AUTHENTICATED
U.S. GOVERNMENT
INFORMATION
GPO

MIXED SIGNALS: THE ADMINISTRATION'S POLICY ON MARIJUANA, PART FOUR—THE HEALTH EFFECTS AND SCIENCE

HEARING

BEFORE THE

SUBCOMMITTEE ON GOVERNMENT OPERATIONS

OF THE

COMMITTEE ON OVERSIGHT AND GOVERNMENT REFORM

HOUSE OF REPRESENTATIVES

ONE HUNDRED THIRTEENTH CONGRESS

SECOND SESSION

JUNE 20, 2014

Serial No. 113–132

Printed for the use of the Committee on Oversight and Government Reform

Available via the World Wide Web: http://www.fdsys.gov
http://www.house.gov/reform

U.S. GOVERNMENT PRINTING OFFICE

89–729 PDF WASHINGTON : 2014

For sale by the Superintendent of Documents, U.S. Government Printing Office
Internet: bookstore.gpo.gov Phone: toll free (866) 512–1800; DC area (202) 512–1800
Fax: (202) 512–2104 Mail: Stop IDCC, Washington, DC 20402–0001

COMMITTEE ON OVERSIGHT AND GOVERNMENT REFORM

DARRELL E. ISSA, California, *Chairman*

JOHN L. MICA, Florida
MICHAEL R. TURNER, Ohio
JOHN J. DUNCAN, JR., Tennessee
PATRICK T. MCHENRY, North Carolina
JIM JORDAN, Ohio
JASON CHAFFETZ, Utah
TIM WALBERG, Michigan
JAMES LANKFORD, Oklahoma
JUSTIN AMASH, Michigan
PAUL A. GOSAR, Arizona
PATRICK MEEHAN, Pennsylvania
SCOTT DESJARLAIS, Tennessee
TREY GOWDY, South Carolina
BLAKE FARENTHOLD, Texas
DOC HASTINGS, Washington
CYNTHIA M. LUMMIS, Wyoming
ROB WOODALL, Georgia
THOMAS MASSIE, Kentucky
DOUG COLLINS, Georgia
MARK MEADOWS, North Carolina
KERRY L. BENTIVOLIO, Michigan
RON DESANTIS, Florida

ELIJAH E. CUMMINGS, Maryland, *Ranking Minority Member*
CAROLYN B. MALONEY, New York
ELEANOR HOLMES NORTON, District of Columbia
JOHN F. TIERNEY, Massachusetts
WM. LACY CLAY, Missouri
STEPHEN F. LYNCH, Massachusetts
JIM COOPER, Tennessee
GERALD E. CONNOLLY, Virginia
JACKIE SPEIER, California
MATTHEW A. CARTWRIGHT, Pennsylvania
TAMMY DUCKWORTH, Illinois
ROBIN L. KELLY, Illinois
DANNY K. DAVIS, Illinois
PETER WELCH, Vermont
TONY CARDENAS, California
STEVEN A. HORSFORD, Nevada
MICHELLE LUJAN GRISHAM, New Mexico
Vacancy

LAWRENCE J. BRADY, *Staff Director*
JOHN D. CUADERES, *Deputy Staff Director*
STEPHEN CASTOR, *General Counsel*
LINDA A. GOOD, *Chief Clerk*
DAVID RAPALLO, *Minority Staff Director*

SUBCOMMITTEE ON GOVERNMENT OPERATIONS

JOHN L. MICA, Florida, *Chairman*

TIM WALBERG, Michigan
MICHAEL R. TURNER, Ohio
JUSTIN AMASH, Michigan
THOMAS MASSIE, Kentucky
MARK MEADOWS, North Carolina

GERALD E. CONNOLLY, Virginia *Ranking Minority Member*
JIM COOPER, Tennessee
MARK POCAN, Wisconsin

CONTENTS

	Page
Hearing held on June 20, 2014	1

WITNESSES

Nora Volkow, M.D., Director, National Institute on Drug Abuse	
Oral Statement	12
Written Statement	15
Doug 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	
Oral Statement	30
Written Statement	32
Carl Hart, Ph.D., Associate Professor of Psychology, Co-Director, Institute for Research in African American Studies, Columbia University	
Oral Statement	46
Written Statement	48

APPENDIX

NE Journal of Medicine Article, "Adverse Health Effects of Marijuana Use," submitted by Rep. Mica	74
Article from CNN by Dr. Sanjay Gupta, "Why I Changed my Mind on Weed," submitted by Rep. Connolly	83
Letters and testimonies from families on medical marijuana benefits, submitted by Rep. Connolly	87
Statement of Mr. Connolly constituent Ms. Elizabeth Collins, submitted by Rep. Connolly	143
Congressional letter to HHS Secretary Burwell, submitted by Rep. Connolly	146
Quesstions for the record from Rep. Blumenauer and Rep. Fleming to Dr. Nora D. Volkow, submitted by Rep. Mica	150
Answers to questions for the record from Dr. Throckmorton from Rep. Fleming and Rep. Blumenauer, submitted by Rep. Mica	158

MIXED SIGNALS: THE ADMINISTRATION'S POLICY ON MARIJUANA, PART FOUR—THE HEALTH EFFECTS AND SCIENCE

Friday, June 20, 2014

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON GOVERNMENT OPERATIONS,
COMMITTEE ON OVERSIGHT AND GOVERNMENT REFORM,
Washington, D.C.

The subcommittee met, pursuant to call, at 9:09 a.m., in Room 2154, Rayburn House Office Building, Hon. John Mica [chairman of the subcommittee] presiding.

Present: Representatives Mica, Turner, Woodall and Connolly.

Also present: Representatives Fleming, Cohen, and Blumenauer.

Staff Present: Melissa Beaumont, Assistant Clerk; Will L. Boyington, Deputy Press Secretary; Molly Boyl, Deputy General Counsel and Parliamentarian; John Cuaderes, Deputy Staff Director; Emily Martin, Counsel; Katy Rother, Counsel; Laura L. Rush, Deputy Chief Clerk; Andrew Shult, Deputy Digital Director; Jaron Bourke, Minority Director of Administration; Courtney Cochran, Minority Press Secretary; Devon Hill, Minority Research Assistant; and Cecelia Thomas, Minority Counsel.

Mr. MICA. Good morning, and I'd like to welcome everyone to the Subcommittee on Government Operations hearing this morning. And the title of today's hearing is "Mixed Signals: The Administration's Policy on Marijuana." And this is actually the fourth hearing that we have conducted on the issue of again changes in policies between State, Federal, and local government on marijuana. And today we're going to focus on the health effects and science.

We have done several other hearings. One focused, I think the most recently, on the District's change—and we have a unique relationship, the Congress does, with the District of Columbia—on the legalization and decriminalization issue, change in their law. We did two other hearings, one with the office of ONDCP, and some of it was prompted, too, by the President and the administration's statements that we have heard over the past few months.

Then I think the other hearing that we did was looking at changes in State laws. This subcommittee deals with Federal issues and laws sometimes that end up in conflict. That's one of our responsibilities in the subcommittee, is sorting out the differences between the different levels of jurisdiction and the Federal Government.

As I said, this is our fourth hearing. I will announce, too, in mid-July, and we'll settle on a date with the minority, we're going to

do a fifth hearing. And that one will look at, I call it trains, planes, automobiles, and marijuana. There are a number of issues in conflict relating to transportation safety that we do want to examine carefully, where we're headed there, as far as the Federal laws conflict and, again, some of the changes in State statutes relating to marijuana use.

The order of business will be, I'll start with an opening statement. Then I will yield to other members. And today we have one panel of witnesses. We welcome them. We will introduce them shortly. And after we hear from those witnesses we'll go to a series of questions. We may be joined by other Members of Congress. We're starting off a little early this morning. Some of whom I heard will be with us, and we'll give them the opportunity to participate through a unanimous consent agreement.

So with that we'll begin the hearing, and let me just state again, we have heard different testimony about, again, conflict between State and Federal law, changes in the law, and some societal changes in attitude toward the legalization question. Part of the hearing is prompted by what we have learned about the state of chaos that exists now between some of the administration's actions and their policy.

The focus today is going to really look at the science of the issue, but we also are concerned about sort of the jumbled messaging about marijuana's effect on public health and also the science involved in classifying marijuana as a Schedule 1 drug. That issue has come up several times during these past hearings.

This was all initiated by the President's own statements, and I think some of that contributed and has contributed to some of the confusion. I've got the President's statement in January. President Obama gave an interview about marijuana, describing marijuana as a bad habit and not very different from cigarettes. And he also added in a statement, again, don't take any additional words or add any words to what he said, but he said, I don't think it's more dangerous than alcohol. Part of what we'll hear today is, again, sorting out the science of marijuana and its use and its effect as a health and safety issue.

However, in our first hearing we heard from the Deputy Director of the Office of National Drug Control Policy, and his testimony, as you may recall, differed from that of the President. He first of all told the committee and testified that marijuana's potency has tripled over the past 30 years. And actually this is a very good article, and I'm going to probably ask that we put this as part of the record. Without objection.

And it just came out June 4. It is the New England Journal of Medicine, and it's entitled "The Adverse Effects of Marijuana Use." But this report, the scientific report differs with what the President has said. And actually if you look at this chart, you can see—and that's also published from this scientific journal—that, in fact, that potency has tripled over the past 30 years. So, in fact, what was testified by ONDCP, in fact, is true, that you have so much more potent marijuana on the streets and in the marketplace today.

They also testified to us that long-term marijuana use when begun during adolescence is associated with an average 8-point lower IQ in later life. And, again, the New England Journal of

Medicine cites again some of the impact on the brain and its impact, particularly on adolescents, in that regard. I was quite taken aback when I heard the Deputy Director of ONDCP testify to us about its effects, again more potent, and it does have some serious implications on the mental capacity of our youth.

The other thing, I don't know if we had it on that chart or not, is the increased use—have we got that chart? I know it's in this report, but it does show marijuana. Put that chart up again.

[Chart]

Mr. MICA. The lower part of it shows marijuana, you've seen some pretty dramatic increases in the youth from 2008 to 2007; also, unfortunately, cocaine, and also heroin. So we have higher use of drugs and also higher incidence of abuse problems cited in this report.

The National Institute—well, first of all, let me also take one other statistic before I finish my opening statement, from this report. This report indicates that 2.7 million Americans are dependent on marijuana and that we have approximately 9 percent of the users who become addicted to marijuana, again from the report. Everybody seems to be chiming in. Today on the way in one of my staffers said that Pope Francis had also actually today issued a statement. And here is a copy of that. He told the delegates attending a Rome drug enforcement conference that even limited steps to legalize recreational drugs are not only highly questionable from a legislative standpoint, but they fail to produce the desired effects. And he went on to say it's only a veiled means of surrendering to the phenomenon; let me state in the clearest possible terms, the problem of drug use is not solved with drugs.

So we have got a lot of folks weighing in on their opinion. And, again, the purpose of this hearing is to look at the science of the use of marijuana. The National Institute on Drug Abuse is tasked with studying drug abuse and addiction and other health effects. We are going to hear from representatives there today. NIDA has found that marijuana use has negative effects on the brain, particularly, again as also mentioned in this journal study, the developing brains of our adolescents. Research shows that adults that smoked marijuana during adolescence have impairment in key brain regions associated with alertness, self-consciousness, awareness, memory, and learning.

The Food and Drug Administration, which assists the council on establishing drug scheduling—and again the question has come up that marijuana continues to be listed as a Schedule 1 drug—but the FDA has found that marijuana has no accepted medical use, again, their findings and reports. We'll hear more about that hopefully today.

Regardless, some 20 States—and again driving in today—no, I think that was shaving. Driving I heard the Pope. Shaving I heard that I think New York, maybe today, the 23rd State to legalize marijuana for medical use. And in addition we have Colorado and Washington States have legalized marijuana for recreational use. You may recall we brought in the U.S. Attorney from Colorado to look at the issues and conflict between State and Federal law and enforcement and prosecution. These States' actions did not change the fact that marijuana still remains illegal under Federal law.

Officials from the Office of National Drug Control Policy, the Drug Enforcement Agency, and the National Institute on Drug Abuse insist that marijuana remains a health risk and should not be made legal. However, officials from the Department of Justice issued guidance that explicitly declines to enforce Federal marijuana laws in States that have legalized marijuana for recreational use and have even issued guidance allowing federally regulated banks about dealing in dollars and money obtained through, unfortunately, illegal marijuana businesses that have sprung up.

The President, Federal law enforcement, DEA, U.S. Attorneys, Food and Drug Administration, National Institute on Drug Abuse, we have heard a whole host of differing messages. Last year DEA Administrator Michele Leonhart affirmed that mixed messaging can be harmful by stating the mixed messages being sent to America's teens and our young people about harmfulness and legality of using record high potency marijuana are sometimes obscuring kids' awareness of the effects that the use of marijuana would have on them. I think America owes it to its children, its young people, to give them the best possible start to life, also a responsible message from all of the various jurisdictions, responsible legal jurisdictions, so they and society aren't hindered in the future.

Today we'll hear from two distinguished government witnesses, and then we also have a third witness who joins us from Columbia University. I look forward to a discussion about how mixed messaging from the administration affects drug abuse prevention and treatment. I will also discuss the process of classifying drugs as a Schedule 1 narcotic. Today I hope we can separate fact from fictions.

Mr. Connolly, I've met with my staff yesterday, and we were talking about what this hearing would be about, and I told them this is going to be like the old television series, law enforcement series, you had Jack Webb, you're old enough to remember, who said, he'd go in and say, all I want is the facts, just the facts, ma'am. And the startling thing was——

Mr. CONNOLLY. I'm really not old enough. I just remember hearing about it.

Mr. MICA. I'll give you that, Mr. Connolly. But my point is that none of the staff had heard that phrase or had heard of Jack Webb and that series. "Dragnet," I guess, was the name of the series. But that's really our purpose here is all we want are the facts, and that's what we are going to deal with hopefully in this and future sessions.

So with that, Mr. Connolly, you're recognized.

Mr. CONNOLLY. Thank you, Mr. Chairman, and thank you for holding this fourth in a series of hearings to examine today the scientific perspective on scheduling marijuana under the Controlled Substances Act. I must say, in this examination what's going to be revealed is that we have some of the most restrictive guidelines in terms of research all skewed toward outcomes that talk about the harmful effects of marijuana, almost none of which talk about the beneficial effects potentially, the positive health effects of marijuana, because we don't allow the research.

And we have one agency that severely restricts for researchers access to marijuana in a way that is almost unique to marijuana.

In fact, we don't do that with other controlled substances. But we're going to examine that today.

I think the title of this hearing shouldn't be about this administration. It really is almost 40 years of U.S. drug policy with respect to marijuana through Republican and Democratic administrations.

Today as you indicated, Mr. Chairman, 22 States and the District of Columbia have actually departed from Federal policy and now have laws on the books that allow for some medical use of marijuana. Since 1970, the Federal Government has classified marijuana alongside heroin, LSD, and Ecstasy as a Schedule 1 drug for which there is, "no currently accepted medical use and a high potential for abuse"—that's interesting, that's quite an interesting message to the 22 States and the District of Columbia who have respectfully decided otherwise—in addition to constituting one of, "the most dangerous drugs of all the drug schedules with potentially severe psychological and physical dependence." That's an astounding statement, and it will be very interesting whether that holds up in terms of science.

I'm neither a doctor nor a scientist—neither is the Pope, I might add—but I surely am not alone in raising my eyebrows over a classification system that would not only group marijuana among heroin, LSD, and Ecstasy in terms of danger for abuse, but would rank cocaine, Oxycontin, and methamphetamines as less dangerous, with less potential for abuse than marijuana. Is that science?

In recent years, there's been a growing acceptance of the potential benefits of medicinal marijuana. Last year Dr. Sanjay Gupta, a staff neurosurgeon at Emory Clinic and CNN's chief medical correspondent, penned an op-ed in support of medical marijuana. And I would ask that his full statement be entered into the record.

Mr. MICA. Without objection.

Mr. CONNOLLY. I thank the chair. In which he stated, quote, "We have been terribly and systematically misled for nearly 70 years in this country, and I apologize for my own role in it." He noted, "While investigating, I realized something else quite important. Medical marijuana is not new, and the medical community has been writing about it for a long time. There were, in fact, hundreds of journal articles, mostly documenting the benefits. Most of those papers, however, were written between the years of 1840 and 1930." And in part it's because we created a system limiting research to skew the outcome so that we downplayed the positive benefits and highlighted the harmful effects.

Meanwhile, on April 28, 2014, my Republican colleague and fellow Virginian, Morgan Griffith, hardly a liberal Democrat, introduced H.R. 4498, the Legitimate Use of Medicinal Marijuana Act, which would reclassify marijuana as a Schedule 2 drug. Currently practitioners that are registered with DEA and have HHS approval may only obtain marijuana for approved research through one single entity, the National Institute on Drug Abuse, NIDA. NIDA acts as the single official source through which researchers may obtain marijuana for research purposes, and it's estimated that more than 90 percent of the marijuana research NIDA approves is to only examine the harmful effects of cannabis. That skews research.

Regrettably, the more I learn about the process, the more I feel we may be trapped in a Catch-22—another reference to an older

era, Mr. Chairman—that would make Joseph Heller proud. As one nonprofit organization noted, "DEA and NIDA have successfully created a Catch-22 for patients, doctors, and scientists by denying that marijuana is a medicine because it is not FDA approved, while simultaneously, of course, obstructing the very research that might be required for FDA approval."

Indeed, in a 2007 ruling that found allowing private production of cannabis for research purposes was in the public interest, a DEA administrative law judge stated, and I quote, "NIDA's system for evaluating requests for marijuana research has resulted in some researchers who hold DEA registrations and the requisite approval from the Department of Health and Human Services being unable to conduct their research because NIDA has refused to provide them with marijuana." Again, skewing research. If this is about science, then let the scientists and the researchers have at it, and let's see what they come up with. But if in advance you prevent them from having the very means to do that research, well, how can any of us be surprised at the outcome?

Thus as it stands today, on the one hand we have the Federal Government that for more than four decades—not just this administration, Mr. Chairman—running has insisted on placing marijuana under the most restrictive drug schedule possible, impeding scientific research into the drug's potential benefits. And that's one of the reasons I guess 22 States and the District of Columbia, and maybe a 23rd State, have rebelled against this heavyhanded Federal approach.

On the other hand, we have very compelling anecdotal evidence and some emergent science that indicates cannabis may well have medicinal properties that can benefit individuals with certain conditions, such as individuals experiencing severe epileptic seizures or veterans suffering post-traumatic stress syndrome. And in the middle stand policymakers such as myself who would love nothing more than to carefully examine and review the evidence, but find ourselves facing an astonishingly barren research environment by design.

It is time for our Nation to approach the debate over marijuana policy with more honesty and less hyperbole and more science. It's a disservice to public discourse when policymakers refuse to grapple with challenging and complex issues in an objective and open manner. We can't ignore the growing evidence of families whose lives have been positively impacted by medicinal marijuana.

For example, one of my constituents in northern Virginia, Ms.Beth Collins, has watched her daughter suffer for years with severe epilepsy. This horrible disease has caused Ms. Collins' teenage daughter, Jennifer, to experience multiple seizures, at times more than 300 seizures in a single day. For years the Collins family tried everything, they tried multiple medication regimes, all of which wrought painful side effects to their daughter and none of which were efficacious in treating her systems.

Today Jennifer's seizures have dramatically dissipated by 85 to 90 percent. That's the good news. The bad news is that Jennifer was forced to leave Fairfax County and move to Colorado Springs because the treatment that has proven quite effective, a daily dose

of medicinal marijuana oil from a syringe, not smoking joints, cannot be legally purchased in the Commonwealth of Virginia.

Our Nation can't continue to ignore compelling stories like that of the Collins family and so many others. In fact, Mr. Chairman, I would also ask unanimous consent, I have a series of letters and pieces of testimony from families attesting to the beneficial effects of medicinal marijuana for their medical conditions.

Mr. MICA. Without objection, it will be part of the record.

Mr. CONNOLLY. I thank the chair, and I'm almost done.

I recognize that anecdote must be reinforced with rigorous scientific data. That's why I believe we should act swiftly to reclassify marijuana in order to allow for legitimate medicinal uses and research and enable rigorous scientific research that will provide a better understanding of how marijuana may be used if proper.

I have long believed that the Federal Government governs best when it truly listens and learns from our States, which have been for decades called the laboratories of democracy. They want their local governments to have the opportunity to innovate and experiment with regulatory and enforcement frameworks governing medicinal marijuana research and use, and I believe it is in our national interest to let those ongoing laboratories of democracy proceed, and to proceed within a rational Federal framework, one which I do not believe exists today. Thank you, Mr. Chairman.

Mr. MICA. Thank you for your opening statement.

And Mr. Turner has left. We have three members, and Mr. Connolly moves that——

Mr. CONNOLLY. Mr. Chairman, I do.

Mr. MICA. —and ask unanimous consent that our colleague from Oregon, Mr. Blumenauer, our colleague from Tennessee, Mr. Cohen, and our colleague from Louisiana, Dr. Fleming, be allowed to participate in today's hearing.

Mr. CONNOLLY. I so move, Mr. Chairman.

Mr. MICA. Without objection, so ordered.

Mr. CONNOLLY. And, Mr. Chairman, just one other thing, a unanimous consent request. Very compelling testimony, and I commend it to you and my colleagues, from my constituent Beth Collins on their story, and I'd ask that that be entered fully into the record.

Mr. MICA. Without objection, so ordered.

Mr. CONNOLLY. I thank the chair.

Mr. MICA. Now, let's see. We heard from Mr. Connolly.

Mr. Fleming.

Mr. FLEMING. Thank you, Mr. Chairman. And I want to thank the panel for allowing me to be here today and welcome the panel.

Yes, the medicinalization, the decriminalization, and the legalization of marijuana has been sweeping the Nation. But it's been happening as a result of myths, mythology about marijuana. And I just want to touch on those from the book from Kevin Sabet, a Ph.D. And an expert on the subject.

Myth number one, marijuana is harmless and nonaddictive. That's simply not true. It's a complete myth. The most common diagnosis today for young people into drug and alcohol centers is for marijuana addiction. It does have a recognized withdrawal syndrome.

Myth number two, countless people are behind bars simply for smoking marijuana. Not true. Yes, there are a lot of people behind bars who smoked marijuana, but that's not why they're behind bars. They're either behind bars for dealing or involved in violence or theft or some other crime.

The legality of alcohol and tobacco strengthens the case for legal marijuana. Terrible myth. If we have problems with tobacco and alcohol, why do we want to add a third problematic substance of addiction and create even more problems in our society? It makes no sense whatsoever.

Also a myth, legal marijuana will solve the government's budgetary problems. The outcomes in terms of health problems, the outcomes in terms of government dependency when people can't get or maintain a job will cost governments a huge amount of money. We'll see our welfare roles, our Medicaid roles, and other things will skyrocket.

Another myth, a common myth, Portugal and Holland provide successful models of legalization. First of all, smoking pot there is not legal. It's decriminalized, not legal, and in recent years they have begun to turn back the time, turn back the clock on the steps of liberalization of that use.

Prevention, intervention, and treatment are doomed to fail. Not true at all. Wherever we see that there is prevention, wherever we see that there is intervention, we see lower use. And, in fact, we talked yesterday in the Addiction Caucus where there is liberalization of thought, where there is less threat to use, we see the use go up and all the other problems that go with it, addiction, drug driving, accidents, deaths from accidents, et cetera.

Now, let's talk about medicinal use. And Mr. Connolly suggests that we just haven't been studying that. Well, I beg to disagree, because my university that I graduated from, the University of Mississippi, both undergraduate and as a physician, this has been studied there in their Pharmacology Department for forty years. The reason why you're not hearing about all the great things that come from marijuana is they're not finding good things coming from marijuana. The only thing they can find is the harm.

Now, there is a discussion about seizures. I have raked across the literature on this. I can't find any authority on this, whether it's rare seize disorders or common ones, where marijuana is used as a treatment, where it's a recognized use. Now, you might say, well, yeah, but it's a Schedule 1 drug. Well, actually no. There is a Schedule 3 drug called Marinol, which is actually an oral form of marijuana, and it is used and it can be used at the same equivalency of, say, Lortab or Oxycontin or a drug like that that's used in more common, everyday medical use.

So you see, it's been there and can be used, and there is a discussion about, well, maybe the oil that doesn't include THC can be used for seizure disorders. Well, sure, that's an extract, and I'm sure we would be able to make that a safely used drug. But no one's been able to prove that the use of marijuana oil has any real benefit. Yeah, we here the anecdotal stories, but that's how the myths come out, is someone tells a story and they tell someone else, and before you know, it's been blown completely out of proportion.

And then lastly, something of which I've studied for years and wrote a book on in 2007, is the fact that we know the earlier in life that the human brain is exposed to addicting substances, again, realizing that the human brain does not mature until age 25 to 30. That's right; half this room have immature brains today. And as a result——

Mr. CONNOLLY. Would my colleague want to tell us which half?

Mr. FLEMING. Don't get me started, sir.

But if you look at the fact that the average age of first use of alcohol, tobacco, and marijuana is 10 years old, then you find that the pathway, the building of the reward system towards addiction begins very early in life. And so when you diagnose someone with an addiction at age 25 or 30, they've been in that process for a decade.

And so as we legalize, decriminalize, or otherwise medicinalize marijuana, that means more and more marijuana will be available to young people, and they will use it. And we're already finding this, looking at California and Colorado, places where this process has been going on.

So I would say to my colleagues today that I look forward to hearing from our panel, but as we study marijuana, all we find is bad news, more heart disease, more lung disease, higher rates of schizophrenic, and many other problems, all apart from addiction, which, of course, is a problem.

And I'll end with this. The other myth is that not only is marijuana non addictive, but it's not a gateway drug. And I'll tell you what a drug addict told me. He said, Doctor, every addicting substance is a gateway drug, and marijuana is no exception to that. Thank you and I yield back.

Mr. MICA. I thank the gentleman.

Mr. MICA. And let me see seniority.

Mr. Blumenaur, thank you for joining us, you're recognized.

Mr. BLUMENAUER. Thank you very much, Mr. Chairman. Chairman Mica, I appreciate your on going efforts to sort of peel back the level of the onion with the these hearings, your courtesy in permitting us to join in, to follow the information. And it's certainly timely, and you've highlighted some areas of contradiction, and in this area I think today's hearing is one that hopefully we can all agree there needs to be some progress.

I appreciate Dr. Fleming not talking about which half of the brain are immature. I just think it may not always deal with chronology or early substance abuse, but I appreciate the benefit of the doubt.

I also appreciate, I think he used the phrase three times in his opening statement that no one has been able to prove, and then had a clause after that. And I think that's exactly the case, and that is why this is such an important hearing. It's because when we have a million people in the United States who are currently using medical marijuana legally under the laws of the 22—it looks like it's going to be 23 states now, in the State of New York and the District of Columbia, and then there are other states that are dealing with variations on this—it's inexcusable that we don't have better information.

I'm embarrassed for this administration and previous administrations for not having a robust, effective program to be able to deal with the facts. I'm embarrassed when I'm at OHSU dealing with neuroscientists and physicians who are talking about patients that they have, similar to what Mr. Connolly was talking about, who are having very positive results, and it is harder for those scientists and doctors to get marijuana to research than it is for parents to self-medicate the kids and really not knowing what they're being given. And part of that is the fault of the Federal Government and stupid policies.

I would note for the record, Mr. Chairman, and ask respectfully that I could enter into the committee's record a letter dated June 17, a bipartisan letter signed by 30 Members of Congress to Secretary Burwell urging that there be changes in the research protocol.

Mr. MICA. Without objection, so ordered.

Mr. BLUMENAUER. Thank you, Mr. Chairman.

It points outs in the letter that only with marijuana and no other Schedule 1 substance is there an additional Public Health Service review for non-NIH-funded protocols established in May 21, 1999, in the guidance for procedures for provision of marijuana for medical research. We have got examples as well of people who are jumping through procedural hoops, people who are approved for research, and we have got this little narrow spigot that does not work.

I'm embarrassed. I'm embarrassed for you having to be here to defend a broken system. I'm embarrassed that we, after years and years and years, and as the States are moving ahead of us, the Federal Government is not an effective partner to be able to have the information.

Now, Dr. Fleming and I have modestly different views about what a sustainable marijuana policy should be, but we are absolutely in accord that we shouldn't be guessing, that we should have facts, we should have effective research, it should work for the American people.

And I, Mr. Chairman, appreciate the courtesy of being able to join. I will be monitoring this. I'm bouncing back and forth between a Ways and Means hearing. I'm going to be here as much as I can. But I really think this is critically important. I appreciate you doing it and you and the ranking member allowing us to participate.

Mr. MICA. Thank you, Mr. Blumenauer.

Let me recognize the gentleman from Tennessee, Mr. Cohen.

Mr. COHEN. Thank you, Mr. Chair. And again, I appreciate your having the hearing and your allowing those that are not on the committee but have an interest in the subject to participate.

First, I want to compliment Dr. Hart for maintaining his demeanor during some of the statements that have been made, rather amazing ability to withhold. My colleague from Louisiana talks about marijuana and says there's been nothing found beneficial. Of course, we know that's not true because the people with epileptic seizures, the mothers who have found that part of that is the cannabinoids, or whatever it is, it definitely helps their children. There's no question about that. And States are falling over them-

selves now, even Tennessee, to study that in Mississippi because kids are having their seizures reduced, which shows that the whole idea of it being Schedule 1 and having no accepted medical benefit is wrong because these kids are benefiting from it.

Montel Williams is pretty strong on beneficial treatment, and a lot of people with cancer find it to help with nausea. I, for one, think that we should expand our horizons and all opportunities we can to people who have cancer and other life-threatening diseases to ease their pain and their anguish, to alleviate their hunger desires for which they may have been limited because of the illness and to give them some type of ability to smile. That would be a nice thing to do.

Mr. Fleming talks a lot about medical marijuana, but doesn't bring up anything about the effects of arrests. Dr. Hart talks about that a lot. You have to balance everything in society and how it affects people. And, yeah, maybe 9 percent, I don't know what the figures that Dr. Volkow mentioned or Dr. Throckmorton, I think it was Dr. Volkow, is that 9 percent may become addicted at some point, et cetera. Well, a great number more than that get arrested and get a scarlet "M" fastened to their chest for life, which means they don't get a job maybe or a college scholarship or an opportunity to live in public housing and other things.

And you have to weigh, no question there are some bad effects of marijuana, but there are some even more harmful effects in taking people's liberty. And you take judgment, informed judgment, and you take depriving people of their liberty and putting them in jail. And there are people in jail for possession. There are lots of people in jail for possession. Even for a short time it's not good. But some of them for a short time. Some of them longer because they don't have money to get bailed out, and they don't have access to attorneys that can get them out. So that's just not accurate.

We talk about 40 years of this policy. Nixon started the war on drugs, and we know that Nixon did it for politics and that Ehrlichman talked to him about it, or Haldeman, I get the two of them confused, the twin devils of that administration. They were not the twin devils, there were lots of devils in that administration, but they were the two poster children for harmful conduct and dirty tricks that were illegal, brought down a President. But they admitted that scheduling as Schedule 1 was for the purpose of politics, and it was a great thing and it had to do with race.

And it really goes back to the 1930s, and while President Roosevelt probably wasn't too aware of it, Harry Anslinger came around, and it was the Hispanics. And Mr. Fleming talked about these myths that get out there, and all of a sudden these myths are out there about medical benefits, and then they become kind of like Goebbels' lie—I can't say that, excuse me, pardon me—kind of like repeating lies over and over again and they become accepted. You know, that's what "Reefer Madness" was, and those lies got perpetrated.

So the bottom line is what Mr. Blumenauer talked about is so true. We need research. We need study. We need study for the States. We need studies for the children. And there's no question children shouldn't be doing, smoking marijuana. That's not what this should be about. They shouldn't be doing alcohol, tobacco,

marijuana, having sex, none of that. It's true some of that happens, but it shouldn't happen, and nobody is suggesting it.

But for adults in a society that prides itself on life, liberty, and the pursuit of happiness, if you make it illegal that's liberty, and some people think it's the pursuit of happiness. Whether that's true happiness or not, whether you find it in a bottle of Jack Daniels or whether you find it in a nice pinot noir or Budweiser or whatever, that's each person's choice in a free society. So I think the study is so important.

Anyway, thank you, Mr. Chairman. I appreciate you, and I hope when you're shaving next you'll hear about the 24th State.

Mr. MICA. Well, thank you, Mr. Cohen, for joining us again.

And I think there are no other opening statements, so what we'll do now is turn to our three witnesses. Again welcome them. Before I do that, let me say that members may have 7 days to submit opening statements for the record. And without objection, we'll include that.

Let me again welcome our three witnesses. And I don't think you all have testified before our panel before. Our method of operation, so to speak, is to allow you about 5 minutes. We only have three witnesses and one panel, so we'll be a little bit generous there. But we ask you, if you have additional lengthy information or data you'd like to be made part of the record, just to request through the chair and we'd accommodate you.

Let me introduce our witnesses, and then I'll swear you in. We have first Dr. Nora Volkow, and the doctor is Director of the National Institute of Drug Abuse. Dr. Doug Throckmorton, and he is the Deputy Director for Regulatory Programs for the Food and Drug Administration. And then we have Dr. Carl Hart. He's an associate professor of psychology at Columbia University. So those are our three witnesses in this panel.

This is an investigation and oversight subcommittee of Congress, so just stand please, and I'll swear you in.

Raise your right hand. Do you solemnly swear or affirm that the testimony you are about to give before this subcommittee of Congress is the whole truth and nothing but the truth?

And all of the witnesses, the record will reflect, answered in the affirmative. And I welcome each of you, and I will recognize you for your testimony. First we'll have our Director of the National Institute of Drug Abuse, Dr. Volkow.

Welcome, and you're recognized.

WITNESS STATEMENTS

STATEMENT OF NORA VOLKOW

Dr. VOLKOW. Good morning. I very much appreciate the opportunity to come to speak with you, and I also very much appreciate your comments, addressing and clearly identifying a subject that is complex and that has evidently polarized very much our perspective. I like the concept of saying where the facts is, and I'm going to try to actually identify where things are, the information is factual, and where the information is currently not fully available or unclear.

Marijuana is used because it activates the endogenous cannabinoid signaling systems in reward areas, and the endogenous cannabinoid system actually is not just in reward areas, but it is involved in multiple functions of the brain and multiple functions of our body. And that's why there has been so much interest in terms of the potential of manipulating the endogenous cannabinoid system for a variety of medical conditions, and that's, I think, at the essence of the debate.

The issue with taking marijuana which activates the system is that it inhibits the individual's endogenous cannabinoid systems, so as a result of that the person may be actually in a state of deprivation when the drug is no longer available. And that is an issue that needs to be addressed as one considers the effects of repeated administration of marijuana.

Marijuana is the most common used elicit drug in our country, and its use is particularly high among adolescents. And this has been increasing over the past years. More high school seniors now smoke marijuana than smoke cigarettes, and we have one of the highest rates of regular use of marijuana that we've had since we've been actually evaluating it; 6.5 percent of 12th graders report regular use of marijuana. So that's almost daily use, which is the one that's most likely to be associated with adverse effects.

This increased use of marijuana we know reflects a decreased perception that marijuana is risky, which then increases the prevalence of its use certainly among teenagers. But this belief is really not backed up by evidence that has evolved over the past 10, 15 years when these changes in perception actually over the past 10 years have dramatically shifted. In fact, there is significant evidence that marijuana can have a deleterious effects.

Now, not everybody will get the deleterious effects. It's like not everybody that smokes cigarettes will get cancer. And yet we don't question it. But we do use that logic in order to actually address the so-called safety of marijuana.

So what is it, how harmful it is, and where is the harmfulness coming from? Well, in addressing marijuana we have to differentiate between acute and chronic effects, repeated effects. Acute effects relate to intoxication. And where is the facts? We know that marijuana impairs motor coordination, perception of time, and we do know that marijuana contributes significantly to car accidents, including fatal ones. And that is basically no question. I mean, the facts are there. There is also evidence that marijuana from studies, if you are intoxicated with marijuana, the risk of being in a car accident is basically double. And if you combine it with alcohol, the risk increases over a dose of each drug alone.

Now, acute intoxication of marijuana is also associated with psychotic episodes, overall most of them short lasting; and we are starting to see reports in the medical literature of medical complications we did not know about, like cerebrovascular and cardiovascular pathology evidently associated with a higher content THC.

So what about the long-term effects of marijuana? Factual, marijuana produces addiction, and as mentioned before, not everybody becomes addicted. Nine percent will become addicted, of those that get exposed; 16 percent if it started when they were teenagers; and 50 percent, they use it regularly.

The discussion of is marijuana gateway drug, very well placed. Marijuana usually precedes the use of other drugs, but this does not negate that the other drugs can actually also act as gateway drugs. Clinical studies in animals indicates that exposure early on actually changes the sensitivity of the reward centers of the brain. Also, animal studies show that exposure to marijuana early on impairs with the connections among neurons, the connections that form in order for neurons to communicate with each other are disturbed by the use of marijuana very early on, cannabinoids.

On human subjects there is evidence that those that were exposed very early on to marijuana have disrupted connectivity in areas of the brain involved with memory and interceptive awareness. There is also evidence from many studies independent that individuals that smoke marijuana regularly during adolescence actually are much more likely to drop out of school and have much lower educational achievement. The mechanisms underlying these associations, however, are not completely understood and could be multifactorial.

Now, because of all of these, and even though there are many, many, many studies that have emerged, many of them have been criticized for one of the factors—they may have not had sufficient sample sizes; they were not controlling for premorbid performance prior to use of marijuana; they actually did not follow individuals long enough or they did not have the sensitivity.

So it is clear in my brain right now as we look forward that we need to actually ask an organization that develops evidence. We need to conduct a properly evaluated study to assess the consequences of marijuana exposure in teenagers, because regardless of what happens with regulations, they are the ones that are more likely to be vulnerable to the adverse effects.

I would like to conclude by the fact that as we look at discussions of where we are and where we are not, the greatest number of cases associated with mortality, morbidity, and economic cost to our society from drugs, by far, by far, are the legal drugs, alcohol and tobacco, much more than all of the other drugs even multiplied. And it's not because alcohol and tobacco, nicotine are more dangerous. Certainly no one will question methamphetamine or cocaine. It is because their legal status makes them more available, and actually perception of risk is much lower.

And I think we have to keep this in mind as we go into these discussions, and whatever the solutions come around, we have to look towards what we have seen in the past of consequences of some of these policies to try to minimize the risk of policies. We all want to do the right thing, and how we look at the data is slightly different. And I think that that is the value of getting together and also very importantly the partnerships among the different agencies.

Thanks very much for having me here, and I will be happy to answer any questions.

Mr. MICA. Thank you.

[Prepared statement of Dr. Volkow follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Mixed Signals: The Administration's Policy on Marijuana, Part Four

Scientific Focus on the Adverse Health Effects of Marijuana Use

Witness appearing before the

House Committee on Oversight and Government Reform

Subcommittee on Government Operations

Nora D. Volkow, M.D.

Director, National Institute on Drug Abuse

June 20, 2014

Mr. Chairman and Members of the Subcommittee. Thank you for inviting the National Institute on Drug Abuse (NIDA), a component of the National Institutes of Health (NIH), to participate in this hearing to share what research tells us about the health effects of marijuana use. In light of the rapidly shifting landscape regarding marijuana use for medical and recreational purposes, it is more important than ever to spread accurate information about marijuana's health effects and to conduct the research needed to fill the gaps in our knowledge.

