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TREATING THE OPIOID EPIDEMIC: THE STATE OF COMPETITION IN THE MARKETS FOR ADDICTION MEDICATION

HEARING

BEFORE THE

SUBCOMMITTEE ON
REGULATORY REFORM,
COMMERCIAL AND ANTITRUST LAW

OF THE

COMMITTEE ON THE JUDICIARY
HOUSE OF REPRESENTATIVES

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TREATING THE OPIOID EPIDEMIC: THE STATE OF COMPETITION IN THE MARKETS FOR ADDICTION MEDICATION

THURSDAY, SEPTEMBER 22, 2016

HOUSE OF REPRESENTATIVES,

SUBCOMMITTEE ON REGULATORY REFORM,
COMMERCIAL AND ANTITRUST LAW

COMMITTEE ON THE JUDICIARY,

Washington, DC.

The Subcommittee met, pursuant to call, at 2 p.m., in room 2237, Rayburn House Office Building, the Honorable Tom Marino, (Chairman of the Subcommittee) presiding.

Present: Representatives Marino, Goodlatte, Collins, Ratcliffe, Bishop, Johnson, Conyers, DelBene, Cicilline, and Peters.

Staff Present: (Majority) Anthony Grossi, Counsel; Andrea Woodard, Clerk: and (Minority) Slade Bond, Minority Counsel.

Mr. MARINO. The Subcommittee on Regulatory Reform, Commercial and Antitrust Law will come to order. Without objection, the Chair is authorized to declare recesses of the Committee at any time. And I would like to make clear for our guests that are here, votes have been moved up and another series has been put in.

We have about 2 hours, maybe a little less, before they are going to call votes and I have asked my colleagues, and they agree we are going to stick to the 5-minute rule on questions. So, when we break, it will be the end of the hearing because I do not want to keep you people here for an hour and a half to 2 hours.

We welcome everyone to today's hearing on "Treating the Opioid Epidemic: The State of Competition in the Markets for Addiction Medicine," and I now recognize myself for my opening statement.

Sadly, the opioid epidemic facing our country is an issue that we are all too familiar with. In 2014, drug overdoses overtook car crashes as the leading cause of accidental death for the first time in history.

In response to this growing epidemic Congress passed a "Comprehensive Addiction and Recovery Act of 2016" which was signed into law on July 22 of this year. This legislation, which included several bills that originated in the Judiciary Committee, is an important measure that will help aid State and Federal authorities in fighting opioid abuse and addiction. However, one aspect on the opioid epidemic that has not received significant attention, is the market for the drugs that treat opioid overdoses and addiction.

Today's hearing will focus on this issue and explore the state of competition in these important markets. There are a number of drugs that are used to treat opioid overdoses and addiction, but two of these drugs have become prominent and will be the principal focus on our hearing. The first is Naloxone and the second is Buprenorphine. Did I have that correct, doctors? Fine, because from now on it is just going to be BUP.

Recently, its primary use has been to treat opioid overdoses in an emergency setting. The next drug that we will touch a little bit on in addition to BUP, as I said earlier, will be Naloxone. Naloxone is a drug that's been around since the 1970s.

Its effect is swift and dramatic, and it can literally bring an overdosed person back to life. BUP has also existed for decades and is a drug that is used in the treatment of opioid addiction. BUP generally is used as part of an "opioid substitution treatment plan" where it replaces a more potent and harmful opioid. The goal of this type of treatment is tapering the patient completely off of all opioids, including BUP. The period that a patient is prescribed the drug can vary greatly, from a little as a few weeks to years. Because BUP is an opioid, it is a regulated and controlled substance by the United States Drug Enforcement Agency, otherwise known as the DEA. Further owning to its abuse potential, BUP oftentimes is combined Naloxone to mitigate the possible misuse of the drugs.

In recent years, demand for these drugs has increased sharply. As a result, there have been reports that they have become hard to obtain, and in some instances prices for these drugs have risen during this period of increased demand. At the same time, innovative new applications of long developed drugs present first responders and family members with the ability to address overdose and addiction. As a strong support of the free markets, I believe that the best remedy to address scarcity and high prices is increased competition.

And so, today we will explore the complex factors that influence competition in the market for addiction medicine. Specifically, we will hear details about whether prices are in fact increasing for these drugs, the level of competition that exists in these markets, how Federal regulation influences competition, whether the antitrust laws are equipped to address any anticompetitive conduct, and whether the Antitrust Enforcement Agencies are appropriately policing unlawful behavior in these markets. We have an excellent panel of witnesses that will provide invaluable insight to these important issues, and I look forward to hearing their testimony.

The Chair now recognizes the Ranking Member of the Subcommittee on Regulatory Reform, Commercial and Antitrust Law, Mr. Johnson of Georgia, for his opening statement.

Mr. JOHNSON. Thank you, Mr. Chairman. Today's hearing is an important and welcome opportunity to discuss drug price competition in the market for treating opioid addiction. Opioid addiction is a devastating public health emergency in many of our communities. Strongly linked to the prescription of opioid pain killers, the Center for Disease Control reports that opioids contributed to the deaths of 28,647 Americans in 2014. While there are many factors that have contributed to this crisis concerns have been raised that common treatments for opioid addiction have become more costly.

