RESEARCHING THE POTENTIAL MEDICAL BENEFITS

AND RISKS OF MARIJUANA

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WEDNESDAY, JULY 13, 2016

United States Senate,

Subcommittee on Crime and Terrorism,

Committee on the Judiciary,

Washington, D.C.

The Subcommittee met, pursuant to notice, at 2:45 p.m., in room SD-226, Dirksen Senate Office Building, Hon. Lindsey Graham, Chairman of the Subcommittee, presiding.

Present: Senators Graham, Grassley, Whitehouse, Klobuchar, and Blumenthal.

OPENING STATEMENT OF HON. LINDSEY GRAHAM, A U.S. SENATOR FROM THE STATE OF SOUTH CAROLINA

Chairman Graham. The hearing will come to order. Our colleagues Senators Booker and Gillibrand are voting, and what I thought we would do, with the permission of my Ranking Member, is just make an opening statement, and we will wait for them to arrive--I think they are on the way--and get started with the hearing.

I appreciate Senator Whitehouse working with us to have this hearing. Let me tell you where I am coming from. I hear a lot of stories about how medical marijuana is providing relief to people who are in very dire straits. I

also hear about how marijuana is a gateway drug that gets people going down the wrong road. So what I am trying to do is to inform myself as much as possible.

Two goals: There is legitimate medical relief to be had from cannabis in a controlled way. That makes sense to me. But I do not want to make medical marijuana a back door to just de facto legalization.

So we are going to hear from some people on the enforcement side and the research side. This is an important issue to many families and I think to the country as a whole. Congress needs to take a stand because 25 States, including the District of Columbia, have some form of medical marijuana that is legally available to their citizens under State law, which is in violation of Federal law, and Federal authorities tend to just not enforce this problem or deal with this problem. So I think it would be good for Congress to get involved and give some direction, and whatever we decide, we enforce, because we are a Nation of laws.

So we see Senator Booker here, and I will turn it over to Senator Whitehouse for an opening statement.

OPENING STATEMENT OF HON. SHELDON WHITEHOUSE, A U.S. SENATOR FROM THE STATE OF RHODE ISLAND

Senator Whitehouse. Thank you very much, Chairman. It is always a treat to work with Chairman Graham on

issues, and this is a good one for us to hold this hearing on. So I thank him, and I also want to thank the witnesses who will testify today.

Our focus will be on marijuana research, specifically on the nature of and the rationale for barriers to research surrounding the benefits and risks of cannabis. While research suggests that THC and other cannabinoids may have potential in the treatment of pain, nausea, epilepsy, obesity, wasting disease, addiction, autoimmune disorders, and other conditions, marijuana's classification as a Schedule I substance means that those interested in conducting research face substantial hurdles.

For starters, there is currently only one facility, in Mississippi, that is licensed to supply the marijuana for federally sanctioned research in the United States. Even minor modifications to a research plan involving cannabis require researchers to submit a supplemental protocol for approval by the DEA. Once researchers receive the approved marijuana, they need to store it in its own securely locked, substantially constructed, kryptonite-proof cabinet--not kryptonite-proof; I was exaggerating--rather than merely in such a way as to, and I quote, "obstruct the theft or diversion of the controlled substance," which is the case for Schedule II, Schedule III, Schedule IV, and Schedule V substances. I doubt anybody present in this room finds

marijuana to be so dangerous as to require that special treatment.

I look forward to hearing from my colleagues and from the Government and academic experts here today, and I trust that while we may not all agree on specific approaches advocated at the State or national levels, we ought to agree that our policies should be informed by robust research and sound science, which we should support.

Chairman Graham. Well said.

Senator Booker, thank you for appearing before the Committee. The stage is yours.

STATEMENT OF HON. CORY BOOKER, A UNITED STATES SENATOR FROM THE STATE OF NEW JERSEY

Senator Booker. I am deeply appreciative of both of the gentlemen, my colleagues sitting before me, and thank you for holding what I think is--when it comes to alleviating human suffering, this is probably one of the more important hearings the Senate has had this year.

So I want to just thank Ranking Member Whitehouse, thank Chairman Graham, I want to thank all the members of the Subcommittee on Crime and Terrorism, and, again, thank you for inviting me here to testify today.

Senator Graham, I want to especially thank you for your support of the bipartisan legislation that Senator Gillibrand, Senator Paul, and I authored, which I will speak about in a moment. But right now, we have a Nation where individuals and families are relying on medical marijuana to treat and manage what are often debilitating medical conditions. This is a fact in America today that sick people are using medical marijuana to alleviate often debilitating conditions.

I am hopeful that today's hearing will be an important step to making this drug more readily available to patients, veterans, children, to families who really need it.

Now, the profound common sense of this issue which is being seen by millions and millions of voters around the

country is that we know that right now veterans, patients, parents, and children could really be benefiting from this. This is not just a hypothetical or a question. We now know from the experience of millions that there are benefits of medical marijuana. We know that broad conditions of medical professionals--broad coalitions, excuse me, of medical professionals believe that marijuana should be an option for medical purposes. And we know from study after study after study and, again, the experience of thousands and thousands of suffering Americans that medical marijuana can treat a variety of life-altering conditions, going from chronic pain to Parkinson's disease, which my father suffered and ultimately died from, post-traumatic stress disorder, epilepsy, and multiple sclerosis.

We also know that Federal policy in this space is out of step with common-sense, fiscally prudent, and compassionate policies that are already existing on the State level. Twenty-five States and the District of Columbia have passed laws establishing medical marijuana programs, and an additional 17 States have either passed laws regarding the use of CBD oil, a compound within marijuana without THC, or limited access to medical marijuana.

Despite all of these developments, Federal barriers and bureaucracies are impeding innovation and potentially life-

saving research on medical marijuana. We must end the classification of marijuana as a Schedule I drug, meaning that it lacks no medicinal value, no medical value whatsoever, and it has a high potential for abuse.

Understand that as a Schedule I drug, marijuana shares the same classification as LSD, as heroin. This actually defies logic and common sense. In fact, we are in the midst of an opioid abuse epidemic when even highly dangerous opioids are not listed as Schedule I; they are actually listed as Schedule II drugs, while leaving marijuana as a Schedule I drug.

And even CBD, as I mentioned earlier, an oil substance made from the marijuana plant that contains virtually no THC, none whatsoever, meaning you cannot experience a high from the drug, is a Schedule I drug. This, again, defies logic and common sense, that CBD, which has been proven to be helpful against horrible seizures like Dravet syndrome, which cripples the development of many children in our country, that they cannot get access to CBD even without the THC in the drug.

And so we also have to just end the DEA monopoly on medical marijuana research. Currently, the University of Mississippi, through a Federal contract, possesses the only DEA license to grow cannabis for medical research in the United States. As Ranking Member Whitehouse was speaking

about, this monopoly on scientific research has really no basis, and without it, drug availability for research would undoubtedly improve.

No person living with a debilitating disease in America should have to have a life of pain when a possible treatment is available and they are barred from accessing it. We must embrace what is just common-sense inquiry, scientific inquiry, broader understanding. We must embrace pathways towards research, and we must do it with a greater sense of urgency in our country because so many are suffering.

How many more people are going to have to suffer because of the Federal bureaucracy, because of Federal inaction, because of congressional inaction? Too many people have already suffered because of continued inaction such as this, like a constituent of mine who had to pick up and move her family out of my State to Colorado just to get the drug that helped control her son's seizures. These folks are marijuana refugees.

And to make matters worse, people using medical marijuana to treat debilitating illnesses and pain may be obeying a State's law, but they are violating Federal law, which is a Catch-22 that puts themselves and their families at a great risk of prosecution and incarceration.

There are so many stories like my constituent's, and as long as there are, we cannot rest until we find a remedy to

this problem. We must put an end to what is not only an abuse of common sense but sheer madness in the face of the suffering that is going on in our country. We must treat our citizens with the respect that they deserve.