Background

Marijuana is the most commonly used illicit drug in the United States, with about 12 percent of people aged 12 and over reporting use in the past year.[1] Rates of use are particularly high (and increasing) in teenagers, corresponding to a diminishing perception of the drug's risks by this age group.[2] In 2009, current (past-month) use of marijuana by 12th graders surpassed cigarette smoking, and according to the 2013 Monitoring the Future (MTF) survey of high school students, 6.5 percent of 12th graders report using marijuana daily or near-daily.[3]

MTF indicates a growing perception among young people that marijuana is a relatively harmless drug, and according to a recent Pew survey, a large majority of adults (69 percent) view alcohol as more dangerous than marijuana.[4] Many studies have reported detrimental effects from marijuana use, but others have not or have left much open to interpretation, and although research is actively underway to address these questions, the extent of marijuana's harms remains hard to specify with as much precision as would be ideal.

We must be careful drawing conclusions from past research on marijuana's effects for several reasons. First, alcohol and tobacco are linked to more morbidity and mortality in our society than other drugs in part due to their widespread availability as legal substances. It is likely that, were patterns of marijuana use by people of all ages to become comparable to that of these other legal

[1] SAMHSA. Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health. , 2013.
[2] MTF
[3] Johnston LD, O'Malley PM, Bachman JG, J.E. S (2013) Overview: key Findings on Adolescent Drug use. 1975-2013. In: Monitoring the Future national Survey Results on Drug Use (University of Michigan).
[4] Pew Research Center, April 2014, "America's Changing Drug Policy Landscape"; available at http://www.people-press.org/files/legacy-pdf/04-02-14%20Drug%20Policy%20Release.pdf

substances, statistics regarding marijuana's impact on automobile accidents (*i.e.,* compared to alcohol), lung diseases (*i.e.,* compared to tobacco), or treatment needs for those addicted (compared to both alcohol and tobacco) would look much different than they do currently. Another reason we must be careful drawing conclusions from past research on marijuana's effects is the dramatic increase in concentrations of the marijuana plant's main psychoactive ingredient, tetrahydrocannabinol (THC) seen over the past couple decades, along with the new ways of administering high THC content (*e.g.,* electronic cigarette devices). The potency of an average marijuana cigarette has steadily increased from roughly 3 percent THC in the early 1990s to 12.5 percent THC in 2013:[5] During this same period, the potency of marijuana extracts (also known as "hash oil") has also climbed to what are now staggering levels: The average marijuana extract contains over 50 percent THC, with some samples containing more than 80 percent THC.[6] This means some historical findings about health and developmental effects from marijuana use may not be relevant when trying to predict effects on contemporary users. A rapid rise in emergency room (ER) admissions linked to marijuana use attests to the greater dangers of acute use than have been seen in the past. There were 128,857 ER visits related to marijuana use in 2011, nearly double the number from 2004 (65,699) and comparable to the number of visits in 2011 related to heroin use (122,517); in the same year, 606,653 visits were related to alcohol use.[7]

Despite some areas of uncertainty, a substantial body of research, most of it supported by NIDA, enables us to say with some confidence that marijuana use may result in a wide range of adverse consequences for health, safety, and other domains, and that by interfering with the endocannabinoid system—an important neuronal signaling system that processes critical information in the brain and the rest of the body—it may have particularly harmful long-term effects when it is used heavily (*e.g.,* on a daily or near-daily basis) during adolescence.[8] I would like to review in this testimony what scientific research enables us to say about the adverse acute (short-term) and chronic (long-term) effects of marijuana use.

---

[5] ElSohly MA (2014) Potency Monitoring Program Quarterly Report Number 124. Reporting Period: 12/16/2013 -03/15/2014 National Institute on Drug Abuse. Contract Number: NO 1 DA-1 0-7773. (HHS, ed): National Center for Natural Products Research, a Division of the Research Institute of Pharmaceutical Sciences.
[6] Id.
[7] SAMHSA. Drug Abuse Warning Network, 2011: National Estimates of Drug-Related Emergency Department Visits. 2011.
[8] FERGUSSON D. M., BODEN J. M. Cannabis use and later life outcomes. Addiction 2008;103:969-76 2008: 103: 969-976.

Acute Effects of Marijuana Use

Health and Safety. Although the reported incidents of death due to the acute influence of marijuana are limited, increasing numbers of ER visits related to marijuana (on its own or in combination with other substances) have been reported. Among the possible causes are involvement in accidents, acute psychotic reactions (paranoia, perceptual distortions, loss of touch with reality), and heart attacks in people with cardiovascular risks or disease.[9] The reported rise in ER visits may be related to the increase in THC content in marijuana, the use of vaporizers that allow users to administer very highly concentrated extracts, and, particularly in the case of children and inexperienced users, the consumption of food products (*e.g.,* candies and baked goods) that contain marijuana extracts. Also troubling are the customary effects of marijuana intoxication, including impairments in memory, judgment, and decision-making ability, which compromise an individual's functioning in various ways that can indirectly have damaging or even devastating impact on their life and health. For example, as is true of alcohol and other drugs, marijuana can increase the likelihood of engaging in risky behaviors such as unsafe sex, which raises the risk of contracting or transmitting sexually transmitted diseases (STDs) including human immunodeficiency virus (HIV).[10] However, the most pronounced immediate threat from marijuana use is through impacting driving ability.

Marijuana significantly impairs coordination and reaction time and is the illicit drug most frequently found to be involved in automobile accidents, including fatal ones.[11] Controlled driving simulation studies have found a direct relationship between blood THC concentration and impaired performance.[12] Recent marijuana smoking and/or blood THC concentrations of 2-5 ng/mL are associated with substantial driving impairment.[13] A meta-analysis of multiple studies

[9] Thomas G, Kloner RA, Rezkalla S. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana inhalation: what cardiologists need to know. Am J Cardiol 2014;113:187-90.
[10] Andrade LF, Carroll KM, Petry NM (2013). Marijuana use is associated with risky sexual behaviors in treatment-seeking polysubstance abusers. American Journal of Drug and Alcohol Abuse 39:266-271.
[11] Brady JE, Li G (2014) Trends in Alcohol and Other Drugs Detected in Fatally Injured Drivers in the United States, 199-2010," American Journal of Epidemiology [Epub ahead of print].
[12] Lenné M, Dietze P, Triggs T, Walmsley S, Murphy B, Redman J. The effects of cannabis and alcohol on simulated arterial driving: Influences of driving experience and task demand. Accid Anal Prev 2010;42:859-66.
[13] Hartman RL, Huestis MA. Cannabis effects on driving skills. Clin Chem 2013;59:478-92.

found that the risk of being involved in an accident roughly doubles after marijuana use.[14] For comparison, one study found that drivers with a blood alcohol level above 0.08 percent, the legal limit in most countries, are at a five-fold risk for having an accident and that this increases to 27-fold for drivers under 21.[15] Accident-involved drivers with THC in their blood, particularly higher levels, are three to seven times more likely to be responsible for the accident than drivers who had not used drugs or alcohol.[16] The risk associated with marijuana in combination with alcohol appears to be greater than that for either drug by itself.[17]

School Performance. By impairing critical cognitive functions including learning, memory, and problem solving—effects which may last for days after acute intoxication[18]—marijuana use may compromise the ability to function in school settings. Its wide use by teenagers (22.7 percent of 12th graders report past-month use[19]) makes marijuana of particular concern when it comes to individual academic success. Failing to learn in school, even as a result of temporary cognitive impairment, interferes with the ability to advance educationally and thus may explain associations that have been found between regular use of marijuana and poorer school performance.[20] The 6.5 percent of 12th graders reporting daily or near-daily marijuana use in the MTF survey likely underestimates the prevalence of regular use among all 17-18-year-olds, as regular marijuana users are more likely to drop out of school[21] and thus not be included in the survey.

Long-Term/Chronic Use

The deleterious impact of marijuana on cognitive performance appears to extend beyond the effects of acute intoxication, accumulating among those who use marijuana heavily and/or over

[14] Ramaekers JG, Berghaus G, van Laar M, Drummer OH. Dose related risk of motor vehicle crashes after cannabis use. Drug Alcohol Depend 2004;73:109-19.
[15] Peck RC, Gebers MA, Voas RB, Romano E. The relationship between blood alcohol concentration (BAC), age, and crash risk. J Safety Res 2008;39:311-9.
[16] Ramaekers J, Berghaus G, van Laar M, Drummer O. Dose related risk of motor vehicle crashes after cannabis use. Drug Alcohol Depend 2004;73:109-19.
[17] Hartman RL, Huestis MA. Cannabis effects on driving skills. Clin Chem 2013;59:478-92.
[18] Crean RD, Crane NA, Mason BJ. An evidence based review of acute and long-term effects of cannabis use on executive cognitive functions. J Addict Med 2011;5:1-8.
[19] MTF
[20] Lynskey M, Hall W (2000) The effects of adolescent cannabis use on educational attainment: a review. Addiction 95:1621-1630.
[21] Bray, J.W., Zarkin, G.A., Ringwalt, C. and Qi, J.F. The relationship between marijuana initiation and dropping out of high school. Health Econ., 9 (2000), pp. 9–18

the long-term, particularly when use is initiated during adolescence. This may reflect the impact THC exposure has on brain development. The human brain undergoes a continuous and protracted process of development from the prenatal period through childhood and adolescence, and it is not done maturing until the mid-20s. Throughout this period the brain is strongly influenced by everything the individual experiences, and its ongoing maturation makes it more vulnerable to the adverse long-term effects of exposure to substances, including THC. The harmful impact of heavy or long-term THC exposure on the developing brain is supported by considerable animal research and a lesser but growing amount of research in humans.

Effects on brain development from prenatal exposure. As the brain is developing, the endocannabinoid system plays a key role in the formation of synapses, and the ability of exogenous cannabinoids (*e.g.,* those found in marijuana) to interfere with this signaling system may explain the alterations in brain development seen in animals prenatally exposed to THC. Studies in rats show that prenatal THC exposure can perturb the establishment of connections between neurons and connections among different parts of the brain[22], including the ventral tegmental area, which contains the dopaminergic cells necessary for responding to natural rewards and responsible for the addictive effects of drugs.[23] The extent to which prenatal exposure to marijuana produces similar effects in humans is still poorly understood. Although an estimated 9 to 22 percent of pregnant women have used marijuana and some studies have linked prenatal exposure to subtle negative effects on higher-order thinking, including problem-solving, memory, planning, impulsivity, and attention, it is difficult to disentangle the effects of marijuana use from various confounding factors, such as a mother's use of other drugs or alcohol.[24]

Effects on brain development in adolescence. We know more about the effects of THC on brain development in adolescence. As in the case of prenatal exposure, studies in rats show that early exposure (comparable to adolescence in human development) to THC is associated with an altered reward system, which increases the likelihood that an animal will self-administer other

[22] Tortoriello G, Morris CV, Alpar A, et al. Miswiring the brain: Δ9-tetrahydrocannabinol disrupts cortical development by inducing an SCG10/stathmin-2 degradation pathway. EMBO J 2014 Jan 27 [Epub ahead of print] 2014.
[23] Dinieri JA, Hurd YL. Rat models of prenatal and adolescent cannabis exposure. Methods Mol Biol 2012;829:231-42.
[24] Brown HL, Graves CR. Smoking and marijuana use in pregnancy. Clin Obstet Gynecol 2013;56:107-13. Jutras-Aswad D, DiNieri JA, Harkany T, Hurd YL. Neurobiological consequences of maternal cannabis on human fetal development and its neuropsychiatric outcome. Eur Arch Psychiatry Clin Neurosci 2009;259:395-412.

drugs (*e.g.,* heroin) when given the opportunity. And imaging studies in humans show that those individuals who consumed marijuana regularly during adolescence (compared to those who did not consume marijuana during adolescence) display impaired neural connectivity in specific brain regions involved in a broad range of cognitive functions like memory, learning, and interoceptive awareness.[25] These neural effects may help explain why adolescent onset of frequent and persistent marijuana use was associated with a significant drop in IQ scores in a large longitudinal study conducted in New Zealand.[26]

We still do not know the full extent of the impact of early marijuana use on long-term cognitive ability and associated life outcomes. Some studies suggest impairments in memory and attention after lengthy heavy marijuana use persist and worsen with increasing years of regular use or with initiation during adolescence; other evidence suggests long-term cognitive deficits could be reversible or remain subtle and not disabling if chronic users discontinue their marijuana use. Inconsistency among studies may be due to the many factors that can modulate the actual relationship between adolescent marijuana use and psychosocial harm (*e.g.,* genetic background, parental and built environment, etc.). Early marijuana use is associated with impaired school performance and increased risk of leaving school early, a harbinger of the established links between heavy marijuana use and other adverse life outcomes including lower income, higher unemployment, greater welfare dependence, increased criminal behavior, and diminished life satisfaction.[27] Whether and to what extent these links are causal remains for further research to determine.

---

[25] Batalla A, Bhattacharyya S, Yücel M, et al. Structural and functional imaging studies in chronic cannabis users: a systematic review of adolescent and adult findings. PLoS One 2013;8:e55821.

[26] Meier MH, Caspi A, Ambler A, Harrington H, Houts R, Keefe RS, McDonald K, Ward A, Poulton R, TE. (2012) Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc Natl Acad Sci U S A 109:E2657-2664.

[27] Brook JS, et al. (2013) Adult work commitment, financial stability, and social environment as related to trajectories of marijuana use beginning in adolescence. Subst Abus. 34:298-305. Brook JS, Lee JY, Finch SJ, Brook DW.Developmental trajectories of marijuana use from adolescence to adulthood: relationship with using weapons including guns. Aggress Behav. 2014 May-Jun;40(3):229-37.

Addiction and other substance use. Approximately nine percent of people who experiment with marijuana will become addicted to it.[28] The number goes up to about one in six among those who start using marijuana as teenagers, with 25-50 percent among those who smoke marijuana daily becoming addicted.[29] The evidence clearly indicates that frequent marijuana use can and often does lead to addiction. According to the 2012 National Survey on Drug Use and Health (NSDUH), an estimated 2.7 million Americans 12 and older met diagnostic criteria for marijuana dependence (equivalent to addiction). Marijuana's ability to cause addiction in some (vulnerable) individuals is consistent with its ability to trigger withdrawal symptoms, including craving, irritability, anxiety, sleeping difficulties, and feeling generally ill or depressed—symptoms that make it hard to quit the drug and cause some people to relapse after they have tried to quit.[30]

The risk of marijuana addiction is increased in young people, particularly when they use the drug regularly. Compared to those who start using marijuana in adulthood, those who start as teenagers are roughly two to four times more likely to experience cannabis addiction symptoms within two years after their first use of the drug. And marijuana addiction, in turn, predicts increased risk of using other illicit drugs.[31] There is suggestive animal evidence that abuse of marijuana in adolescence could facilitate subsequent addictive behaviors in adulthood. For example, animal studies show that early THC exposure can weaken the dopamine system in the reward areas of the brain—an effect that, in humans, would explain early marijuana initiates' increased likelihood of developing other substance use disorders later in life.[32]

However, other drugs, such as alcohol and nicotine, also prime the brain for a heightened response to other substances, and thus could also be categorized as gateway drugs. There may be nothing

---

[28] Anthony, J.; Warner, L.A.; and Kessler, R.C. *Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: Basic findings from the National Comorbidity Survey.* Exp Clin Psychopharmacol 2:244–268, 1994.
[29] Hall, W.; and Degenhardt, L. *Adverse health effects of non-medical cannabis use.* Lancet 374:1383–1391, 2009. Hall, W. *The adverse health effects of cannabis use: What are they, and what are their implications for policy?* Int J of Drug Policy 20:458–466, 2009.
[30] Gorelick DA, Levin KH, Copersino ML, et al. Diagnostic criteria for cannabis withdrawal syndrome. Drug Alcohol Depend 2012;123:141-7.
[31] Agrawal A, Neale MC, Prescott CA, Kendler KS. A twin study of early cannabis use and subsequent use and abuse/dependence of other illicit drugs. Psychol Med 2004;34:1227-1237
[32] Agrawal A, Neale MC, Prescott CA, Kendler KS (2004) A twin study of early cannabis use and subsequent use and abuse/dependence of other illicit drugs. Psychol Med 34:1227-1237

special about marijuana in this respect: One interpretation of the links between early marijuana (or tobacco or alcohol) use and subsequent substance use trajectories would be that those who are more vulnerable to substance use may simply be more likely to start with substances that are readily available. Resulting social interactions with other drug users may then make them more likely to try other substances.

Other Mental and Physical Health Effects Associated with Marijuana Use

Mental illness risk. There is an association between regular marijuana use and anxiety and depression. However, it is inherently difficult to confidently demonstrate causality in studies that link marijuana use and mental illness. There is a stronger link between marijuana use and psychoses (including schizophrenia), particularly if users have a preexisting vulnerability to that disease.[33] Marijuana can also worsen the course of schizophrenia. The disease trajectory can be negatively affected by stronger potency, heavier use, and younger onset, which may advance the time of an initial psychotic episode by anywhere from two to six years.[34] It is possible that heavy marijuana use may arise from some of the same factors that predict increased risk of mental illness, rather than being a cause.

Cancer and other diseases. An area of obvious concern given that marijuana is most commonly smoked is its short- and long-term impacts on lung health. Large airway inflammation, increased airway resistance, and lung hyperinflation are associated with marijuana smoking, and regular marijuana smokers report more symptoms of chronic bronchitis than non-smokers.[35] Smoking marijuana may also reduce the immunological competence of the user's respiratory system, increasing the likelihood of acquiring respiratory infections, including pneumonia.[36]

---

[33] Caspi, A. et al. (2005) Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: longitudinal evidence of a gene X environment interaction. Biol Psychiatry 57:1117-1127. Di Forti, M. et al. (2012) Confirmation that the AKT1 (rs2494732) Genotype Influences the Risk of Psychosis in Cannabis Users. Biol Psychiatry 72:811–816. Compton, M. (2014) Teen Marijuana Use Linked to Earlier Psychosis Onset. Medscape May 14, 2014.

[34] Casadio, P., Fernandez, C., Murray, R.M., Di Forti, M. (2011) Cannabis use in young people: The risk for schizophrenia. Neuroscience and Biobehavioral Reviews 35:1779–1787.

[35] Tashkin DP. Effects of marijuana smoking on the lung. Ann Am Thorac Soc 2013;10:239-47.

[36] Owen KP, Sutter ME, Albertson TE. Marijuana: respiratory tract effects. Clin Rev Allergy Immunol 2014;46:65-81.

At this point, however, the long-term impact of low levels of marijuana exposure on respiratory health does not appear to be significant, and we do not yet know if even heavy marijuana smoking over a long period of time raises a person's risk for lung cancer. One study found that users who smoked the equivalent of one joint or one pipeful of hashish per day for at least 30 years (or "30 joint-years") had a higher rate of lung and several upper respiratory and digestive tract cancers; however, this association did not hold up after potential confounding factors like cigarette smoking were adjusted for.[37]

Research is however showing a link between adolescent marijuana use and rare but fast-growing form of testicular cancer (non-seminomatous testicular germ cell tumor) in young men. One case-control study showed that any lifetime use of marijuana approximately doubled the risk for this cancer[38], and another study found that risk increased with frequent use and earlier initiation of use.[39]

Marijuana use has also been associated with vascular disease that may put a user at higher risk for heart attack, stroke, and transient ischemic attacks after using marijuana, although we do not fully understand the mechanisms by which this may occur.[40]

What Is NIDA Doing About Marijuana?

Information dissemination and outreach. A critical component of NIDA's mission is to ensure the rapid and effective dissemination of research results to significantly improve prevention, treatment, and policy as it relates to drug abuse and addiction. To inform and educate the public on marijuana and its potential harms, NIDA has published a number of reports about marijuana for professional care providers and policy makers as well as easy-to-read fact sheets and

[37] Hashibe M, et al (2006) Marijuana use and the risk of lung and upper aerodigestive tract cancers: results of a population-based case-control study. Cancer Epidemiol Biomarkers Prev 15:1829-1834.

[38] Lacson, J. C. A., Carroll, J. D., Tuazon, E., Castelao, E. J., Bernstein, L. and Cortessis, V. K. (2012), Population-based case-control study of recreational drug use and testis cancer risk confirms an association between marijuana use and nonseminoma risk. Cancer, 118: 5374–5383. doi: 10.1002/cncr.27554

[39] Daling, J. R., Doody, D. R., Sun, X., Trabert, B. L., Weiss, N. S., Chen, C., Biggs, M. L., Starr, J. R., Dey, S. K. and Schwartz, S. M. (2009), Association of marijuana use and the incidence of testicular germ cell tumors. Cancer, 115: 1215–1223. doi: 10.1002/cncr.24159

[40] Thomas G, Kloner RA, Rezkalla S. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana inhalation: what cardiologists need to know. Am J Cardiol 2014;113:187-90.

informational pamphlets aimed at young people and parents. Other dissemination efforts include serving as a resource for the press, responding to public information queries, conducting, social media outreach, and coordinating public education initiatives such as National Drug Facts Week.

NIDA's marijuana research portfolio. NIDA funds a wide range of research on marijuana and on THC and other cannabinoid chemicals, including:

- Patterns and trends in marijuana use and attitudes, particularly among adolescents
- Short- and medium-term effects of THC on the brain and behavior
- Driving under the influence of cannabis
- Long-term effects of prenatal and adolescent cannabis exposure on brain development
- The development and impact of prevention programs on marijuana use
- Screening and brief assessment for marijuana abuse to prevent escalation
- Medications and behavioral treatments for cannabis use disorder
- The working of the brain's cannabinoid system, including its role in pain and HIV
- Potential therapeutic uses of THC and other cannabinoids in treatment of pain, HIV, and addiction (see section below)
- Social, behavioral, and public health impacts of state-level policy changes related to marijuana (*i.e.,* both "medical marijuana" and recreational use)

Research on the therapeutic benefits of cannabis and cannabinoids. THC and other chemicals in the marijuana plant have a potentially wide range of medicinal properties, and thus the possible therapeutic uses of marijuana are a subject of increasingly intense interest by researchers and the wider public. The challenge is to learn how to optimally harness the potential medical benefits of marijuana's chemical constituents without exposing healthy or sick people to the various intrinsic risks of smoking or otherwise ingesting marijuana in its crude form (particularly when product quality, composition, purity, and dosing are inconsistently standardized and regulated, as may be the case with "medical marijuana"). While acknowledging that smoked marijuana has been anecdotally reported to be useful in certain cases (*i.e.,* in stimulating appetite, particularly in AIDS-related wasting syndrome; in combating chemotherapy-induced nausea and vomiting, severe pain, and some forms of spasticity), the authoritative Institute of Medicine report on "Marijuana and

Medicine" stressed the greater potential of non-smoked, rapid-onset delivery systems for cannabis and urged the field to concentrate on investigating the therapeutic potential of synthetic or pharmaceutically pure cannabinoids, not smoked marijuana.[41]

As of January 31, 2014, seven NIH institutes are supporting 54 NIH active grants related to the therapeutic uses of cannabis or cannabinoids, (approximately half of them were funded by NIDA), in 9 different disease categories. Many of these studies are using animal models or cell culture systems. The vast majority are examining the medical benefits of individual cannabinoid chemicals derived from or related to those in the marijuana plant, not the plant itself, although a handful of studies use unprocessed plant material. Individual cannabinoid chemicals may be isolated and purified from the marijuana plant or synthesized in the laboratory, or they may be naturally occurring (endogenous) cannabinoids found in the body (*i.e.,* as part of the endocannabinoid signaling system) and modified using other, non-cannabinoid chemicals.

FDA-approved medicines based on THC for the treatment of wasting syndrome and to control nausea in chemotherapy patients are already available, and there is currently a great deal of active interest in developing medications based on another constituent of the cannabis plant called cannabidiol (CBD). This non-psychotropic chemical does not directly interact with cellular receptors of the body's endocannabinoid signaling system, on which THC acts, and it may even mitigate some of the psychoactive effects of THC. CBD has shown some promise in controlling seizures in children with severe forms of epilepsy (Dravet and Lennox-Gastaut syndromes), and preliminary trials of a CBD-based drug are currently underway, although those trials are not funded by NIH.

Limitations and Need for Further Research

Most of the long-term effects of marijuana use summarized in this testimony have been observed among those who use the drug heavily and/or over a long period of time, but most of the human studies so far have not been large or prospective, and various (often hidden) confounding

[41] IOM (1999) Marijuana and Medicine: Assessing the Science Base. Janet E. Joy, Stanley J. Watson, Jr., and John A. Benson, Jr., Editors. Division of Neuroscience and Behavioral Health, Institute of Medicine. NATIONAL ACADEMY PRESS Washington, D.C.

factors—including the frequent use of marijuana in combination with other drugs—often make it difficult to establish causality or determine the strength of marijuana's unique effects. This is particularly the case when trying to assess the true impact of intrauterine exposure to marijuana or understand the relationship between marijuana use and mental illness, as discussed earlier. There is also the difficulty, also mentioned, of knowing the current relevance of published study findings of long-term outcomes that were conducted when the potency of the cannabis available was less than what it is today.

Research is needed in several areas. For example, it is important to learn more about long-term marijuana use by vulnerable populations, such as those who may use marijuana for medical purposes (despite the limited scientific evidence, as yet, for these benefits)—such as AIDS patients, cardiovascular disease patients, patients with multiple sclerosis or other neurodegenerative diseases, and elderly persons. We do not yet know if people whose health has been compromised by disease or its treatment (*e.g.,* chemotherapy) are at greater risk for adverse health outcomes from marijuana use. We also need to know more about the potential harms of marijuana to individuals prenatally exposed to the drug.

More research is also needed to shed light on the influence of marijuana policy on public health and other outcomes. Our understanding of the impact of marijuana policy on market forces (*e.g.,* youth-targeted advertising, the allure of new sources of tax revenue, pricing wars, and the emergence of FDA-approved cannabis-based medicines) is very limited, as is our understanding of how perception, use, and outcomes interrelate around this drug. Getting a better grasp of this will be crucial, given the striking decades-long trend in epidemiological data (Monitoring the Future)[42] showing that whenever adolescents report diminished perception of risk, prevalence of teen marijuana use increases. Would current or anticipated shifts in culture/policy around marijuana cause more young people to be regularly exposed to cannabis and thus use it more than they already do?

[42] Johnston LD, O'Malley PM, Bachman JG, J.E. S (2013) Overview: key Findings on Adolescent Drug use. 1975-2 013. In: Monitoring the Future national Survey Results on Drug Use (Michigan, U. o., ed).

Most importantly, there have thus far been no large-scale longitudinal studies beginning in childhood, prior to first exposure to marijuana, that track individuals through adolescence and examine links between drug use behaviors and brain development and other outcomes. NIDA in partnership with the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Cancer Institute (NCI), and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) has recently proposed a large, prospective study that would use current brain-imaging and other technologies to study the impact of marijuana and all other forms of substance use on teenagers. This study, provisionally called the National Longitudinal Study of the Neurodevelopmental Consequences of Substance Use, will follow a large cohort, beginning in late childhood, prior to drug exposure, through young adulthood. By gathering neuroimaging data as well as a broad range of substance use, mental health, and other outcomes such as IQ and cognition, the study will clarify the impact of marijuana use on development, reveal the effects of multiple substance exposures, and disentangle the effects of marijuana and other drugs from various confounding factors (particularly prior exposure to substances), as well as giving us insight into the mechanisms by which substances change the brains of young users.

Conclusion

Scientific research has linked marijuana use to a range of significant adverse effects on health and well-being. For example, its acute effects during intoxication interfere with cognitive and motor processes needed for driving a vehicle, and thus marijuana use significantly raises the risk for automobile accidents. Frequent marijuana use during adolescence may have a prolonged or even permanent deleterious impact on brain function and may jeopardize a young person's educational, professional, and social achievements. Like other drugs of abuse, marijuana can be addictive. Additionally, marijuana use is associated with increased risk of some psychiatric conditions as well as various pulmonary and vascular health effects. We still need to understand more fully to what extent rising potency of marijuana may exacerbate these risks.

The health impact of any substance (legal or illegal) is determined not only by its inherent toxicity and how it acts in a user's brain but also by how available and socially acceptable it is, how it is advertised/marketed, how people use it (and how often), and so on. Alcohol and tobacco—legal

substances—provide a useful perspective here, since these two substances overwhelmingly account for the greatest burden of drug-associated death and disease due in part to their widespread access afforded by their legal status.. As state policies around marijuana shift, it is reasonable to predict that increasing numbers of people will use the drug, including young people, and thus that increasing numbers of Americans will experience the types of consequences discussed above.[43]

We appreciate the opportunity to testify on the health effects of marijuana. The key to minimizing negative outcomes lies, on one hand, in the intensification of efforts to educate the public about the real dangers associated with marijuana use and, on the other, in the deployment of multipronged, evidence-based strategies to prevent and treat the abuse of and addiction to marijuana and other drugs.

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

[43] Richter KP, Levy S. Big Marijuana - Lessons from Big Tobacco. N Engl J Med. (2014, June)
Morris RG, TenEyck M, Barnes JC, Kovandzic TV. The effect of medical marijuana laws on crime: evidence from state panel data, 1990-2006. PLoS One. 9(3):e92816. (2014)
Schuermeyer J et al. Temporal trends in marijuana attitudes, availability and use in Colorado compared to non-medical marijuana states: 2003-11. Drug Alcohol Depend. 140:145-55. (2014)
Salomonsen-Sautel Set al. Trends in fatal motor vehicle crashes before and after marijuana commercialization in Colorado. Drug Alcohol Depend.140:137-44. (2014)

Mr. MICA. And we'll hold them until we have heard from the other witness. I'll recognize next the Deputy Director for Regulatory Programs of Food and Drug Administration, Dr. Doug Throckmorton.

STATEMENT OF DOUG THROCKMORTON

Dr. THROCKMORTON. Mr. Chairman, Ranking Member Connolly, members of the subcommittee, thank you for this opportunity to discuss the role that the FDA plays in regulating marijuana in the United States. In addition to important work overseeing the approval of prescription drugs and use of drugs derived from marijuana and its constituents, FDA understands the importance of supporting efficient and scientific assessment of marijuana in connection with drug development.

Marijuana contains compounds with potential to provide important new treatments for important diseases, and rigorous studies are needed to assess their potential, and where appropriate, deliver new drugs for use by Americans. FDA continues to believe that the drug approval process established by Congress represents the best way to ensure that safe and effective new medicines from marijuana are available as soon as possible for the largest numbers of patients.

First, FDA is the agency that is responsible for the assessment and regulation of new drugs in the United States. The Food, Drug, and Cosmetic Act requires that drugs be shown to be safe and effective for their intended uses before being marketed. 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 derived from a botanical source such as marijuana.

As a part of our work to regulate prescription drugs, FDA also provides scientific 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 the appropriate controls for those substances.

To make these recommendations, FDA is responsible for preparing what's called an 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 for marijuana and recommended that marijuana remain in Schedule 1, the most restrictive schedule, both because of its high potential for abuse and because there was not sufficient evidence that marijuana had an accepted medical use in treatment in the United States.

Next let me turn to the FDA work to support the efficient development of drugs from marijuana. As a part of our mission to promote availability of safe and effective medical products for all Americans in all therapeutic areas, FDA is actively streamlining regulatory processes at various steps along the path from drug dis-

covery to delivery to a patient. We understand that this is an important part of our mission.

We have developed and successfully used a number of flexible and innovative approaches intended to expedite drug development. These approaches are being applied to developing drugs derived from marijuana. For example, FDA granted fast-track designation to Sativex, composed primarily of two cannabinoids, being studied for the treatment of pain in patients with advanced cancer. More recently, in June of this year FDA granted fast-track designation to the investigational cannabidiol product Epidiolex, being developed for the treatment of childhood epilepsy.

As a part of this work to encourage efficient drug development, FDA recognizes that many patients are urgently waiting for new potentially beneficial drugs, and we are committed to supporting timely patient access to them. FDA's expanded access mechanisms are designed to facilitate the availability of investigational drug products to patients while those drugs are being studied for approval.

These mechanisms are also being used in the area of marijuana drug development. For example, GW Pharmaceuticals has announced that they have established 21 expanded access INDs for Epidiolex to treat patients with epilepsy syndromes, and to date over 300 patients have received Epidiolex through those programs.

In support of scientific research into marijuana and its constituents, FDA also works with researchers who are developing new drugs from marijuana. Recently several States have announced their intentions to study it for therapeutic purposes, and the FDA is providing ongoing assistance to support their efforts. I have had the opportunity to speak with many of those researchers from those States myself. For example, Georgia and New York have recently announced their intention to develop clinical trials using Epidiolex to help treat patients diagnosed with epilepsy.

Finally, the FDA is working with other Federal agencies on marijuana. In addition to the work I mentioned earlier on drug scheduling with NIDA and DEA, our scientific staffs work closely together to understand the effects of marijuana. FDA also participates in regular meetings with the Office of National Drug Control Policy and other Federal agencies discussing marijuana.

To close my remarks then, there is considerable public interest in developing new therapies from marijuana. FDA understands this and will support the continuing development of specific new drugs that are safe, effective, and manufactured to a high quality. Drug development grounded in rigorous scientific research is essential to determining the appropriate uses of marijuana and its constituents in the treatment of human disease. We are committed to making this process as efficient as possible and looking for ways to speed the availability of new drugs from marijuana for the American public.

Thank you for your interest in this important topic. I'd be happy to answer any questions that I can.

Mr. MICA. Thank you. And we will get back to you with questions.

[Prepared statement of Dr. Throckmorton follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

STATEMENT

OF

DOUGLAS C. THROCKMORTON, M.D.
DEPUTY DIRECTOR FOR REGULATORY PROGRAMS

CENTER FOR DRUG EVALUATION AND RESEARCH

FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

SUBCOMMITTEE ON GOVERNMENT OPERATIONS

COMMITTEE ON OVERSIGHT AND GOVERNMENT REFORM

U.S. HOUSE OF REPRESENTATIVES

"Mixed Signals: The Administration's Policy on Marijuana—Part Four—the Health Effects and Science"

JUNE 20, 2014

RELEASE ONLY UPON DELIVERY

INTRODUCTION

Mr. Chairman, Ranking Member Connolly, and Members of the Subcommittee, I am Dr. Douglas Throckmorton, Deputy Director of the Center for Drug Evaluation and Research (CDER) 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 be here today to discuss the important role that FDA plays in the regulation of researching marijuana for potential medical uses in the United States, as part of FDA's mission to protect and promote the public health by ensuring the safety, efficacy, and quality of medical products, including drugs.

I would like to discuss two aspects of the work FDA does related to the regulation of marijuana. First, FDA plays a critical role in regulating the development and potential use of marijuana and its constituents as prescription drugs in the United States. Second, FDA plays a critical role, alone and in partnership with other Federal agencies, in supporting the efficient and scientific assessment of marijuana and its constituents to support needed drug development. Both of these activities are critical if safe and effective drugs are to be developed from marijuana. FDA continues to believe that the drug approval process represents the best way to ensure that safe and effective new medicines from marijuana are available as soon as possible for the largest numbers of patients, and it is important and appropriate to apply these same scientific standards to the development and assessment of any therapeutic uses of marijuana.

FDA's Role in Regulating Marijuana as a Potential Prescription Drug

The first role for FDA in the regulation of marijuana as a potential prescription drug relates to our larger responsibility for the regulation of all drugs intended for human use. The Agency reviews drug product applications to determine whether drugs are safe and effective for their

intended uses. Any product that is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease is classified by FDA as a drug. This applies, regardless of the product's form and the way in which the manufacturer chooses to market and label the product.

The Federal Food, Drug, and Cosmetic Act (FD&C Act) requires that drugs be shown to be safe and effective for their intended uses before being marketed in the United States. In approving a drug for marketing, FDA reviews important information about the drug, including:

1. The indication for which the drug has been shown to be effective at treating, including specific uses in children or the elderly, if any
2. What patients may benefit from its use, including information about whether the drug has been tested in children
3. What adverse effects have been reported for individuals taking the drug
4. How the drug should be taken (*e.g.,* orally, intravenously)
5. The dose of the drug that is recommended to be used
6. How the drug is made (*e.g.,* as a pill, liquid) and what is in the drug, including both active and inactive ingredients

Getting a drug approved requires the collection and submission to FDA of clinical and non-clinical data about the proposed use of the drug for review as part of a New Drug Application (NDA) or Biologics License Application (BLA). Usually, the first step that a sponsor takes to obtain approval for a new drug is to use non-clinical tests to determine drug toxicity. The sponsor then takes those testing data, along with additional information about the drug's composition and manufacturing, to develop a plan for testing the drug in humans. The sponsor then submits these data to FDA in the form of an Investigational New Drug (IND) application

that includes protocols describing proposed studies, the qualifications of the investigators who will conduct the clinical studies, and assurances of informed consent and protection of the rights, safety, and welfare of the human subjects. FDA then reviews the IND to ensure that the proposed studies, generally referred to as clinical trials, do not place human subjects at unreasonable risk of harm. FDA also verifies that there are adequate assurances of informed consent and human subject protection. At that point, the drug testing in humans can begin.[1]

Briefly, the initial clinical trials assess how to safely administer and dose the drug when used in small numbers of healthy volunteers. If those trials are successful, later studies explore the effectiveness of the drug for a particular indication over a range of doses and determine short-term side effects. These studies typically involve a few hundred subjects. If later studies are successful, pivotal studies are then designed to build on the information learned in the earlier studies to further study safety and assess the efficacy of the investigational drug for a particular indication in a defined patient population. These studies can also provide additional safety data, including long-term experience effects of the drug in certain patient groups, and efficacy of different doses of the drug. These later trials can sometimes enroll several thousand subjects to provide the needed information about the investigational drug's safety and efficacy. Following the completion of these studies, the data might be submitted to FDA as an NDA or BLA for the Agency to review. Throughout the development process, FDA strongly encourages sponsors to work closely with the Agency to support efficient drug development.

In addition to establishing the safety and efficacy of the investigational drug, manufacturers also must demonstrate that they are able to consistently manufacture a high-quality drug product.

[1] In the case of controlled substances, practitioners must first register with the Drug Enforcement Administration before proceeding with clinical trials using controlled substances. Registration requirements applicable to Schedule I controlled substances differ from those for drugs controlled in Schedules II-V (21 U.S.C. 823(f)).

This is an essential part of drug development and presents special challenges when the drug is derived from a botanical source, such as marijuana. Botanicals include herbal products made from leaves, roots, stems, seeds, pollen or any other part of a plant. Botanical products pose challenges that are unique to this class of product, including lot-to-lot consistency. These unpurified products, which may be either from a single plant source or from a combination of different plant substances, can have effects through mechanisms that are either unknown or undefined, making it difficult to determine if the product is causing the change in a patient's condition, or the change is related to some other factor. For these reasons, a focus of drug development from botanicals is identifying a source that will provide the necessary assurance of consistent quality, lot-to-lot. To support development of drugs derived from botanical sources, FDA has released guidance providing information on the development and approval of such drugs that addresses these issues as well as providing more general recommendations on studying botanicals.[2]

Another important consideration is the need to identify a method to consistently provide a given dose of a drug. When the Institute of Medicine (IOM) reviewed the clinical use of marijuana, it identified the problems associated with obtaining consistent dosing using smoked products and recommended that clinical trials involving marijuana should be conducted with the goal of developing safe, alternative delivery systems:[3]

> "If there is any future for marijuana as a medicine, it lies in its isolated components, the cannabinoids and their synthetic derivatives. Isolated cannabinoids will provide more reliable effects than crude plant mixtures. Therefore, the purpose of clinical trials of smoked marijuana would not be to develop marijuana as a licensed drug but rather to serve as a first step toward the development of nonsmoked rapid-onset cannabinoid delivery systems."