In November 2014, the New York Times reported that Naloxone——

Mr. MARINO. There are several ways to say that, believe me. I checked it on the Internet there are multiple ways to say it.

Mr. JOHNSON. Naloxone, okay. It has been reported that this drug, a common treatment for opioid addiction and overdoses, had experienced severe price spikes. Alarmingly in my home State of Georgia police departments report that the price of drug kits containing Naloxone have increased from $22 to $40. I am concerned that in addition to costing States millions of dollars, these spikes have decreased access and undermined the ability of law enforcement agencies and local health responders to combat exploding opioid crisis.

Unfortunately, for many, these concerns extend to the markets for other lifesaving treatments as well. For example, I am personally concerned about the high cost of the new treatment for Hepatitis C, a virus that affects more than 4 million Americans and which costs nearly $75,000.

While this form of treatment is a significant advancement, particularly for patients with a form of the disease that is difficult to treat, there is little doubt that Americans should not have to choose between liver disease and extreme financial hardship when making healthcare choices. As millions of American struggle in the fight against this silent epidemic, treatments must be accessible and affordable.

According to a study by Dr. Aaron Kesselheim and others recently published in the Journal of American Medical Association, one of the driving forces in high drug prices is protection from competition through market exclusivity. Our patent system is designed to promote innovation by conferring a limited monopoly on inventions that are novel, useful, and non-obvious. It is critical that our polices continue to place a high value on innovation. As the Department of Health and Human Services found in 2012, leading research indicates that the economics literature generally indicates that innovation in medical products has produced tremendous benefits for U.S. consumers lead longer and healthier lives.

But it is equally important that patent extension applications are carefully scrutinized to ensure competition in drug markets through generic drug availability. As Dr. Kesselheim's study noted, there is little evidence that pro-competitive policies will hamper innovation. In fact, they may even drive new therapies to market. I look forward to today's hearing. We have a truly excellent panel of witnesses and I yield back the balance of my time.

Mr. MARINO. Thank you. The Chair now recognizes the Ranking Member of the full Judiciary Committee, Mr. Conyers of Michigan, for his opening statement.

Mr. CONYERS. Thank you, Mr. Chairman. Welcome to our distinguished panel, particularly Professor Feldman of the Hastings College of Law. Sudden and sharp increases in the cost of lifesaving prescription medications have caused much public outcry. Most recently regarding substantial spike in the price of EpiPen which is used to treat life threatening allergic reactions.

Although today's hearing focuses on competition in the markets for a particular set of lifesaving drugs, namely those that treat

opioid addiction, I hope that there are some broader lessons that we can draw from our discussion today.

To that end, I would like our witnesses to address, if they can, the following issues. The witnesses should discuss the real life consequences of the opioid addiction epidemic and the impact of rising prices for medications that treat opioid addiction. According to the Centers for Disease Control and Prevention, there are more than 28,000 deaths in 2014 resulting from opioid overdoses. In fact, 6 out of 10 drug overdose deaths that year resulted from opioid overdoses.

Medications like Naloxone revive an opioid overdose victim in the critical moments after he or she stops breathing as the result of an overdose. Yet, the price of this drug, in both its generic and branded forms, has skyrocketed in recent years. According to public health and police officials, prices for the drug have increased by 50 percent or more according to some reports.

As a result, the ability of emergency responders and individuals to purchase this critical lifesaving medication is being jeopardized. Other generic and branded medicines that are designed to gradually ween addicts from their opioid use have also seen similar price increases. As the statistics demonstrate, addressing the consequences of these price increases is no mere academic matter. It is beyond the dispute that such price increases have had a devastating impact on patients, their families, insures, first responders, and healthcare providers.

In addition, I would like the witnesses to consider the current law whether the current law strikes a proper balance between incentivizing investment in new pharmaceutical products and ensuring vigorous competition.

Under both our patent and regulatory systems manufactures of brand name drugs are entitled to temporary exclusivity periods for their products, during which other firms are prevented from offering competing products. These exclusivity periods are designed to provide an economic incentive for manufacturers to invest in developing new products. But the result is that prices for brand name drugs remain high. After the exclusivity periods end, competition in the form of the introduction of generic versions of the brand name drug is supposed to lead to decreases in drug prices.

Indeed, the availability of generics is the primary means of insuring competition in low prices in pharmaceutical markets. Nevertheless, there is a concern that some brand name manufacturers have manipulated the current patent and regulatory regimes to extend what our supposed to be their time-limited monopolies. We ought to explore whether there should be a better balance.

And finally, the witnesses should, if they can, address the factors responsible for the skyrocketing cost of generic opioid addiction drugs and the actions that Congress should take in response. Prices for almost all opioid addiction medicines have risen, not just for those for brand name products. This situation undermines the competition based rational for encouraging generics to enter the market in the first place. We and Congress need to focus on constructive ways to respond to this problem.

And so accordingly I look forward to hearing the thoughtful suggestions that I know will come from our witnesses today. Thank them for their participation and thank the Chairman.

Mr. MARINO. Thank you. The Chairman of the full Committee, Mr. Goodlatte, will be here shortly so we will reserve time for his opening statement. But without objection, other Members' opening statements will be made part of the record.