And so we have a bill, the Compassion Access to Research Expansion and Respect States Act, the CARERS Act, which is comprehensive, it is rational, and it should become law. The bill would, among other provisions, lift barriers on marijuana treatment for patients and families. Under current law, our veterans are banned from getting the medical treatment they so desperately need to relieve their pain, even if they are in States that allow medical marijuana. Too many parents are unable to get the medical treatment their children need. Highly trained professionals, doctors, and scientists are unable to prescribe and recommend drugs that they know could alleviate suffering for their patients. And otherwise law-abiding citizens, like many in my State, are fearful of unnecessary, expensive, and life-disrupting litigation.

What our bill would do is reschedule marijuana from Schedule I to Schedule II to accepted medical use, allow States to import CBD, recognized treatment for epilepsy and seizures. It would provide veterans access to prescribed medical marijuana in certain States. And it would permit financial services and banking for marijuana dispensaries

and, finally, expand opportunities for research, which would allow experts to test the drug to understand the effects of the drug and how it can be best utilized.

Americans are struggling with these life-altering conditions. They deserve Federal laws that are fair and compassionate, not ones that add additional burdens on research and science, as well as add to the extreme stress many patients and families face.

We as a Nation are better than this. We are instead a Nation that seeks to help and not hinder, heal and not hurt. We must change these laws. It is time to fix our broken drug policy that lacks compassion for those in pain. It is time for Congress to support abundant research. It is time to allow States' medical professionals, scientists to make these decisions, decisions that are rooted in facts and evidence.

The CARERS Act would move our country forward, end senseless barriers to medical research, and help countless individuals gain access to the care they need. And so I urge this Committee and encourage this Committee in the pathway that you have taken to take up these issues and to work to pass the CARERS Act.

I want to thank you for allowing me to testify, and I am happy to see right now I am joined by my colleague from that State across the Hudson River--"New York," I think it

is called--and I am grateful to see you here.

Chairman Graham. Thank you, Senator Booker. Thank you very much.

Senator Gillibrand.

STATEMENT OF HON. KIRSTEN GILLIBRAND, A UNITED STATES SENATOR FROM THE STATE OF NEW YORK

Senator Gillibrand. Thank you, Chairman Graham and Ranking Member Whitehouse, for holding this vital hearing about the science behind medical marijuana. I have met with many families in my State who desperately need access to this medicine. Many of them have severely ill children, and some of these children have literally 100 seizures a day. These families have met with doctors who have told them that medical marijuana could drastically reduce the number of seizures that their children suffer from. But if they take that advice, these families would have to break a Federal law to get access. That does not make any sense.

I know some people are saying that we should wait until there is more research before changing the laws, but the one thing that is blocking the research is the law. Federal law defines cannabis as a Schedule I drug, which, by definition, means no medical use. Schedule I designation also triggers the most restrictive limitations on research. It means that for someone to perform medical research on marijuana, they first have to obtain that Schedule I license. This is more difficult to get than a Schedule II license. Schedule I means that researchers have to identify a Schedule I manufacturer to supply the study. In the case of marijuana, there is only one supplier allowed by the DEA in the whole

country, the University of Mississippi, through the National Institute of Drug Abuse.

Schedule I means researchers have a much higher bar to meet for preventing diversion when the DEA inspects their facilities, including installing bolted safes, which are not practical for most clinical settings.

Schedule I also means if a researcher makes any change to his study or protocol at any point, they have to stop the study until the DEA approves the change without any timeline for those approvals, creating costly delays and impeding research.

Finally, Schedule I means that a researcher must personally administer the drug to each patient, which is extremely difficult to do if a study has large numbers of patients.

On top of this, Federal sources such as the NIH and the VA are much less likely to fund research on therapeutic uses for Schedule I substances because, by definition, they have no accepted medical use.

Because of these unnecessary barriers, last year only two researchers in the entire country were able to legally obtain cannabis for research in humans. How can we get the information we need about this medicine if our laws are blocking scientists from doing the basic research? The Federal Government needs to catch up with the medical

community and the public.

State lawmakers and voters in 42 States, including New York, my home State, have already recognized that medical research is showing that medical marijuana can alleviate symptoms and even treat a variety of illnesses, from MS to cancer to severe forms of epilepsy. Unfortunately, the Federal laws do not allow any medical use of marijuana even in the States where it is legal.

Under current law, patients and doctors have no treatment options or must use dangerous alternatives that often have severe side effects, such as opioids. Many patients are substituting medical marijuana for addictive prescription opioids, and they are avoiding those severe side effects while saving taxpayers' dollars.

A recently published study shows that States that have implemented medical marijuana laws have saved over $160 million in Medicare Part D costs. I have introduced a bill with Senator Booker and Senator Paul that would lift these barriers to research and allow doctors, not the Government, to decide if medical marijuana is the best option for their patients. The bill is called the "CARERS Act," and it would finally allow patients and families in States where medical marijuana is legal to access the medical care without fear of prosecution.

Families should not have to violate the Federal law and

risk arrest just to get the medicine they need. And just to describe a couple of these families, when I have met the children, their mothers say to me, "My child has 100 seizures a day. Any one of those seizures could kill her. If I get access to CBD oil, those seizures stop, and she gets one or two a month."

So you can imagine how important that medicine is to them. One little girl named Charlotte Figi is the reason why it is called "Charlotte's Web," which is one of these CBD oils. It had a miracle effect on her. So you cannot say these drugs do not have effects. They have medical effects. And for this one particular class of patient, it is life-saving effects.

Thank you.

Chairman Graham. Thank you very much, Senator Gillibrand.

We are ready for our next panel.

Chairman Graham. While we wait to have the panel seated, I would ask unanimous consent to put in the record testimony from Aaron Smith, executive director of the National Cannabis Industry Association; Institute for Behavior and Health, testimony of Robert DuPont; Cannabis and Medical Properties, Bertha Madras; and Robert Capecchi, to the United States Judiciary Subcommittee on Crime and Terrorism, the Director of Federal Policies, Marijuana Policy Project. So I ask that those statements be submitted for the record.

Senator Whitehouse. Without objection. And may I ask also that Ranking Member Patrick Leahy's statement join those in the record.

Chairman Graham. Without objection. Any other member who wants to submit statements, we will allow them to do that.

[The statements follows:]

/ SUBCOMMITTEE INSERT

Chairman Graham. Our first panel, we are going to stipulate that you are very smart people, have done a lot of things in your lives, so I am just going to introduce where you work.

Dr. Susan Weiss, Ph.D., Associate Director for Scientific Affairs, National Institute on Drug Abuse, National Institute of Health.

Dr. Douglas Throckmorton, Deputy Center Director for Regulatory Programs, Food and Drug Administration.

The floor is yours. You have great academic backgrounds and real-world experience, and thank you for coming. Dr. Weiss.

STATEMENT OF HON. SUSAN R.B. WEISS, PH.D.,
DIRECTOR, DIVISION OF EXTRAMURAL RESEARCH,
NATIONAL INSTITUTE ON DRUG ABUSE, NATIONAL
INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES, BETHESDA, MARYLAND

Ms. Weiss. Thank you. Chairman Graham, Ranking Member Whitehouse, and members of the Subcommittee, thank you for inviting me to participate in this hearing to review the state of the science on the therapeutic potential of marijuana and its constituent compounds and to discuss ways of facilitating more research in this important area.

In light of the rapidly evolving landscape regarding the medical use of marijuana and marijuana-derived compounds, it is important to review what we do and do not know about their therapeutic potential.

The marijuana plant contains more than 400 compounds, including over 100 cannabinoids. The majority of the research on the therapeutic potential of marijuana has focused on two cannabinoids: delta-9-THC and cannabidiol, or CBD.

Most cannabinoids exert their effects by interacting with cannabinoid receptors which come in two variations: CB1 and CB2. These are found in the brain and the immune system, respectively. The euphoric effects of THC are caused by its activation of CB1 receptors. CBD, however,

has a very low affinity for these receptors and, consequently, does not produce euphoria or intoxication. Its mechanisms of action are not well understood.

There is significant research suggesting the potential therapeutic value of cannabinoids in numerous health conditions. To date, the FDA has approved three cannabinoid medications: dronabinol, a synthetic form of THC; and very recently a liquid version of dronabinol; and nabilone, a synthetic that is similar to THC. These are approved to treat severe nausea and vomiting in cancer patients undergoing chemotherapy and wasting in patients with AIDS.

