that be available under an expanded use?

Dr. GOTTLIEB. Well, I don't—it depends on is it a circumstance where the company made a decision not to go forward with the further development of product or the company is continuing to develop the product and then they are going to provide it subsequent to the clinical trial in sort of an open label fashion.

In the latter circumstance, we see a lot of companies doing that. In the former circumstance, when companies do curtail development of products in clinical trials it's because they've deemed them not to work but certain patients felt they are deriving a benefit, this doesn't address it.

I think it would take something that Congress would have to do to address that kind of a circumstance.

Mr. BURGESS. Very well. Good to know.

I do want to thank you for being here and your indulgence through the testimony and the questions.

We are going to transition without a break to our third panel, and we are ready to hear from Mr. John Dicken, director of health care in the United States Government Accountability Office.

Dr. Dicken, we'll give you a moment to get situated and then you'll be recognized for 5 minutes whenever you're ready.

**STATEMENT OF JOHN E. DICKEN, DIRECTOR, HEALTH CARE,
GOVERNMENT ACCOUNTABILITY OFFICE**

Mr. DICKEN. Great. Thank you, Chairman Burgess, and members of the subcommittee.

I am pleased to be here today to discuss GAO's recent report on FDA's expanded access program. As you have been hearing this morning, this program allows patients with serious or life-threatening ailments and no other comparable medical options to obtain

access to investigational drugs and biologics—that is, those that are not yet approved for FDA marketing.

FDA receives and reviews these expanded access requests and determines whether to allow them to proceed. It's also important to note that other entities also have roles.

For example, manufacturers decide whether to give patients access to their investigational drugs, Institutional Review Boards must approve their investigational access treatment plans, and physicians treat the patients with the investigational drugs and monitor their progress.

My testimony today briefly highlights three key findings from our July report. First, I will speak about what is known about the number, type, and time frames of expanded access requests received by FDA; second, what actions FDA and other stakeholders have taken to improve expanded access; and third, how FDA uses data from expanded access in the drug approval process. In addition, I will highlight a recommendation we have made to FDA to improve the program.

First, we found that FDA allowed to proceed nearly all, 99 percent, of the nearly 5,800 expanded access requests that were submitted from fiscal years 2012 through 2015.

Almost 96 percent of these requests were for single patients with more than 2,400 requested on an emergency basis. FDA typically responded to these emergency requests within hours and responded to all other requests within 30 or fewer days.

In the rare cases when FDA did not allow a request to proceed, the most common reasons were incomplete applications, unsafe dosing, the treatments demonstrated lack of efficacy, or the availability of adequate alternative therapies.

We also found that FDA and others have taken steps to improve patient access through this program. For example, in response to concerns that the process to request expanded access was cumbersome, FDA simplified its Web site, guidance, and forms.

Efforts by other stakeholders include a project to educate and streamline the process by which Institutional Review Boards approve treatment plans for expanded access use and the creation of an advisory group to help drug manufacturers manage expanded access requests.

Finally, we examined FDA's use of safety reports based on the use of drugs allowed through expanded access. Manufacturers sponsoring clinical trials included—including any expanded access use must submit safety reports to FDA that include adverse events data.

FDA reported using adverse events data from expanded use in a few cases during the drug approval process but not more widely because expanded access use does not have the same controls as clinical trials.

For example, FDA data show that there were only two instances from 2005 through 2014 in which adverse events from expanded access use contributed to FDA delaying a drug's development by imposing a clinical hold on the drug's use.

However, several manufacturers and other stakeholders we interviewed raised concerns that FDA is not consistently clear

about how it uses expanded access adverse events data during the drug approval process.

Our review of documents that FDA uses to communicate with drug manufacturers about expand access found that only one included a reference to FDA's use of these data.

Manufacturers know that this lack of clear information can influence their decision whether or not to give patients access to their drugs.

Based on this finding, we recommended that FDA should clearly communicate how the agency will use adverse events data from expand access use when reviewing drugs and biologics for approval.

FDA agreed with our recommendation and I was pleased to hear FDA Commissioner Gottlieb announce this morning new guidance in response to GAO's recommendation.

We believe that this additional clarity could help allay manufacturers' concerns and help meet the goal of FDA facilitating expanded access to drugs for patients with serious or life-threatening conditions when appropriate.

Chairman Burgess and members of the subcommittee, this concludes my statement. I will be pleased to respond to any questions you may have.

[The prepared statement of Mr. Dicken follows:]

United States Government Accountability Office



Testimony
Before the Subcommittee on Health,
Committee on Energy and Commerce,
House of Representatives

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INVESTIGATIONAL NEW DRUGS

FDA's Expanded Access Program

Statement of John E. Dicken
Director, Health Care

Chairman Burgess, Ranking Member Green, and Members of the Subcommittee:

I am pleased to be here today to discuss our recent report on the Food and Drug Administration's (FDA) expanded access program.¹ As you know, through FDA's expanded access program, patients with serious or life-threatening ailments and no other comparable medical options can obtain access to investigational drugs—drugs not yet approved by FDA for marketing in the United States—outside of a clinical trial when appropriate. FDA receives and reviews expanded access requests, and determines whether to allow them to proceed. Other entities also have roles in the process. For example, manufacturers decide whether to give patients access to their investigational drugs; institutional review boards must approve patients' expanded access treatment plans; and physicians treat the patients with the investigational drugs, and monitor their progress.

FDA's expanded access program has been criticized by some physician and patient advocacy groups for being too burdensome and confusing to the entities involved, which could pose a barrier to individuals' access to investigational drugs. Additionally, manufacturers have raised questions about how FDA might consider data from expanded access use in its process for approving the drug for marketing in the United States. However, stakeholders—including physicians, patients, and patient advocates—have also highlighted steps FDA and other stakeholders have taken to improve the program.

My testimony today summarizes the findings from our July 2017 report examining FDA's expanded access program. Accordingly, this testimony addresses (1) what is known about the number, type, and time frames of expanded access requests received by FDA; (2) what actions FDA and other stakeholders have taken to improve expanded access; and (3) how, if at all, FDA uses data from expanded access in the drug approval process. In addition, I will highlight a recommendation we made to help FDA meet its goal of facilitating expanded access to investigational drugs by patients with serious or life-threatening conditions.

¹GAO, *Investigational New Drugs: FDA Has Taken Steps to Improve the Expanded Access Program but Should Further Clarify How Adverse Events Data Are Used*, GAO-17-564 (Washington, D.C.: July 11, 2017).

To conduct the work for our report, we reviewed regulations and FDA documents, and analyzed FDA data on the numbers and types of expanded access requests it received from fiscal year 2012 through 2015, the most recent available at the time of the review. We also interviewed FDA officials and other stakeholders, including a non-generalizable selection of nine drug manufacturers—selected to represent large and small companies—and patient and physician representatives. The work this statement is based on was performed in accordance with generally accepted government auditing standards. Further details on our scope and methodology are included in our report.

FDA Allowed Nearly All Expanded Access Requests to Proceed from Fiscal Year 2012 through 2015

In our July 2017 report, we found that of the nearly 5,800 expanded access requests that were submitted to FDA from fiscal year 2012 through 2015, FDA allowed 99 percent to proceed.² Almost 96 percent of these requests were for single patients (either emergency or non-emergency), while the rest were for multiple patients. (See table 1.) FDA typically responded to emergency single-patient requests within hours, and responded to all other requests within 30 days. According to a study using FDA data, in the rare cases when FDA did not allow a request to proceed, the most common reasons were incomplete applications, unsafe dosing, the requested drug's demonstrated lack of efficacy for its intended use, the availability of adequate alternative therapies, and inadequate information provided in the application on which to base a decision.³

²The agency reports data separately on four categories of expanded access requests that FDA defines as: (1) single-patient; (2) single-patient emergency, for example, for a patient who is not expected to live long enough for an institutional review board to review a typical single-patient expanded access request; (3) intermediate-size, generally for two patients to potentially hundreds of patients; and (4) treatment for larger widespread populations.

³Jonathan P. Jarow, Steven Lemery, Kevin Bugin, and Naomi Lowy, "Ten-Year Experience for the Center for Drug Evaluation and Research, Part 2: FDA's Role in Ensuring Patient Safety," *Therapeutic Innovation & Regulatory Science*, vol. 51, no. 2 (2016).

Table 1: Total Expanded Access Requests Reviewed and Allowed to Proceed by the Food and Drug Administration's (FDA) Center for Drug Evaluation and Research and Center for Biologic Evaluation and Research, by Type, Fiscal Years 2012 through 2015.

| Type of request | | Number reviewed | Allowed to proceed | Percent allowed to proceed |
|-------------------|------------------------|-----------------|--------------------|----------------------------|
| Single Patient | Emergency | 2,451 | 2,436 | 99.4 |
| | Non-emergency | 3,047 | 3,016 | 99.0 |
| Multiple Patients | Intermediate-sized | 204 | 194 | 95.1 |
| | Treatment (widespread) | 51 | 51 | 100.0 |
| Total | | 5,753 | 5,697 | 99.0 |

Source: GAO analysis of FDA data | GAO-18-157T

Note: Intermediate-sized requests are generally for two patients to potentially hundreds of patients, and treatment requests are for larger widespread populations.

FDA and Others Have Taken Steps to Improve the Expanded Access Program and Patient Access to Investigational Drugs

We found that FDA and other stakeholders, including a non-profit organization and a drug manufacturer, have taken steps to improve the expanded access process and patient access to drugs. For example, in response to concerns that the process to request expanded access to drugs was complex and cumbersome, FDA simplified its website, guidance, and the forms required for the most common types of expanded access requests. Efforts by other stakeholders include a project to educate and streamline the process by which institutional review boards approve treatment plans for expanded access drug use, and a pilot advisory group to help a drug manufacturer manage expanded access requests.

Some states have also enacted "Right-to-Try" laws to facilitate patient access to investigational drugs. These laws provide liability and licensing protections for manufacturers and providers under state law if an adverse event—such as an adverse reaction to the drug—occurs with patients who were allowed access to investigational drugs. However, some stakeholders we interviewed cited concerns that these laws may not help patients access drugs, in part because they do not compel a manufacturer to provide access.

FDA Reported Limited Use of Expanded Access Safety Data in its Drug Approval Process, and Some Manufacturers Have Asked for More Clarity on This Use by FDA

Manufacturers sponsoring clinical trials must submit safety reports to FDA that include adverse events data resulting from clinical trials, as well as from any expanded access use, to be used in assessing the safety of a drug within the drug approval process.⁴ FDA reported using adverse events data from expanded access use in a few cases during the drug approval process, but not more widely, because expanded access use does not have the same controls as clinical trials. For example, according to a study using FDA data, there were only two instances from 2005 through 2014 in which adverse events from expanded access use contributed to a decision to have a clinical hold put on a drug.⁵ However, several stakeholders we spoke with, including the selected manufacturers we interviewed, raised concerns that FDA is not clear about how it uses expanded access adverse events data in its review of drugs being considered for sale and marketing in the United States.

FDA officials reported that they communicate with manufacturers on how they will use expanded access adverse events data. However, our review of documents FDA uses to communicate with drug manufacturers about the expanded access program found that only one included a reference to FDA's use of these data, and the document did not include specific examples of how the data might be used. Further, some of the manufacturers we interviewed told us the guidance was unclear. These manufacturers noted that the lack of clear information can influence their decision whether to give patients access to their drugs, because of their concerns that an adverse event will result in FDA placing a clinical hold on their drug, which could delay its development. This could impact FDA's goal of facilitating expanded access to drugs for treatment use by patients with serious or life-threatening diseases or conditions, when appropriate.

Based upon this finding, we recommended that FDA should clearly communicate how the agency will use adverse events data from expanded access use when reviewing drugs and biologics for approval for marketing and sale in the United States. FDA agreed with our recommendation, noting that, while there have only been two instances in

⁴The process by which a drug or biologic is developed and considered for approval for marketing in the United States involves a number of steps, which include the clinical testing of the drug's safety and effectiveness on human volunteers.

⁵Jonathan P. Jarow, Steven Lemery, Kevin Bugin, Sean Khozin, and Richard Moscicki, "Expanded Access of Investigational Drugs: The Experience of Drug Evaluation and Research Over a 10-Year Period," *Therapeutic Innovation & Regulatory Science*, vol. 50, no. 6 (2016).

which adverse event data have contributed to decisions to temporarily put development of investigational drugs on partial clinical holds, additional clarity on how FDA uses such data from expanded access use may allay manufacturers' concerns.

Chairman Burgess, Ranking Member Green, and Members of the Subcommittee, this concludes my prepared statement. I would be pleased to respond to any questions you may have at this time.

**GAO Contacts and
Staff
Acknowledgments**

If you or your staff members have any questions concerning this testimony, please contact me at (202) 512-7114 or dickenj@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this statement. Other individuals who made key contributions to this testimony include Gerardine Brennan (Assistant Director), Nick Bartine (Analyst-in-Charge), George Bogart, and Carolyn Garvey.

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Mr. BURGESS. I thank you for your testimony.

We will move into the question and answer portion of the hearing. I would like to recognize Mr. Guthrie from Kentucky, 5 minutes for his questions, please.

Mr. GUTHRIE. Thank you very much. Thank you, Mr. Dicken, for being here. Appreciate you being here today.

And what are some of the ways, like the 14 other stakeholders you spoke with—what are the ways they are working to improve the expanded access process?

Mr. DICKEN. Right. We heard of several efforts that were ongoing. Certainly, some deal with the transparency and education about the program.

There's an effort by the Reagan-Udall Foundation that's working with FDA to create a Navigator that will allow more information.

Certainly, the effort by this committee and Congress and the 21 Century Act make legislation that requires manufacturers to include information about their policy for expanded access also adds two kinds of transparency in the information that's available.

There are other efforts that we heard about that deal with streamlining the Institutional Review Board process or having assistance from manufacturers' pilot program.

I think a witness in the last panel will speak more about efforts to help manufacturers consider and manage these types of requests.

Mr. GUTHRIE. OK. Thank you. And you got sort of to the answer of this next question but I am going to ask it again and give you a chance to elaborate at the very end of your—of your comments there.

It says your report found the FDA does not consistently and clearly communicate how it uses adverse effects data from expanded access used in the drug approval process.

Can you please summarize how FDA communicates currently, which you sort of did, and how GAO recommends they change? If you can elaborate again.

Mr. DICKEN. Sure. We—during the course of our work, we reviewed a range of materials that FDA provides to communicate with manufacturers and others about the expanded access program. That includes various guidance documents as well as acknowledgments when they are expand access requests.

Across those multiple documents we found that FDA had updated one that provides some general information. They had a question and answer that provides some information at a general level about how they would use adverse events data.

But we continued to hear from drug manufacturers' and others' concerns that was not as consistent or as clear as possible.

So we were pleased that FDA did agree with the recommendation and, certainly, Commissioner Gottlieb's testimony in the case that they intend to clarify more guidance, going forward.

Mr. GUTHRIE. OK. Thank you.

And your report indicates that FDA allowed 99 percent of expanded access requests they received to proceed. Did you look at the reasons for why FDA would not allow a request to proceed and if so, what did you find?

Mr. DICKEN. Yes. We looked at FDA's data on why. They indicated that they did not allow the exceptions—the 1 percent that did not proceed.

The types of issues that FDA indicated were either the FDA had identified that there was evidence that was ineffective for the incident treatments—either that there might have been availability of other treatments including clinical trials that individuals may have been able to participate in or also incomplete information or safety concerns.

Mr. GUTHRIE. Well, I think Dr. Gottlieb mentioned earlier when he was here that part of the reason was that there was a confidential hold because there were some adverse effects that was identified but wasn't public knowledge.

Did you see that and I guess what I am getting at it appeared that unless there was a specific reason that people weren't getting approved to go into the right—were getting the right to try unless there was some specific adverse effect.

I think you said—I think you said two things—one, there was nonavailability. Two was that there was some confidential—I forget the term that he used but a hold—that they knew there was an adverse effect but they couldn't put that out publicly.

And so is that what you found and, you know, it seems like everybody, unless there's a specific reason not to, are getting the chance to try.

Mr. DICKEN. And so I think that's a fair characterization—that it's only in very isolated incidences that they had additional information that may have raised concerns about the safety.

I will note that this is not the only player, that there are other decisions including that they need to have approval from the manufacturer before proceeding with an expanded access request.

Mr. GUTHRIE. OK. Thank you.

That concludes my questions and I yield back.

Mr. BURGESS. Gentleman yields back. Chair thanks the gentleman.

Chair recognizes the gentleman from Texas, Mr. Green, 5 minutes for questions, please.

Mr. GREEN. Thank you, Mr. Chairman, and thank you for being here, and looking at the GAO helps us in looking at what we may do with this legislation.

The report found that some manufacturers expressed concerns regarding how adverse events associated with expanded access would impact the drugs' development or ultimate approval.

GAO recommended the FDA should clearly communicate how it uses adverse events data from expanded use in the drug approval process, a recommendation that FDA just a few minutes ago agreed with.

Can you elaborate on this recommendation and how will greater clarity from the FDA on the use of adverse event data from expanded use improve upon patient access to these investigational therapies?

Mr. DICKEN. Yes. This was a concern that as we interviewed manufacturers and other participants in the process that several raised that this was affecting their decision making about agreeing to expanded access requests.

We also heard, and you have heard testimony today, that there have been very rare instances—only two instances—when there has been a delay or a clinical hold.

And so that led to the if there were more clarity as to what the circumstances where FDA would consider that information that in many cases, because this information does not have the same controls that a clinical trial has, I think Commissioner said it's often not useful in the drug development and approval process.

But when it is, there was concern and so more clarity that it's only in isolated circumstances and that that would be a concern the appropriate context seemed important to help allay those manufacturers' concerns and hopefully help improve access for patients that could get investigational therapies when appropriate.

Mr. GREEN. OK. Thank you.

A central component of the 2017 report focused on what's known as number type and the time frames of expanded access requests received by the FDA.

The bills we are considering today would take the FDA out of the process altogether. Would it be possible to even know the universe of expanded access or Right to Try requests made absent any FDA involvement and do you think this lack of accountability by a company potentially illegitimate claiming to have an IND expose patients to bad actors.

If the FDA is out of the picture, how do we know the adverse actors?

Mr. DICKEN. So on the first part of that about the total universe, you know, we know the data on how many are reaching FDA. We reported on that.

We did also talk to manufacturers—a subset of nine manufacturers—with experience in the process and their experiences really varied. There was no consistent data on how much requests they are getting.

But, certainly, they had requests, from dozens to hundreds of requests in some cases, for expand access. But there is not consistent information across all manufacturers of how often they would be getting these requests.

Certainly, under current authority FDA's key part of developing—the drug development approval requires a clinical trial and approvals in that process and looking at information from other sources including, where appropriate, expanded access use.

Mr. GREEN. OK. And you mentioned in your testimony the use of this data by FDA, while limited, is still a source of concern for manufacturers looking to get their products approved.

Could you elaborate on the concerns expressed in your interviews with manufacturers regarding FDA's guidance on this issue?

Mr. DICKEN. Yes. I think the concerns were that if there is uncertainty as to whether or not and how FDA would consider a situation where the therapy doesn't work.

These are terminally ill individuals. There will be outcomes that no one wants but that are negative. And so in the uncertainty of how FDA would consider that information, that led them to have concerns about making some of the approvals.

That's where we think more clarity on the limited circumstances in which FDA does consider this is very important and recognition

of the context that these are individuals that are not in clinical trial settings, that are terminally ill, and how—whether or not that is relevant information that FDA could—would find useful.

Mr. GREEN. Thank you. Thank you, Mr. Chairman.

Mr. BURGESS. Chair thanks the gentleman. Gentleman yields back.

The Chair recognizes the gentleman from Virginia, Mr. Griffith, 5 minutes for questions, please.

Mr. GRIFFITH. Thank you, Mr. Chairman.

Let me just say I appreciate your report. I appreciate the fact that the FDA—Dr. Gottlieb, earlier today, said he's going to take a number of those recommendations and they are announcing some steps that may improve the process.

We have already heard from other witnesses that—or from other members of Congress who have asked you about the concerns of manufacturers and I think you covered that, which is where some of my questions were going to go.

Let me ask a little bit of a follow-up in a slightly different direction. Does the FDA also require that safety data include the reporting and use of data on patients that benefited from the expanded access treatment?

So previously we've talked about all the concerns about manufacturers about the adverse. Does the FDA use the things that turned out well and how did manufacturers—if so, and how did manufacturers respond to that?

Mr. DICKEN. Right. There are requirements and then this, as you've acknowledged, on safety reporting. I think we heard from FDA that there were circumstances when they saw other information such as dosage or other information that might be useful and they can prove it and that there were limited instances that's also limited here where the information could be used by the manufacturer in supporting its application for approval.

And so in those cases, if the manufacturer is providing information to FDA in some limited cases this also helps support FDA's decision for approval or labeling or dosing.

Mr. GRIFFITH. Well, and I do think that it's important that FDA consider both because, you know, it may not be the best evidence. We might want to have the full clinical trial to get the best evidence.

But when you have somebody who is using this process it is at least some evidence of whether it's good or bad or helpful or not helpful, and I do appreciate it.

With that, Mr. Chairman, I yield back.

Mr. BURGESS. Chair thanks the gentleman. The gentleman yields back.

And Mr. Dicken, let me just ask you. You heard Commissioner Gottlieb—Dr. Gottlieb and I discussed a little bit and he didn't want to steal the testimony that you were—you were going to provide.

It didn't bother me at all. I was perfectly willing to pre-empt any impact that you might make. But do you feel that the answer that I got was that satisfactory? Was that fulsome in that response as far as the adverse reporting issue?

Mr. DICKEN. Yes. Certainly, it did not—I was pleased to have that discussion happen earlier as well and agree that, you know, certainly, the adverse event reporting I think was a fair characterization. So yes, thank you.

Mr. BURGESS. And I am going to—again, your preface or your premise, as you started out with your report, was that there was the perception that the program has been criticized by physician and patient advocacy groups for being too burdensome and confusing.

But now as we've worked through this process with the guidance that the FDA is going to be providing with perhaps some of the legislative products that are out there, do you feel like we are generally moving in the correct direction to get—to get therapies to patients in a timely fashion that will actually impact their clinical course?

Mr. DICKEN. Yes. I think we heard from patients and groups and providers and manufacturers that they thought progress was being made in improving the expanded access program and, certainly, continued to streamline and educate providers, individuals, and manufacturers about that.

We still are hearing, still, during the course of our work, that even though FDA has streamlined their application that some others, such as Institutional Review Boards occasionally may still ask for the more complex information, and there have been efforts to kind of educate so that more streamlined information can be used not only by FDA but other entities that need to approve this expanded access use.

Mr. BURGESS. So, I mean, the Institutional Review Board, that's a—that's a good thing. We want that independent look at a request for expanded use.

At the same time, I mean, if someone is not—if someone is just out practising in the community and they have a patient who has this request, it can be difficult for them, that—the IRB itself becomes a barrier, does it not?

Mr. DICKEN. And that is where I think there were some efforts to help educate IRBs who may only in some cases experience these requests occasionally and so some efforts to both educate IRBs to perhaps have some specialized IRBs that would have more experience with this process and help minimize and streamline that as an obstacle.

Mr. BURGESS. And to even provide some flexibility within the IRB structure itself where something needs to happen in a more—where time becomes a critical factor. Do I understand that correctly?

Mr. DICKEN. That is correct.

Mr. BURGESS. Now, you did not—at least—well, let me just see if I can ask this in the right way. It really wasn't your function to assess the liability concerns that some manufacturers might have. Is that correct?

Mr. DICKEN. That's correct.

Mr. BURGESS. Is that a fair statement? That's why it's not really addressed in your report?

Mr. DICKEN. Yes. We did not independently assess that. We did ask manufacturers and others about what their concerns were and I think you've heard about some of those concerns.

Others are outlined in our report and those dealt more with supply, with concern about any public backlash if they should deny it, about risks and potential benefits.

Mr. BURGESS. Yes. I think we are going to hear a little bit more about that.

Well, seeing no other members wishing to ask questions, I do want to thank you for your testimony today. Thank you for your participation in the—in the hearing.

We are going to transition to our final panel, again doing so without a break in the action. It will take a few minutes more because we do have a little bit larger panel now for our final panel.

But I ask our witnesses to take their seats and each witness—after you get a chance to get situated each witness will have an opportunity to give a statement followed by questions from Members.

And there is no pressure on the technical challenge to get the name—and, again, each witness is going to be recognized for 5 minutes to give a general statement, and then we'll follow that with questions from the Members.

On our fourth and final panel, we are going to hear from Ms. Naomi Lopez Bauman, director of Healthcare Policy at the Goldwater Institute; Lieutenant Commander Matthew Bellina, United States Navy, patient advocate; Mr. Kenneth Moch, president and CEO of Cognition Therapeutics; Dr. Alison Bateman-House, assistant professor, Department of Population Health, New York University, Langone Health; and Dr. Ellen Sigal, chairperson and founder, Friends of Cancer Research.

We appreciate each of you being here with us today and you will each be recognized 5 minutes for an opening statement.

Ms. Lopez Bauman, we will recognize you for 5 minutes.

STATEMENTS OF NAOMI LOPEZ BAUMAN, DIRECTOR OF HEALTHCARE POLICY, GOLDWATER INSTITUTE; LCDR MATTHEW BELLINA, U.S. NAVY (RETIRED); KENNETH I. MOCH, PRESIDENT AND CHIEF EXECUTIVE OFFICER, COGNITION THERAPEUTICS, INC.; ALISON BATEMAN-HOUSE, PH.D., ASSISTANT PROFESSOR, DIVISION OF MEDICAL ETHICS, DEPARTMENT OF POPULATION HEALTH, NEW YORK UNIVERSITY LANGONE HEALTH; ELLEN V. SIGAL, PH.D., CHAIR AND FOUNDER, FRIENDS OF CANCER RESEARCH

STATEMENT OF NAOMI LOPEZ BAUMAN

Ms. LOPEZ BAUMAN. Chairman Burgess, Ranking Member Green, and other members of the committee, thank you for the opportunity to address you today.

My name is Naomi Lopez Bauman and I am the director of healthcare policy at the Goldwater Institute. We began our work on Right to Try about 5 years ago.

Doctors and patients approached the institute because dying patients were not getting access to the innovative treatments. Meanwhile, the wealthy and well-connected could seek innovative treatment overseas, leaving most others behind with few options.

Diego Morris, who was diagnosed with osteosarcoma at age 10, is one of those lucky few. His family relocated to England for an entire year so that he could obtain a leading treatment that 7 years later has yet to receive U.S. approval.

It's also considered the standard of care in many countries around the world. Diego is now a healthy 17-year-old who is now helping to ensure that other patients like him are not left behind.

Something is desperately wrong when terminal patients who are out of options are required to stand in line for permission to seek an investigational treatment that their doctor is recommending and that a manufacturer is willing to make available.

Right to Try is about the terminal patients who don't fit into a control group, who can't afford to travel overseas or move to another country, and who simply want permission to seek the same treatments that other patients, sometimes in the same medical facility, are already receiving.

This inequity occurs despite the fact that one of the bedrock principles of medical ethics is patient autonomy. When a life hangs in the balance, decisions about healthcare are ultimately for the patient to make.

That is the basis of the State Right to Try laws, and I am very happy to report that yesterday the Senate in Pennsylvania unanimously passed Right to Try, so now in Pennsylvania it has passed both chambers unanimously and we hope will be the 38th State that will be a Right to Try State, and we are still proceeding in the additional States as well.

But under these State laws, if you have a terminal diagnosis and you have exhausted all other options, you may seek, under your doctor's care and direction, investigational treatments that have passed Phase 1 of the FDA clinical trials and are continuing to undergo FDA evaluation.

Simply put, this law extends to all terminal patients who are dying and out of options the same right to try to save one's own life that is already enjoyed by the wealthy and well-connected and the lucky few that are in the clinical trials.

At the worst time of his life, Mark Hayutin of California was facing terminal cancer and insurmountable odds when he became a patient of Dr. Ebrahim Delpassand, a nuclear medicine physician who was testing a promising treatment.

Then the FDA terminated the study that Mark was participating in because there was no longer a need for more patient data. Mark was left without the ability to complete his treatment.

It is because of the Texas Right to Try law that Mark was eventually able to complete the treatments. Today, Mark credits Dr. Delpassand and the Texas Right to Try law for saving his life.

The Federal Right to Try legislation under consideration today is not a call to ignore research or undermine science or for doctors to abandon their obligations to their patients or for drug companies to disregard the complex ethical questions such as how to distribute limited supplies of drugs.

And, obviously, Right to Try is not a guarantee that an investigational medicine will work or that patients and doctors will have perfect information to make these informed decisions. And as the FDA admits, no system can ensure against all risks.

But that isn't the question for us today. The question is who should ultimately decide what level of risk is acceptable to a dying patient: Federal officials or the patients themselves, in consultation with their doctors?

Thank you for your consideration of Senate Bill 204, the Right to Try Act. I yield back to the Chair.

[The prepared statement of Ms. Lopez Bauman follows:]

Testimony of Naomi Lopez Bauman
Director of Healthcare Policy
Goldwater Institute
Phoenix, Arizona

Before the United States House
Energy and Commerce Subcommittee on Health
Examining Patient Access to Investigational Drugs

October 3, 2017

Chairman Burgess, Ranking Member Green, and other Members of the Committee thank you for the opportunity to address you today:

My name is Naomi Lopez Bauman, and I am the director of healthcare policy at the Goldwater Institute. We began our work on Right to Try about five years ago. Doctors and patients approached the Institute because dying patients were not getting access to innovative treatments while the wealthy and well-connected could seek innovative treatment overseas, leaving most others behind with few options.¹

Diego Morris, who was diagnosed with osteosarcoma at age 10, is one of the lucky few. His family relocated to England for an entire *year* so that he could obtain a leading treatment that, seven years later, has yet to receive U.S. approval.² Diego is now a healthy 17-year-old who is helping to ensure that other patients are not left behind.³

Something is desperately wrong when terminal patients who are out of options are required to stand in line for permission to seek an investigational treatment that their

¹ Olsen, Darcy, [The Right to Try: How the Federal Government Prevents Americans from Getting the Lifesaving Treatments They Need](#) (New York: HarperCollins, 2015), pp. 61-82 and 87-93 and Statement of Dr. Ebrahim Delpassand before the United States Senate Committee on Homeland Security and Governmental Affairs, "Exploring a Right to Try for Terminally Ill Patients," September 22, 2016 at <https://www.hsgac.senate.gov/hearings/exploring-a-right-to-try-for-terminally-ill-patients>.

² Statement of Diego Morris before the United States Senate Committee on Homeland Security and Governmental Affairs, "Connecting Patients to New and Potential Life Saving Treatments," February 26, 2016 at <https://www.hsgac.senate.gov/download/testimony-morris-2016-02-25>.

³ Olsen, pp. 80-82.

doctor is recommending and that a manufacturer is willing to make available. Right to Try is about the terminal patients who don't fit into a control group, who can't afford to travel or move to another country, and who simply want permission to seek the same treatments that other patients — sometimes in the same medical facility⁴ — are already receiving.

This inequity occurs despite the fact that one of the bedrock principles of medical ethics is patient autonomy: when a life hangs in the balance, decisions about health care are ultimately for the patient to make.⁵ That is the basis of state Right to Try laws.⁶

Right to Try is now law in 37 states and counting.⁷ Under these state laws, if you have a terminal diagnosis and you have exhausted all other options, you may seek, under your doctor's care, investigational treatments that have passed phase 1 of FDA clinical trials

⁴ Flatten, Mark, "Dead on Arrival: Federal "Compassionate Use" Leaves Little Hope for Dying Patients," Goldwater Institute Investigative Report, February 24, 2016, p. 10 at https://goldwater-media.s3.amazonaws.com/cms_page_media/2016/2/24/Dead%20on%20Arrival%20downloadable%20PDF.pdf.

⁵ See, e.g., Runzheimer, Jane and Larsen, Linda Johnson, Medical Ethics for Dummies, (Hoboken, NJ: Wiley, 2010).

⁶ Right to Try model legislation at <http://scienceblogs.com/insolence/files/2014/10/GoldwaterInstituteRighttoTryModel.pdf>.

⁷ In just four years, Right to Try has passed in 37 states, often near unanimously and with bipartisan support. The current Right to Try states are: Alabama, Arizona, Arkansas, California, Colorado, Connecticut, Florida, Georgia, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Maryland, Michigan, Minnesota, Mississippi, Missouri, Montana, Nevada, New Hampshire, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, South Carolina, South Dakota, Tennessee, Texas, Utah, Virginia, West Virginia, Washington and Wyoming.

and are continuing to undergo FDA evaluation.

Simply put, this law extends to *all* terminal patients who are dying and out of options the same Right to Try to save one's own life that is already enjoyed by the wealthy and well-connected and the lucky few in clinical trials.

At the worst time of his life, Marc Hayutin was facing terminal cancer and insurmountable odds when he became a patient of Dr. Ebrahim Delpassand, a nuclear medicine physician who was testing a promising treatment. Then, the FDA terminated the study that Marc was participating in because there was no longer a need for more patient data. Marc was left without the ability to complete his treatment.⁸

It is because of the Texas Right to Try law that Marc was eventually able to complete the treatments. Today, Marc credits Dr. Delpassand and the Texas Right to Try law for saving his life.