I will begin by swearing in our witnesses before introducing them. Would you please stand and raise your right hand?

Do you swear that the testimony that you are about to give before this Committee is the truth, the whole truth, and nothing but the truth, so help you God? Let the record reflect that the witnesses have responded in the affirmative. Please be seated.

Dr. Anne McDonald Pritchett is the vice president of Policy and Research at the Pharmaceutical Research Manufacturers of America. Prior to joining PhRMA, she worked in the Office of National Drug Control Policy for almost 8 years.

Dr. Pritchett earned her bachelor's degree in English and Graphic Design from Virginia Tech, her master's in Public Policy from George Mason University, and her doctorate in Public Policy and Public Affairs from Virginia Tech. Welcome, doctor.

Mr. David Gaugh is the senior vice president of Science and Regulatory Affairs for the Generic Pharmaceutical Association. Prior to joining GPhA, Mr. Gaugh was the vice president and general manager of Bedford Laboratories and has otherwise been engaged in the pharmaceutical industry for years. Mr. Gaugh is a registered pharmacist and a graduate of the University of Wyoming School of Pharmacy. Welcome.

Mr. Mark Merritt has served as the president and CEO of the Pharmaceutical Care Management Association, PCMA, since 2003, which is the National Association representing America's Pharmacy Benefit Managers, or known as PBMs, that collective administrative prescription drug plan for more than 266 million Americans.

Prior to joining PCMA Mr. Merritt served as a senior strategist with America's Health Insurance Plan and PhRMA. Mr. Merritt received both his bachelor's degree and his master's degree from Georgetown University. Welcome, sir.

Dr. Eric Ketcham, M.D., is the current president of the New Mexico Chapter of the American College of Emergency Physicians. Dr. Ketcham is also the medical director of the Emergency Department and Urgent Care and the Co-Medical Director of the EMS at the San Juan Regional Medical Center in New Mexico.

Dr. Ketcham also served our country in the U.S. Navy as a second-class petty officer, aviation ordnanceman in the Strike Fighter Squadron 11 and later in the Naval Reserve as a first-class petty officer.

Dr. Ketcham earned his bachelor's degree in economics and Russian studies from the University of Colorado; his MBA from the University of Texas at Dallas; and his medical degree from the University of Colorado School of Medicine. He completed his residency at the University of Michigan Hospital and Saint Joseph's Mercy Hospital. Welcome, sir.

Professor Robin Feldman holds the Harry and Lillian Hastings chair and is also the director of the UC Hastings Institute for Innovation Law. Professor Feldman is a prolific author on among other things, intellectual property, antitrust and pharmaceutical issues. She has provided testimony and commentary for other congressional Committees, the Federal Trade Commission, the Department of Justice, the Patent and Trademark Office, and the National Academy of Sciences.

Professor Feldman earned her bachelor's degree from Stanford University and her J.D. from Stanford Law School where she graduated Order of the Coif. Welcome.

Each of the witnesses' statements will be entered into the record in its entirety. I ask that each witness summarize his or her testimony in the 5 minutes or less. And to help you stay within that time, there is a timing light in front of you. The light will switch from green to yellow indicating that you have 1 minute to conclude your testimony. When the light turns red, it indicates that the witness' 5 minutes have expired.

Again, I want to thank you for being here and I diplomatically will pick up the gavel here if you are running over your 5 minutes. I will not hit anything; it is just a little polite indication to you, would you please wrap up because I do not look at the lights when I know I have 5 minutes. I am thinking about what I am asking or saying, and I know you may do the same thing. So there will just be a polite little gesture. I have not thrown this yet. Dr. Pritchett, will you please make your opening statement?

TESTIMONY OF ANNE McDONALD PRITCHETT, Ph.D, VICE PRESIDENT, POLICY AND RESEARCH, PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA (PhRMA)

Ms. PRITCHETT. Good afternoon Chairman Marino, Ranking Member Johnson, and Members of the Subcommittee. As mentioned, my name is Anne Pritchett. I am the vice president of Policy and Research at the Pharmaceutical Research and Manufacturers of America, also known as PhRMA. We represent the Nation's leading biopharmaceutical research companies which are dedicated to making new treatment and cures for some of the most of our most challenging diseases. Our members have invested half a trillion dollars in R&D since 2000 alone, and about $58.8 billion in the last year alone.

PhRMA is committed to supporting the appropriate use of prescription medicines and to making the R&D investments needed to develop new therapies including new medications to treat addiction and overdose reversal agents. Before speaking specifically to addiction treatments, I wanted to give a sense of what we see as the key policies necessary to address this overall epidemic.

First, we feel that prescribers immediately undergo ongoing education and training on the appropriate prescribing of controlled substances and effective pain management. They need training on how to identify those at risk for prescription drug abuse, for overdose, and those in need of treatment. We need more prescribers to be using evidence based clinical guidelines to inform opioid selection dosage and duration of treatment. Second, we feel that State prescription drug monitoring programs have been demonstrated

through peer review research to be one of the most effective tools in detecting potential doctor shoppers.

But, they are only useful if their being used. We need to mandate training in the use of PDMPs and we need to adjust those barriers to their use. Third, we need to encourage the development of abuse to current formulations not opioid pain medications and medications to treat addictions and prevent overdose.