However, for the most part, patients across the country are using marijuana plant products or extracts that have not undergone rigorous clinical trials, are not regulated for consistency or quality, and are being used for medical conditions within an insufficient or no evidence base supporting these products' effectiveness.

What does research tell us about the therapeutic potential of marijuana and cannabinoids? In March of 2016, NIH convened a research summit to review the state of the science on both the harms and therapeutic potential of marijuana and other cannabinoids. While there has been remarkable progress in our understanding of how the endocannabinoid system works, which holds great promise for new medications development, there remains a dearth of

evidence from clinical studies regarding the benefits of marijuana or its components. One of the notable exceptions is the mounting evidence for cannabidiol in the treatment of severe forms of pediatric epilepsy.

Within the published scientific literature, there have been more than 70 clinical trials exploring the therapeutic effects of marijuana or its constituent cannabinoids for various health conditions. These studies have suggested potential therapeutic value for the treatment of Tourette syndrome, sleep disorders, substance use disorders, social phobia, neuropathic pain, and psychosis in patients with schizophrenia.

While this sounds like a lot, most of these trials would not meet the rigor required for FDA approval because of small numbers of participants, short durations, or other factors that were not well controlled. However, multiple recent reviews, including one by the American Academy of Neurology, concluded that there is strong evidence for the efficacy of marijuana-derived cannabinoids for spasticity and pain associated with multiple sclerosis and moderate evidence for THC and nabiximols, which is a combination extract of THC and CBD, also known as Sativex, for neuropathic pain.

Additionally, preclinical research studies in animals or cells has provided evidence that some cannabinoids may

have antioxidant, neuroprotective, anti-inflammatory, anti-tumor, and anti-anxiety properties.

NIH supports a broad portfolio of research on cannabinoid compounds and other possible tools to manipulate the function of the endocannabinoid system. In fiscal year 2015, NIH supported 281 projects totaling over $111 million on cannabinoid research, including 49 projects examining the therapeutic properties of cannabinoids.

There is a pressing need for more cannabinoid research related to various compounds, dose levels, therapeutic outcomes, and adverse effects. However, the progress of therapeutics development and clinical trials has been slow. This is due in part to the increased time, costs, and administrative efforts associated with research on these and other Schedule I compounds, as you have already heard, and also the currently limited diversity of marijuana supply for research purposes, and the conflicting Federal and State laws which hinder the ability to do research with marijuana from State dispensaries or other sources.

Though the research is not yet sufficient to support additional drug approval for marijuana or other cannabinoid compounds, addressing these challenges will facilitate more rigorous clinical research and accelerate progress. NIDA will continue to work closely with other Federal agencies to do so, and NIH will continue to support research on the

therapeutic and harmful effects of marijuana and cannabinoids.

Thank you again for inviting me here, and I look forward to any questions you may have.

[The prepared statement of Ms. Weiss follows:]

Chairman Graham. Thank you.

Dr. Throckmorton?

Senator Whitehouse. You might want to move your microphone a little closer to your mouth.

STATEMENT OF DOUGLAS C. THROCKMORTON, M.D., DEPUTY DIRECTOR FOR REGULATORY PROGRAMS, CENTER FOR DRUG EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, SILVER SPRING, MARYLAND

Dr. Throckmorton. Chairman Graham, Ranking Member Whitehouse, members of the Subcommittee, thank you for this opportunity to discuss the role that the FDA plays in regulating marijuana in the United States.

First, let me be clear. In addition to the important work the FDA has in overseeing the approval and use of prescription drugs from marijuana and its constituents, we understand the importance of supporting the efficient and scientific assessment of marijuana and drug development. Marijuana contains compounds with real potential to provide new treatments for important diseases, and rigorous studies are needed to assess their potential and, where appropriate, develop and deliver those new drugs for use by Americans.

FDA continues to believe that the drug approval process established by Congress represents the best way to ensure the safe and effective new medicines for marijuana are available as soon as possible for the largest numbers of the U.S. public.

First, FDA is the agency that is responsible for the assessment and regulation of new drugs in the United States.

The Federal Food, Drug, and Cosmetics Act requires that drugs be shown to be safe and effective for their intended use before marketing. In addition, drugs must be shown to be manufactured consistently, lot to lot, with high quality. Because many factors influence the makeup of plant materials, such as temperature, time of year, and location, this essential part of drug development presents special challenges when the drug is being developed from a botanical source, such as marijuana.

To address these challenges and to speed development, FDA has established a Botanical Review Team and revised and recently published guidance to investigators to give recommendations on how to study plant-derived drugs.

As a part of our work to regulate prescription drugs, FDA also provides specific recommendations to the Drug Enforcement Administration, or DEA, on drugs and other products that have the potential to be abused, so-called controlled substances, including marijuana. While DEA is the lead Federal agency responsible for regulating controlled substances and enforcing the Controlled Substances Act, FDA, working with NIDA provides scientific recommendations about appropriate controls for drugs with abuse potential.

To make this recommendation, we are responsible for preparing the so-called eight-factor analysis, which is a

document that is used to assess how likely a drug is to be abused. At the request of DEA, in 2001 and again in 2006, FDA conducted a review of the available data on marijuana and an eight-factor analysis and recommended that marijuana remain in Schedule I, the most restrictive schedule, both because of its high risk for abuse and because there was not sufficient evidence that marijuana had an accepted medical use in the United States. DEA is currently in the process of evaluating two citizen petitions regarding the scheduling of marijuana.

Next, let me turn to the work FDA is doing to support efficient development of drugs derived from marijuana as a part of our larger mission to promote the availability of safe and effective medical products for Americans in all therapeutic areas.

To accomplish this, we have developed and are using a number of flexible and innovative approaches to expedite drug development. In this area, for example, FDA has granted fast-track designation, a provision intended to facilitate the development and expedited review of promising new therapies to the investigational cannabidiol product Epidiolex. One goal of these expedited mechanisms is to speed drug availability for patients. I have also spoken personally to the parents of children with seizure disorders. I understand the importance of making

investigational products like Epidiolex available to patients quickly, even while the products continue to be studied for approval whenever possible.

To this end, FDA has strongly supported the work done by GW Pharmaceuticals which has announced that they have established more than 20 expanded access programs for Epidiolex to treat these patients with epilepsy syndromes. To date, well over 400 patients have received Epidiolex through these programs.

While doing what we can to speed the pace of development for promising investigational products, we are also mindful of protecting consumers and have taken actions in 2015 and again earlier this year against unapproved products making egregious health care claims that allegedly contained cannabidiol and other cannabinoids. Some of these products allegedly containing cannabidiol claimed to be effective in the treatment of cancer, rheumatoid arthritis, and Ebola. We tested and found that some of them contained no cannabidiol. In other cases, they contained different levels than what the manufacturers claimed. Marketing such products does more than simply defraud customers. These products and their marketing create false hope in those seeking relief from serious medical conditions for themselves or their loved ones, including children.

Finally, FDA understands the importance of working with

other Federal agencies on marijuana. In addition to the work I mentioned on scheduling with NIDA and DEA, our scientific staffs work closely together to understand the effects of marijuana-derived compounds such as cannabidiol. Through this week, FDA has identified a specific clinical study for cannabidiol that is needed to assess its risks for abuse, and with NIDA we are working to find ways to complete it.

To close my remarks, there is considerable public interest in developing new therapies for marijuana. FDA will continue to support the efficient development of new drugs from marijuana that are safe, effective, and manufactured to a high quality to speed their availability for the American public.

Thank you very much for your interest in this important topic. I am happy to answer any questions I can.

[The prepared statement of Dr. Throckmorton follows:]

Chairman Graham. Thank you both very much. Very impressive.

As sort of a general overview here, do you have an opinion as to whether we should change--is there enough information now to go from Schedule I to Schedule II? Dr. Weiss.

Ms. Weiss. Well, that is something that--

Senator Whitehouse. Microphone.