The federal Right to Try legislation under consideration today is not a call to ignore research or undermine science, or for doctors to abandon obligations to patients, or for drug companies to disregard complex ethical questions such as how to distribute limited supplies of drugs. And obviously, Right to Try is not a guarantee that investigational medications will work, or that patients and doctors will have perfect information to inform their decisions.

⁸ Letter from Marc I. Hayutin to Susan Cork, Therapy Patient Coordinator at Excel Diagnostics dated June 2, 2017 at <https://s3.amazonaws.com/goldwater-website-links/RTT+testimonial+Marc+Hayutin>.

As the FDA admits, no system will ensure against all risks.⁹ But that isn't the question. The question is: Who should ultimately decide what level of risk is acceptable to a dying patient—federal officials or patients themselves, in consultation with their doctors?

Respectfully submitted,

Naomi Lopez Bauman
Director of Healthcare Policy
Goldwater Institute
500 E. Coronado Road
Phoenix, AZ 85004
(602) 462-5000
www.goldwaterinstitute.org

⁹ U.S. Food and Drug Administration, "Guidance for Industry and Food and Drug Administration Staff: Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approvals and *De Novo* Classifications," August 24, 2016, p. 11 at <https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm517504.pdf>.

Mr. BURGESS. Chair thanks the gentlelady for yielding back. Lieutenant Commander Bellina, you are recognized for 5 minutes for a statement, please.

STATEMENT OF LCDR MATTHEW BELLINA

LCDR BELLINA. Ladies and gentlemen, thank you for inviting me here to speak today in my—I don't think I am on.

Is that better? Yes, way better. All right.

And my diaphragm is failing a bit here so if I get hard to hear, Mr. Moch, if you'd give me a poke I will speak up.

Ladies and gentlemen, thank you for inviting me to speak here today. I also want to extend a heartfelt thank you to my representative, Congressman Brian Fitzpatrick. He has been a tireless advocate not only for the ALS community but for all terminally ill Americans.

In my advocacy work, I have met literally thousands now terminally ill people and their families and the vast majority ask me how can anybody oppose the Right to Try bill.

I appreciate that sentiment, but I also do respect the fact that they are well-meaning people with ideological differences. I would like to illustrate the arguments I've heard and why I believe they are based on faulty logic.

The one that I hear all the time—and it's been thrown around a lot today—is, you know, we had this expanded access program—we already approved 99 percent, you know, why do we need this bill?

On average, there are less than 2,000 applications per year, by conservative estimates. There are nearly 30 million Americans living with incurable conditions. I would like to draw an analogy.

Imagine there were 30 million Americans eligible for food stamps. Two thousand applied and were approved. The other 29,998,000 never completed an application, and they starved to death.

Would we be congratulating ourselves on that kind of stat? That never offends me. The major difference I see is that food stamp reform would involve a fiscal note, and this bill doesn't. So, in my mind, it's better.

The FDA's involvement—and, really, Dr. Gottlieb, I think, did a great job. Their involvement—they've tried so hard but their involvement has a chilling effect on the manufacturers, and that is the supply issue that he was talking about.

The other argument I hear pretty often is that the State Right to Try bills have had little impact, so why should we pursue a Federal bill? The hundred or so case patients in Texas that you mentioned would have a very different opinion.

But let's assume for argument's sake that that hundred people is not enough for us to make an effort here today. I think the big issue is the courts and their broad interpretation of the interstate commerce clause.

Most pharmaceutical companies are trying to sell a drug in more than one State. So, you know, we need a Federal law to protect them in that case.

I am sympathetic. You're going to hear from Mr. Moch here in a minute and other pharmaceutical executives. I know this makes their job harder when, you know, you have patient communities

and social media calling them out—you know, why aren't you giving the drug to this person or that?

I would say the issue is that, you know, they have to have the courage and tell the community what they think is right and wrong, and sometimes the answer is no. And I do appreciate that, but we can't let the FDA be the bad guy.

And I will sum up by saying I know it's probably too late for me. I made my peace with that.

I need to know before I die that if my children find themselves in this unenviable position, this Nation that I proudly serve will respect their liberties and the right to make their own decision about their medical treatments.

Thank you for having me. God bless.

[The prepared statement of LCDR Bellina follows:]

USN LCDR (Ret.) Matthew Bellina testimony: 10/3/2017

Ladies and Gentlemen, thank you for inviting me to speak here today. I also want to extend a heartfelt "thank you" to my representative, Congressman Brian Fitzpatrick. He has been a tireless advocate for not only the ALS Community but for all terminally ill Americans.

In all of my advocacy work the question I am asked most often is "How could anybody oppose the Right To Try Bill?". While I appreciate the sentiment, I respect the fact that there are well-meaning people with ideological differences. I would like to illustrate their arguments and why I feel they are based on false logic.

The argument I hear most often is that we already have an Expanded Access Program in the FDA that approves over 99% of applications. On average, this is less than 2,000 applications per year. By conservative estimates there are nearly 30 million Americans living with incurable conditions. I would like to draw an analogy here. Imagine there were 30 million Americans eligible for food stamps. 2,000 people applied and were approved. The other 29,998,000 Americans never completed an application and starved to death. Would we be patting ourselves on the back for a successful program? I should hope not. The major difference here is that food stamp reform would involve a sizeable fiscal note and the Right To Try Bill does not. The FDA's involvement in the Compassionate Use of Medicine has an unintended chilling effect on the pharmaceutical industries willingness to operate outside of the boundaries of the clinical trial system. This obstacle can and should be removed.

The other argument I hear often is that the State Right To Try Bills have had little impact, so why should we pursue a Federal bill? The 100 or so cancer patients in Texas would have a very different opinion about the overall impact, but for arguments sake let's assume that number is not significant enough to make a federal effort. If anybody can point me to a case in the last 50 years where the courts have sided with State over Federal law on matters of Interstate Commerce, I would concede that there is no value added to passing this bill. As it is, no respectable pharmaceutical company would jeopardize their ability to participate in Interstate Commerce for the sole purpose of providing their drug in a single state. This bill is needed to protect the pharmaceutical industry from litigation and allow them to respect the individual state laws. Once this bill is passed we should see more widespread use of the 37 state laws. I have no illusion that this will solve the entire problem but it is absolutely a step in the right direction and a step we need to take now.

I am sympathetic to the position of Mr. Kenneth Mochs and other pharmaceutical executives. Often times the greater good is to put the trial over the rights of the individuals. This however is not a one-size-fits-all situation. The processes for all trials and drugs are unique and must be treated that way. Pharmaceutical executives make enough money that they need to have the courage to explain these decisions to the patients and families and not hide behind a government agency to make these ethical decisions easier for them.

I know that it is probably too late for me and I have made my peace with that. I need to know before I die that if my children find themselves in this unenviable position, that this nation that I proudly served will respect their liberties and their right to make their own decisions about their medical treatments. Thank you for having me here. God Bless you and God Bless this great nation of ours.

Mr. BURGESS. We thank the gentleman for his service and thank him for his testimony.

Mr. Moch, you are recognized for 5 minutes, please.

STATEMENT OF KENNETH I. MOCH

Mr. MOCH. That's a tough start for me.

Good afternoon, Chairman Burgess, Ranking Member Green, and members of the subcommittee.

My name is Kenneth Moch and I am the president and CEO of Cognition Therapeutics, a company developing what we hope is a new medicine for Alzheimer's disease.

Over the course of my career, I have been the CEO or co-founder of five biotechnology companies focussed on developing new medicines for terminal or life-threatening diseases including serving as CEO of an antiviral therapeutics company called Chimerix.

Starting in late 2009, Chimerix provided its experimental antiviral called brincidofovir under expanded access to 430 critically ill individuals.

This was one of the largest expanded access programs undertaken by a biotech company, at its peak accounting for an estimated 6 percent of the expanded access requests to the entire FDA and an estimated 30 percent of the requests to the antiviral drug division.

The FDA was never a hindrance to granting these requests and the FDA staff we dealt with including the division director were extraordinary in their help and their compassion and their clear understanding of the critical needs of the patients.

Right to Try legislation would not have changed anything that we did during this multiyear program. At the end of 2012, we made the difficult decision to cease the expanded access program and focus on the pathway to FDA approval.

Fifteen months later in March of 2014, the family of a critically ill 7-year-old boy named Josh Hardy started a social media campaign access to brincidofovir.

The high profile #SaveJosh campaign catalysed international debate on issues of ethics and equity in expanded access and raised questions regarding the role of patient advocacy and social media and, in many ways, led to the ongoing discussion today about Right to Try.

Let me state clearly that I am an advocate of expanded access—what I prefer to call preapproval access—when it is appropriate for the medicine under development.

The testimony today has been heartfelt, truly heartfelt, and I believe that everybody in this room, if we had a family member who was critically ill—a child, a parent, a sibling—or if we were critically ill ourselves would do everything in our power to gain access to an experimental medicine that might increase the chance of survival.

That being said, expanded access programs raise social, ethical, and moral conflicts and dilemmas regarding access to experimental medicines.

How does society or a company balance the immediate needs of a critically ill individual, in many cases a child, versus the potential needs of many future patients?

Who is advocating for those future patients who might not receive a needed medicine because FDA approval is delayed by even a week or a month?

And I am not talking about the FDA delaying the approval process—the review process—but rather, what might happen if because of an unexpected finding our outcome some percentage of potential participants choose not to enroll in a clinical trial, slowing down the development time line?

Being very granular, what would have happened to the brincidofovir clinical development program and even to Chimerix if, after a global social media campaign, Josh Hardy had received brincidofovir and shortly thereafter died?

We live in a world of social media, and while the FDA might not react to patient—to the—might not react, the patient community likely would have.

In other words, you can't look at Right to Try legislation without looking at all of the implications and applications of this law.

At the time of the #SaveJosh campaign, I characterized this ethical dilemma as not being about Josh but about the many future Joshes. This question is the challenge that faces each of you as you discuss and think about Right to Try legislation.

Let me also say that I am not a supporter of Right to Try legislation. In my opinion, this legislation does nothing to help patients in need.

I believe there are things that need to be done but Right to Try is not in any way addressing the complexities of drug development.

And given that the FDA only considers expanded access requests when it is received by the drug sponsor and approves over 99 percent of these requests, the decision to grant expanded access requests fall to the leadership of the company developing the new medicine, not the FDA.

It is crucial to understand the extraordinary complexity of developing new medicines as well as the fragility of the biotechnology companies that are the predominant sources of these innovations.

No ethical company that I know of would ever release an experimental medicine outside the FDA's regulatory process. A basic mantra is that all drugs have side effects and cutting scientific corners creates unbounded risks.

There is simply no monolithic answer to the question of when circumstances and timing are right to undertake an expanded access program because each experimental medicine is different, the safety and efficacy parameters are different, the clinical development processes and regulatory pathways are different, and the patient populations in need are different.

Expanded access is not drug development, and Right to Try is not drug development, and given this fact, it is not unreasonable for a company to decide not to initiate an expanded access program until there is sufficient data demonstrating the efficacy and safety of an experimental medicine.

In closing, I believe that Right to Try legislation as currently crafted is not the answer to any of the questions that have been raised about providing experimental medicines to critical or terminally ill patients.

Bypassing the FDA is not in anyone's interest and no ethical company I know would do so. At the best, Right to Try will not help people and at the worst, I believe, it could do harm.

I thank you for your time.

[The prepared statement of Mr. Moch follows:]

TESTIMONY OF KENNETH I. MOCH
PRESIDENT & CEO
COGNITION THERAPEUTICS, INC.

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON ENERGY AND COMMERCE
SUBCOMMITTEE ON HEALTH

OCTOBER 3, 2017

"EXAMINING PATIENT ACCESS TO EXPERIMENTAL DRUGS"

Chairman Burgess and Ranking Member Green, Members of the Committee, my name is Kenneth Moch, President and Chief Executive Officer of Cognition Therapeutics, headquartered in Pittsburgh, Pennsylvania. Thank you for having me here today. This hearing is looking at patients' access to experimental drugs, and I have a great deal of experience with expanded access from my roles in leadership at small, innovative biotechnology companies.

I have spent my career at the interface of science and business, having been the CEO or co-founder of 5 biotechnology companies focused on developing new medicines for life-threatening diseases, including Alzheimer's disease (Cognition), the first liposome company, the first cord blood stem cell bank and, prior to Cognition, an antiviral therapeutics company called Chimerix. In my years building and leading emerging biotechnology companies, I have overseen several expanded access programs, and in my position as a Board Member for the Biotechnology Innovation Organization (BIO), I have

engaged with many other CEO's to draft principles for expanded access programs.

While I am a strong supporter of expanded access programs, I am NOT a supporter of Right to Try legislation. In my opinion, this is feel-good legislation which gives false hope to patients in need, without actually helping them.

There are few issues with more emotional and moral impact than "Right to Try." I applaud the Committee for its willingness to examine this issue in depth, from all perspectives. While the idea of a patient's "right to try" has become a very popular idea in this country and, since 2014 37 states have passed "right to try" laws and the U.S. Senate passed legislation earlier this year, there is shockingly little discussion about the social, ethical and moral conflicts and dilemmas in the use of experimental medicines to treat life threatening medical conditions.

For patients and their loved ones, there is no moral quandary. They want access to a drug they believe could save or extend their life. I fully understand that. All of us, if we had a family member who was critically ill - a child, a parent, a sibling - or if we were critically ill ourselves, would do everything in our power to gain access to any experimental medicine that

might increase the chance of survival. That being said, for the company engaged in the drug development, the Food and Drug Administration (FDA) and lawmakers, it is our moral imperative to not just think of that one patient, but of all the patients. We must consider, beyond the risks to an individual, how does society or a company balance the immediate needs of a critically ill individual, in many cases a child, versus the potential needs of many future patients?

In 1987, mostly in response to the AIDS crisis, the FDA instituted expanded access guidelines where an unapproved medicine could be made available to an individual with a serious or immediately life-threatening disease. In 2009, the guidelines were substantially revised and three categories of use were outlined. With the revision, the FDA was seeking to balance the desire of sick and vulnerable patients to get access to drugs with safety and without compromising the clinical trials process. The FDA's statement on this topic: *"Expanded access, sometimes called "compassionate use," is the use of an investigational drug outside of a clinical trial to treat a patient with a serious or immediately life-threatening disease or condition who has no comparable or satisfactory alternative treatment options. The drug manufacturer and the patient's doctor must make special arrangements to obtain the drug for*

the patient. These arrangements must be authorized by the FDA. These safeguards are in place to avoid exposing patients to unnecessary risks.”¹

In practice, however, the FDA’s role is not always as clear. According to Richard Klein, former Director of FDA’s Patient Liaison Program, the FDA’s role is to provide a “mechanism” for expanded access. Indeed, the FDA approves over 99% of the requests it receives for expanded access. From 2009 to 2013, the period of time when Chimerix first had an expanded access program, the FDA approved 4017 expanded access requests, both individual patients and larger expanded access protocols, and denied 24. In 2014 the FDA approved approximately 2000 more requests. While the number of IND submissions and protocol requests declined in 2015 and 2016, the approval rate remains at a similar percentage.

Given that the FDA only processes an expanded access request when it has been received from the drug’s sponsor, almost always a company which is developing the experimental medicine, what these approval percentages clearly illustrate is that the decision as to whether or not to grant an expanded access request falls to the leadership of the company developing the new medicine, not the FDA.

¹ Access to Investigational Drugs Outside of a Clinical Trial (Expanded Access). <http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/AccessToInvestigationalDrugs/ucm176098.htm>; Statement language is from May 2014, at the time of the #SaveJosh social media campaign.

For companies, decisions around whether to grant or deny expanded access requests are heart wrenching. In many circumstances, it is making the decision around practical aspects of drug approval and the desire to treat all the patients with an approved medicine, against an emotional plea from a patient who is out of options. Additionally, there are regulatory and legal implications for companies in their decision to grant or not grant preapproval access to experimental medicines.

First and foremost, a biotechnology company's top priority is getting a drug through the FDA approval process, so that it is available to ALL patients. We cannot lose sight of that mission in this discussion, and "right to try" cannot supplant this mission. We must continue to work to innovate clinical trials and streamline the FDA approval process so that drugs can make it to market quickly and safely. I applaud this Committee for their efforts in this regard. Both 21st Century Cures and The FDA Reauthorization Act will move this forward.

Second, a company may not be willing or able to take the risk of providing its experimental drugs to patients due to legitimate financial and personnel constraints that prevent them from doing so—particularly for small companies. While this may sound cruel against the plea from a dying

patient, the experimental medicine may simply not be well enough understood to be provided outside of the confines of well controlled clinical testing.

It is important to always remember that in developing new medicines you are attempting to alter a biochemical process in a finely tuned organism called human beings that took millions of years to evolve, and you're trying to do so without having effects that are outside of your specific target process.

No ethical company that I know of would ever release an experimental medicine outside of the FDA's regulatory process. A basic mantra is that "all drugs have side effects." Right to Try legislation has been written with the assumption that the safety of an experimental medicine is well characterized after initial Phase 1 testing, and the clear evidence is that this is simply not the case. Nor is the efficacy of an experimental medicine well understood after Phase 1 testing. Yes the issue is the risk/benefit profile of a critically ill or terminally ill patient, but this decision must be made on a case by case basis for each experimental medicine as it is developed.

Additionally, there are circumstances where companies do not have the resources, the experimental medicine itself or the personnel to provide oversight, to simultaneously conduct clinical trials and participate in expanded access.

I often say that biotech companies are "research and development pipelines unencumbered by revenue" – we conduct years and often decades of research and development on unproven experimental medicines, and spend hundreds of millions and often over a billion dollars in investment capital before hopefully reaching FDA approval and generating product revenue. The practical result of this is a fragility of the company and limited resources that must be dedicated to getting the product to approval. Additionally, expanded access programs require dedicated, trained personnel to handle requests, assist requesting physicians, dispense the drug, field questions, and handle paperwork and reporting, and many companies simply cannot handle this additional personnel and workload.

Third, the company has to consider the ramifications of a critically ill patient that gets worse or dies, related or unrelated, to the experimental drug. This can cause other patients to decline to participate in clinical trials, or put the approval of the product in jeopardy. Giving experimental medicines to critically ill individuals under less or in some cases completely uncontrolled

conditions is inherently risk creating. With the increasing awareness of expanded access, heightened by the Right-to-Try legislation, individuals are likely to be asking for experimental medicines earlier in the development process and for conditions that are further separated from the primary conditions for which the medicine is being developed. If things go badly, future patients might not receive a needed medicine because FDA approval is derailed or delayed. Biotechnology companies, the FDA and legislators must advocate for the needs of those patients as well.

Finally, the role of social media must be considered, as it is interlinked with the explosion of "right to try" laws. In the era of Facebook and Twitter, where people can express their opinions and interact with others in real-time, the moral and ethical issues created by these situations are complicated by a hyper-immediacy that increases the intensity and scrutiny under which these issues must be addressed.

I have had very personal experiences with this. My former company, Chimerix, Inc., went through a very public ordeal with a young boy whose parents undertook a social media campaign which resulted in extreme pressure on Chimerix to grant access to an experimental antiviral drug.

Chimerix was founded in 2002 to develop an oral form of a potent intravenously administered antiviral drug as a medical countermeasure against smallpox. At the time that I joined Chimerix in June 2009, the company was beginning to expand its development program to look at the potential for its drug, brincidofovir, to treat other viruses within the double-stranded DNA viral family, including herpes viruses such as cytomegalovirus, papilloma viruses, polyoma viruses and adenovirus. Soon thereafter, the decision was made to focus the Company's clinical development efforts on the potential use of brincidofovir to prevent the reactivation of cytomegalovirus in bone marrow stem cell transplant recipients, a pathological event that was known to significantly increase post-transplant mortality.

The first compassionate use of brincidofovir occurred in March 2009, when Chimerix provided brincidofovir to help save a soldier who, after receiving a smallpox vaccination, had a life-threatening breakthrough of the vaccinia pox virus. From this single event and the subsequent publication by the Center for Disease Control in May 2009², interest in and requests for brincidofovir grew through word of mouth within the medical community and led to a significant expanded access program by Chimerix.

² Progressive Vaccinia in a Military Smallpox Vaccinee --- United States, 2009. CDC Morbidity and Mortality Weekly Report, May 19, 2009. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm58e0519a1.htm>

Starting in September 2009, approximately 50 individual requests for brincidofovir were received over a 9-month period, increasing to approximately 50 requests over next 3-month period. This was one of the largest individual patient expanded access programs undertaken by a biotech company, at its peak accounting for an estimated 6% of the expanded access request to the entire FDA and an estimated 30% of the requests to the Antiviral Drugs Division. Because of this, in late 2010 the FDA asked Chimerix to establish a formal "intermediate size" Expanded Access program that would be listed on clinicaltrials.gov.

In February 2011, Chimerix received an \$88.1 million contract from the Biomedical Research Advanced Development Authority (BARDA), a portion of which was designated to pay for the 200-patient clinicaltrials.gov expanded access protocol in order to gain insights into emergency situations which were closely analogous to a potential smallpox outbreak. In late 2012, when funding under the BARDA program ended, Chimerix closed the expanded access program for brincidofovir to focus its resources on the formal regulatory approval process. At the time, Chimerix was still a private company, and had limited financial resources.

In total, brincidofovir was provided via expanded access to approximately 430 patients [215 individual requests plus 215 under the BARDA funded

program] to treat many different dsDNA viruses. During 2013 into 2014, after the cessation of the brincidofovir expanded access program, more than 300 additional requests were received and denied by the Chimerix Medical Department.

On February 12, 2014, doctors at St. Jude Children's Hospital in Memphis requested that Chimerix provide brincidofovir for a seven-year-old patient, Josh Hardy. Josh Hardy had been diagnosed at the age of 9 months with a malignant, highly aggressive, and rare form of kidney cancer. He subsequently survived three other bouts of cancer but, as a result of the treatments he had earlier in his life, in November 2013 a bone marrow biopsy revealed that he had a bone marrow failure. On January 10th, 2014, he received a bone marrow transplant at St. Jude Children's Hospital in Memphis, Tennessee. While he had heart and kidney issues before, the transplant caused further complications. Several days after the bone marrow transplant later, he was moved to the ICU for heart failure and five days later was put on a ventilator. He then developed an adenovirus infection as a result of his compromised immune system. As a result, Josh's doctors recommended that he receive brincidofovir under expanded access.

At that time, Chimerix had 55 employees. The expanded access program had closed and all of the resources were focused on completing the ongoing

Phase 3 clinical trial. Therefore this request, as with the hundreds before it, was denied by the Chimerix Medical Department.

Another request was made on March 5th by the St. Jude's Vice President, Clinical Trials Administration stating that "it is likely that after having fought against childhood cancer for so long, he may succumb to this infection without a non-nephrotoxic medication with superior efficacy proven in clinical trials." This second request was also denied.^{3,4}

It is at this moment that the importance of adhering to the process of developing new medicines intersects with the expanding world of a patient's "right to try" to get access to preapproved drugs. And while none of the policies being discussed in the states or at the Federal level would force companies into giving patients experimental drugs, they do work to encourage situations that we quickly found ourselves in at Chimerix.

On March 6th, one day after the second denial, Josh's mother Aimee Hardy wrote the following post on her Facebook page:

³ Facebook, #SaveJosh, March 7, 2014.

<https://www.facebook.com/SaveJoshHardy/photos/pch.666481523393017/666481483393021/?type=1&theater>

⁴ Young cancer survivor's family pleads with company for experimental drug, Ryan Jastrow, CBS News, March 11, 2014
<http://www.cbsnews.com/news/young-cancer-survivors-family-pleads-with-drug-company-chimerix-for-experimental-drug/>

"Our son, Josh Hardy, who recently had a bone marrow transplant has developed the adenovirus. This [is] a deadly virus for people who have weak immune system[s]. There is a drug called Brincidofovir that has been proven to treat the adenovirus effectively. Our doctor at St Jude told us they ran the study for the drug company and he knows it will work. However, the drug company has refused to release the drug for compassionate care because they are trying to take it to market. Basically they are not going to save a child's life for money. The company is Chimerix Inc out of Durham, NC. And the main contact is Dr. Herve Mommeja-Marin. And the drug is called Brincidofovir. The child that absolutely needs it to save his life is Josh Hardy. He is currently in the ICU at St Jude Children's Research Hospital. If anyone with influence can help us convince the Chimerix Inc to release the drug for compassionate care for our son, we would be forever grateful. The phone # of Chimerix Inc is 919-806-1074 and the email is compassionateuserequest@chimerix.com"⁵

Mrs. Hardy posted her plea for help on another website, Caringbridge:

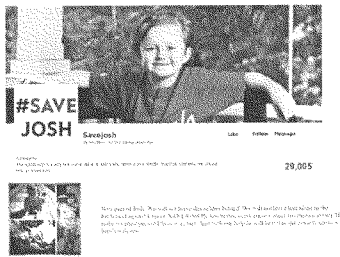
"We are asking everyone to think of any US representatives they might know or pharmaceutical connections that might help us. If

⁵ Aimee Hardy Facebook page. https://www.facebook.com/aimee.hardy.5?hc_location=timeline

anything, if 500 people or so just called Chimerix and told them they should send the Brincidofovir to Josh Hardy at St Jude's, it might be helpful”⁶

Overnight, into the morning of March 7th, Josh Hardy’s uncle created a Facebook page and twitter campaign called “#SaveJosh.” (Figure 1) His first post on the Facebook page was the letter from St. Jude’s Vice President to Chimerix containing the second request for brincidofovir.

Figure 1, the #SaveJosh campaign



By midday on Friday, March 7th, Chimerix employees and Board members had already received hundreds of phone calls and emails in support of Josh.⁷ This included emails from friends of Chimerix employees and Chimerix

⁶ Aimee Hardy Caringbridge page. <http://www.caringbridge.org/visit/joshuahardy/journal/view/id/5319641ecb16b40c20fb0945>

⁷ Fredericksburg first-grader fighting for his life. Robyn Sidersky, Fredericksburg.com News Desk, March 7, 2014.

investors, as well as calls from politicians including a US Congressman and the Speaker of the Virginia House of Delegates.

Over the next two days, there was a barrage of statements on social media and within traditional media such as CNN, which ran an 8-minute segment on Josh Hardy and the family's request for brincidofovir. CNN's print headline was "Company denies drug to dying child." FoxNews carried the headline "Company Denies Drug to 7-Year-Old Boy Struggling Against Curable Virus,"⁸ ignoring the fact that brincidofovir was still in the experimental phase and thus the ability to "cure" an adenovirus infection was unproven.

On Monday March 10th, the #SaveJosh campaign trended in the top 5 on twitter, based in part on the participation of social media "amplifiers," individuals with large followings who retweeted the #SaveJosh message. By March 13th over 25,000 people had "liked" the Facebook page, which had been viewed by over 1.3 million people.⁹ The social media campaign was not only targeted at Chimerix's employees and board, but also at politicians and the FDA. Within these messages, a darker side of social media was exposed, one based on threats of violence.

⁸ Company Denies Drug to 7-Year-Old Boy Struggling Against Curable Virus. Fox News Insider, March 10, 2014. <http://foxnewsinsider.com/2014/03/10/drug-maker-chimerix-refuses-release-drug-7-year-old-josh-hardy-struggles-against-curable>

⁹ Facebook Savejosh – Posts March 7, 2017 to March 13, 2014. <https://www.facebook.com/SaveJoshHardy/photos/a.666481530059683.1073741827.666476203393549/669181626456340/?type=1&theater>

In the face of this media storm, I tried to explain the ethical dilemma that Chimerix was facing, stating that “this is not only about Josh, it is about the many Joshes.”¹⁰ This approach did nothing to quell the uproar.

While the very public and highly negative social and traditional media frenzy pleading for access for Josh was ongoing, behind the scenes there were active conversations between Chimerix and the FDA about how to proceed, during which Chimerix maintained its position that for a multitude of reasons it did not have a clear path to make brincidofovir available to Josh Hardy under a single patient expanded access protocol. In response, the FDA proposed a novel solution. On Tuesday evening, March 11th, 120 hours after the first Facebook post by Mrs. Hardy, Chimerix announced in a press release that *“it has reached agreement with the FDA for the immediate initiation of a pilot trial of open-label brincidofovir for the treatment of adenovirus infections in immunocompromised patients.....This study is expected to begin with Josh Hardy as the first patient enrolled on Wednesday, March 12, 2014.”*¹¹

¹⁰ When unapproved drugs are the only help: A case for compassionate use. Jennifer Miller, Ethics Illustrated, August 18, 2014. <http://www.bioethics.net/2014/08/when-unapproved-drugs-are-the-only-help-a-case-for-compassionate-use/>

¹¹ Chimerix to Provide Brincidofovir to Josh Hardy as First Patient in New Open-Label Study in Patients With Adenovirus Infections. Chimerix Press Release, March 11, 2014. <http://ir.chimerix.com/news-releases/news-release-details/chimerix-provide-brincidofovir-josh-hardy-first-patient-new-open>

The ability to craft such a novel solution is rare, and would not have happened without the specific involvement of senior level FDA personnel.¹² As opposed to “conceding” in the face of social media pressure, the solution found was the initiation of a new Phase 3 clinical trial that in addition to treating Josh had the potential to provide data that could be used for the benefit of future patients who were faced with life threatening adenovirus infections- “the many future Joshes.”

I also want to take this opportunity to push back on the idea that the FDA is slow and ineffective with regard to expanded access, as is intimated in many “right to try” bills. The FDA approves more than 99 percent of these requests, on average, within four days¹³. For emergency requests, the agency responds in one day or less. The idea that these bills will give patients faster access to experimental drugs by cutting out the bureaucracy, which is a tenant in most of the Right to Try bills, is simply wrong. In reality, ending FDA oversight over experimental drugs would “expose the patients to exploitation without guaranteeing access to the drugs they seek. And weakening the FDA puts everyone else who takes drugs or uses medical devices or vaccines at grave risk.”¹⁴

¹² Chimerix Issues Statement Thanking the FDA for Collaboration in Developing Protocol to Treat Patients With Life-Threatening Adenovirus Infection, Chimerix Press Release, March 14, 2014. <http://ir.chimerix.com/news-releases/news-release-details/chimerix-issues-statement-thanking-fda-collaboration-developing>

¹³ “Expanded Access of Investigational Drugs: The Experience of the Center of Drug Evaluation and Research Over a 10-Year Period” Jonathan P. Jarow, Steven Lemery, MD, MHS, Kevin Bugin, MS, RAC, Sean Khozin, MD, MPH. Sage Journals, June 29, 2016

¹⁴ “Expanded Access of Investigational Drugs: The Experience of the Center of Drug Evaluation and Research Over a 10-Year Period” Jonathan P. Jarow, Steven Lemery, MD, MHS, Kevin Bugin, MS, RAC, Sean Khozin, MD, MPH. Sage Journals, June 29, 2016

Josh Hardy received his first dose of brincidofovir on Wednesday night March 12th. His progress and response were reported by his mother through multiple Facebook posts¹⁵ and by March 31st, when Josh turned 8, adenovirus was undetectable.¹⁶ On April 10th, after fewer than 10 doses of brincidofovir and a month after his first dose, Josh was released from St. Jude, although he was required to remain in Memphis to be near his physicians.¹⁷ On July 17, he was allowed to return to his home in Virginia. Sadly, on September 22, 2016, 2 ½ years after receiving brincidofovir, Josh Hardy died of further complications of his underlying disease. He was 10 years old.

While brincidofovir provided Josh Hardy with additional time, many cases do not work out this way. And continuing to create policies that will encourage more patients to try and access unapproved drugs without FDA oversight, while well intentioned, is the wrong solution to such a serious issue. The laws will unlikely make a difference in the lives of patients, but will encourage this growing phenomenon of using social media to shame companies into providing access to unapproved drugs.

¹⁵ Aimee Hardy Facebook page. <https://www.facebook.com/aimee.hardy.5?ref=ts>

¹⁶ St. Jude Patient Celebrates Birthday And Improving Health, WREG Memphis, March 31, 2014. <http://wreg.com/2014/03/31/st-jude-patient-celebrates-birthday-and-improving-health/>

¹⁷ Josh Hardy released from hospital, Fredericksburg.com News Desk, April 11, 2014

The #SaveJosh social media campaign brought considerable publicity to expanded access and “right to try,” and much was written by bioethicists and others about the #SaveJosh social media campaign and its impact and implications for on expanded access, Right to Try and the development of experimental medicines. My learning experiences and observations will be more fully discussed in a soon to be published article in Medicine Access @ Point of Care entitled, “Ethical Crossroads: Expanded Access, Patient Advocacy and the #SaveJosh Social Media Campaign.”¹⁸

Hopefully, this expanded body of writings will provide more support and guidance to corporate leaders who are trying to make decisions about expanded access. However, at the time that Chimerix was faced with these questions very little had been written, and thus I relied on my own expanded access experiences at prior companies, on several Chimerix colleagues and on a number of industry leaders who had relevant experience in expanded access and crisis management, as well as on the “Statement of Ethical Principles on Early Access Programs” that had been published in 2010 by the Biotechnology Innovation Organization’s (BIO) Standing Committee on Bioethics.¹⁹

¹⁸ Ethical Crossroads: Expanded Access, Patient Advocacy and the #SaveJosh Social Media Campaign. Kenneth I. Moch, Under Revision, to be published in Medicine Access @ Point of Care, 2017. <http://medicine-access.pointofcarejournals.com/>

¹⁹ Early Access Programs: Points to Consider, Biotechnology Innovation Organization Standing Committee on Bioethics, April 16, 2010, <https://www.bio.org/sites/default/files/files/20100416.pdf>

Additionally, since the experience with Chimerix, considerable progress has been made on both the regulatory front by the FDA and in the legislative arena through the 21st Century Cures Act. 21st Century Cures now requires that all companies in the business of developing, manufacturing, and distributing drugs publish the policies and processes under which they will make their investigational unapproved medicines available to very sick patients. Importantly, they are required to provide a specific contact point where doctors can discuss the patient's need for the experimental medicine. It is policies like these that Congress should be focused on in continuing their work.