Given more than 90 percent of the most abused medicines are generic opioids; we think it is critically important that the FDA finalize its guidance to assist generic manufactures in the development of abuse deterrent formulations products as well. And we need coverage and access polices that reflect the public health benefits of these products.

And finally, we need to expand access to the full range of treatment and recovery services needed to break the cycle of addiction. A couple of key points. Despite the fact that a large body of research is documented the cost effectiveness of medication assisted treatments for addictions, and despite the fact that opioid abuse is widely recognized as a chronic disease, prescription drug benefit designs often include prior off step therapy, or as I call it, fail first.

The consequences of which in this case can be deadly and a number of State Medicaid programs impose lifetime limits on the use of addiction treatments. These polices are in direct conflict with the public health goal of expanding access and breaking the cycle of addiction.

Now, I wanted to take just a moment to talk about the nature of competition in the biopharmaceutical market, overall. I would say in contrast to Mr. Kesselheim, respectfully, the competitive market is structured to take maximum advantage of savings from brand competition.

We have brand medicines facing competition before they come to market. About 88 percent of medicines that are deemed first in class had competitors in development at the time of launch. In Hepatitis C, we saw multiple competitors within less than a year with payers negotiating discounts between 40 and 65 percent. We do to continue, though, to have challenges related to coverage and access to these critical medicines.

In following generic entry, payers quickly shift utilization to generics. The reality is, more than 90 percent of all medicines prescribed in the U.S. are generics, and once a drug loses its exclusivity, within less than a year 93 percent of market share is generic based. But, we have a drug cycle that balances the need for incentives innovation with a desire for increased competition.

I would note that with the coming loss of IP protection between now and 2020, were going to have about 93 billion U.S. brand sales that will be facing generic competition. In the case of addiction treatments, we have a substantial number of generic medicines available in these well-established classes. But we have also seen a number of new drug applications that are providing significant medical advances for addressing opioid abuse and addiction in terms of more convenient delivery systems.

In recent years, the market has signaled a need for new treatment options in this space that can improve patient adherence and quality of life by providing more convenient dosing and delivery

methods. And companies are beginning to respond as we have seen from the recent approvals, and from what we have seen in the pipeline.

When you look at the pipeline we have 31 abuse deterrent determinations in development of pain so that we avoid ever getting to this point. There are 35 addiction medicines in development and 49 opioid pain medications in development potentially providing important treatment alternatives to what is currently on the market. But the demand for treatment in the addiction spaces has dramatically increased. It has increased unfortunately because opioid overdose rates have increased the growing burden on communities and families around the country.

On the positive, we have seen increased awareness in education removing some of the stigma related to addiction. In addition, we have seen State and Federal policy changes, the Care Act was mentioned as critical to expanding access. I would say that we think there is robust competition in this space one of the key barriers we have seen when we look at products in this space is the challenges related to ensuring coverage and access to these. When we have lifetime limits and we have Fail First, that creates tremendous challenges and one of our concerns is how the dynamics of coverage and access policies impact incentives to enter the market. Thank you.

[The prepared statement of Ms. Pritchett follows:]

Testimony of

Anne Pritchett, PhD, Vice President, Policy and Research,
Pharmaceutical Research and Manufacturers of America (PhRMA)

Before the U.S. House of Representatives, Committee on the Judiciary,
Subcommittee on Regulatory Reform, Commercial and Antitrust Law

Hearing on "Treating the Opioid Epidemic: The State of Competition in the Markets for Addiction Medicine"

September 22, 2016

Good afternoon Chairman Marino, Ranking Member Johnson, and the Members of the Subcommittee:

My name is Anne Pritchett, Vice President, Policy and Research, at the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA represents the country's leading innovative biopharmaceutical research companies, which are devoted to developing medicines that enable patients to live longer, healthier and more productive lives. Since 2000, PhRMA member companies have invested more than half a trillion dollars in the search for new treatments and cures, including an estimated $58.8 billion in 2015 alone.

I have spent a substantial portion of my career focused on substance abuse issues including almost 8 years in the Office of National Drug Control Policy before joining PhRMA. The adverse health effects of the misuse of prescription opioids, including abuse, dependence, and overdose are a well-documented public health crisis. According to the Centers for Disease Control and Prevention, the rate of deaths from drug overdoses has increased 137%, including a 200% increase in the rate of overdose deaths involving opioids (opioid pain relievers and heroin) since 2000.[i] The total economic burden related to the abuse of prescription opioids is estimated to be as high as $78.5 billion, which includes health care, substance abuse treatment, and criminal justice costs.[ii] Of course these statistics do not begin to fully consider the impact on families and communities across the country nor the challenges and suffering of individuals seeking to break the cycle of addiction. Given the growing toll related to the abuse of prescription opioids and heroin, we must collectively redouble our efforts to prevent the misuse, abuse, and diversion of prescription medicines. While more than 90 percent of the prescription medicines most susceptible to abuse are generic,[iii] PhRMA and its members are committed to supporting the appropriate use of prescription medicines and working with others to collectively address the growing problem of opioid abuse and addiction.