---

[2] FDA guidance document on the development of botanical drug products: *http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm070491.pdf*.
[3] IOM Report, p. 11 (1999), *Marijuana and Medicine: Assessing the Science Base*.

Another consideration related to the regulation of marijuana as a potential medicine is its status as a controlled substance. Under section 202 of the Controlled Substances Act (CSA), marijuana is currently listed as a Schedule I controlled substance.[4] Schedule I includes those substances that have a high potential for abuse, have no currently accepted medical use in treatment in the United States, and lack accepted safety for use under medical supervision.[5] Nevertheless, Schedule I substances, including drugs that are derived from botanical sources such as marijuana, can be and are the subject of clinical trials under the FD&C Act, provided, among other things, that the sponsor successfully submits an IND to FDA and successfully registers with the Drug Enforcement Administration (DEA).[6]

Through the drug development processes described above, FDA has approved two drugs for human use which contain active ingredients that are present or similar to those present in botanical marijuana: Marinol and Cesamet. FDA approved Marinol Capsules in 1985 for the treatment of nausea and vomiting associated with cancer chemotherapy in patients who had failed to respond adequately to conventional antiemetic treatments. Marinol Capsules include the active ingredient dronabinol, a synthetic delta-9-tetrahydrocannabinol, or THC, which is a psychoactive component of marijuana. Marinol Capsules were approved in 1992 for the treatment of anorexia associated with weight loss in patients with AIDS. FDA approved Cesamet Capsules for the treatment of nausea and vomiting associated with chemotherapy in 1985. Cesamet Capsules contain the synthetic cannabinoid nabilone as the active ingredient.

---

[4] 21 U.S.C. 812

[5] 21 U.S.C. 812(b)(l)(A)-(C)

[6] 21 U.S.C. 823(f) (stating that registration applications by practitioners wishing to conduct Schedule I research shall be referred by the Secretary of HHS, who shall determine the qualifications and competency of each practitioner, as well as the merits of the research protocol); *see also* 21 CFR 1301.18 (outlining specific application procedures and information to be provided by Schedule I researcher applicants).

These products have undergone FDA's rigorous approval process and have been determined to be safe and effective for their respective indications, and reflect the views of the IOM that the future of marijuana as a potential medicine lies in classical pharmacological drug development.[7] As a result, patients who need medication can have confidence that any approved drug will be safe and effective for its indicated uses.

FDA's Role Under the CSA With Regard to Marijuana

An additional role for FDA in the regulation of marijuana is in making scientific recommendations about the appropriate controls for controlled substances. Under the CSA, controlled substances are listed in one of five schedules, depending on their abuse potential, among other criteria. As noted above, marijuana is currently listed as a Schedule I substance, due not only to its high abuse potential, but also because it currently has no accepted medical use in treatment within the United States and lacks accepted safety for use under medical supervision.

While DEA is the lead Federal Agency responsible for regulating controlled substances and enforcing the CSA, HHS has a number of responsibilities under the CSA, several of which are performed by FDA on behalf of HHS. As a part of this work, FDA provides scientific recommendations to HHS about the appropriate controls for controlled substances, including marijuana. To make this recommendation, CDER, including the Controlled Substance Staff (CSS), is responsible for preparing the "eight-factor analysis" that serves as the basis for the scheduling recommendation to HHS and DEA. This analysis includes the following areas of assessment with regard to a drug or other substance: (1) its actual or relative potential for

[7] Institute of Medicine, Marijuana and Medicine: Assessing the Science Base (IOM Report), p.193 (2003).

abuse;[8] (2) scientific evidence of its pharmacological effect, if known; (3) the state of current scientific knowledge regarding the drug or other substance; (4) its history or current pattern of abuse; (5) the scope, duration, and significance of abuse; (6) what, if any, risk there is to the public health; (7) its psychic or physiological dependence liability; and (8) whether the substance is an immediate precursor of a substance already controlled under the CSA.[9]

At the request of DEA, in 2001[10] and again in 2006,[11] FDA conducted a review of the available data for marijuana, analyzed the eight factors, and recommended that marijuana remain in Schedule I[12] because of its high potential for abuse, the fact that it has no currently-accepted medical use in treatment in the United States, and because it lacks accepted safety for use under medical supervision.[13]

If an NDA is submitted to FDA for a drug that FDA believes may require rescheduling (*e.g.*, from Schedule I to Schedule II), FDA, working with NIDA and the Assistant Secretary of Health in HHS, prepares a scientific analysis, including a recommendation for scheduling (as discussed above). This analysis is based in part on a review of data on abuse potential submitted by the applicant. The recommendation on scheduling is transmitted from HHS to DEA, which makes

[8] The term "abuse" is not defined in the CSA; however, the legislative history of the CSA suggests the following factors, which FDA considers in determining whether a particular drug or substance has a potential for abuse: (a) individuals are taking the substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community; (b) there is a significant diversion of the drug or substance from legitimate drug channels; (c) individuals are taking the substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such substances; and (d) the substance is so related in its action to a substance already listed as having a potential for abuse to make it likely that it will have the same potential for abuse as such substance; thus, making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community. (The Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., Sess. 1 (1970), reprinted in U.S.C.C.A.N. 4566, 4603.

[9] 21 U.S.C. 811(c).

[10] *66 Federal Register 20038 (April 18, 2001)*

[11] *76 Federal Register 40552 (July 8, 2011)*

[12] Once the recommendation is completed by FDA, it is then forwarded to the National Institute on Drug Abuse (NIDA) and then to HHS, which, in turn, makes a final recommendation to DEA. The HHS scheduling recommendation is binding on DEA as to scientific and medical matters. Once HHS has transferred to DEA a scheduling recommendation, where the recommendation is to add a drug to a schedule or to transfer a drug to another schedule, DEA goes through a rulemaking process to schedule the drug.

[13] See 74 FR 40552; 66 FR 20038.

the final determination of the appropriate schedule for the substance by scheduling the substance through the rulemaking process prescribed by statute.[14]

FDA's Role in Investigations and Enforcement Actions With Regard to Controlled Substances

In addition to its role in scheduling drugs, FDA sometimes works with the Department of Justice (DOJ), including DEA, and other state and Federal agencies on criminal investigations involving the illegal sale, use, and diversion of controlled substances. FDA recognizes that DEA is the lead Federal Government Agency for enforcement matters related to the diversion of controlled substances, including marijuana. Historically, FDA has deferred to DEA regarding the illegal sale and use of illicit drugs of abuse that have no currently-accepted medical use (*i.e.,* Schedule I drugs).

At present, more than 20 states and the District of Columbia have passed legislation to provide for medical use of marijuana and its derivatives, and several others are considering whether to do so.

FDA's Role in Supporting Development of New Therapies

FDA also plays a role in supporting the development of new drugs, including drugs derived from marijuana and its constituents. This role broadly affects all of drug development. Because of FDA's role as both a regulator and as a public health agency, FDA has a unique perspective on drug development, a perspective we use to identify and facilitate the development of new, innovative products to meet the needs of patients and the American public. We recognize that

[14] *See* 21 U.S.C. 811.

many scientific discoveries still need to be translated into treatments while patients are urgently waiting for new lifesaving therapies, and FDA is committed to helping bridge this gap.

As a part of this activity to streamline drug development, FDA has been actively scrutinizing, strengthening, and streamlining our regulatory processes at various steps along the path from drug discovery to delivery—including the clinical development phase, the longest and most expensive period of drug development. We have developed and successfully used a number of flexible and innovative approaches to expedite the development and review of drugs—to the benefit of millions of American patients. For instance, in 2013, almost three quarters (74 percent) of the 27 new molecular entities approved by FDA were approved first in the United States before any other country.[15]

FDA has four programs that facilitate and expedite development and review of new drugs that address unmet medical needs in the treatment of serious or life-threatening conditions, including Fast Track,[16] Accelerated Approval,[17] Priority Review,[18] and Breakthrough Designation.[19] A look at recent drug approvals suggests that these programs have played an important role in

[15] "President's Fiscal Year 2015 Budget Request for the FDA" Testimony of Commissioner Margaret Hamburg before the Senate Committee on Appropriations (April 3, 2014) at *http://www.fda.gov/newsevents/testimony/ucm392262.htm*.

[16] Fast-track designation: Providing for more frequent meetings and communications with FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval, including such things as the design of the proposed clinical trials and use of biomarkers.

[17] Accelerated Approval: Basing approval not on a clinical endpoint but on an agreed-upon surrogate marker that is a measure, such as blood test or urine marker that is believed to be indicative of a disease state and treatment effect, but not demonstrative of a direct health gain to the patient.
Since its inception in 1992, more than 80 new products have been approved under the Accelerated Approval pathway. It has long been successful in driving innovation in cancer and HIV therapies, but we are encouraging its broader application in other areas, helped by the Food and Drug Administration Safety and Innovation Act (FDASIA), which clarified that FDA has the authority to consider epidemiologic, pharmacologic, or other evidence developed using biomarkers or other scientific methods or tools in determining whether an endpoint can support accelerated approval.

[18] Priority Review: Acting on drug applications within six months instead of 10 months for standard review

[19] Breakthrough Therapy designation: Providing all of the benefits of Fast-Track designation plus intensive guidance on an efficient drug development program, beginning as early as Phase 1, and the commitment from FDA's review staff, including senior managers, to work closely together throughout the drug development and review process. FDA's new Breakthrough Therapy Designation, was created as part of the 2012 FDA Safety and Innovation Act (FDASIA) As of May 5, 2014, FDA received 186 requests for designation, and granted 48. Six drugs have been approved, including a late-stage lung cancer drug that was approved—four months ahead of its goal date, using evidence from a trial with 163 patients.

bringing innovative drugs to market. Nearly half of the 27 novel drugs approved by FDA last year took advantage of at least one of these expedited drug development and review approaches.

Development programs for drugs derived from marijuana are eligible for these expedited review and development programs under appropriate circumstances, and some are being used to aid the development of drugs derived from marijuana. For example, in April 2014, GW Pharmaceuticals announced that FDA granted Fast-Track designation[20] to its investigational drug product Sativex®, composed primarily of two cannabinoids: CBD (cannabidiol) and THC, administered as a metered-dose oromucosal spray, for the treatment of pain in patients with advanced cancer, who experience inadequate analgesia during optimized chronic opioid therapy. Sativex is currently in Phase 3 clinical trials for this indication. In addition, on June 6, 2014, GW Pharmaceuticals announced that FDA granted Fast-Track designation to its investigational CBD product, Epidiolex®, in the treatment of Dravet syndrome, a rare and catastrophic treatment-resistant form of childhood epilepsy.[21]

FDA also understands the interest in making investigational products available to patients while they are being studied for approval, and there are expanded access provisions in both FDA's statute and its regulations to make this possible. FDA's expanded-access mechanisms are designed to facilitate the availability of investigational products to patients with serious diseases or conditions when there is no comparable or satisfactory alternative therapy available, either because the patients have exhausted treatment with or are intolerant of approved therapies, or when the patients are not eligible for an ongoing clinical trial.[22] FDA

[20] *http://www.gwpharm.com/GW%20Pharmaceuticals%20Announces%20that%20Sativex%20Receives%20Fast%20Track%20Designation%20from%20FDA%20in%20Cancer%20Pain.aspx*
[21] *http://www.gwpharm.com/GW%20Pharmaceuticals%20Announces%20Epidiolex%20Receives%20Fast%20Track%20Designation%20from%20FDA%20for%20the%20Treatment%20of%20Dravet%20Syndrome.aspx*
[22] *http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/SpeedingAccesstoImportantNewTherapies/ucm177138.htm*

cannot mandate or require a drug company to provide an unapproved drug to patients, and the availability of an investigational product through expanded access depends on the agreement of the drug company to make the drug available for the expanded access use, either through the company's own expanded access program or to a treating physician for administration to his or her patient.

The expanded access program is being used in the area of marijuana. Epidiolex, containing CBD, is being developed for the treatment of certain seizure disorders in children.[23] GW Pharmaceuticals has announced that there are now 21 active expanded access INDs for Epidiolex treating approximately 300 patients with epilepsy syndromes. Approximately 95 percent of these INDs are for patients between 1 and 17 years of age.[24]

FDA is working with researchers, who are conducting studies on the development of new drugs derived from marijuana, meeting with them regularly as they plan and carry out the trials as a part of their INDs. Although marijuana is a Schedule I substance, it can be, and is being, used in clinical trials, provided that the sponsor submits an IND and registers with DEA. A number of government-funded research projects involving marijuana or its component compounds have been completed or are currently in progress, many of which are listed on the *ClinicalTrials.gov* website. NIDA also permits and funds studies on potential therapeutic benefits of marijuana or its constituent chemicals and lists such studies on its website.[25]

---

[23] Epidiolex received orphan product designation for treatment of Dravet syndrome. *http://www.accessdata.fda.gov/scripts/opdlisting/oopd/OOPD_Results_2.cfm?Index_Number=409313* and more recently for treatment of Lennox-Gastaut syndrome: *http://www.accessdata.fda.gov/scripts/opdlisting/oopd/OOPD_Results_2.cfm?Index_Number=421213*

[24] *http://www.gwpharm.com/Epidiolex.aspx*

[25] *http://www.drugabuse.gov/drugs-abuse/marijuana/nida-research-therapeutic-benefits-cannabis-cannabinoids*.

As a part of encouraging appropriate research into marijuana and its constituents, FDA has also worked with investigators to provide clear information on how to conduct research in this area. To help address common questions about research into marijuana, FDA, NIDA, and DEA all have created materials online to help researchers.[26] We also know that a number of states are interested in allowing access to cannabinoid oil, or CBD, to treat childhood epilepsy. FDA encourages and supports medical research into the safety and effectiveness of marijuana products through adequate and well-controlled clinical trials conducted under an IND and consistent with DEA requirements for research on Schedule I substances. FDA has talked with representatives from several states that are considering support for medical research of marijuana and its derivatives to provide scientific advice and to help ensure that their research is rigorous and appropriate. For example, Georgia Governor Nathan Deal recently announced that Georgia Regents University-Augusta is planning to conduct clinical trials of Epidiolex.[27] Also, Governor Andrew M. Cuomo announced an agreement between New York State and GW Pharmaceuticals to develop clinical trials using Epidiolex to help treat children diagnosed with epilepsy who suffer from seizures and other medical complications.[28]

Collaboration with Other Agencies

Another role FDA plays in the regulation of marijuana for potential medical use is our work to support scientific advances related to drug abuse with our sister agencies. FDA and other Federal agencies, including DEA and NIDA, work together on several issues related to marijuana. For example, as described above, FDA works with NIDA and DEA as a part of drug

---

[26] *http://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/ucm362986.htm; http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM198650.pdf*; "Guidance for Industry: Botanical Drug Products" at *http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm070491.pdf.http://www.drugabuse.gov/drugs-abuse/marijuana/marijuana-research-nida; http://www.deadiversion.usdoj.gov/drugreg/faq.htm#sched1*

[27] *http://gov.georgia.gov/press-releases/2014-04-10/deal-leads-state-path-forward-cannabis-oil-treatment*

[28] *http://www.governor.ny.gov/press/06032014-new-medical-treatments*

scheduling. FDA sometimes works with the Department of Justice (DOJ), including DEA, and other state and Federal agencies on criminal investigations involving the illegal sale, use, and diversion of controlled substances. FDA and NIDA also participate in meetings with the Office of the National Drug Control Policy, along with DEA. Finally, FDA participates in the interagency work group that the HHS Office of the Assistant Secretary for Health coordinates to review non-federally funded scientific research proposals that require the use of research-grade marijuana. This committee is composed of a number of HHS agencies, as relevant to the topic of the research, and routinely includes individuals from FDA, NIDA, other NIH components, and the Substance Abuse and Mental Health Services Administration.

CONCLUSION

FDA appreciates this opportunity to discuss FDA's work in the regulation of marijuana for potential medical uses in the United States, which is a part of FDA's larger mission to protect and promote the public health by ensuring the safety, efficacy, and quality of medical products, including drugs. There is considerable public interest in developing new therapies from marijuana and its constituents. FDA will continue to support development of such new therapies that are safe, effective, and manufactured to a high quality, applying the drug development paradigm that continues to provide important new medicines for patients. This paradigm, grounded in rigorous scientific research, is essential to determining the appropriate uses of marijuana and its constituents in the treatment of human disease. As a part of this important work, we are committed to collaborating with Federal and state agencies, researchers, and manufacturers also working on issues related to the use of marijuana in the United States, including cooperation to help speed the development of safe and effective new drugs. Thank you for your interest in this important topic, and I am happy to answer any questions.

Mr. MICA. I want to now recognize the Associate Professor of Psychology at Columbia University, Dr. Carl Hart.

Welcome. And you are recognized.

STATEMENT OF CARL HART, PH.D.

Mr. HART. Chairman Mica, Ranking Member Connally, and distinguished members of the subcommittee, it is a privilege and honor to offer my expertise in your quest to more comprehensively understand the impact of marijuana on the individual as well as our society.

As you all pointed out, I am a tenured professor at Columbia University in the Departments of Psychology and Psychiatry. I also serve as a research scientist in the division on substance abuse at the New York State Psychiatric Institute.

I am also a member of the National Advisory Council on Drug Abuse, and I am on the board of directors for the College of Problems of Drug Dependence and, also, for Drug Policy Alliance.

As you all may know, I am a trained neuropsychopharmacologist who has spent the past 16 years studying the neurophysiological, psychological, and behavioral effects of marijuana.

As part of my research, I have given thousands of doses of marijuana to people and I have carefully studied the immediate and delayed effects on the drug on them. My findings are published in some of the most prestigious scientific journals.

I have coauthored a popular college-level textbook that focuses on drugs in society. My most recent book, "High Price," is aimed at educating the general public about drugs and preventing drug-related tragedies.

But I want to be clear here today that my remarks will focus primarily on the effects of marijuana on adults, since we all agree that recreational use of marijuana as well as other drugs by children should be discouraged.

So, to be clear, marijuana is a psychoactive drug. That means that it alters the functioning of brain cells and influences our thinking, mood and behavior. It can have both positive as well as negative effects. This is true of all psychoactive drugs, including alcohol and tobacco.

A major potential negative consequence of marijuana use is addiction. As has been pointed out correctly, marijuana—about 9 percent of the people who use marijuana will become addicted. By comparison, however, about 15 percent of the people who use alcohol will become addicted and a third of the people who smoke tobacco will become addicted.

The point is, yes, marijuana is addictive. However, when you compare it to our legally available drugs, its addictive potential is lower.

Another concern related to marijuana is disruption of cognitive functioning. As is the case with alcohol, during marijuana intoxication, some cognitive operations, such as response time, may be temporarily slowed, but the intoxicated individual is able to respond to environmental stimuli in appropriate manners.

Marijuana intoxication typically lasts no more than 2 to 4 hours, depending upon the individual's level of experience with the drug. It is important to understand that, even during periods of intoxica-

tion, the user is able to carry out his or her usual behavioral repertoire. That means engaging in appropriate social behaviors, including responding to emergencies.

After the intoxicating effects of marijuana have dissipated, there are no detectable physiological or behavioral effects of the drug in recreational and casual users. This is similar to what is observed following alcohol intoxication.

In fact, many of the people who I have studied who participate in our research studies where we actually give the drug, they are responsible members of their community. They are graduate students. They are actors. They are schoolteachers. They are waitresses, waiters, professors, lawyers, among other professions.

One of the least discussed effects of our current approach to marijuana deals with arrest rates. It was briefly mentioned here today.

Each year there are more than 700,000 marijuana arrests, which account for half of all the drug arrests in the country.

By the way, the overwhelming majority of people who are arrested for marijuana, 80 percent or so, are arrested for simple drug possession.

But what is worse is that, at the State level, black people are 2 to 7 times more likely to be arrested for marijuana than their white counterparts.

And at the Federal level, Hispanics represent two-thirds of all the people arrested for marijuana violation, despite the fact that blacks, Hispanics and whites use the drug at similar rates.

The scientific community has virtually ignored this shameful marijuana-related effect. The National Institute on Drug Abuse could help remedy this situation by requesting research applications that explicitly focuses on race, for example, trying to understand the long-term consequences of marijuana arrests on black and Hispanic people, especially as they relate to disrupting one's life trajectory.

So as we move forward here to develop a more rational approach to marijuana in our society, it is my most sincere hope that we not only focus on the potential negative effects of the drug, but we also include some of the beneficial effects of the drug and, most importantly, the consequences of our current policies on certain communities of color.

Thank you, guys.

Mr. MICA. Thank you.

[Prepared statement of Dr. Hart follows:]

Chairman Mica, Ranking member Connolly, and distinguished members of the subcommittee, it is a privilege and honor to offer my expertise in your quest to understand more comprehensively the impact of marijuana on the individual as well as society. Currently, I am a tenured Associate Professor of Psychology at Columbia University in both the Departments of Psychology and Psychiatry. I also serve as a research scientist in the Division on Substance Abuse at the New York State Psychiatric Institute. I am a member of the National Advisory Council on Drug Abuse and am on the board of directors for the College on Problems of Drug Dependence and for the Drug Policy Alliance.

As you know, I am trained as a neuropsychopharmacologist who has spent the past 16 years studying the neurophysiological, psychological and behavioral effects of marijuana. As part of my research, I have given thousands of doses of marijuana to people and have carefully studied their immediate and delayed responses. My findings are published in some of the most prestigious scientific journals. I have also co-authored a college-level textbook focused on Drugs and society. My most recent book, *High Price*, is aimed at educating the general public about drugs and preventing drug-related tragedies.

I would like to point out that my remarks today will focus primarily on the effects of marijuana on adults since most agree that marijuana use – as well as other drug use - by children should be discouraged.

To be clear, marijuana is a psychoactive drug. That is, it alters the functioning of brain cells and influences our thinking, mood, and behavior. It can have both negative and positive effects. This is true of all psychoactive drugs, including nicotine and alcohol.

A major potential negative consequence of marijuana use is addiction. About 9 percent of all marijuana users will become addicted to the drug. By comparison, about 15 percent of alcohol users and 33 percent of tobacco smokers will become addicted. The point is: yes, marijuana is potentially addictive, but its addictive potential is lower than our current legal drugs alcohol and tobacco.

Another concern related to marijuana use is disruption of cognitive functioning. As is the case with alcohol, during marijuana intoxication some cognitive operations, such as response time, may be temporarily slowed, but the intoxicated individual is able to respond to environmental stimuli in an appropriate manner. Marijuana intoxication typically lasts no more than 2-4 hours, depending upon the individual's level of experience with the drug. It is important to understand that even during the period of intoxication, the user is able to carry out her/his usual behavioral repertoire, e.g., engage in appropriate social behaviors, including responding to emergencies.

After the intoxicating effects of marijuana have dissipated, there are no detectable physiological or behavioral effects of the drug in recreational and causal users. This is similar to what is observed following alcohol intoxication. In fact, many of the individuals who have served as research participants in my studies on marijuana (during which they were administered the drug) are responsible members of their communities.

They are graduate students, actors, schoolteachers, waiters/waitresses, professors, and lawyers, among other professionals.

One of the least discussed effects of our current approach to marijuana deals with arrest rates. Each year, there are more than 700,000 marijuana arrests, which account for half of all drug arrests. By the way, the overwhelming majority of these arrests are for simple drug possession. But what's worse is that – at state level - black people are two to over seven times more likely to be arrested for marijuana than their white counterparts. And at the federal, Hispanics represent 2/3 of the individuals arrested for marijuana violations, despite the fact that blacks, Hispanics, and whites all use marijuana at similar rates.

The scientific community has virtually ignored this shameful marijuana-related effect. The National Institute on Drug Abuse could help remedy this situation by requesting research applications that focus explicitly on race—for example, trying to understand the long-term consequences of marijuana arrests on black and Hispanic people, especially as they relate to disrupting one's life trajectory.

So, as we forward to develop a more rational approach to marijuana in our society, it is my hope that we not only discuss potential negative effects of the drug, but that we also include potential benefits and the unintended consequences of our current policies on certain communities of color.

Mr. MICA. And I thank all three of our witnesses for their testimony.

And we will start with some questions.

First of all, I will start with our Director of the National Institute on Drug Abuse and ask the question: President Obama had said that smoking marijuana is not very different from smoking cigarettes, and he also said that marijuana is less dangerous than alcohol—or intimated that. I think we had up on the screen his exact comments.

How would you respond, Doctor?

Dr. VOLKOW. Well, we all use our own experience to actually get conclusions. And, as I mentioned, for cigarette smoking, not everybody that smokes cigarettes is going to get lung cancer. And so, in their experience, this is not a harmful drug.

And there are very significance differences, we know, variability, probably determined by genetic factors that make some people more vulnerable and others more resilient.

To the comment of whether marijuana is more or less harmful than alcohol and tobacco—and, again, I do agree with my colleague, Dr. Hart—there is always positive and negatives.

I think one of the issues in those comparisons, which I don't like, to start with, is that you are comparing the percentage of people that become addicted to marijuana when they get exposed to it, which is 9 percent, versus, say, 15 percent for alcohol, which is much higher.

But alcohol is legal and marijuana is illegal, and the legal status affects the norms and the willingness of people to get exposed to it.

So in order to really compare the likely—the relative potency of one drug versus the other vis—vis how humans end up consuming it, you have to have similar social conditions for both of them.

And so, in animal models, nicotine is not very addictive. It is very hard to make animals addicted to nicotine.

But it is a very widely available drug. It is dispersed to groups through an administration that leads to very high concentration, which is smoking, just like marijuana.

And, also, finally, the other aspect that we need to consider, which was brought by Mr.—Dr. Fleming, is that the marijuana that he may have smoked is likely to have had, we know, probably very low content of 9–THC opposed to the marijuana that we currently have now.

And we do know that the higher the content of 9–THC, the higher the likelihood that you will develop adverse effects and much more likely to become addicted to it.

So I think that all of these factors——

Mr. MICA. You also testified that marijuana becomes—is responsible for being a gateway drug.

Dr. VOLKOW. Well, epidemiological data has shown that most individuals that smoke cocaine or take heroin started with marijuana, but they also show that they started with alcohol and nicotine.

So there is—this could be just a social phenomena of which is the drug that is the most readily available or a pharmacological effect of the drug that, when you take it when you are an adolescent

brain, when your brain is developing very rapidly, influences, primes, your brain in such a way that then you become more vulnerable to other drugs, which would then explain why, for example, individuals that get exposed to marijuana before age 17 are not only at greater risk of becoming addicted to marijuana, but they are also at greater risk of becoming addicted to other drugs of abuse, even when you control for genetic backgrounds and environmental backgrounds.

So there is evidence to suggest that there may be a priming effect that could account for this concept of a gateway drug.

Mr. MICA. I am not a scientist. But we have had testimony now. And I guess some of these reviews also indicate that there is—particularly when used by adolescents, that there is a diminution in the level of intelligence.

Do you—is there evidence to that?

Dr. VOLKOW. This study was actually—the one that you are referring to was a study done in New Zealand in 1,050 individuals that were monitored periodically from age 13 until age 32. So they were evaluating the cognitive performance actually before they took marijuana.

And what they found, that those that consistently took marijuana during adolescence have overall lower—8 points lower I.Q. When they were consistently taking it.

Mr. MICA. Okay.

Dr. VOLKOW. So that is a strong study. But like anything else in science, you need to replicate. But it is evidence we cannot ignore because it actually does address many of the criticisms that have been done by prior studies.

Mr. MICA. Okay. Now, Dr. Throckmorton, you don't set marijuana as a Schedule I narcotic, but you do participate in the process which you described, and I guess you recommend to DEA and DOJ.

And you are not prepared to make any other recommendation but to keep it in Schedule I?

Dr. THROCKMORTON. So in 2001 and, again, in 2006——

Mr. MICA. Right. 2001, 2006, you did the last studies.

But right now the question around the country is: This is classified as a Schedule I drug. We had DEA in. We didn't have DOJ. We had a U.S. attorney. But the DEA was adamantly opposed to taking it, I think, out of a Schedule I classification.

What is your position? Has it changed from the 200-—you said 2001 they studied it, 2006 they studied it. Where are we now?

Dr. THROCKMORTON. So if I could say, there are two reasons why the FDA conducts an 8-factor analysis, why we look at the scheduling of a product. And I think it might worthwhile just making sure that we understand both of those because they both relate to, potentially, marijuana.

The first is if we have a drug submitted to us for approval. So a new drug and—for an indication comes to us, including a drug that comes from marijuana. We would be required to conduct an analysis.

Mr. MICA. And you also testified that you are looking at several of—I don't know if—I am not a scientist—at derivatives or—one was Epidiolex——

Dr. THROCKMORTON. "Epidiolex."

Mr. MICA. "Epidiolex."

— that you are looking at that and, again, several others I think you indicated. And that is the first time I have heard testimony about, again, the direction you are taking on medical marijuana.

But, again, as—and that is part of your responsibility. I mean, I don't know how soon it is going to be before we see "FDA approved" stamp on—well, maybe you can talk about that.

But the process, too, of the Schedule I is part of what has been at issue here. We have DEA. We have the Department of Justice. We have—just in the District of Columbia we have 26 Federal law enforcement agencies enforcing Federal law. And it is still an illegal narcotic in the highest classification.

Are you about to change that?

Dr. THROCKMORTON. I wouldn't be able to comment about potential changing of our recommendation. First, my recommendation would go through layers above me.

Mr. MICA. How would we get—can we get the——

Dr. THROCKMORTON. That was what I wanted to—that was why I wanted to talk a little about the two pathways. So——

Mr. MICA. Well, one is—I mean, you do have some studies that you are conducting about the medical benefits of some derivatives and you are on the path.

But the—again, the major question is the Schedule I classification. And you are not prepared to say there is going to be any change?

Dr. THROCKMORTON. What I am prepared to say is that, under two possible scenarios, we would have to conduct another 8-factor analysis on marijuana or its constituents.

And either of those scenarios——

Mr. MICA. Do you plan to do a factor analysis? The last one was done in 2006. Right?

Dr. THROCKMORTON. The last one requested for us by the DEA. So there are—the—there are—the two ways are, one, a drug company submits a drug for application to us and we conduct an 8-factor——

Mr. MICA. That is not what we are talking about.

Dr. THROCKMORTON. And the second one—I understand that is the center of your interest—is the one where the DEA requests that we conduct an additional 8-factor analysis. They have done—2001, 2006, did those at those points. Recommended that it remain in Schedule I.

It is public knowledge that the DEA has received additional citizens petitions asking them to look again at the medical evidence surrounding the safety and effectiveness——

Mr. MICA. But that would bounce back to you.

Dr. THROCKMORTON. And that has been sent to us, and we are in the process of conducting that 8-factor analysis. We have not yet come to a conclusion there.

Mr. MICA. So you are conducting an 8-factor analysis, an update?

Dr. THROCKMORTON. Yes.

Mr. MICA. When do you expect that would be done?

Dr. THROCKMORTON. I wouldn't be able to comment, partly because it is a recommendation first. So we make a recommendation

to Health and Human Services after we consult with the National Institute on Drug Abuse. And then that recommendation goes to the DEA. Things out of my control.

Mr. MICA. Are you able to tell us, Dr. Volkow, your recommendation at this point?

Dr. VOLKOW. Well, I have to see——

Mr. MICA. I am moving forward.

Dr. VOLKOW. I have to see exactly what the data is and then definitely will act swiftly with that information.

Mr. MICA. So you're going to rely on the first data that's produced by the 8-factor analysis and then you would respond to that? That's the order?

Dr. VOLKOW. Correct.

Mr. MICA. Okay. Dr. Hart, did you want to respond to anything?

Mr. HART. Yeah. It seems to me that we need to clarify some of the—there's been some misinformation stated.

There was a comment made about the average age of people who smoke marijuana now—begin smoking marijuana is, like, 10. That's just not true. It's about 17 or 18.

And, also, as we think—move forward and think about the increasing amount of marijuana potency, it certainly has increased. But the question becomes: What does that mean?

When you think about potency and you think about people smoking marijuana, one of the advantages of smoking a drug compared to some other route of administration is that, when you smoke a drug, you can quickly detect the potency or the strength of the psychoactive effects. So that means you will decrease the amount you intake.

It's like drinking a stiff drink versus drinking a beer. You don't drink the two the same way. So this issue of potency has been overstated.

Second point. When we think about gateway drug, as has been talked about here, it is true that the majority of the people who go on to use heroin and cocaine may have used marijuana first.

That's true. That's a fact. But it is also a fact that the majority of the people who smoke marijuana don't go on to cocaine or heroin.

And if we are calling marijuana a gateway drug, we have to think about this fact: The last three occupants of the White House all smoked marijuana.

If we use this logic about gateway, we could very well say that marijuana is a gateway drug to the White House. It just doesn't make sense.

Finally——

Mr. MICA. Okay.

Mr. HART. Finally, when we think about I.Q.—the study that has shown the decrease in I.Q. Points, it's important to note that the group that has shown the decrease in I.Q. Points—there were 20 people in that group.

And when you look at the I.Q. Range that they have decreased to, they remained within the normal range. They are normal. And so it's important for people to understand what the science actually says.

Mr. MICA. Thank you. And we'll yield now to Mr. Connally.

Mr. CONNOLLY. Thank you.

And I do want to remind Dr. Hart that one of those three Presidents never inhaled.

Mr. MICA. That's what he said.

Mr. CONNOLLY. Dr. Throckmorton, I think the chairman and I were both struck by your testimony because, if we understood your testimony, you were acknowledging that, in fact, there were positive medicinal benefits in terms of medicinal treatment with a derivative of marijuana for epileptic seizures. Was that correct?

Dr. THROCKMORTON. No. What I was saying was that there are people who are very enthusiastic about the potential for cannabidiol and THC and some of its derivatives to treat a number of important medical conditions. My job, given that potential, is to make sure that that development happens as quickly as possible.

Mr. CONNOLLY. Okay. But your testimony does not dismiss that possibility?

Dr. THROCKMORTON. Absolutely not. I look forward to seeing the full data.

Mr. CONNOLLY. Okay. And I don't want to put words in your mouth because both the chairman and I thought we heard you acknowledge that at least there is some preliminary data beyond the placebo effect with respect to the treatment for epileptic seizures.

Dr. THROCKMORTON. I really wouldn't be able to comment. I'm sorry.

Mr. CONNOLLY. You think the science is too early?

Dr. THROCKMORTON. It's important science to get right and——

Mr. CONNOLLY. But, conversely, neither are you testifying that it is, in fact, only a placebo effect?

Dr. THROCKMORTON. We have approved drugs from plants. And this plant has several compounds in it that people have identified as very promising.

Our job is to take those developments——

Mr. CONNOLLY. I think that is really important because my colleague, Dr. Fleming, seemed to suggest it could only have a placebo effect and, in fact, the science doesn't tell us that necessarily.

The science may very well lead us to the fact that there is an empirical, efficacious, medical effect that can benefit people like my constituent, Jennifer Collins, who suffers 300 seizures a day. It would come as news to her family that the effect is only a placebo effect.

Mr. FLEMING. Would the gentleman yield?

Mr. CONNOLLY. And let me just say that family had to move their daughter to another State. She's separated from her friends at school. She's separated from her family for medical reasons, not to get a high, not for recreational use, but because her body is tormented 300 times a day with epileptic seizures.

And we owe it to her and the other families in this country that may suffer from similar medical conditions. So put aside the politics, put aside the bias scientifically that has prevented us from genuinely researching this topic to see whether, in fact, there can be an efficacious effect.

Mr. FLEMING. Would the gentleman yield?

Mr. CONNOLLY. I would briefly yield to my colleague.

Mr. FLEMING. Yeah. I never suggested that there was a placebo effect at all. All I said was that we have no proven benefit to seizures or otherwise and that to simply go out and mass-produce this, allow the population as a whole to use it, when, in fact, it is in research and we are trying to find answers on this makes no sense at all.

Mr. CONNOLLY. Reclaiming my time. And I thank my colleague.

And, by the way, I'd be delighted to have my colleague meet my constituent so that he could hear their story directly.

Mr. FLEMING. I would be happy to as well. But it's still an anecdotal——

Mr. CONNOLLY. Okay. But I would also just point out my friend has just created a straw man. No one has talked about mass production and letting everyone use it anyway they want. That's not the topic of this hearing nor——

Mr. FLEMING. That is medicinal marijuana, sir.

Mr. CONNOLLY. Well, actually, talk to the 22 States that——

Mr. FLEMING. There are more marijuana——

Mr. CONNOLLY. Excuse me. This is my time.

But I would just suggest to my colleague you can talk to the 22 States who have decided otherwise. And if Louisiana doesn't want to do it, that's its choice.

But there are 22 States and the District of Columbia that have decided otherwise because they feel they have been held back at the Federal level.

Now, Dr. Volkow——

Dr. VOLKOW. Yes.

Mr. CONNOLLY. —your testimony seems to completely disregard lots of other data. You referred to marijuana, as Dr. Hart said, as a gateway drug.

Is there any evidence that marijuana is uniquely so, any more or less than other controlled substances?

Dr. VOLKOW. I think that in my testimony I explicitly stated that we have no evidence that marijuana, as a gateway drug, is different from alcohol and tobacco and that tobacco, in fact——

Mr. CONNOLLY. But isn't it even misleading to call it a gateway drug?

I mean, if you've got an addictive personality, you started with something. It might be prescription drugs. It might be alcohol. It might be tobacco.

I mean, there's no evidence that marijuana stands out among those other substances if you've got an addictive personality and you're going to go on to an addiction, is there?

Dr. VOLKOW. No. Absolutely. And if you have an addictive personality, it may just be what's more available as a young person that will just start to take it first.

Mr. CONNOLLY. I guess I'm suggesting to you, however, given the data—for example, you only cited the addiction rate for marijuana. You didn't mention in contrast to what.

So 9 percent of the people who start out with marijuana become addicted. But you didn't mention that 33 percent of people who start out with tobacco become addicted and, as Dr. Hart pointed out, 15 percent with alcohol.

What is it if you started out with cocaine? What's the addiction rate of that?

Dr. VOLKOW. Cocaine is probably, like, 20, 25 percent.

Mr. CONNOLLY. Okay. So in all of these case so far, they are much higher than marijuana.

Dr. VOLKOW. Cocaine, methamphetamine, heroin are much higher than marijuana. But you need to—when you are making these comparisons, you have to compare with an illegal and legal because the social changes make the perception different and make it much more available.

Mr. CONNOLLY. I understand.

But for you to only cite the addiction rate with marijuana seems to me to be cherry-picking statistics for a purpose.

Dr. VOLKOW. I only have 5 minutes, and I apologize for not saying it, because I always present all of the data. But I had 5 minutes.

Mr. CONNOLLY. All right. Dr. Hart had the same 5 minutes and managed to somehow put it in context.

Let me ask you about NIDA. Right now NIDA has a monopoly on the production of marijuana to be used for FDA-approved research for medical purposes, and that's been the case since 1974. Is that correct?

Dr. VOLKOW. That is my understanding.

Mr. CONNOLLY. That's your understanding.

Dr. VOLKOW. Yes.

Mr. CONNOLLY. Your title is director?