State and Federal legislators must be coming up with solutions that will ensure that all patients can get access to groundbreaking new treatments. Unfortunately, I believe that ultimately the potential confusion and complexities caused by states passing different variations of Right-to-Try laws will need to be addressed and corrected, which is another reason why I urge Congress to proceed with caution in this space. At its essence, expanded access is not drug development, and it cannot be used as an alternative to fully demonstrate the efficacy and safety of experimental medicines. The goal must not change – and that is to get a drug approved by the FDA so that it is available to be used in all appropriate patients.

There is no simple, monolithic answer to the question of when the circumstances and timing are right to undertake an expanded access program, because each experimental medicine is different, the safety and efficacy parameters are different, the clinical development processes and regulatory pathways are different, and the patient populations in need are different. Expanded access is not drug development and, given this fact, it is not unreasonable for a company to decide not to initiate an expanded access program until there is sufficient data demonstrating the efficacy and safety of an experimental medicine.

As I have noted, expanded access programs raise social, ethical and moral conflicts and dilemmas regarding access to experimental medicines. How does society or a company balance the immediate needs of a critically ill individual, in many cases a child, versus the potential needs of many future patients? Who is advocating for future patients who might not receive a needed medicine because FDA approval is delayed by even a week or a month?

I am not talking about the FDA delaying the review process, but rather what might happen if, because of an unexpected finding or outcome, some percentage of potential participants choose not to enroll in a clinical trial, slowing down its timeline. Being very granular, what would have happened

to the brincidofovir clinical development program and even to Chimerix if, after the global social media campaign, Josh Hardy had received brincidofovir and shortly thereafter died?

The ethical decisions should not rest solely on the corporate leadership in biotechnology companies. Instead, there needs to be a focused effort to create a more equitable approach to expanded access. In 2015, in a Wall Street Journal article, I laid out several proposals, some of which have already been adopted. ²⁰

- “Life-science companies should publicly state their policy on expanded access. It must be recognized that a company has the right not to make an experimental medicine available if it believes the greater good is served by this decision.”

This was actually a proposal adopted in 21st Century Cures, which I applaud.

- “Regulatory guidance should provide a framework so companies can consider the risks to the drug development timeline and approval

pathway in the face of unforeseen or unfortunate consequences from granting expanded access.”

While the FDA has done a great deal to provide guidance, there needs to be a greater partnership and coordination with the agency.

- “Especially for smaller companies whose drug or device may be their only product, there should be an optional system to provide support for these complex decisions that would look at multiple factors, including equitable access and availability, cost, and the short- or long-term risks and benefits to a development program.”

Complex situations are often best analyzed in hindsight. Now, over 3 ½ years after the #SaveJosh social media campaign, it is clear to me that I would not change any of the key decisions that I made in dealing with the external forces and interests.

Key learning experiences stand out. First, despite all the hope and desire, not all experimental medicines succeed in clinical testing. Brincidofovir did not achieve the level of effectiveness in either of its two Phase 3 clinical trials, and the company has had to reposition its development efforts for the compound to progress towards regulatory approval. This highlights one of

the underlying complexities of the use of experimental medicines, as stated above: expanded access is not drug development. While there is evidence of a high approval rate for drugs provided under expanded access²¹, the understanding of safety and efficacy of an experimental medicine is still evolving, and there are no guarantees that the experimental medicine will have the desired effect without undesired side effects. For growing biotech companies with voracious capital requirements, successful market structure reform would lead to scientific advancement, novel medicines, and life-saving treatments for patients in need.

Also, as I mentioned earlier, the FDA is not an impediment in patients getting access to experimental medicine. Rather, they are a necessary partner and must be engaged in the process as a partner with the company, for the safety of all patients.

Finally, social media cannot and must not drive these decisions. The social media uproar regarding Josh Hardy exploded and reached a conclusion over the course of five days, just 120 hours, and as a result, there was much analysis over the power of social media in influencing the decision-making process regarding access to health care. On March 23, The Washington Post published an article entitled, "Crowdsourcing medical decisions: Ethicists

²¹ Characterizing expanded access and compassionate use programs for experimental drugs, Miller et al. BMC Res Notes, July 28, 2017. <https://www.ncbi.nlm.nih.gov/pubmed/28754150>

worry Josh Hardy case may set bad precedent” in which the author noted that “critics of the strategy say they sympathize with Josh’s parents and admire them for being willing to do anything to save their child, but they decry the crowdsourcing of medical decisions and warn that the case may set a dangerous precedent.”²²

I know firsthand that collective public opinion marshalled by social media can create immediate pressure which is difficult if not impossible to ignore. And these new laws are encouraging and rewarding these actions, resulting in individual companies being forced to make decisions on an ad hoc basis, which will only continue to fuel suspicions among patients, family members and the public about the motives when access is denied.”²³ The climate of innovation needs to be fostered, not vilified. These growing biotech companies are trying to drive scientific advancement, and bring novel medicines and life-saving treatments for ALL patients in need.

I do not want to end this testimony without providing a concept for consideration, a potential way to work with and embrace the intent of Right to Try legislation.

²² Crowdsourcing medical decisions: Ethicists worry Josh Hardy case may set bad precedent. Ariana Eunjung Cha, The Washington Post, March 23, 2014. https://www.washingtonpost.com/national/health-science/crowdsourcing-medical-decisions-ethicists-worry-josh-hardy-case-may-set-bad-precedent/2014/03/23/f8591446-ab81-11e3-adbc-88c8010c799_story.html

²³ Viral Crossroads, Steve Usdin, BioCentury, March 31, 2014. <https://www.biocentury.com/biocentury/regulation/2014-03-31/hardy-case-shows-flaws-compassionate-use-system-provides-catalyst>

One way to meld the intent of Right to Try laws with the existing expanded access process would be to create a more explicit regulatory pathway which allows expanded access safety and efficacy data to be incorporated into the label of a new medicine once it is formally approved for its primary indication via “traditional” placebo controlled trials. In this way, companies could balance the risks and benefit to individual patients with the needs of future patients.

Under current expanded access regulations and Right to Try legislation, safety and efficacy data gained through expanded access programs is viewed as uncontrolled data that can provide only limited support to the drug development and approval process. As demand for expanded access increases, the lack of specific incentives to offset the costs and risks can and most likely will become a factor in the decision to allow expanded access, a decision that, as noted, rests primarily with the sponsor companies.

This might require legislative and/or regulatory changes to existing guidelines for intermediate- or large-scale expanded access programs. Rather than circumventing the FDA oversight process, companies would have to reach agreement with the FDA as to the parameters under which “real-world evidence” collected from patients enrolled in these larger-scale expanded access trials could be used to support additional label claims for a new medicine. These programs would be “open label” trials, conducted

without placebo controls, but overseen as if they were formal clinical trials designed to provide full input into the drug development process.

Such programs would also have the benefit of obviating the need for incremental funding from third parties, unlike an oft-proposed national pool from which drug development companies would be paid for the cost of providing experimental medicines and managing Right to Try programs. Under this amended expanded access proposal, companies would be incented to undertake these programs because they could determine how the expanded access program would potentially lead to the ability to treat a larger future patient population.

All of us who are committed to creating life-saving medicines would like to see our medicines made available to as many people as possible as quickly as possible. In order for that to happen, we need to conduct rigorous clinical trials so that both the efficacy and safety are well understood by doctors and their patients. However, we also recognize that this drug development process is lengthy and complex, and that there are patients in need now who cannot wait for the approval process to be completed. Rather than skirting regulatory oversight through Right to Try legislation, creating the potential for label claims which build on the data from larger expanded access programs may save their lives.

Thank you again for allowing me the opportunity to testify today.

Mr. BURGESS. And we thank you for your testimony.
Dr. Bateman-House, you are recognized for 5 minutes, please.

STATEMENT OF ALISON BATEMAN-HOUSE

Dr. BATEMAN-HOUSE. Mr. Chairman, Ranking Member Green, and the members of the Health Subcommittee, I am Dr. Alison Bateman-House, an assistant professor of medical ethics at NYU Langone Health.

Thank you, first, for having this hearing and also for the opportunity to be here with you today. It's wonderful to see so many people engaged in trying to help patients who find themselves in exceedingly dire straits.

I co-chair a working group on compassionate use and preapproval access. This group is composed of patient advocates, members of the pharmaceutical industry, individuals with clinical trial and compassionate use experience, bioethicists, lawyers, venture capitalists, and individuals with both experience at the FDA or the Reagan-Udall Foundation for the FDA.

This working group was formed before the Right to Try movement began and there was no litmus test of any sort on Right to Try or any other topic for members to pass to be invited to the group. And yet, every member of our group opposes Right to Try on ethical, legal, and pragmatic grounds.

The working group was founded in the aftermath of Josh Hardy's quest to gain access to brincidofovir that Mr. Moch just spoke of. That case and others made public headlines and indicated that there was dissatisfaction with the existing system for accessing investigational medicines outside of clinical trials.

So our task was a specific mission—to study access to investigational drugs outside of clinical trials from the vantage point of all stakeholders to identify what problems existed and to propose solutions.

We have identified many concerns with the current system and we have proposed several ways to address these concerns. I will review some of these briefly. But before I go any further, I want to make two points very clear.

First, after more than 3 years of studying all facets of compassionate use or preapproval access, including the right to try, the working group has found that the FDA's expanded access program has been doing an excellent job in helping patients obtain access to experimental drugs.

Earlier today, we heard Representative Fitzpatrick say that Right to Try would "prevent the Government from blocking access to potentially lifesaving treatments."

This is a solution for a problem that does not exist. We have heard repeatedly today that the Government is not the barrier to people getting access.

The second point I want to drive home is that no piece of Right to Try legislation either on the State or Federal level addresses the myriad issues the working group has identified in this space.

So what issues have we found? First, as we've heard today, there's a widespread lack of knowledge about the expanded access program.

My working group has tried to address this dearth of knowledge by hosting webinars, publishing and speaking extensively and partnering with patient organizations for events like Ask an Expert sessions.

But, obviously, our small volunteer group is unable to fill a national educational gap.

So we have told the FDA that it needs to step up and to make sure that there's more understanding in this process. But this responsibility for increased education cannot rest solely on the FDA.

Doctors and nurses organizations, pharmaceutical trade associations, and all sorts need to step up and be involved.

Another especially troubling issue is that of rampant, inaccurate, even mythological beliefs. Some patients believe the FDA can force companies to give access to drugs. This is not true.

Another widespread myth is that the FDA is slow in handling requests. This is not true. Another myth is that the United States somehow has an incredibly small number of patients being served.

We don't know if this is true or not. When people say that less than 2,000 requests have been approved, those are protocols. We don't know how many patients are in those protocols.

We know about half the protocols are single patients, so just one, but the others could be anywhere from hundreds to thousands of patients. We don't know.

And the last myth that I have heard is that, you know, focussing on legal liability prosecution is necessary—that somehow we need to protect companies from legal risk. This is also a myth.

And because these myths are persistent, widespread, and may well be leading companies, doctors, or hospitals to turn down patient requests, they have to be dealt with.

So these among others are some of the problems that the working group has identified and you will note that I have not identified Right to Try much in what I've said because none of these issues are dealt with in any of the Right to Try laws.

I will quote a recent letter from 22 patient organizations that say, quote, "Our organizations support patient access to unapproved therapies."

But S. 204 and H.R. 878 do not effectuate policy changes that would afford our patients greater access to promising investigational therapies. Instead, these bills would likely do more harm than good.

In closing, I want to point out one way that Right to Try laws have already caused harm, and that is by taking what was already a confusing situation and making it even more confusing.

We now have 37 State laws—it's not one coherent law, they are each individually different—plus a potential for a Federal law.

You know, especially when patients cross State lines to seek health care or when you have hospital or insurance organizations that span State lines, such complexity is the enemy of patients.

I thank you for your time, and I look forward to your questions and I yield back to the Chair.

[The prepared statement of Dr. Bateman-House follows:]



STATEMENT
OF
ALISON BATEMAN-HOUSE, PHD, MPH, MA
ASSISTANT PROFESSOR, DIVISION OF MEDICAL ETHICS
DEPARTMENT OF POPULATION HEALTH, NYU LANGONE HEALTH
BEFORE THE
HEALTH SUBCOMMITTEE OF THE
COMMITTEE ON ENERGY AND COMMERCE
U.S. HOUSE OF REPRESENTATIVES
“EXAMINING PATIENT ACCESS TO INVESTIGATIONAL DRUGS”
OCTOBER 3, 2017



Mr. Chairman, Ranking Member Green, and Members of the Health Subcommittee, I am Dr. Alison Bateman-House, an assistant professor of medical ethics at NYU Langone Health. Thank you for the opportunity to be here today to discuss the various "Right to Try" proposals that have been introduced in the House of Representatives.

I co-chair the Working Group on Compassionate Use and Pre-Approval Access. This group is composed of patient advocates, members of the pharmaceutical industry, individuals with clinical trial and compassionate use experience, bioethicists, lawyers, venture capitalists, and individuals with experience at the FDA and the Reagan-Udall Foundation for the FDA. The Working Group was formed before the Right to Try movement began, and there has been no litmus test of any sort, on Right to Try or any other topic, that members had to pass. And yet, every member of the group opposes Right to Try on ethical, legal, and pragmatic grounds.

The Working Group was founded in the aftermath of Josh Hardy's quest to gain access to brincidofovir.¹ That case and others that made public headlines indicated that there was dissatisfaction with the existing system for accessing investigational medicines outside of clinical trials. The group was founded with a specific mission: to study access to investigational drugs outside of clinical trials from the vantage point of all stakeholders; to identify problems; and to propose solutions.

We have identified many concerns with the current system and have proposed several ways to address them. I will review some these briefly, but before I go any further, I want to make three points very clear. First, after more than three years of studying all facets of compassionate use/pre-approval access, including Right to Try, the Working Group has found that the FDA's expanded access program has been doing an excellent job of

¹ Elizabeth Cohen, "Company denies drug to dying child," *CNN*, March 11, 2014.



helping patients obtain access to experimental drugs. Second, no piece of Right to Try legislation, either on the state or federal level, addressed the concerns the Working Group has identified.

So, what issues have we found? First, there's a widespread lack of knowledge of the FDA's expanded access program. Consistently, in speaking with patients, doctors, reporters, and even personnel in the pharmaceutical industry, people have not known that it is possible to access investigational drugs outside of clinical trials, much less how to do so. Patient advocacy groups tend to be more knowledgeable about expanded access, but there is a vast range in knowledge when you move from large organizations like the American Cancer Society and the National Organization for Rare Diseases to smaller, more regional or community-based organizations. The Working Group has tried to address this dearth of knowledge by hosting webinars, publishing and speaking extensively, and partnering with patient organizations for events like "Ask an Expert" sessions, but our small volunteer group is obviously unable to fill a national educational gap. We have therefore called for the FDA to be more proactive in educating industry, doctors, patient advocacy organizations, and patients about this potentially very beneficial resource that it offers. We're happy to report that they've listened: Over the last 2 years the FDA has made its website more user-friendly and has introduced a new, much shorter application form for compassionate use requests for single patients. So while we applaud the agency's process, we also call on it to be more proactive in informing stakeholders about it. However, the responsibility for this education should not rest solely on the FDA. Doctors' and nurses' organizations need to step up in educating their members about expanded access. Likewise, pharmaceutical trade associations should continue their recent efforts to make sure their members understand all aspects of expanded access.

Another, especially troubling issue we have identified is that of rampant inaccurate, even mythological, beliefs about compassionate use. Some patients believe the FDA can force drug companies to make their investigational products available. This is not true. The FDA can merely approve a request to proceed; if the



company says no, there is no higher power to which a patient can appeal. Another widespread myth is that the FDA is slow in handling requests for compassionate use. This is untrue. Another myth, promulgated by Right to Try legislation's focus on shielding all involved from legal liability prosecution, is that engaging in expanded access may expose companies to legal risks. Our research has found no instances in which a drug company, doctor, or hospital was sued with regard to expanded access; a recent journal article also found no such lawsuits.² A particularly pernicious myth is that if a company provides its drugs outside of clinical trials, and a patient has a serious problem or dies, then the drug's eventual FDA approval will be threatened, if not ruined. After spending years and an enormous sum of money developing a new drug, it would be understandable if a company were to think that providing its drugs via compassionate use is simply too much of a business risk. But the FDA has studied this extensively over the past few years, and it has found *zero* instances in which a compassionate use drug that was linked to a death or serious problem was rejected based on that incident. It also has found *zero* instances in which a drug that was linked to a death or serious problem was ordered by the FDA to undergo additional clinical studies. Furthermore, the FDA has found *zero* instances in which a drug that was tied to a death or serious problem ended up with more restrictive labeling based on that incident. The FDA found only 2 instances in 10 years in which development of a drug was paused due to a death or serious problem in a compassionate use patient, a minuscule number.

Because these myths are persistent, widespread, and may well be leading companies, doctors, or hospitals to turn down patient requests for compassionate use, they must be dealt with head-on.

Another issue that the Working Group has identified is patient, family, and advocate frustration over not

² Amy E. McKee, Andre O. Markon, Kirk M. Chan-Tack, and Peter Lurie, "How Often Are Drugs Made Available Under the Food and Drug Administration's Expanded Access Process Approved?" *Journal of Clinical Pharmacology* (2017), 57(510): S136-S142.



knowing how to request an experimental drug from a company. Just stating the issue reveals another knowledge gap, as we don't know of a single company that will grant compassionate use access requests made by a patient: rather, the requests need to be made by a health care professional. So, as previously mentioned, health care professionals need training on this matter. But in the meantime, to help these professionals and all other interested parties, we have been advocating for companies to make public their access policies. We are very pleased that this provision was included in the 21st Century Cures Act, thanks to the work of Representative Michael McCaul and his colleagues, particularly Representative Upton and Representative Degette. We are, however, dismayed that the provision apparently has no enforcement mechanism and there is less than 100% compliance with the rule.

These are some of the problems that the Working Group has identified and for which we have proposed possible solutions. You will note that I have not mentioned Right to Try much, **because none of these issues are addressed in those laws**. Indeed, if I were to analyze the Right to Try laws, I would point out much that is misleading, unnecessary, confusing, vague, or downright harmful. I'm happy to do so during the Q&A, but now I'll simply quote a recent letter from 22 patient advocacy organizations that says, "Our organizations support patient access to unapproved therapies, but S.204 and H.R.878 do not effectuate policy changes that would afford our patients greater access to promising investigational therapies. Instead, these bills would likely do more harm than good."³ These are 22 groups whose sole reason for being is to help save the lives of patients.

I do want to point out that one huge way that Right to Try laws have already caused harm is through the confusion created by 37 different state laws that have been enacted. These vary from state to state on crucial matters: for example, while advocates of Right to Try often use children as examples of patients needing access to experimental drugs, 5 state right to try laws don't apply to those 18 and younger. In 19 states, patients using

³ To Rep. Greg Walden, 9/19/2017 (appended)



an investigational drug obtained via right to try can lose their hospice coverage, and 6 states say these patients may be denied coverage for home healthcare assistance. These laws apply to terminally ill patients—the very people who would naturally be dependent on hospice, home healthcare, and insurance. These are not humane, patient-centered provisions for people who are facing death. And the inconsistency in laws from state to state have real implications for patients who might travel across state lines seeking care, for healthcare institutions that operate in more than one state, and for patient advocacy groups who advise patients from a range of states.

Every Working Group member has witnessed the suffering of patients and their families when they are confronted with serious or life-threatening conditions and are out of FDA-approved treatment options. We understand why patients would want to try experimental drugs. For 3 decades, the FDA has had in place a system to help such patients gain access these drugs. Between 2010-2015, the agency has allowed more than 99 percent of the “compassionate use” requests it received from drug companies to proceed. And while such a large number of approvals may suggest that the FDA “rubber stamps” requests, this is far from the case. A recent study found that 11% of these requests had been modified after input from FDA experts, with regard to such issues as drug dosage or frequency of dosing.⁴ These modifications are made for the sole purpose of trying to improve the likelihood that these compassionate use drugs will help—and, importantly, not hurt—the patients using them. In short, the FDA’s expanded access program works, assisting patients who choose to try experimental drugs.

Of course, there will always be some requests for investigational drugs that companies will deny. In many cases this is reasonable. For instance, if the drug is available via a clinical trial in which the patient is eligible to participate, it is appropriate to tell the patient that they must obtain the drug via the trial, not

⁴ Jonathan P. Jarow, Peter Lurie, Sarah Crowley Ikenberry, Steven Lemery, “Overview of FDA’s Expanded Access Program for Investigational Drugs,” *Therapeutic Innovation & Regulatory Science* (2017), 51(2): 177-179.



compassionate use. If drug quantity is limited, it is appropriate for a company to deny a request. But it is essential that companies deny requests based on sound reasons, not on myths or unfounded fears.

The best, safest way to speed access to drugs in development to the largest number of patients is through the clinical trial process. Clinical trials are vital to the pharmaceutical industry's creation of safe and effective drugs, and once approval is secured for a new drug, all patients with the condition are able to receive it, thereby helping the largest number of patients. However, not all patients who are willing to participate in clinical trials are able to do so. In some cases, this is because no trials are available where they live, or patients are considered too young or old, or because they have something in their medical history that renders them ineligible to participate. The Working Group has called for an investigation into what can be done to make clinical trials available on an equitable basis for all patients, and we are gratified to see such a provision included in the recently enacted FDA User Fee Reauthorization Act. By expanding clinical trial access, you will reduce the number of patients forced to seek access to investigational drugs outside of clinical trials. And by educating all stakeholders, combatting myths, and continuing to review the current system for ways it can be even more streamlined, the Working Group is convinced that compassionate use will become more accessible, more transparent, and more patient-friendly.

CONCLUSION

Clinical trials remain the best option for patients wishing to gain access to investigational products, and bringing new, innovative products to market through the FDA approval process remains the best way to assure the development of and access to safe and effective new medical products for *all patients*. For those patients who cannot participate in trials and who have no other therapeutic options, the FDA's expanded access program



works. However, it faces challenges, especially a widespread lack of knowledge and confusion about the program. We need to fix this. But we do not need to undermine a working program that benefits patients by creating a deeply flawed alternative program that will only lead to further confusion and strip patients of crucial protections they currently have. Right to Try laws do not solve the problems the Working Group has identified in its years of research. And the laws not only fail to address these current problems, they will create additional, new problems. Instead of promoting Right to Try as a way to help patients, we need to focus on making the current expanded access system even better: letting people know what it is, how to use it, that they need to work with their doctor to request access, and so on. And finally, since the ultimate decision to grant access is up to individual companies, we need to work with these companies to find out why they deny requests and what, if any, policies would make them more likely to say yes.

Thank you. I look forward to your questions.

September 19, 2017

The Honorable Greg Walden, Chairman
2125 Rayburn House Office Building
U.S. House Committee on Energy and Commerce
Washington, DC 20515

The Honorable Frank Pallone, Ranking Member
2471 Rayburn House Office Building
U.S. House Committee on Energy and Commerce
Washington, DC 20515

Dear Chairman Walden and Ranking Member Pallone,

The undersigned organizations collectively represent millions of patients with serious and life-threatening diseases. We write to express our strong opposition to S.204, the *Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017*, as well as H.R.878, the *Right to Try Act of 2017*, currently under consideration in the House Energy and Commerce Committee. We urge the Committee to proceed through regular legislative order to facilitate discussion and consideration of alternative policies that would genuinely increase access to promising investigational therapies for the communities we represent.

Our organizations support patient access to unapproved therapies, but S.204 and H.R.878 do not effectuate policy changes that would afford our patients greater access to promising investigational therapies. Instead, these bills would likely do more harm than good. We encourage the Committee to hold hearings to examine these issues more closely, as well as consider other policy options to improve the ability of patients to safely access unapproved therapies.

We do not believe S.204 or H.R.878 would successfully increase access to promising investigational therapies for those in need. Both of these bills remove the Food and Drug Administration (FDA) from the initial approval process for accessing an investigational therapy outside of a clinical trial. Removing FDA from this process is not likely to facilitate increased access to investigational therapies because FDA currently approves 99.7 percent of all expanded access requests submitted by physicians and companies for patients with immediately life-threatening illnesses who cannot participate in clinical trials.¹ The Government Accountability Office (GAO) recently released a report examining the current FDA expanded access program, and found that substantial changes were not needed within the program, aside from greater clarity on the use of adverse event data.²

When access to a therapy is denied to a patient, it is generally the company that denies the request, and for reasons that appear to be reasonable, such as a determination that the benefits do not outweigh the risks, an unavailability of sufficient product to offer outside of clinical trials, costs, or concerns about adversely affecting clinical trial enrollment.

¹ Jarow, Jonathan P., et al. "Expanded access of investigational drugs: the experience of the Center of Drug Evaluation and Research over a 10-year period." *Therapeutic innovation & regulatory science* 50.6 (2016): 705-709.

² GAO, "FDA Has Taken Steps to Improve the Expanded Access Program but Should Further Clarify How Adverse Events Data Are Used," July 2017.

It is important to remember that the current regulatory system for medical products and research in the United States was created as a result of serious patient harm and exploitation that occurred early in the 20th Century. Birth defects resulting from Thalidomide are an example of what happens when drugs are given to humans without proper safety review and approval. While obtaining unapproved therapies outside of a clinical trial is not about research, the products themselves remain experimental and have not been shown to be safe and effective. Clinical research subject protections are in place when experimental products are being tested to ensure the safe and ethical treatment of research participants. Patients seeking expanded access to unapproved therapies outside of clinical trials must be afforded the same ethical standards and protections as patients taking part in clinical trials.

Existing expanded access policies are not without room for improvement. We encourage the Committee to examine the predominant reasons why patients interested in access to experimental therapies are ultimately unable to obtain them by enrolling in clinical trials or through the current expanded access process. We also ask the Committee to provide oversight as FDA moves forward with implementation of relevant provisions enacted within the past year that improve the expanded access system. These include the requirements within the *21st Century Cures Act* for the public posting of expanded access policies on company websites, and greater clarity from FDA on the use of adverse event data. Several provisions in the *Food and Drug Administration Reauthorization Act (FDARA)* will also improve access to investigational therapies, such as the allowance for IRBs to appoint one individual to review applications rather than a fully convened IRB. FDARA also directs FDA to further investigate inclusion/exclusion criteria within clinical trials, a key factor in the number of individuals able to access investigational therapies.

We are eager to work with the Committee as it considers these proposals, and endeavors to ensure patients gain greater access to investigational therapies. We welcome the opportunity to work with members of the Committee, as well as the sponsors of this legislation, to improve and increase access to both approved and unapproved innovative, lifesaving therapies.

Sincerely,

Alliance for Aging Research
American Cancer Society Cancer Action Network
American Lung Association
American Society of Clinical Oncology
Association of Pediatric Hematology/Oncology Nurses
Cancer Support Community
Children's Brain Tumor Foundation
Children's Cause for Cancer Advocacy
Cystic Fibrosis Foundation
Fight Colorectal Cancer
Friedreich's Ataxia Research Alliance
Friends of Cancer Research
Grandparents in Action
Leukemia & Lymphoma Society
Lung Cancer Alliance
LUNgevity Foundation

Max Cure Foundation, Inc.
National Comprehensive Care Network
National Health Council
National Organization for Rare Disorders (NORD)
TargetCancer Foundation
United Mitochondrial Disease Foundation

CC: The Honorable Paul Ryan, Speaker
The Honorable Kevin McCarthy, Majority Leader
The Honorable Nancy Pelosi, Minority Leader
The Honorable Steny Hoyer, Minority Whip

September 5, 2017

Dear Members of the United States House of Representatives:

The undersigned groups respectfully urge you to oppose S. 204 — which is deceptively titled the “Right to Try Act of 2017” but should instead be called the “False Hope Act of 2017.”

We recognize the desire of patients with terminal illness who have exhausted available treatment options to access experimental medical products that have not been approved or cleared by the Food and Drug Administration (FDA). However, the best way for patients to gain such access is through the FDA’s Expanded Access Program, which allows seriously ill patients to receive treatment with experimental medical products while also providing basic safeguards to protect patients’ rights and welfare. Importantly, the recently enacted FDA Reauthorization Act of 2017, which renewed the FDA’s user fee programs, included responsible bipartisan language intended to enhance the agency’s Expanded Access Program.

We are concerned that S. 204, as amended and passed by the U.S. Senate on August 3, 2017, would put countless patients at risk by undermining important FDA safety rules related to the use and oversight of unapproved, experimental medications. Such legislation would expose vulnerable patients to risks of serious harm, including dying earlier and more painfully than they otherwise would have, without appropriate safeguards.

FDA’s Current Expanded Access Program

Currently, the FDA oversees the use of all experimental drugs and biological products in the U.S. The FDA’s Expanded Access Program allows patients across the country to gain access to such products, provided that each patient’s doctor believes such access is appropriate and that the manufacturer of the product agrees to provide it for that use.

To protect patients, the FDA and an institutional review board (IRB) must approve each use of an experimental drug or biological product under the Expanded Access Program. As conditions of approval, there must be sufficient evidence of the safety and effectiveness of the experimental drug to support its use in a particular patient, and the probable risk to the patient from the drug must not be greater than the probable risk from the disease or condition. The program further protects patients by requiring a robust informed consent process that is similar to the consent process for a clinical trial, as well as monitoring and reporting of serious adverse events. The FDA grants 99 percent of all Expanded Access Program requests and, in urgent circumstances, can respond to such requests within one or two days. The agency also recently streamlined the program to require less paperwork. In addition, the 21st Century Cures Act of 2016 included useful provisions that require drug manufacturers to publicly post their expanded access policies and provide points of contact for requests. The potential impact of these streamlining efforts has yet to be fully realized.

It is also important to recognize that many of the experimental products made available through this program ultimately are not shown to be safe and effective in clinical testing and are not approved or cleared by the FDA.

Undermining Patient Protections While Offering False Hope

The false-hope legislation passed by the Senate and now being considered by the House would create a dangerous, uncharted pathway for access to experimental drugs and biological products that essentially bypasses the protections of the FDA's Expanded Access Program for patients diagnosed with life-threatening diseases or conditions — a patient population that is much broader than “patients diagnosed with a terminal illness,” which was the patient population covered by the original version of S. 204.

Of particular concern, this alternative pathway for accessing experimental drugs and biological products would put vulnerable patients at risk and undermine their rights by:

- Specifying completion of a single phase I clinical trial as the evidentiary threshold for allowing use of experimental drug products under the legislation. Such a threshold is insufficient for allowing use of an experimental drug outside the context of a clinical trial because initial phase I clinical trials often only involve healthy volunteers, typically involve testing of a single dose of an experimental drug, provide no meaningful data on efficacy, and yield only very limited preliminary data on safety.
- Eliminating the requirements for review and approval by the FDA and an IRB, which help to ensure that proposed uses of experimental drugs do not pose unacceptable risk to patients and that the patients are fully informed of the risks and other key information when their consent is sought.
- Eliminating the requirements that (a) the consent of the patient be sought only under circumstances that provide the patient with sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence; (b) the information given to the patient when consent is sought be understandable to the patient; and (c) the consent process exclude exculpatory language through which the patient is made to waive or appear to waive any of his or her legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.
- Broadly immunizing sponsors, manufacturers, prescribers, and dispensers from liability for any alleged acts or omissions related to eligible experimental drugs, unless the relevant conduct constitutes reckless or willful misconduct, gross negligence, or an intentional tort under applicable state law. This provision would bar suits in a variety of situations in which state law might reasonably impose liability. For example, it would immunize manufacturers from being held accountable for harm caused by contamination of an investigational drug product, which can be serious. It also would bar state-law negligence suits against the physician prescribers; for example, if the physician negligently prescribed an investigational drug that was known to be contraindicated for a particular patient's set of circumstances, but the situation did not arise to “gross negligence.” Decisions about liability in such situations are properly based on consideration of the specific facts, and the bill's immunity provision may cause physicians to be less careful in making prescribing decisions for seriously ill patients.
- Eliminating the requirement that the treating physician report immediately to the manufacturer or sponsor any serious adverse events regardless of whether they are considered drug-related.

Letter to Congress Regarding S. 204

September 5, 2017

In closing, we urge you to oppose S. 204 and any similar false-hope legislation that is introduced in the future. Thank you for considering our views on this important matter.