I am pleased to appear before you to provide PhRMA's perspective on the critical issue of prescription drug abuse and medications to help prevent overdose and treat addiction. Our Industry is committed to the research and development of new therapies, including the development of non-opioid analgesics, abuse deterrent formulations (ADFs) of medicines that are intended to help prevent abuse, and various medicines to treat addiction and prevent overdose.

Today, I will briefly speak to the following areas:

- PhRMA's perspective on the overall policy framework for addressing opioid abuse
- Competition dynamics for medication assisted-treatments including opioid overdose reversal agents
- Current market for medication assisted treatments for overdose reversal
- Current market for other medication-assisted treatments for addiction

Policy Framework to Stop Opioid Abuse

We need a balanced approach that ensures appropriate access and use of prescription medicines by patients for legitimate medical needs under the direction and care of a licensed health care professional, but that also reduces the potential for misuse, abuse and diversion. Prescription drug abuse is a complex problem with no single solution—rather it requires a multi-pronged approach. To combat prescription drug abuse and particularly opioid abuse, PhRMA supports the following policies (for more detail, please see PhRMA's policy recommendations at http://www.phrma.org/policy-paper/for-a-healthier-america-strategies-to-combat-prescription-drug-abuse):

- *Expand education and training related to prescription drug abuse, pain management, and treatment options.* Physicians and other prescribers are often on the frontlines of the fight against prescription drug abuse. Prescribers need ongoing training to ensure they meet the legitimate medical needs of patients while reducing the potential for abuse, but increasingly first responders including friends and family are best positioned to assist an overdose victim. In addition to continuing to increase awareness of the dangers of prescription abuse and the signs of overdose and how to assist an overdose victim, public policies need to:

  - *Require ongoing prescriber education and training* to ensure appropriate prescribing of controlled substances, effective pain management, identification of patients at risk for prescription drug abuse and overdose, identification of those in need of treatment, and awareness of available treatment options.

  - *Foster the development and dissemination of evidence-based clinical guidelines* to inform opioid selection, dosage, duration, follow up, and discontinuation, including guidance on the first opioid prescription for patients for acute pain to ensure that no greater quantity than needed is prescribed for the expected duration of pain severe enough to require opioids. In considering initiation or continuation of opioid therapy, prescribers should be informed by evidence based clinical guidelines that include guidance on whether and under what circumstances a non-opioid analgesic, an abuse-deterrent formulation (ADF) (which makes the drug more difficult to abuse), or a non-medical treatment is appropriate.

- *Prevent and detect potential doctor shoppers.* One of the most promising tools in preventing and detecting potential doctor shoppers while allowing for legitimate medical use of needed prescription medicines by patients is Prescription Drug Monitoring Programs (PDMPs). These state-run data bases collect, analyze, and share dispensing information on controlled substances, providing critical information to providers to inform their prescribing. We support mandated training and use of PDMPs, efforts to expand the timeliness and quality of data included in these data bases, and efforts to increase interoperability and standardization of key elements to facilitate the generation of information to assist all prescribers in easily identifying potentially problematic behavior.

- *Encourage the development of ADF products, non-opioid pain medications, and medications to treat addiction and prevent overdose.* Despite ADF products' role in preventing widespread abuse by impeding delivery of the active ingredient, we continue to see non-ADF versions of the same drug on the market despite an ADF product being available. We encourage the FDA to use its existing authority to remove non-ADF generic versions of the product from the market in those circumstances and to expeditiously finalize guidance for generic manufacturers on the development of generic ADF products. We urge that the FDA use its existing authorities to expedite the review of and encourage the development of non-opioid pain medications, ADF products, products to treat opioid addiction, and products that can prevent opioid drug overdose and death, including generic products. Further, we need to ensure policies regarding coverage and access of these medicines is appropriate a given the public health benefits of such products.

- *Clarify regulations to support law enforcement efforts to shut down key sources of diversion, including rogue online pharmacies and "pill mills," and prosecute the perpetrators.* Clarifying the regulations related to legitimate pain management clinics would facilitate law enforcement's ability to shut down and prosecute those operating "pill mills." For example, "pill mills" pose as legitimate pain management clinics but inappropriately provide controlled substances often on a cash-only basis and without requiring a prescription solely for financial gain. The National Association of Board of Pharmacy has reported that "despite the perception that illegal purchases of prescription opioids only take place with drug dealers on the street, rogue internet drug outlets serve as dealers hiding behind sleek websites that look safe to people trying to purchase CS [controlled substance] medications.[iv]

- *Expand treatment capacity, coverage, and access.* The National Institute on Drug Abuse (NIDA) defines "addiction as a chronic, relapsing brain disease that is characterized by compulsive drug seeking and use, despite harmful consequences. It is considered a brain disease because drugs change the brain; they change its structure and how it works."[v] While this reinforces the challenges associated with treating this disease, addiction is a treatable, chronic disease that can be managed successfully. As documented by the peer-reviewed research, behavioral therapy combined with medication-assisted treatment can help ensure success for most patients. However, treatment approaches must be individualized to address each patient's particular circumstances and any other medical, psychiatric, and social problems. Importantly while many patients relapse that does not mean treatment failed, rather it suggests that the treatment plan needs to be reevaluated. The nature of addiction also underscores the importance of having multiple treatment options that can be tailored to prescriber and patient needs.