Ms. Weiss. That is something that is being considered under the eight-factor analysis which Dr. Throckmorton referred to and which we are not yet--which is still in a pre-decisional state.

What I would state is that we still do not have the clinical trials to show that marijuana as a plant is effective for any specific indication. So I think we still need to get more information.

However, what we are very interested in is trying to find ways to support research and to expedite research, whether it is by changing the schedule or by finding a way of streamlining processes within the Schedule I process that will help us get there, and this is something that we have been in discussions with many of our Federal partners, including the DEA, who are also interested in working with us to try and facilitate Schedule I research.

Chairman Graham. So your advice to the Committee, if I

have got this right, is that we need more research. There are some promising applications, but there is also a chance for abuse, too.

Ms. Weiss. Correct.

Chairman Graham. I mean, we need to know what we are doing here.

Ms. Weiss. Correct.

Chairman Graham. Dr. Throckmorton, what is your view about do we know enough now to make the change?

Dr. Throckmorton. I would agree with Dr. Weiss, first, that the DEA is in the process of finalizing their decision, and so it would not be something that I would be able to comment on directly.

I would also agree with Dr. Weiss we do not know as much as we would like to about the specific compounds found in marijuana and the specific potential values that they may hold. So additional research, we need to be sure that whatever the Federal agencies do, we are not getting in the way of that research.

Chairman Graham. Okay. I think the two previous Senators suggested that, you know, politicians should not make these decisions, scientists will. I think politicians will ultimately make this decision, but I think both of us want to make an informed decision. And if you have doubts about the state of play, I do not know how we could not have

doubts. Does that make sense?

Ms. Weiss. Yes. I think we see a lot of potential for this system, and I think there is a lot of promising data out there, and there are a few areas where I suggested that the data are stronger than others, for example.

Chairman Graham. But we need a process.

Ms. Weiss. But we need a process.

Chairman Graham. Here is an--I do not mean to advertise for this guy, but Dr. Reefer has a billboard--I think this is in Las Vegas: "Get your medical marijuana card." "Out-of-State MMJ cards accepted. Left on Naples to Grove." I want to introduce these into the record, but I will get more.

[The information follows:]

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Chairman Graham. Some States that have legalized medical marijuana seem to have not gone down the scientific route--unless Dr. Reefer knows more than you all do. So what do we do about that? How does the system work? States that have, you know, legalized medical marijuana, I have been told stories about where somebody will come up to you on the beach and want to know if you need a prescription. Is that true?

Ms. Weiss. Those are the stories that we hear as well and the reasons that we are very concerned that people might make choices of using marijuana when there are actually proven effective treatments that could benefit patients. And we hear this from parents who are interested in treating their children with ADHD with marijuana rather than with some of the stimulant medications that have been shown to be effective.

Chairman Graham. Dr. Throckmorton, are you familiar with Dr. Reefer?

Dr. Throckmorton. I have not had the pleasure.

Chairman Graham. Okay. Do you know if he has published any--

Dr. Throckmorton. I will say, however, we have had good interactions with the States, and I think you characterized where we are with State medical marijuana well. Each of the States has made different decisions about

what areas to allow under medical marijuana.

Chairman Graham. Here is where I do not want to go. I do not want to go to the Dr. Reefer route. If you can prove to me and the Committee that marijuana has medical applications for those in need through a scientific process, I am very open-minded because my mother passed of cancer, and I have been told anecdotally about how this drug helps people with seizures. But I also have been a prosecutor, and I understand that this has been a gateway drug. So I think I understand both sides. What I do not want is this. I do not want this. [Holds up documents.]

So thank you both for your testimony, and you have given us information about how we could change to increase research. That is what I am looking for. I do not want to make a Schedule I/Schedule II decision just based on the fact you cannot have adequate research. Maybe there are ways to get research without changing the schedule until we know more. Is that a fair statement?

Ms. Weiss. I think it is a fair statement, and I think that is really what we have been trying to work with our other Federal agencies on, ways of looking at the laws to be able to, for one thing, you know, perhaps increase the number of manufacturers of marijuana, which you have already heard about. NIDA right now is the single source. We have been working with the DEA and others to look at ways to see

if this is possible, and we are hopeful.

Chairman Graham. Thank you.

Senator Whitehouse?

Senator Whitehouse. Thank you, Chairman.

Are you both here testifying on behalf of your agencies?

Ms. Weiss. Yes.

Dr. Throckmorton. Yes.

Senator Whitehouse. So you are speaking officially when you give your testimony. It is not personal views. It is FDA and NIH.

Chairman Graham. Is that true?

Dr. Throckmorton. I would industry anything that was a personal view of mine, yes.

Senator Whitehouse. Just one factual question. Dr. Throckmorton, your testimony is that at the request of DEA, in 2001 and again in 2006, FDA conducted a review of the eight-factor test for scheduling marijuana. Are you conducting that review for DEA now?

Dr. Throckmorton. As a part of the citizen petition responses that I mentioned in my testimony, the DEA asked the FDA to conduct another eight-factor analysis, and that eight-factor analysis was performed and did include a review of all of the available scientific literature at that time.

Senator Whitehouse. And did it draw a conclusion?

Dr. Throckmorton. We did draw a conclusion.

Senator Whitehouse. What conclusion did you draw?

Dr. Throckmorton. Like we talked before, because out recommendation goes to HHS and then to the DEA, who makes the final decision, it is not something that I am able to talk about at this time.

Senator Whitehouse. Because?

Dr. Throckmorton. It is pre-decisional.

Senator Whitehouse. Okay.

Dr. Throckmorton. The DEA takes our recommendation along with other factors and then makes that final decision.

Senator Whitehouse. From a practical point of view, assuming that the purpose of this hearing is to consider reducing marijuana from Schedule I level to Schedule II level, not liberalization of marijuana laws or anything beyond that, what do you believe the practical results would be from a research perspective and from an abuse perspective of that simple step to have it be Schedule II instead of Schedule I? Dr. Weiss first.

Ms. Weiss. Well, there are certainly additional barriers or additional hurdles that have to be passed for somebody to do research, and we also--

Senator Whitehouse. So from a research--

Ms. Weiss. For research purposes.

Senator Whitehouse. --perspective, it would be--

Ms. Weiss. It would be helpful.

Senator Whitehouse. But do you think some obstacles--it would be helpful to have it go to Schedule II?

Ms. Weiss. Yes, or it would--

Senator Whitehouse. Okay.

Ms. Weiss. Well, I am sorry. May I just step back for a second? There are certainly obstacles that are associated with Schedule I. Whether the only solution to that is to move it to Schedule II I would not be willing to say at this point.

Senator Whitehouse. I did not ask you to consider other options, just if you move from Schedule I to Schedule II, conclusion one is that it would facilitate research. And on the abuse side, how much do you think the difference between Schedule I treatment and Schedule II treatment would open up the flood gates to marijuana abuse?

Ms. Weiss. It would depend, because if it were made Schedule II without any FDA approval for any kind of medical use--which would be the situation because it has not gone through the FDA process--then it would still be illegal for abuse--it would still be illegal to use. However, the message that would be given to people around the country would be that it--regardless of whether it had been approved by the FDA for medical use, that would be the message that many people around the country would take, that if it were

moved into Schedule II, that it had a medical use.

Senator Whitehouse. Could you tell me--

Ms. Weiss. And that could increase--

Senator Whitehouse. --some of the other drugs that are Schedule II?

Ms. Weiss. Excuse me?

Senator Whitehouse. What are some of the other drugs that are Schedule II?

Ms. Weiss. Amphetamine, methamphetamine, cocaine.

Senator Whitehouse. Methamphetamine and cocaine you think send a really strong signal by being on Schedule II that they are okay to use?

Ms. Weiss. No, I do not think that, but I think that those drugs--but I think that there are many issues around marijuana that are more subtle than they are for methamphetamine, for example, that make it a very challenging drug to talk about and to convince people about its harms, despite the fact that we know a lot about its harms and the fact that it is an addictive substance and can affect brain development.

Senator Whitehouse. Dr. Throckmorton, same question. From a point of view of research, what would the move from Schedule I to Schedule II do?