Sincerely,

Public Citizen
ACTUP New York
Breast Cancer Action
Doctors For America
END AIDS NOW
Government Accountability Project
Health GAP
Jacobs Institute of Women's Health
MedShadow Foundation
National Consumers League
National Physicians Alliance
National Women's Health Network
Richard N. Gottfried, Chair, Committee on Health, New York State Assembly
Social Security Works
The Annie Appleseed Project
The Society for Patient Centered Orthopedics
Treatment Action Group
Washington Advocates for Patient Safety



1600 20th Street, NW • Washington, D.C. 20009 • 202/588-1000 • www.citizen.org

March 6, 2017

Dear Members of the United States Senate and House of Representatives:

Public Citizen, a consumer advocacy organization with more than 400,000 members and supporters nationwide, respectfully urges you to oppose S. 204, H.R. 878 and H.R. 1020, bills with various names that would most appropriately each be titled the “False Hope Act of 2017.”

These bills provide false hope to patients and are related to a nationwide lobbying effort funded by the Goldwater Institute, which has deceptively branded such laws as “Right to Try” legislation.

We recognize the desire of patients with terminal illness who have exhausted available treatment options to access experimental medical products that have not been approved or cleared by the Food and Drug Administration (FDA). However, the best way for patients to gain such access is through the FDA’s Expanded Access Program, which allows seriously ill patients to receive treatment with experimental drugs, biological products or medical devices while also providing basic safeguards to protect patients’ rights and welfare and maintaining strong incentives for careful clinical testing and timely product development.

We are concerned that false hope legislation like S. 204, H.R. 878 and H.R. 1020 would put countless patients at risk by dramatically undermining the FDA’s role in ensuring that medical products are safe and effective before they become widely used. Such legislation would expose vulnerable patients to risks of serious harm, including dying earlier and more painfully than they otherwise would have, without appropriate safeguards. It also would undermine incentives for companies to swiftly develop life-saving products for FDA approval and impair review of these products by limiting the agency’s access to unfavorable information.

FDA’s Current Expanded Access Program

The FDA’s Expanded Access Program allows patients across the country to gain access to experimental drugs, biological products and medical devices, provided that each patient’s doctor believes such access is appropriate and the manufacturer of the product agrees to provide it for that use. The program protects patients by requiring informed consent, ethical review by an institutional review board, safety monitoring and the reporting of adverse events to the FDA. It also prevents manufacturers from profiting from the use of experimental products, which helps to maintain incentives to continue rigorous clinical testing aimed at FDA approval.

The FDA grants 99 percent of all Expanded Access Program requests and, in urgent circumstances, can respond to such requests within 1 or 2 days. The agency also recently streamlined the program to require less paperwork. In addition, the 21st Century Cures Act of 2016 included useful provisions that require drug manufacturers to publicly post their expanded access policies and provide points of contact for requests. The potential impact of these streamlining efforts has yet to be fully realized.

It is also important to recognize that many of the experimental products made available through this program ultimately are not shown to be safe and effective in clinical testing and are not approved or cleared by the FDA. Despite patients’ hopes, there is no evidence that the current Expanded Access Program helps more patients than it harms.

Public Citizen

March 6, 2017, Letter to Congress Regarding
S. 204, H.R. 878, and H.R. 1020**Broadly Attacking Patient Protections While Offering False Hope**

Rather than proposing further improvements to the existing program, the false hope legislation now before Congress would undermine the FDA's fundamental authority to oversee the use of experimental medical products and to ensure they are safe and effective before they become widely used.

The legislation would put vulnerable patients at risk by:

- Offering manufacturers broad rights to sell experimental medical products after only very preliminary clinical testing, when very little is known about a product's potential risks, let alone its benefits.
- Eliminating important federal safeguards intended to protect the rights and welfare of patients exposed to such products, including appropriate, fully informed consent; ethical review by an IRB; and safety monitoring.
- Allowing manufacturers to charge high prices for experimental medical products, which forces patients to take financial risks for unproven benefits.
- Stripping away legal protections for patients by immunizing manufacturers, doctors and others against liability, even if they failed to exercise reasonable care or inform vulnerable patients about potential risks and benefits of the experimental products.
- Preventing the FDA from enforcing good manufacturing practices or intervening to stop the sale of tainted or otherwise substandard experimental medical products.

The legislation also would slow the development and impair FDA review of new medical products by:

- Reducing incentives to continue rigorous clinical testing in pursuit of FDA approval.
- Discouraging patients from enrolling in placebo-controlled clinical trials by providing them with access to experimental medical products in the general marketplace.
- Prohibiting the agency from considering (S. 204 and H.R. 878) or requesting (H.R. 1020) information about side effects, injuries or deaths in patients treated with experimental medical products under the legislation.

Congress should stop these attacks on the FDA's authority to regulate experimental medical products, an effort that will only encourage false hope for patients while ultimately doing them more harm than good.

We urge you to oppose S. 204, H.R. 878 and H.R. 1020 and any similar false hope legislation that is introduced in the future. Thank you for considering our views on this important matter.

Sincerely,



Michael A. Carome, M.D.
Director
Public Citizen's Health Research Group



Sarah Sorscher, J.D., M.P.H.
Researcher
Public Citizen's Health Research Group

TAG

Treatment Action Group

October 3, 2017

The Honorable Michael C. Burgess, MD
Chairman, Health Subcommittee
Energy and Commerce Committee
United States House of Representatives
Washington, DC 20515

The Honorable Gene Green
Ranking Member, Health Subcommittee
Energy and Commerce Committee
United States House of Representatives
Washington, DC 20515

Dear Chairman Burgess and Ranking Member Green:

Treatment Action Group (TAG) appreciates the opportunity to submit these comments to the Health Subcommittee of the U.S. House of Representatives Energy and Commerce Committee, in association with its hearing, "Examining Patient Access to Investigational Drugs," and the deliberations of H.R. 1020, the Compassionate Freedom of Choice Act of 2017, and S. 204, the Right to Try Act of 2017. TAG is an independent, activist and community-based research and policy think tank fighting for better treatment, prevention, a vaccine, and a cure for HIV, tuberculosis (TB), and hepatitis C virus (HCV). For 25 years, TAG has strongly advocated for expedited access to drugs and biologics with the greatest potential to save human lives. However, we also remain committed to stringent regulatory practices designed to minimize risk, confirm efficacy, and to protect consumers from harmful commercialization practices.

In July 2017, TAG joined with National Center for Health Research in urging the Senate to reject S. 204.¹ We reiterate here that any legislation aiming to circumvent existing expanded access processes authorized and monitored by the Food and Drug Administration (FDA) to help and protect patients with serious or life-threatening illnesses is unnecessary and dangerous.

In the early 1990s, due in large part to the influence of HIV/AIDS activism, the FDA formalized compassionate use and expanded access programs to provide patients with serious or life-threatening diseases with access to experimental drugs that have demonstrated reasonable safety and potential efficacy in phase II clinical trials, and are undergoing further investigation in phase III trials. These programs have been a lifeline for U.S. residents living with HIV, particularly those with virus resistant to approved antiretrovirals (ARVs), those unable to tolerate approved ARV options, and those unable to access phase III

¹ National Center for Health Research. Patient, consumer, and public health coalition letter to senators opposing the "Right to Try" law. July 31, 2017. Available from: <http://www.center4research.org/coalition-letter-senators-opposing-right-try-law/>

trials due to enrollment, distance, or entry criteria restrictions. They have also been vital for people affected by other life-threatening conditions, such as forms of TB and cancer that approved treatment options cannot cure.

There is empirical evidence that existing expanded access programs are sufficient for patients with serious or life-threatening illnesses. A 2016 analysis conducted by the FDA Center for Drug Evaluation and Research (CDER) found that more than 1,000 expanded access applications are received by the agency each year, the vast majority of which (99.7%) are allowed to proceed.² A follow-up analysis confirmed the high number of expanded access applications approved by CDER, while also underscoring FDA commitments to patient protections.³ Between January 2005 and December 2014, 99.3% of almost 9,000 expanded access applications were approved, with only 38 emergency treatment investigational new drugs (INDs) denied and 23 non-emergency treatment INDs not allowed to proceed. The most common reasons for denying emergency INDs was that the patient was stable on current therapy and that it was not deemed an emergency. The most common reasons for not allowing non-emergency expanded access INDs to proceed were incomplete application, unsafe dosing, demonstrated lack of efficacy for intended use, availability of adequate alternative therapies, and inadequate information provided in the application on which to base a decision.

TAG strongly supports the needs of people living with HIV, TB, and HCV to access promising drugs and biologics as quickly as possible and remains committed to the continuity of ethical and scientifically sound mechanisms in place to ensure patients with limited or no treatment options have access to the most promising investigational agents. Right-to-Try legislation in no way improves on these mechanisms and only stands to compromise patient safety and, additionally, create a lax legal and regulatory environment for the pharmaceutical industry. We urge the Health Subcommittee of the Energy and Commerce Committee to consider the following:

- **H.R. 1020 and S. 204, effectively undermine the current requirement that pharmaceutical companies develop, implement, and complete the registrational trials necessary to confirm safety and efficacy in patients with serious and life-threatening illnesses.** Not only are these data necessary to support FDA approval indications, they are essential to clinicians and patients in making informed treatment decisions. Legislation that allows manufacturers to circumvent stringent regulatory approval requirements to instead focus on commercializing its products to desperate patients—particularly with statutory language freeing manufacturers of any liability⁴—

² Jarow JP, Lemery S, Bugin K, Khozin S, Moscicki R. Expanded access of investigational drugs: the experience of the Center of Drug Evaluation and Research Over a 10-year period. *Ther Innov Regul Sci*. 2016 Nov; 50(6):705-9. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5135086/>

³ Jarow JP, Lemery S, Bugin S, Lowy N. Ten-year experience for the Center for Drug Evaluation and Research, Part 2: FDA's role in ensuring patient safety. *Ther Innov Regul Sci*. 2017 Mar; 51(2):246-9. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5443559/>

⁴ H.R. 1020, Sec. 561B

is a step in the wrong direction.

- **No risk analysis or evidence of potential efficacy is required in H.R. 1020 or S. 204.** In fact, the proposed legislation stipulates the removal of the FDA from any safety and efficacy determinations and, no less worrisome, would prevent the agency from collecting data from clinicians treating patients with an investigational agent that can be used in safety and efficacy determinations if/when the agent is submitted for approval.⁵ Existing expanded access programs not only allow for access to experimental agents, they contribute to the data sets that inform approval, labeling, and best practices—which protect patients, their providers, and companies alike.

TAG believes it is reasonable and necessary to allow the FDA to retain its regulatory oversight for expanded access and compassionate use programs in order to help mitigate safety concerns, ensure preliminary efficacy to guide risk-benefit determinations, and buttress the need for clinical trial data to inform registrational approval and prescribing practices. Especially since the agency approved more than 99% of expanded access requests, FDA's role in reviewing preapproval access requests is clearly not an impediment, and provides important oversight. H.R. 1020 and S. 204 do nothing for people who are terminally ill. It instead aims to curtail vital FDA stringency requirements that have not only largely succeeded in protecting public health, but continue to be effectively streamlined to hasten access to investigational and approvable drugs and biologics for those who need them most.

Respectfully submitted,

Tim Horn
Deputy Executive Director, HIV & HCV Programs

Erica Lessem
TB/HIV Project Director

⁵ H.R. 1020, Sec. 561A

The Honorable Michael C. Burgess, MD
Chairman, Health Subcommittee
Energy and Commerce Committee
United States House of Representatives
Washington, DC 20515

The Honorable Gene Green
Ranking Member, Health Subcommittee
Energy and Commerce Committee
United States House of Representatives
Washington, DC 20515

2 October 2017

Re: Examining Patient Access to Investigational Drugs

Dear Chairman Burgess and Ranking Member Greene,

As an American citizen and the sister of a patient who suffered from a nearly incurable form of extensively drug-resistant tuberculosis (XDR-TB), I write you in advance of the hearing "Examining Patient Access to Investigational Drugs" on October 3, 2017 to thank you for your interest in promoting the health and well-being of the American public, and to urge you **not** to pass H.R. 1020.

My brother was diagnosed with a severe case of terminal and infectious XDR-TB in 2013. Even less severe cases of TB require multi-drug therapy, and my brother was nearly out of options. His brilliant doctor, Dr. Caitlin Reed of Los Angeles, cobbled together a regimen for him, but needed access to a new drug in phase IIb development called delamanid. Unfortunately, Otsuka, the company that manufactures delamanid, would not grant access to delamanid to my brother, because it had not yet been studied with another drug in his regimen called bedaquiline. Dr. Reed and I and several clinicians and activists pressured the company for a year for access, to no avail (finally, Otsuka changed their policy about co-administration with bedaquiline, but not in time to help my brother). As a result, my brother was stuck on an inferior regimen that, while he managed to survive, caused him to develop psychosis, left him with painful permanent nerve damage, and required him to have a lobectomy to remove some of the disease in absence of enough powerful drugs, so he has permanent limited lung capacity. Meaning he cannot travel himself to be at your event tomorrow. He is actually in the hospital right now for related lung issues.

Our story painfully illustrates frustrations with pre-approval access to novel drugs. However, none of the barriers to access were caused by the U.S. Food and Drug Administration's regulations. Rather, the issue was a company's unwillingness to provide drug. They did not cite any concern about the cost of doing so. And it is well-established that the overwhelming majority of—in fact, nearly all—expanded access applications are approved by the FDA, and that data from such pre-approval use has very rarely resulted in a product not receiving approval. H.R. 1020 gives drug developers full permission to charge for access to a drug, even one that has only been in one clinical trial of unspecified size. But it does not compel them to provide access, even for desperate cases like my brother, which is what we would have needed. We need a more, not less, empowered FDA to be involved in cases of pre-approval access.

Not only would H.R. 1020 not have helped my brother's case, it could have made it worse. H.R. 1020 allows companies to charge for drugs pre-approval. So if H.R. 1020 had been enacted when my brother needed treatment, if Otsuka had decided to grant access, they could have charged the nearly \$25,000-32,000 that delamanid costs on the European market, where it is approved. We would have not had the recourse to pay for it.

The so-called "Compassionate Freedom of Choice Act of 2017" will provide neither freedom nor compassion to the thousands of Americans suffering difficult choices like my brother, our family, and Dr. Reed faced.

I urge you to please, not pass this bill, and to instead to uphold the existing expanded access policies and work to ensure an efficient, empowered, and fully funded FDA that can balance access needs with ensuring sufficient safety and efficacy of new products before they reach the market.

I appreciate your willingness to hear my concerns, and look forward to your assurance that this unhelpful and potentially dangerous legislation not be passed.

Thank you in advance,
Stephanie Aleksanyan

'Examining Patient Access to Investigational Drugs'
House Energy & Commerce Committee
Subcommittee on Health

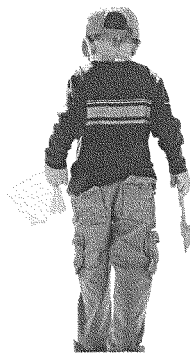
Andrew McFadyen | The Isaac Foundation

October 3, 2017



[October 3, 2017] The Isaac Foundation

Dear Chairman Burgess, Ranking Member Green, and members of the House Energy & Commerce Committee's Subcommittee on Health:



The Isaac Foundation is an organization based in Canada dedicated to finding a cure for a rare and devastating disease called Mucopolysaccharidosis, or MPS. Our work pushes international boundaries, with the bulk of our advocacy and patient support taking place in Canada and the United States. This is an organization that is very dear to me, because it is named after my son – my hero, and the bravest person I know – Isaac McFadyen, who suffers from MPS Type VI.

When Isaac was diagnosed at the age of 18 months, we were told that he was going to live a life of pain and suffering, and that we would endure many years of heartache and heartbreak. Essentially, every bone, muscle, organ, and tissue in his body would be ravaged by this disease until he eventually succumbed to the condition, probably in his early to late teens.

During the past decade he's battled - we've battled - to stave off the inevitable. And we've been lucky. In 2006, after a lot of work and determination, we were able to bring a new life-prolonging treatment to Canada - an enzyme replacement therapy that was approved by the FDA but not by Health Canada - to fight his disease. Isaac is now 13 years old, and the 13 that we see today is very different than the 13 we were told to prepare for.

After our success bringing Isaac's treatment to Canada, other families began contacting our organization so that we could help them obtain access to rare disease medications, and provide advocacy and support throughout their journey. Our successes brought many more families our way - families battling other forms of MPS, as well as other diseases - from Duchenne Muscular Dystrophy, to Batten Disease, to Gaucher Disease, to rare pediatric cancers. Our mission to find a cure for our son became a multi-faceted one that crossed both borders and disease families. It became a mission to help those suffering from any rare disease and in need, and we've dedicated ourselves to that mission ever since.

Today, I'm proud to say that we've never been unsuccessful gaining access to rare disease treatments for children in Canada, and our work alongside pharmaceutical companies is helping patients see similar results for countless children in the United States. We've achieved this success in part because I understand the world that our families are living in, and I understand the unbearable burden that a potentially terminal diagnosis brings. I understand because I live each and every day facing the mortality of my son. I understand because after 10 years, I still wake up every night and check to be sure that my son is still breathing, crippled by the fear that one day I'll walk in and he won't be. I understand because I've walked this lonely road, searching for hope when all hope seemed lost.

From our experience in the patient advocacy community, we understand the unbearable burden of a potentially terminal diagnosis and can see the appeal of Right to Try legislation for those with nowhere else to turn. The Goldwater Institute does a marvelous job of promoting its policy as the last chance for people to extend their lives. Goldwater claims that "Right To Try laws help patients get

immediate access to the medical treatments they need before it's too late," suggesting their legislation "restores life-saving hope back to those who've lost it."

This utopian vision of access to medications for millions of Americans who desperately need them is laudable. However, an analysis of the state Right to Try bills that have already been passed reveals that many laws leave many patients in danger of losing access to home health care, hospice care or even insurance coverage should they try an experimental product. Beyond this often-overlooked aspect of the laws, the cruel reality of Right to Try is that it does not grant patients immediate access to any treatments. Right to Try traffics in false hope, and as the advocates for desperate patients, we believe they deserve better.

Although Right to Try laws have been passed in 37 states, there is no concrete evidence of a single patient ever receiving a life-saving medication under Right to Try that they otherwise wouldn't have through the existing FDA expanded access program. Over 300 million Americans currently live in states with Right to Try laws. Why then, with nearly 80 percent of Americans having, as Goldwater claims, "immediate access to medical treatments they need," do we still have no evidence to suggest these state laws actually do what their defenders purport the laws do? The answer is simple: they aren't. If they were, people like [Jack Fowler](#), a 7-year-old with a rare metabolic disease called Hunter syndrome, would be receiving the life-saving medication he needs. Jack lives in Illinois, which has a Right to Try law, but despite the agreement of his physician, a hospital review board, and the FDA that he needs a certain drug, he is unable to begin treatment. Shire Pharmaceuticals, the company that makes the drug he needs, refuses to give him access.

Indeed, legislation does not guarantee access to investigational therapies for those in need - it never has. Right to Try legislation provides nothing to patients except the "right not to be barred from seeking access to experimental products."¹ Legislation has, however, created a misguided belief among vulnerable patients that the help they have been searching for has arrived. Right to Try is a misnomer, implying an entitlement to patients: "If a person asks, someone or some entity has a duty to provide."²

A more apt title would be "Right to Ask," because this is the only entitlement Right to Try legislation provides patients. This right to ask has been formally codified since 1987 through the FDA's Expanded Access Program. In both the FDA program and under proposed Right to Try legislation, pharmaceutical companies are under no obligation to make their investigational drugs available to patients.³ Thus, investigating what disincentives prevent companies from making their drugs available – and what incentives could be put in place to positively influence these decisions – would be a more fruitful approach than legislating a theoretical "Right to Try."

¹ Bateman-House, Alison et al. "Right-to-Try Laws: Hope, Hype, and Unintended Consequences." *Annals of internal medicine* 163.10 (2015): 796-797.

² Bateman-House, Alison et al. "Right-to-Try Laws: Hope, Hype, and Unintended Consequences." *Annals of internal medicine* 163.10 (2015): 796-797.

³ Rubin, Rita. "Experts critical of America's right-to-try drug laws." *The Lancet* 386.10001 (2015): 1325-1326.

We should be promoting enhancements to the FDA's existing Expanded Access Program, which shows promise for its high approval rates, transparent data collection, and focus on patient safety.

As patient advocates, we know that Right to Try laws can't and won't help our loved ones, some of whom are fighting for their lives. What supporters tout as a beacon of hope does nothing to change the reality for patients in need – and risks making Americans' access to healthcare even more unequal. And not only does Right to Try not work, it actually strips vulnerable patients of valuable assistance.

We urge members of the House of Representatives to vote against any form of Right to Try legislation and instead focus on measures that will provide assistance, not empty words, to everyone with serious need.

Sincerely,

Andrew McFadyen
Executive Director
The Isaac Foundation



560 Sylvan Avenue, Suite 1225
 Englewood Cliffs, New Jersey 07632
 Phone (201) 569 5595 | Fax (201) 569 5597
 www.MaxCure.org

September 29, 2017

Members of the House Subcommittee on Health of
 the Energy and Commerce Committee
 C/O The Honorable Greg Walden, Chairman
 2125 Rayburn House Office Building
 U.S. House Committee on Energy and Commerce
 Washington, DC 20515

Dear Chairman Walden and Members of the Health Subcommittee of the Energy and Commerce
 Committee,

I am Vice Chairman and Co-Founder of Max Cure Foundation, Inc., a pediatric cancer foundation formed in 2008 in honor of my grandson Max who was diagnosed with cancer and is now a 10 year pediatric cancer survivor. I retired from the practice of law in 2008 to devote my life to assisting children diagnosed with cancer and their families. Given my background as a trial lawyer, I have been actively involved in advocating before Congress and to the public as to the needs of children with cancer. I am personally credited with leading the effort to obtain the experimental drug for 7 year old Josh Hardy that cured the Adenovirus that threatened his life back in March 2014. The Biotech firm, Chimerix, that provided the drug (Brincidofovir) had rejected over 300 prior requests for the drug. The former CEO of Chimerix (Ken Moch) was fired as a result of providing the drug to young Josh and others as part of a hastily formed clinical trial. He told me he is often asked what distinguished the Josh Hardy request for the experimental drug from the over 300 requests that were declined. He told me he answers in two words, "Richard Plotkin." The worldwide attention given to the Josh Hardy matter was a significant factor in causing Congress to address the issue of expanded access under 21st Century Cures Act.

Despite the Virginia Right to Try law not having anything to do with the Josh Hardy matter, the Goldwater Institute, the main proponent H.R. 2368, implies Josh was given the drug under that state law. This is just one of the many falsehoods promulgated by The Goldwater Institute in its effort to "pull the wool over the eyes of Congress" in order to get the Federal Right to Try law passed.

For the Committee's consideration, I wish to highlight the following:

1. In a recent study of 150 requests, selected randomly, made to the FDA to approve the use of experimental drugs in seriously ill and terminally ill patients, the FDA made suggested changes in 11% of those applications, demonstrating that it does not "rubber stamp" the



560 Sylvan Avenue, Suite 1225
 Englewood Cliffs, New Jersey 07632
 Phone (201) 569 5595 | Fax (201) 569 5597
 www.MaxCure.org

applications (one could conclude that given that the FDA approves over 99% of the applications submitted). That test, among many other examples, demonstrates that the FDA serves a very important function as the “gatekeeper” and “safety net” for those who are terminally ill and seek experimental drugs.¹ Extrapolating the 11% figure to the 1,562 applications to the FDA in 2015 for compassionate use waivers with respect to experimental drugs results in 172 of those terminally ill and seriously ill patients receiving a safer product due to the involvement of the FDA.

2. Following my involvement with the Josh Hardy matter in March 2014, I attended a meeting later that year in DC among pediatric cancer advocates. The issue of giving experimental drugs to dying children was raised. I stated, “What difference does it make, these children are going to die.” An oncologist at the meeting responded, “You would not be taking that position if you had seen as I have children being given experimental drugs who were ‘tortured’ leading to their deaths.” I have over the last 4 years educated myself to the point that I recognize the importance of the FDA in the approval process for giving experimental drugs to terminally ill patients;
3. As a trial lawyer, I have concluded that H.R. 2368 (successor to H.R. 878) exposes many unsuspecting entities and persons to lawsuits who would be involved in giving experimental drugs to terminally ill patients. I had written an article in *The Hill.com*² that covered that issue with respect to an earlier draft of the legislation. H.R. 2368 continues to leave unsuspecting individuals and entities, including hospitals, IRB’s, and others exposed to lawsuits based on a claim of negligence. There is clearly an issue as to who is included, and who excluded, under H.R. 2368, Section 2 (c) (1), where it states, “No liability shall lie against a producer, manufacturer, distributor, prescriber, dispenser, possessor, or user of an experimental drug” As a former trial lawyer, I would, as noted, be concerned that many folks/entities would be subject to a claim of negligence. Also, without the involvement of the FDA, I question whether any manufacturer of experimental drugs or devices, plus others, including doctors, hospitals, IRB’s, could obtain liability insurance. Absent product liability insurance or insurance for malpractice or other negligent acts, I suggest without the FDA’s involvement, there will not be any patients who would receive the experimental product – except perhaps if prescribed by less than reputable physicians working in concert with equally disreputable companies. In any event, those subject to lawsuits would not have as a defense that the

¹ Jarow, Jonathan P., et al. “Ten-Year Experience for the Center for Drug Evaluation and Research, Part

2: FDA’s Role in Ensuring Patient Safety.” *Therapeutic Innovation and Regulatory Science* (2016) 1-4

² Plotkin, Richard. “‘Right to Try’ is a Sham.” *The Hill*, February 13, 2017. Accessed September 12, 2017

250 Ashland Pl., 37E
Brooklyn, NY 11217

October 3, 2017

The Honorable Michael Burgess
Chairman of the House Energy & Commerce Committee subcommittee on Health
2336 Rayburn House Office Building
Washington, DC 20515

The Honorable Gene Green
Ranking Member of the House Energy & Commerce Committee subcommittee on Health
2470 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Burgess and Ranking Member Green:

I am the institutional review board and bioethics director at Lehman College.

My job is to evaluate proposed experiments and determine whether they are ethically compatible with the Belmont Report and applicable United States Code provisions. My position was born of the federal recognition that experimental drugs and procedures need to be held to stringent ethical safeguards - abuses such as Dr. Mengele's torture chambers in Auschwitz proved the need to supervise and build ethical boundaries around scientific research.

Right to try essentially bypasses these safety and ethics measures in two ways.

First, and contrary to the Belmont Report, it spreads benefits of biomedical research unevenly among members of society. Persons with means can gain access to research participation and potential health benefits while indigent individuals are left out of the loop. This exacerbates already extreme levels of social and economic inequality.

Second, right to try marries the understandable human desire - often a desperate desire - to get well, with the often corrupting influence of wealth. Implementing right to try procedures runs the risk of human nature taking its ugly course as common swindle the desperate and affluent. Perhaps, if Bernard Madoff went to medical school, he may have become a right to try advocate.

Finally, right to try provides no guarantee that a terminally ill patient will get well. It is cruel to tell people that they can try unapproved medical treatments without mentioning that these treatments may be out of their reach anyway due to cost barriers. In a sense, right to try is like giving me the right to drive a Maserati without mentioning that my chances of being in a position where I will get to drive a Maserati are slim indeed.

I'm not unsympathetic to the ill and their loved ones. I had a serious brain injury in infancy and almost died. I remain learning and physically disabled. Were I offered a pill or procedure to cure

these disabilities, I would perhaps do almost anything to obtain them, but predators who lurk in every office building in the land would no doubt salivate over this possibility.

Sincerely,

A solid black rectangular box redacting the signature of Zoltan Boka.

Zoltan Boka
IRB & Bioethics Director
Lehman College
Bronx, New York

Mr. BURGESS. Thank you for testimony.

Dr. Sigal, you're recognized for 5 minutes for a statement, please.

STATEMENT OF ELLEN V. SIGAL

Dr. SIGAL. Chairman Burgess, Ranking Member Green, I am honored to be here today, and members of the committee.

I am Ellen Sigal, chair of Friends of Cancer Research, a group—a nonprofit that is committed to innovation, accelerating better treatments for patients that are safe and effective.

I founded Friends over 20 years ago, driven by the profound loss of my dear sister, Gale. After many years battling cancer, Gale had exhausted every option.

As metastatic breast cancer raged through her body, defeating all conventional treatments she found, she faced a final decision—succumb to the disease or wage one last battle with an experimental bone marrow transplant known to kill 20 percent of patients.

Gale chose to fight. In Gale's case, the side effects of the treatment were swift and violent. Within two days, at the age of 40 she was dead, leaving her 4-year-old daughter and husband behind.

All of us here today agree on the basic premise—more must be done to save patients' lives. We must continue to ensure our regulatory system is expediting therapies as safely and quickly as possible.

Friends of Cancer Research took huge steps towards this beginning 5 years ago, when we worked with many on this committee to create the breakthrough therapies designation. It has been incredibly successful.

This is progress, but I will acknowledge much more needs to be done. In addition, a predominant reason why patients seek expanded access to experimental therapies in the first place is that they are unable to attain them by enrolling in clinical trials.

By expanding eligibility criteria and taking down barriers that oftentimes disqualify a patient from participating in a trial to begin with, we can make additional progress.

Legislation before Congress seeks to grant all terminally ill patients the right to try experimental therapies once approved alternatives have failed, even though the FDA authorizes 99 percent of compassionate use requests.

Serious changes to today's legislative proposal are needed before this law is safe for patients. First, provisions for informed consent are essential.

A significant majority of early-phase drugs are dangerous and ultimately prove ineffective with upwards of 90 percent never being brought to the market.

Any legislation that goes forward cannot circumvent the FDA and must be carefully crafted to assure that we do not create a loophole for those seeking to profit off the sick by offering false hope. This is reprehensible.

Second, the limits of Right to Try must be clear. Even if patients receive the right to request an experimental therapy, the drug company developing the therapy is under no obligation to provide it.

Patients petitioning for expanded access deserve accurate information about whether the potential benefits outweigh the risks.

This is highly personal calculus. It's impossible if drug companies do not monitor and report side effects.

A key component is transparency. Patients have long been frustrated that they could not find information about expanded access on sponsor Web site and didn't know how to make a request for the sponsor.

The Reagan-Udall Foundation, which I am honored to chair, recently launched an expanded access Navigator for compassionate use of experimental therapies.

The Navigator is currently being piloted in oncology with the goal of increasing accessibility to information for patients and providers.

We have already—we already have three dozen companies that contribute their information and had 10,000 visitors to the site. In the very near future, this program will expand to include rare diseases.

While I fully believe that dying patients should have access to promising treatments, we must not subject patients to false hope or unacceptable side effects. With significant adjustments, Federal Right to Try legislation could help very sick patients.

One of these adjustments is that patients must have more and immediate access to information about significant adverse events or death of patients that have previously been given the therapy.

Another adjustment would be the establishment of the designated central Institutional Review Board with the predominant focus of coordinating and dealing with expanded access requests.

The current legislative proposals would likely do more harm than good. I encourage the committee to consider other policy options that would truly improve the ability for patients to safely access unapproved therapies.

Thank you very much.

[The prepared statement of Dr. Sigal follows:]



**Testimony of Dr. Ellen V. Sigal
Chair & Founder
Friends of Cancer Research
Washington, DC**

**Before the U.S. House of Representatives
Committee on Energy and Commerce**

October 3, 2017

Chairman Walden, Ranking Member Pallone and members of this distinguished committee- I am honored to be testifying before you today on this vital topic. I am Ellen Sigal, Chair and Founder of Friends of Cancer Research, a nonprofit advocacy organization ensuring patients receive the best treatments in the fastest and safest way possible.

I founded *Friends* over 20 years ago, driven by the profound loss of my dear sister Gale who was only 40 with a 4 year-old-daughter.

After many years battling cancer Gale had exhausted every option. As metastatic breast cancer raged through her body, defeating all conventional treatments, she faced a final decision: succumb to the disease or wage one last battle with an experimental bone marrow transplant known to kill 20 percent of patients.

Gale chose to fight, opting to use the unproven therapy at a time when institutional review boards and scientific peer review regulated this experimental therapy rather than the Food and Drug Administration (FDA).

Now, three decades later, the FDA has an expanded access policy, also known as "compassionate use," that seeks to ensure the quality of unproven therapies used by dying patients. In Gale's case, the side effects of the treatment were swift and violent. Within two days, she was dead. Clinical trials have since demonstrated that the therapy had limited efficacy and a greater risk of lethality than reported at the time.

All of us here today agree on the basic premise that more must be done to save patients lives. We must take steps to allow patients to gain access to clinical trials and to continue to ensure our regulatory system is expediting therapies as safely and quickly as possible. My organization, took huge steps toward this 5 years ago when we worked with many members of this committee to create the breakthrough therapy designation. Breakthrough that has truly changed the way the FDA approves and industry develops life-saving therapies for patients that so desperately need them. Because of this designation there have already been over 60 new drugs approved for serious and life-threatening diseases. This is progress, but I will acknowledge, much more needs to be done.