Dr. VOLKOW. Yes. That's my understanding. It's a use of words.

Mr. CONNOLLY. All right. Is there any other Schedule I drug used for research purposes that's available only for—only from one government source like yours?

Dr. VOLKOW. You were correct. And I don't think there is.

Mr. CONNOLLY. So, again, unique to marijuana, you have exclusive control for research purposes, unlike any other substance?

Dr. VOLKOW. Correct. In the United States, yes.

Mr. CONNOLLY. What's the rationale for that? Is there any rationale for that?

Dr. VOLKOW. I guess that one of the rationales—the reasons why this is described to be the case is that you want to be able to have control over the material that you are providing for research.

Mr. CONNOLLY. Why wouldn't that be true about cocaine?

Dr. VOLKOW. Cocaine has different mechanisms for—I mean, it is a drug that is regulated differently vis—vis where we get it for researchers. The production of marijuana is based on plants.

Mr. CONNOLLY. Well, all right. DEA has licensed privately funded manufacturers, privately funded manufacturers, to produce methamphetamines, LSD, MDMA, heroin, cocaine and a host of other controlled substances for research purposes. Is that not correct?

Dr. VOLKOW. They are for research purposes. Yes. And most of those go to—for clinical studies, laboratory animals.

Mr. CONNOLLY. Right now HHS guidelines prohibit the use of NIDA-produced marijuana for use in research designed to develop marijuana into an FDA-approved prescription medicine. Is that correct?

Dr. VOLKOW. Not to my understanding. To—my understanding is we can—we are—we provide the marijuana for clinical research that has been approved by the committee of the DEA, the FDA, and by——

Mr. CONNOLLY. There's no restriction that says but you can't use it for research that's aimed at producing an FDA-approved prescription medicine. Is that correct?

Dr. VOLKOW. Well, there the wording—I don't want to be imprecise because, when you say the FDA-approved medications, since it is a Schedule I, I don't want to say something that is incorrect.

We can fund research that can provide the evidence that then can be brought into the FDA to bring up an argument about why this should be considered as a medical application. That's what we do. And there's no—and we will——

Mr. CONNOLLY. Dr. Throckmorton——

I'm sorry, but I have a limited time. I appreciate your answer.

Dr. Throckmorton, is that correct?

Dr. THROCKMORTON. Could you just ask briefly again. I'm sorry.

Mr. CONNOLLY. Yes.

The HHS guidelines prohibit the use of NIDA-produced marijuana—and it has a monopoly on it—for use in research that could be designed—or is designed to develop marijuana into an FDA-approved prescription medicine.

Dr. THROCKMORTON. No. I don't believe that's true. I believe, in fact, we do see applications that make use of the NIDA marijuana.

Mr. CONNOLLY. I would ask you both to get back to the committee for the record.

Dr. THROCKMORTON. Absolutely.

Mr. CONNOLLY. Because that would be at variance with our understanding, but that's good to know.

Human studies on Schedule I drugs have to be approved by the FDA. Is that not correct?

Dr. THROCKMORTON. That's correct.

Mr. CONNOLLY. But studies involving marijuana, additional approval also has to be sought from NIDA and HHS. Is that not correct?

Dr. VOLKOW. Scientifically, they have to be approved by a committee on NIDA.

Mr. CONNOLLY. Is that true about heroin, cocaine and methamphetamines? Do they have to go through that triple-tier approval process for research as well——

Dr. VOLKOW. No. The——

Mr. CONNOLLY. —on human studies?

Dr. VOLKOW. The approval for those human studies—most of it comes from review committees at the NIH. And if the DEA approves of giving them the drug, then it's a—it's a different procedure.

Mr. CONNOLLY. But don't we—yes. It's a different process and it's less cumbersome.

What is it about marijuana?

You know, I asked the deputy director of the DEA at one of our previous hearings, "Name a single death in America due to an overdose from marijuana." He couldn't do it. Prescription drugs,

legal, every 19 minutes. We could—we could cite other substances as well.

Now, that's not to say, therefore, we shouldn't be concerned about marijuana, but it does raise the question of whether our behavior has been appropriate with respect to marijuana.

The restrictions on research, the extraordinary incarceration—prosecution and incarceration rates, look at what we've unleashed. We've created a subclass of criminal behavior in America that seems out of proportion to the fact that, as Dr. Hart says, 80 percent are for small, you know, possession.

Now, ideally, they wouldn't have it at all. But we have really skewed the system and we've created all kinds of special barriers with respect to marijuana as if it were the uber alles of all drug abuse when, in fact, it is not.

And we've impeded the abilityto have legitimate research that could benefit human health, and it just doesn't—it's very hard for me to frankly understand why we continue to insist it's a class 1 substance.

I yield back, Mr. Chairman.

Mr. MICA. Thank you.

And, Mr. Turner, gentleman from Ohio.

Mr. TURNER. Thank you, Mr. Chairman.

I appreciate the passion that Mr. Connally has, but I'm going to return the hearing back to members asking questions and the panel testifying.

Thank you for having this hearing.

Mr. CONNOLLY. I hope that's what we have all the time.

Mr. TURNER. It should be our goal.

So public health encompasses a wide range of considerations. And I'm certainly pleased that we have the National Institute on Drug Abuse and the Food and Drug Administration representatives today.

As it stands, what role does the FDA play in providing consumer protections for individuals who use recreational drugs in the United States?

Dr. Throckmorton, for example, does the FDA mandate that the products sold in Colorado or Washington State bear warning labels? What about statements as to the potency or strength of the product? Is there information provided to the user at all?

What information does the FDA currently have relating to the strength of various marijuana strains? And how is that information provided to consumers? And should State governments have it? And how does the FDA work with States to make certain that they have that information?

Dr. Throckmorton?

Dr. THROCKMORTON. I hope I got all four of those down. I'll try to respond to them——

Mr. TURNER. It's very simple.

What do you know? And how does it get to a user?

Dr. THROCKMORTON. So as far our role in terms of the State's activities going on in Colorado, they are very limited.

We do communicate with the Public Health Department there because they are doing important work to understand the impact

of marijuana, the impact of the State laws there and things and the access of marijuana in Colorado.

With regards to labeling, we have—we have no role in terms of labeling of the products that are approved under State law in Colorado, including things like strength, purity, any assurances like that. I think that's an important feature of approved drug development that differs from some of the things that are going on in Colorado.

And then, finally, you asked about our interactions with Colorado. As I said, we work with the Public Health Department there because it's important for us to understand where marijuana is going, the kinds of experiences they're having——

Mr. TURNER. Dr. Throckmorton, I just want to go back to that.

You just said nothing to do with labeling. Interestingly enough, food can be harmless or not harmless, and you're very active in its labeling.

But here this clearly is a drug and you're not active at all in any of the information sharing or with respect to the issues of labeling.

Dr. THROCKMORTON. No. To be clear, the products in Colorado are not approved drugs. They've not come before the Agency. We haven't reviewed them for safety effects or security——

Mr. TURNER. And so there's a process that's been skipped so that there's no interaction——

Dr. THROCKMORTON. Those are the things that my Agency oversees. Those are the things we're trying to encourage to the fullest extent possible.

Mr. TURNER. But if I went to go buy a bottle of ketchup—I mean, that labeling is an issue that's been under the FDA, but, yet, we have this as a product and it has not.

Dr. Volkow, in the absence of warning labels or a statement of some kind as to the potency or strength of the marijuana an individual is using, it seems that some very basic consumer protections are absent here.

For example, marijuana can be directly linked to impaired driving. Even Dr. Hart would indicate from his own research that it would have that.

But, again, back to no labeling, no warning, with regard to this serious safety concern, are you aware of any existing methodology that might enable a law enforcement officer with probable cause to assess whether a driver is operating a vehicle under the influence of marijuana? How do they determine that?

Dr. VOLKOW. Well, it's much harder—with marijuana, it's particularly difficult because you actually have—marijuana and its constituents can be in your body for a long period of time, up to 1 week or sometimes even 2 weeks, but that does not mean that you are impaired.

So whereas with alcohol you can measure a certain level and you know that that is associated with the impaired functioning, with marijuana, it is much more complex.

So there's research going on to try to get biomarkers that will allow us to know that someone has smoked marijuana, but that someone is within the range that is dangerous.

Mr. TURNER. And, obviously, with alcohol use, as we understand, it would be the Breathalyzer that can be applied.

But law enforcement in this area is left without any real specific tools that make it very difficult to apply what is the law and what clearly, even in Dr. Hart's research, shows an effect on the impairment of driving and operating a vehicle.

Mr. Chairman, I yield back.

Mr. MICA. Thank you.

Mr. Cohen.

Mr. CONNOLLY. Mr. Cohen, would you yield?

Mr. COHEN. Yes.

Mr. CONNOLLY. Just want to observe that last comment sounded like a comment, not a question to the panel. Thank you.

Mr. COHEN. Mr. Turner, as a denizen of 400 Mass, would you like to respond?

We share the same condo unit. Thank you.

Dr. Volkow, one thing I can't grasp real well is, when Dr. Hart pointed out that the studies say 9 percent of people who smoke marijuana get addicted and 15 percent of people who do alcohol get addicted, you've talked about legal and illegal as if, if it was—marijuana was legal, more people would smoke, which is true.

How does that affect a ratio of 9 percent when it's not about the people, it's about the drug and its interaction with people?

Is there not a large enough class of people that made up the 9 percent to be an accurate gauge of those that would become addicted?

Are you suggesting that those who have not smoked because it's illegal are more likely to get addicted and will run the level from 9 percent up to 15 percent?

Dr. VOLKOW. Two factors. Actually, many people don't smoke because—marijuana because it is illegal. So the moment that it's legalized, they do adapt to social norms and that modulates their behavior.

But, more importantly, I think that what determines the extent to which a person gets exposed to a drug and becomes addicted is not that you get exposed once, but the likelihood that you will be exposed repeatedly.

So by having a drug that is legal, particularly in adolescence, they are actually much more likely to get exposed to it repeatedly, that is, that drug is elicit.

So the more that you get exposed to it, the greater the likelihood that you could become addicted. And that's why, as I say, if you are going to compare it, you have to compare it in the similar——

Mr. COHEN. I understand what you're saying. I just simply—I don't agree.

And I think Dr. Hart—Dr. Hart, how would you respond to that?

Mr. HART. I don't know how to respond.

I agree with your point in terms of we—as has been pointed out accurately, marijuana is the most frequently smoked illicit drug. We have about 18 million current users in the country.

I think those numbers are sufficient to determine what the addictive potential will be. But, you know, it's an empirical question. But I think that there is—it is sufficient.

Mr. COHEN. Thank you, Doctor.

You talked, Dr. Volkow, about—you said—and I guess there are car accidents involved in marijuana. But you said marijuana, car accidents, and particularly fatal accidents, and that those are facts.

What are the facts? What are the facts you're relying upon?

Dr. VOLKOW. Well, this is data from the Department of Transportation. And, in fact——

Mr. COHEN. And what's that data say?

Dr. VOLKOW. That data says that, unequivocally, the use of marijuana is associated with doubling your risk for getting into a car accident. And the data——

Mr. COHEN. Doubling your risk of getting in car accident as distinguished from not smoking marijuana?

Dr. VOLKOW. From not being intoxicated when you are driving the car.

Mr. COHEN. Right.

But how does it relate to alcohol?

Dr. VOLKOW. Alcohol is much greater risk.

Mr. COHEN. Right.

And let me submit—because these are kind of somewhat red herrings.

Nobody in the world, I don't think—nobody I know in Congress or anywhere I know in the world that's dealing with this is suggesting that adolescents should be doing—smoking marijuana or that anybody should be driving a car while under the influence.

And the whole problem may be solved by Uber Cars. You just pick up and you get more people. That may take care of the problem. But nobody is suggesting that that should happen.

Dr. Throckmorton, I think you said that y'all are doing some study on possibly looking at Schedule I and marijuana?

Dr. THROCKMORTON. There's—we've been requested to conduct another 8-factor analysis, and that requires that we look at eight sets of data that Congress laid out.

They said, "Look at these factors and then make a recommendation to the DEA about what the appropriate schedule is." And so we are working through those factors.

Mr. COHEN. Right.

Is there no question, even without studying, to know that cocaine is a more likely addictive substance than marijuana and that heroin is, too?

Dr. THROCKMORTON. Scheduling isn't just about comparative risk, though. The other aspect about scheduling and the reason why cocaine has features that allow it to be at a different schedule is that it has ascribed benefits.

So there are approved uses for cocaine as a topical anesthetic and things like that. With those approved uses comes accepted medical use in the United States.

And that's—that's the thing that's fundamentally missing at present from the—you know, our current conclusions regarding marijuana is that absence of accepted medical use.

Typically, the best way to demonstrate accepted medical use has been through a drug approval. So with an approval comes accepted medical use.

And that's why I started out saying that that's another pathway to think about as far as rescheduling of marijuana, looking at other

avenues to encourage better science, fully understand its benefits and risks and, as a part of that, reconsider the scheduling.

Mr. COHEN. Thank you.

Mr. Chairman, I want to thank you once again for this hearing. I think that both Dr. Volkow and Dr. Throckmorton have done a splendid job.

I do think, to some extent, they have remained, which is understandable because of their position in the government, within the silos in which they are authorized. And so they've talked about marijuana and health and marijuana and addiction and marijuana and these areas.

But Dr. Hart has taken a holistic approach. He's not siloed by his government job and his superiors. And it is a holistic approach we need to take in this case.

And to judge it as against the merits of incarcerating hundreds of thousands of people and putting millions of people in a secondary class for the rest of their lives because of what might have been an adolescent or young or mature choice or mistake, however you want to look at it, should they be punished? Is the punishment relative to the action merited?

And so I thank Dr. Hart for his holistic approach.

And I know y'all would probably take the same ones if you didn't have the straightjacket of government jobs.

Thank you.

Mr. MICA. Thank you.

And now we'll turn to Dr. Fleming. You're recognized.

Mr. FLEMING. Thank you, Mr. Chairman.

Dr. Hart, you're obviously a very strong advocate for the decriminalization, even legalization, of marijuana. Would that be correct?

Mr. HART. I'm an advocate for justice and science.

Mr. FLEMING. Well, that's—again, it's a "yes" or "no."

Are you an advocate for legalization of marijuana?

Mr. HART. No. I'm not an advocate. I wrote a book——

Mr. FLEMING. Are you an advocate for decriminalizing?

Mr. HART. Wait. Wait. If you're going to ask me questions——

Mr. FLEMING. It's a "yes" or "no" question, sir.

Mr. HART. If you ask me a question, I'm going to answer it.

Mr. FLEMING. It's a "yes" or "no."

Are you——

Mr. HART. I am an advocate for decriminalization. Yes, I am. And I wrote that in my book.

Mr. FLEMING. But not legalization?

Mr. HART. No.

Mr. FLEMING. Okay. Now——

Mr. HART. But I am not against legalization. I am for what makes sense for the society as a whole.

Mr. FLEMING. Okay. But, again, along the way, we have to make a decision "yes" or "no."

So you're saying that you are in favor of decriminalization and you're not against the legalization. Is that a correct characterization?

Mr. HART. That is correct.

Mr. FLEMING. Okay. Now, you make a strong argument taking the data, turning it on its side and doing a lot of things with it.

But I would suggest to you a lot of it is inaccurate and out of date. For instance, you say the beginning use age of marijuana is 17. That may have been true 20 years ago when it wasn't being legalized or medicinalized.

But what we're finding out today is, like alcohol and tobacco, the average starting age is in the range of 9 to 12. That is the average starting range.

In places where marijuana is widely available through decriminalization and through legalization, medicinalization, we are seeing that age close in on tobacco and alcohol.

In fact, just the other day, they reported 4-year-olds ingesting marijuana through the goodies, the baked goods and so forth and even fourth-graders dealing marijuana.

So, you see, what Dr. Volkow is suggesting is quite true. And that is, as the threats go away, as it becomes legalized or decriminalized and the stigma is removed, the usage rates go up and so do the addiction rates.

So, again, that explains the 9 versus 15 percent. If you put marijuana at the same status as alcohol and tobacco, you're going to see similar, if not greater, rates.

But the thing that I think is unforgivable in your statement——

Mr. HART. Can I respond to that?

Mr. FLEMING. No, sir.

The thing that I find unforgivable in your statement is that you said that—let me see if I get this correct—marijuana only remains in a person's system for a few hours.

Mr. HART. No. No. No. You misunderstood.

I have to—you cannot—you cannot——

Mr. FLEMING. No, sir.

Mr. HART. You cannot——

Mr. FLEMING. No, sir. I have the——

Mr. HART. That's wrong. I did not say that. I did not say that.

Mr. FLEMING. All right. Specifically, how long does marijuana stay in the system?

Mr. HART. Marijuana can stay in your system for as long as 30 days, depending upon the level of the users.

Mr. FLEMING. That is correct.

You suggested——

Mr. HART. Of course it's correct. I do these studies.

Mr. FLEMING. But you suggested otherwise. You suggested otherwise.

And we also heard from testimony yesterday in the addiction caucus that not only does it remain in the body, but it remains active longer than alcohol.

So to suggest that marijuana is less active and for a shorter period of time than alcohol is simply incorrect. Do you concede that?

Mr. HART. I don't know what you heard.

Mr. FLEMING. All right. But I'm asking you specifically. Which stays in the body longer? Alcohol or marijuana?

Mr. HART. Marijuana, of course.

Mr. FLEMING. Okay. Very good. We got that.

All right. Now, Dr. Volkow, you said something I thought was very interesting and something I very agree with, and it's the theme in my book in 2007.

You said that marijuana and other drugs, anything addicting, has a priming effect in the brain. The human brain, particularly the immature brain, is still open to all sorts of stimuli that may occur, whether it's cannabinoid receptors, dopamine receptors, norepinephrine, whatever the receptors are.

And so would you elaborate on this priming effect and the fact that younger—the younger people are who use addicting substances, the more likely they are to have problems down the road.

And, again, that's in a context of decriminalization and legalization. Because we all know that, if it's illegal, it's less likely to be in the home, available to kids through their parents, but if it's legal, it is more likely to be there.

So would you please comment on that.

Dr. VOLKOW. Yeah. What we know—and this is true—but certainly for alcohol, nicotine and marijuana, is the earlier initiation, the greater the likelihood of addiction.

And this is, in part, from the fact that these drugs stimulate endogenous signaling systems that during those developmental stages are specifically involved in creating the architecture of the brain, and it changes very dramatically in the transition from childhood into adulthood.

So cannabinoids specifically, for example, will determine how a particular neuron will connect with another one. And so, if you saturate and bombard with marijuana, what you're going to be doing is having a state of hyperstimulation followed by an inhibition.

So that, in turn, disrupts this very, very perfectly orchestrated process, which is why—one of the reasons why there is concern about cannabinoids.

Similarly with nicotine you also have this role. So it's not something that's unique to marijuana, but it is clear both nicotine and marijuana can be interfering with a normal process of brain development.

Mr. FLEMING. So not only do we have epidemiological data that suggests that a forerunner to heroin and crack cocaine use or methamphetamine is marijuana, but, also, if you look at the—the pump-priming effect of drugs even as common as nicotine, that we see that there's really a scientific pathway, there's a brain pathway in development that certainly explains that likelihood?

Dr. VOLKOW. Yeah. And it's exactly why we are particularly focused on understanding what are the consequences of exposure to the adolescent brain of these drugs in their individual trajectories.

And I completely agree. Nobody's here saying we are expecting—we're approving the use of these drugs in adolescents.

Unfortunately, when we make decisions that are targeted to adults, we are changing also the attitudes of the adolescents and we are influencing.

So we need to be cognizant of that, and we need to actually obtain the information that can lead us to prevention efforts, whatever finally the regulations or policy are.

Mr. FLEMING. Right.

And, Dr. Throckmorton, you talk about the fact we actually are working on extracts and even fast-tracking extracts particularly for seizure disorders.

And was there other uses as well?

Dr. THROCKMORTON. There's also fast-track designation that's been given to another product called Sativex being developed for cancer pain.

Mr. FLEMING. For cancer pain.

So what we're really doing is what we typically do for other drugs and, as we find some potential benefit, we begin to try to focus and extract and purify a drug to do that.

So, again, that begs the question. My colleague before suggested that, well—because I said, well, look, we have the—we have the mass use now of medicinal marijuana. We have more marijuana dispensaries in California and Denver than we do Starbucks.

So aren't we putting the cart before the horse? Why are we widely distributing this to millions of Americans as a treatment when we haven't done the research and extracted and purified and really gone to the very target treatment that we're really trying to achieve?

What is your response to that?

Dr. THROCKMORTON. As I said in my opening statement, drug development is the best way to assure safe, effective, high-quality medicines are available for the U.S. public as quickly as possible. I think that's got—I think that's everyone's goal in this room.

Mr. FLEMING. Would that be consistent with I, as a physician treating patient with penicillin, giving them a purified product by mouth or by injection rather than giving them, say, moss or mold?

Dr. THROCKMORTON. I don't think I want to comment about the other paths.

Mr. FLEMING. Yes.

Dr. THROCKMORTON. My job at the FDA is to make sure that the drug development pathway works and is being applied efficiently.

Mr. FLEMING. Right. I appreciate that. And I want you to continue to do that. That's really the safe pathway to go down.

Also, something we really haven't talked about—and, Dr. Volkow, I'll come back to you—is recent studies are rolling out that are telling us very terrifying things about even casual use of marijuana.

For instance, you alluded to structural changes of the brain. We're seeing that, even in moderate users or even—casual, I think, is the term they use—twice-a-day smokers, huge changes in the structure of the brain, a tremendous spike now in disease of the heart and the lungs in users.

Would you elaborate on some of this data.

Dr. VOLKOW. Well, in the data of brain imaging studies, which actually is the one that I've personally been involved with and I can look at it critically, I think that the—the studies that show evidence of harm are studies that relate to the regular use of marijuana, heavy use of marijuana.

There was a recent study on adolescents that were not very frequent users, once a month or twice a month, and they reported changes. But, in science, one needs to replicate.

So I see it's valuable. It's the first one to document that perhaps not-so-frequent use could create harm. But I would be caution—cautious until we get a replication study.

With respect to the other area that has generated a lot of interest is schizophrenia because, if you give high enough doses of THC, you are going to make someone psychotic. Most of those episodes are short-lasting. But there is a group that goes into chronic psychosis that then results as the diagnosis of schizophrenia.

So there's been a lot of interest to determine can marijuana produce schizophrenia. And what the data seems to suggest is it triggers an episode. It may advance it in someone that has the vulnerability. And that is associated also with a higher content THC.

So while Dr. Hart says correctly a lot of people say you can model it, the data actually seems to show otherwise. We're seeing higher content of plasma, content of 9–THC, over all of these years.

Mr. FLEMING. The stronger the drug gets——

Dr. VOLKOW. The higher the plasma content——

Mr. FLEMING. —the higher the——

Dr. VOLKOW. —the 9–THC, the higher the consequences.

Mr. FLEMING. Yeah. There's no science to suggest that, just because marijuana—the THC level is higher, that people are using it less to compensate. That simply isn't the case.

Before I yield back, Mr. Chairman, I just wanted to say, in terms of what Dr. Hart says, even if you take what Dr. Hart says at face value, which I think a lot of what he said is incorrect and the wrong direction, he still makes a very compelling case to keep this as a Schedule I drug. It is a dangerous drug.

And I yield back.

Mr. MICA. Thank the gentleman.

Let me yield for wrap-up Mr. Connolly.

Mr. CONNOLLY. Yes. You know, I respect my colleague from Louisiana. I don't think he makes any such case.

In fact, I think this whole hearing and the other hearings we've had, certainly for this member of Congress, who started out not wanting to touch marijuana, leave it where it is—I've been forced to study this.

I've been forced to look at it. I've been forced to look at the science of it when I didn't want to, really. I had plenty of other things I was worried about.

And I am—I don't believe that we—that the testimony we've heard today in any way reinforces how dangerous this drug is and it needs to be a Substance I drug. Quite the opposite.

I think it raises profound questions about the policy of the United States in the last 30 or 40 years with respect to marijuana as a gross overreaction.

The fact that cocaine is Substance II and marijuana is Substance I tells you a lot about how skewed the United States' policy—Federal policy is with respect to this drug.

And I again suggest that's one of the reasons why 22, maybe 23, States are going in a different direction. And there's danger to that because being out of sync with the Federal Government creates some problems.

My friend is still here. And he's a doctor. And I know he has a good heart and wants to hear patient stories.

I hope he will indulge me if I just share for the record with him and with the panel the testimony of my constituent, Beth Collins,

about her daughter's experience in Colorado under treatment with a derivative of marijuana, Jennifer.

Jennifer's medication administered as an oil under her tongue is called THCA, an inactive form of THC. So it has no psychoactive effect. However, it is scheduled the same as heroin precisely because it's a Schedule I drug.

Marinol, a synthetic form of THC, is Schedule III. Marinol is used to help control pain and nausea for cancer patients, but it does not help with seizures.

We're currently seeing a significant decrease in Jennifer's seizers. Her neurologist here in Colorado, who is very supportive, feels that in the next few months she may be ready to start weaning from the heavy pharmaceuticals that are causing her physical, cognitive, and emotional damage, that is to say, the non-marijuana-derivative pharmaceuticals.

I'm witnessing a great deal of success with other epilepsy cases using various Cannabis extracts here in Colorado.

Of the approximately 200 pediatric patients using Cannabis oil from the Realm of Caring—trademark—in Colorado, 78 percent show a reduction in seizures. 78 percent.

Of that 78 percent, 25 percent have had a greater than 90 percent reduction in seizures or are seizure-free. Most of these patients have exhibited a significant increase in cognition.

Now, here's where—the Federal regulation problem because it's a Substance I abuse and because we so skew against marijuana in our so-called research.

Rescheduling marijuana to a Schedule III drug would enable Jennifer to leave the State of Colorado for visits home to her friends and family back in Virginia. It would also allow doctors to begin studies of the efficacy of marijuana in pediatric epilepsy.

While Jennifer's neurologist here is supportive, he's unable to provide us with the advice on dosing and compile his findings and observations into usable research as this is against Federal law.

I and other parents are nervous about making these decisions with very little input from our children's doctors. We'd really like the guidance of our physicians because this is a serious medical concern with serious ramifications. Current Federal law prohibits us from receiving such guidance.

Mr. FLEMING. Would the gentleman yield?

Mr. CONNOLLY. Of course.

Mr. FLEMING. Because I'd like to agree, to an extent, to what you say. You know, a little over a century ago medicine moved to the direction of modern science.

You know, we want to research these things. And just as Dr. Throckmorton has said, these things that hold promise should be studied.

And in the case of this little girl, if we want to use rigorous scientific evaluation, enter her into a study—I have a grandson, by the way, who has cystic fibrosis.

And I would love for him to get some of the experimental drugs, but he doesn't qualify at this point. So we hope that he will qualify or a new drug will come out. But what I don't want to do is to see us throw medication at children.

And so that's why I say, to me, it conflates the reality by saying that we should have medicinal pharmacies all across the Nation where millions of people get a drug that is really being used for recreational use.

We really need to be honest with that. To conflate that with a specific situation where a child may benefit from a nonactive THC product, we all agree. I just, as a physician, ask that we go through the rigor of research.

Mr. CONNOLLY. But I—you know, I very much appreciate your comment, and I agree with you. I don't have any agenda here. I'm not one who is in favor, necessarily, of recreational use or just legalizing it everywhere, not at all.

But I have been, as I said, because of these hearings, actually forced to re-examine what I thought I knew about marijuana.

And I agree with my friend that we should have rigorous empirical studies to convince ourselves that it is—can be used in limited circumstances or broad circumstances, whatever it may be.

But I hope my colleague has heard through this hearing that marijuana, though—if we—we both agree that rigorous scientific research ought to occur here, it should occur in an unbiased fashion.

Marijuana is not treated like any other substance. In fact, cocaine is more liberally treated for research purposes than is marijuana. And it is clear marijuana is not more dangerous.

Mr. FLEMING. As a point of order, I think that crack cocaine is still a Schedule I drug. Correct? There's a medicinal form of cocaine that is classified differently. The same would be true of Marinol, which is a Schedule III. It's the same thing.

Mr. CONNOLLY. My point wasn't that it's not a Class I. It is that the research allowed on cocaine has a lower standard.

NIDA is the—marijuana is the only drug that NIDA has an exclusive research control over. In the case of cocaine, it's actually easier to do research. And if you and I both agree that we want rigorous research, I think we have to re-examine the control of NIDA.

Mr. FLEMING. I agree with my colleague.

Mr. CONNOLLY. Okay. That was the point I was making.

Mr. FLEMING. I think we should allow as much research on marijuana as we would cocaine.

Mr. CONNOLLY. I thank my friend.

Dr. VOLKOW. And, if I may answer, because—just to clarify, I mean, definitely—I mean, we do a lot of research as it relates to cannabinoids.

And we speak about marijuana, but marijuana is a series of chemicals, many cannabinoids. So what we are interested in is extracting the active ingredients.

So, for example, for the cases of this very intractable epilepsy in children, Dravet's, the compound—the cannabinoid compound that appears to be responsible is cannabidiol.

Cannabidiol content of the marijuana you get out there is decreasing and decreasing, and it's not rewarding, it doesn't produce a high.

Mr. CONNOLLY. Dr. Volkow, my chairman has been very generous with me on this. So I'm going to just make one point.

Okay. But the mission of your agency is drug abuse.

Dr. VOLKOW. Correct.

Mr. CONNOLLY. It's not medical research into the possible efficacy of derivatives from otherwise dangerous or semi-dangerous drugs.

And given the fact that you have a monopoly over the control of marijuana for research purposes in the Federal family, one could—a reasonable inference could be drawn that you are less than motivated, as an agency, to assist us in that rigorous medical research Dr. Fleming and I were just talking about.

I'm not calling into question the legitimacy of your mission. I am saying, however, that your mission is not the same as that of those wishing to pursue medical research as to the beneficial effects. Your own testimony never even mentioned beneficial effects or even the potentiality of it.

Dr. VOLKOW. And you're absolutely right. We're the Institute of Drug Abuse. And you're absolutely right. We have the farm that has to provide with the marijuana for research purposes, and that was something that was determined many years ago. And I think that—I mean, you are bringing it up as an issue, I think.

Mr. CONNOLLY. I thank you.

And I thank my colleague, Dr. Fleming.

Thank you, Mr. Chairman.

Mr. MICA. Thank you, both.

Let me just conclude with a couple of things.

First of all, I take away from this—I've heard for the first time that FDA is actually going to—is in the process of conducting another 8-factor analysis.

Is that correct, Dr. Throckmorton?

Dr. THROCKMORTON. That's correct.

Mr. MICA. Okay. So we heard that they are—they did it in 2001. They said "no." They did it in 2006. And that is a scientific evaluation.

And then you consult with NIDA. And I'll give—and we heard again the director say that they would look at your findings and make a recommendation.

So as far as the Schedule I, that analysis is underway. Correct, everyone?

Dr. THROCKMORTON. That's correct.

Mr. MICA. Okay. And you have enough funds and research capability of conducting that in a thorough manner?

Dr. THROCKMORTON. Yes.

Mr. MICA. Okay. And the second thing is across the country there's been a wave of votes and legislative actions to take us into using marijuana or some of its derivatives—I'm not going to be technically accurate here—for medical beneficial purposes.

You don't study that, right, at NIDA?

Dr. VOLKOW. We study it as it pertains to two conditions, can we use some of these derivatives for the treatment of drug addiction and when we use them for the treatment of pain.

Mr. MICA. Okay. Okay. Well, then—okay. Then, you do some review of its capability.

We also heard—I heard for the first time that FDA has several drugs that contain either a derivative or some form of marijuana

for medical purposes and that's under consideration for the FDA stamp of approval, for lack of a better term. Is that correct?

Dr. THROCKMORTON. We talked about two drugs that are——

Mr. MICA. Yes. Two.

Dr. THROCKMORTON. Yes.

Mr. MICA. Okay. So there—and you have enough funds. You have that research going on. You couldn't tell us when the 8-factor analysis would be complete.

If we could—we could ask them a question and then if you want to respond, if you have some estimate or guesstimate you could provide for the record, a timeline.

And then—you don't. Well, we're going to ask you the question anyway. And then I'll subpoena your butt back here.

Mr. CONNOLLY. Yeah. Maybe you should.

Mr. MICA. But, seriously, what we're trying to find out—because people say, "Well, what's going on with the Schedule I?" And this has big implications.

I mean, we've had law enforcement people, we've had prosecutorial folks, we have the head of the DEA, we've got ONDCP, a whole bunch of people going in different directions on this.

So, again, we'll hear at some time on both the rescheduling and then we'll hear on the efficacy or the acceptance of using some of these substances that contain marijuana for medical purposes.

So that's where we are in that regard. I think that's been helpful for me. And, again, I have not heard some of this before.

Both of you have enough resources? Because then people say, "Well, they're not able to study. They're not able to conduct."

Is there a shortage in anything you're doing, Dr. Throckmorton?

Dr. THROCKMORTON. Both of these are important parts of our mission.

Mr. MICA. Are you okay, Dr. Volkow? You can always use more money?

Dr. VOLKOW. I'm smiling. I'm just smiling. I mean, the amount of resources allows us to expedite——

Mr. MICA. Do you need more resources? Tell us.

Dr. VOLKOW. Faster. You can always do things much faster if you have more resources.

Mr. MICA. Okay. Well, I think that's something I'd ask the staff to look at. Because, again, you want good review, good studies, and people have to have the adequate resources to conduct that responsibly.

Mr. CONNOLLY. Mr. Chairman, I mean, you've got a Republican chairman asking if you have enough money in your budgets. Run all the way to the bank with that question.

Mr. MICA. Well, again, I feel a little bit like Solomon. I'm trying to get the answers. Many questions have been raised. And we have an important oversight responsibility. Societal impressions about this are changing, and attitudes are changing.

Now, one of the things that—and I thought—Dr. Fleming brought up something we didn't talk about. But FDA has a responsibility over consumer safety.

And we now have products on the market, some being dispensed with alleged medical benefits, not controlled by you. Right?

Dr. THROCKMORTON. Depending on what they're claiming, they could fall under our jurisdiction.

Mr. MICA. I find very little today that you can eat or consume or buy off the shelf for medical remedies that has no labeling, no disclosure. So I think that we've got to look at that particular aspect, too, and see where we're headed there. You do have a couple of drugs, as you said, that you're looking at specifically. But the lack of consumer information.

The other thing, too, is going down this path of legalization, kids are very impressionable. Everybody, Dr. Hart, Dr. Throckmorton, Dr. Volkow, all of our panelists, everyone starts out we don't want this in the hands of adolescents. But the statistical data that we have is you're seeing more and more use of this narcotic by young people. Lack of information, but again more promotion as far as its acceptability. And then it's hitting our most vulnerable, young people.

And there are consequences. We'll get into some of them. We're going to look at differences in law and enforcement. We don't have tests that can tell us how stoned people are or how incapacitated they are that are uniform or acceptable, and then we have the residual aspect that Dr. Hart, Dr. Fleming got into.

The other thing, too, is now this is being touted. I talked about driving, shaving, and then watching TV today, I see the ad with a candidate in Maryland who is going to balance the budget, pay for education, just by taxing marijuana. So there are a whole host of implications of what is happening. If you try to get a job and you use marijuana or you have it in your system, or join the military, there is a whole other set of subpenalties that we currently have. So, again, we raise questions.

And now, Mr. Connolly, we have the return of one of our subcommittee members who has not had an opportunity to participate. The gentleman from Georgia, Mr. Woodall, has asked for time, so I'll yield to him. Thought I was going to close, but that didn't work out.

Mr. WOODALL. I appreciate the chair's indulgence. I appreciate the ranking member as well.

I had to rush back, Mr. Chairman, because had things been going wrong and we dragged the FDA in here today, we'd be the first one to talk about all the delays, all the paperwork, all the folks who could have been helped if only FDA had been done things differently. But I come from the great State of Georgia, and when you talk to the regulators down in Georgia, when you talk to folks trying to make a difference in people's lives in Georgia, in fact, I talked to them before this hearing and they said, I don't know who you're going to have testify, but have you have Dr. Throckmorton testify I want you to know he's been the most helpful Federal Government person that we have worked with in our tenure. And he is all about making a difference, wants to do it safely, wants to do it wisely, but if it's worth doing, wants to do it rapidly.

And it means a lot with all the frustration and mistrust that oftentimes government rightly deserves, when we have an opportunity to brag on folks who are doing everything they can to restore that trust, everything they can to fulfill the mission of their agency, I want to be a part of saying thank you for that. Generally,

when we find those folks, they get promoted out of that job on to do something where they are not nearly as effective as they used to be. So I don't wish those promotions upon you, Dr. Throckmorton. I want to tell you that candidly.

And with that, Mr. Chairman, I'm grateful for your indulgence, and I encourage you all to watch the partnership that we have, GW Pharmaceutical, Regents University, Georgia, New York. It's going to be something worth paying attention to.

Mr. MICA. I'm sort of in shock. I don't think we have ever had—well, first of all, Mr. Woodall, the gentleman from Georgia, is a tiger on anyone from the Federal bureaucracy, so that holds me in awe with his statement of you. Then, I've been on the committee longer than anyone in Congress, and I don't think I've ever heard such a compliment before this committee of someone who works in an agency or a bureaucrat, no offense. So it's a rare occasion. I may need medical treatment.

Mr. CONNOLLY. So two record-shattering events have occurred, Mr. Throckmorton, here. One is a Republican chairman has said, do you have enough money, do you need more? And secondly, a Georgian Republican is praising a Federal official. I'm telling you, run to the bank.

Mr. MICA. Well, again, we end on sort of a light and positive note, which is good. But, again, this series of hearings is to review some important questions. Our subcommittee in particular has jurisdiction over State-Federal relations and conflicts and laws. And I think, again, we'll be having another hearing in July.

And I thank each of our witnesses. I thank the members who've participated. There being no further business before the Government Operations Subcommittee, this hearing is adjourned.

[Whereupon, at 11:23 a.m., the subcommittee was adjourned.]

APPENDIX

Material Submitted for the Hearing Record

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Adverse Health Effects of Marijuana Use

Nora D. Volkow, M.D., Ruben D. Baler, Ph.D., Wilson M. Compton, M.D., and Susan R.B. Weiss, Ph.D.

From the National Institute on Drug Abuse, National Institutes of Health, Bethesda, MD. Address reprint requests to Dr. Volkow at the National Institute on Drug Abuse, 6001 Executive Blvd., Rm. 5274, Bethesda, MD 20892, or at nvolkow@nida.nih.gov.

N Engl J Med 2014;370:2219-27.
DOI: 10.1056/NEJMra1402309
Copyright © 2014 Massachusetts Medical Society.

IN LIGHT OF THE RAPIDLY SHIFTING LANDSCAPE REGARDING THE LEGALIZATION of marijuana for medical and recreational purposes, patients may be more likely to ask physicians about its potential adverse and beneficial effects on health. The popular notion seems to be that marijuana is a harmless pleasure, access to which should not be regulated or considered illegal. Currently, marijuana is the most commonly used "illicit" drug in the United States, with about 12% of people 12 years of age or older reporting use in the past year and particularly high rates of use among young people.[1] The most common route of administration is inhalation. The greenish-gray shredded leaves and flowers of the *Cannabis sativa* plant are smoked (along with stems and seeds) in cigarettes, cigars, pipes, water pipes, or "blunts" (marijuana rolled in the tobacco-leaf wrapper from a cigar). Hashish is a related product created from the resin of marijuana flowers and is usually smoked (by itself or in a mixture with tobacco) but can be ingested orally. Marijuana can also be used to brew tea, and its oil-based extract can be mixed into food products.