We support a comprehensive treatment approach that includes:

- Expanding treatment capacity
- Increasing coverage and access to the full range of treatment and recovery services needed, which range from a range of in-patient and out-patient treatment options, medication-assisted treatment, including opioid reversal agents, and medication-assisted therapies in combination with other treatment options.

Competitive Dynamics for Medication-Assisted Treatments including Opioid Reversal Agents

There are currently a range of medications available to (1) reverse the effects of an opioid overdose and (2) treat addiction, with some of the medications in the latter category also approved to treat alcohol addiction. Demand for these products has increased substantially in a relatively short period of time. Among the drivers of demand is the increased rate of deaths from overdose, which is creating a tremendous burden on families, our health care and law enforcement infrastructure, and communities around the country; efforts to reduce the stigma associated with addiction which is encouraging more people to seek treatment as well as increased awareness and education; and changes in policy at the state and federal levels that have sought to broaden access to therapies.

Before delving into the specifics of these markets, it is important to put into perspective the overall U.S. biopharmaceutical market where substantial competition exists—both brand to brand and brand to generic. A few key facts:

- The competitive market is structured to take maximum advantage of savings from brand competition. Brand medicines face competition well before approval, as companies race to be first to market. Multiple companies simultaneously compete to research, develop, and secure FDA approval of first-in-class treatments. In fact, 88% of first-in-class medicines launched between 2005 and 2011 already had a competitor in Phase II clinical development at the time of their launch. Once launched, the time a medicine is alone in its class is 2.3 years for drugs approved between 2005 and 2011.[vi]

- Following generic entry, the U.S. market continues to drive long-term affordability by taking maximum advantage of the savings provided by generic drugs.
  - Today, more than 90% of all medicines prescribed in the U.S. are generics—due largely to the concentration of purchasing power by payers and the aggressive use of utilization management tools to rapidly shift utilization towards generics.
  - Continued competitive pressure resulting from the loss of intellectual property (IP) protection and the entry of more generics and biosimilars is expected to continue to fuel this dynamic in the years ahead. Between now and 2020, an estimated $93 billion of U.S. brand sales are projected to face generic competition.

- For brand medicines facing generic entry in 2013-2014, generics captured an average of 93% of the market (by volume) within a year of entry, compared to 56% in 1999-2000.[vii][viii] In other words, brand medicines retained an average of only 7% of market share at one year post-generic entry in 2013-2014, compared to brand medicines maintaining a market share of 44% in 1999-2000.

In both the market for overdose reversal agents and medicines to treat addiction, generics have been available for decades and comprise the majority of medicines prescribed today. In addition, there are several brand or innovative drugs currently available in these therapeutic areas that constitute significant medical advances for addressing opioid abuse and addiction .

In recent years, there has been an increasing public health need for ADF versions of pain medicines, non-opioid analgesics, as well as new therapies to help treat addiction and to reverse opioid overdose. This increased demand is being driven by a number of factors, including changes to policies at the federal and state levels to address the rising epidemic related to addiction and overdose, such as the recently passed Comprehensive Addiction and Recovery Act of 2016, which included a range of provisions aimed at expanding access among first responders to opioid reversal agents as well as efforts to expand access to medication-assisted treatments for addiction. In addition, there are many new innovative medicines in development to address this growing demand. According to a September 2016 search of the Adis R&D Insight Database, there were an estimated 31 ADF products for the treatment of pain, 35 addiction medicines, and close to 40 non-opioid pain medicines in clinical development. While only 12% of drugs in development reaching clinical trials are ultimately approved by the FDA,[ix] the pipeline speaks to the potential for additional new options for patients in the coming years and the potential for increased competition in this space.

As companies assess whether to invest in R&D in a particular area they consider the potential market and whether there will be demand for their medicine. Federal and state policies have increasingly been focused on seeking to expand access, which creates an incentive for the development of new therapies, which in turn drives brand to brand competition and ultimately generic competition as well. Companies must ultimately assess an array of factors in determining whether or not to enter a market, including whether they can develop a medicine that is an improvement over existing treatments (e.g., whether the product can result in better health outcomes, improve patient adherence and quality of life, reduce side effects, or provide more convenient dosing and delivery methods), whether they can make the case to payers of the value of the treatment.

A brief overview of the current marketplace for some of the existing therapies for opioid reversal and addiction treatment are detailed below.

Medication-Assisted Treatments for Overdose Reversal

Opioids in high doses can lead to respiratory depression and death. The effects of opioid overdose can be reversed if the person receives basic life support and the timely administration of the medication naloxone. Naloxone products sometimes referred to as "rescue drugs" or "overdose reversal agents" are used to counter the effects of overdose from heroin and other opioids. These medications are not controlled substances, meaning they have no potential for abuse. They only have an effect in a person that has opioids in his/her system.

Naloxone currently is purchased by a number of different stakeholder groups with differing needs and preferences, including acute care settings such as hospitals and clinics, jails, first responders, community-based groups, and caregivers. Each stakeholder group differs in terms of preferred method of delivery for the medicine, with acute care settings more likely to prefer to administer the medicine via syringe whereas caregivers and many first responders prefer the use of other delivery mechanisms such as via auto-injector or nasal spray.