It is imperative to examine a predominant reason why patients are interested in expanded access to experimental therapies; they are unable to obtain them by enrolling in clinical trials. We at Friends of Cancer Research, working with the American Society of Clinical Oncology (ASCO), have taken steps to address this problem through the work we have done on issues surrounding expanding eligibility criteria – taking down barriers that often times disqualify a patient from participating in a trial to begin with.

While these do not, by any means, solve all of the issues we are discussing here today, it is important to acknowledge the work being done by so many. Still I acknowledge that challenges remain.

The legislation before Congress seeks to grant all terminally ill patients the "Right to Try" experimental therapies once approved alternatives have failed. Although the FDA authorizes 99 percent of compassionate use requests, advocates of Right to Try claim

the process is too slow. The FDA has streamlined the current process so that requests are reviewed within 24 hours; filling out an application now takes less than an hour. Unfortunately, the proposed federal legislation provides almost no protections for patients. Everyone with a late-stage terminal illness like my sister deserves the chance to try an experimental therapy. However, serious changes to today's legislative proposal are needed before this law is safe for patients.

First, provisions for informed consent are essential. Upwards of 90 percent of new drugs never make it to market because they are found to be dangerous or ultimately proven ineffective. Right-to-Try laws allow patients to request from companies therapies that have passed a Phase I trial with the FDA. But this is only a preliminary step in which a small group of patients receive the experimental therapy under carefully controlled conditions. The trial is designed to detail obvious toxicities and identify a tolerable range of potentially effective doses before the drug advances to a larger, Phase II trial.

Before the results of that second phase of study, there is no reliable data on whether the therapy works and, even after clearing a Phase I trial, toxicities can be discovered in later phases.

Any legislation that goes forward cannot circumvent the FDA and must be carefully crafted to assure that we don't create a loophole for charlatans and snake oil salesman to take advantage of desperate patients. Profiting off of the sick by offering false hope is reprehensible, but there is a long history of such occurrences to this very day. Without proper protections we risk a market outside of the FDA approval system.

Meanwhile, patients like Gale who receive the therapy may risk a sudden and painful death from unanticipated side effects, as early-phase trials rarely evaluate the risks of extended or repeated administration. Key information about the safety or efficacy of experimental therapies is typically not made public until after drug approval. Provisions insuring informed consent would guarantee that patients requesting expanded access can judge the magnitude of their decision.

Second, the limits of Right to Try must be clear.

Today patients have the right to request an experimental therapy from a sponsor, but the sponsor is under no obligation to provide it. Under the proposed legislation there is no new "right". A patient still has the right to ask, but a sponsor still has the right to say no. While the term "Right to Try" sounds appealing, this legislation grants no such right.

There are legitimate reasons for a sponsor to say no, including supply shortages, a lack of financial incentives, and concerns that negative "compassionate use" outcomes could be used by the FDA to delay or deny approval (which is protected against by the Right-to-Try legislation). Development roadblocks would stop therapies from reaching patients.

However, the FDA cannot simply ignore expanded access outcomes. Patients petitioning for expanded access deserve accurate information about whether the potential benefits of an experimental treatment outweigh the risks. What are the side effects? What are the chances of success? This highly personal calculus is impossible if drug companies do not monitor and report side effects.

A key component of effective Right to Try legislation is transparency. The Reagan-Udall Foundation for the FDA (RUF), which I am honored to chair, is a nonprofit created by Congress to modernize regulatory science, promote public health and help the US Food and Drug Administration achieve its mission. This year, RUF launched an Expanded Access Navigator to raise awareness among doctors, patients and families when it comes to the compassionate use of experimental therapies. The Navigator is currently being piloted in oncology with the goal of increasing the accessibility of information to patients and providers.

Patients have long been frustrated that they could not find information about expanded access on sponsor websites and didn't know how to make a request of the sponsor. The Navigator is the most comprehensive tool available for patients and physicians to research single-patient expanded access in part because companies list their EA policies, contact information and available therapies in one, consolidated Directory. The 21st Century Cures Act required greater transparency on the part of sponsors, and we have already had 3 dozen companies contribute their information and had 10,000 visitors to this site. In the very near future RUF will expand this program to include rare diseases.

Everyone agrees that dying patients should have access to promising experimental therapies when all available options have been exhausted. Right to Try is a path to achieving that goal; in pursuing it, however, we must not subject patients to false hope or unacceptable side effects. Informed consent and transparency—currently lacking from the proposed legislation—are essential.

With significant adjustments, federal Right-to-Try legislation could help very sick patients easily obtain necessary information to decide what is best for them and improve

processes to access otherwise unavailable drugs. One of these adjustments is that patients must have more immediate access to information about significant adverse events or death of patients that have previously been given the therapy they are seeking access to. This must be done in a much more efficient way. Another adjustment would be the establishment of a designated central institutional review board (IRB) with the predominant focus of coordinating and dealing with expanded access requests.

In its current form, however, Right-to-Try does nothing for patients other than allow them to request a drug they may never receive. This drug may be more likely to hurt them than to help them.

I want to reiterate how important it is to support patient access to unapproved therapies, however, S.204 and HR 878 do not accomplish policy changes that would afford patients greater access to promising investigational therapies. Instead these bills would likely do more harm than good.

I encourage the committee to consider other policy options that would truly improve the ability for patients to safely access unapproved therapies.

Thank You for the committee's efforts on this vital issue to patients.

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For further information or inquiries contact:

Ryan Hohman, JD

Vice President – Public Affairs

Friends of Cancer Research

202.944.6708

rhohman@focr.org

ABOUT FRIENDS OF CANCER RESEARCH:

Friends of Cancer Research drives collaboration among partners from every healthcare sector to power advances in science, policy, and regulation that speed life-saving treatments to patients.

During the past 20-plus years, Friends of Cancer Research (*Friends*) has been instrumental in the creation and implementation of policies ensuring patients receive the best treatments in the fastest and safest way possible. We've been successful due to our ability to convene the right people at the right time and put forth revolutionary, yet realistic ideas. We are energized now more than ever to continue this critical work with our trusted partners, creating innovative solutions to overcome barriers standing in the way of conquering cancer.

Mr. BURGESS. I want to thank each of you for your testimony. It's been a very powerful panel. We will begin the Member question portion by recognizing the gentleman from Kentucky for 5 minutes for his questions.

Mr. GUTHRIE. Thank you, Mr. Chairman.

Lieutenant Commander, thank you for your service.

LCDR BELLINA. Thank you.

Mr. GUTHRIE. We appreciate what you do and appreciate your service. I am one that's—we need to figure out how to handle expanded access.

I think, Dr. Sigal, you summed it up. We need to do it right, do it correct, and give people opportunities to make informed decisions within what we have to sort out and try to figure out so we don't do more harm than good.

I think, as you mentioned, so we need to do it right, and that's why I think this hearing has been important and your willingness to testify has really been helpful and we appreciate that.

One thing that—that when you start getting into this that some of the unknown, not just in the FDA or all the other issues is just other things and, one, I understand that hospice services are provided once you've exhausted all options, and then after you've exhausted all options you get hospice services for care and comfort until the end of life—kind of end-of-life care.

And my understanding is it could jeopardize hospice services if you go into an experimental treatment. And so the question I get to, I think—in Dr. Bateman-House's testimony, you said that 19 State patients receiving expanded access drugs lose their hospice coverage and six States say these patients may be denied coverage for home health assistance.

So my question—I think you talked about it too, Ms. Lopez Bauman—if both of you would talk about this, and two questions.

How would a Federal Right to Try Act impact access to hospice services, and the second, how do States who have passed this legislation balance access to hospice services with a right to try? Do you want to start first?

Ms. LOPEZ BAUMAN. Thank you for your question—and the Right to Try Act, Senate Bill 204, was amended prior to the Senate vote in order to address and accommodate a lot of these concerns and such as specifying how adverse event data can be used, requiring reporting to the FDA, capping allowable charges to direct costs only, and limiting manufacturer reliability.

I can tell you that that is—that in the insurance area, end-of-terminal and end-of-life and hospice benefits and those things, those are terms under the insurance—under the State insurance laws and regulations.

And so, even if you might technically not be eligible for hospice because you are continuing to seek treatment, it doesn't mean that that patient will not get that treatment.

I would also like to point out that these laws have undergone 4 years of addressing these kinds of stakeholder concerns and in the 37 States and counting where it is now law, and the message from across the country is really loud and clear that terminal patients shouldn't have to beg the Federal Government for permission to pursue these options.

And I would also like to point out something. We've heard a lot about opposition to Right to Try because of—based on false hopes.

But I would like to point out that we've heard a lot today about how the FDA is addressing the adverse event issue.

I very quickly took a look at the guidance that they issued today, and it's really important to point out—and I direct you to questions 25 and 26 in the guidance—where they are actually—they are changing basically the standard for reporting adverse events. But they are—they are not addressing how they are going to actually deal with those adverse events.

So after a GAO report, after years of patients talking to Congress and the FDA about the need for actually clarifying how the FDA will address adverse events, it's still not done, not even today, even though we've heard about it all morning.

Mr. GUTHRIE. OK. I only have just a little bit amount of time. So I want to give Dr. Bateman-House a chance to answer the question about access to hospice services.

Dr. BATEMAN-HOUSE. Right. So in addition to potentially losing access to hospice services under some of these State bills, you could lose, as you mentioned, access to home health care.

You also, under a few of the bills, could actually lose access to health insurance for six months post, you know, this treatment that you get through Right to Try.

Mr. GUTHRIE. Are States trying to address—then fix, as Dr. Lopez Bauman kind of—

Dr. BATEMAN-HOUSE. Well, so as—

Mr. GUTHRIE. Once that's been passed, they look at it and they say, oh, unintended consequence and we try to fix—

Dr. BATEMAN-HOUSE. I always say, unfortunately, we are working in a data-free environment. Despite our best efforts as a group, we have only found two doctors who admit to giving treatments to patients under Right to Try. They're both in the State of Texas. Texas does not have a reporting requirement.

We have no idea what happened with those individual patients. One of the States that does have a reporting requirement, Oregon, we contacted them to try to find out, you know, the experience of the patients, and did they lose access to anything, et cetera.

They had no record of anyone being treated under Right to Try. California also has a reporting requirement, but the law has only been in effect for about a year or so.

Mr. GUTHRIE. And we've got about 30 seconds. I know your opposition to the bills before us. But is there a protocol or, as Dr. Sigal kind of suggested—is it "Seegal" or "Segall"? "Seegal"?

Dr. SIGAL. "Seegal." Whichever.

Mr. GUTHRIE. "Seegal"—Dr. Sigal. I had a professor named Dr. "Segall," spelled the same way. That can be put in place so this could be—this could work? Or is this just something you don't think can work at all?

Dr. BATEMAN-HOUSE. Well, the thing that I don't think has been said today is that it's not supplanting the FDA. What it's doing is it's doing an alternative pathway.

So if you want to go through expanded access you still can. If you want to go through Right to Try, you can't—I mean, you can also do that if the Federal bill were to pass.

Honestly, as Ken Moch said, I have said all along I don't think any reputable company will give access to drugs this way. So I really think it's a moot issue.

Mr. GUTHRIE. Well, thank you. My time has expired so I yield back.

Mr. BURGESS. Chair thanks the gentleman. Gentleman yields back.

The Chair recognizes the gentleman from Texas, Mr. Green, 5 minutes for questions.

Mr. GREEN. Thank you, Mr. Chairman, and having served 20 years in the Texas legislature and had a number of issues when I was serving there, whether it be cancer treatment with peach pits—laetrile—DMSO, who had—and States have an ability to do that, whereas on the Federal level we have an FDA since 1906 and so it may be easier for States to say, well, you have the right to try.

And, basically, I agree with that. If I was terminally ill or needed—I would want that. But I also know we have this agency that has tried to protect us for over a hundred years, and to do it.

Dr. Sigal, I know that you've spent considerable time and effort on working with researchers and sponsors to help enroll patients in clinical trials.

I represent a district in Houston and we have some great clinical trials whether it be at MD Anderson, Methodist Hospital, any of ours. In fact, our chairman actually went to medical school in Houston.

But I am greatly concerned that the Right to Try legislation would confuse families and patients on what role the FDA plays and how they can access the FDA, and let me give you an example.

A couple of years ago when we had the Ebola scare, I was concerned that there was something on a lab table that would treat these patients, and I checked with them and I was told that they did that and the FDA gave 24 hours' notice that they could give that.

These patients were U.S. citizens. They were doctors. They were cognizant of what they were doing, and the sad part is we don't know whether that medication helped them or not because, you know, it wasn't a trial. It didn't have a comparison.

So but what would the impact on increasing access to investigational drugs through Right to Try legislation outside the clinical trials have on clinical trial enrollment, and do you believe it would endanger or delay clinical trial enrollment?

Dr. SIGAL. The answer is yes. The clinical trial system is not perfect but it is the gold standard and we do need to work on exclusionary criteria on it.

However, if patients think they can circumvent it and get this drug off a clinical trial through Right to Try, clearly, they are going to try to do it.

Unfortunately, there will be probably no company—reputable company that will allow their drug to be used that way. But I do think we can do a lot about clinical trials and we can do a lot more in informed consent.

But in fact the clinical trial system is the best we have. We need to have more patients enrolled in it. We know that. We need to

look carefully at exclusionary criteria, and also we are doing a lot about innovation.

FDA now is—we are working on lung cancer master protocols. There are single arm trials. There's seamless drug development. There's a lot going on in this field to expedite drug development so patients can have the benefit of these treatments earlier because that's what we want.

Mr. GREEN. OK. And another concern I have is that pediatrics—we also have the great hospital, Texas Children's, and those facilities all over the country, and just because, you know, children are different than adults and we need to have trials with children, and I know Congress over the years has encouraged that. Would that also impact pediatric clinical trials?

Dr. SIGAL. The answer is yes. We need more of them. We know we need more. Twenty-first Century Cures just have really important provisions to expedite that and to really handle with drug development on it.

But, again, the same issue—if people think that they can access a drug through Right to Try, they are going to circumvent the clinical trial process and then we won't know the data.

We won't know exactly what happened on it and, again, the ability for the patients to access these trials is—or this Right to Try is going to be highly limited and really very worrisome.

Mr. GREEN. OK. Thank you, Mr. Chairman. I yield back.

Mr. BURGESS. Chair thanks the gentleman. Gentleman yields back.

Chair recognizes the gentleman from Virginia, Mr. Griffith, 5 minutes for questions, please.

Mr. GRIFFITH. Thank you. Thank you very much. I have to say I don't think that patients who are dying are going to be confused, particularly if we say this has not yet been approved by the FDA. Would you agree with that, Ms. Lopez Bauman?

Ms. LOPEZ BAUMAN. Thank you for your question. Yes. The Right to Try Act, Senate Bill 204, actually works in tandem with the current updated process and that is why Right to Try is only available to patients who have exhausted approved treatments, who are unable to participate in the clinical trial, and why Right to Try only applies to medicines that are already being considered by the FDA and are continuing to be evaluated by the FDA, and I would like—

Mr. GRIFFITH. So by the time a patient has gotten to that point, they are fairly well educated on the issues, at least related to their condition and disease?

Ms. LOPEZ BAUMAN. I think that's true, but I think that the words of Dr. Razelle Kurzrock—who at one point ran one of the Nation's largest clinical trials, actually, at MD Anderson—explained that the process was so burdensome that they only submitted one application per year.

This was a clinical trial of more than 1,000 patients, and to quote Dr. Kurzrock, that there were so many barriers that even at one of the best places in the world and one of the largest apartments that this, as their day-in and day-out job, it was still very challenging.

Mr. GRIFFITH. And I appreciate that.

I also think that it's important that we do have informed consent. Both House bills have that, and so any language that you might want to provide to make that stronger for us I would greatly appreciate that, Dr. Sigal.

But I would appreciate any language that you could provide. Unfortunately, time is of the essence so I can't get that language right now later if you could provide us with some opportunities.

Lieutenant Commander, again, thank you for your service. You mentioned that you hoped that it would be different when your children were grown up. How old are your kids?

LCDR BELLINA. All right. I have a 6-year-old, a 4-year-old, and a 7-month-old at home—three boys.

Mr. GRIFFITH. Well, I know that's got to be a great joy for you.

LCDR BELLINA. It is, and I do want to also throw out there, and I hope everybody hears this: There's this notion floating around that expanded access isn't getting used because people don't know or can't figure it out.

I find that deeply offensive. I would say the ALS patients I know are bright, well-informed. A lot of them know more than the researchers and the doctors they work with, and the idea that they wouldn't apply because they can't figure it out, I don't even know what to say.

Mr. GRIFFITH. Yes, I appreciate that.

Back to you, Ms. Lopez Bauman. What legal protections do patients in the 37 States that have passed Right to Try laws have that patients in other States do not? And we are running out of time, so if you could keep it as quick as possible.

Ms. LOPEZ BAUMAN. So, really, what it comes down to is that in the States where Right to Try is now law, it's about allowing terminal patients more freedom to access the right treatment at the right time.

And it's not a guarantee but it is an assertion that patients have a right to medical autonomy and that bureaucratic and administrative barriers shouldn't be standing in the way.

And I'd like to point out that earlier this year, this very own legislative body implicitly endorsed the right to try for terminal patients to seek investigational treatments to save their own lives.

Remember little Charlie Gard, who was granted residency to seek an investigational treatment here in the United States. He was granted residency after the U.K. blocked his parents' right to seek an investigational treatment.

And so this has already been implicitly endorsed by your legislative body. We have the vehicle and it has been vetted and stakeholder concerns have been addressed. It's time to act.

Mr. GRIFFITH. I am going to open this up for anybody to send me a response afterwards. But I do want the lieutenant commander to respond to this.

In your article—I believe it's your article—in the Washington Post you indicated that in 2014 nearly 25,000 people in France were using investigative treatments through the French government's equivalent program, and yet we had less than 2,000—I think that was your reference earlier—to the food stamp program.

LCDR BELLINA. That is correct.

Mr. GRIFFITH. And what are the differences in the French program that allow them to get access to them, even though they have a much smaller population than we do, that we don't have?

LCDR BELLINA. Well, I think Dr. Gottlieb was 100 percent correct that it's a supply issue. It's not a demand issue, and I think their legislation allows for the demand—the market to drive this supply is what we see there and we don't have that here. I think this bill is a big step in addressing that.

Mr. GRIFFITH. I appreciate that.

My time is up, but if anybody else would like to give me a written response to that of what they see as either pros or cons with the French law versus the American law I would appreciate it.

And with that, Mr. Chairman, I yield back.

Mr. BURGESS. Chair thanks the gentleman. Gentleman yields back.

Dr. Sigal, let me ask you—and thank you for bringing the case of your sister to us. It was very powerful.

I was actually in practice in the 1990s, so I remember that controversy very well, not with your sister but with the high-dose chemotherapy and rescue with stem cell transfer for metastatic breast cancer.

And it was quite controversial, and there was a sense—perhaps relating to what Mr. Moch encountered—there was a sense that, hey, here's something that will work when nothing else will, but it's expensive and so therefore it's denied.

Can you tell us what has now happened with the therapy that your sister received? Is that still a viable clinical pathway for patients to follow?

Dr. SIGAL. Well, the answer is no. I mean, at the time she had metastatic disease. There were no options. But she did go into that knowing that there was a 20 percent fatality. This was the decision that she made and, of course, she died from it.

Later on when we did do clinical trials we realized that that therapy was not effective. But because patients refusing to go into clinical trials at the time it took us a much longer time.

I mean, today our system is swifter. We are, at the FDA, approving drugs in single arms, some with 10 and 15 patients. When we have the breakthrough mechanism and when we see really good evidence early, it's all hands on deck and they are getting to market earlier.

We are the fastest in the world. We published at *Friends* 5 years ago EMA versus FDA, because we were told that we were slower than Europe, and we were shocked.

We went back and did the study ourselves and were shocked that we were faster, and when we told the FDA they said nobody will believe you—you have to publish this in a peer review journal, and we did. And, in fact, the importance is not faster, but the issue is better and gold standard.

So we all understand the burden of disease and particularly for dying patients who have no risks. So the ability to get them on trials, to look at exclusionary criteria, and to look at treatments that work.

But most importantly, patients really need to have information—
informed consent. They may decide they want to take the risk.

But they can't make that decision with their doctor unless they have the data, and if they don't have the data in Phase 1, where it is really only safety and no efficacy, and if that's not available to them, what decision that's informed will be made by that patient and the physician? You need data, and then it is up to the patient if they want to participate.

Mr. BURGESS. Well, let me ask a question then, Ms. Lopez Bauman. The case that you reference—Diego, with the osteosarcoma who's now 17 and was diagnosed when he was age 10, and you said that medicine is still not available in the United States, is that correct?

Ms. LOPEZ BAUMAN. That's correct. If I recall correctly, it has passed Phase 3 and this summer there was an FDA advisory council that voted against approval. Of course, the ultimate approval has not been made by the FDA.

But I think it is really important to point out that the current process only serves less than one half of 1 percent of terminal patients in this country and it is only the well-connected and the affluent that are able to go to other countries to get this kind of treatment.

And Right to Try is about making this available to everyone to at least pursue. I mean, obviously, there are no guarantees.

I would also like to point out something about safety. We've been talking about safety quite a bit, and Dr. Gottlieb explained how he was treated off-label for his own cancer, and I'd like to just explain to the committee that doctors can prescribe FDA-approved treatments for off-label uses, where medicines that are used to treat conditions other than what the FDA says it is approved for.

So what that means is that these are—these are prescribed and this is completely legal and lawful and it is actually very common, particularly in areas where there's a very serious disease, where there's—without proof of efficacy.

And this—and this is done very frequently. About one-fifth of all off-label prescriptions are—about one-fifth of all prescriptions are written off label and in cases where—in cases where there aren't a lot of options, particularly the more serious types of cancer, it is the majority of the time.

And so this idea that we can't allow doctors with their patients to make decisions about what might be an appropriate treatment and, really, just run roughshod over patient autonomy is, I think, is really the wrong—

Mr. BURGESS. I am just going to interrupt you for a second because, again, I am getting such a completely different story, Dr. Sigal, and your story on Diego's osteosarcoma medication. Is there a question of the efficacy of the medication and that's why it hasn't been approved?

Ms. LOPEZ BAUMAN. Well, I mean, there certainly isn't in other countries. It's available in Mexico, Israel, all over Europe. He went to the U.K. and in, I believe, 2014 it actually won the—

Mr. BURGESS. But let me—I am going to stop you for a second. There really wouldn't be an off-label option for Diego.

Ms. LOPEZ BAUMAN. Not in his case. But what I am saying is that this idea of talking about risk or that you can't prescribe something without knowing the efficacy is actually not true.

In our current system, it is perfectly legal for a physician to prescribe off-label and it is actually very common.

Mr. BURGESS. Sure. Very common.

Ms. LOPEZ BAUMAN. And so Right to Try, I don't believe, poses, you know, additional risks and burdens on the doctors and the patients in terms of a lack of information or not having perfect information, because we are already using off-label treatments in a lot of different areas of health care, and, in fact, one-fifth of all prescriptions are off-label.

So this idea that you have to have efficacy or you have to have more data before you can give a patient permission to use it is, I think, absolutely unacceptable and that the default should be that patients should have the right to try to save their own lives.

Mr. BURGESS. And I don't disagree. But, again, as Dr. Sigal so eloquently pointed out in her sister's case, that perhaps was premature to be utilizing that type of therapy.

And I agree, we are much better now. Put the United States breast cancer statistics up against anyone in the world. That is truly one of the bright spots, as far as developmental therapeutics is concerned.

Mr. Moch, I just have to ask you, sort of the last—the last tier about the issue of the legal liability, and what is—you're the one who served as—I guess on the board or the CEO of an actual company that had to deal with this.

So that's a real concern for a company, is it not, that someone will come back after the fact and say, "I was harmed by your product"?

Mr. MOCH. So I've actually been CEO of five companies involved in this space.

The answer is no. I think that's not the argument, and it is not one of the reasons that I've looked at for not making an experimental medicine available, and I've done it in multiple companies.

You have informed consent. There are going to be side effects. I think everybody knows in these cases these are terminally ill patients.

Again, I think—and I just—I have no other way to say this. As being right between this debate, I cautioned everybody that you're looking at a specific issue in a vacuum.

I see—the plural of anecdote is not data. I can pull out lots of examples of people who survived or died or have been problems, and you're looking at a particular case that's a statement that's made to make a point.

You have to look at the totality. That's not being done in this discussion in a way that really is—for me, as a drug developer in five companies—is frustrating, I will be clear.

There are lots of reasons that people will make or will not make a drug available under expanded access. The Right to Try laws address none of those reasons, and I think that is—in my original statement, I said this is feel-good legislation for legislators, and I am sorry to say it so bluntly.

The percentage of legislators who voted for Right to Try legislation is about equal to the percentage of FDA approvals of expanded access applications. It's not a relevant comparison, but it is a very relevant comparison.

The problem here is that drug development is very complex. You do now know, in most cases—in fact, you do not know the safety of a drug after Phase 1. I have taken drugs through Phase 3 and had them fail for safety issues in Phase 3.

Hundreds of millions of dollars are spent. You think you know the answer, and 40 or 50 percent of drugs still fail in Phase 3.

The drug development process where you're trying to alter a biological system that's evolved over how many hundreds of millions of years, and you're trying to alter one system in a human being.

Doesn't happen that way. You get side effects. You get issues. You don't know what the number is or percentage is.

So the argument that Right to Try legislation is going to make more people have access to experimental medicines does not exist in my mind as a drug developer nor in anybody I know, and I can't say it more bluntly than that.

I know it is a very emotional thing. I know we all want—look, I've done more expanded access than most drug developers with a biotechnology company.

I want to see it happen. This doesn't do anything. If you want to talk about at some point how to do things that are helpful, then you've got to get a group of people in a room and have a meaningful discussion.

This discussion really doesn't address those issues.

Mr. BURGESS. Well, I actually look forward to having that discussion. So you have set the stage for perhaps our second hearing in this regard.

But this has been fascinating today and, clearly, we haven't heard the end—this is not the end of the story. But very powerful panel, and I thank you all for spending time with us today.

I don't see any other Members who have not yet asked questions. So, again, I will thank you for being here today. We have received outside feedback from a number of organizations on these bills.

So I'd like to submit statements from the following, for the record: Right to Try, the National Conference of State Legislatures as well as a letter from our Senate colleagues—Senator Johnson and Senator Donnelly.

Without objection, so ordered.

[The information appears at the conclusion of the hearing.]

Mr. BURGESS. Pursuant to committee rules, I remind Members they have 10 business days to submit additional questions for the record, and I ask the witnesses to submit their response within 10 business days upon receipt of the questions.

And without objection, the subcommittee is adjourned.

[Whereupon, at 1:34 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

PREPARED STATEMENT OF HON. GREG WALDEN

Today, our Health Subcommittee is reviewing an important and often emotional topic—patient access to experimental drugs for our family members, friends, and other loved ones battling serious or immediately life-threatening illnesses.

Having lost close family members in such circumstances, I understand the passion people have for finding a life-saving cure.

Previous barriers to investigational drugs led to a nationwide movement, resulting in the establishment of the Food and Drug Administration's expanded access program. Commonly referred to as compassionate use, this 1980s-era process has

helped patients who do not meet the guidelines of clinical trial participation receive experimental access to unapproved drugs. The individual's physician and the drug developer must agree the potential benefits outweigh any patient safety concerns with the FDA facilitating the process. According to the nonpartisan Government Accountability Office, 99 percent of the nearly 5,800 applications were approved from 2012 through 2015.

However, there is ongoing concern that some patients may not be allowed to access investigational drugs even after exhausting all other treatment options. We must examine whether there are regulatory, legal, or commercial barriers to patient access for experimental drugs.

This has led some advocates to promote a nationwide grassroots movement for State Right to Try laws. To date, 37 States have enacted such laws, according to the National Conference of State Legislatures, including my home State of Oregon. Many patients, like Navy veteran Matt Bellina, here with us today, have moving stories to tell. And they deserve a voice in this complex discussion.

Ultimately, this issue is about fairness. As a representative body, our responsibility is to strike the delicate balance of individual liberty, and patient safety in public policy.

For many on this committee, today marks your first formal exposure to patient access to investigational drugs. Today is an opportunity for all of us to learn more.

Thank you, Mr. Chairman, for holding this hearing. And thank you to our four panels of witnesses, I appreciate you taking the time to be with us today. I yield the balance of my time.



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115TH CONGRESS
1ST SESSION

S. 204

IN THE HOUSE OF REPRESENTATIVES

AUGUST 4, 2017

Referred to the Committee on Energy and Commerce

AN ACT

To authorize the use of unapproved medical products by patients diagnosed with a terminal illness in accordance with State law, and for other purposes.

1 *Be it enacted by the Senate and House of Representa-*
2 *tives of the United States of America in Congress assembled,*

1 **SECTION 1. SHORT TITLE.**

2 This Act may be cited as the “Trickett Wendler,
3 Frank Mongiello, Jordan McLinn, and Matthew Bellina
4 Right to Try Act of 2017”.

5 **SEC. 2. USE OF UNAPPROVED INVESTIGATIONAL DRUGS BY**
6 **PATIENTS DIAGNOSED WITH A TERMINAL**
7 **ILLNESS.**

8 (a) IN GENERAL.—Chapter V of the Federal Food,
9 Drug, and Cosmetic Act is amended by inserting after sec-
10 tion 561A (21 U.S.C. 360bbb–0) the following:

11 **“SEC. 561B. INVESTIGATIONAL DRUGS FOR USE BY ELIGI-**
12 **BLE PATIENTS.**

13 “(a) DEFINITIONS.—For purposes of this section—
14 “(1) the term ‘eligible patient’ means a pa-
15 tient—

16 “(A) who has been diagnosed with a life-
17 threatening disease or condition (as defined in
18 section 312.81 of title 21, Code of Federal Reg-
19 ulations (or any successor regulations));

20 “(B) who has exhausted approved treat-
21 ment options and is unable to participate in a
22 clinical trial involving the eligible investigational
23 drug, as certified by a physician, who—

24 “(i) is in good standing with the phy-
25 sician’s licensing organization or board;
26 and

1 “(ii) will not be compensated directly
2 by the manufacturer for so certifying; and

3 “(C) who has provided to the treating phy-
4 sician written informed consent regarding the
5 eligible investigational drug, or, as applicable,
6 on whose behalf a legally authorized representa-
7 tive of the patient has provided such consent;

8 “(2) the term ‘eligible investigational drug’
9 means an investigational drug (as such term is used
10 in section 561)—

11 “(A) for which a Phase 1 clinical trial has
12 been completed;

13 “(B) that has not been approved or li-
14 censed for any use under section 505 of this
15 Act or section 351 of the Public Health Service
16 Act;

17 “(C)(i) for which an application has been
18 filed under section 505(b) of this Act or section
19 351(a) of the Public Health Service Act; or

20 “(ii) that is under investigation in a clin-
21 ical trial that—

22 “(I) is intended to form the primary
23 basis of a claim of effectiveness in support
24 of approval or licensure under section 505

1 of this Act or section 351 of the Public
2 Health Service Act; and

3 “(II) is the subject of an active inves-
4 tigational new drug application under sec-
5 tion 505(i) of this Act or section 351(a)(3)
6 of the Public Health Service Act, as appli-
7 cable; and

8 “(D) the active development or production
9 of which is ongoing and has not been discon-
10 tinued by the manufacturer or placed on clinical
11 hold under section 505(i); and

12 “(3) the term ‘phase 1 trial’ means a phase 1
13 clinical investigation of a drug as described in sec-
14 tion 312.21 of title 21, Code of Federal Regulations
15 (or any successor regulations).

16 “(b) EXEMPTIONS.—Eligible investigational drugs
17 provided to eligible patients in compliance with this section
18 are exempt from sections 502(f), 503(b)(4), 505(a), and
19 505(i) of this Act, section 351(a) of the Public Health
20 Service Act, and parts 50, 56, and 312 of title 21, Code
21 of Federal Regulations (or any successor regulations), pro-
22 vided that the sponsor of such eligible investigational drug
23 or any person who manufactures, distributes, prescribes,
24 dispenses, introduces or delivers for introduction into
25 interstate commerce, or provides to an eligible patient an

1 eligible investigational drug pursuant to this section is in
2 compliance with the applicable requirements set forth in
3 sections 312.6, 312.7, and 312.8(d)(1) of title 21, Code
4 of Federal Regulations (or any successor regulations) that
5 apply to investigational drugs.

6 “(c) USE OF CLINICAL OUTCOMES.—

7 “(1) IN GENERAL.—Notwithstanding any other
8 provision of this Act, the Public Health Service Act,
9 or any other provision of Federal law, the Secretary
10 may not use a clinical outcome associated with the
11 use of an eligible investigational drug pursuant to
12 this section to delay or adversely affect the review or
13 approval of such drug under section 505 of this Act
14 or section 351 of the Public Health Service Act un-
15 less—

16 “(A) the Secretary makes a determination,
17 in accordance with paragraph (2), that use of
18 such clinical outcome is critical to determining
19 the safety of the eligible investigational drug; or

20 “(B) the sponsor requests use of such out-
21 comes.

22 “(2) LIMITATION.—If the Secretary makes a
23 determination under paragraph (1)(A), the Sec-
24 retary shall provide written notice of such deter-
25 mination to the sponsor, including a public health

1 justification for such determination, and such notice
2 shall be made part of the administrative record.
3 Such determination shall not be delegated below the
4 director of the agency center that is charged with
5 the premarket review of the eligible investigational
6 drug.