The regular use of marijuana during adolescence is of particular concern, since use by this age group is associated with an increased likelihood of deleterious consequences[2] (Table 1). Although multiple studies have reported detrimental effects, others have not, and the question of whether marijuana is harmful remains the subject of heated debate. Here we review the current state of the science related to the adverse health effects of the recreational use of marijuana, focusing on those areas for which the evidence is strongest.

ADVERSE EFFECTS

RISK OF ADDICTION

Despite some contentious discussions regarding the addictiveness of marijuana, the evidence clearly indicates that long-term marijuana use can lead to addiction. Indeed, approximately 9% of those who experiment with marijuana will become addicted[3] (according to the criteria for dependence in the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition [DSM-IV]). The number goes up to about 1 in 6 among those who start using marijuana as teenagers and to 25 to 50% among those who smoke marijuana daily.[4] According to the 2012 National Survey on Drug Use and Health, an estimated 2.7 million people 12 years of age and older met the DSM-IV criteria for dependence on marijuana, and 5.1 million people met the criteria for dependence on any illicit drug[1] (8.6 million met the criteria for dependence on alcohol[1]). There is also recognition of a bona fide cannabis withdrawal syndrome[5] (with symptoms that include irritability, sleeping difficulties, dysphoria, craving, and anxiety), which makes cessation difficult and contributes to relapse. Marijuana use by adolescents is particularly troublesome. Adolescents' increased vulnerability to adverse long-term outcomes from marijuana use is probably related

The New England Journal of Medicine
Downloaded from nejm.org by SAM BUTMAN on June 4, 2014. For personal use only. No other uses without permission.
Copyright © 2014 Massachusetts Medical Society. All rights reserved.

Table 1. Adverse Effects of Short-Term Use and Long-Term or Heavy Use of Marijuana.

Effects of short-term use
Impaired short-term memory, making it difficult to learn and to retain information
Impaired motor coordination, interfering with driving skills and increasing the risk of injuries
Altered judgment, increasing the risk of sexual behaviors that facilitate the transmission of sexually transmitted diseases
In high doses, paranoia and psychosis
Effects of long-term or heavy use
Addiction (in about 9% of users overall, 17% of those who begin use in adolescence, and 25 to 50% of those who are daily users)*
Altered brain development*
Poor educational outcome, with increased likelihood of dropping out of school*
Cognitive impairment, with lower IQ among those who were frequent users during adolescence*
Diminished life satisfaction and achievement (determined on the basis of subjective and objective measures as compared with such ratings in the general population)*
Symptoms of chronic bronchitis
Increased risk of chronic psychosis disorders (including schizophrenia) in persons with a predisposition to such disorders

* The effect is strongly associated with initial marijuana use early in adolescence.

to the fact that the brain, including the endocannabinoid system, undergoes active development during adolescence.[6] Indeed, early and regular marijuana use predicts an increased risk of marijuana addiction, which in turn predicts an increased risk of the use of other illicit drugs.[7] As compared with persons who begin to use marijuana in adulthood, those who begin in adolescence are approximately 2 to 4 times as likely to have symptoms of cannabis dependence within 2 years after first use.[8]

EFFECT ON BRAIN DEVELOPMENT

The brain remains in a state of active, experience-guided development from the prenatal period through childhood and adolescence until the age of approximately 21 years.[9] During these developmental periods, it is intrinsically more vulnerable than a mature brain to the adverse long-term effects of environmental insults, such as exposure to tetrahydrocannabinol, or THC, the primary active ingredient in marijuana. This view has received considerable support from studies in animals, which have shown, for example, that prenatal or adolescent exposure to THC can recalibrate the sensitivity of the reward system to other drugs[10] and that prenatal exposure interferes with cytoskeletal dynamics, which are critical for the establishment of axonal connections between neurons.[11]

As compared with unexposed controls, adults who smoked marijuana regularly during adolescence have impaired neural connectivity (fewer fibers) in specific brain regions. These include the precuneus, a key node that is involved in functions that require a high degree of integration (e.g., alertness and self-conscious awareness), and the fimbria, an area of the hippocampus that is important in learning and memory.[12] Reduced functional connectivity has also been reported in the prefrontal networks responsible for executive function (including inhibitory control) and the subcortical networks, which process habits and routines.[13] In addition, imaging studies in persons who use cannabis have revealed decreased activity in prefrontal regions and reduced volumes in the hippocampus.[14] Thus, certain brain regions may be more vulnerable than others to the long-term effects of marijuana. One study showed that selective down-regulation of cannabinoid-1 (CB1) receptors in several cortical brain regions in long-term marijuana smokers was correlated with years of cannabis smoking and was reversible after 4 weeks of abstinence.[15] Changes in CB1 receptors were not seen in subcortical regions.

The negative effect of marijuana use on the functional connectivity of the brain is particularly prominent if use starts in adolescence or young adulthood,[12] which may help to explain the finding of an association between frequent use of marijuana from adolescence into adulthood and significant declines in IQ.[16] The impairments in brain connectivity associated with exposure to marijuana in adolescence are consistent with preclinical findings indicating that the cannabinoid system plays a prominent role in synapse formation during brain development.[17]

POSSIBLE ROLE AS GATEWAY DRUG

Epidemiologic and preclinical data suggest that the use of marijuana in adolescence could influence multiple addictive behaviors in adulthood. In rodents exposed to cannabinoids during adolescence, there is decreased reactivity of the dopamine neurons that modulate the brain's reward regions.[18] The exposure of rodents to

The New England Journal of Medicine
Downloaded from nejm.org by SAM BUTMAN on June 4, 2014. For personal use only. No other uses without permission.
Copyright © 2014 Massachusetts Medical Society. All rights reserved.

cannabis in utero alters the developmental regulation of the mesolimbic dopamine system of affected offspring.[19] If reduced dopamine reactivity in the brain's reward regions does follow early exposure to marijuana, this effect could help to explain the increased susceptibility to drug abuse and addiction to several drugs later in life, which has been reported in most epidemiologic studies.[20] This theory is also consistent with animal models showing that THC can prime the brain for enhanced responses to other drugs.[21] Although these findings support the idea that marijuana is a gateway drug, other drugs, such as alcohol and nicotine, can also be categorized as gateway drugs, since they also prime the brain for a heightened response to other drugs.[22] However, an alternative explanation is that people who are more susceptible to drug-taking behavior are simply more likely to start with marijuana because of its accessibility and that their subsequent social interactions with other drug users would increase the probability that they would try other drugs.

RELATION TO MENTAL ILLNESS

Regular marijuana use is associated with an increased risk of anxiety and depression,[23] but causality has not been established. Marijuana is also linked with psychoses (including those associated with schizophrenia), especially among people with a preexisting genetic vulnerability,[24] and exacerbates the course of illness in patients with schizophrenia. Heavier marijuana use, greater drug potency, and exposure at a younger age can all negatively affect the disease trajectory (e.g., by advancing the time of a first psychotic episode by 2 to 6 years).[25]

However, it is inherently difficult to establish causality in these types of studies because factors other than marijuana use may be directly associated with the risk of mental illness. In addition, other factors could predispose a person to both marijuana use and mental illness. This makes it difficult to confidently attribute the increased risk of mental illness to marijuana use.

EFFECT ON SCHOOL PERFORMANCE AND LIFETIME ACHIEVEMENT

In the 2013 Monitoring the Future survey of high-school students,[26] 6.5% of students in grade 12 reported daily or near-daily marijuana use, and this figure probably represents an underestimate of use, since young people who have dropped out of school may have particularly high rates of frequent marijuana use.[27] Since marijuana use impairs critical cognitive functions, both during acute intoxication and for days after use,[28] many students could be functioning at a cognitive level that is below their natural capability for considerable periods of time. Although acute effects may subside after THC is cleared from the brain, it nonetheless poses serious risks to health that can be expected to accumulate with long-term or heavy use. The evidence suggests that such use results in measurable and long-lasting cognitive impairments,[16] particularly among those who started to use marijuana in early adolescence. Moreover, failure to learn at school, even for short or sporadic periods (a secondary effect of acute intoxication), will interfere with the subsequent capacity to achieve increasingly challenging educational goals, a finding that may also explain the association between regular marijuana use and poor grades.[29]

The relationship between cannabis use by young people and psychosocial harm is likely to be multifaceted, which may explain the inconsistencies among studies. For example, some studies suggest that long-term deficits may be reversible and remain subtle rather than disabling once a person abstains from use.[30] Other studies show that long-term, heavy use of marijuana results in impairments in memory and attention that persist and worsen with increasing years of regular use[31] and with the initiation of use during adolescence.[32] As noted above, early marijuana use is associated with impaired school performance and an increased risk of dropping out of school,[27,29] although reports of shared environmental factors that influence the risks of using cannabis at a young age and dropping out of school[33] suggest that the relationship may be more complex. Heavy marijuana use has been linked to lower income, greater need for socioeconomic assistance, unemployment, criminal behavior, and lower satisfaction with life.[2,34]

RISK OF MOTOR-VEHICLE ACCIDENTS

Both immediate exposure and long-term exposure to marijuana impair driving ability; marijuana is the illicit drug most frequently reported in connection with impaired driving and accidents, including fatal accidents.[35] There is a relationship between the blood THC concentration

The New England Journal of Medicine
Downloaded from nejm.org by SAM BUTMAN on June 4, 2014. For personal use only. No other uses without permission.
Copyright © 2014 Massachusetts Medical Society. All rights reserved.

and performance in controlled driving-simulation studies,[36] which are a good predictor of real-world driving ability. Recent marijuana smoking and blood THC levels of 2 to 5 ng per milliliter are associated with substantial driving impairment.[37] According to a meta-analysis, the overall risk of involvement in an accident increases by a factor of about 2 when a person drives soon after using marijuana.[37] In an accident culpability analysis, persons testing positive for THC (typical minimum level of detection, 1 ng per milliliter), and particularly those with higher blood levels, were 3 to 7 times as likely to be responsible for a motor-vehicle accident as persons who had not used drugs or alcohol before driving.[38] In comparison, the overall risk of a vehicular accident increases by a factor of almost 5 for drivers with a blood alcohol level above 0.08%, the legal limit in most countries, and increases by a factor of 27 for persons younger than 21 years of age.[39] Not surprisingly, the risk associated with the use of alcohol in combination with marijuana appears to be greater than that associated with the use of either drug alone.[37]

RISK OF CANCER AND OTHER EFFECTS ON HEALTH

The effects of long-term marijuana smoking on the risk of lung cancer are unclear. For example, the use of marijuana for the equivalent of 30 or more joint-years (with 1 joint-year of marijuana use equal to 1 cigarette [joint] of marijuana smoked per day for 1 year) was associated with an increased incidence of lung cancer and several cancers of the upper aerodigestive tract; however, the association disappeared after adjustment for potential confounders such as cigarette smoking.[40] Although the possibility of a positive association between marijuana smoking and cancer cannot be ruled out,[41] the evidence suggests that the risk is lower with marijuana than with tobacco.[40] However, the smoking of cigarettes that contain both marijuana and tobacco products is a potential confounding factor with a prevalence that varies dramatically among countries.

Marijuana smoking is also associated with inflammation of the large airways, increased airway resistance, and lung hyperinflation, associations that are consistent with the fact that regular marijuana smokers are more likely to report symptoms of chronic bronchitis than are nonsmokers[42]; however, the long-term effect of low levels of marijuana exposure does not appear to be significant.[43] The immunologic competence of the respiratory system in marijuana smokers may also be compromised, as indicated by increased rates of respiratory infections and pneumonia.[44] Marijuana use has also been associated with vascular conditions that increase the risks of myocardial infarction, stroke, and transient ischemic attacks during marijuana intoxication.[45] The actual mechanisms underlying the effects of marijuana on the cardiovascular and cerebrovascular systems are complex and not fully understood. However, the direct effects of cannabinoids on various target receptors (i.e., CB1 receptors in arterial blood vessels) and the indirect effects on vasoactive compounds[46] may help explain the detrimental effects of marijuana on vascular resistance and coronary microcirculation.[47]

LIMITATIONS OF THE EVIDENCE AND GAPS IN KNOWLEDGE

Most of the long-term effects of marijuana use that are summarized here have been observed among heavy or long-term users, but multiple (often hidden) confounding factors detract from our ability to establish causality (including the frequent use of marijuana in combination with other drugs). These factors also complicate our ability to assess the true effect of intrauterine exposure to marijuana. Indeed, despite the use of marijuana by pregnant women,[48] and animal models suggesting that cannabis exposure during pregnancy may alter the normal processes and trajectories of brain development,[49] our understanding of the long-term effects of prenatal exposure to marijuana in humans is very poor.

The THC content, or potency, of marijuana, as detected in confiscated samples, has been steadily increasing from about 3% in the 1980s to 12% in 2012[50] (Fig. 1A). This increase in THC content raises concerns that the consequences of marijuana use may be worse now than in the past and may account for the significant increases in emergency department visits by persons reporting marijuana use[51] (Fig. 1B) and the increases in fatal motor-vehicle accidents.[35] This increase in THC potency over time also raises questions about the current relevance of the findings in older studies on the effects of marijuana use, especially studies that assessed long-term outcomes.

The New England Journal of Medicine
Downloaded from nejm.org by SAM BUTMAN on June 4, 2014. For personal use only. No other uses without permission.
Copyright © 2014 Massachusetts Medical Society. All rights reserved.

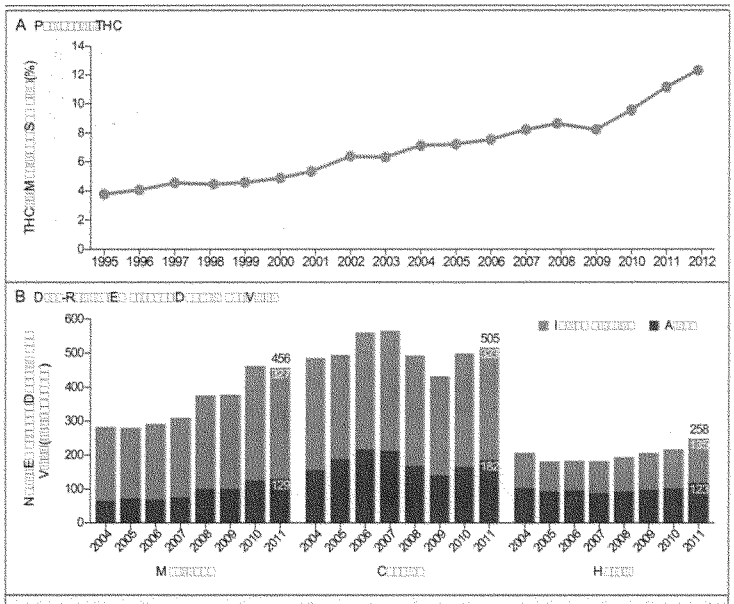


Figure 1. Increases over Time in the Potency of Tetrahydrocannabinol (THC) in Marijuana and the Number of Emergency Department Visits Involving Marijuana, Cocaine, or Heroin.

Panel A shows the increasing potency of marijuana (i.e., the percentage of THC) in samples seized by the Drug Enforcement Administration (DEA) between 1995 and 2012.[50] Panel B provides estimates of the number of emergency department visits involving the use of selected illicit drugs (marijuana, cocaine, and heroin) either singly or in combination with other drugs between 2004 and 2011.[51] Among these three drugs, only marijuana, used either in combination with other drugs or alone, was associated with significant increases in the number of visits during this period (a 62% increase when used in combination with other drugs and a 100% increase when used alone, $P<0.05$ for the two comparisons).

There is also a need to improve our understanding of how to harness the potential medical benefits of the marijuana plant without exposing people who are sick to its intrinsic risks. The authoritative report by the Institute of Medicine, *Marijuana and Medicine*,[52] acknowledges the potential benefits of smoking marijuana in stimulating appetite, particularly in patients with the acquired immunodeficiency syndrome (AIDS) and the related wasting syndrome, and in combating chemotherapy-induced nausea and vomiting, severe pain, and some forms of spasticity. The report also indicates that there is some evidence for the benefit of using marijuana to decrease intraocular pressure in the treatment of glaucoma. Nonetheless, the report stresses the importance of focusing research efforts on the therapeutic potential of synthetic or pharmaceutically pure cannabinoids.[52] Some physicians continue to prescribe marijuana for medicinal purposes despite limited evidence of a benefit (see box). This practice raises particular concerns with regard to long-term use by vulnerable populations. For example, there is some evidence to suggest that in patients with symptoms of human immunodeficiency virus (HIV) infection or AIDS, marijuana use may actually exacerbate HIV-associated cognitive deficits.[75] Simi-

The New England Journal of Medicine
Downloaded from nejm.org by SAM BUTMAN on June 4, 2014. For personal use only. No other uses without permission.
Copyright © 2014 Massachusetts Medical Society. All rights reserved.

Clinical Conditions with Symptoms That May Be Relieved by Treatment with Marijuana or Other Cannabinoids.*

Glaucoma

Early evidence of the benefits of marijuana in patients with glaucoma (a disease associated with increased pressure in the eye) may be consistent with its ability to effect a transient decrease in intraocular pressure,[53,54] but other, standard treatments are currently more effective. THC, cannabinol, and nabilone (a synthetic cannabinoid similar to THC), but not cannabidiol, were shown to lower intraocular pressure in rabbits.[55,56] More research is needed to establish whether molecules that modulate the endocannabinoid system may not only reduce intraocular pressure but also provide a neuroprotective benefit in patients with glaucoma.[57]

Nausea

Treatment of the nausea and vomiting associated with chemotherapy was one of the first medical uses of THC and other cannabinoids.[58] THC is an effective antiemetic agent in patients undergoing chemotherapy,[59] but patients often state that marijuana is more effective in suppressing nausea. Other, unidentified compounds in marijuana may enhance the effect of THC (as appears to be the case with THC and cannabidiol, which operate through different antiemetic mechanisms).[60] Paradoxically, increased vomiting (hyperemesis) has been reported with repeated marijuana use.

AIDS-associated anorexia and wasting syndrome

Reports have indicated that smoked or ingested cannabis improves appetite and leads to weight gain and improved mood and quality of life among patients with AIDS.[61] However, there is no long-term or rigorous evidence of a sustained effect of cannabis on AIDS-related morbidity and mortality, with an acceptable safety profile, that would justify its incorporation into current clinical practice for patients who are receiving effective antiretroviral therapy.[62] Data from the few studies that have explored the potential therapeutic value of cannabinoids for this patient population are inconclusive.[62]

Chronic pain

Marijuana has been used to relieve pain for centuries. Studies have shown that cannabinoids acting through central CB1 receptors, and possibly peripheral CB1 and CB2 receptors,[63] play important roles in modeling nociceptive responses in various models of pain. These findings are consistent with reports that marijuana may be effective in ameliorating neuropathic pain,[64,65] even at very low levels of THC (1.29%).[66] Both marijuana and dronabinol, a pharmaceutical formulation of THC, decrease pain, but dronabinol may lead to longer-lasting reductions in pain sensitivity and lower ratings of rewarding effects.[67]

Inflammation

Cannabinoids (e.g., THC and cannabidiol) have substantial antiinflammatory effects because of their ability to induce apoptosis, inhibit cell proliferation, and suppress cytokine production.[68] Cannabidiol has attracted particular interest as an antiinflammatory agent because of its lack of psychoactive effects.[58] Animal models have shown that cannabidiol is a promising candidate for the treatment of rheumatoid arthritis[58] and for inflammatory diseases of the gastrointestinal tract (e.g., ulcerative colitis and Crohn's disease).[69]

Multiple sclerosis

Nabiximols (Sativex, GW Pharmaceuticals), an oromucosal spray that delivers a mix of THC and cannabidiol, appears to be an effective treatment for neuropathic pain, disturbed sleep, and spasticity in patients with multiple sclerosis. Sativex is available in the United Kingdom, Canada, and several other countries[70,71] and is currently being reviewed in phase 3 trials in the United States in order to gain approval from the Food and Drug Administration.

Epilepsy

In a recent small survey of parents who use marijuana with a high cannabidiol content to treat epileptic seizures in their children,[72] 11% (2 families out of the 19 that met the inclusion criteria) reported complete freedom from seizures, 42% (8 families) reported a reduction of more than 80% in seizure frequency, and 32% (6 families) reported a reduction of 25 to 60% in seizure frequency. Although such reports are promising, insufficient safety and efficacy data are available on the use of cannabis botanicals for the treatment of epilepsy.[73] However, there is increasing evidence of the role of cannabidiol as an antiepileptic agent in animal models.[74]

* AIDS denotes acquired immunodeficiency syndrome, CB1 cannabinoid-1 receptor, and CB2 cannabinoid-2 receptor, HIV human immunodeficiency virus, and THC tetrahydrocannabinol.

larly, more research is needed to understand the potential effects of marijuana use on age-related cognitive decline in general and on memory impairment in particular.

Research is needed on the ways in which government policies on marijuana affect public health outcomes. Our understanding of the effects of policy on market forces is quite limited (e.g., the allure of new tax-revenue streams from the legal sale of marijuana, pricing wars, youth-targeted advertising, and the emergence of cannabis-based medicines approved by the Food and Drug Administration), as is our understanding of the interrelated variables of perceptions about

The New England Journal of Medicine
Downloaded from nejm.org by SAM BUTMAN on June 4, 2014. For personal use only. No other uses without permission.
Copyright © 2014 Massachusetts Medical Society. All rights reserved.

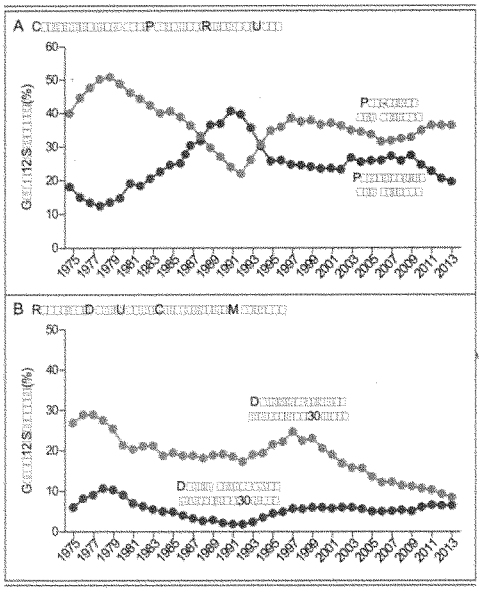


Figure 2. Use of Marijuana in Relation to Perceived Risk and Daily Use of Tobacco Cigarettes or Marijuana among U.S. Students in Grade 12, 1975–2013.

Panel A shows the inverse correlation between the perception of the risk associated with marijuana use and actual use. Perceived risk corresponds to the percentage of teenagers who reported that the use of marijuana is dangerous. Panel B shows the percentage of students who reported daily use of tobacco cigarettes or marijuana in the previous 30 days. Data for both graphs are from Johnston et al.[26]

use, types of use, and outcomes. Historically, there has been an inverse correlation between marijuana use and the perception of its risks among adolescents (Fig. 2A). Assuming that this inverse relationship is causal, would greater permissiveness in culture and social policy lead to an increase in the number of young people who are exposed to cannabis on a regular basis? Among students in grade 12, the reported prevalence of regular marijuana smoking has been steadily increasing in recent years and may soon intersect the trend line for regular tobacco smoking (Fig. 2B). We also need information about the effects of second-hand exposure to cannabis smoke and cannabinoids. Second-hand exposure is an important public health issue in the context of tobacco smoking, but we do not have a clear understanding of the effects of second-hand exposure to marijuana smoking.[76] Studies in states (e.g., Colorado, California, and Washington) and countries (e.g., Uruguay, Portugal, and the Netherlands) where social and legal policies are shifting may provide important data for shaping future policies.

CONCLUSIONS

Marijuana use has been associated with substantial adverse effects, some of which have been determined with a high level of confidence (Table 2). Marijuana, like other drugs of abuse, can result in addiction. During intoxication, marijuana can interfere with cognitive function (e.g., memory and perception of time) and motor function (e.g., coordination), and these effects can have detrimental consequences (e.g., motor-vehicle accidents). Repeated marijuana use during adolescence may result in long-lasting changes in brain function that can jeopardize educational, professional, and social achievements. However, the effects of a drug (legal or illegal) on individual health are determined not only by its pharmacologic properties but also by its availability and social acceptability. In this respect, legal drugs

Table 2. Level of Confidence in the Evidence for Adverse Effects of Marijuana on Health and Well-Being.

Effect	Overall Level of Confidence*
Addiction to marijuana and other substances	High
Abnormal brain development	Medium
Progression to use of other drugs	Medium
Schizophrenia	Medium
Depression or anxiety	Medium
Diminished lifetime achievement	High
Motor vehicle accidents	High
Symptoms of chronic bronchitis	High
Lung cancer	Low

* The indicated overall level of confidence in the association between marijuana use and the listed effects represents an attempt to rank the strength of the current evidence, especially with regard to heavy or long-term use and use that starts in adolescence.

The New England Journal of Medicine
Downloaded from nejm.org by SAM BUTMAN on June 4, 2014. For personal use only. No other uses without permission.
Copyright © 2014 Massachusetts Medical Society. All rights reserved.

(alcohol and tobacco) offer a sobering perspective, accounting for the greatest burden of disease associated with drugs[77] not because they are more dangerous than illegal drugs but because their legal status allows for more widespread exposure. As policy shifts toward legalization of marijuana, it is reasonable and probably prudent to hypothesize that its use will increase and that, by extension, so will the number of persons for whom there will be negative health consequences.

No potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

REFERENCES

1. Center for Behavioral Health Statistics and Quality. National survey on drug use and health. Rockville, MD: Substance Abuse & Mental Health Services Administration, 2013.
2. Fergusson DM, Boden JM. Cannabis use and later life outcomes. Addiction 2008;103:969-76.
3. Lopez-Quintero C, Pérez de los Cobos J, Hasin DS, et al. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Drug Alcohol Depend 2011;115:120-30.
4. Hall W, Degenhardt L. Adverse health effects of non-medical cannabis use. Lancet 2009;374:1383-91.
5. Gorelick DA, Levin KH, Copersino ML, et al. Diagnostic criteria for cannabis withdrawal syndrome. Drug Alcohol Depend 2012;123:141-7.
6. Mechoulam R, Parker LA. The endocannabinoid system and the brain. Annu Rev Psychol 2013;64:21-47.
7. Hall W, Degenhardt L. Prevalence and correlates of cannabis use in developed and developing countries. Curr Opin Psychiatry 2007;20:393-7.
8. Chen CY, Storr CL, Anthony JC. Early-onset drug use and risk for drug dependence problems. Addict Behav 2009;34:319-22.
9. Gogtay N, Giedd JN, Lusk L, et al. Dynamic mapping of human cortical development during childhood through early adulthood. Proc Natl Acad Sci U S A 2004;101:8174-9.
10. Dinieri JA, Hurd YL. Rat models of prenatal and adolescent cannabis exposure. Methods Mol Biol 2012;829:231-42.
11. Tortoriello G, Morris CV, Alpar A, et al. Miswiring the brain: Δ9-tetrahydrocannabinol disrupts cortical development by inducing an SCG10/stathmin-2 degradation pathway. EMBO J 2014;33:668-85.
12. Zalesky A, Solowij N, Yücel M, et al. Effect of long-term cannabis use on axonal fibre connectivity. Brain 2012;135:2245-55.
13. Filbey F, Yezhuvath U. Functional connectivity in inhibitory control networks and severity of cannabis use disorder. Am J Drug Alcohol Abuse 2013;39:382-91.
14. Batalla A, Bhattacharyya S, Yücel M, et al. Structural and functional imaging studies in chronic cannabis users: a systematic review of adolescent and adult findings. PLoS One 2013;8(2):e55821.
15. Hirvonen J, Goodwin RS, Li C-T, et al. Reversible and regionally selective downregulation of brain cannabinoid CB1 receptors in chronic daily cannabis smokers. Mol Psychiatry 2012;17:642-9.
16. Meier MH, Caspi A, Ambler A, et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc Natl Acad Sci U S A 2012;109(40):E2657-E2564.
17. Gaffuri AL, Ladarre D, Lenkei Z. Type-1 cannabinoid receptor signaling in neuronal development. Pharmacology 2012;90:19-39.
18. Pistis M, Perra S, Pillolla G, Melis M, Muntoni AL, Gessa GL. Adolescent exposure to cannabinoids induces long-lasting changes in the response to drugs of abuse of rat midbrain dopamine neurons. Biol Psychiatry 2004;56:86-94.
19. DiNieri JA, Wang X, Szutorisz H, et al. Maternal cannabis use alters ventral striatal dopamine D2 gene regulation in the offspring. Biol Psychiatry 2011;70:763-9.
20. Agrawal A, Neale MC, Prescott CA, Kendler KS. A twin study of early cannabis use and subsequent use and abuse/dependence of other illicit drugs. Psychol Med 2004;34:1227-37.
21. Panlilio LV, Zanettini C, Barnes C, Solinas M, Goldberg SR. Prior exposure to THC increases the addictive effects of nicotine in rats. Neuropsychopharmacology 2013;38:1198-208.
22. Levine A, Huang Y, Drisaldi B, et al. Molecular mechanism for a gateway drug: epigenetic changes initiated by nicotine prime gene expression by cocaine. Sci Transl Med 2011;3:107ra109.
23. Patton GC, Coffey C, Carlin JB, Degenhardt L, Lynskey M, Hall W. Cannabis use and mental health in young people: cohort study. BMJ 2002;325:1195-8.
24. Caspi A, Moffitt TE, Cannon M, et al. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: longitudinal evidence of a gene X environment interaction. Biol Psychiatry 2005;57:1117-27.
25. Di Forti M, Sallis H, Allegri F, et al. Daily use, especially of high-potency cannabis, drives the earlier onset of psychosis in cannabis users. Schizophr Bull 2014 March 19 (Epub ahead of print).
26. Johnston LD, O'Malley PM, Miech RA, et al. Monitoring the Future: national survey results on drug use, 1975-2013 — overview, key findings on adolescent drug use. Ann Arbor: Institute for Social Research, University of Michigan, 2014 (http://monitoringthefuture.org/pubs/monographs/mtf-overview2013.pdf).
27. Bray JW, Zarkin GA, Ringwalt C, Qi J. The relationship between marijuana initiation and dropping out of high school. Health Econ 2000;9:9-18.
28. Crean RD, Crane NA, Mason BJ. An evidence based review of acute and long-term effects of cannabis use on executive cognitive functions. J Addict Med 2011;5:1-8.
29. Lynskey M, Hall W. The effects of adolescent cannabis use on educational attainment: a review. Addiction 2000;95:1621-30.
30. Macleod J, Oakes R, Copello A, et al. Psychological and social sequelae of cannabis and other illicit drug use by young people: a systematic review of longitudinal, general population studies. Lancet 2004;363:1579-88.
31. Solowij N, Stephens RS, Roffman RA, et al. Cognitive functioning of long-term heavy cannabis users seeking treatment. JAMA 2002;287:1123-31. [Erratum, JAMA 2002;287:1651.]
32. Schweinsburg AD, Brown SA, Tapert SF. The influence of marijuana use on neurocognitive functioning in adolescents. Curr Drug Abuse Rev 2008;1:99-111.
33. Verweij KJ, Huizink AC, Agrawal A, Martin NG, Lynskey MT. Is the relationship between early-onset cannabis use and educational attainment causal or due to common liability? Drug Alcohol Depend 2013;133:580-6.
34. Brook JS, Lee JY, Finch SJ, Seltzer N, Brook DW. Adult work commitment, financial stability, and social environment as related to trajectories of marijuana use beginning in adolescence. Subst Abus 2013;34:298-305.
35. Brady JE, Li G. Trends in alcohol and other drugs detected in fatally injured drivers in the United States, 1999-2010. Am J Epidemiol 2014;179:692-9.
36. Lenné MG, Dietze PM, Triggs TJ,

The New England Journal of Medicine
Downloaded from nejm.org by SAM BUTMAN on June 4, 2014. For personal use only. No other uses without permission.
Copyright © 2014 Massachusetts Medical Society. All rights reserved.

Walmsley S, Murphy B, Redman JR. The effects of cannabis and alcohol on simulated arterial driving: influences of driving experience and task demand. Accid Anal Prev 2010;42:859-66.
37. Hartman RL, Huestis MA. Cannabis effects on driving skills. Clin Chem 2013; 59:478-92.
38. Ramaekers JG, Berghaus G, van Laar M, Drummer OH. Dose related risk of motor vehicle crashes after cannabis use. Drug Alcohol Depend 2004;73:109-19.
39. Peck RC, Gebers MA, Voas RB, Romano E. The relationship between blood alcohol concentration (BAC), age, and crash risk. J Safety Res 2008;39:311-9.
40. Hashibe M, Morgenstern H, Cui Y, et al. Marijuana use and the risk of lung and upper aerodigestive tract cancers: results of a population-based case-control study. Cancer Epidemiol Biomarkers Prev 2006; 15:1829-34.
41. Callaghan RC, Allebeck P, Sidorchuk A. Marijuana use and risk of lung cancer: a 40-year cohort study. Cancer Causes Control 2013;24:1811-20.
42. Tashkin DP. Effects of marijuana smoking on the lung. Ann Am Thorac Soc 2013;10:239-47.
43. Pletcher MJ, Vittinghoff E, Kalhan R, et al. Association between marijuana exposure and pulmonary function over 20 years. JAMA 2012;307:173-81.
44. Owen KP, Sutter ME, Albertson TE. Marijuana: respiratory tract effects. Clin Rev Allergy Immunol 2014;46:65-81.
45. Thomas G, Kloner RA, Rezkalla S. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana inhalation: what cardiologists need to know. Am J Cardiol 2014;113:187-90.
46. Stanley C, O'Sullivan SE. Vascular targets for cannabinoids: animal and human studies. Br J Pharmacol 2014;171:1361-78.
47. Rezkalla SH, Sharma P, Kloner RA. Coronary no-flow and ventricular tachycardia associated with habitual marijuana use. Ann Emerg Med 2003;42:365-9.
48. Brown HL, Graves CR. Smoking and marijuana use in pregnancy. Clin Obstet Gynecol 2013;56:107-13.
49. Jutras-Aswad D, DiNieri JA, Harkany T, Hurd YL. Neurobiological consequences of maternal cannabis on human fetal development and its neuropsychiatric outcome. Eur Arch Psychiatry Clin Neurosci 2009;259:395-412.
50. ElSohly MA. Potency Monitoring Program quarterly report no.123 — reporting period: 09/16/2013-12/15/2013. Oxford: University of Mississippi, National Center for Natural Products Research, 2014.
51. Drug Abuse Warning Network, 2011: national estimates of drug-related emergency department visits. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2011 (http://www.samhsa.gov/data/2k13/DAWN2k11ED/DAWN2k11ED.htm).
52. Joy JE, Watson SJ Jr, Benson JA Jr, eds. Marijuana and medicine: assessing the science base. Washington, DC: National Academy Press, 1999.
53. Merritt JC, Crawford WJ, Alexander PC, Anduze AL, Gelbart SS. Effect of marihuana on intraocular and blood pressure in glaucoma. Ophthalmology 1980;87:222-8.
54. Hepler RS, Frank IR. Marihuana smoking and intraocular pressure. JAMA 1971;217:1392.
55. Chen J, Matias I, Dinh T, et al. Finding of endocannabinoids in human eye tissues: implications for glaucoma. Biochem Biophys Res Commun 2005;330:1062-7.
56. Song ZH, Slowey CA. Involvement of cannabinoid receptors in the intraocular pressure-lowering effects of WIN55212-2. J Pharmacol Exp Ther 2000;292:136-9.
57. Nucci C, Bari M, Spanò A, et al. Potential roles of (endo) cannabinoids in the treatment of glaucoma: from intraocular pressure control to neuroprotection. Prog Brain Res 2008;173:451-64.
58. Zuardi AW. Cannabidiol: from an inactive cannabinoid to a drug with wide spectrum of action. Rev Bras Psiquiatr 2008;30:271-80.
59. Sallan SE, Zinberg NE, Frei E III. Antiemetic effect of delta-9-tetrahydrocannabinol in patients receiving cancer chemotherapy. N Engl J Med 1975;293:795-7.
60. Parker LA, Kwiatkowska M, Burton P, Mechoulam R. Effect of cannabinoids on lithium-induced vomiting in the Suncus murinus (house musk shrew). Psychopharmacology (Berl) 2004;171:156-61.
61. D'Souza G, Matson PA, Grady CD, et al. Medicinal and recreational marijuana use among HIV-infected women in the Women's Interagency HIV Study (WIHS) cohort, 1994-2010. J Acquir Immune Defic Syndr 2012;61:618-26.
62. Lutge EE, Gray A, Siegfried N. The medical use of cannabis for reducing morbidity and mortality in patients with HIV/AIDS. Cochrane Database Syst Rev 2013;4:CD005175.
63. Chiou LC, Hu SS, Ho YC. Targeting the cannabinoid system for pain relief? Acta Anaesthesiol Taiwan 2013;51:161-70.
64. Wilsey B, Marcotte T, Tsodikov A, et al. A randomized, placebo-controlled, crossover trial of cannabis cigarettes in neuropathic pain. J Pain 2008;9:506-21.
65. Wallace M, Schulteis G, Atkinson JH, et al. Dose-dependent effects of smoked cannabis on capsaicin-induced pain and hyperalgesia in healthy volunteers. Anesthesiology 2007;107:785-96.
66. Wilsey B, Marcotte T, Deutsch R, Gouaux B, Sakai S, Donaghe H. Low-dose vaporized cannabis significantly improves neuropathic pain. J Pain 2013;14:136-48.
67. Cooper ZD, Comer SD, Haney M. Comparison of the analgesic effects of dronabinol and smoked marijuana in daily marijuana smokers. Neuropsychopharmacology 2013;38:1984-92.
68. Nagarkatti P, Pandey R, Rieder SA, Hegde VL, Nagarkatti M. Cannabinoids as novel anti-inflammatory drugs. Future Med Chem 2009;1:1333-49.
69. Esposito G, Filippis DD, Cirillo C, et al. Cannabidiol in inflammatory bowel diseases: a brief overview. Phytother Res 2013;5:633-6.
70. Collin C, Davies P, Mutiboko IK, Ratcliffe S. Randomized controlled trial of cannabis-based medicine in spasticity caused by multiple sclerosis. Eur J 2007; 14:290-6.
71. Centonze D, Mori F, Koch G, et al. Lack of effect of cannabis-based treatment on clinical and laboratory measures in multiple sclerosis. Neurol Sci 2009;30:531-4.
72. Porter BE, Jacobson C. Report of a parent survey of cannabidiol-enriched cannabis use in pediatric treatment-resistant epilepsy. Epilepsy Behav 2013;29:574-7.
73. Kogan NM, Mechoulam R. Cannabinoids in health and disease. Dialogues Clin Neurosci 2007;9:413-30.
74. Hill TD, Cascio MG, Romano B, et al. Cannabidivarin-rich cannabis extracts are anticonvulsant in mouse and rat via a CB1 receptor-independent mechanism. Br J Pharmacol 2013;170:679-92.
75. Cristiani SA, Pukay-Martin ND, Bornstein RA. Marijuana use and cognitive function in HIV-infected people. J Neuropsychiatry Clin Neurosci 2004;16:330-5.
76. Niedbala S, Kardos K, Salamone S, Fritch D, Bronsgeest M, Cone EJ. Passive cannabis smoke exposure and oral fluid testing. J Anal Toxicol 2004;28:546-52.
77. Degenhardt L, Hall W. Extent of illicit drug use and dependence, and their contribution to the global burden of disease. Lancet 2012;379:55-70.
Copyright © 2014 Massachusetts Medical Society.