Dr. Throckmorton. So there are two things that people have suggested--and I think Dr. Weiss mentioned both of

them--that would change if marijuana was moved from Schedule I to Schedule II:

One, there are registration requirements for Schedule I products that do not exist for Schedule II, so they would go away. Now, they are there for a reason, so it would be important to talk to DEA and understand, you know, the rationale for those to exist.

The second is perception, and there is a perception that being in Schedule I, marijuana is somehow less attractive for research. And I have heard that, and I think Dr. Weiss has heard that. Changing that perception I think has the potential to be powerfully important as far as supporting better research. And, again, my goal in terms of drug development is to get more people to be doing the kinds of studies that we want to have to develop drugs.

One other small point--

Senator Whitehouse. Why don't I, since I am over my time, interrupt you at that point so that other Senators have a chance, because both our Chairman, Senator Grassley, and Senator Klobuchar from Minnesota are here.

Chairman Graham. Thank you.

Senator Grassley?

Chairman Grassley. Mr. Chairman, I am not going to ask any questions. You know, we had that vote that screwed up our schedule, and down the hall here I have got a meeting on

Alzheimer's disease with the Senate Finance Committee. So I came along to put a statement in the record.

Chairman Graham. Without objection.

Chairman Grassley. And to thank not only this panel of witnesses but the first panel, our colleagues, and the next panel that is going to come. But I would like to highlight a couple things that I have in my statement.

Number one, through the Drug Caucus that Senator Feinstein and I chair, we have been working on this issue, particularly as it relates to epilepsy, for a long time. And so I want to point that out in my statement, so I hope people will be brought up to date on where we are on that issue.

That is all the time I need right now.

[The prepared statement of Chairman Grassley follows:]

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Chairman Graham. Thank you, Mr. Chairman. Thank you very much.

And I will also put into the record a statement by Senator Hatch.

[The prepared statement of Senator Hatch follows:]

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Chairman Graham. Senator Klobuchar.

Senator Klobuchar. Thank you very much, Mr. Chairman. Thank you to both of you.

According to the National Conference of State Legislatures, 25 States and the District of Columbia allow for comprehensive public medical marijuana programs. My State is one of them. I know that each of these medical marijuana programs which are not classified as comprehensive approach the issue of medical marijuana differently. For instance, the medical marijuana law that Minnesota passed in 2014 limited the program to patients with one of nine medical conditions, such as cancer, and also limited delivery methods to exclude smoking. This year, the State made amendments to that law, including adding intractable pain as a qualifying condition effective next month, and I think that is one example.

Given the broad diversity of medical marijuana laws throughout the country, what lessons have we learned or have you learned by observing and comparing the results in each of these States? Do you see one that is a model that we should be looking at? Dr. Weiss. You probably do not want to pick out one State.

Ms. Weiss. So I do not think we have all of the answers yet. I think that we need to--I know this is what the scientists always say, but I think we do need to have

more research.

I think that we are very concerned about the States that have very liberal policies about medical marijuana. Particularly California, for example, is one that we do hear that the average medical marijuana user is about 35 with low back pain, and that may be a very different situation from what you have in Minnesota and from what some of the other States have.

But at this point, I think we are still talking about products that are not being regulated and that it is unclear what the appropriate dosage would be for any of these different conditions. So we have grave concerns about patients using medical marijuana without additional research and additional guidance on how to use it.

Senator Klobuchar. So along that line--and if you want to add something, Dr. Throckmorton, maybe I will get to that, but it just goes into my next question, and that is about research. What do you think are the most effective steps we could take to expand medical research?

Ms. Weiss. So apart from always the need for additional funding, we also, I think, could be--I think we could--there are ways to streamline the research process so that investigators would feel that it was less burdensome and that it was less of a threatening process and would encourage them to go into research. One of the things that

NIH did this past year was hold a summit, and part of the reasons for having this summit was to show that NIH as a whole is supportive of research and is supportive of research not only into the harmful effects of marijuana, but also into the therapeutic effects.

Senator Klobuchar. And so how do our research laws compare to other countries, what they are doing? Are there other countries that are doing more with research on medical marijuana? And can we use some of that research?

Ms. Weiss. I think some of these other countries are also struggling with it. These are laws that are changing. I recently read an article by somebody in Israel who was actually the person who first isolated THC from the marijuana plant back in the 1960s, and he has talked about the fact that in Israel the laws have gotten easier for doing research, and yet still there are not sufficient clinical trials to be able to make strong recommendations as to which products can be used for what illnesses.

So I think we still have a ways to go, but I certainly think that making it possible for--you know, having additional growers, which was already discussed, and which is something that we are looking into with our colleagues from other agencies, is something that would be helpful, as well as ways of helping people get through the Schedule I licensing process in a way that can expedite things.

Senator Klobuchar. And, Dr. Throckmorton, there are currently two FDA-approved drugs that contain cannabinoid chemicals in pill form. Is that right?

Dr. Throckmorton. There are three.

Senator Klobuchar. Three?

Dr. Throckmorton. We approved a third a few weeks ago.

Senator Klobuchar. Okay. And I know one of them treats nausea caused by chemotherapy, and another one is regarding appetite loss with patients with AIDS. What was the process that the FDA would have gone through to approve those three drugs?

Dr. Throckmorton. So those three drugs would have had the same process used that we would apply to drug development from any other source, any other plant, for instance. We have developed drugs from plants in the past, and we applied that same process.

What we are doing now is making sure that process is as efficient as it possibly can be for things like marijuana, so I have a Botanicals Team. I have one individual that helps identify all of the investigational uses of marijuana and connects those investigators up with the right divisions and the right manufacturing consultants and things so they are able to get the work done as quickly as possible.

I would say one other piece that has given me some hope, I would say, has been the work that we have had going

on with the States. So some of the States that have passed medical marijuana laws, Louisiana, for instance, and States that have passed laws regarding recreational marijuana use, like California--or, sorry, Colorado, have come to us because they also want to make sure that they are encouraging and supporting research to the extent they can. And we have been able to tie them with our development team to make sure that that research is as robust and as efficient as possible.

Senator Klobuchar. And do you see this as expanding research because of the work of the States? Or do you think there are things that you could be doing differently with the FDA to expand the research?

Dr. Throckmorton. If there are things that we could be doing at the FDA, I would like to know about them, because we would try to do them.

Senator Klobuchar. No, that is why I was just asking if--

Dr. Throckmorton. No, I genuinely would be interested, because we have looked very carefully to try to make sure we are not in the way, that we are, in fact, supporting the efficient research to the extent we can.

I am cautiously encouraged by the work that the States are doing. In Louisiana, we had an opportunity to talk to one of their research institutes as a follow-up to the

things that they had done, work with that institute, put them in touch with the right people, to hopefully get the research that is really needed done.

Senator Klobuchar. All right. Thank you very much.

Chairman Graham. Thank you.

Anything, Senator Whitehouse?

Senator Whitehouse. I am all set. We can go to the next panel.

Chairman Graham. All right. Thank you both. Thank you both for coming.

Chairman Graham. Thank you all. Our next panel, I will try not to butcher your name, and you are all very highly qualified, so I will just kind of give a brief summary of what you do.

Dr. Daniele--how do you say your name, sir?

Mr. Piomelli. "Daniel."

Chairman Graham. The last name?

Mr. Piomelli. "Piomelli."

Chairman Graham. All right. Thank you. You are professor of anatomy and neurobiology, University of California, Irvine.

Dr. Situation Gitlow, M.D., is executive director, Annenberg Physician Training Program in Addictive Disease.

And Mr. Barber, D. Linden Barber, J.D., partner with Quarles and Brady.

Thank you all for coming. You have very distinguished backgrounds, and I will put that into the record, but we will start with you, sir.

STATEMENT OF DANIELE PIOMELLI, PH.D., PROFESSOR, DEPARTMENTS OF ANATOMY AND NEUROBIOLOGY, PHARMACOLOGY AND BIOLOGICAL CHEMISTRY, UNIVERSITY OF CALIFORNIA, IRVINE, CALIFORNIA

Mr. Piomelli. Chairman Graham, Ranking Member Whitehouse, and Committee members, thank you for the opportunity to appear before you today to address the very important issue of medical marijuana.