7 “(d) REPORTING.—

8 “(1) IN GENERAL.—The manufacturer or spon-
9 sor of an eligible investigational drug shall submit to
10 the Secretary an annual summary of any use of such
11 drug under this section. The summary shall include
12 the number of doses supplied, the number of pa-
13 tients treated, the uses for which the drug was made
14 available, and any known serious adverse events.
15 The Secretary shall specify by regulation the dead-
16 line of submission of such annual summary and may
17 amend section 312.33 of title 21, Code of Federal
18 Regulations (or any successor regulations) to require
19 the submission of such annual summary in conjunc-
20 tion with the annual report for an applicable inves-
21 tigational new drug application for such drug.

22 “(2) POSTING OF INFORMATION.—The Sec-
23 retary shall post an annual summary report of the
24 use of this section on the internet website of the
25 Food and Drug Administration, including the num-

1 ber of drugs for which clinical outcomes associated
2 with the use of an eligible investigational drug pur-
3 suant to this section was—

4 “(A) used in accordance with subsection
5 (e)(1)(A);

6 “(B) used in accordance with subsection
7 (e)(1)(B); and

8 “(C) not used in the review of an applica-
9 tion under section 505 of this Act or section
10 351 of the Public Health Service Act.”.

11 (b) NO LIABILITY.—

12 (1) ALLEGED ACTS OR OMISSIONS.—With re-
13 spect to any alleged act or omission with respect to
14 an eligible investigational drug provided to an eligi-
15 ble patient pursuant to section 561B of the Federal
16 Food, Drug, and Cosmetic Act and in compliance
17 with such section, no liability in a cause of action
18 shall lie against—

19 (A) a sponsor or manufacturer; or

20 (B) a prescriber, dispenser, or other indi-
21 vidual entity (other than a sponsor or manufac-
22 turer), unless the relevant conduct constitutes
23 reckless or willful misconduct, gross negligence,
24 or an intentional tort under any applicable
25 State law.

1 (2) DETERMINATION NOT TO PROVIDE DRUG.—
2 No liability shall lie against a sponsor manufacturer,
3 prescriber, dispenser or other individual entity for its
4 determination not to provide access to an eligible in-
5 vestigational drug under section 561B of the Fed-
6 eral Food, Drug, and Cosmetic Act.

7 (3) LIMITATION.—Except as set forth in para-
8 graphs (1) and (2), nothing in this section shall be
9 construed to modify or otherwise affect the right of
10 any person to bring a private action under any State
11 or Federal product liability, tort, consumer protec-
12 tion, or warranty law.

13 **SEC. 3. SENSE OF THE SENATE.**

14 It is the sense of the Senate that section 561B of
15 the Federal Food, Drug, and Cosmetic Act, as added by
16 section 2—

17 (1) does not establish a new entitlement or
18 modify an existing entitlement, or otherwise estab-
19 lish a positive right to any party or individual;

20 (2) does not establish any new mandates, direc-
21 tives, or additional regulations;

22 (3) only expands the scope of individual liberty
23 and agency among patients, in limited cir-
24 cumstances;



115TH CONGRESS
1ST SESSION

H. R. 1020

To allow the manufacture, importation, distribution, and sale of investigational drugs and devices intended for use by terminally ill patients who execute an informed consent document, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

FEBRUARY 13, 2017

Mr. GRIFFITH (for himself and Mr. BRAT) introduced the following bill; which was referred to the Committee on Energy and Commerce

A BILL

To allow the manufacture, importation, distribution, and sale of investigational drugs and devices intended for use by terminally ill patients who execute an informed consent document, and for other purposes.

1 *Be it enacted by the Senate and House of Representa-*
2 *tives of the United States of America in Congress assembled,*

3 **SECTION 1. SHORT TITLE.**

4 This Act may be cited as the “Compassionate Free-
5 dom of Choice Act of 2017”.

1 **SEC. 2. DRUGS AND DEVICES FOR USE BY TERMINALLY ILL**
2 **PATIENTS.**

3 The Federal Food, Drug, and Cosmetic Act is amend-
4 ed by inserting after section 561 (21 U.S.C. 360bbb) the
5 following:

6 **“SEC. 561A. DRUGS AND DEVICES FOR USE BY TERMINALLY**
7 **ILL PATIENTS.**

8 “(a) IN GENERAL.—Nothing in this Act or section
9 351 of the Public Health Service Act prevents or restricts,
10 and the Food and Drug Administration shall not imple-
11 ment or enforce any provision of law preventing or re-
12 stricting, the manufacture, importation, distribution, or
13 sale of an investigational drug or device intended for use
14 by a terminally ill patient in accordance with subsection
15 (b).

16 “(b) PATIENT REQUIREMENTS.—In order for an in-
17 vestigational drug or device to be intended for use in ac-
18 cordance with this subsection, such drug or device must
19 be intended for use by a patient who has—

20 “(1) been diagnosed with a terminal illness by
21 a licensed physician;

22 “(2) been informed by a licensed physician that
23 no drug or device that is lawfully marketed in the
24 United States is likely to cure the illness; and

25 “(3) executed a written informed consent docu-
26 ment that states—

1 “(A) the known and potential risks and
2 benefits of such drug or device; and

3 “(B) any indications of the illness for
4 which a drug or device is lawfully marketed, or
5 for which treatment is otherwise available, in
6 the United States.

7 “(c) PROHIBITION ON REQUIRING THE DISCLOSURE,
8 COLLECTION, AND REPORTING OF CERTAIN INFORMA-
9 TION BY FOOD AND DRUG ADMINISTRATION.—

10 “(1) IN GENERAL.—The Commissioner of Food
11 and Drugs may not require the disclosure, collection,
12 or reporting of—

13 “(A) any information related to the deliv-
14 ery, administration, or use of an investigational
15 drug or device pursuant to this section; or

16 “(B) any information related to the clinical
17 outcomes experienced by a terminally ill patient
18 supplied an investigational drug or device pur-
19 suant to this section.

20 “(2) EXCEPTION.—Nothing in this subsection
21 prevents the sponsor of a clinical trial from volun-
22 tarily disclosing, collecting, or reporting information
23 to the Food and Drug Administration.

1 “(d) DEFINITION OF INVESTIGATIONAL DRUG OR
2 DEVICE.—In this section, the term ‘investigational drug
3 or device’ means a drug or device that—

4 “(1) has not yet been approved, licensed, or
5 cleared for commercial distribution under section
6 505, 510(k), or 515 of this Act or section 351 of the
7 Public Health Service Act, and cannot otherwise be
8 lawfully marketed in the United States; and

9 “(2) is or has been the subject of one or more
10 clinical trials.”.

11 **SEC. 3. LIABILITY PROTECTION.**

12 The Federal Food, Drug, and Cosmetic Act (21
13 U.S.C. 301 et seq.) is amended by inserting after section
14 561A, as inserted by section 2 of this Act, the following:

15 **“SEC. 561B. LIABILITY PROTECTION.**

16 “Except in the case of gross negligence or willful mis-
17 conduct, any person who manufactures, imports, distrib-
18 utes, prescribes, dispenses, or administers an investiga-
19 tional drug or device in accordance with section 561A shall
20 not be liable in any action under Federal or State law for
21 any loss, damage, or injury arising out of, relating to, or
22 resulting from—

23 “(1) the design, development, clinical testing
24 and investigation, manufacturing, labeling, distribu-

1 tion, sale, purchase, donation, dispensing, prescrip-
2 tion, administration, or use of the drug or device; or
3 “(2) the safety or effectiveness of the drug or
4 device.”.

○

September 19, 2017

The Honorable Greg Walden, Chairman
2125 Rayburn House Office Building
U.S. House Committee on Energy and Commerce
Washington, DC 20515

The Honorable Frank Pallone, Ranking Member
2471 Rayburn House Office Building
U.S. House Committee on Energy and Commerce
Washington, DC 20515

Dear Chairman Walden and Ranking Member Pallone,

The undersigned organizations collectively represent millions of patients with serious and life-threatening diseases. We write to express our strong opposition to S.204, the *Trickett Wender, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017*, as well as H.R.878, the *Right to Try Act of 2017*, currently under consideration in the House Energy and Commerce Committee. We urge the Committee to proceed through regular legislative order to facilitate discussion and consideration of alternative policies that would genuinely increase access to promising investigational therapies for the communities we represent.

Our organizations support patient access to unapproved therapies, but S.204 and H.R.878 do not effectuate policy changes that would afford our patients greater access to promising investigational therapies. Instead, these bills would likely do more harm than good. We encourage the Committee to hold hearings to examine these issues more closely, as well as consider other policy options to improve the ability of patients to safely access unapproved therapies.

We do not believe S.204 or H.R.878 would successfully increase access to promising investigational therapies for those in need. Both of these bills remove the Food and Drug Administration (FDA) from the initial approval process for accessing an investigational therapy outside of a clinical trial. Removing FDA from this process is not likely to facilitate increased access to investigational therapies because FDA currently approves 99.7 percent of all expanded access requests submitted by physicians and companies for patients with immediately life-threatening illnesses who cannot participate in clinical trials.¹ The Government Accountability Office (GAO) recently released a report examining the current FDA expanded access program, and found that substantial changes were not needed within the program, aside from greater clarity on the use of adverse event data.²

When access to a therapy is denied to a patient, it is generally the company that denies the request, and for reasons that appear to be reasonable, such as a determination that the benefits do not outweigh the risks, an unavailability of sufficient product to offer outside of clinical trials, costs, or concerns about adversely affecting clinical trial enrollment.

¹ Jarow, Jonathan P., et al. "Expanded access of investigational drugs: the experience of the Center of Drug Evaluation and Research over a 10-year period." *Therapeutic innovation & regulatory science* 50.6 (2016): 705-709.

² GAO, "FDA Has Taken Steps to Improve the Expanded Access Program but Should Further Clarify How Adverse Events Data Are Used," July 2017.

It is important to remember that the current regulatory system for medical products and research in the United States was created as a result of serious patient harm and exploitation that occurred early in the 20th Century. Birth defects resulting from Thalidomide are an example of what happens when drugs are given to humans without proper safety review and approval. While obtaining unapproved therapies outside of a clinical trial is not about research, the products themselves remain experimental and have not been shown to be safe and effective. Clinical research subject protections are in place when experimental products are being tested to ensure the safe and ethical treatment of research participants. Patients seeking expanded access to unapproved therapies outside of clinical trials must be afforded the same ethical standards and protections as patients taking part in clinical trials.

Existing expanded access policies are not without room for improvement. We encourage the Committee to examine the predominant reasons why patients interested in access to experimental therapies are ultimately unable to obtain them by enrolling in clinical trials or through the current expanded access process. We also ask the Committee to provide oversight as FDA moves forward with implementation of relevant provisions enacted within the past year that improve the expanded access system. These include the requirements within the *21st Century Cures Act* for the public posting of expanded access policies on company websites, and greater clarity from FDA on the use of adverse event data. Several provisions in the *Food and Drug Administration Reauthorization Act (FDARA)* will also improve access to investigational therapies, such as the allowance for IRBs to appoint one individual to review applications rather than a fully convened IRB. FDARA also directs FDA to further investigate inclusion/exclusion criteria within clinical trials, a key factor in the number of individuals able to access investigational therapies.

We are eager to work with the Committee as it considers these proposals, and endeavors to ensure patients gain greater access to investigational therapies. We welcome the opportunity to work with members of the Committee, as well as the sponsors of this legislation, to improve and increase access to both approved and unapproved innovative, lifesaving therapies.

Sincerely,

Alliance for Aging Research
American Cancer Society Cancer Action Network
American Lung Association
American Society of Clinical Oncology
Association of Pediatric Hematology/Oncology Nurses
Cancer Support Community
Children's Brain Tumor Foundation
Children's Cause for Cancer Advocacy
Cystic Fibrosis Foundation
Fight Colorectal Cancer
Friedreich's Ataxia Research Alliance
Friends of Cancer Research
Grandparents in Action
Leukemia & Lymphoma Society
Lung Cancer Alliance
LUNgevity Foundation

Max Cure Foundation, Inc.
National Comprehensive Care Network
National Health Council
National Organization for Rare Disorders (NORD)
TargetCancer Foundation
United Mitochondrial Disease Foundation

CC: The Honorable Paul Ryan, Speaker
The Honorable Kevin McCarthy, Majority Leader
The Honorable Nancy Pelosi, Minority Leader
The Honorable Steny Hoyer, Minority Whip

September 5, 2017

Dear Members of the United States House of Representatives:

The undersigned groups respectfully urge you to oppose S. 204 — which is deceptively titled the “Right to Try Act of 2017” but should instead be called the “False Hope Act of 2017.”

We recognize the desire of patients with terminal illness who have exhausted available treatment options to access experimental medical products that have not been approved or cleared by the Food and Drug Administration (FDA). However, the best way for patients to gain such access is through the FDA’s Expanded Access Program, which allows seriously ill patients to receive treatment with experimental medical products while also providing basic safeguards to protect patients’ rights and welfare. Importantly, the recently enacted FDA Reauthorization Act of 2017, which renewed the FDA’s user fee programs, included responsible bipartisan language intended to enhance the agency’s Expanded Access Program.

We are concerned that S. 204, as amended and passed by the U.S. Senate on August 3, 2017, would put countless patients at risk by undermining important FDA safety rules related to the use and oversight of unapproved, experimental medications. Such legislation would expose vulnerable patients to risks of serious harm, including dying earlier and more painfully than they otherwise would have, without appropriate safeguards.

FDA’s Current Expanded Access Program

Currently, the FDA oversees the use of all experimental drugs and biological products in the U.S. The FDA’s Expanded Access Program allows patients across the country to gain access to such products, provided that each patient’s doctor believes such access is appropriate and that the manufacturer of the product agrees to provide it for that use.

To protect patients, the FDA and an institutional review board (IRB) must approve each use of an experimental drug or biological product under the Expanded Access Program. As conditions of approval, there must be sufficient evidence of the safety and effectiveness of the experimental drug to support its use in a particular patient, and the probable risk to the patient from the drug must not be greater than the probable risk from the disease or condition. The program further protects patients by requiring a robust informed consent process that is similar to the consent process for a clinical trial, as well as monitoring and reporting of serious adverse events. The FDA grants 99 percent of all Expanded Access Program requests and, in urgent circumstances, can respond to such requests within one or two days. The agency also recently streamlined the program to require less paperwork. In addition, the 21st Century Cures Act of 2016 included useful provisions that require drug manufacturers to publicly post their expanded access policies and provide points of contact for requests. The potential impact of these streamlining efforts has yet to be fully realized.

It is also important to recognize that many of the experimental products made available through this program ultimately are not shown to be safe and effective in clinical testing and are not approved or cleared by the FDA.

Undermining Patient Protections While Offering False Hope

The false-hope legislation passed by the Senate and now being considered by the House would create a dangerous, uncharted pathway for access to experimental drugs and biological products that essentially bypasses the protections of the FDA's Expanded Access Program for patients diagnosed with life-threatening diseases or conditions — a patient population that is much broader than “patients diagnosed with a terminal illness,” which was the patient population covered by the original version of S. 204.

Of particular concern, this alternative pathway for accessing experimental drugs and biological products would put vulnerable patients at risk and undermine their rights by:

- Specifying completion of a single phase I clinical trial as the evidentiary threshold for allowing use of experimental drug products under the legislation. Such a threshold is insufficient for allowing use of an experimental drug outside the context of a clinical trial because initial phase I clinical trials often only involve healthy volunteers, typically involve testing of a single dose of an experimental drug, provide no meaningful data on efficacy, and yield only very limited preliminary data on safety.
- Eliminating the requirements for review and approval by the FDA and an IRB, which help to ensure that proposed uses of experimental drugs do not pose unacceptable risk to patients and that the patients are fully informed of the risks and other key information when their consent is sought.
- Eliminating the requirements that (a) the consent of the patient be sought only under circumstances that provide the patient with sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence; (b) the information given to the patient when consent is sought be understandable to the patient; and (c) the consent process exclude exculpatory language through which the patient is made to waive or appear to waive any of his or her legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.
- Broadly immunizing sponsors, manufacturers, prescribers, and dispensers from liability for any alleged acts or omissions related to eligible experimental drugs, unless the relevant conduct constitutes reckless or willful misconduct, gross negligence, or an intentional tort under applicable state law. This provision would bar suits in a variety of situations in which state law might reasonably impose liability. For example, it would immunize manufacturers from being held accountable for harm caused by contamination of an investigational drug product, which can be serious. It also would bar state-law negligence suits against the physician prescribers; for example, if the physician negligently prescribed an investigational drug that was known to be contraindicated for a particular patient's set of circumstances, but the situation did not arise to “gross negligence.” Decisions about liability in such situations are properly based on consideration of the specific facts, and the bill's immunity provision may cause physicians to be less careful in making prescribing decisions for seriously ill patients.
- Eliminating the requirement that the treating physician report immediately to the manufacturer or sponsor any serious adverse events regardless of whether they are considered drug-related.

Letter to Congress Regarding S. 204

September 5, 2017

In closing, we urge you to oppose S. 204 and any similar false-hope legislation that is introduced in the future. Thank you for considering our views on this important matter.

Sincerely,

Public Citizen
ACTUP New York
Breast Cancer Action
Doctors For America
END AIDS NOW
Government Accountability Project
Health GAP
Jacobs Institute of Women's Health
MedShadow Foundation
National Consumers League
National Physicians Alliance
National Women's Health Network
Richard N. Gottfried, Chair, Committee on Health, New York State Assembly
Social Security Works
The Annie Appleseed Project
The Society for Patient Centered Orthopedics
Treatment Action Group
Washington Advocates for Patient Safety



1600 20th Street, NW • Washington, D.C. 20009 • 202/588-1000 • www.citizen.org

March 6, 2017

Dear Members of the United States Senate and House of Representatives:

Public Citizen, a consumer advocacy organization with more than 400,000 members and supporters nationwide, respectfully urges you to oppose S. 204, H.R. 878 and H.R. 1020, bills with various names that would most appropriately each be titled the “False Hope Act of 2017.”

These bills provide false hope to patients and are related to a nationwide lobbying effort funded by the Goldwater Institute, which has deceptively branded such laws as “Right to Try” legislation.

We recognize the desire of patients with terminal illness who have exhausted available treatment options to access experimental medical products that have not been approved or cleared by the Food and Drug Administration (FDA). However, the best way for patients to gain such access is through the FDA’s Expanded Access Program, which allows seriously ill patients to receive treatment with experimental drugs, biological products or medical devices while also providing basic safeguards to protect patients’ rights and welfare and maintaining strong incentives for careful clinical testing and timely product development.

We are concerned that false hope legislation like S. 204, H.R. 878 and H.R. 1020 would put countless patients at risk by dramatically undermining the FDA’s role in ensuring that medical products are safe and effective before they become widely used. Such legislation would expose vulnerable patients to risks of serious harm, including dying earlier and more painfully than they otherwise would have, without appropriate safeguards. It also would undermine incentives for companies to swiftly develop life-saving products for FDA approval and impair review of these products by limiting the agency’s access to unfavorable information.

FDA’s Current Expanded Access Program

The FDA’s Expanded Access Program allows patients across the country to gain access to experimental drugs, biological products and medical devices, provided that each patient’s doctor believes such access is appropriate and the manufacturer of the product agrees to provide it for that use. The program protects patients by requiring informed consent, ethical review by an institutional review board, safety monitoring and the reporting of adverse events to the FDA. It also prevents manufacturers from profiting from the use of experimental products, which helps to maintain incentives to continue rigorous clinical testing aimed at FDA approval.

The FDA grants 99 percent of all Expanded Access Program requests and, in urgent circumstances, can respond to such requests within 1 or 2 days. The agency also recently streamlined the program to require less paperwork. In addition, the 21st Century Cures Act of 2016 included useful provisions that require drug manufacturers to publicly post their expanded access policies and provide points of contact for requests. The potential impact of these streamlining efforts has yet to be fully realized.

It is also important to recognize that many of the experimental products made available through this program ultimately are not shown to be safe and effective in clinical testing and are not approved or cleared by the FDA. Despite patients’ hopes, there is no evidence that the current Expanded Access Program helps more patients than it harms.

Public Citizen

March 6, 2017, Letter to Congress Regarding
S. 204, H.R. 878, and H.R. 1020**Broadly Attacking Patient Protections While Offering False Hope**

Rather than proposing further improvements to the existing program, the false hope legislation now before Congress would undermine the FDA's fundamental authority to oversee the use of experimental medical products and to ensure they are safe and effective before they become widely used.

The legislation would put vulnerable patients at risk by:

- Offering manufacturers broad rights to sell experimental medical products after only very preliminary clinical testing, when very little is known about a product's potential risks, let alone its benefits.
- Eliminating important federal safeguards intended to protect the rights and welfare of patients exposed to such products, including appropriate, fully informed consent; ethical review by an IRB; and safety monitoring.
- Allowing manufacturers to charge high prices for experimental medical products, which forces patients to take financial risks for unproven benefits.
- Stripping away legal protections for patients by immunizing manufacturers, doctors and others against liability, even if they failed to exercise reasonable care or inform vulnerable patients about potential risks and benefits of the experimental products.
- Preventing the FDA from enforcing good manufacturing practices or intervening to stop the sale of tainted or otherwise substandard experimental medical products.

The legislation also would slow the development and impair FDA review of new medical products by:

- Reducing incentives to continue rigorous clinical testing in pursuit of FDA approval.
- Discouraging patients from enrolling in placebo-controlled clinical trials by providing them with access to experimental medical products in the general marketplace.
- Prohibiting the agency from considering (S. 204 and H.R. 878) or requesting (H.R. 1020) information about side effects, injuries or deaths in patients treated with experimental medical products under the legislation.

Congress should stop these attacks on the FDA's authority to regulate experimental medical products, an effort that will only encourage false hope for patients while ultimately doing them more harm than good.

We urge you to oppose S. 204, H.R. 878 and H.R. 1020 and any similar false hope legislation that is introduced in the future. Thank you for considering our views on this important matter.

Sincerely,



Michael A. Carome, M.D.
Director
Public Citizen's Health Research Group



Sarah Sorscher, J.D., M.P.H.
Researcher
Public Citizen's Health Research Group

How Often Are Drugs Made Available Under the Food and Drug Administration's Expanded Access Process Approved?

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 2017, 57(S10) S136–S142
 © 2017, The American College of
 Clinical Pharmacology
 DOI: 10.1002/jcph.960

Amy E. McKee, MD¹, André O. Markon, PhD, MPH², Kirk M. Chan-Tack, MD¹,
 and Peter Lurie, MD, MPH³

Abstract

In this review of individual patient expanded-access requests to the Center for Drug Evaluation and Research for the period Fiscal Year 2010 to Fiscal Year 2014, we evaluated the number of applications received and the number allowed to proceed. We also evaluated whether drugs and certain biologics obtained under expanded access went on to be approved by the Food and Drug Administration. Finally, we considered concerns that adverse events occurring during expanded access might place sponsors at risk for legal liability. Overall, 98% of individual patient expanded-access requests were allowed to proceed. During the study period, among drugs without a previous approval for any indication or dosage form, 24% of unique drugs (ie, multiple applications for access to the same drug were considered to relate to 1 unique drug), and 20% of expanded-access applications received marketing approval by 1 year after initial submission; 43% and 33%, respectively, were approved by 5 years after initial submission. A search of 3 legal databases and a database of news articles did not appear to identify any product liability cases arising from the use of a product in expanded access. Our analyses seek to give physicians and patients a realistic perspective on the likelihood of a drug's approval as well as certain information regarding the product liability risks for commercial sponsors when providing expanded access to investigational drugs. The US Food and Drug Administration (FDA)'s expanded-access program maintains a careful balance between authorizing patient access to potentially beneficial drugs and protecting them from drugs that may have unknown risks. At the same time, the agency wishes to maintain the integrity of the clinical trials process, ultimately the best way to get safe and effective drugs to patients.

Keywords

expanded access, compassionate use, US Food and Drug Administration

A core mission of the FDA is the premarket assessment of the safety and effectiveness of investigational new drugs and biological products (referred to collectively as “drugs” in this paper). However, the FDA understands that patients, particularly those with life-threatening diseases or conditions, may have an interest in obtaining access to drugs that have not yet been approved.

Wherever possible, the FDA believes enrollment in clinical trials remains the best option for patients who wish to gain access to investigational drugs. Clinical trial enrollment helps to provide adequate protection for patients and leads to the collection of data that may result in the approval of the investigational drug and, consequently, to wider availability. However, when patient enrollment in a clinical trial is not possible (eg, a patient is not eligible for any ongoing clinical trials, there are no ongoing clinical trials, or the patient does not live near an ongoing trial and cannot travel to participate), patients have the option to seek access to unapproved drugs if they have serious or life-threatening diseases or conditions and no comparable or satisfactory alternative treatment is available.

In 1987, the FDA formalized its expanded-access process, which facilitates access to investigational new drugs and biological products for patients with serious or immediately life-threatening diseases or conditions and who lack therapeutic alternatives. Expanded access can also be used to secure access to an approved drug where availability is limited by a risk evaluation and

¹Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD, USA

²Center for Food Safety and Applied Nutrition, Food and Drug Administration, College Park, MD, USA

³Office of Public Health Strategy and Analysis, Food and Drug Administration, Silver Spring, MD, USA

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Corresponding Author:

Amy E. McKee, MD, Acting Deputy Office Director, FDA/CDER/OND/OHOP, White Oak, Building 22 Room 2249, 10903 New Hampshire Avenue, Silver Spring, MD 20993
 Email: amy.mckee@fda.hhs.gov

Disclaimer

The views expressed in this manuscript are those of the authors and do not necessarily reflect those of the Food and Drug Administration.

mitigation strategy and patients cannot obtain the drug under this strategy.

In expanded access, sometimes termed “compassionate use,” the primary purpose is to treat a patient rather than to obtain data about the drug, as would be the case in a clinical trial. In operating the expanded-access process the FDA seeks to maintain a careful balance between facilitating patient access to potentially beneficial drugs and protecting these patients from drugs that may have unknown risks.

In August 2009, the FDA revised its expanded access regulations to increase awareness and knowledge about expanded-access processes and to streamline the procedures for obtaining investigational drugs for treatment use. Under those regulations, the FDA identified 3 categories of expanded-access investigational new drug (IND) applications¹⁻⁵ (In addition, the FDA accepts expanded-access protocols, which permit expanded access through reference to an existing, typically commercial, IND. These follow different procedures and are not considered in this analysis.):

1. Expanded access for individual patients (frequently referred to as “single patients”) including for emergency use. Unless the FDA notifies the sponsor (typically the patient’s requesting physician) that treatment may begin earlier, there is a 30-day period from the date that the FDA receives the application before treatment may begin. Under the regulations’ emergency use provisions, treatment is typically initially requested and authorized by telephone (or other rapid means of communication such as email) and may start immediately on FDA authorization. The physician must agree to submit a written application within 15 working days of authorization.
2. Expanded access for intermediate-size patient populations. These are generally for more than an individual patient but for fewer patients than in the third category described below. FDA regulations do not have specific numerical limitations for when intermediate-size patient population expanded access may be appropriate. This determination generally depends on whether the drug is under development for marketing for the expanded access use and the number of patients with the disease or condition.
3. Expanded access for widespread treatment use. These are designed for use in larger patient populations and often bridge the gap between trial completion and potential approval while a marketing application is under review at the Agency.

This article focuses on the first category (individual patient expanded-access INDs).²⁻⁵ For such applications, the FDA must determine that:

- The patient to be treated has a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;
- The potential patient benefit justifies the potential risks of the treatment use, and those potential risks are not unreasonable in the context of the disease or condition to be treated;
- Providing the investigational drug for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded-access use or otherwise compromise the potential development of the expanded-access use; and
- The patient cannot obtain the investigational drug under another IND or protocol;

In addition, the patient’s physician must determine that the probable risk to the patient from the investigational drug is not greater than the probable risk from the disease or condition.

An important component of the expanded-access application process is a letter of authorization from the commercial sponsor of the investigational drug. The letter of authorization permits the FDA to refer to the commercial sponsor’s application for information to satisfy submission requirements. The FDA has personnel who help requesting physicians to identify the appropriate FDA review division, locate contacts at companies, find company policies regarding expanded access, engage an Institutional Review Board, and determine whether there are ongoing clinical trials.²⁻⁵ An FDA review of expanded-access requests includes knowledge of the totality of data and information that the commercial sponsor has submitted to the FDA for the development program, including data (eg, safety/toxicity data, dosing considerations) that may not be publicly available. The FDA does not provide clinical advice for the individual patient (this is the responsibility of the requesting physician), but the FDA can recommend revisions to the treating physician’s desired treatment plan to better protect the patient’s safety.⁵

The FDA acts quickly in response to individual patient expanded access requests and allows the vast majority of requests to proceed. For an emergency use application, access to the drug may begin on verbal authorization (usually over the telephone) by the reviewing FDA staff.⁴ For nonemergencies, the FDA strives to respond promptly and has a median response time of 4 days. As noted above, if the FDA does not respond within 30 days, treatment may proceed.⁶ (Certain expanded access protocols are not subject to

the 30-day requirement.) Although expanded-access submissions represent approximately one-third of all IND submissions, the vast majority of these are for individual patients and do not typically require substantial agency resources to review.

For this study, the FDA conducted a review of the expanded-access applications to the Center for Drug Evaluation and Research for the period Fiscal Year (FY) 2010-2014. We also evaluated whether drugs obtained under expanded access went on to be approved by the FDA. Finally, we considered concerns that adverse events occurring during expanded access might place sponsors at risk for legal liability.

Methods

A data set containing all expanded-access requests between FY 2010 and FY 2014 was obtained from the Center for Drug Evaluation and Research. This database included all individual patient, intermediate-size, and treatment use expanded-access INDs and protocols (6054 unique entries) and included both drugs and biologic products regulated by the Center for Drug Evaluation and Research. This project focused only on individual patient INDs, including individual patient INDs for emergency use, and thus excluded intermediate-size and treatment INDs and all protocols submitted to existing INDs.

The first step in cleaning this data set involved the removal of nonsubmitted INDs and duplicates. Nonsubmitted INDs included submissions in which an IND number was issued in error, submissions that were withdrawn by the sponsor, submissions where drug development under the IND had been suspended, or those where an IND number had been preassigned but no supporting documents had been received. We also removed 14 entries that were listed as both individual patient and emergency INDs. Exclusion of these entries, in combination with the removal of intermediate and treatment INDs and all protocols, resulted in a final data set with 5394 unique entries.

We next sought to standardize drug names for each remaining IND, as multiple drug names were present in the IND submissions—sponsoring physicians may have submitted expanded-access INDs for drugs identified by their commercial names in the United States or abroad, commercial veterinary names, code names of drugs used by the sponsors in investigational studies, or the chemical names of the active ingredient(s). A master drug list was therefore derived using the following 2-step process:

1. The provided drug name was entered into the Drugs@FDA search engine (<https://www.access.data.fda.gov/scripts/cder/drugsatfda/index.cfm>),

which provides labels and other pertinent information on previously approved prescription drugs, over-the-counter drugs, and therapeutic biological products. If the drug was found, the initial drug approval date was abstracted and added to the drug master list. To be considered approved for this study, drugs had to be approved by September 30, 2015.

2. If the drug was not found, a simple search was conducted using Google, PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>), and/or the National Cancer Institute's NCI Drug Dictionary (<http://www.cancer.gov/publications/dictionaries/cancer-drug>) to assess potential misspellings and similar errors. Alternative drug names found via this step were then entered in the Drugs@FDA search engine, as above. If the drug was not found after this step, the drug's potential commercial drug name, active ingredient, or drug code name (in that order) was added to the master list, and the drug was listed as not having been approved by September 30, 2015.

We calculated the numbers of INDs allowed to proceed and those not allowed to proceed. Additional analyses conducted focused only on INDs that were allowed to proceed, using both the individual IND and the unique drug (in this analysis, multiple applications for access to the same drug were considered to relate to a single unique drug) as the unit of analysis. Drug names are not presented in this document because of confidentiality protections associated with information about unapproved products, but aggregate data are presented by review division.

We produced Kaplan-Meier-style curves that described what percentage of INDs and unique drugs went on to be approved for any indication at various time junctures. For these analyses we included only drugs that had not been approved in any dosage form or for any indication at the time of the initial expanded-access application. For fixed-combination drugs, the drug was considered unapproved if at least 1 of the drugs in the combination had not yet been approved. All analyses were conducted using Microsoft Excel 2010 and SAS version 9.4.

To identify instances in which a tort allegedly arose in the context of expanded access, we searched WestlawNext, Google Scholar/Case Law and HeinOnline/Law Journals, not limited by date, using such terms as "tort liability," "product liability," "expanded access," "compassionate use," "investigational new drug," and "FDA." An analogous search for news articles using the same search terms was conducted using WestlawNext's news sources.