IMAGES IN CLINICAL MEDICINE

The *Journal* welcomes consideration of new submissions for Images in Clinical Medicine. Instructions for authors and procedures for submissions can be found on the *Journal*'s website at NEJM.org. At the discretion of the editor, images that are accepted for publication may appear in the print version of the *Journal*, the electronic version, or both.

The New England Journal of Medicine
Downloaded from nejm.org by SAM BUTMAN on June 4, 2014. For personal use only. No other uses without permission.
Copyright © 2014 Massachusetts Medical Society. All rights reserved.

CNN Health

Why I changed my mind on weed

By **Dr. Sanjay Gupta,** CNN Chief Medical Correspondent
Updated 8:44 PM EDT, Thu August 8, 2013

Over the last year, I have been working on a new documentary called "Weed." The title "Weed" may sound cavalier, but the content is not.

I traveled around the world to interview medical leaders, experts, growers and patients. I spoke candidly to them, asking tough questions. What I found was stunning.

Long before I began this project, I had steadily reviewed the scientific literature on medical marijuana from the United States and thought it was fairly unimpressive. Reading these papers five years ago, it was hard to make a case for medicinal marijuana. I even wrote about this in a TIME magazine article, back in 2009, titled "Why I would Vote No on Pot."

Well, I am here to apologize.

I apologize because I didn't look hard enough, until now. I didn't look far enough. I didn't review papers from smaller labs in other countries doing some remarkable research, and I was too dismissive of the loud chorus of legitimate patients whose symptoms improved on cannabis.

Instead, I lumped them with the high-visibility malingerers, just looking to get high. I mistakenly believed the Drug Enforcement Agency listed marijuana as a schedule 1 substance because of sound scientific proof. Surely, they must have quality reasoning as to why marijuana is in the category of the most dangerous drugs that have "no accepted medicinal use and a high potential for abuse."

They didn't have the science to support that claim, and I now know that when it comes to marijuana neither of those things are true. It doesn't have a high potential for abuse, and there are very legitimate medical applications. In fact, sometimes marijuana is the only thing that works. Take the case of Charlotte Figi, who I met in Colorado. She started having seizures soon after birth. By age 3, she was having 300 a week, despite being on seven different medications. Medical marijuana has calmed her brain, limiting her seizures to 2 or 3 per month.

I have seen more patients like Charlotte first hand, spent time with them and come to the realization that it is irresponsible not to provide the best care we can as a medical community, care that could involve marijuana.

We have been terribly and systematically misled for nearly 70 years in the United States, and I apologize for my own role in that.

I hope this article and upcoming documentary will help set the record straight.

On August 14, 1970, the Assistant Secretary of Health, Dr. Roger O. Egeberg wrote a letter recommending the plant, marijuana, be classified as a schedule 1 substance, and it has remained that way for nearly 45 years. My research started with a careful reading of that decades old letter. What I found was unsettling. Egeberg had carefully chosen his words:

"Since there is still a considerable void in our knowledge of the plant and effects of the active drug contained in it, our recommendation is that marijuana be retained within schedule 1 at least until the completion of certain studies now underway to resolve the issue."

Not because of sound science, but because of its absence, marijuana was classified as a schedule 1 substance. Again, the year was 1970. Egeberg mentions studies that are underway, but many were never completed. As my investigation continued, however, I realized Egeberg did in fact have important research already available to him, some of it from more than 25 years earlier.

High risk of abuse

In 1944, New York Mayor Fiorello LaGuardia commissioned research to be performed by the New York Academy of Science. Among their conclusions: they found marijuana did not lead to significant addiction in the medical sense of the word. They also did not find any evidence marijuana led to morphine, heroin or cocaine addiction.

We now know that while estimates vary, marijuana leads to dependence in around 9 to 10% of its adult users. By comparison, cocaine, a schedule 2 substance "with less abuse potential than schedule 1 drugs" hooks 20% of those who use it. Around 25% of heroin users become addicted.

The worst is tobacco, where the number is closer to 30% of smokers, many of whom go on to die because of their addiction.

There is clear evidence that in some people marijuana use can lead to withdrawal symptoms, including insomnia, anxiety and nausea. Even considering this, it is hard to make a case that it has a high potential for abuse. The physical symptoms of marijuana addiction are nothing like those of the other drugs I've mentioned. I have seen the withdrawal from alcohol, and it can be life threatening.

I do want to mention a concern that I think about as a father. Young, developing brains are likely more susceptible to harm from marijuana than adult brains. Some recent studies suggest that regular use in teenage years leads to a permanent decrease in IQ. Other research hints at a possible heightened risk of developing psychosis.

Much in the same way I wouldn't let my own children drink alcohol, I wouldn't permit marijuana until they are adults. If they are adamant about trying marijuana, I will urge them to wait until they're in their mid-20s when their brains are fully developed.

Medical benefit

While investigating, I realized something else quite important. Medical marijuana is not new, and the medical community has been writing about it for a long time. There were in fact hundreds of journal articles, mostly documenting the benefits. Most of those papers, however, were written between the years 1840 and 1930. The papers described the use of medical marijuana to treat "neuralgia, convulsive disorders, emaciation," among other things.

A search through the U.S. National Library of Medicine this past year pulled up nearly 2,000 more recent papers. But the majority were research into the harm of marijuana, such as "Bad trip due to anticholinergic effect of cannabis," or "Cannabis induced pancreatitits" and "Marijuana use and risk of lung cancer."

In my quick running of the numbers, I calculated about 6% of the current U.S. marijuana studies investigate the benefits of medical marijuana. The rest are designed to investigate harm. That imbalance paints a highly distorted picture.

The challenges of marijuana research

To do studies on marijuana in the United States today, you need two important things.

First of all, you need marijuana. And marijuana is illegal. You see the problem. Scientists can get research marijuana from a special farm in Mississippi, which is astonishingly located in the middle of the Ole Miss campus, but it is challenging. When I visited this year, there was no marijuana being grown.

The second thing you need is approval, and the scientists I interviewed kept reminding me how tedious that can be. While a cancer study may first be evaluated by the National Cancer Institute, or a pain study may go through the National Institute for Neurological Disorders, there is one more approval required for marijuana: NIDA, the National Institute on Drug Abuse. It is an organization that has a core mission of studying drug abuse, as opposed to benefit.

Stuck in the middle are the legitimate patients who depend on marijuana as a medicine, oftentimes as their only good option.

Keep in mind that up until 1943, marijuana was part of the United States drug pharmacopeia. One of the conditions for which it was prescribed was neuropathic pain. It is a miserable pain that's tough to treat. My own patients have described it as "lancinating, burning and a barrage of pins and needles." While marijuana has long been documented to be effective for this awful pain,

the most common medications prescribed today come from the poppy plant, including morphine, oxycodone and dilaudid.

Here is the problem. Most of these medications don't work very well for this kind of pain, and tolerance is a real problem.

Most frightening to me is that someone dies in the United States every 19 minutes from a prescription drug overdose, mostly accidental. Every 19 minutes. It is a horrifying statistic. As much as I searched, I could not find a documented case of death from marijuana overdose.

It is perhaps no surprise then that 76% of physicians recently surveyed said they would approve the use of marijuana to help ease a woman's pain from breast cancer.

When marijuana became a schedule 1 substance, there was a request to fill a "void in our knowledge." In the United States, that has been challenging because of the infrastructure surrounding the study of an illegal substance, with a drug abuse organization at the heart of the approval process. And yet, despite the hurdles, we have made considerable progress that continues today.

Looking forward, I am especially intrigued by studies like those in Spain and Israel looking at the anti-cancer effects of marijuana and its components. I'm intrigued by the neuro-protective study by Raphael Meschoulam in Israel, and research in Israel and the United States on whether the drug might help alleviate symptoms of PTSD. I promise to do my part to help, genuinely and honestly, fill the remaining void in our knowledge.

Citizens in 20 states and the District of Columbia have now voted to approve marijuana for medical applications, and more states will be making that choice soon. As for Dr. Roger Egeberg, who wrote that letter in 1970, he passed away 16 years ago.

I wonder what he would think if he were alive today.

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

Today we bring you these letters, which represent the smallest fraction of the children suffering while marijuana remains a Schedule I substance. In these letters, you will find bravery, resilience, and strength. You will also see parents who mourn. We mourn the loss of our children's good years. We mourn the smiles, the first words, the first steps, taken away by seizures and seizure medications.

Throughout these letters, there is a common thread of hope. That hope is medical marijuana. We desperately need marijuana to be rescheduled to Schedule III or lower to allow for more research so that children like ours can have access.

Over three million Americans suffer from epilepsy. Of those, over one million have seizures that are not adequately controlled by the medications, diets, and surgeries available in the United States today. Over one million Americans are suffering.

Because of marijuana's status as a Schedule I drug, patients using medical marijuana, even legally, are being kicked out of hospitals, refused treatment by their physicians, and/or forced to discontinue this valuable, life-saving treatment due to a lack of clarity from the Department of Justice. Whole-plant research is stymied, despite very clear anecdotal evidence that it is saving lives and improving lives throughout the country. People are finding themselves forced to leave their homes in one state – families in some cases are being torn apart – so that a patient can become a medical refugee who cannot go home and cannot cross a state line with his or her medication. Some parents have chosen through these circumstances to become criminals to save their children and chance losing the same children they've risked everything to save.

Meet with us, please, to discuss the issue. We've researched it extensively, and we are happy to share our knowledge with you.

We are running out of time. We never had much to begin with. Please, Mr. Holder – don't delay. Our children are depending on you.

With great hope,

Anonymous	Lisa Glass	Nicole Mattison	Melissa Rhoden
Rachel Ablondi	Gwen Hartley	Penn Mattison	Travis Rhoden
Cady Coe	Lauren Hoehn	Susan Meehan	Riccardo Rivera
Elizabeth Collins	Joan Jones	Dr. Tom Minahan	Sarah Robinson
Patrick Collins	Wrayanne Leslie	Shannon Moore	Lisa Smith
William Davis	Lisa Leyden	Courtney Moser	Jennie Stormes
Suzanne De Gregorio	Dara Lightle	Michele Pulaski	Adrianne Woods
Teresa Elder	Marisa Kiser	Gail Rand	

And the untold thousands of parents of children across the United States who suffer every day, every hour, every minute.

The Honorable Eric Holder

Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

I'm writing to you anonymously, because I am a criminal in order to save my daughter's life.

I must protect myself and my beautiful child, who is now six years old.

She requires full time care. She cannot nor ever will be able to take care of herself. She began to have seizures when she was six months old. Seizures are debilitating. Once she had a status epilepticus seizure that, combined with an overdose of diazepam, sent her into a coma that had her in PICU for six weeks. She almost did not survive.

We have tried Phenobarbital, Clonazepam, Valproic Acid, Trileptal, Prednisone, Sabril, and Keppra. Nothing worked. Because of Trileptal, she landed in the hospital with her sodium levels drastically low as a result of a side effect of the drug. When she was on all these drugs she was in a different world – not present, not looking us in the eye.

Since January 2, 2014, we have been using Cannabidiol oil, and it has reduced her seizures by 85%. We have weaned her off of Valproic Acid and are beginning to wean her off Keppra with the blessing of our Neurologist, who tells us "whatever you are doing, keep doing it."

We have our kid back. She smiles, follows books, she is active and moving her arms and legs more than ever. She is a different child since beginning the oil. Why in the world would we want to continue to give her poisonous drugs that cause many complications and problems to her health? It is miraculous what the oil has done for our daughter, and her neurologist can hardly believe the change they see in her.

PLEASE FREE THE PLANT. It is vital to our society and to the health of our children that this plant be free to investigate and research further.

Sincerely,

Anonymous

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

Andrew, our first son was born full term, but after a very long delivery in July of 1999. We were first-time parents and were thrilled to meet our son and get started with this special time in our lives. I was breastfeeding Andrew on his second day of life, when things changed. He was having trouble, and right there in front of me he turned blue. Andrew was rushed to the NICU. I will never forget following the nurse there and her shutting the window curtain closed so that we could not see them admit Andrew to the NICU.

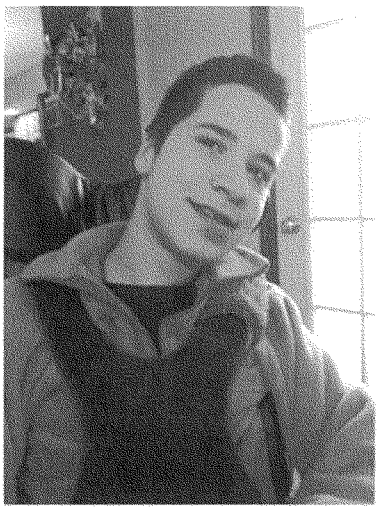
The doctors called my husband and me in our hospital room within in an hour to ask if they could perform a spinal tap on Andrew. Suddenly our lives turned upside down. Andrew, our perfect newborn baby boy, was in distress.

Turns out Andrew's brain bled in several areas. After a 14-day NICU stay, Andrew was sent home with us. We were not told much then, and over the years an answer as to why Andrew's brain bled has yet to be found. Andrew smiled and rolled over on time, meeting those milestones as he should, but that would be the last developmental milestone he would meet. Andrew's first year of life was filled with countless doctor's appointments, therapy appointments and home visits from county developmental specialists. Just as we were acclimating ourselves to caring for Andrew and celebrating the happy occasion of Andrew's first birthday, this day instead brought an unexpected and dreadful event: a cluster seizure. Andrew's tiny body twitched forward in a frightening rhythm repeatedly for twenty minutes. His eyes were dazed.

Andrew was diagnosed with a severe form of epilepsy, Infantile Spasms, and his journey of fighting epilepsy had begun. Our beautiful, one-year-old baby had a devastating diagnosis – and we were told that this would lead to "severe and profound mental retardation".

Andrew seizes in cluster patterns. He seizes hundreds of times of day with quick jerking movements. He has and does seize so hard shaking his arms and legs and gasping for air so many times now that we often wonder how his body can survive this. Andrew seizes thousands of times every single day.

Over the years we have been across the country, even to Canada to provide the best possible treatment for Andrew. We have tried alternative diets, supplements, therapies, and at least fifteen anti-seizure medications. Nothing has worked.



Medicine side effects have included vomiting, weight gain, weight loss, swallowing issues, weak immune system, fatigue, drowsiness, sleepless nights, irritability and so much more. Andrew is currently at the developmental level of a six-month-old (chronological age is 15 years) with a diagnosis of Lennox-Gastaut Syndrome and several other disabilities. His daily seizures interfere with every part of his life, and our family life.

He takes three anti-seizure medicines three times a day. We are at a stage in our lives where we have to accept Andrew taking all of this harsh medication and still seizing daily. We feel we have tried it all. We are desperate.

We are excited and intrigued to find out if medical marijuana will help Andrew. We've seen results in kids like Andrew. We have been through so much as parents, but obviously our precious son is suffering as no one should. Just like any other parent out there our job is to care for our child and provide any treatment which will in turn give our son the quality of life he deserves.

Thank you.

Sincerely,

Rachel Ablondi
Maryland

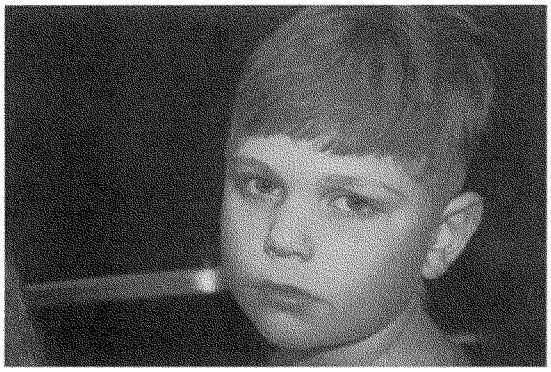
The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

My name is Cady Coe and my son Charlie has a form of Epilepsy called Doose Syndrome. Charlie was born in 2005, a typical little bundle of joy. He progressed normally until one day, at almost 4 years old, his life changed forever with a simple head jerk and eye roll. We rushed him to his doctor and thus began a 3-year odyssey of trying numerous medications and undergoing countless tests. Finally it was determined that the seizures that Charlie suffered from daily were linked to Doose Syndrome.



Today at age 9 Charlie functions as a 3-year-old, as his brain is besieged with over one hundred seizures every day. Some of his seizures cause him to suddenly drop to the floor and shake uncontrollably; some cause him to stare off into space for minutes at a time, unable to communicate. Other seizures cause his arms and legs to fly wildly around and for him to lose control of his balance and bowels. Then there are the "quiet seizures" that come in clusters of head bobs and eye rolls. The seizures have no regard for time of day, activity, holiday or event. They happen anywhere, all day even during sleep. And because of this a happy playground or a simple set of stairs become dangerous places for Charlie.

Charlie has seen doctors at DC Children's Hospital, the Medical College of VA, the Cleveland Clinic, Johns Hopkins, and at UVA Medical Center in Charlottesville, VA. He has had countless tests run and has tried 17 different pharmaceuticals, as well as many combinations of these drugs. He has been on the highest version of the Ketogenic diet and currently lives on a modified version of the Atkins diet. After 6 years, NOTHING HAS WORKED. Charlie has not had a seizure free day in 6 long years. His doctors now say that the only options left for him are implanting medical devices or undergoing a brain surgery that disconnects the hemispheres of the brain. Neither are shown to be successful in Doose kids, but we are out of options.

Each drug that Charlie has tried comes with ENORMOUS side effects. Some cause his body to be unable to regulate his temperature making him unable to sweat. Some cause double vision, sensitivity to light

and sound, or loss of appetite. Almost all come with severe behavioral side effects, and some drugs caused him to be so "out of it" that all he could do was stare off into space and drool. Twice, drugs have caused him to have life threatening rashes and hives. We have tried all of the drugs made available to him. He has endured all of the side effects. And still the seizure count grows.

So now our family is faced with another difficult decision. In order to save our son, we are going to have to uproot all of our children, and move to Colorado to try Medical Cannabis. Our family will endure the stress and financial costs of selling our home in VA, moving ourselves across the country, finding new jobs, schools and doctors for all of the family, and specialists for Charlie. Of course we will be leaving behind an extensive web of support made up of family and friends. Just to try something that could save our seriously ill child's life, we are being made to leave our home.

It should not be this hard.

It should not be this hard to try a therapy that could save our little boy from the daily struggles to learn and live happily. It should not be this hard to treat your child and live together as a family. It should not be this hard to provide quality of life for a child who has exhausted every drug that the FDA has approved for Epilepsy.

Please help us. Please help save Charlie. Please.

Thank you,

Cady Coe
Virginia

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

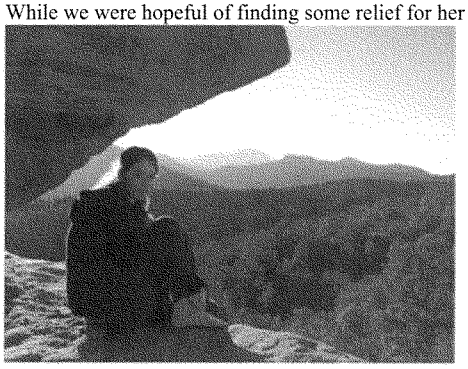
May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

I would like to ask your help in reuniting my family and saving children's lives. On December 2, 2013 my 14-year-old daughter Jennifer and I moved from Fairfax, Virginia to Colorado. Like over a hundred others, we left our home, my other 16-year-old daughter, my husband, our family, doctors, and friends, to give Jennifer the opportunity to find relief from her seizures and the harmful side effects of her current medications through medical marijuana. We have exhausted all other treatments. Despite her current daily regimen of 14 pills, Jennifer still suffered from over 300 seizures daily. In addition, the side effects of her medication include cognitive functioning issues, depression, weight gain, and ovarian issues, to name a few. Her neurologist, Dr. Philip Pearl, now Director of Epilepsy and Clinical Neurophysiology at Boston Children's Hospital, gave us his blessing and said, "If I could legally obtain this for you, I would. It is worth a try."

While we were hopeful of finding some relief for her through medical marijuana, if it worked for her, she would be unable to leave the state because medical marijuana is a Schedule I drug. She was afraid the new medicine would work, and she would be forced to live here. To say the least, this has been a difficult and painful decision. Quite frankly, it is one we shouldn't have had to make.



Jennifer's medication is from the cannabis plant, but it contains no active THC, so it has no psychoactive effect, and yet, it is considered to be in the same class as heroin.

We are currently seeing an approximately 85-90% decrease in her seizures. Her neurologist here in Colorado, who is very supportive of this treatment, feels that in the next few months she will be ready to start weaning from the heavy pharmaceuticals that are causing her physical, cognitive, and emotional damage. Despite this good news, Jennifer is having a very difficult time emotionally. She wants to go home. She has even said, "I would rather have the seizures, and

have my dad and friends every day." This is heartbreaking. Jennifer asks daily to go home. She misses her father and sister. She misses her friends and teachers.

Rescheduling marijuana to a Schedule III drug or lower would enable Jennifer to leave the state of Colorado for visits home to her friends and family. It would also enable doctors to begin studies on the efficacy of marijuana in pediatric epilepsy. While Jennifer's neurologist here is supportive, he is unable to provide us with advice on dosing and he is not able to compile his findings or observations into usable research as this is against Federal law.

Our story was featured in a front-page article in the Metro section of the Washington Post a few Sundays ago. We are hoping that this helps Federal Lawmakers, Virginia leadership, and citizens understand the importance of this issue. We hope that the Federal Government begins taking steps to reschedule marijuana from a Schedule I drug to Schedule IV, so that much needed research and better access can occur. Here is a link to the online version of the article: http://www.washingtonpost.com/local/northern-va-families-move-to-colorado-to-get-medical-marijuana-for-children-with-epilepsy/2014/04/12/859b65a6-bf60-11e3-b195-dd0c1174052c_story.html.

There are so many children in this country who need this medication. For some, it truly is a life or death issue. I am constantly receiving emails and talking to parents whose children are potentially one seizure away from death. For the 1 million people living with epilepsy that is not controlled by pharmaceuticals, this is truly a last hope. For Jennifer, it has been a miracle, and a curse. I am witnessing a great deal of success with other epilepsy cases here in Colorado.

Here is an NBC story that aired in May which includes our family and two other Virginia families: http://www.nbc12.com/story/25447368/controversial-treatment-helps-children. I know that Lucy's mother, Melissa Rhoden; and Haley's mother, Lisa Smith have written to you as well.

I would like to ask if you can help in rescheduling this medicine. I assure you, after 5 months on medical marijuana, Jennifer is doing much better and has no side-effects. I cannot say this for ANY of the pharmaceuticals she has been on during the course of her illness.

Thank you for your time and consideration.

Beth Collins
Virginia and Colorado

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

My name is Teresa Elder, and I am writing to you today on behalf of my son Tommy. If Tommy could communicate to others - - - this is what I believe he would say:

> Dear Mr. Attorney General:
>
> Please help me and kids like me. Please reschedule medical marijuana to allow for scientific studies and medical use.
>
> My name is Tommy and I have a severe seizure disorder. I am 21 years old. I started having seizures at the age of 6 months old. Over the past 21 years, I have been on 16 medications (which have horrific side effects), including many different combinations, had 3 Vagus Nerve Stimulators, been on the Ketogenic Diet several times, and, when I was 11, I had brain surgery.
>
> NOTHING helps me!
>
> I have been on life support machines 37 times. After all that, I am generally a pretty happy guy.
>
> It shouldn't be like this. I know it shouldn't.
>
>
>
> I hear my mom talking to the doctors. I heard the doctor tell my mom that I probably wouldn't live until I was 3 years old . . . then 13 . . . then 20. I'm scared. And I know my mom is terrified too.
>
> Sometimes, I have an aura, meaning I know when the seizures are coming on, and I go to my mom and grab onto her. I see the pain in her face. I hear her heart start to race with fear. I know she is holding back tears. She wants to help me, she really does, but nothing she does can help me. She gives me lots of Ativan or Valium, which the doctors call "rescue drugs" – but they don't work either.

A few months ago, my mom was so excited when she heard about medical marijuana and how it is helping the kids in Colorado. The problem is that we live in Virginia, and medical marijuana is illegal here.

My mom is a good mom. She would never let me "smoke pot," she doesn't want to get me high, she wants access to medical marijuana because she is just trying to find something that can save my life.

So, I would like to ask you: why won't you reschedule medical marijuana to help people like me? Is it because we aren't important? Or do you not understand medical marijuana? I have tried so many different treatments, and nothing works. The doctors are amazed that I am still here.

You can help me!!! This is my chance. Maybe this is what I have been waiting for – medical marijuana. But, you see, the problem is, I may not have a lot of time. The fact is that one of these seizures is going to kill me. That makes me sad, because I don't want to die, and I don't want my mom to have to go through that.

Please consider rescheduling medical marijuana so that people and kids like me can get involved in a scientific study and/or use it medically. We really NEED your help.

Thank you,

Tommy Elder

Because Tommy cannot speak for himself anymore, he depends on us to speak for him and act for him. We cannot wait any longer.

Thank you,

Teresa Elder
Virginia

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

I'm sick of feeling sad, depressed, and anxious. It's been rough to have to take medication that helps keep me alive and seizure-free, but they prescribe me more medication to keep me "normal." It's a terrible system when the medications that the government allows doctors to give me have such soul-sucking side effects.

It has been emotionally draining for the last 12 years to have to have a condition that can be so easily treated with non-psychoactive CBD oil, and yet where is the government to deliver research and or actual assistance? Meanwhile parents and children suffer needlessly while the pharmaceutical companies line their wallets with the thousands of dollars my family and countless others have spent trying to keep their loved ones healthy. Words cannot express my gratitude to my friends and family for their support and assistance, but also my mother Jennifer Oram for always helping me get though the roller coaster of living with epilepsy and keeping a positive attitude throughout it all. Hopefully this letter makes an impact, because unless we act and educate, nothing will improve.

I'm attaching a picture of me from the hospital – I had a seizure and fell, and had a concussion. All while taking my prescription medications.

My heart goes out to all the people and families who have or been affected by epilepsy. Please reschedule marijuana to Schedule 3 or lower so that all the patients can benefit.

Sincerely,

William Davis
Virginia

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, D.C. 20530-0001

May 30, 2014

RE: Rescheduling Marijuana

Dear Mr. Attorney General,

My name is Suzanne De Gregorio. My twelve year old son Alex has severe autism and epilepsy. It was not always this way. Alex was a typical, healthy baby before he regressed into autism. At three he was so high functioning that his therapists thought he might be a genius, so we had every reason to believe his future could still be bright. But by six my son was severely autistic and back in diapers, with an IQ of 52. Undiagnosed petite mal epilepsy had battered his brain for years, robbing him of speech, cognition, and coping skills. My once happy, gentle son now becomes so aggressive during neurological episodes that he has to be restrained. He grows bigger and stronger by the year and it is harder to restrain Alex now. He bites his arms up and down until they bruise. My son is in so much pain that it is often hard for him to function outside of his home.

Anticonvulsant medications alone do not cut it and their side effects are devastating. Depakote raised his liver enzymes and made him obese, so he switched medications. They were worse. Topamax made him lose what little language he had while on it. Lamictal gave him a potentially fatal rash and such impulse control problems that Alex darted in front of cars, tried to pull boiling pots of water onto himself and put his hand in the garbage disposal. So, he was eventually put back on the first medication that makes him obese and carries the risk of liver damage. Alex was also on steroids for two years to control his seizures, but long term use risks osteoporosis, diabetes, and adrenal disease. It was a terrible decision for a mother to have to make: risk my child's health to spare his brain.

Medical Cannabis is helping children like mine live happier, more functional lives without the debilitating side effects. Please reschedule medical cannabis so it can be researched in the United States and so that patients can have safe access.

Sincerely,

Suzanne M. De Gregorio
Louisville, Kentucky

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

I'm writing to you to ask that you reschedule marijuana to Schedule III or lower.

I moved from Spartanburg, SC to Colorado with my two-year-old son, Ezra Gault, to try medical marijuana. He has a diagnosis of Generalized Intractable Epilepsy & Infantile Spasms, and may possibly have Lennox-Gastaut Syndrome.

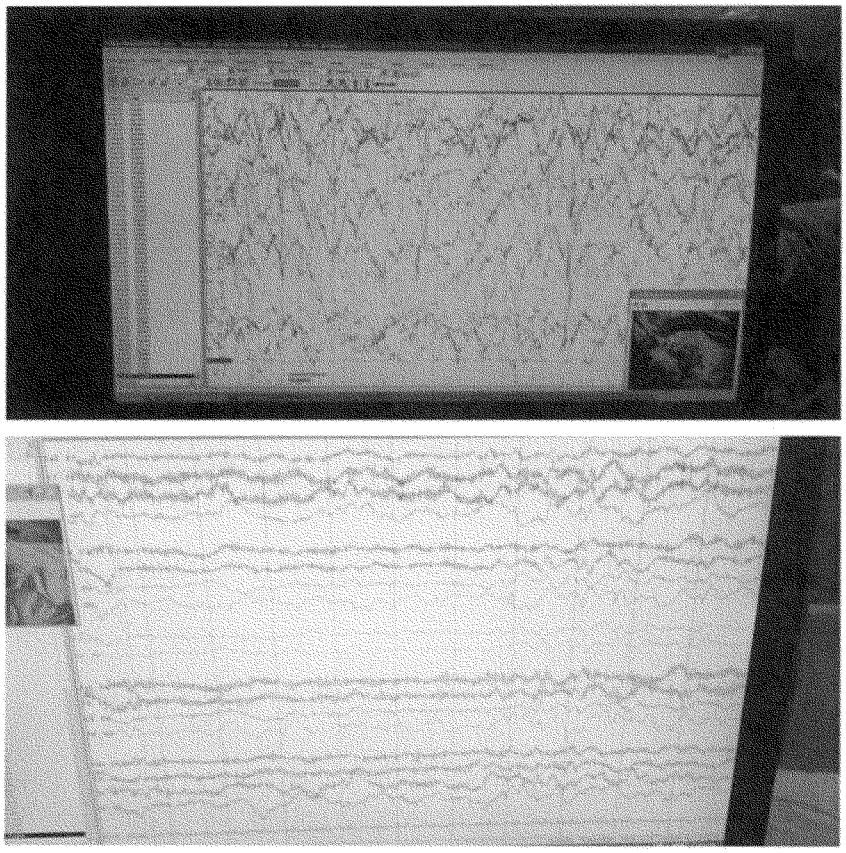
He started THC oil in September 2013, Charlotte's Web oil (a CBD oil) in October 2013, and THCa in March 2014. Currently, he uses all three oils for a variety of ailments.

Previously, he had 300 to 500 seizures per day. Now, he has approximately five seizures every two weeks. I see dramatic improvements across the board. He's now beginning to hold his head up for the first time, and he's gaining trunk strength. Despite being legally blind, he's beginning to track objects, and has slightly improved vision – his last eye exam required a new prescription. He has an improved appetite, and has been weaned to a minimal amount of pharmaceuticals. He currently only takes 5mg. of Onfi per day.

On the page below are two EEGs – the first is obviously before medical marijuana, and the second is after. You can see that the constant seizure activity has quieted thanks to marijuana.

Sincerely,

Marisa Kiser
South Carolina and Colorado



Ezra Gault's EEGs Before and after Medical Cannabis

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

Our son Christian is 4 1/2 years old. He was diagnosed with Dravet Syndrome, a catastrophic pediatric epilepsy syndrome, when he was just a little over a year old. Although we've done pretty well taking things one day at a time, we now are faced with the challenges of his older years and it's frightening. He has extreme developmental disabilities and has been to four neurologists. The latest neurologist told us that he will not ever get to a teen or adult age cognitively. He will always need assistance and they think he has autism as well. What we find is that the anti-seizure medications all have terrible side effects. The one that makes life most difficult is Topamax which has been known to cause problems with speech. Christian was on it long before it was time to talk so he's never had a chance to learn to speak. We are hoping that with the use of medical marijuana he will be more clear-minded and open to speech.

We pray that he will be one of the lucky kids for whom this will work. We need you to make this possible for him. We are one of the families that would benefit from the rescheduling of marijuana to allow scientific studies and medical use. Thank you so much for listening to us.

Sincerely,

Lisa Glass
Maryland

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

My name is Gwen Hartley, and my family of 5 lives in Kansas. My husband and I have three children -- a typical son who is 15, a daughter who is 12, and another daughter who is 8. Both of our daughters have a rare genetic condition which causes them to have a variety of health problems including dwarfism, microcephaly, cerebral palsy, epilepsy, and more. Due to their extreme sensitivity and fragility, both girls are unable to take medicine, as even Tylenol and Benadryl over the counter make them seize even more.

Our 12-year-old, Claire, has approximately 10 seizures a week, lasting from 5-20 minutes in length. Our 8-year-old, Lola, has many more seizures (too many to count) which occur in clusters and at times affect her ability to even eat. In those instances, we have to place a nasogastric tube down her nose to nourish her (she is unable to get a g-tube placed in her stomach, as she is too fragile to go under anesthesia). Both are very tiny and very sensitive. Claire is 23 pounds at age 12 ½, and Lola is 10 pounds at age 8.

We have had to go a more natural route with the girls due to their size and their reactions to medicines. We have even opted to not vaccinate them, for fear of causing further damage to their brains and bodies. We keep them at home, and neither attends school; instead, therapists come to us at home. We were told initially that both girls would not live to be 1 year old due to their condition, so we feel proud of the fact that they are still here now, defying odds and changing the lives of everyone around them. We have used chiropractic, homeopathic remedies, craniosacral therapy, hydrotherapy, hippotherapy, vitamin and mineral supplements, Reiki and more to try to help their lives in a positive way and to optimize all we can for each of our daughters. That has been effective, though we are unable to control their seizures using these methods. Prescription drugs are simply not an option, as I'm not sure either of our daughters would survive the use of something so harsh. (Not

to mention that my friends' kids who have similar conditions and use seizure medications have many health problems, toxic livers, and the seizures are still present -- how is that HELPING?)

Due to the fact that we live in Kansas, medical marijuana (which is completely natural and something I think the girls would handle well) is illegal. Our hands are tied. We are unable to pick up and move our family to another state due to family situations, work, having an entire care team in place here in Kansas to help care for our daughters, and our needs are being met in this state in EVERY WAY except for this.

I completely understand why marijuana is not being legalized for recreational use -- it is a drug. However, CBD oil does not contain the parts of the plant which causes a "high" -- it only contains the therapeutic CBD which has been proven to dramatically help seizures. I would NEVER subject my daughters to a drug or something I felt would be harmful to their well-being. It is something I have researched thoroughly and would work with educated, caring, knowledgeable growers to be sure my daughters were receiving the highest quality form of CBD oil. I would also be in contact with a Harvard-trained doctor to manage their care and be SURE they were being watched over closely.

I refuse to sneak medical marijuana/CBD oil across state lines for fear of being reported and possibly losing the very children I was trying so hard to save. I cannot understand the reasoning behind why something like this would not be considered for families such as ours, whose possible ONLY HOPE lies in a very safe, natural treatment that would still be monitored closely. Why would someone prevent me from trying a natural, safe PLANT to help control my girls' seizures? It is safe for me to use other herbal remedies which contain no drugs – why then is this also not OK?

Please help legalize medical marijuana for Claire, Lola and all of the other children who need this for their survival.

THANK YOU!
Gwen Hartley
Benton, Kansas
www.thehartleyhooligans.com

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

This is the story of Shane, a 14-year-old boy residing in Maryland and battling intractable epilepsy.

Shane was a perfectly happy and healthy little boy until the age of 7. When he began going blind, we started at the eye doctor for extensive eye exams. We moved to a neurologist after everything in his eyes checked out OK. As soon as they hooked him up to an EEG - the brain spikes were evident. Shane was diagnosed with Occipital lobe epilepsy on his 7th birthday.

For the past 7 years we have tried what feels like every drug out there to help decrease Shane's seizures - to no avail. He has tried all of the epilepsy diets, acupuncture, and has been made sick from all the medications we pump into his tiny body. Nothing slows his seizures down. Shane still has seizures every single day. They vary in complexity, length, and severity but he has had seizures now for half of his life! A day when he only has 6-8 is considered a good day and a day when he has 50-70 is a not-so-good day.

We have run out of options. We have given up hope with the medications out there (none have worked in 7 years) - or do we try something more natural? I have seen the faces of these children suffering from epilepsy and other neurological disorders. Visit the pediatric neurology department at Children's National Hospital for a day and you would run out of there trying to reschedule this possible miracle for these kids.

Help stop the seizures.

Sincerely,

Lauren Hoehn
Maryland

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

I'm writing to you on behalf of my daughter, Hannah Grace Jones. She was born July 9, 1995 with a rare chromosome deletion 1q 24-31. When she was 11 months old she had her first of many status seizures. Looking back now 18 years later I realized she might have been having Infantile Spasms but was never diagnosed. She continued to have status epilepticus (extremely long, potentially fatal) seizures for years. She had a toxic reaction to valproic acid because she was getting 10 times more medication than she should have had. I'm not sure how that slipped through the cracks. She suddenly had petechiae all over her body and was unresponsive, and the doctors thought she had streptococci meningitis. It took a long time to recover from that.

When she was 4 years old, we changed hospitals and got a new neurologist. During an EEG, we discovered that she was having a seizure every time she blinked her eyes – she was seizing constantly. They put her on a new medication (by this time she had been on most of them) and they seemed to be under control. When she was 8 years old she started precocious puberty and started having seizures every day that were different than the eye blinking. We were constantly changing medications and adding new ones. Nothing seemed to work for long.

She has been on every medication possible except Felbatol. She was on 6 medications and still having lots of seizures so in November 2012 she started the ketogenic diet. She was on it exactly one year. Her seizures were still bad and her potassium and sodium levels were out of control so we had to stop the diet. The only good thing is she got off of 2 of her medications during that year. Now she is on 4 seizure meds and still has daily seizures. I also think she is having a lot more than we see. Getting ready to transition into the adult world of medicine is scary, mainly because of her size. At 18years old she is 3 feet, 4 inches tall and weighs 40 pounds.

Medical Marijuana is our last resort. She used to sit alone and roll all over the place, she would laugh when tickled or when he sisters were around, but now, she just sits in her chair, once in a while playing with her hands, but never laughing or smiling at all, not even crying. We want our old Hannah back from the seizure monster!

Sincerely,

Joan Jones
Hannah's Mom
Maryland

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, D.C. 20530-0001

May 30, 2014

RE: Rescheduling Marijuana

Dear Mr. Attorney General,

My 14 year old daughter has a rare form of intractable epilepsy called Lennox Gastaut syndrome. At 6 months old she began having seizures. Her first diagnosis was idiopathic infantile spasms, a rare and very damaging epileptic syndrome that likey progresses into Lennox Gastaut.

Morgan has tried multiple medications and has never been seizure free. She is developmentally an infant. She can walk, and feed herself, but she's 100% in need of total care. She has had many seizure related accidents which needed facial stitches and caused her to be without her front teeth. Here smile is amazing but the seizures have broken it.
She has multiple seizures and seizure types daily. We et through it, but it's heart breaking. She as well as many children deserve the opportunity to be recipients of Cannibidiol. Please hear us, please stand with us in an effort to seize the seizures.