The marketplace for naloxone products is unique compared to many other therapeutic areas. At the state level, access to naloxone products historically has been limited to circumstances in which there was a direct physician-patient relationship and providing the drug to anyone other than the patient was prohibited by law. In recent years, however, many states have sought to update their laws to expand access to naloxone among those likely to be in a position as first responder such as paramedics and other emergency medical services personnel, law enforcement, pharmacists, and parents and other caregivers. Many states' regulations allow pharmacies to dispense naloxone without a patient being present with a prescription through standing order or collaborative practice agreements with prescribers.

This has resulted in a bifurcated system in which many states permit the purchase of naloxone outside of the normal drug distribution system and often without a prescription. CVS,[x] for example, announced in 2015 that naloxone will be available without a prescription in 14 states, and in 2016, Walgreens announced the roll out of a program across 35 states to make naloxone available without a prescription by the end of the year.

Other key aspects of the naloxone market:

- Naloxone is produced and sold by 8 different biopharmaceutical manufacturers. There are 6 generic manufacturers in a range of dosage forms and there are also 2 brand naloxone medications offering convenient delivery systems (see below). Relative to the market in early 2015, the number of manufacturers in this space has close to doubled.

- The branded products include:

  - Narcan, approved in 2015, is the first nasal form of the drug that enables users to administer the medication without the use of a syringe. In the approval letter for this

medicine, the FDA noted that many first responders and caregivers felt that a nasal spray formulation of naloxone was easier to deliver, and avoided the risk of contaminated needles. As a result, prior to the approval of Narcan, there had been widespread use of unapproved naloxone kits using an injectable formulation of naloxone along with an atomizer to deliver the medicine off-label nasally. Today, according to FDA, "people have access to an FDA-approved product for which the drug and its delivery device have met the FDA's high standards for safety, efficacy and quality."[xi] Also of note, in late 2015, the FDA denied approval of another nasal form of the medication.

- Evzio, approved in 2014, is the first drug-device combination product that delivers a single dose of naloxone via a hand-held auto-injector. Once turned on, the device provides verbal instruction to the user describing how to deliver the medication.[xii]

- Since 2011, naloxone sales have increased from 4.4 million units to 6.1 million units:
  - In the past 2 years, there has a 40% increase in volume.
  - While there's been growth across all channels, the vast majority has been in retail pharmacy—where growing demand for more convenient delivery mechanisms has resulted in the entry of new branded products—particularly among first responders and non-healthcare professionals.

As demand increases along with heightened interest in alternative forms of delivery to meet various user needs, it is likely that competition will increase in this space.

Medication Assisted Treatments for Addiction

Medications to treat addiction include the following:

- **Buprenorphine and buprenorphine-naloxone**—These medicines seek to suppress withdrawal symptoms and cravings—it is primarily used for the withdrawal phase of opioid dependence. The combination products compete with other opioids by suppressing withdrawal symptoms and cravings and are combined with naloxone to diminish the potential for misuse.
- **Naltrexone**—These medicines block opioid receptors involved in opioid's euphoric effects.
- **Methadone**--These medicines compete with other opioids by suppressing withdrawal symptoms and cravings.

Key aspects of the market include the following:

- Buprenorphine and buprenorphine-naloxone products comprise more than 70% of medication-assisted treatments by volume and sales (based on unpublished analysis from IMS Health).

- Since 2011, sales of buprenorphine and buprenorphine-naloxone combination products have grown from 226 million extended units to 368 million extended units, with unit referring to a standardization of the various forms of the products—indicating a relatively steady growth in demand of about 63% over the past 5 years.

- Generics have become a growing share of the market as demand has grown:
  - Since 2011, sales of generic buprenorphine products have grown from 30 million units to 148 million units.
  - Today generic products represent more than 40% of the buprenorphine market whereas, 5 years ago they represented just 13%.

- There are currently 19 manufacturers of buprenorphine and buprenorphine-naloxone combination products currently on the market to treat addiction, including 4 manufacturers of brand medications:
  - Bunavail, approved in 2014, is the first and only formulation of buprenorphine and naloxone for buccal (inside of the cheek) administration providing an important delivery alternative.
  - Zubsolv, approved in 2013, is a once-daily, sublingual tablet formulation that fully dissolves within minutes.
  - Suboxone sublingual film was approved in 2010 as a maintenance treatment for opiate addiction.
  - The first buprenorphine implant, Probuphine, for the maintenance treatment of opioid dependence was approved in May 2016. Probuphine is designed to provide a constant, low-level dose of buprenorphine for 6 months in patients who are already stable and on low-to-moderate doses of other forms of buprenorphine, as part of a complete treatment program. The FDA approval letter noted that this medicine "provides a new treatment option for people in recovery who may value the unique benefits of a six-month implant compared to other forms of buprenorphine, such as the possibility of improved patient convenience from not needing to take medication on a daily basis." [xiv]

- There are currently 11 manufacturers of naltrexone products on the market, but there is only one extended-release product, Vivitrol, an innovative product, that is approved to treat and prevent relapse after patients with opioid dependence have undergone detoxification treatment. This extended-release formulation of naltrexone administered by intramuscular

injection once a month. In announcing approval of this new medicine, the FDA stated that "This drug approval represents a significant advancement in addiction treatment."[xiv]

- All available methadone products are generic and the overall market share in the addiction space for these medicines has remained stable at between 3 and 4% since 2011.