Humans have used marijuana as a medicine for at least 5,000 years. Under the scientific name of cannabis, marijuana was added to the pharmacopeias of Europe and the United States in the 1840s. It was recommended to alleviate pain, stimulate appetite, suppress nausea, and treat opiate withdrawal.

All medical marijuana use came abruptly to an end in 1937 when the Marijuana Tax Act effectively banned it. At the time we knew close to nothing about marijuana. What do we know now?

Well, first of all, we know that the chemical composition of marijuana is complex, as you have heard. But we also know that two chemicals take the lion's shares of its pharmacology. Those are tetrahydrocannabinol, THC, and cannabidiol. THC is the main reason why people use marijuana recreationally and is also responsible for many, but not all, of its potential useful effects.

How does THC work? Research in the past 30 years has provided a firm answer to this question, revealing the existence of a previously unsuspected signaling system that serves crucial functions in the brain and actually throughout the body. The system is called the "endogenous cannabinoid system" or "endocannabinoid system." In my lab at UC-Irvine, I have had the privilege to study this for over 25 years.

At the core of the encocannabinoid system are the cannabinoid receptors. These proteins recognize THC just like a lock recognizes its own key. They are found on cells in the brain and other organs and mediate the pharmacological effects of THC.

The other crucial component of the endocannabinoid system are the endocannabinoids, chemical transmitters made in our body that, like THC, are recognized by cannabinoid receptors. The endocannabinoids are the legitimate key for the cannabinoid receptor lock, which THC observes.

So why do we have a cannabinoid system? Well, let me assure you endocannabinoids are not there to get us high. Research has shown that the system regulates essential bodily function. For example, it controls pain. It makes us more resilient in the face of psychological stress, allaying anxiety and improving mood. It strengthens our response to a vast array of stimuli that we find

pleasurable, from Twinkies to cocaine. It finely tunes our ability to learn and retain new information.

So what does this new knowledge teach us about the potential utility of cannabis as a medicine? Well, first, it provides us a strong scientific ground on which we can base possible medical uses. Most prominent, in my opinion, is chronic pain, a life-shattering condition that afflicts millions of Americans and costs billions of dollars to our economy. Opiate medications are effective at reducing chronic pain, but they are addictive, and their excessive use has created an epidemic that kills more people than car accidents do. Clinical studies suggest that marijuana can alleviate chronic pain at dosages that cause only modest side effects. But we need more research to confirm these results and understand better the value of marijuana as an analgesic.

Besides chronic pain, other possible indications for medical marijuana which are supported by our knowledge of the endocannabinoid system include post-traumatic stress disorder, nausea and vomiting, for example, caused by anti-cancer drugs, and inflammatory bowel disease. But also in those cases, more research is needed to confirm real benefits.

Our understanding of the cannabinoid system can also guide us in assessing the risks that are inevitably

associated with the medicinal use of marijuana like any other drug. An important concern with acute marijuana use is the negative impact the drug can have on memory. Maybe it does not matter very much if you forget what you had for dinner last night, but what about forgetting stuff while you are driving a car? Automobile driving is a challenging cognitive task, and we still do not fully understand how marijuana affects it.

A serious potential side effect of prolonged marijuana use is addiction. Marijuana is less addictive than opiate painkillers are, but it is an addictive substance, and we do not know how the addictive properties of marijuana play out when the drug is combined with opioids, as it would happen if it became a medicinal compound.

But at present, the most pressing concern I see with medical marijuana is its potential long-term impact on the adolescent brain. The adolescent brain is still very much in development, and so is the endocannabinoid system inside it. Overstimulation by marijuana might interfere with the normal development of this system and with brain development, and the persistent consequences that we might end up having are not understood.

So one objective of a large human study funded by NIDA called ABCD is to bring light to this question, and our lab is working with NIDA to put together a research program that

would look deeply into the same issue at the mechanistic level.

In closing, I must briefly consider the second most important chemical constituent of marijuana, cannabidiol, which is, of course, as you have heard, the main constituent of Charlotte's Web. There is a lot of confusion about this molecule, even in the medical profession. Here are some facts on which scientists agree and some open questions that we all ask:

First, unlike THC, CBD does not recognize cannabinoid receptors. As a result, it does not have mind-altering effects and does not have addictive effects.

Second, CBD exerts interesting pharmacological effects that include the ability to alleviate psychotic symptoms in people with schizophrenia, reduce anxiety, control seizures in some forms of epilepsy, as we heard before, and suppress skin acnes. The receptor mechanism by which CBD brings about these effects is unknown.

Now, lastly, but importantly, while CBD appears to be relatively safe after short-term administration, its long-term effects remain undetermined. So in light of the promising therapeutic potential of CBD, it will be important to address this question in future research.

Thank you.

[The prepared statement of Mr. Piomelli follows:]

Chairman Graham. Thank you.

Dr. Gitlow.

STATEMENT OF STUART GITLOW, M.D., EXECUTIVE DIRECTOR, ANNENBERG PHYSICIAN TRAINING PROGRAM IN ADDICTIVE DISEASE, AMERICAN SOCIETY OF ADDICTION MEDICINE, WOONSOCKET, RHODE ISLAND

Dr. Gitlow. We live in a society where some 15 percent of our population has addictive disease. These individuals generally do not know it until they are exposed to the substance which will eventually prove their downfall. If the substance is prohibited, most of them will not try it or use it regularly, and the actual number of people who become addicted will be comparatively low. If a substance is freely available, as in alcohol or tobacco or even prescribed opioids, we see the number of people who try the substance rise. And the number of individuals who end up going down the addictive disease path, therefore, rises as well.

Now, we have run this experiment many times, and we know that two of the leading causes of preventable death in our society are drugs with no benefit whatsoever. Half a million Americans die per year due to tobacco use; 88,000 die per year due to excessive alcohol use. How insidious an assault this has been, where right under our noses, nearly 600,000 of us die every year due to use of products that have no benefit and enormous burdens of cost and risk.

Which brings me to marijuana. Marijuana, as has been

said, is a plant with hundreds of molecular components rather like the willow tree. Now, the willow tree's bark has a component that acts as an anti-inflammatory very much like aspirin. But we do not refer to willow tree bark as "medical willow." We do not prescribe it to patients for their headaches. We do not find willow trees in the wild to have had their barks stripped by people who then stood nearby afterward smoking the willow bark as a way of combating whatever inflammatory process they might have.

There are three reasons we do not see that:

The first is that there is no such thing as medical willow bark because willow bark has not been demonstrated in double-blind, placebo-controlled studies to have sufficient benefit and absent risk sufficient to be acceptable as a medication.

Second is that we have legitimate medications which have demonstrated efficacy for treating inflammation, medications which are comparatively safe and which have comparatively fewer risks.

But third, and perhaps the crux of the matter, is that no one gets high from smoking willow bark. And let me be clear. There is no such thing as medical marijuana. The American Medical Association, the American Psychiatric Association, the American Society of Addiction Medicine are all in agreement: There have been no placebo-controlled,

double-blind studies demonstrating the plant marijuana to have sufficient benefit and absent risk sufficient to be acceptable as a medicine. What has been legislated into existence in 25 States and in the District of Columbia is not medical marijuana. It is recreational marijuana being said to be used for some other purpose.

The dangers and risks of marijuana use are well known by the scientific community, even as they are downplayed by the corporate interests. Apathy, lost productivity, addictive disease, deterioration in intellectual function, motor vehicle accidents, and psychosis in a small minority are all among the negative outcomes. All from a product with no statistically demonstrated benefit.

Now, for nearly all conditions for which marijuana has purported benefits, we already have existing medications--safe medications--demonstrated to have value. But people get high from using marijuana, and so they are asking us to bypass the very system that has been in place for many years that protects us from drugs coming to market before they have been demonstrated as being valuable and useful in treating disease.

So it behooves us to research the plant to find out if, indeed, some component of marijuana is found to have value. If so, we can produce it in a form that does not have the many risks present with respect to use of the whole plant.