Wrayanne Lesslie

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

As I write this letter, I am sitting at home watching over my beautiful 11-year-old son Jackson. I am a small business owner, but unable to work because my son suffers from catastrophic epilepsy and he suffers from uncontrollable seizures throughout the day.

The seizures and the harsh side effects associated with antiepileptic drugs are preventing him from going to school and are robbing him of his childhood. He is still suffering many seizures and other problems, despite currently being on two antiepileptic drugs (one of which is Felbamate, which can lead to liver failure and aplastic anemia, both life-threatening), trying and failing with 10 other antiepileptic drugs, and receiving intravenous immunoglobulin infusions at Children's National Medical Center every other weekend.

My husband and I take turns sleeping with Jackson each night so that we are able to administer rescue medication if he has a severe seizure or a cluster of seizures, out of concern for sudden unexplained death in epilepsy (SUDEP), which steals lives of about 10% of children in Jackson's situation every year.

Jackson's little brother, Declan, wishes to be able to share his room with his brother again. This is the most stressful and emotionally draining job there is, as we never know if one of the seizures will take Jackson away from us and we deal with this every single day and night. We desperately need the scheduling of cannabis to be changed in the hope of saving our son's life as nothing else has worked.

Jackson was a typically developing child until epilepsy came into our lives when he was 8 years old. We have had every possible test done and multiple opinions from some of the best doctors in the nation (Johns Hopkins, NYU, Children's National Medical Center, Georgetown University Hospital), and the cause of his condition remains unknown.

Our family continues to mourn what we lost and we live in fear of what may happen in the future. The change in the scheduling of cannabis would give families like us more options for our children and allow the medical professionals the ability to perform much-needed research. We need to have appropriate strains of medical cannabis that are high in cannabidiol (CBD) and low in THC available for Jackson or we may have to relocate out of the District of Columbia, as our current life is unsustainable.

Our family is in constant crisis and suffering. Thank you for listening to our story and please help us in gaining access to this potentially life-saving medicine by rescheduling medical cannabis.

Sincerely,
Lisa Leyden (Mom)
District of Columbia

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

I'm writing to you to ask that you reschedule marijuana to Schedule III or lower.

I moved from South Riding, VA to Colorado to try medical marijuana for my daughter, Madeline, age nine. She's been on Charlotte's Web since October 24, 2013, and on THCa for about three weeks.

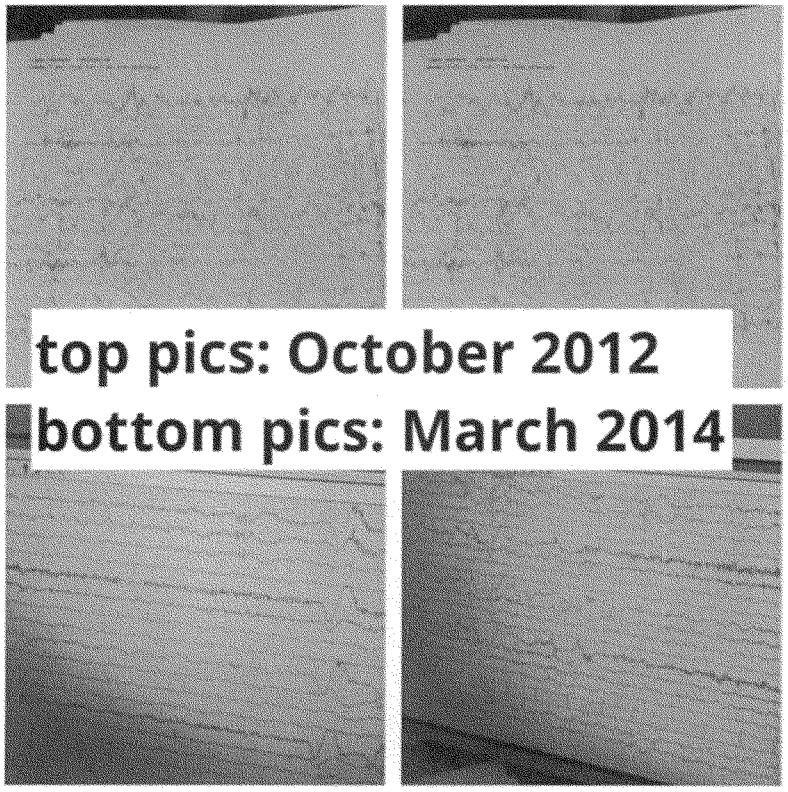
Seizure reduction is hard to see in her case, because 80% of her seizure activity would happen in her sleep. She would have them for hours on end even when we couldn't tell according to Johns Hopkins. They told us the next step was to remove the entire left side of her brain. Instead, we moved to Colorado.

Below are two EEGs – the first is obviously before medical marijuana, and the second is after. You can see that the constant seizure activity has quieted thanks to marijuana.

Sincerely,

Dara Lightle
Virginia and Colorado

Madeline Lightle's EEGs



The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

I am writing today to petition you to reschedule (hopefully deschedule) cannabis.

I would like to engage you on behalf of my two-year-old daughter Millie. She has been diagnosed with intractable infantile spasms. Infantile Spasms is a rare form of early onset epilepsy in which the brain is shown to seize constantly. Intractable is a term used by the medical community to describe a patient whose seizures cannot be controlled by medication. Some families dealing with epilepsy have used up to 14 different medications. Millie has been on 8 different medications, starting since the age of 3 months. That is a total of three quarters of her life on powerful medications.

She started out on what are considered conservative antiepileptic medications; Trileptal, Topamax and Keppra. It became clear that these were not helping so she was then put on Clonazepam, a benzodiazepine which is a psychoactive medication used to treat anxiety, depression and a variety of other psychiatric conditions. She was also put on a large doses of Sabril, a medication whose main side effect is blindness and even at up to 2,000 mg a day the medication had no effect on Millie's seizures or EEG.

The Neuroscience Center at Nationwide Children's Hospital in Columbus Ohio has researched tirelessly to provide the following statistic: The first seizure medication chosen has about a 60% chance of controlling seizures. If that medication fails, the chance of seizure control drops to 10%. If 2 medications fail then there is only a 1-2% chance of controlling seizures; at which point there currently are 2 other options: diet and brain surgery.

At 3 months old Millie was also prescribed the ketogenic diet; a specialty diet designed to adjust the body's chemistry by producing ketones to fuel the body, as opposed to the typical fuel of glucose. The diet is successful in a large number of patients; however, Millie was not one of these cases. For 9 months she

gained weight only in ounces, not in pounds and grew only in centimeters; for her 1st birthday she was still in 3-6 month clothing. However slow growth and weight loss is not uncommon for the ketogenic diet, it also causes bone deterioration and osteoporosis-like symptoms resulting in bone fractures in a number of young and old patients. The diet did not work at all. In June of 2013 Millie's body started going into metabolic acidosis, though the root cause was misdiagnosed, and in August of 2013 Millie's kidneys shut down. Through the summer of 2013 she required 9 blood transfusions, had 5 PICU stays, 6 PICC lines, 1 staph infection and 1 central line. Upon request of our nutritionist at Cincinnati Children's hospital, the staff at Vanderbilt removed her from the ketogenic diet.

It was at this point in November of 2013 that we further investigated the rumors of medical cannabis in the treatment of epilepsy. We consulted our neurology team at Cincinnati Children's hospital and they felt we had nothing to lose. The firsthand personal experiences are nothing short of miraculous – not only great decline in seizure activity but increases in cognitive, developmental and behavioral skills even in those with irreparable brain damage. We sold our landscape business and moved our family of 5 to Colorado in January. Millie has now been on THCa oil for 4 months and high CBD oil for 3 months. Her seizure activity has decreased 85-90%.

THCa is a whole plant (not strain specific) medication showing significant results in Australia for treating seizures along with THC which acts identically to benzodiazepines in patients who require such medications; however, it works without the harsh side effects.

Previously our daughter was in a "Sabril coma." Sabril, as mentioned above, is a harsh medication. For those similar to Millie, with cryptogenic/idiopathic infantile spasms (no known cause), Sabril puts them to sleep for upwards of 23 hours a day. Now that Millie is on THCa and high CBD oil, she is on a regular wake/sleep schedule. She is vocalizing, she is moving all body parts, sucking on a pacifier and swallowing her saliva, holding her head up and even sitting up. This may not sound like a lot, but to a parent who is told

their child has a .1% chance of surviving, this is HUGE!! She is not only surviving, she is on her way to thriving!! She was considered deaf, but is jumping at more and more noises. She was also considered cortically visually impaired (her brain was not comprehending what she sees) but she is tracking toys and faces and looking at things, she is smiling when she sees us!

Patients young and old need other medical options, especially one such as medical cannabis that has been studied and has documented positive results from around the world. I do not believe our daughter is beyond help. I believe that she and the multitude of others like her have hope in medical cannabis. We have been told by doctors time and time again, as have all of the families in Colorado, that there is nothing we can do; however, medical cannabis is proving them wrong. We refuse to give up!

Thank you again for your time.

Sincerely, The Mattison Family
Penn, Nicole, Neal, Sam and Millie
Tennessee and Colorado

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

My Facebook page, Cyndimae S'miles (https://www.facebook.com/groups/Cyndimae/) was created to document the life and times of our baby girl, Cyndimae, and her life with Dravet Syndrome, vaccine-induced epilepsy and the high-THC cannabis medicine that has saved her life. Indeed, cannabis has given her a life to live. While not every day is seizure-free, many days are, and all of our days do not revolve around seizures and heavily-sedating Antiepilepsy Drugs (AEDs).

At 10 months old, Cyndimae's first seizure occurred 27 hours after her 3rd set of childhood vaccinations. At age 10 (2013), she was having 20,000 to 40,000 "spikes" on her EEG in a 24-hour period -- these "spikes" correlated with myoclonic jerks. The best way I have ever heard a myoclonic jerk described is "A myoclonic jerk is like a sneeze, but imagine sneezing about 1067 times an hour." Try eating or sleeping while having over 1000 sneeze-like events an hour. Besides these continuous disturbances in her brain and her daily life that clinically presented as sharp jerks or startles, Cyndimae also had anywhere from 4 to 12 (sometimes more, occasionally less) generalized tonic clonic seizures a day requiring medical intervention including Diastat (rectally administered valium) and Versed (nasally administered midazolam, a sedative often used for surgery).

After a 2012 surgical implant called a Vagus Nerve Stimulator, Cyndimae was experiencing "only" 2000 to 4000 "spikes" and myoclonic jerks a day which correlated to "only" 107 of these sneeze-like interruptions per hour. While this was a 90% reduction in seizures, Cyndimae still required 4 pharmaceutical medications that drugged her to the point she was often wheelchair-bound, could not communicate her needs, needed help eating when she was able to eat, and could never walk without her seizure helmet. By October 2013, Cyndimae was losing weight (again) instead of gaining, and doctors were discussing a g-tube. Doctors were discussing the last two AEDs that Cyndimae had not tried: Sabril which potentially causes blindness; and Felbatol, which destroys a patient's liver function and ultimately causes death. A last-attempt surgical option involved slicing the connections between the two halves of Cyndimae's brain. Because Cyndimae's seizures fire off from multiple locations on both sides of her brain, this option would NOT stop her seizures, but it might lessen the intensity of some of her generalized seizures. At this time, Cyndimae's neurologist, Dr. John Gaitanis, from Hasbro Children's Hospital in Providence, RI, strongly recommended the family get Cyndimae access to medical marijuana. The family and Dr. Gaitanis had many times discussed medical marijuana as a

possibility, but this time, there were no other options the family or Dr. Gaitanis felt were real options.

Cyndimae came very close to becoming a Colorado resident to access a high CBD strain of medical marijuana known as Charlotte's Web. A very special friend in Maine continuously pointed out options in closer-to-Connecticut (where we are from), Maine. While Maine did not have this very high CBD option, Maine had many very compassionate caregivers willing to help Cyndimae's family dial in the right medical marijuana treatment for Cyndimae. Today, the family is very thankful to be "fractured" by only a 5 hour drive rather than a 4 hour flight. Additionally, Cyndimae does not respond well to high-CBD strains like Charlotte's Web. Even low to moderate doses of CBD aggravate Cyndimae's myoclonic jerks. Another cannabis option is a marijuana extract made without activating the THC -- it is a THCa extract that leaves the carbon molecules attached to the THC molecule. This THCa marijuana extraction has been used to treat pediatric epilepsy in other countries for a couple of years. Dave Mapes, a resident of Michigan, operates a company called Epsilon. Epsilon publishes free instruction and education guides for many homeopathic options including THCa extraction from a full grown, flowered marijuana plant. Cyndimae has thrived on a combination of THCa extracts, THC to treat breakthrough GTC seizures and a VERY low dose of CBD.

Cyndimae's new "baseline" is amazing to her family and friends. Gone are the pink helmet days and the child who could not walk or eat by herself. Cyndimae runs, pumps her own swing, jumps and hops even on one foot, buttons her shirt, zips her coat, and eats by herself! She is finally a healthy weight for her frame! She still has her most difficult-to-control seizure MOST mornings, her myoclonic cluster that used to convert to a GTC most mornings. With a rescue dose of THC and THCa, this seizure rarely generalizes nowadays. Her "Cannabis 911" tincture leaves her hungry for breakfast and ready to face the day!

The incredible improvements Cyndimae has experienced in only 6 months using medical cannabis are due to a few things. The first thing is the 90% reduction in pharmaceuticals. I wonder why folks want to know if cannabis makes her "high." No one ever asks if valium makes her groggy, or dull, or makes her drool, or causes massive developmental delays. When keppra made my sweet child a raging homicidal 8-year-old, no one helped me wrestle her to the bed all day long, 24-7, until the drug was finally tapering in her system – no one asked about the bruises I endured from this legal drug that made her so angry she was a threat to herself and to humanity. No one asks about the drugging effects of Phenobarbital, a drug sometimes used as a date rape drug because such a small dose renders the person unable to move or talk – a zombie-like remnant of a whole person – but no legislators cared when she spent day after day couch locked by these legal pharmaceuticals or when she slept 20 of 24 hours a day. Every medication, even a botanical like cannabis, has side effects. Pharmaceuticals –legal FDA approved double blind clinically tested DRUGS – have directly caused Cyndimae's developmental delays physically, emotionally and educationally. Cyndimae was so drugged, she could not feed herself – the family was consulting with doctors about a g-tube to provide nutrition to this child who was

unable to feed herself ONLY due to the legal drugs used to attempt to control her seizures. Even this drugged by legal anti-seizure drugs, Cyndimae was having 1 to 4 generalized tonic clonic (gtc) seizures a day, and thousands of "little" myoclonic jerks a day.

Cannabis has reduced her seizures to 1 gtc every 4-7 days and about 10 myoclonic seizures a day. Cannabis' side effects have been a very positive impact on her life. She is happy. She finally has enough appetite to be a healthy weight – she has gained 15 needed pounds on cannabis. Cyndimae can walk, does not fall much, and does not need to wear her seizure helmet unless she is participating in an activity that calls for a helmet like riding a bike or climbing. Cyndimae sleeps most nights from 10pm to 7am without sleep aids, and Cyndimae is awake all day most days without a nap. This is the impact of cannabis. If we want to call this 'stoned' then so be it. Cannabis has caused all of these positive side effects: eating, smiling, walking, talking, and sleeping a normal schedule. It is a huge disservice – or worse, perhaps it is abuse, that we consider these legal poisons firsthand and cannabis last.

Sincerely,

Susan Meehan
Connecticut and Maine

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

I'm an Emergency Medicine Physician at one of the busiest trauma centers in Southern California. I continually see drugs used and abused, and I see the damage they do to this country.

My daughter, 11 year-old Mallory, had failed about a dozen drugs to try and control her seizures. The next drug to try was so toxic that it required blood draws every 3-4 weeks to watch for a nasty side effect. The side effect had a death rate of 20-30%.

Someone suggested medical marijuana. As an ER doctor, I knew it was just a ruse for legally getting high.

But I was losing my daughter – her seizures had jumped to 30-40/month, and she was unable to attend school. She was getting worse with time. I am including pictures of Mallory with facial injuries from seizures. As you can see, these were pretty traumatic.

I discovered my daughter could try medical marijuana that's an oil. She could ingest it. And it's low in THC, so, she won't be getting high. She went from 30-40 seizures/month to 1 in the last 3 weeks. And she's back in school!

I got my daughter back!

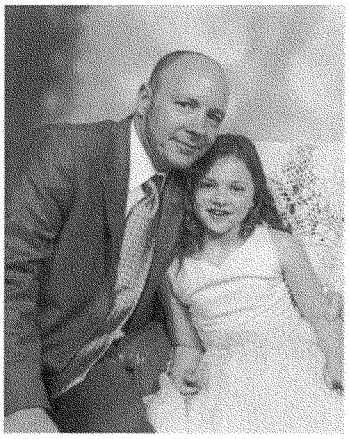
Our last picture, at the bottom of page two, is of her smiling, and present. It's after she began using cannabis oil to control her seizures.

Please consider moving this plant to Schedule III or lower. Pure THC (Marinol) is Schedule III, but when you add the rest of the plant, it moves it to Schedule 1,

which creates too many problems. To help fellow physicians remove the "anecdotal" stigma and do some real research on this plant, please consider moving it.

Sincerely,

Tom
Dr. Thomas F. Minahan
Program Director
Emergency Medicine Residency
Arrowhead Regional Medical Center
Colton, CA 92324



The Honorable Eric Holder
US Attorney General
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

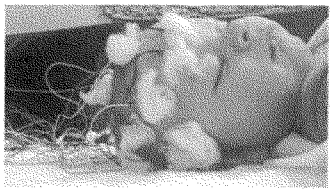
May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

My name is Shannon Moore. I am a resident of Frederick, Maryland and the mother of three-year-old twins named Nicolas and Byron. We call them Nico and Bebo. The boys have a rare genetic condition called Miller-Dieker Syndrome. They cannot walk or talk and are wheelchair-bound. They have severe, life-threatening seizures on a daily basis. http://bit.ly/1h16Il9

The boys take five different seizure medicines. These medicines have terrible side effects like permanent peripheral blindness, liver failure, other organ failure, respiratory failure, addiction, and death. Despite all of these powerful medicines, the seizures are breaking through.



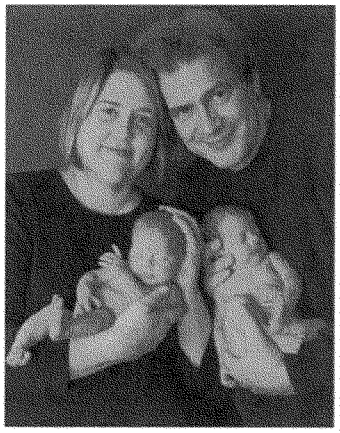
In January, the boys had surgery for feeding tubes at Children's Hospital because seizures had robbed them of the ability to eat. After surgery, we visited the boys' neurologist, and she informed us that it was time for us to choose between quantity and quality of life with seizure control. I knew we had another option because many parents I personally knew were using medical marijuana to treat their children's seizures to great effect. I asked her about medical marijuana, but she was uncomfortable with the fact that it was a Schedule I substance that could not be subjected to double-blind, placebo-controlled tests.

I became an advocate for medical marijuana as a result of this experience and helped organize other parents to legalize it in the state of Maryland through an effort called StoptheSeizures, http://www.stoptheseizures.com/. Our efforts were successful and the law was signed by Governor O'Malley in April http://wj.la/1p6bAYn.

It is not right that children in some states are able to legally receive this life-saving medicine but that children in other states cannot. It is also not right that parents should become criminals in

order to receive the life-saving plant their children need or that they should expose themselves to legal and physical risks to access medicine.

Medical marijuana is working for seizures. If we wait, more parents will go on the black market to find this medicine at great risk, more children will become medical refugees trapped in legal states, more opportunities to study the medical benefits of this amazing plant will be lost, and more children legally using cannabis will be turned away from receiving medical care in hospitals. More children will die. ***PLEASE REMOVE MARIJUANA FROM SCHEDULE I AND PLACE IT AS SCHEDULE III OR LOWER. WE CANNOT WAIT.***



Thank you so much for listening to my story. I would be happy to meet with you to discuss ways to remedy this difficult situation, and to serve in any capacity to help with policy development.

Sincerely,

Shannon Moore
Maryland

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

At 20 months old, my daughter Chloe is having about 200 seizures every day. She had her first one at 9 months old and has been getting worse as time goes on. She is currently on 2.5 mL of keppra, 2.5 mL valproic acid, 2.9 mL of trileptal and is now on valium and xanax as rescue drugs if Chloe has a seizure that lasts more than twenty seconds. Even while on all these medications she is still having 200 seizures a day. They have held her back from trying to hold her head up and from having a normal childhood.

Chloe has recently been diagnosed with Aicardi Syndrome, a very rare genetic disorder that is characterized by brain malformations and Infantile Spasms, a type of seizure. She also has schizencephaly, abnormal clefts in the brain that result in developmental delays and hydrocephalus, an excessive accumulation of cerebral-spinal fluid.

Medical marijuana could help control her seizures and give her some relief.

Thank you for your time.

Sincerely,

Courtney Moser
Maryland

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

My name is Michele Pulaski and I am the mother of a beautiful 7-year-old-girl, Sarah. She was born on March 6, 2007 with her twin brother Joshua. Sarah and Joshua were born at 32 weeks premature; however, both of them were very strong and did quite well after birth.

After a 3 week stay in the NICU at the hospital both Sarah and Joshua came home and I was the happiest mom in the world. Little did we know that two weeks later Sarah would start to die in my arms. Sarah contracted Late Onset Group B Strep Meningitis, which is very rare and we will never know how this happened. My son fortunately was spared.

It all started at 5am one morning when Sarah didn't want to eat. By 7am she looked a little pale, but no fever. By 8am when I went to take her into the doctor she started turning blue and stopped breathing. We did CPR and called the ambulance, which rushed her to the emergency room. For 72 hours we weren't sure if she would survive.

They conducted a CT scan and an EEG. The results were devastating and we were told that Sarah would be profoundly disabled and probably never even smile or laugh. She was left with spastic quadriplegic cerebral palsy, intractable epilepsy, cortical visual impairment and global delay in all areas. Once the shock was over, I decided I wasn't going to listen to the doctors and I was going to do all that I could to help Sarah recover as much as possible.

Since then Sarah has done amazing things such as learn to say words, take steps and her laugh and smile are contagious. Her determination is there, but what is holding her back are her horrible seizures. Sarah has up to 30-40 seizures a day that cannot be treated with medicine. We have tried over 8 different medications during the last seven years and not one of them can reduce or eliminate her seizures. Due to the seizures, Sarah cannot make much progress. Most importantly, every time she has a seizure, her life is in danger. I go into her room every night to see if she is still breathing. No mother should ever have to worry about that.

We know someone personally who has had 80% seizure reduction within 2 months by using CBD (the variation of medical marijuana that our kids need). I have to be allowed to give Sarah that chance to live a better life and be here with her family for a long time. Every day is one more day that she may not be here due to a seizure and we don't have the luxury of time. We need to move forward as soon as possible. Please consider re-classifying marijuana to a Schedule III drug. It does have value and kids all over the country are waiting for help. Thank you for your time and consideration.

Sincerely,

Michele Lewis Pulaski
Maryland

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

Our third child Logan was born in 2009, and we watched with deep gratitude as this happy, beautiful baby hit his developmental milestones. Logan has always been a sweet and happy little guy. After his first birthday Logan experienced his first seizure and everything changed – our child, our family, and our world would never be the same again.

Logan's seizures started as quick, "staring" seizures and quickly progressed to "drop" seizures. Logan would simply drop as if he were a marionette whose strings were cut. He now has all kinds of seizures, in all kinds of places -- on the stairs, in his bath, at school, on a walk. We watch helpless and heartbroken as the agony of the seizures is compounded by the injuries he accidentally receives when they occur. Following the seizures he is exhausted and sometimes takes hours to recover. It is impossible to find the words to describe the anguish we feel at our inability to help our son.

To date, Logan has had over 12,000 seizures and his development has been dramatically impacted because we cannot find a way to minimize or stop the seizures. We do our best to give Logan every opportunity to reach his potential – including thousands of hours of speech, occupational, and physical therapy as well as therapeutic riding on horses, but Logan can barely communicate verbally.

We've sought out the best medical care we could find – seeing 8 neurologists, including specialists at the world-renowned Johns Hopkins Pediatric Epilepsy Center. Out of desperation we have given our little angel some nasty, heavy-hitting, mind-altering drugs prescribed by the neurologists and epilepsy specialists. ***Sadly, these toxic drugs haven't worked; in fact, Logan has suffered some tremendous consequences from the side effects. Some medicines even made the seizures worse.*** Other drugs have caused strange behaviors, lack of balance, and interrupted sleep. We even tried the "ketogenic diet," a strict high-fat, difficult to administer diet that repulsed Logan. ***Nothing helps…nothing has stopped the seizures. Yet we won't give up. We can't give up. He is our son.***

Medical cannabis has worked for our friend, Zaki, who suffers from Doose Syndrome, the same type of epilepsy with which Logan was diagnosed. Since taking medical cannabis, Zaki has been seizure-free for over a year and a half and his EEG, which monitors brainwaves, has cleared up

significantly. Zaki and Logan present in very similar ways – and that gives us great hope that it could work for Logan as well. Our hearts break because he is being denied the opportunity to live up to his greatest potential.

Think for just one moment what it would be like to walk in Logan's shoes and please open your heart and your mind to allow him to get access he needs as soon as possible to this life-changing medicine.

Sincerely,

Gail Rand
Maryland

MELISSA CROWDER RHODEN

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

I'm writing to tell you a story about my daughter, Lucy. I was asked to write a half a page, but I'm an English teacher and a writer, and I'm afraid I am loquacious.

September 3, 2011, Baby Girl Rhoden was born in the Shenandoah Valley in Virginia. We had been waiting for her for a long time, planning and hoping and wishing for this little miracle. We named her Lucinda, which means "light," because she is the light of our lives.

Her first few months seemed uneventful, though in hindsight I suppose we could have identified signs if only we had known to look for them. But we were absolutely delighted with our beautiful little girl. We took her on her first big road trip to visit her Grandma and Grandpa Rhoden in Kentucky on Thanksgiving, and then she had a seizure.

Kids with Lucy's particular syndrome typically have a prolonged generalized tonic-clonic seizure -- a very long grand mal seizure -- as their first event. Lucy does not do things typically. So her first event did not even make the word seizure enter my mind. We simply saw that her right arm was very stiff, and in an odd position, moving rhythmically. My husband and I weren't even sure what to do. We decided to take her to the hospital because she seemed really out of it, and because that side of her body was very limp. We drove her to the nearest hospital, and because we were in rural Kentucky, that was 45 minutes away. The doctor there refused to admit us and instead called the University of Kentucky Hospital.

He told us to drive her there as fast as we could, and that he'd contacted the state police to let them know we'd be on the way. He couldn't send us in the ambulance because they only have one and it was on a call. I think that's what told us that things were bad.

UK Hospital admitted us through the Emergency Room after midnight and took blood for labs. They kicked us out of the room to perform a lumbar puncture because they told us she would associate the pain with us, but I wish I hadn't left. I can still hear that particular scream in my soul. The next day, they performed an MRI which required us to meet with the chief of surgery because general anesthesia isn't safe on a baby that small; and finally an EEG.

All of Lucy's tests came back negative. Nothing was wrong.

When the doctors discharged us, they told us to follow up with our pediatrician, and to videotape any more events. I made an appointment for a few days after our return, and we drove home.

The day we returned, she did that arm thing again. And then again, on the other side. And then her leg. Then her other leg. Then half of her body. Then her whole body. So I called the doctor's office.

The nurse listened and said that since all the tests were negative that we could wait until our appointment the next day. Seizures are, after all, extremely rare in babies.

But these events kept happening with no other connection but time. Approximately three hours after the last one, Lucy would have another. My husband and I stayed awake all night. I think we knew, but neither of us wanted to say. However, our good doctor took one look at the videos we brought and said it: "I think she's having seizures." And then she sent us to UVA hospital, where we spent the next three days. It was agonizing to watch Lucy have a seizure every three hours, but as the day turned into night, things grew steadily worse – the seizures grew steadily longer and closer together. An EEG had been scheduled for first thing the next morning, and the doctors were trying to not medicate her prior, but by the early morning of the next day, she was having seizures ninety minutes apart and nearly three minutes in length. At about 3:00am, they decided to go ahead and give her Keppra, an anti-epileptic drug. The seizures stopped immediately. Her EEG came back normal. We were sent home with a prescription for Keppra, a prescription for Diastat (a rescue medication to stop seizures which I REALLY hoped we'd never need) and a diagnosis of "seizure disorder." Lucy had occasional breakthrough seizures now and then, but as we figured out her appropriate Keppra dosage and as she grew, we simply dealt with these.

In May 2012, Lucy began doing some odd shrugging movements. Again, they were unlike anything we had ever seen, so we reported them to her neurologist, who had us bring her in for a 48-hour video EEG. It didn't capture the movement, and she stopped doing it after a while. We also took her to see a developmental pediatrician because we were having some concerns about her. When he looked at the "shrugging" on video, he said it was possibly a form of dystonic posturing. He also diagnosed Lucy with hypotonia (low muscle tone), and sent us to genetics for testing, just to double-check a suspicion of his.

Around this time, we found a wonderful neurologist in Richmond, who's been taking excellent care of Lucy since then. Lucy had two prolonged seizures in August 2012 which were precipitated by fevers, and both needed Diastat and required trips to the emergency room. This became a trend – we simply couldn't get back in control of her seizures.

September 14, 2012, Lucy had her first episode of status epilepticus (SE is a life-threatening medical emergency). This seizure lasted two hours, and we can identify no trigger. In November, she got sick and had another seizure, during which she probably aspirated some fluid. In December she had a second episode of SE and was admitted to our local hospital with pneumonia. Later that afternoon she went into SE again and was medflighted to VCU hospital, where the next day she had her fourth status. We were there for nine days, and she spent most of that time on a ventilator. On December 21, a kind nurse helped me hold my daughter while she was still on the vent. It was the first time she'd been in my arms in over a week. While I was looking at her still face, with the tubes

coming out of her nose and mouth, listening to the machine breathe for her, my cell phone rang. I thought about ignoring it, but since it was a hospital number, I answered. It was our genetics counselor – Lucy had tested positive for an SCN1A mutation. She had Dravet Syndrome, a catastrophic epilepsy condition marked by difficult to control seizures, developmental delays, and a 20% mortality rate. We had our answers – and we had the most devastating news.

January of 2013 was, in many ways, a repeat of December – Lucy got RSV and went into SE. She was medflighted to the university hospital and we were there for a week, during which time she had yet another episode of SE. At this point, we knew that daycare and possibly other children were too much a danger for her and made some changes to make it possible for her to be safe and at home more.

Lucy continues to have seizures, and her development is a challenge. She receives a lot of therapy, and because of that therapy she can frequently regain what she loses, though a major seizure can take it away again. The dystonia is still a problem, but we can't treat it without putting undue stress on her heart, which will place her at an even higher risk for SUDEP (Sudden Unexpected Death in Epilepsy). She has many different kinds of seizures, and new seizure types develop nearly every 6-8 months. When she has a convulsive seizure, she nearly always goes into Status Epilepticus. Our local emergency squad's "Lucy Protocol" includes alerting a helicopter to be on standby.

Now she's on really high (adult) doses on both of her anti-seizure medications, one of which is a benzodiazepine and the other which is not FDA-approved for use in children, and uses an adult dose of valium as an at-home rescue drug for prolonged seizures. It rarely stops them. She's also dealing with the side effects from those, which include a total loss of appetite (we've had to add another prescription medication to stimulate her appetite), dizziness, sleepiness, rage, psychosis, mania, extreme lethargy, inability to regulate body temperature or sweat, and hair loss.

Dravet Syndrome is marching on – and despite all of this, Lucy remains loving, affectionate, funny, and sensitive. She's still a beautiful, bright light – but she deserves a better quality of life. I believe she can get it from medical marijuana. I know that the pharmaceuticals she takes keep changing her.

When I was with in the PICU, and the EEG was showing continuous seizure activity, I would have done anything to hear her say "mama" again. To giggle again. To open her eyes. I would do anything to protect her, but I don't want to have to move away from the doctors she loves and knows, and who love and know her; from the community here that support us and love us, in order to seek the treatment that will give her more time.
Please, please help me keep her with me.

Sincerely,
Melissa Crowder Rhoden
Melissa Crowder Rhoden
Lucy's Mom

www.vaparents4mmj.org
Virginia

P. S. Lucy's giggle is infectious. You're welcome to experience it anytime – whether you'd like us to come to you, or you'd like to visit us in Staunton or our hospital room.

Tatyana Rivera

The Honorable Eric Holder
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 29, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

Tatyana Angelique Rivera was born January 17, 2007. She was full term and was completely healthy. She was meeting all of her milestones: holding her head up, rolling over, sitting up on her own and crawling. This all changed when she hit 10 months, when she had her first Grand mal seizure.

Tatyana's first hospital stay would be one of many. She would have about 25 seizures by lunch time and has been recorded on EEG's (Electroencephalogram) up to over 300 in a 24 hour period. Leaving her in a comatose and bed ridden state.

Tatyana was diagnosed with Lennox Gastaut Syndrome. Which is a difficult-to-treat form of childhood-onset epilepsy. This condition is often accompanied by developmental delay, psychological and behavioral problems. Mortality rates ranges from 8.5 to 9.7 years. Deaths are often related to accidents caused by seizure activity.

Over the past 7 years we have been fighting for the survival of our only child. She's been on several anti-seizure medications: Keppra, Dilantin, Depakote, Banzel. She has also been on Corticosteroids as well. All of these drugs has had bad side effects on my daughter. Her memory, attention span, thinking cognitive, sleeplessness, weight loss, weight gain, extreme irritability. These meds have also caused tooth decay, resulting in surgical dental restoration. If these medications are doing this to her healthy teeth then imagine what they are doing to her organs and soft tissue.

With my little girls life expectancy this is no quality of life, not for her or anyone else for that matter.

Medicinal Marijuana has been proven to provide children like Tatyana (aka Tuffy) a chance at a better

quality of life. There are children that have been deemed worse than Tuffy, that are actually going down to 0 seizures being on this miracle drug. With over 25 different combinations of drugs which resulted in not helping the seizure activity. My question is why can't she try one more drug that could possibly save her life? Please reschedule marijuana for our future's sake.

Sincerely,

Ricardo Rivera
New Jersey

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

My nine-year-old son Mason was diagnosed with Lissencephaly (smooth brain) at 2 ½ months old when he began having seizures. Since then I have watched him struggle daily with multiple seizures, I have watched him turn blue and struggle to breathe, and I have watched him sleep for hours on end only to wake up, have another seizure and go back into seizure-induced sleep. We have tried 16 different seizure medications or combinations thereof. He has been on the Ketogenic diet and had a Vagus Nerve Stimulator (VNS) implanted, all in attempt to control his seizures and allow him a better quality of life where he can be allowed to participate in daily activity and not continually lose any progress gained.

With every medication change we have to weigh the benefits: "what are the risks?", "will the medications cause more damage than the seizures?", "will they cause him to sleep all day and not enjoy life?" As parents these decisions are heart-wrenching but we will always choose quality of life over length of life. Currently, Mason is on four seizure medications that he takes twice a day and his seizures remain to be a daily occurrence. When we were in Arizona, we were working with a doctor to obtain medical marijuana, but we had to move due to my husband's military service and lost our opportunity.

The possible side effects of these medications include, but are not limited to: vision loss, rashes, nausea, permanent cognitive impairment, behavior changes, headaches, fatigue, dizziness, abdominal cramps, appetite change, hair loss, swollen gums, nausea, tremulousness, poor coordination, muscle weakness, constipation, diarrhea, swelling, skin discoloration and liver damage/failure. After receiving this concoction of "Schedule III" drugs you can watch his body weaken, his eyes droop and he will lose the ability to focus and track. Within a half hour he will fall asleep for a couple of hours or more.

Medical Marijuana is safer for his body than any one of his medications and will not result in any of the side effects of his current medications. Cannabis has been proven over and over again to have significant benefits for treating seizure disorders in children with multiple diagnoses,

including that of my son's. Considering Marijuana to have no medicinal benefit and classified with drugs such as Heroin, LSD, and Meth is beyond irrational and irresponsible. How can marijuana be considered as one of "the most dangerous drugs of all?" Having this classification is keeping a lifesaving medicinal drug, with minimal side effects, from those who so desperately need it.

Sincerely,

Sarah Robinson
Maryland

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:

I'm writing to you on behalf of my daughter, Haley Smith. Haley came into this world on August 20, 2000. It was an easy, healthy pregnancy and uneventful birth. Haley developed normally and was a happy little baby. However, on January 29th, 2001 around 5:00pm, the lives we knew changed forever. Haley had a seizure. My husband and I rushed her to our local ER which was about eight minutes away from our home. They ER team brought us back right away and started to work on Haley. The seizure continued for over 25 minutes and was stopped only by administering IV Ativan. Once the convulsions stopped the ER team ran numerous tests on our baby. Fortunately our pediatrician happened to be in the ER too and helped answer our questions. We were told the seizure was probably febrile due to an ear infection. We were also told it was unusual for an infant to have a febrile seizure that lasted that long. We left in the pre-dawn hours and went home with the thought this was an isolated incident that should not happen again.

Unfortunately, it did. Haley continued to have seizure after seizure, and after a very long road in which we tried many different drugs and medical diets, Haley was diagnosed with Dravet Syndrome in 2007. In the years since our diagnosis, we have seen some more regression in her fine motor skills. She is unable to draw shapes and she still writes her names as she did when she was two. She receives weekly therapies in Speech, Occupational, and Physical therapies, as well as attending therapeutic horseback riding.

Her ability to get around has been greatly hindered over the years. She is unable to walk far distances and has a wheelchair for

outings. She has tried orthotics for the severe pronation of her feet, but they have not stopped the progression. She has also had surgery on both feet to reconstruct an arch to create stability. The surgery was successful in helping her have better balance, but as she ages we are seeing the collapse of her feet again. There is a more invasive surgery that we could try if she begins to fall more regularly, which we are beginning to see.

Her seizures have migrated to being almost all nocturnal or anytime when she falls asleep. This began about age 6-7 years. We had fairly good control (which is a relative term) until 2012-13. In the summer of 2012, we saw the beginning of severe clusters of seizures coming back and the rescue drugs did not stop them. In January and February 2013, Haley was hospitalized four times due to the clusters. Her neurologist finally prescribed Versed as a rescue drug that we would be able to administer at home via intramuscular injection. During one cluster series we gave her 20 mg of Diastat and she continued to seize. We then gave her 5mg Versed and took her to the ER. She continued to seize there and the ER doctor administered 4 mg of Ativan. The seizures persisted and he had to give her two more doses of Ativan for a total of 12 mg of Ativan prior to us being transported by ambulance to MCV. Upon arrival at MCV, Haley had a few more seizures which were finally stopped by a bolus of Keppra. The amount of medication she received and still seized was remarkable. It could very well put a few full-grown adults on their bottoms. For us this was very scary and we needed to find another option to help control the seizures.