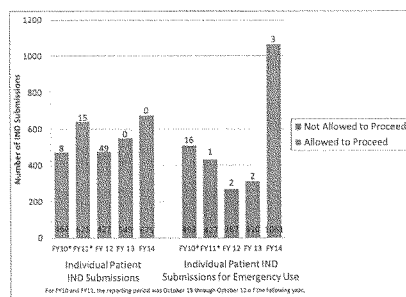


Figure 1. Individual patient expanded-access INDs, Fiscal Years 2010-2014. IND indicates investigational new drug.

Results

Analysis of FDA Expanded-Access Data

There were 5394 unique individual patient expanded-access IND applications during the study period, almost evenly split between individual patient INDs ($n = 2812$, 52%) and individual patient INDs for emergency use ($n = 2582$, 48%). Figure 1 presents these INDs by IND type. The average annual number of applications was 548 for individual patient and 512 for emergency use, with the highest number for each, 675 and 1061, respectively, occurring in FY 2014. During FY 2010-2014, the FDA authorized more than 98% of individual patient expanded-access requests received (99% and 97% allowed to proceed for emergency use and individual patient INDs, respectively). (These numbers are slightly different from what the FDA has presented elsewhere due to minor differences in methodology.)

Table 1 shows the top 10 FDA review divisions that received expanded access INDs, which together accounted for approximately 95% of individual patient expanded-access INDs; the remaining 12 divisions to which expanded access requests were submitted accounted for slightly less than 5% of applications. The majority of INDs were submitted to divisions that focus on infectious diseases (45%) and on oncology/hematology (37%). Table 2 presents the review divisions of the 10 most requested drugs during the study period. Together these 10 drugs accounted for almost 60% of all INDs submitted.

Overall, 3365 of the 5298 INDs allowed to proceed (64%) requested drugs that were approved for any indication by September 30, 2015. Figure 2 displays approval rates for INDs requested by application year and IND type. In each year except FY 14, approval rates were higher for individual patient INDs than for individual patient INDs for emergency use (range 46% to 71% for individual patient INDs and 46% to 83% for emergency-use INDs).

There were 408 unique drugs or unique fixed-combination drugs requested between FY 2010 and FY 2014. Table 3 shows that, overall, more unique drugs were requested using individual patient INDs than individual patient INDs for emergency use (305 and 182, respectively), whereas Figure 3 shows somewhat higher approval rates for drugs requested under individual patient INDs for emergency (range 36% to 48%) than for individual patient INDs for every year (range 32% to 40%). Overall, 30% (122/408) of all unique drugs for which expanded access was sought had been approved by September 30, 2015, including 39% of those originating in FY 2010 and 30% of those originating in FY 2014.

Figures 4 and 5 show the rate of approval over time, measured as the time since the first expanded-

Table 1. Top 10 Divisions to Which Individual Patient Expanded-Access INDs That Were Allowed to Proceed Were Submitted, FY 2010-2014

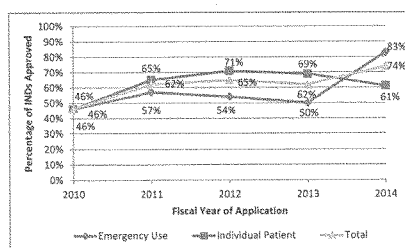
| Rank | Review Division | Number | Percentage |
|------|---|-------------|------------|
| 1 | Antiviral products | 1226 | 23 |
| 2 | Anti-infective products | 997 | 19 |
| 3 | Hematology products | 885 | 17 |
| 4 | Oncology products 1 | 848 | 16 |
| 5 | Gastroenterology and inborn errors products | 434 | 8 |
| 6 | Oncology products 2 | 223 | 4 |
| 7 | Gastroenterology products | 175 | 3 |
| 8 | Special pathogen and transplant products | 143 | 3 |
| 9 | Transplant and ophthalmology products | 128 | 2 |
| 10 | Neurology products | 103 | 2 |
| | Other divisions | 136 | 3 |
| | Total | 5298 | 100 |

Oncology products 1 include Division of Oncology Products 1 (DOP1) and Division of Drug Oncology Products (DDOP). Oncology products 2 include Division of Oncology Products 2 (DOP2) and Division of Biologic Oncology Products (DBOP), respectively, which were combined due to division restructuring and renaming during the study period. DBOP indicates biologic products; FY, fiscal year; IND, investigational new drug.

Table 2. Ten Most Requested Drugs Under Individual Patient Expanded-Access INDs That Were Allowed to Proceed, Presented by Review Division and Their Approval Status as of September 30, 2015, FY 2010-2014^a

| Rank | Review Division (Number of INDs) ^a | Number of Requests | Percentage of Requests | Approved for Any Indication ^b |
|------|--|--------------------|------------------------|--|
| 1 | Anti-infective products (727) Special pathogen and transplant products (81) Transplant and ophthalmology products (54) | 869 | 16.4 | Yes |
| 2 | Antiviral products (573) | 573 | 10.8 | No |
| 3 | Hematology products (437) | 442 | 8.3 | Yes |
| 4 | Gastroenterology and inborn errors products (232) Gastroenterology products (71) | 304 | 5.7 | No |
| 5 | Antiviral products (235) | 235 | 4.4 | No |
| 6 | Gastroenterology and inborn errors products (119) Gastroenterology products (54) | 173 | 3.3 | Yes |
| 7 | Drug oncology products (98) Oncology products 1 (36) Oncology products 2 (14) | 156 | 2.9 | Yes |
| 8 | Hematology products (94) Oncology products (50) | 153 | 2.8 | Yes |
| 9 | Transplant and ophthalmology products (24) Anti-infective products (89) Special pathogen and transplant products (21) | 134 | 2.5 | No |
| 10 | Antiviral products (120) | 120 | 2.3 | Yes |

IND indicates investigational new drug.

^aIncludes only divisions with more than 10 requests.**Figure 2.** Percentages of expanded-access INDs that were allowed to proceed for which the investigational drugs were approved for any indication by September 30, 2015, by IND type and application year, FY 2010-2014 (n = 5298). FY indicates fiscal year; IND, investigational new drug.

access application rather than by cohort year, for those INDs associated with drugs without a previous approval for any indication or dosage form. Figure 4 shows that 20% of INDs were for drugs that were approved within 1 year after the initial expanded access IND was submitted and that 33% were approved by 5 years after the initial submission. Figure 5 presents the same data by unique drug and shows that almost one-quarter of drugs requested under individual patient expanded-access INDs (including those for emergency use) received marketing approval by 1 year after the initial expanded-access IND was submitted, and 43% received approval by 5 years.

Table 3. Number of Unique Drug Expanded-Access Requests That Were Allowed to Proceed by IND Type and Year of Initial Request, FY 2010-2014

| Emergency Use | 2010 | 2011 | 2012 | 2013 | 2014 | All Years ^a |
|---------------------------------------|------|------|------|------|------|------------------------|
| Drug approved ^b by 9/30/15 | 29 | 28 | 25 | 27 | 26 | 74 |
| Drug not approved by 9/30/15 | 35 | 31 | 31 | 35 | 46 | 108 |
| Total | 64 | 59 | 56 | 62 | 72 | 182 |
| Individual patient | | | | | | |
| Drug approved by 9/30/15 | 30 | 36 | 33 | 40 | 38 | 86 |
| Drug not approved by 9/30/15 | 45 | 64 | 70 | 66 | 81 | 219 |
| Total | 75 | 100 | 103 | 106 | 119 | 305 |
| All INDs^c | | | | | | |
| Drug approved by 9/30/15 | 49 | 50 | 49 | 56 | 49 | 122 |
| Drug not approved by 9/30/15 | 78 | 91 | 93 | 94 | 114 | 286 |
| Total | 127 | 141 | 142 | 150 | 163 | 408 |

FY indicates fiscal year; IND, investigational new drug.

^a"All Years" total does not always add up to the sum of individual years, as drugs could have been requested in multiple years.^bFor any indication.^c"All INDs" total does not always add up to the sum of individual patient INDs and individual patient INDs for emergency use as unique drugs because drugs could have been requested under both.

Product Liability Information

A search of the 3 legal databases identified 58 items in WestlawNext, 18 items in Google Scholar, and 69 items in HeinOnline. On closer inspection, none of these represented product liability cases against pharmaceutical companies relating to personal injuries allegedly sustained while using drugs obtained under the expanded-access process. The search of Westlaw Next's news sources yielded no relevant articles.

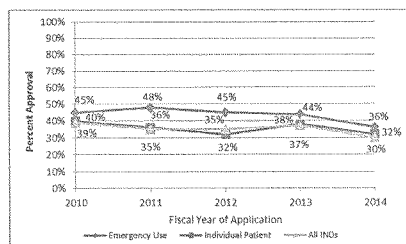


Figure 3. Percentage approval for any indication by September 30, 2015 of unique drugs for which expanded-access INDs were allowed to proceed by year of application, FY 2010-2014 (n = 408). FY indicates fiscal year; IND, investigational new drug.

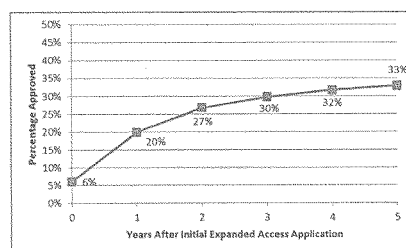


Figure 4. Percentage approval for any indication by September 30, 2015 for drugs for which expanded-access INDs were allowed to proceed, FY 2010-2014 (n = 2882). FY indicates fiscal year; IND, investigational new drug.

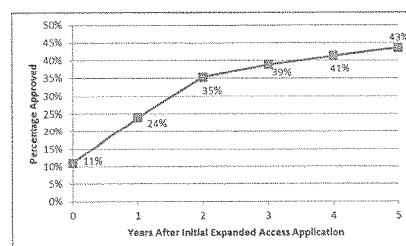


Figure 5. Percentage approval for any indication by September 30, 2015 for unique drugs for which expanded-access INDs were allowed to proceed, FY 2010-2014 (n = 471). FY indicates fiscal year; IND, investigational new drug.

Discussion

During FY 2010-2014, the FDA allowed more than 98% of the 5394 individual patient expanded-access requests received to proceed. As our analysis demonstrates, physicians and patients should not assume that

these drugs will later be approved for marketing by FDA. During the study period, for drugs not previously approved in any dosage form or for any indication, 24% of unique drugs and 20% of INDs received marketing approval by 1 year after initial submission; 43% and 33%, respectively, were approved by 5 years after initial submission. Expanded access provides just that: access. There is no guarantee that the product sought will be effective and/or safe, much less that it will be effective and/or safe for the particular patient, and these individual INDs are not purposed to collect data on the drug.⁷⁻¹⁰

The FDA's consideration of an expanded-access application generally comes only after the commercial sponsor has agreed to provide the investigational drug. The FDA cannot require the commercial sponsor to provide its investigational drug for expanded access use. Sponsors may choose not to do so for various reasons, including lack of available drug, lack of adequate safety information, or a desire to focus their attention on completing the clinical trials necessary to support an FDA marketing application. There is some emerging evidence that individual companies have rejected more applications for a single drug than the FDA has rejected for all drugs over this entire study period. For example, 1 company indicated that it had turned down 98 of 160 applications for a single drug in a 6-month period.¹¹ Another company turned down "hundreds" of applications for its drug over 2 years.¹² In contrast, in only 96 instances over the 5-year study period did the FDA not allow the expanded-access use to proceed.

Some have cited potential liability concerns as another reason companies may not provide expanded access to their drugs, but we did not identify information about product liability cases involving the use of a drug in an expanded-access program.

The FDA is also aware of concerns that adverse events occurring during expanded access could place a drug development program in jeopardy. In fact, the safety data from individual patient expanded access requests can be informative to the commercial sponsor and can contribute to the overall development program for the investigational drug. From a public health perspective, early identification of important adverse events is beneficial and is critical in the FDA's evaluation of a drug's benefit-risk profile. Moreover, the agency understands that patients who do not meet the entry criteria for clinical trials but are treated under expanded access might be at increased risk for serious adverse events because of their advanced disease, concomitant medications, and/or comorbidities. FDA reviewers of these adverse-event data understand the context in which the expanded-access use was permitted and evaluate any adverse event data obtained from an expanded-access submission within that context.²

A recent analysis by the FDA revealed that, over the last decade, spanning almost 11,000 expanded access requests, there were only 2 instances in which a clinical hold was placed on commercial drug development due to adverse events occurring under expanded access. In both instances the development of the drugs continued shortly after these issues were addressed and the holds were lifted.¹³

Recent FDA Efforts to Improve the Expanded Access Process

The FDA has undertaken several initiatives to streamline the process for physicians to request expanded access for individual patients. In response to feedback that the expanded-access application form was challenging for physicians to complete, in June 2016 the FDA finalized a streamlined form (Form FDA 3926) for individual patient expanded access that is estimated to take 45 minutes to complete and also reduces the number of required attachments from 7 to 1.³ At the same time, the FDA revamped its website and finalized 3 guidances (1 on the new form, 1 on charging for investigational drugs under an IND, and a more general guidance clarifying various aspects of expanded access).^{2,3,5} The agency also developed simple information sheets for patients and physicians. The FDA welcomes stakeholder input in our ongoing efforts to balance the potential benefits of expanded access to investigational drugs against their potential risks.

Conclusion

This analysis seeks to give physicians and patients a realistic perspective on the likelihood of a drug's approval as well as to provide certain information regarding the product liability risks for commercial sponsors in providing expanded access to investigational drugs. The FDA maintains a careful balance between permitting patients to obtain access to potentially beneficial drugs and protecting them from drugs that may have unknown risks. At the same time, the agency wishes to maintain the integrity of the clinical trials process, ultimately the best way to get safe and effective drugs to patients.

Acknowledgments

The authors wish to thank Daniel Sigelman for assistance in gathering the data related to product liability and Joanne Berger for research assistance.

Declaration of Conflicting Interests

Dr McKee, Dr Markon, Dr Chan-Tack, and Dr Lurie have no potential conflicts of interest related to this article.

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Right to Try ACRO Policy Statement

Over the past few years, legislation that would give terminally ill patients access to unapproved treatments, known as “Right-to-Try,” has gained momentum in a number of states and now in the U.S. Congress. As the organization representing the world’s leading clinical research organizations that each year conduct more than 7,000 clinical trials involving 1.3 million patients in more than 100 countries, ACRO is deeply committed to ensuring treatments are made available to patients in need, to the full extent possible, through the established clinical trials process in order to effectively monitor safety and efficacy. ACRO also supports measures to accelerate the drug discovery, development and approval process without sacrificing patient safety.

As such, ACRO’s view is that proposed Right-to-Try legislation is deeply flawed because it:

- contains insufficient patient protections;
- compromises the clinical trial process; and
- undermines the FDA’s authority to assess safety and effectiveness;

ACRO has significant concerns that including Right-to-Try provisions in the upcoming user fee reauthorization or any subsequent legislation would be detrimental to patients.

The Food and Drug Administration (FDA) currently administers a program for Expanded Access, also known as “Compassionate Use,” which gives patients the ability to access an investigational product, i.e., one that has not been approved by FDA, outside of a clinical trial. Compassionate Use is often used when a patient cannot participate in a clinical trial, because of “exclusion criteria” such as having more than one life-threatening disorder. Unlike Right-to-Try, under Expanded Access, a patient must meet certain conditions to participate, including: that the patient’s physician determines that there is no comparable therapy available to diagnose, monitor, or treat the patient’s disease or condition; that FDA determines that the probable risk to the patient from the investigational product is not greater than the probable risk from the disease or condition; and that the FDA determines that providing the investigational product will not interfere with the conduct of clinical trials to support marketing approval.

Clinical trials provide the pathway for a thorough assessment of the safety and efficacy of a drug, ensuring that patients and their health care providers have adequate information about a product’s risks and benefits. Yet, Right-to-Try efforts may exacerbate the problem of recruitment for those trials. According to the Tufts Center for the Study of Drug Development, 37% of clinical trial sites do not meet enrollment goals and 11% fail to enroll a single patient.

Patient recruitment and retention are two of the biggest challenges to clinical trials today. With Right-to-Try, patients could start taking an investigational therapy without ever pursuing the traditional trial route, making it even more difficult to meet enrollment goals. This would create an especially large recruitment hurdle for rare disease, orphan drug and pediatric trials. Compared to trials for other diseases, rare disease trials – those for diseases affecting less than 200,000 patients in the US -- are even harder to recruit for due to limited patient populations. If even a few rare disease patients were to opt for “Right-to-Try” rather than a clinical trial, for example, this could severely delay or compromise the entire drug development effort, placing the entire patient population at risk.



In 2015, all but 10 of 1,278 Compassionate Use requests (99.2%) were approved by the FDA. Applicants usually receive responses within four days of applying, and a recently streamlined FDA form takes about 45 minutes to complete.¹ Additionally, average response time for emergency use is one day or less. Provisions in the 21st Century Cures Act will further strengthen the FDA's Expanded Access program by requiring greater clarity on the policies of pharmaceutical companies and enhancing communication.

To further improve the accessibility of information about Expanded Access programs for patients and their providers, the Reagan-Udall Foundation plans to introduce an Expanded Access navigator, a portal of online resources that includes educational content, tools, and a contact directory. The Foundation hopes to promote the use of Compassionate Use through this effort. This portal is expected to launch in June, 2017.

Given the FDA's implementation of its current Compassionate Use policy, it is unclear that Right-to-Try legislation would provide any added benefit for individual patients in terms of access. Such legislation would, however, create potentially significant concerns for patient safety. This legislation could also lead to ethical challenges for future clinical research, weakening the informed consent process by diminishing the safety and risk/benefit data that should be available to every patient.

By circumventing the FDA, Right-to-Try eliminates utilizing the agency's objectivity, expertise and knowledge of treatments in various stages of development, in presenting the best options to the patient. Conversely, under Expanded Access, FDA review can require changes to treatment plans that are most beneficial to patients.

The mission of ACRO member companies is to ensure the safety of human subjects and maintain data integrity in clinical research; however, Right-to-Try places both objectives at risk. Recent federal Right-to-Try proposals would prevent FDA from considering adverse events arising out of the use of a product through the Right-to-Try path. This would undermine patient safety protections not only for the patients accessing the product outside of a clinical trial but also for the patients using the product once it is on the market.

ACRO notes the European Medicines Agency (EMA) has also provided recommendations on Compassionate Use. Similar to FDA's Compassionate Use policy, the EMA recommendation states that such compassionate access to investigational (non-approved) drugs should only be used when a patient is left without other treatment options. ACRO generally supports policies that conform to international norms for patient safety and best practices for clinical research.

ACRO believes that any effort to make investigational therapies available to patients outside of a clinical trial should include proper patient protections and avoid compromising the current FDA safety and effectiveness review process. For these reasons, ACRO does not support Right-to-Try legislation.

¹ Lurie P. Committee on Homeland Security and Government Affairs Hearing Testimony, U.S. Food and Drug Administration, available at <https://www.fda.gov/NewsEvents/Testimony/ucm522044.htm>

Adopted May 22, 2017



U.S. Department of Health & Human Services
U.S. Food and Drug Administration

Patient Access to Investigational Therapies

Many states across the country are considering so-called “Right to Try” legislation to provide patients with access to investigational therapies before they are approved by FDA. However, for over two decades, FDA has had processes in place to do just that. Expanded access, which is sometimes called “compassionate use,” supplements the clinical trials process. FDA believes enrollment in clinical trials remains the best option for patients wishing to gain access to investigational drugs—it assures adequate protection for patients and leads to the collection of data that could eventually result in FDA approval of the investigational therapy, which provides the broadest availability to patients. Patients who are not eligible for a clinical trial because of where they live, their age, or some other disqualifying factor have the option to seek expanded access if they have serious or life-threatening conditions and no comparable or satisfactory alternative is available.

FDA acts quickly in response to expanded access requests and allows almost all of them to proceed. In fact, FDA authorized more than 99 percent of individual patient expanded access requests received in Fiscal Years 2010-14. Emergency requests are often granted immediately over the phone. For non-emergencies, the Agency strives to respond promptly and, in general, does not take longer than 30 days. Moreover, FDA continues to improve its processes. In response to feedback from physicians that the expanded access form was challenging, in February 2015, FDA announced the development of a new draft form for individual patient expanded access that is estimated to take only about 45 minutes to complete.

Expanded access to investigational treatments requires the active involvement and cooperation of parties other than FDA, including drug companies and healthcare providers. FDA can encourage drug companies to offer expanded access to their investigational therapies, but companies may choose not to do so for various reasons, including lack of available drug or a desire to focus their attention on completing the clinical trials necessary to support FDA approval.

Facts:

- FDA has a longstanding and well-established process for individual patients to obtain access to investigational therapies—expanded access, which is sometimes called compassionate use.
- FDA allows almost all expanded access requests to proceed: more than 99 percent of individual patient expanded access requests made from 2010-14 were granted.
- FDA responds to individual patient expanded access requests quickly; emergency requests are often granted immediately over the phone. For non-emergencies, the Agency strives to respond promptly and, in general, does not take longer than 30 days.
- FDA is improving expanded access to make it easier to apply; a new form for individual patient expanded access requests is estimated to take physicians only about 45 minutes to complete.

FDA is an important part of the process and helps to ensure patients are adequately protected from unnecessary risk. The independent scientific review provided by FDA is an essential component of patient protection, particularly because one is considering treatments for which safety and efficacy have not been demonstrated.

Contact Us

For more information, please contact FDA’s Office of Legislation at 301-796-8900, or see FDA’s website: <http://www.fda.gov/ExpandedAccess>.

Updated: June 2016

| | | |
|---|---|--|
| DEPARTMENT OF HEALTH AND HUMAN SERVICES Food and Drug Administration Individual Patient Expanded Access Investigational New Drug Application (IND) <i>(Title 21, Code of Federal Regulations (CFR) Part 312)</i> | | Form Approved: OMB No. 0910-0814 Expiration Date: April 30, 2019 See PRA Statement on last page. |
| 1. Patient's Initials | | 2. Date of Submission (mm/dd/yyyy) |
| 3.a. Initial Submission <input type="checkbox"/> Select this box if this form is an initial submission for an individual patient expanded access IND, and complete only fields 4 through 8, and fields 10 and 11. | 3.b. Follow-Up Submission <input type="checkbox"/> Select this box if this form accompanies a follow-up submission to an existing individual patient expanded access IND, and complete the items to the right in this section, and fields 8 through 11. | Investigational Drug Name Physician's IND Number |
| 4. Clinical Information | | |
| Indication | | |
| Brief Clinical History (Patient's age, gender, weight, allergies, diagnosis, prior therapy, response to prior therapy, reason for request, including an explanation of why the patient lacks other therapeutic options) | | |
| 5. Treatment Information | | |
| Investigational Drug Name | | |
| Name of the entity that will supply the drug (generally the manufacturer) | | |
| FDA Review Division (if known) | | |
| Treatment Plan (Including the dose, route and schedule of administration, planned duration, and monitoring procedures. Also include modifications to the treatment plan in the event of toxicity.) | | |
| 6. Letter of Authorization (LOA), if applicable (generally obtained from the manufacturer of the drug) | | |
| <input type="checkbox"/> I have attached the LOA. (Attach the LOA; if electronic, use normal PDF functions for file attachments.) Note: If there is no LOA, consult the Form Instructions. | | |
| 7. Physician's Qualification Statement (Including medical school attended, year of graduation, medical specialty, state medical license number, current employment, and job title. Alternatively, attach the first few pages of physician's curriculum vitae (CV), provided they contain this information. If attaching the CV electronically, use normal PDF functions for file attachments.) | | |
| 8. Physician Name, Address, and Contact Information | | |
| Physician Name (Sponsor) | | Email Address of Physician |
| Address 1 (Street address, No P.O. boxes) | | Telephone Number of Physician |
| Address 2 (Apartment, suite, unit, building, floor, etc.) | | |
| City | State | Facsimile (FAX) Number of Physician |
| ZIP Code | | Physician's IND number, if known |

9. Contents of Submission

This submission contains the following materials, which are attached to this form (select all that apply). If none of the following apply to the follow-up communications, use Form FDA 1571 for your submission.

- | | |
|---|--|
| <input type="checkbox"/> Initial Written IND Safety Report | <input type="checkbox"/> Change in Treatment Plan |
| <input type="checkbox"/> Follow-up to a Written IND Safety Report | <input type="checkbox"/> General Correspondence |
| <input type="checkbox"/> Annual Report | <input type="checkbox"/> Response to FDA Request for Information |
| <input type="checkbox"/> Summary of Expanded Access Use (treatment completed) | <input type="checkbox"/> Response to Clinical Hold |

10. Request for Authorization to Use Form FDA 3926

- I request authorization to submit this Form FDA 3926 to comply with FDA's requirements for an individual patient expanded access IND.

11. Certification Statement: I will not begin treatment until 30 days after FDA's receipt of a completed application and all required materials unless I receive earlier notification from FDA that treatment may begin. I also agree not to begin or continue clinical investigations covered by the IND if those studies are placed on clinical hold. I also certify that I will obtain informed consent, consistent with Federal requirements, and that an Institutional Review Board (IRB) that complies with the Federal IRB requirements will be responsible for initial and continuing review and approval of this treatment use. I understand that in the case of an emergency request, treatment may begin without prior IRB approval, provided the IRB is notified of the emergency treatment within 5 working days of treatment. I agree to conduct the investigation in accordance with all other applicable regulatory requirements.

WARNING: A willfully false statement is a criminal offense (U.S.C. Title 18, Sec. 1001).

Signature of Physician

To enable the signature field, please fill out all prior required fields. For a list of required fields which have not yet been filled out, please click here.

Date

For FDA Use Only

| | | |
|---------------------|--|---|
| Date of FDA Receipt | Is this an emergency individual patient IND? <input type="checkbox"/> Yes <input type="checkbox"/> No | Is this indication for a rare disease (prevalence < 200,000 in the U.S.)? <input type="checkbox"/> Yes <input type="checkbox"/> No |
| IND Number | | |

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Statement of Diana Zuckerman, PhD, President
On behalf of the National Center for Health Research
Regarding Right to Try Legislation
House Energy and Commerce Subcommittee on Health
October, 3, 2017

Chairman Burgess, Ranking Member Pallone, and distinguished Subcommittee Members:
Thank you for the opportunity to submit hearing testimony for the record. The National Center for Health Research is a non-profit organization which analyzes medical and scientific data and produces original health-related research to inform patients, the general public, and policymakers. We advocate for patients and consumers to have access to safe, effective, and affordable drugs and medical devices. We accept no funding from the pharmaceutical or medical device industries.

We all agree that terminally ill patients should receive the best medical treatment as quickly as possible. Some terminally ill patients are willing to take big risks to have a chance to live longer. Unfortunately, many of us know desperate patients whose efforts to “try anything” made their remaining days miserable and left their families even more devastated. What can and should Congress do to make sure that desperate patients won’t be exploited, or suffer even more painful deaths as a result of legislation? That is the key question before you today.

It is essential that all Members of Congress understand what the various Right to Try bills would do. A key issue is to understand what it means to give access to any experimental treatment that has been in **at least one clinical trial**. The earliest clinical trials (known as **Phase I**) **often don’t include even one patient**. Instead Phase I trials can include “healthy volunteers” that are much less likely to be harmed by an experimental drug or device than a terminally ill patient would.

In addition, these first (Phase I) clinical trials study **very small numbers of people**, and **do not study whether or not a product works**. They are designed to determine the immediate risks on just a few healthy volunteers or patients. Since so few people are studied, even **if a treatment is immediately and painfully fatal to 10% of patients, for example, these first clinical trials probably would not be able to provide that crucial information**.

The Right to Try bill introduced by Representatives Griffith and Brat do not even require that a first clinical trial be completed – it can have just started. In other words, there is no way that a patient could be warned about any terrible risks of those treatments.

The Johnson Right to Try bill (S 204) requires that a Phase I clinical trial be completed. That is an improvement over the Griffith and Brat bill, but it is important to know that 85% of drugs that successfully complete Phase I clinical trials are **later found to be unsafe or ineffective and are therefore never approved by the FDA. So neither version would help most patients.**

In contrast, the FDA's current expanded Access Program requires at least some evidence that an experimental treatment might possibly be helpful. That's not a very restrictive safeguard, but it does help protect many patients. The FDA routinely utilizes what the agency terms "compassionate waivers" for very ill patients when doctors request them, and FDA grants such requests 99% of the time.

Another important issue for Congress to consider is whether these bills would exploit patients financially. The experimental drugs provided through the current FDA Expanded Access program are provided for free most of the time, or "at cost." The same is true for clinical trials. The Johnson bill also protects patients from financial exploitation by limiting what experimental treatments can cost. The Griffith and Brat bill allows **companies to charge whatever they want** to dying patients desperate for access to any experimental drug or device – even one that has absolutely no evidence that it is either safe or effective. **That means that desperate patients could be required to pay exorbitant fees for the "Right to Try" to be treated like guinea pigs. Many families would feel tremendous guilt if they could not afford to do so.**

FDA's compassionate use program could be improved, and improvements are already underway thanks to the Navigator program that the FDA has recently initiated with the Reagan Udall Foundation. Other access issues are inherent in the situation where patients want drugs that are not yet being manufactured in large numbers or when the companies are reluctant to provide drugs that they fear will be harmful to patients who are too ill to benefit. The GAO's July 2017 report was generally supportive, with a few recommendations for improvement. And, GAO pointed out that most experimental drugs distributed under Expanded Access eventually obtain FDA approval. In other words, the program is doing what was intended – giving patients earlier (usually free) access to experimental drugs that will eventually be proven safe and effective.

In addition to harming individual patients, making unsafe treatments available for sale harms our entire drug development enterprise, by eliminating the incentive for patients to participate in clinical trials that would help millions of patients in the future. If HR 1020 was to become law, then it is likely that the richest patients will buy access to experimental treatments and only the middle-class and low-income patients will participate in clinical trials. Reputable companies would continue to study new drugs and devices in clinical trials, but progress would be slowed because of difficulty attracting enough patients to participate in clinical trials. Meanwhile, scam artists and fly-by-night companies would be motivated to make as much money as possible on dangerous or worthless experimental drugs for as long as they are available, and HR 1020 and would make it impossible to gather information about how dangerous their products are.

Such problems have long been documented regarding unproven treatments sold at outrageously high prices in Mexico and elsewhere, where some patients have been irreparably harmed or killed because they sought unproven treatments that were marketed dishonestly. Indeed, tragedies arising from the “right to try” unregulated medical sales of the 19th Century and early 20th Century were the reason FDA was created, to protect patients and consumers.

To improve Right to Try legislation, Congress should:

1. Ensure that experimental treatments cannot be sold at a profit by companies or medical professionals;
2. Ensure that all experimental treatments have been proven safe in completed Phase I or Phase II trials conducted on a reasonable number of patients (not healthy volunteers);
3. All experimental drugs and devices available through RTT should be studied as part of FDA’s regulatory process;
4. Information about harmful side effects and adverse events should be required to be reported to the FDA by the physicians.

We strongly urge this Committee to reject the Right To Try legislation that is currently under consideration, because it would undermine the successful FDA compassionate waiver program already in place to enable patients to have access to experimental drugs for free or at cost.

Thank you for the opportunity to present our views.



September 12, 2017

Dear Members of the U.S. House:

As advocates for Americans facing terminal and life-threatening illnesses, we write to urge your support for S. 204, the Trickett Wendler, Frank Mongiello, Jordan McLinn & Matthew Bellina Right to Try Act of 2017, that was passed unanimously by the U.S. Senate. This bill will help protect the right of sick Americans to try to save their own lives. Fewer than 3 percent of cancer patients can participate in clinical trials, and for less common diseases like ALS and deadly Duchenne muscular dystrophy, the numbers are even lower. Right to Try gives people who cannot participate in trials a new path to access promising treatments.

Right to Try is Bipartisan: As of this writing, 37 states have adopted Right to Try laws with overwhelming bipartisan support. In half of those states the laws have passed with unanimous support in the state House and Senate; in Arizona, voters approved the measure with nearly 80% of the popular vote. The laws have been signed by 25 Republican Governors and 11 Democratic Governors.

Right to Try is Safe: The doctor-recommended treatments available to patients under Right to Try laws must have passed an FDA-approved Phase I clinical trial and be in an active Phase II or Phase III trial or under active consideration by the FDA. The risk for a patient trying an investigational treatment under Right to Try is the same as for those in clinical trials because they are the same treatments. Right to Try simply allows more patients to have access to treatments that are being safely used in clinical trials.

Right to Try Protects Clinical Trials & FDA-Authority: Right to Try laws rely on the FDA's approval process to determine which treatments in clinical trials terminal patients can access. Right to Try only applies to treatments that have successfully completed the FDA's first phase of trials and remain in ongoing FDA-sanctioned phase II or III trials where they are ultimately working towards approval. This alternative and limited pathway leaves the FDA trial system intact. Only treatments that the FDA itself has determined are worthy of continued investigation are eligible. If at any point or for any reason a treatment no longer remains in a clinical trial and is no longer working towards FDA approval, a patient cannot access it under Right to Try.

Right to Try Patient Data will be Collected & Reported: Drug manufacturers will be required to report adverse events to the FDA. But, this data alone cannot be used to stop a trial, or to delay or deny approval of the treatment, unless the FDA believes not using the data will create a significant public health risk. The FDA will still be allowed to have conversations with the manufacturer about the adverse events, request more

2

Right To Try Letter of Support

information, and even recommend changes in trial protocols. Simply put, the FDA will still decide whether to approve or reject a treatment based on the clinical trial results.