And we can do this by following the same path that we follow for development of medications in this country, a path we have used for decades, a path that has been protecting our Nation's public health in the process. We can and we should make this process less obstructive in this case because we do need the robust basic and clinical research to develop more information about marijuana's potential to treat various conditions. The recently introduced MEDS Act, for example, makes sense. It encourages legitimate research for the purpose of producing an FDA-approved drug that utilizes a component of marijuana. And it does this in a constructive manner as we would for any other medication, as opposed to a destructive manner in which we let loose a psychoactive drug that has enormous potential to harm our public health. And by following that pathway, we will demonstrate the same concern that we do in all other aspects of our Nation's health.

[The prepared statement of Dr. Gitlow follows:]

Chairman Graham. Thank you.

Mr. Barber.

STATEMENT OF D. LINDEN BARBER, PARTNER, AND DIRECTOR, DEA COMPLIANCE AND LITIGATION PRACTICE, QUARLES AND BRADY, LLP, INDIANAPOLIS, INDIANA

Mr. Barber. Good afternoon, Chairman Graham, Ranking Member Whitehouse, and Senator Blumenthal. Thank you for the opportunity to appear and speak about the DEA regulatory requirements that apply to Schedule I research, including research involving marijuana.

I am the director of the DEA Compliance and Litigation Practice at Quarles and Brady, and I represent registrants, including some who are engaged in Schedule I research. Sometimes that position puts me at odds with DEA, but I have a history with DEA where I was representing them. I worked in the Office of Chief Counsel for 12 years and during that time was exclusively involved in matters involving the regulated community, including researchers. And there is no doubt that research with Schedule I drugs, including marijuana, is important. We know that THC has medical benefits because of the FDA-approved drugs like dronabinol. The rescheduling of dronabinol is a good example of allowing science to dictate when to move a drug or a product that comes from a particular controlled substance into a different schedule so that it is available for medical use.

Certainly the research with cannabidiol is promising, and it is important that the regulatory requirements of DEA

and other Federal agencies do not raise unreasonable barriers to research with marijuana. And it is also important that any steps taken to reduce perceived regulatory barriers or real regulatory barriers do so in a manner that continue to provide for the protection of public health and safety.

As my written statement indicates, the congressional findings contained in the Controlled Substances Act back in 1970 emphasized the necessity of regulating controlled substances in a manner that, one, allows the American people to benefit from the medical uses and legitimate scientific uses of those products; but, two, provides that the Act is to protect the public health and safety from the harms of the misuse of controlled substances. And we have 46 years under the Controlled Substances Act in which there is significant evidence of the misuse of marijuana.

The regulatory system established in DEA's regulations actually provides for a great deal of flexibility. It is not always used by registrants or by the agencies, but there is great flexibility that allows the agency to meet the underlying purposes of the Controlled Substances Act.

For example, DEA regulations permit any person to request that the agency waive any provision of the regulations. Now, of course, the agency cannot waive statutory requirements that Congress has passed, but it can

waive its own regulations. And the agency has done so in order to lift some of the barriers to research with cannabidiol.

For example, the regulatory requirement for modification and multi-agency review of the protocol for Schedule I research was waived by DEA on nearly 40 occasions over the last 7 months. And this is important. Having spoken with the father of Patient 1 in one of the clinical trials who told me how the seizures of his son were reduced in this clinical trial from hundreds a day to less than 10, it is critical that the agency be responsive in the manner that it was in waiving some of these research requirements that tend to pose barriers on the researchers.

Another example of the flexibility in the current DEA regulatory scheme is the security requirements. Yes, the requirement is a securely locked, substantial container, and yet substantial compliance is what the regulations require. And, again, there is a waiver provision that permits the agency to do so when requested.

It is important to consider how any proposals that are designed to facilitate research will be carried out under existing statutory and regulatory schemes. If marijuana were a Schedule II drug, researchers would still be required to obtain registration; DEA would still be required to establish the aggregate production quota; and researchers

would still have to have physical security which is identical to the Schedule I physical security requirements of having a securely locked, substantial container. And as I noted in my written statement, the only meaningful difference between Schedule I and Schedule II research is that Schedule I researchers are required to submit a protocol to DEA at the time of applying.

But DEA has registered more than 300 researchers to conduct research with marijuana, marijuana extracts, and cannabidiol. And according to DEA officials, registration is not a barrier. In the last year, the average time from approval by FDA of the research protocol from application to registration is less than 5 weeks at DEA.

In the 46 years of the Controlled Substances Act, science has determined the schedule in which drugs will be placed. Science has determined what constitutes legitimate use of a controlled substance. And it has determined the formulations that will be used for the health and safety of the American people.

I look forward to your questions, and I thank the Committee for the opportunity to appear.

[The prepared statement of Mr. Barber follows:]

Chairman Graham. Thank you all very much.

Let me see if I can see where we agree. Do all of you agree that it would be a good thing to have more double-blind, scientifically proven research on marijuana in terms of its medical benefits?

Mr. Piomelli. I do.

Dr. Gitlow. I do.

Mr. Barber. I am not qualified as a scientist. I am a lawyer, and I can tell you about the legal--

Chairman Graham. Okay. Fair enough. So that seems to be everybody is in that boat. The best way to do that is to change the schedule or just to come up with different protocols?

Mr. Piomelli. I do not have an answer to that, but what I can say is that there is a huge psychological impact of the scheduling that makes a lot of us researchers--

Chairman Graham. That is what Dr. Weiss--

Mr. Piomelli. --very hesitant.

Chairman Graham. Do you agree with that?

Dr. Gitlow. Well, changing the schedule presumes that there is a demonstrated medical benefit to the substance, the substance in this case being the entire plant marijuana as opposed to any component of it.

Chairman Graham. Right.

Dr. Gitlow. That has not happened yet. So there are

any of a number of things that could be done. For instance, there might be a Schedule I-A, a schedule that would still be for a substance--

Chairman Graham. Could you do me a favor and kind of write that down and give it to us?

Dr. Gitlow. Sure.

Chairman Graham. Okay.

[The information follows:]

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Dr. Gitlow. But that would give you an opportunity to say it does not have a known medical benefit, but the research--

Chairman Graham. I got you.

Dr. Gitlow. Okay.

Chairman Graham. Do you all agree--is it M-A-R-I-N-=O-L? How do you say that?

Mr. Barber. Marinol or dronabinol.

Chairman Graham. Okay, Marinol. Do you all agree that it has some medical benefit?

Mr. Piomelli. Yes, of course.

Dr. Gitlow. Yes.

Mr. Barber. Yes, sir.

Chairman Graham. Okay. So there is part of this marijuana that we know has some medical benefit.

CBD, do you all agree that it does not get you high?

Mr. Piomelli. I do.

Dr. Gitlow. I do.

Chairman Graham. You are a lawyer, so we do not care what you think, right?

[Laughter.]

Chairman Graham. All right. So here is the goal: to try to find out in a scientific way how much you can get from CBD, how much you can get from THC, and make sure societally we are making a good decision. That is the goal.

You all agree that is a good goal for this Committee.

Now, we are on the floor arguing among ourselves. Senator Whitehouse has been a great leader on this. Apparently there is an epidemic of prescription drug abuse from opiates. Do you all agree with that?

Mr. Piomelli. Very much.

Dr. Gitlow. Yes.

Mr. Barber. Yes.

Chairman Graham. Are you cautioning us do not go down this road until you really understand what you are doing?

Dr. Gitlow. Yes. The key here to recognize is that if I take a hammer and hit a patient on the head, lightly but hard enough for him to notice, the pain that he has in his lower back will disappear. And if the only question I ask him after I have hit him in the head with a hammer is, "How is the pain in your lower back?" the subjective report is going to be hitting him in the head with a hammer is an effective way of treating lower back pain. So we have to ask the right questions.

Chairman Graham. I got you. So do you all agree that Dr. Reefer is probably not the way to go?

Mr. Piomelli. Yes.

Dr. Gitlow. Yes.

Mr. Barber. I agree.