In May 2013, we took Haley to MCV to have a Vagus Nerve Stimulator (VNS) implanted. This device is implanted in her armpit region and has electrode from the battery pack to her Vagus nerve on the left side of her neck. The surgery was a success and we were able to see at least another form of "rescue" from the seizures. For when Haley had a seizure we were able to swipe the battery pack with a magnet and stop the seizure. However, in July we started to see infection at the wound site. Long story short, the device was infected and after three surgeries to wash out, the surgeons had to remove the device in August. Fortunately, we were able to successfully have it re-implanted in October. It helped us stop some seizures, but Haley's seizures are truly out of control.

In 2013 Haley experienced over 800 seizures and had eight hospitalizations. She has tried over 21 medications or combination of them. In February 2014 we had a neurology visit where we received some devastating news. We had her Vagus Nerve Stimulator upped to its highest setting and then were told there is nothing left for her to try. At the age of 13 years old Haley has exhausted ALL treatments that are "legal" for her condition, which actually is not an accurate statement in that there is no "treatment" for Dravet syndrome. ALL the medications she has been on with the exception of the Stiripentol, a non-FDA approved medication, have been

used "off-label," meaning they are NOT meant to be prescribed for Dravet syndrome. Haley's present neurologist, Dr. Larry Morton, did suggest that he might try Fycompa for Haley.

Fycompa's side effects state: "serious or life-threatening psychiatric and behavioral adverse reactions including aggression, hostility, irritability, anger, and homicidal ideation and threats have been reported in patients taking Fycompa". I quickly said "NO" to ever trying this drug. Presently there are a number of families that have volunteered their children to be a "guinea pig" for Dravet using a form of Medical Marijuana called "Charlotte's Web", named after Charlotte Figi, a child with Dravet syndrome. These children are having remarkable results in seizure control and increased cognition. Overall their lives are improved.

We are asking that you would consider helping Haley and our family to have an increase in quality of life. Haley recently suffered over 60 seizures in ONE night. We accept the fact that Haley might always have seizures, but 60 seizures in one night is not acceptable. The only thing stopping Haley's ability to get the medication that can help her is our zip code.
Moving sounds like an easy solution, but it is not as simple as it seems. My husband is self-employed and starting over at 50 years old is not a great option. If we did move we would have to split the family. That is not fair to deprive my three kids of a two-parent household. Not to mention the fact the financial strain, we would have to have a mortgage payment and a rental payment. We also would lose our support system that consists of a wide medical community of neurologists, pediatricians, gynecologist, orthopedist, ENT doctor, speech therapist, occupational therapist, physical therapists, caregivers, religious support, and friends. We would have to uproot and leave all them behind. The bittersweet part is that IF the medical marijuana works, Haley could NEVER leave Colorado and either could the parent that went with her. We have never left her to this day overnight with anyone. Imagine, if one of my parents pass away, I could not leave and be with my family. That is not "freedom." That is not what America is about.

Haley continues to be a happy young lady. She is blissfully ignorant of her condition and knows nothing but love. She has taught us so much about what truly is important in life. Our goal is to make her life, how long she lives, enjoyable. Presently, she cannot attend school due to her severe seizures. Her neurologist classifies her seizures as "life threatening." It is our goal to find something to bring relief to her condition.

Please know that this is not an issue that I have entered into lightly. The risk/benefit has been considered. What would you do IF this was your child and were told there is NOTHING left…that is legal?

Thank you for your time.

Sincerely,

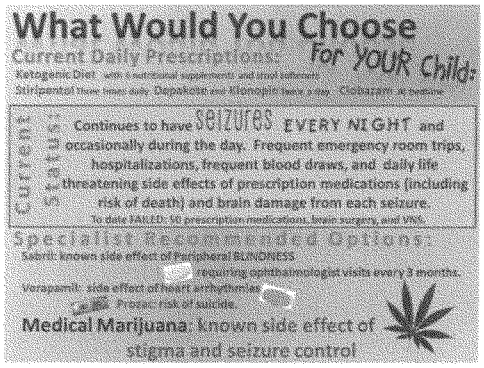
Lisa Smith
Virginia

The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

Dear Mr. Attorney General:



Cannabis is controversial, but it is medication and it is the only medication which has worked in the 14 years my son has been alive. It is the first time he has had a quality of life and the ability to grow and learn without being medically addicted to narcotics. I get asked by many, "Are you afraid of cannabis because the FDA has not approved it?" My honest answer is that my son has been on 50+ combinations of medication beginning at the age of 4 months old. None have been FDA-approved for children under 12 years old. I already considered this situation when my son was 4 months old and placed on phenobarbital, a powerful and mind-altering narcotic. The cannabis plant profile has such a lower harm profile that it is safer than Tylenol. As a pediatric registered nurse, I am confident in using this medication. When cannabis is used properly with the guidance and direction of a physician willing to learn about the human endocannabinoid system and the application of cannabis, the healing potential is huge and compassionate.

Here is our story:
Jackson "Jaxs" is a 14-year-old with Dravet Syndrome. He has suffered with relentless, changing, and prolonged seizures since he was 4 months old. Since 1999, Jaxs he has failed over 50 mono/poly pharmacological combination of prescription medications, 2 brain surgeries in 2008, a Vagus Nerve Stimulator in 2005 and 2012 (battery replacement), and restrictive, nutritionally incomplete diet treatment without success. We have grasped at any hope of treatment, including importing a Non-FDA approved medication from France (stiripentol) which is the only medication known to treat Dravet Syndrome. That medication stopped working soon enough with unbearable side effects such as gastrointestinal upset and anorexia, muscle wasting, and rapid weight loss of 11 lbs in 2 weeks. The side effects of the other drugs Jaxs has taken include aggression, self-abuse, severe behaviors, increased seizures, insomnia, blood disorders, and death: all of these are listed side-effects from the FDA approved drugs.

In October 2012 Jaxs had a Video EEG (VEEG) completed which was typical for him at this point in time with multiple spike waves and slowing every second. He was having about 10+ seizures every night once he fell asleep.

In November 2012 Jaxs started on cannabis high in cannabidol (CBD) and low in tetrahydrocannabinol (THC). He did remarkably well. He was able to be weaned off of the phenobarbital which he was medically addicted to and been weaning for 3 years. He went from 120mg of phenobarbitol three years ago to 75 mg and weaning with cannabis. Four months later, he was successfully weaned from the phenobarbital and his seizure control improved. His school noticed immediately his ability to pay attention to the task at hand and to concentrate unlike before. His vocabulary and language skills increased tremendously and he was learning, participating, and engaged in his world.

While on the high CBD cannabis he was hospitalized with another VEEG in January 2013. The epileptologist was surprised to see the huge improvements in background activity with literally a normal background with an occasional spike wave.

There seem to be plateaus or withdrawal symptoms which require more CBD, THC or even THCa (non-psychoactive acid form of THC). In February 2014, He was still recovering from the benzodiazepine withdrawal and seemed to be suffering from doses that were too high of other pharmaceuticals. Jaxs's cannabis treatment course added the inactivated form of THC, as THCa and the improvement were immediate. The week prior Jaxs could not throw a basketball more than 2 feet in front of himself with the Parkinson-like tremors he was suffering from. 5 days after beginning the THCa, he was launching the ball across the living room into the hallway. Just last month he was outside throwing basketballs into the basket almost every attempt.
To date, Jaxs is no longer on

- Phenobarbital ($45/mo)
- Klonopin ($51/mo)
- Clobazam ($601/mo)
- Stiripentol ($1700/mo)
- Banzel ($950/mo)
- Ketogenic Diet and 6 nutritional supplements ($300/mo)
- Versed Intranasal ($157/mo) average usage
- Diastat Rectal Valium ($3000/mo) average usage

His most recent VEEG (17 months later) now has one spike wave per hour compared to the multiple every second and no slowing. He is on 50% lower dose of Depakote ($99/mo) with cannabis. His seizure control has improved and has not required an emergency rescue medication or hospitalization since November 2013.

At the age of 14, the damage from the ineffective pharmaceuticals, the relentless seizures, the brain surgeries, and other treatments have done their damage. He will not be able to fulfil his potential from when he was born or at the age of 5 when he was beginning the decline in abilities and skills. The question remains: what if prohibition, based on racism and business politics of the 1930's, was not in place when his seizures began in 1999? Could his life have been different? Could he have better seizure control and better learning capacity? That question will never have an answer, but please be aware that my son is the future of these small children who need the appropriate medication from their specialist to adequately care for and treat the diseases which do not age discriminate.

The cost saving to the state of NJ in monthly pharmaceuticals is tremendous, since this cannabis medication is working so effectively and the medications have been weaned and are no longer necessary, including the emergency meds. The discontinued medications alone are greater than $7,000 if you include the decrease in dosing for Depakote. The medical flights, emergency room visits, and hospital admission have ceased to occur with the improved seizure control.

Many challenges exist with the conflict between state and federal rights and laws. **Last week, for the second time since being on cannabis, the hospital attempted to kick Jackson out of the hospital for using his state-permitted cannabis oil in an edible form because of the Schedule I classification.** The other option was to abruptly stop the cannabis medication if he were to stay in the hospital since he was not stable enough to return home. Both of these options are extremely dangerous and both could cause death. Having to choose between lifesaving medication made with cannabis and medical care at a level 4 epilepsy center is not a decision any parent should have to make. Living with a chronic illness is difficult enough without having to make life or death decisions based on policies and prohibition from the 1930's. When I refused to leave and refused to not administer his lifesaving medication, the hospital threatened placing a security guard in the room to ensure he was not given his cannabis which the state of NJ allows with the strictest program in the US. Newspaper coverage of this can be found here: http://www.northjersey.com/news/relief-of-medical-marijuana-off-limits-at-n-j-hospitals-1.1022114?page=all#sthash.ONXyuk8m.dpuf.

Something has to change or more children will die without the proper medication they need. Cannabis is medication and should be allowed for use when needed and compassion is the objective. No child or adult should have to suffer through years of seizures and experimental drugs to control seizures when cannabis is known to effectively treat and offer a quality of life. This includes the whole plant with all the components regardless of the age of the patient. Children grow up and will eventually be adults with the same medical needs with the same medications being required once they are over 18. The age does not make the child un-disabled. The same compassionate medication should continue to be available and offered to all those in need.

Sincerely,

Jennie Stormes, RN

www.JacksonStormes.com ● FB @JaxsCannaJourney ● TW @JacksonStormes

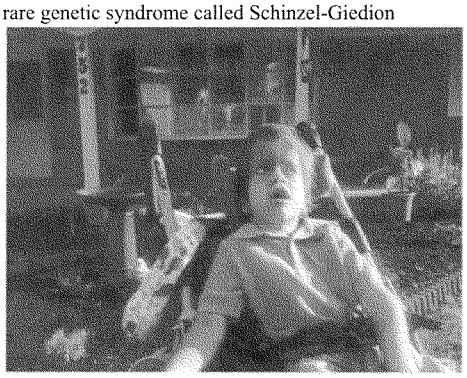
The Honorable Eric Holder
Attorney General of the United States
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

May 27, 2014

Re: Rescheduling Marijuana

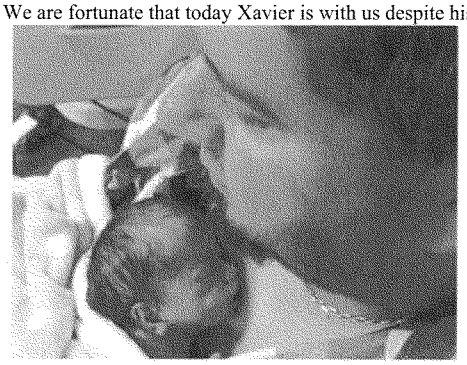
Dear Mr. Attorney General:

Our son, Xavier, is 5 years old. Xavier has a rare genetic syndrome called Schinzel-Giedion Syndrome. He is one of 3 confirmed children in the US, 10 world-wide, and approximately 50 children to *ever* have been diagnosed with this syndrome.



SGS is a random gene mutation and is not something that is inherited or we (the parents) are carriers for. SGS is complex and has a constellation of symptoms. Children with SGS suffer from a severe seizure disorder, severe developmental delay, feeding problems, genitourinary issues, as well as other medical complications. Children with SGS typically do not survive past infancy.

We are fortunate that today Xavier is with us despite his struggles. He cannot walk or talk. He has a feeding tube and is completely dependent for all of his needs. His biggest obstacle is the intractable epilepsy that he has had since birth. Despite pharmaceuticals, his seizures are not controlled and he has multiple seizures daily. His brain is in a constant state of chaos with subclinical seizure activity.

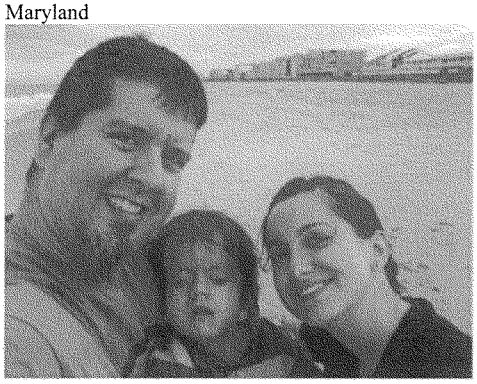


We believe that medical marijuana could hold potential to helping Xavier and other children who fight seizures every single day. Therefore we strongly urge

and support the reclassification of marijuana to a Schedule III or lower substance. This would ease restrictions on researchers and allow them to grasp a better understanding of the potential of marijuana. Please consider this important step forward for the future of our children.

Sincerely,

Adrianne Woods
Maryland



Corrected version 6/11/2014
Added Dr. to Thomas Minahan
Corrected spelling of Marisa Kiser's Name
Corrected home state of Joan Jones to Maryland
Teresa Brogan name corrected to Teresa Elder
Added three letters sent individually to AG Holder after the original send

- Suzanne M. De Gregorio
- Wrayanne Leslie
- Ricardo Rivera

Ms. Elizabeth Collins
Statement for the Record
Subcommittee on Government Operations
Committee on Oversight and Government Reform
Mixed Signals: the Administration's Policy on Marijuana, Part Four – the Health Effects and Science
June 20, 2014

Chairman Mica and Ranking Member Connolly, thank you for holding today's hearing examining the administration's policy on marijuana.

I am Beth Collins, wife of Patrick Collins, mother of Alexandra, 16 and Jennifer, 14. I work as a training manager, and hold a Master's Degree in Education. I am also becoming an epilepsy and medical marijuana expert and advocate. That is why I am submitting this testimony to you today.

There are over three million Americans with epilepsy. Approximately one million of those have seizures that are not controlled by the pharmaceuticals, medical diets, and surgeries available in the United States today. My 14-year-old-daughter, Jennifer, falls into this group. Despite her daily regimen of 14 pills, Jennifer still experienced between two and three hundred seizures daily. In addition, the side effects of her medication include suicidal thoughts, rages, a decrease in cognitive functioning, depression, weight gain, and ovarian issues, just to name a few.

Before her current combination of medications, Jennifer failed to respond to 9 different medications as well as a highly restrictive diet. While trying these medications, we witnessed our academically, socially, and athletically successful child decline. The medications she takes make her cognitively slow. She now requires special education services. They also cause her to have erratic behavior and depression, making it difficult for her to form and maintain friendships. They make her uncoordinated and make her have low energy, inhibiting her once strong ability in sports. What's worse, they don't control all of her seizures.

We were told by doctors at John's Hopkins and Children's Medical Center that this was the best they could do. We were out of options. But we would not give up on her. She deserves the opportunity to reach her full God-given potential. So, on December 2, 2013, Jennifer and I, and only Jennifer and I, moved from Fairfax, Virginia to Colorado to try medical marijuana treatment. Like over 100 others, we left our home, my other 16–year-old daughter, my husband, our family, doctors, and friends, to give Jennifer the opportunity to find relief from her seizures and the harmful side-effects of her current medications through medical marijuana.

We are hopeful of finding some relief for her through medical marijuana. However, if it works for her, because medical marijuana is a schedule one drug, she will be unable to leave the state.

To say the least, this has been a difficult and painful decision. And, quite frankly, one that we feel we shouldn't have had to make. Jennifer asks daily to go home. She misses her father and sister. She misses her friends and teachers. She is afraid the new medicine will work, and she will be forced to live here.

Jennifer's medication, administered as an oil under her tongue, is called THCa, an inactive form of THC, so it has no psychoactive effect. However, it is scheduled the same as heroin. Marinol, a synthetic form of THC, is schedule three. Marinol is used to help control pain and nausea for cancer patients; but it does not help with seizures.

We are currently seeing a significant decrease in Jennifer's seizures. Her neurologist here in Colorado, who is very supportive of this treatment, feels that in the next few months she may be ready to start weaning from the heavy pharmaceuticals that are causing her physical, cognitive, and emotional damage. I am witnessing a great deal of success with other epilepsy cases using various cannabis extracts here in Colorado. Of the approximately 200 pediatric patients using cannabis oil from the Realm of Caring™ in Colorado, approximately 78% show a reduction in seizures. Of that 78%, approximately 25% have had a greater than 90% reduction in seizures or are seizure free. Most of these patients have also exhibited a significant increase in cognition.

Rescheduling marijuana to a schedule three drug or lower would enable Jennifer to leave the state of Colorado for visits home to her friends and family. It would also allow doctors to begin studies on the efficacy of marijuana in pediatric epilepsy. While Jennifer's neurologist here is supportive, he is unable to provide us with advice on dosing and compile his findings and observations into usable research as this is against Federal law. I and the other parents here are nervous about making these decisions with very little input from our children's doctors. We'd really like the guidance of our physicians, because this is a serious medical concern with serious ramifications. Current Federal law prohibits us from receiving this guidance.

The United States Controlled Substances Act states that in order for a substance to be classified as schedule one, "The drug or other substance has no currently accepted medical use in treatment in the United States." There are thousands of studies showing medical marijuana's efficacy in treating numerous illnesses. In fact, the Federal Government currently grows and distributes marijuana to four patients, all with different ailments, through the Compassionate Investigational New Drug Program. The disconnect between state laws and Federal laws needs to be rectified. Even in states like Colorado, where medical marijuana is legal, patients run into difficulties when trying to administer medical marijuana to their children in hospitals. In many cases, they have been reported to social services when they've tried to do so.

There are so many children in this country who need this medication. For some, it truly is a life or death issue. I am constantly receiving emails and talking to parents whose children are potentially one seizure away from death. Children are dying while waiting for this medicine.

For the 1 million people living with epilepsy that is not controlled by pharmaceuticals, this is truly a last hope. For Jennifer, it has been a miracle, and a curse. I assure you, after 5 months on medical marijuana, Jennifer is doing much better and has experienced no harmful side effects. I cannot say this for ANY of the pharmaceuticals she has been on during the course of her illness. Despite this good news, Jennifer is having a very difficult time emotionally. She wants to go home, and that is the curse of medical marijuana for her – she is stuck in Colorado

I urge you to reschedule marijuana to schedule three. Families like ours should not be forced to make a choice between home and their children's health. Jennifer has said, "I would rather have the seizures, and have my dad and sister and friends every day."

Is this really her only option?

Thank you,

Beth Collins

Congress of the United States
Washington, DC 20515

June 17, 2014

The Honorable Sylvia Mathews Burwell, Secretary
Department of Health and Human Services
200 Independence Ave. SW
Washington, D.C. 20201

Dear Secretary Burwell,

We write to express our support for increasing scientific research on the therapeutic risks and benefits of marijuana. We ask that you take measures to ensure that any non-National Institutes of Health (NIH) funded researcher who has acquired necessary Food and Drug Administration (FDA), Institutional Review Board (IRB), Drug Enforcement Administration (DEA) and appropriate state and local authority approval be able to access marijuana for research at-cost without further review.

Twenty-two states and the District of Columbia have passed laws allowing for the use of medical marijuana. Over one million Americans currently use medical marijuana at the recommendation of their physician. There is overwhelming anecdotal evidence from patients, their family members, and their doctors of the therapeutic benefits of marijuana for those suffering from cancer, epilepsy, seizures, Post-Traumatic Stress Disorder, glaucoma, anxiety, chronic pain, and more.

We believe the widespread use of medical marijuana should necessitate research into what specific relief it offers and how it can best be delivered for different people and different conditions. Yet, the scientific research clearly documenting these benefits has often been hampered by federal barriers.

Researchers seeking to develop prescription drugs in the United States must go through FDA and IRB approval processes. To conduct research using Schedule I substances such as marijuana, LSD, psilocybin and MDMA, researchers must also seek a DEA registration, as well as any required state and local licenses. The review process required to gain these approvals is robust and ensures that researchers are weighing the risks as well as the possible benefits of their potential medications.

Only with marijuana, and no other Schedule I substances, is there an additional Public Health Service review for non NIH-funded protocols, established in the May 21, 1999, Department of Health and Human Services (HHS) "Guidance on Procedures for the Provision of Marijuana for Medical Research[1]." This review process grants access to the only source of marijuana that can

[1] Guidance on Procedures for the Provision of Marijuana for Medical Research: http://grants.nih.gov/grants/guide/notice-files/not99-091.html

PRINTED ON RECYCLED PAPER

be legally used for research – grown by the University of Mississippi under contract with the National Institute on Drug Abuse (NIDA).

In light of the fact that substances like opioids and barbiturates have been researched and developed for human use, it would seem that we should investigate the legitimate medical uses of marijuana. We request that you review and revise the HHS Guidance to eliminate what we believe to be an unnecessary additional review process. NIDA should provide marijuana at-cost to all non-NIH funded marijuana research protocols that have successfully obtained necessary FDA, DEA, IRB and appropriate state and local authority approval.

Considering the number of states with medical marijuana laws and the number of patients who use marijuana medicinally in the United States, it is clear that we need more scientific information about the therapeutic risks and benefits of marijuana.

Thank you for your attention to this request, and we look forward to your response.

Sincerely,

Earl Blumenauer
Member of Congress

H. Morgan Griffith
Member of Congress

Dana Rohrabacher
Member of Congress

Jan Schakowsky
Member of Congress

Dan Benishek
Member of Congress

Julia Brownley
Member of Congress

Matt Cartwright
Member of Congress

William Lacy Clay
Member of Congress

Steve Cohen
Member of Congress

John Conyers
Member of Congress

Diana DeGette
Member of Congress

Sam Farr
Member of Congress

Raul Grijalva
Member of Congress

Alan Grayson
Member of Congress

Jared Huffman
Member of Congress

James R. Langevin
Member of Congress

Barbara Lee
Member of Congress

Alan Lowenthal
Member of Congress

Michelle Lujan Grisham
Member of Congress

Thomas Massie
Member of Congress

George Miller
Member of Congress

James P. McGovern
Member of Congress

James P. Moran
Member of Congress

Beto O'Rourke
Member of Congress

Chellie Pingree
Member of Congress

Mark Pocan
Member of Congress

Jared Polis
Member of Congress

Eric Swalwell
Member of Congress

Dina Titus
Member of Congress

Peter Welch
Member of Congress

Questions for the Record for
Nora D. Volkow, M.D.
Director, National Institute on Drug Abuse
"Scientific Focus on the Adverse Health Effects of Marijuana Use"
House Committee on Oversight and Government Reform
Subcommittee on Government Operations
June 20, 2014

Rep. Earl Blumenauer

1. During the hearing on Friday, June 20th, I submitted a letter for the record that I, along with 29 of my colleagues, recently sent to Department of Health and Human Services (HHS) Secretary Burwell, requesting the removal of the HHS review process that grants access to marijuana for research, established in the May 21, 1999 HHS "Guidance on Procedures for the Provision of Marijuana for Medical Research." The Food and Drug Administration (FDA) is required to review research protocols for new drug applications. Why is it necessary for there to be an additional HHS review process for non-National Institutes of Health funded researchers, which grants access to marijuana under the control of the National Institute on Drug Abuse (NIDA)? This is unique to marijuana and an additional step for researchers to go through. Has there been any consideration of eliminating this additional step?

Answer: This issue is outside the scope of the mission of the National Institute on Drug Abuse.

2. Why is it necessary for NIDA to hold a monopoly on marijuana grown for research purposes?

Answer: Articles 23 and 28 of the Single Convention on Narcotic Drugs[1] (the "Single Convention") – an international narcotics control treaty to which the United States is a party – specify the "system of controls" to be applied when a country permits the cultivation of the cannabis plant. Among other things, this "system of controls" stipulates the establishment and maintenance of "one or more government agencies to carry out the functions" listed in Article 23, which applies to cannabis cultivation as provided in Article 28. Article 23 of the Single Convention also states that "only cultivators licensed by the agency shall be authorized to engage in ... cultivation."

Through the Controlled Substances Act, the Attorney General has authority to regulate manufacturing, distribution, and dispensing of controlled substances. The U.S. Drug

[1] http://www.unodc.org/pdf/convention_1961_en.pdf (PDF, 680kb).

Enforcement Administration (DEA) oversees the implementing regulations for the Controlled Substances Act.

DEA has determined that the United States meets its obligations under the Single Convention with respect to marijuana cultivation through the actions of two agencies: DEA and NIDA. With respect to NIDA, it currently oversees the cultivation of research-grade marijuana on behalf of the United States Government.

3. Is the HHS review process that grants access to NIDA marijuana subject to any response-time requirements? The FDA is required to respond in writing to an Investigational New Drug (IND) sponsor within 30 calendar days of receipt of the sponsor's request. On average, how long does it take for the HHS reviewers to respond to a non-NIH funded researcher who applies to use NIDA marijuana?

Answer: This issue is outside the scope of the mission of the National Institute on Drug Abuse.

4. In 2007, Drug Enforcement Agency (DEA) Administrative Law Judge, Mary Ellen Bittner, found the existing supply of marijuana made available by NIDA for research to be inadequate, but DEA rejected that finding. Over one million people use marijuana medically in accordance with state law, and it is imperative that we understand how it is helping people and how it can best be delivered. Can NIDA guarantee an adequate supply of marijuana, in whatever strain a researcher wishes to use, to approved researchers? How quickly can it be made available and at what cost?

Answer: NIDA contracts with the University of Mississippi to cultivate, harvest, process and distribute marijuana under controlled and secure conditions. The contractor maintains a secure and DEA approved facility with the capacity to grow up to 12 acres of plants. However, the actual production is dependent upon demand, availability of funds, and approval of DEA. DEA is responsible for establishing the aggregate production quota of marijuana that may be produced each calendar year.

The base costs for running the facility is approximately $850,000. This covers the current small-scale indoor cultivation, processing, and testing of marijuana for research. The contract can also support growing outside at an additional cost of approximately $400,000 per 1.5 acres or $570,000 per 6 acres. This cost does not include the additional costs that would be required for storage, processing, testing, or distribution. The total costs would be dependent upon the specific requirements necessary to support the research. To exercise this contract option NIDA would need to notify the University of Mississippi by March of a given year to initiate spring

planting for harvest in the fall of that year. Assuming DEA approvals and regulatory requirements are in place and sufficient funds are available NIDA would be able to support the cultivation of up to 12 acres of plants each year. All costs related to this effort compete with other NIDA priorities for our research funding.

5. During the hearing, the subject of GW Pharmaceuticals Phase III clinical trials on Sativex was raised. This has been used as an example of FDA-approved drug development research on cannabinoids being conducted in the United States. However, GW Pharmaceuticals is a British company and the marijuana was grown in Britain by GW Pharmaceuticals. Is any marijuana, or derivative or marijuana, grown in the United States being used in any Phase III trial?

Answer: There are no Phase 3 Clinical Trials of marijuana or marijuana-derived products funded by NIH currently underway; however, other private companies located inside and outside of the U.S. are continuing research in this area. Details on some clinical trials of marijuana or marijuana-derived products can be found at ClinicalTrials.gov.[2] The advance search feature allows users to focus specifically on Phase 3 Clinical Trials and any intervention of interest under investigation.

6. If a researcher used NIDA marijuana for Phase III trials and the product was approved, would it be possible for that product to make it to market, considering that NIDA is only authorized to grow marijuana for research but not for commercial sale?

Answer: It is beyond the scope of NIDA's mission to manufacture marketable medicinal products. Under the Controlled Substances Act, marijuana is a Schedule I controlled substance. Schedule I substances have a high potential for abuse, no currently accepted medical use in the United States, and lack accepted safety for use under medical supervision. If an NDA for marijuana or a marijuana-derived drug product is approved by FDA, then FDA and DEA could be asked to revisit the scheduling of marijuana or the marijuana-derived product. The requirements applicable to marketing the drug would be dependent upon the scheduling of the substance under the Controlled Substances Act, and in addition would include any statutory and regulatory provisions applicable to the production, marketing, and distribution of drug products.

[2] http://clinicaltrials.gov/.

Rep. John Fleming

1. During the course of the hearing, the question about NIDA's role in approving and/or permitting marijuana research and providing marijuana for an approved study was raised more than once. Can you explain NIDA's role in approving marijuana research and NIDA's role in providing marijuana for an approved study? Please also explain the interaction and impact of both federal law and international treaty on NIDA's role.

Answer: NIDA supports a drug supply program, which provides controlled substances, including research-grade marijuana, to researchers for scientific purposes. The marijuana supply program operates pursuant to the Single Convention on Narcotic Drugs[3] (the "Single Convention"), which, among other things, requires each party-nation to designate one or more government agencies to oversee the cultivation of marijuana.

DEA has determined that the United States meets its obligations under the Single Convention with respect to marijuana cultivation through the actions of two agencies: DEA and NIDA. With respect to NIDA, it currently oversees the cultivation of research-grade marijuana on behalf of the United States Government and, to that end, contracts with the University of Mississippi to grow marijuana for use in research studies. The University designates a secure plot of land where marijuana crops are grown as needed based on demand. The marijuana is grown, harvested, stored, and made into cigarettes or other purified elements of marijuana to use for research.

To obtain research-grade marijuana through the NIDA drug supply program, all applicants must fulfill the following three requirements:

1. Demonstrate scientific validity and ethical soundness:
   a. For NIH-funded projects – through NIH peer review, consisting of three steps: (1) the NIH peer-review system, which assesses the scientific and technical merit of all grant applications; (2) the Institute's National Advisory Council, comprising eminent scientists as well as public members from the community; and (3) the Institute Director, who makes the final decision on the merit of an application for funding, based on peer review, public health significance, and Institute priorities.
   b. For studies not funded by NIH – through a scientific-review panel of staff from across the Department of Health and Human Services (HHS) with expertise relevant to the research being proposed. The final decision as to whether or not to approve a proposal is based on the consensus of the experts on the review committee.

[3] http://www.unodc.org/pdf/convention_1961_en.pdf (PDF, 680kb)

2. An Investigational New Drug application on file with FDA (for human research only); and

3. A DEA registration for a Schedule I controlled substance.

When the above steps have been completed, investigators then contact the NIDA Drug Supply Program to place an order for marijuana with specific THC concentrations. The program official verifies that the application is complete (with all the above-mentioned steps fulfilled), and forwards the order on to the contractor responsible for shipping the marijuana.

2. Please provide a list for the types of marijuana research NIDA funds. Does NIDA allow and/or fund studies on potential therapeutic benefits of marijuana or its components?

Answer: NIDA funds a wide range of research on both adverse effects and potential therapeutic effects of marijuana (cannabis); its main psychoactive ingredient, delta-9-tetrahydrocannabinol (THC); and chemicals related to THC (cannabinoids),[4] including:

- Patterns and trends in marijuana use and attitudes, particularly among adolescents
- Short- and medium-term effects of THC on the brain and behavior
- Driving under the influence of cannabis
- Long-term effects of prenatal and adolescent cannabis exposure on brain development
- The development and impact of prevention programs on marijuana use
- Screening and brief assessment for marijuana abuse
- Medications and behavioral treatments for cannabis use disorder
- The working of the brain's cannabinoid system, including its role in pain and HIV
- Potential therapeutic uses of THC and other cannabinoids in treatment of pain, HIV, and addiction
- Social, behavioral, and public-health impacts of policy changes related to marijuana (*e.g.*, "medical marijuana" and recreational legalization)

[4] See http://www.drugabuse.gov/drugs-abuse/marijuana/marijuana-research-nida.

Research suggests that THC and/or other cannabinoids (chemicals that act on the same receptors as THC in the brain and body) may have potential in the treatment of pain, nausea, obesity, wasting disease, addiction, autoimmune disorders, and other conditions. NIDA, as well as other NIH institutes, funds studies on the potential therapeutic benefits of marijuana and its constituent chemicals.[5]

3. Can you explain the roles and responsibilities of the FDA, NIDA, DEA and other relevant federal agencies when it comes to marijuana research for medicinal purposes or health effects under the Controlled Substances Act?

Answer: NIDA, along with several other institutes of the NIH support research studies on the adverse effects and possible therapeutic uses of marijuana and its constituent cannabinoid chemicals. NIDA supports a drug supply program, which provides controlled substances, including research-grade marijuana, to researchers for scientific purposes. The marijuana supply program operates pursuant to the Single Convention on Narcotic Drugs[6] (the "Single Convention"), which, among other things, requires each party-Nation to designate one or more government agencies to oversee the cultivation of marijuana.

Pursuant to the Single Convention on Narcotic Drugs, and the DEA's implementation of the Controlled Substances Act, NIDA is responsible for overseeing cultivation of marijuana for research.

To obtain research-grade marijuana through the NIDA drug supply program, all applicants must fulfill the following three requirements:

4. Demonstrate scientific validity and ethical soundness:
   c. For NIH-funded projects – through NIH peer review, consisting of three steps: (1) the NIH peer review system, which assesses the scientific and technical merit of all grant applications; (2) the Institute's National Advisory Council, comprising eminent scientists as well as public members from the community; and (3) the Institute Director, who makes the final decision on the merit of an application for funding, based on peer review, public health significance, and Institute priorities.

[5] A list of current NIDA-funded projects related to the potential therapeutic benefits of cannabis or cannabinoids can be viewed at http://www.drugabuse.gov/drugs-abuse/marijuana/nida-research-therapeutic-benefits-cannabis-cannabinoids.

[6] http://www.unodc.org/pdf/convention_1961_en.pdf (PDF, 680kb)

d. For studies not funded by NIH – through a scientific-review panel of staff from across HHS with expertise relevant to the research being proposed. The final decision as to whether or not to approve a proposal is based on the consensus of the experts on the review committee.

5. An Investigational New Drug application on file with FDA (for human research only); and

6. A DEA registration for a Schedule I controlled substance.

When the above steps have been completed, investigators then contact the NIDA Drug Supply Program to place an order for marijuana with specific THC concentrations. The program official verifies that the application is complete (with all the above-mentioned steps fulfilled), and forwards the order on to the contractor responsible for shipping the marijuana.

SEP 0 5 2014

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

The Honorable Darrell Issa
Chairman
Committee on Oversight and Government Reform
House of Representatives
Washington, D.C. 20515-6143

SEP 0 3 2014

Dear Mr. Chairman:

Thank you for providing the Food and Drug Administration (FDA or the Agency) with the opportunity to testify at the June 20, 2014, hearing entitled "Mixed Signals: The Administration's Policy on Marijuana, Part 4 – the Health Effects and Science," before the Subcommittee on Government Operations, Committee on Oversight and Government Reform. This letter is a response for the record to questions posed by Representatives Earl Blumenauer and John Fleming in both of your letters, dated June 30, 2014.

If you have further questions, please let us know.

Sincerely,

Thomas A. Kraus
Associate Commissioner
for Legislation

Enclosure

cc: The Honorable Elijah Cummings
Ranking Member

We have restated each Member's questions below in bold type, followed by FDA's responses.

The Honorable Earl Blumenauer

1. **During the hearing on Friday, June 20th, I submitted a letter for the record that I, along with 29 of my colleagues, recently sent to Department of Health and Human Services (HHS) Secretary Burwell, requesting the removal of the HHS review process that grants access to marijuana for research, established in the May 21, 1999 HHS "Guidance on Procedures for the Provision of Marijuana for Medical Research." The Food and Drug Administration (FDA) is required to review research protocols for new drug applications. Why is it necessary for there to be an additional HHS review process for non-National Institutes of Health funded researchers, which grants access to marijuana under the control of the National Institute on Drug Abuse (NIDA)? This is unique to marijuana and an additional step for researchers to go through. Has there been any consideration of eliminating this additional step?**

   Please reference the National Institute on Drug Abuse (NIDA) response to this question.

2. **Why is it necessary for NIDA to hold a monopoly on marijuana grown for research purposes?**

   Please reference the NIDA response to this question.

3. **Is the HHS review process that grants access to NIDA marijuana subject to any response time requirements? The FDA is required to respond in writing to an Investigational New Drug (IND) sponsor within 30 calendar days of receipt of the sponsor's request. On average, how long does it take for the HHS reviewers to respond to a non-NIH funded researcher who applies to use NIDA marijuana?**

   Please reference the NIDA response to this question.

4. **In 2007, Drug Enforcement Agency (DEA) Administrative Law Judge, Mary Ellen Bittner, found the existing supply of marijuana made available by NIDA for research to be inadequate, but DEA rejected that finding. Over one million people use marijuana medically in accordance with state law, and it is imperative that we understand how it is helping people and how it can best be delivered. Can NIDA guarantee an adequate supply of marijuana, in whatever strain a researcher wishes to use, to approved researchers? How quickly can it be made available and at what cost?**

   Please reference the NIDA response to this question.

5. **During the hearing, the subject of GW Pharmaceuticals Phase III clinical trials on Sativex was raised. This has been used as an example of FDA-approved drug development research on cannabinoids being conducted in the United States.**

However, GW Pharmaceuticals is a British company and the marijuana was grown in Britain by GW Pharmaceuticals. Is any marijuana, or derivative or marijuana, grown in the United States being used in any Phase III trial?

Consistent with long-standing Agency policy, FDA does not discuss the substance of matters pending before the Agency, including the contents of any INDs, such as information about Phase III clinical trials.

6. **If a researcher used NIDA marijuana for Phase III trials and the product was approved, would it be possible for that product to make it to market, considering that NIDA is only authorized to grow marijuana for research but not for commercial sale?**

   The Office of National Drug Control Policy (ONDCP) may be able to better address the question as to whether it would be possible for a marijuana drug product to make it to market if FDA approved the product, given the various roles that different agencies play in the regulation of marijuana and its derivatives.[1]

The Honorable John Fleming

1. **Can you explain the roles and responsibilities of the FDA, NIDA, DEA and other relevant federal agencies when it comes to marijuana research for medicinal purposes or health effects under the Controlled Substances Act?**

   FDA plays a critical role, alone and in partnership with other Federal agencies, in supporting the efficient and scientific assessment of marijuana and its constituents to support needed drug development. FDA plays a role in supporting the development of new drugs, including drugs derived from marijuana and its constituents. Schedule I substances, including drugs that are derived from botanical sources such as marijuana, can be and are the subject of clinical trials under the Federal Food, Drug, and Cosmetic Act, provided, among other things, that the sponsor successfully submits an Investigational New Drug (IND) application to FDA. Clinical trials with Schedule I substances are also subject to Drug Enforcement Administration (DEA) registration requirements.[2] FDA is working with researchers, who are conducting studies on the development of new drugs derived from marijuana, meeting with them regularly as they plan and carry out the trials as a part of their INDs. A number of government-funded research projects involving marijuana or its component compounds have been completed or are currently in progress, many of which are listed on the *ClinicalTrials.gov* website.

   To encourage appropriate research into marijuana and its constituents, FDA has also worked with investigators to provide clear information on how to conduct research in this area. To help address common questions about research into marijuana, a number of

---

[1] *http://www.whitehouse.gov/ondcp/frequently-asked-questions-and-facts-about-marijuana#research*

[2] 21 U.S.C. 823(f); *see also* 21 CFR 1301.18 (outlining specific application procedures and information to be provided by Schedule I researcher applicants).

○