Right to Try is a Last Resort: Right to Try is only for patients whose doctors have determined are facing a life-threatening illness, who have exhausted all available treatments, and who cannot participate in a clinical trial. This law is aimed at helping a narrow set of patients who have truly run out of options, but who might be helped by a treatment that is helping people in clinical trials. Right to Try is the opposite of Right to Die: it is for people who are not ready to stop fighting. We owe them the opportunity to try treatments that are being given to the lucky few in clinical trials.

Right to Try is Voluntary: No patient, doctor, or drug manufacturer is required to seek or provide treatment under a state Right to Try law. If a patient wants to try an investigational treatment that his or her doctors and the manufacturer do not think will be helpful, they are under no obligation to provide that treatment. Right to Try can only be used in situations where the patient signs an informed consent document that fully explains all the risks the patient is assuming, and the doctor and manufacturer agree that the treatment could be helpful to the patient.

Right to Try is Working: While most state laws do not include central reporting requirements, we know the law is being used to successfully treat patients. Dr. Ebrahim Delpassand, an oncologist in Houston, and his colleagues at Excel Diagnostics, have used the Texas Right to Try law to treat nearly 100 terminal neuroendocrine cancer patients with a new compound that is under final review by the FDA. Many of these patients were given only months to live and two years later are still with us and enjoying a robust quality of life.

Right to Try provides a new path for people who are out of options to access promising and safe investigational treatments. We urge you to support this critical law that will help the Americans we represent at no cost to the government.

Sincerely,

Abigail Alliance for Better Access to Developmental Drugs
 Athletes for Care
 Coalition for Access Now
 Cures Within Reach
 Digestive Disease National Coalition
 Dystrophic Epidermolysis Bullosa Research Association of America
 Federal Law Enforcement Officers Association
 Fire Fighters with Parkinson's Disease
 Foundation to Open Access to Cancer Cures
 Gastroparesis Patient Association for Cures and Treatments, Inc.

3

Right To Try Letter of Support

Hope Now for ALS
KK125 Ovarian Cancer Research Foundation
Little Hercules Foundation
METAvivor Research and Support, Inc.
Have a Heart Foundation
One Woman Many Lakes
Patients for Stem Cells
Rare Disease United Foundation
Teen Cancer America
Tomorrow's Cures Today Foundation



September 28, 2017

Dear U.S. House Members:

As advocates for individual rights, human dignity, and limited government representing millions of Americans, we write to urge your support for S. 204, the Trickett Wendler, Frank Mongiello, Jordan McLinn Right to Try Act of 2017. This bill will help protect the right of sick Americans to try to save their own lives. Fewer than 3 percent of cancer patients can participate in clinical trials, and for less common diseases like ALS and deadly Duchenne muscular dystrophy, the numbers are even lower. Right to Try gives people who cannot participate in trials a new path to access promising treatments.

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Right To Try Letter of Support

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Right to Try provides a new path for people who are out of options to access promising and safe investigational treatments. When you're fighting for your life, you shouldn't have to fight the government too. We urge you to support these critical laws that will help the Americans we represent at no cost to the government.

Sincerely,

Goldwater Institute
 Americans for Prosperity
 Campaign for Liberty
 Cascade Policy Institute
 Competitive Enterprise Institute
 Freedom Partners Chamber of Commerce
 FreedomWorks
 Generation Opportunity
 Georgia Public Policy Center

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Right To Try Letter of Support

Idaho Freedom Foundation
James Madison Institute
Libertas Institute
Liberty Coalition
Mississippi Center for Public Policy
Rio Grande Foundation
The LIBRE Initiative

RON JOHNSON, WISCONSIN, CHAIRMAN
 JOHN M. CAHN, ARIZONA
 JIM PORTMAN, OHIO
 AND PAUL KENTUCKY
 ANNE S. LANKFORD, OKLAHOMA
 DONALD B. ENZI, WYOMING
 JOHN HOEVEN, NORTH DAKOTA
 TREV DAINES, MONTANA
 CLAIRE M. CASILL, MISSOURI
 THOMAS R. CARPER, DELAWARE
 JON TESTER, MONTANA
 HEIDI HEITKAMP, NORTH DAKOTA
 GARY C. PETERS, MICHIGAN
 MARGARET WOOD-HASSAN, NEW HAMPSHIRE
 KAMALA D. HARRIS, CALIFORNIA

CHRISTOPHER R. HIXON, STAFF DIRECTOR
 MARGARETE E. DAUBS, MINORITY STAFF DIRECTOR

United States Senate
 COMMITTEE ON
 HOMELAND SECURITY AND GOVERNMENTAL AFFAIRS
 WASHINGTON, DC 20510-6250

October 2, 2017

The Honorable Greg Walden
 Chairman
 Committee on Energy & Commerce
 U.S. House of Representatives
 2125 Rayburn House Office Building
 Washington, DC 20515

The Honorable Frank Pallone, Jr.
 Ranking Member
 Committee on Energy & Commerce
 U.S. House of Representatives
 2322A Rayburn House Office Building
 Washington, DC 20515

The Honorable Michael C. Burgess, M.D.
 Chairman
 Subcommittee on Health
 U.S. House of Representatives
 2336 Rayburn House Office Building
 Washington, DC 20515

The Honorable Gene Green
 Ranking Member
 Subcommittee on Health
 U.S. House of Representatives
 2470 Rayburn House Office Building
 Washington, DC 20515

Dear Congressmen Walden, Pallone, Burgess, and Green:

We write to provide additional information to consider as part of the Subcommittee on Health's hearing on October 3, 2017.¹ We understand this hearing will include discussion of S. 204, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017,² a bill that passed the Senate unanimously on August 3rd.

As the sponsors of S. 204, named after just a few of the amazing patients who have inspired our work on this issue, you can understand we are passionate about opening potential pathways to treatment for terminal patients when no other alternatives are available. We are proud of this measure's bipartisan support in the U.S. Senate, including 46 cosponsors. Over two-thirds of states have already adopted versions of this legislation, with over 97 percent of state legislators voting in favor.

When Chairman Lamar Alexander and Ranking Member Patty Murray of the Senate Committee on Health, Education, Labor & Pensions raised concerns about certain provisions in the bill, we were happy to work with them in a collaborative fashion to successfully address those issues. As such, the bill as passed by the Senate reflects sensible changes, including:

- (1) greater transparency surrounding reporting serious adverse events;

¹ U.S. House Committee on Energy & Commerce, Subcommittee on Health, "Examining Patient Access to Investigational Drugs," Hearing, October 3, 2017.

² S. 204, 115th Cong. (2017). The bill is an update of a previous bill introduced in May 2016 which garnered 43 bipartisan cosponsors. S. 2912, 114th Cong. (2016).

Reps. Walden, Pallone, Burgess, and Green
 October 2, 2017
 Page 2

- (2) a uniform federal definition of eligible patients;
- (3) a cap on the price charged for treatments;
- (4) further clarification that other provisions governing regulation of drugs still apply (e.g., good manufacturing practices, labeling requirements, etc.);
- (5) provisions maintaining the FDA's use of adverse outcomes; and
- (6) clarified liability provisions to protect good actors and exclude bad actors.

These changes were made in addition to the bill's existing provisions that explicitly maintain incentives for patients to participate in clinical trials and pursue other available treatments, require certification by a doctor that the patient has exhausted available options, and limit eligible treatments to those that have completed a Phase I clinical trial.

Last Congress, the Senate Committee on Homeland Security and Governmental Affairs, which has jurisdiction over the regulatory process, held two hearings on this issue. We heard testimony from terminally ill patients across the country—such as Matt Bellina of Bucks County, Pennsylvania and Jordan McLinn of Indianapolis, Indiana—for whom the FDA's status quo is not working. We also heard from a brave doctor in Texas who successfully treated patients under his state's Right to Try law despite risk of federal sanction.³

We have always been careful not to represent Right to Try as a promise for a cure—Congress cannot legislate a miracle. This pursuit has always been about protecting hope. Patients (along with their doctors) are informed, capable of making rational decisions, and have the right to do whatever they can to try to save their own lives.

Finally, we understand that there may be some discussion regarding who ought to be eligible to participate in Right to Try—whether the definition contained in the legislation is too broad. Our test has always been a simple one: will the legislation benefit Jordan McLinn, a seven year-old boy with Duchenne Muscular Dystrophy, a terminal disease by anyone's standards, but not one that will likely take his life within six months, one year, or even two.

Every day that Congress fails to act is a day during which potentially thousands of patients lose hope. As Frank Mongiello, who suffers from amyotrophic lateral sclerosis, pled when we first introduced the Senate bill over 16 months ago, “We don't have the luxury of time.”⁴ On behalf of Frank, Matt, Jordan, and Trickett's family, we must do whatever we can to ensure that Right to Try is passed by the House and signed into law as soon as possible. We are urging the House to take up and pass S. 204 without amendment.

Thank you for working with us on this legislation.

³ U. S. Senate Committee on Homeland Security and Governmental Affairs, “Exploring a Right to Try for Terminally Ill Patients,” Hearing, September 22, 2016 (statement of Dr. Ebrahim Delpassand), <https://www.hsgac.senate.gov/hearings/exploring-a-right-to-try-for-terminally-ill-patients>.

⁴ U.S. Senate Committee on Homeland Security & Governmental Affairs, “ICYMI: Johnson Introduces the Trickett-Wendler Right to Try Act,” May 11, 2016, <https://www.hsgac.senate.gov/media/majority-media/icymi-johnson-introduces-the-trickett-wendler-right-to-try-act>. The full details of the Committee's efforts related to Right to Try can be found here: <https://www.hsgac.senate.gov/media/majority-media/johnson-right-to-try-bill-passes-senate>.

Reps. Walden, Pallone, Burgess, and Green
October 2, 2017
Page 3



Ron Johnson
Chairman

Sincerely,



Joe Donnelly
U.S. Senator

cc: The Honorable Joe Barton
The Honorable Fred Upton
The Honorable John Shimkus
The Honorable Tim Murphy
The Honorable Marsha Blackburn
The Honorable Steve Scalise
The Honorable Robert Latta
The Honorable Cathy McMorris
Rodgers
The Honorable Gregg Harper
The Honorable Leonard Lance
The Honorable Brett Guthrie
The Honorable Pete Olson
The Honorable David McKinley
The Honorable Adam Kinzinger
The Honorable Morgan Griffith
The Honorable Gus Bilirakis
The Honorable Bill Johnson
The Honorable Billy Long
The Honorable Larry Bucshon
The Honorable Bill Flores
The Honorable Susan Brooks
The Honorable Markwayne Mullin
The Honorable Richard Hudson
The Honorable Chris Collins
The Honorable Kevin Cramer
The Honorable Tim Walberg
The Honorable Mimi Walters
The Honorable Ryan Costello
The Honorable Buddy Carter

The Honorable Bobby Rush
The Honorable Anna Eshoo
The Honorable Eliot Engel
The Honorable Diana DeGette
The Honorable Michael Doyle
The Honorable Janice Schakowsky
The Honorable G.K. Butterfield
The Honorable Doris Matsui
The Honorable Kathy Castor
The Honorable John Sarbanes
The Honorable Jerry McNerny
The Honorable Peter Welch
The Honorable Ben Lujan
The Honorable Paul Tonko
The Honorable Yvette Clarke
The Honorable David Loebsack
The Honorable Kurt Schrader
The Honorable Joseph Kennedy
The Honorable Tony Cárdenas
The Honorable Raul Ruiz
The Honorable Scott Peters
The Honorable Debbie Dingell

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FIFTEENTH CONGRESS
Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115
Majority (2017) 275-2927
Minority (2017) 228-3841
November 17, 2017

Dr. Scott Gottlieb
Commissioner of Food and Drugs
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

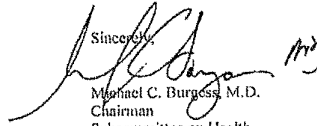
Dear Dr. Gottlieb:

Thank you for appearing before the Committee on Energy and Commerce on October 3, 2017, to testify at the hearing entitled "Examining Patient Access to Investigational Drugs."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on December 5, 2017. Your responses should be mailed to Zack Dareshori, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, DC 20515 and e-mailed in Word format to zack.dareshori@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Committee.

Sincerely,

Michael C. Burgess, M.D.
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment

[Dr. Gottlieb did not answer submitted questions for the record by the time of printing.]

Attachment — Additional Questions for the Record

The Honorable Chris Collins

1. I posed this question to Mr. Gottlieb in the second panel but I would also like to get your thoughts. When going through the drug development process, it is important to design a clinical trial that will have statistical significance. It is from my understanding that trials must have a P value of 0.05. Meaning, I am confident that “x” drug will be effective 95 percent of the time... based on these clinical trials.

Question: Have you all, as stakeholders, considered coming together on alternative measures, like requesting the scientific community to change the designation of statistical significance for drugs that treat terminally-ill patients? If so, could you please explain?

2. There is a common frustration among some patients who are desperate to gain access to a potential life-saving drug. No government can compel companies to make clinical trials available beyond their capacity - due to a lack of resources and other factors. In addition, there is no standard for evaluating patient requests exists in the industry.

Question: How would you advise the FDA or industry to streamline this process to allow 100 percent of applications to pass through?

The Honorable Frank Pallone, Jr.

1. Adverse Events

Some of the country's largest and most reputable physician and patient advocacy organizations are opposed to the recently passed Senate “Right-to-Try” legislation. In addition to your organization, the American Society of Clinical Oncology, the Cancer Action Network of the American Cancer Society, the National Organization for Rare Disorders, and Public Citizen have all written in opposition to this Committee. As I understand it, one of the main concerns related to this legislation is the potential for patient harm as a result of removing FDA from the role of reviewing Expanded Access requests. I am also worried about the limits on FDA's ability to access information regarding adverse events and other clinical outcomes.

You note in your testimony that patients pushing for Expanded Access deserve accurate information about whether the potential benefits outweigh the risks, however, I am concerned that patients may be unable to do this unless they have access to complete information.

- a) Dr. Sigal, how should information on adverse events regarding investigational products be shared with FDA and the patient community? And do you believe that such information should be taken into consideration when evaluating a drug for approval?
- b) Although the Senate "Right to Try" legislation allows FDA to consider adverse events --after jumping through considerable hurdles --and requires manufacturers to report on an annual basis about known serious adverse events, is there anything in the bill that requires doctors or distributors to report these adverse events? If a patient suffers a horrible adverse event related to the use of a drug under "Right-to-Try, are there any protections in place under this bill to ensure that the next patient using this drug and his or her physician knows about that adverse event and can make a truly informed choice?

2. Informed Consent

Although the Senate "Right to Try" legislation allows FDA to consider adverse events --after jumping through considerable hurdles --and requires manufacturers to report on an annual basis about known serious adverse events, is there anything in the bill that requires doctors or distributors to report these adverse events? If a patient suffers a horrible adverse event related to the use of a drug under "Right-to-Try, are there any protections in place under this bill to ensure that the next patient using this drug and his or her physician knows about that adverse event and can make a truly informed choice?

- a) Dr. Sigal, do you believe that the recently passed Senate legislation would ensure that patients provide adequate informed consent and are fully informed regarding the use of an eligible investigational drug as defined in the legislation?
- b) What further patient protections do you believe are needed to ensure that truly "informed" consent is received from eligible patients?

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FIFTEENTH CONGRESS
Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115
Majority (202) 225-2327
Minority (202) 225-3841
November 17, 2017

Mr. John Dicken
Director of Health Care
U.S. Government Accountability Office
441 G Street, N.W.
Washington, DC 20548

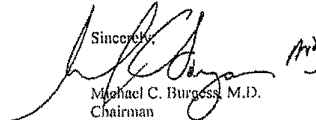
Dear Mr. Dicken:

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Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

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Sincerely,

Michael C. Burgess, M.D.
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment

[Mr. Dicken did not answer submitted questions for the record by the time of printing.]

Attachment --- Additional Questions for the Record

The Honorable Frank Pallone, Jr.

1. Adverse Events Under S. 204

As you state in your testimony and the July 2017 report, manufacturers noted that the lack of clear information related to the use of adverse events data can influence their decision to give patients access to their drugs due to concerns with the potential for a clinical hold on the drug and a delay in its development.

The Senate passed "Right-to-Try" legislation would prevent FDA from utilizing adverse event data unless the agency could justify that it is "critical to determine safety". Manufacturers would also be required to submit annual reports summarizing adverse event data.

- a) GAO recommended that FDA clearly communicate how the agency intended to use adverse event data from expanded access. In your opinion, does the requirement in the Senate passed legislation that FDA can only use such data when it is "critical to determine safety" help to address the concerns GAO heard from manufacturers?
- b) Although the Senate "Right to Try" legislation allows FDA to consider adverse events --after jumping through considerable hurdles --and requires manufacturers to report on an annual basis about known serious adverse events, is there anything in the bill that requires doctors or distributors to report these adverse events? If a patient suffers a horrible adverse event related to the use of a drug under "Right-to-Try, are there any protections in place under this bill to ensure that the next patient using this drug and his or her physician knows about that adverse event and can make a truly informed choice?

2. GAO's Recommendation for FDA's Expanded Access Program

As you know, manufacturers are required to submit safety data to FDA with information on adverse events from clinical trials in addition to adverse events from expanded access use. This data could then potentially be taken into consideration in FDA's approval process for the product.

- a) In your review of the program how often did you find that FDA considered adverse event data from expanded access use in the approval process? Will you

also further elaborate on why FDA noted it may not use adverse event data from expanded access use?

- b) What guidance is currently available from FDA on their use of adverse event data from expanded access use?

3. GAO's Findings

As you stated in your testimony GAO released an extensive report on FDA's expanded access program last July. GAO's report found that of the nearly 5,800 expanded access requests received by FDA from 2012 to 2015, FDA approved 99 percent. This incredibly high approval rate seems to demonstrate that FDA is highly responsive to the Expanded Access requests that agency receives. In addition to the rate of approval, I want to better understand the timeline by which FDA responds to those submitting Expanded Access requests.

- a) In your findings how quickly did FDA respond to both emergency and non-emergency requests?
- b) Though we know it's extremely rare for FDA to deny an expanded access request could you expand on why, in a handful of cases, FDA might not allow a request to move forward?

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FIFTEENTH CONGRESS
Congress of the United States
House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115

Majority (202) 225-2827
Minority (202) 225-3641

November 17, 2017

Ms. Naomi Lopez-Bauman
Director of Healthcare Policy
Goldwater Institute
500 East Coronado Road
Phoenix, AZ 85004

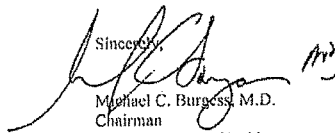
Dear Ms. Lopez-Bauman:

Thank you for appearing before the Committee on Energy and Commerce on October 3, 2017, to testify at the hearing entitled "Examining Patient Access to Investigational Drugs."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

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Thank you again for your time and effort preparing and delivering testimony before the Committee.

Sincerely,

Michael C. Burgess, M.D.
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment

Attachment – Responses to Questions for the Record

Questions from the Hon. Chris Collins

1. N/A. The Goldwater Institute is not seeking to change or alter the current FDA approval process nor have we explored alternative standards for drug approvals for terminally-ill patients.

2. Whether the FDA approves 99 percent or 100 percent of all Expanded Access applications, the current process ignores two important, fundamental issues:

1) Expanded access is so tangled in red tape that only about 1,200 patients per year are even able to submit compassionate use requests to the FDA—even though over half a million Americans die annually of cancer alone, for example.

2) The federal government should not require dying patients who have exhausted all government-approved options to beg the government for permission to obtain treatment to save their lives—treatment that is already being given to the patients in clinical trials or to those who can afford to travel overseas – if their physician is recommending an investigational treatment and if the manufacturer is willing to make the treatment available.

3. S. 204 reflects changes made as part of the stakeholder process that occurred in the U.S. Senate, including the addition of language addressing how the FDA will treat adverse events and additional liability protections.

Because Right to Try participation requires manufacturer participation, physician certification is duplicative in that a manufacturer will already evaluate a patient's eligibility to participate in a trial.

It is important to recognize that stakeholder processes have also occurred in the 39 states where Right to Try is now law. While these state laws are modeled after Goldwater Institute Right to Try legislation, variations reflect the stakeholder processes that took place in each state.

While it is heartening to see the recent FDA improvements to the expanded access program which are the result of the heightened attention and awareness that are the result of the Right to Try movement, the expanded access application process continues to fall short. Shorter forms are not fixing the system's fundamental flaws. The current system fails to acknowledge the potentially millions of patients who don't have the opportunity to submit the application and requires the terminal patient to navigate federal bureaucracy and red tape for the chance to save their own life.

4. The proposed legislation retains the federal authority to use adverse event information, but clarifies the circumstances and procedures for how the information will be used to halt or end a trial, for example. Despite repeated requests, the current FDA

guidance and policy has not clarified if and how adverse events stemming from compassionate use will be used. Absent this clarity, there is little incentive for companies to provide investigational treatments.

5. The Goldwater Institute acknowledges that the FDA approves almost all Expanded Access/Compassionate Use applications that it receives. We contend that a program that is supposed to serve millions of potential terminal patients is an obstacle when only 1,200 patients per year are even able to apply. More important, the federal government should not require dying patients who have exhausted all government-approved options to beg the government for permission to obtain treatment to save their lives.

GREG WALDEN, OREGON
CHAIRMAN

FRANK FALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FIFTEENTH CONGRESS
Congress of the United States
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COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115
Majority (203) 225-2927
Minority (203) 225-3941
November 17, 2017

Lieutenant Commander Matthew Bellina, USN, Ret.
38 Heron Road
Holland, PA 18966

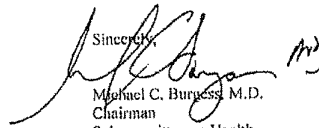
Dear Lieutenant Commander Bellina:

Thank you for appearing before the Committee on Energy and Commerce on October 3, 2017, to testify at the hearing entitled "Examining Patient Access to Investigational Drugs."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

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Sincerely,

Michael C. Burgess, M.D.
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment

[LCDR Bellina did not answer submitted questions for the record by the time of printing.]

Attachment — Additional Questions for the Record

The Honorable Chris Collins

1. I posed this question to Mr. Gottlieb in the second panel but I would also like to get your thoughts. When going through the drug development process, it is important to design a clinical trial that will have statistical significance. It is from my understanding that trials must have a P value of 0.05. Meaning, I am confident that “x” drug will be effective 95 percent of the time... based on these clinical trials.

Question: Have you all, as stakeholders, considered coming together on alternative measures, like requesting the scientific community to change the designation of statistical significance for drugs that treat terminally-ill patients? If so, could you please explain?

2. There is a common frustration among some patients who are desperate to gain access to a potential life-saving drug. No government can compel companies to make clinical trials available beyond their capacity - due to a lack of resources and other factors. In addition, there is no standard for evaluating patient requests exists in the industry.

Question: How would you advise the FDA or industry to streamline this process to allow 100 percent of applications to pass through?

3. Some have argued that because the expanded access program is burdensome and difficult to navigate, many physicians are discouraged from applying. I understand that Cures has a provision that requires manufacturers to have publicly accessible compassionate use policies for drugs treating serious or life-threatening conditions.

Question: Could first explain this discouragement and expand on how this expanded access policy will affect this community?

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

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WASHINGTON, DC 20515-6115
Majority (202) 225-2827
Minority (202) 225-3641
November 17, 2017

Mr. Kenneth I. Moch
President & CEO
Cognition Therapeutics, Inc.
2403 Sidney Street
Pittsburgh, PA 15203

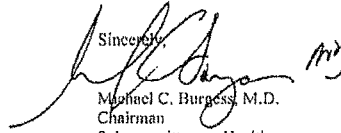
Dear Mr. Moch:

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Sincerely,

Michael C. Burgess, M.D.
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment

Answers to Additional Questions for the Record from The Honorable Chris Collins

1. I posed this question to Mr. Gottlieb in the second panel but I would also like to get your thoughts. When going through the drug development process, it is important to design a clinical trial that will have statistical significance. It is from my understanding that trials must have a P value of 0.05. Meaning, I am confident that "x" drug will be effective 95 percent of the time... based on these clinical trials.

Question: Have you all, as stakeholders, considered coming together on alternative measures, like requesting the scientific community to change the designation of statistical significance for drugs that treat terminally-ill patients? If so, could you please explain?

There have been many discussions and analyses, by a broad range of interested and involved parties, as to what is the best way to design and implement clinical trials and whether the traditional measure of "statistical significance" is the correct approach.

To date, no new approach has prevailed.

One suggestion I have is that for diseases that are designated as imminently life threatening, the p value that is acceptable for initial clinical trials could be modified to "less than 0.1", versus less than 0.05. This asks the question of whether a person would accept a 90 percent probability that the activity seen in a clinical trial was due to the activity of the experimental medicine as opposed to a 95% probability.

Also, please see the attached Opinion Piece from [The Hill](#), which I would like included in the record. This article addresses the role of expanded access and the potential to use data from these open label trials to increase the breadth of availability of an experimental medicine after it has been approved for a different indication.

2. There is a common frustration among some patients who are desperate to gain access to a potential life-saving drug. No government can compel companies to make clinical trials available beyond their capacity - due to a lack of resources and other factors. In addition, there is no standard for evaluating patient requests exists in the industry.

Question: How would you advise the FDA or industry to streamline this process to allow 100 percent of applications to pass through?

I would not do this. The issue of availability of investigational medicines under expanded access will not in any way be impacted by having the FDA approve 100

percent of the applications it receives. Please see the attached Op-Ed from The Wall Street Journal, which I also would like included in the record. This addresses the complexities of the development process for new medicines and role and complexities of expanded access in this process.

As I wrote in this Op-Ed, "Each drug is different, the testing and data required for FDA approval are different, and patient populations are different. Expanded access is not a substitute for clinical trials."

3. Some have argued that because the expanded access program is burdensome and difficult to navigate, many physicians are discouraged from applying. I understand that Cures has a provision that requires manufacturers to have publicly accessible compassionate use policies for drugs treating serious or life-threatening conditions.

Question: Could first explain this discouragement and expand on how this expanded access policy will affect this community?

While I am a strong proponent of expanded access, I am not in favor of the proposed Right to Try legislation for reasons that I described in my testimony before the Health Subcommittee last October.

That being said, I believe that the sole benefit of this Right to Try legislation to date has been to increase the awareness of expanded access, and this is a good thing. There are many reasons that patients and/or physicians do not pursue expanded access for a critically or terminally ill patient, from lack of awareness of the process, to lack of awareness of potentially available experimental medicines, to paperwork within institutions, to concerns about the cost of this process. None of these issues is addressed by the current State or proposed Federal Right to Try legislation.

While I cannot speak for all companies developing experimental medicines, I can say that most of the companies that I am aware of have programs to help physicians understand and navigate the application for expanded access.

However, it is also clear that there are additional burdens within the physician's hospital/medical institution - additional layers of paperwork and approvals from hospital risk management (such as Institutional Review Boards) that are required in order to dose a critically or terminally ill individual with an experimental medicine. Gaining these approvals may just take hours, but can also take much longer depending on the institution and the medical professionals involved in the expanded access request.

GREG WALDEN, OREGON
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

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COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115
Majority (201) 225-2927
Minority (202) 225-3641

November 17, 2017

Dr. Alison Bateman-House
Assistant Professor
Department of Population Health
New York University (NYU) Langone Health
227 East 30th Street
7th Floor, #754A
New York, NY 10016

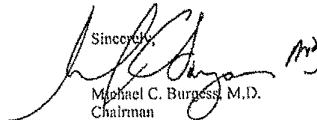
Dear Dr. Bateman-House:

Thank you for appearing before the Committee on Energy and Commerce on October 3, 2017, to testify at the hearing entitled "Examining Patient Access to Investigational Drugs."

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Thank you again for your time and effort preparing and delivering testimony before the Committee.

Sincerely,

Michael C. Burgess, M.D.
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment

[Dr. Bateman-House did not answer submitted questions for the record by the time of printing.]

Attachment — Additional Questions for the Record

The Honorable Chris Collins

1. I posed this question to Mr. Gottlieb in the second panel but I would also like to get your thoughts. When going through the drug development process, it is important to design a clinical trial that will have statistical significance. It is from my understanding that trials must have a P value of 0.05. Meaning, I am confident that “x” drug will be effective 95 percent of the time... based on these clinical trials.

Question: Have you all, as stakeholders, considered coming together on alternative measures, like requesting the scientific community to change the designation of statistical significance for drugs that treat terminally-ill patients? If so, could you please explain?

2. There is a common frustration among some patients who are desperate to gain access to a potential life-saving drug. No government can compel companies to make clinical trials available beyond their capacity - due to a lack of resources and other factors. In addition, there is no standard for evaluating patient requests exists in the industry.

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Question: Could first explain this discouragement and expand on how this expanded access policy will affect this community?

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CHAIRMAN

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RANKING MEMBER

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WASHINGTON, DC 20515-6115
Majority (202) 225-2927
Minority (202) 225-3641

November 17, 2017

Dr. Ellen V. Sigal
Chairperson and Founder
Friends of Cancer Research
1800 M Street, N.W.
Suite 1050 South
Washington, DC 20036

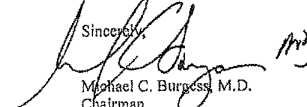
Dear Dr. Sigal:

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Sincerely,

Michael C. Burgess, M.D.
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment

[Dr. Sigal did not answer submitted questions for the record by the time of printing.]

Attachment — Additional Questions for the Record

The Honorable Chris Collins

1. Single-patient expanded access requests for both emergency and non-emergency generally occur during or after phases I, II, or III clinical trials. Phase I includes 20-80 patients, Phase II ranges between a few dozen to hundreds of patients, and Phase III includes hundreds to thousands of patients.

Question: For those that apply to the Expanded Access Program, at what Phase do patients typically apply to most?

2. As noted, FDA granted over 99% of the expanded access requests it has received since 2010.

Question: For the 1% that are not approved, which criteria are patients not meeting to allow them to be granted access?

3. As you know, the 21st Century Cures Act included monumental bipartisan reform on patient-focused drug development, advancing new drug therapies, modern trial design and evidence development, and patient access to therapies and information. And it would appear you have already begun that work based on your Work Plan of the FDA Innovation Account submitted to Congress in June.

Question: How will your efforts in this mass overhaul help terminally ill patients gain access to life saving drugs or clinical trials?

4. When going through the drug development process, it is important to design a clinical trial that will have statistical significance. It is my understanding that trials must have a P value of 0.05. Meaning, I am confident that “x” drug will be effective 95 percent of the time... based on these clinical trial.

Question: Has the FDA or scientific community considered changing the designation of statistical significance for drugs that treat terminally-ill patients?

5. Some have argued that because the expanded access program is burdensome and difficult to navigate, many physicians are discouraged from applying. I understand that Cures has a provision that requires manufacturers to have publically accessible compassionate use policies for drugs treating serious or life-threatening conditions.

Question: Could you explain this “discouragement” and expand on how this expanded access policy will affect this community?

The Honorable Frank Pallone, Jr.

1. Adverse Events:

GAO's recent report on FDA's Expanded Access program noted several times that one of the concerns from manufacturers, if not the main concern for manufacturers, was the potential use of adverse event data disrupting the clinical development of the new drug.

- a) How frequently are adverse events reported as a part of the Expanded Access Program?
- b) According to FDA data, there have only been two cases of adverse events associated with expanded access use that led to any disruption of the drug's FDA development process. Will you provide details related to these two cases and how the FDA used the adverse event data?
- c) In general, the GAO report also found that greater clarity as to how FDA would use adverse event data associated with expanded access would help manufacturers to make decisions regarding whether or not to make their treatment available in an expanded access situation. On the day of the hearing, FDA released revised guidance to provide greater clarity on this issue. Do you believe that this action will be sufficient to provide greater clarity to manufacturers, or will the agency be taking additional actions?

2. Expanded Access Program Requests and Approvals

In your testimony you noted that FDA has allowed almost all Expanded Access requests the agency receives to proceed. I understand last year that the agency received 1,554 Expanded Access requests, and approved 1,545 of these requests.

- a) Can you provide an example of why FDA would have not approved a request for expanded access?
- b) In your opinion, have state laws, such as the Right to Try laws in 37 states, helped improve patient access to investigational drugs they would not have had otherwise? Have these laws impacted the FDA's approval process or request approval rate?
- c) In your opinion, is federal legislation necessary to improve patients' ability to receive investigational drugs, or are there additional steps you could take administratively that would help to achieve this goal?

3. Eligible Treatments

I want to better understand when it may be appropriate to provide access to an investigational treatment. Many of the State "Right-to-Try" laws would allow any investigational drug that has completed a Phase 1 Clinical Trial to be made available without FDA oversight. This is also true of S. 204. However, legislation introduced in the House, H.R. 1020, would allow any drug or device that has been the subject of any clinical trial to be eligible for Expanded Access.

- a) Will you discuss at what point in the clinical development process it may be appropriate to make available an investigational drug to patients?
- b) Can you explain what is typically learned about a drug during Phase 1 Clinical Trials?
- c) Are you concerned about exposing patients to investigational drugs that have not demonstrated any efficacy or that may lack meaningful safety data?