Chairman Graham. So what I am trying to do--and then I

will turn it over to Senator Whitehouse--is to find out where the science is at, where it needs to go, and get it there as reasonably quick as possible, do it in a sound way, and stop this Dr. Reefer crap, because that is not where I am at. If you are excited about me being part of the cause, good. If you are excited about me wanting to legalize marijuana, you should not be excited.

So, Dr. Gitlow, what do you tell the people who come to me in large numbers and say anecdotally this substance helps their family?

Dr. Gitlow. Anecdotally, it may well. Or it may well be that they have misunderstood what they have seen because the human brain is programmed--

Chairman Graham. That is why we need the research.

Dr. Gitlow. Exactly.

Chairman Graham. Mr. Barber, could you very quickly tell the Committee from your expertise in terms of scheduling and legal advice, what do you think is the best way forward to ensure more research without sending the wrong message that Dr. Piomelli is worried about?

Mr. Barber. I think using the existing regulatory system and the flexibility that is built into it is something that can be done. It is not always done. Some of that is a result of how registrants approach that. Some of it is how regulators approach it. But there is already

flexibility, and I do share concerns that a rescheduling of marijuana not only sends a societal message, but Schedule II drugs can be prescribed even though they are not in an FDA-approved formula.

For example, there are compounded drugs--licensed physicians are permitted to prescribe a drug to be compounded that is in a formulation not approved by FDA. Dr. Reefer is the prototypical bad example of what would happen, and as you mentioned, the opioid abuse problem, which is drugs in Schedule II, gives us an idea of what happens when bad prescribers are involved in the prescribing of Schedule II drugs. They find that the root of the epidemic in opioids is bad prescribing.

Chairman Graham. Apparently, we are just giving this stuff out like candy, and a lot of people are getting addicted on the opiate side. And no doubt in my mind it does help people with their pain and other problems.

Senator Whitehouse?

Senator Whitehouse. The first thing I want to do is to thank Senator Graham. We achieved cloture on the Comprehensive Addiction and Recovery Act today. With any luck, we will get the final vote perhaps today, perhaps tomorrow. I am not sure when that is going to be scheduled. But one of the reasons that we are there is because Senator Graham and he recruited Senator Hatch and they were willing

to cosponsor the bill so it had Judiciary Committee cosponsors, and that was a critical step in moving the bill forward. If you cannot bring it up in the Judiciary Committee without bipartisan cosponsorship, you do not have a very clear path to the floor, and it was Senator Graham and Senator Hatch who stepped forward on this Committee to serve as Republican Committee cosponsors, and from here we went to the floor and ended up 94-1. But Senator Graham was there right at the beginning, and I want to thank him for that.

The question that I have is for Mr. Barber. You have considerable experience in this area, both from your history at DEA and as a practicing lawyer in this area now. There is a wide array of legal enforcement that criminalizes or regulates the recreational, non-prescribed use of marijuana. It is at the State level, and it is at the Federal level. In what respect would a move from Schedule I to Schedule II change that enforcement regime that is already out there? If you were to move it from Schedule I to Schedule II, would you be required to go to other Federal statutes to make an adjustment in order to make sure that we were not inadvertently tearing down those criminal and regulatory laws?

Mr. Barber. No, the move from Schedule I to Schedule II would still subject in this case marijuana to the

Controlled Substances Act. And just like trafficking in oxycodone or other FDA-approved opiates is illegal and prosecutable and regularly prosecuted by U.S. Attorneys around the country, the illicit use of marijuana, if it were in Schedule II, would be subject to the same criminal laws.

Senator Whitehouse. State and Federal?

Mr. Barber. State and Federal.

Senator Whitehouse. Very good. That is what I wanted to hear. Thank you very much.

Chairman Graham. Senator Blumenthal.

Senator Blumenthal. Thanks, Mr. Chairman.

I want to read to you, if I may, an article that was in the New Haven Register a few months ago, not read the story but tell you about the article that appeared about Sean Hearn, 11 years old, of Stratford, Connecticut, who suffers from 50-plus seizures in a day because of a severe rare form of epilepsy. He uses a wheelchair. He cannot walk, talk, or survive without a feeding tube. He has to eat pureed food. He takes five medications. All of them have severe side effects. And I am quoting his mother: "The problem with seizure meds is every bit you give him, he loses a little of himself." That is what his mother, Kim, said. She, her husband, Sean's doctor are considering the use of CBD oil when it becomes legal this October for minor patients in Connecticut following a vote by our State

legislature.

So perhaps you can help me to understand, number one, in your view, is marijuana, when it is smoked and inhaled, addictive? Number two, is CBD oil addictive? And, number three, should it be treated in the same way that marijuana is for regulatory purposes?

Dr. Gitlow. So marijuana itself as a plant, when smoked, generally has a fairly significant THC level in it. THC is the euphoric-producing substance within marijuana. So, yes, it is addictive. People use it. They grow tolerant to it. They need greater amounts in order to achieve the same effect over a period of time.

CBD oil, because of its nature and not being a euphoric, is not known to be addictive and does not have that same issue of tolerance known to be attributed to it. However, a good deal of research would be necessary to determine whether or not it has the benefits purported to have in that article and anecdotally described on several occasions.

Senator Blumenthal. You mentioned earlier that the research has to ascertain whether--I think you used the words whether these marijuana-based potential medical treatments are "useful and valuable." The standard in the FDA is, of course, safe and effective. Are those two standards interchangeable? Did you mean them to be

interchangeable?

Dr. Gitlow. I meant them interchangeably, yes.

Senator Blumenthal. Okay. But it is not your position that a different standard should be applied to--

Dr. Gitlow. No, sir. In fact, I would recommend the same standard be applied.

Senator Blumenthal. Right. Let me ask all of you, but particularly Mr. Barber, one of the challenges for Connecticut, which legalized medical marijuana some years ago, I think 2012, is the financial transactions that take place to enable the system to work, and the reason that issues have arisen is, in fact, some of the financial institutions may be reluctant to finance or enable these kinds of transactions to take place. For whatever reasons, financial transactions have been, at least at the beginning, an issue. Is that something that has occurred widely and has been of concern to the DEA? I know that you are no longer with the DEA, but in your present position, perhaps you have some insight.

Mr. Barber. Senator Blumenthal, unfortunately, I do not have any insight. I know the banking industry is heavily regulated, as is the pharmaceutical industry. But I do not have any insight into the agency's thinking around the restrictions on financial institutions.

Senator Blumenthal. Any of the other witnesses have

any?

[No response.]

Senator Blumenthal. Thank you, Mr. Chairman.

Chairman Graham. Thank you.

One last question. Dr. Piomelli, what is the effectiveness and the risk associated with how you take THC or CBD, whether it is oral, topical, smoked, or otherwise? Can you tell us anything about that?

Mr. Piomelli. Is your question related to the high levels of THC?

Chairman Graham. Just is it better--how you administer it, does it really matter? Is it orally administered? Do you smoke it? Is it topical? Does one form of administering the THC or CBD at the same levels, does it matter how you administer it?

Mr. Piomelli. It does. It does very much. In fact, it is one of the major problems in assessing marijuana and its products, the fact that the pharmacokinetics--that is the technical name for these things--can be dramatically different depending on the route of administration. Typically, a route of administration such as smoking, which is a form of inhalation, causes a very high level of the active products in blood within a few seconds or minutes; whereas, administration through the oral route takes a much longer time, usually many minutes to hours.

Now, this has impact not just in, if you wish, the duration and onset of action, but really on the pharmacodynamics. The effects are substantially different. If you hit very quickly the brain with a high level of a compound, you usually end up having effects that are different from those that are obtained when you achieve a certain level over a period of many minutes. This can be best exemplified with the case of cocaine where snorted cocaine or base cocaine, which is crack cocaine, the latter is much faster in its onset of action and is much more addictive in that regard.

So these considerations apply to THC as they apply to any other compound that has rewarding effects, so can induce addiction.

Chairman Graham. Thank you all very much. You have been very helpful to the Committee.

The hearing is adjourned, and we will keep the record open for 7 days for anybody who would like to submit information. Thank you all very much.

[Whereupon, at 4:10 p.m., the Subcommittee was adjourned.]

C O N T E N T S