This very high level review of the marketplace for medications to treat addiction demonstrates there are a large number of generic entrants as well as growth in the entry of new branded therapies that are providing valuable new delivery mechanisms expanding treatment options for prescribers and patients. As mentioned previously, based on the evolving market dynamics and review of the pipeline, competition is expected to further expand and evolve in response to the needs of various purchasers.

More research is needed to determine the impact that insurer tools, such as formulary placement, prior authorization, quantity limits, step therapy, and other tools influence utilization and market incentives. Benefit design should be carefully considered as it can pose barriers to access. Further, it can create disincentives for companies to engage in research to bring new therapies to market if there is not a willingness to cover and reimburse for innovative new treatments.

Conclusion

PhRMA applauds your continued commitment to addressing opioid abuse. Just as overdose prevention and addiction treatment and the recovery process are multi-faceted, so too is the overall challenge of preventing diversion and abuse of prescription medicines. We look forward to continuing to work with the Subcommittee, members of Congress, and other stakeholders on these important issues.

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[i] http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm

[ii] Curtis, F, et al. The Economic Burden of Prescription Opioid Overdose, Abuse, and Dependence in the United States, 2013, Medical Care 2016(54)10: 901-6.

[iii] Among the most abused prescription medicines (opioids, CNS drugs, and stimulants) an estimated 93.6% of prescriptions at the retail level were for generic medicines in calendar year 2013. PhRMA analysis IMS National Prescription Audit, June 2014.

[iv] National Association of Boards of Pharmacy. *Internet Drug Outlet Identification Program Progress Report for State and Federal Regulators: July 2016* cited in http://www.news-medical.net/news/20160730/NABP-report-points-rogue-internet-drug-outlets-serve-as-dealers-to-people-purchasing-controlled-substances.aspx

[v] https://www.drugabuse.gov/publications/media-guide/science-drug-abuse-addiction-basics

[vi] Tufts Center for the Study of Drug Development. First in class drugs in competitive development races with later entrants. Tufts CSDD Impact Report. 2015(17):6.

[vii] Grabowski, G, et al. "Updated Trends in US Brand-Name and Generic Competition," Journal of Medical Economics, April 11, 2016, http://www.tandfonline.com/doi/abs/10.1080/13696998.2016.1176578.

[viii] Generic erosion for all NMEs was 88% as brand medicines retained an average of 12% of market share (by volume) at 1 year post-generic entry 2013-2014.

[ix] Tufts Center for the Study of Drug Development. Briefing: Cost of Developing a New Drug, November 18, 2014. Tufts Center for the Study of Drug Development & Tufts School of Medicine.

[x] In 2015, CVS announced that it would sell Naloxone without a prescription in Arkansas, California, Minnesota, Mississippi, Montana, New Jersey, North Dakota, Pennsylvania, South Carolina, Tennessee, Utah and Wisconsin. The company already sold naloxone without a prescription in Massachusetts and Rhode Island. States where naloxone will be available through Walgreens without a prescription at its pharmacies: Alabama, Arkansas, California, Colorado, Connecticut, District of Columbia, Idaho, Illinois, Indiana, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Minnesota, Mississippi, Montana, Nebraska, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, and Wisconsin.

[xi] http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm473505.htm

[xii] http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm391465.htm

[xiv] http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm503719.htm

[xv] http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm229109.htm

Mr. MARINO. Thank you. Mr. Gaugh.

TESTIMONY OF DAVID R. GAUGH, R.Ph., SENIOR VICE PRESIDENT FOR SCIENCE AND REGULATORY AFFAIRS, GENERIC PHARMACEUTICAL ASSOCIATION

Mr. GAUGH. Thank you. Good morning, Chairman Marino—afternoon excuse me—Ranking Member Johnson, and Members of the Subcommittee. I would like to first begin by commending the Committee for your continued focus on these important issues that we are going to discuss today. The Generic Pharmaceutical Association is the Nation's leading trade association for manufactures and distributors of generic medicines.

GPhA's mission is to improve the lives of patients in the U.S. healthcare system through access to affordable generic medicines. Eighty-eight percent of all prescriptions dispensed in the United States are generic; however, generics account for only 28 percent of the totals of drugs span. GPhA is strongly committed to addressing the improving treatment options for patients suffering from addiction. This includes combating drug abuse by supporting community anti-drug coalitions, encouraging safe disposal of unused drugs, and through the development of abuse deterrent drug formulations.

As part of this response, including ensuring the availability of high quality low cost generics. I am here to discuss the GPhA conviction that the best way to achieve the goals of patient access to use lifesaving treatments is through the development of policies to promote robust competitive markets. As GPhA represents multiple competing generic manufactures, we are not privileged to member company information about individual products or any pricing decisions around those projects.

We can; however, provide some insight to what we believe is a proven solution to rapidly inflating drug prices. Competition. Competition from generic drugs savings is access and not cost. In fact, a variety of healthcare stakeholders have found a trend of overall price decreases for generics. Last week, the government accountability office publishes a report examining drugs in Medicare, part D. That report echoes the findings of multiple previous independent reports. That generic drug prices continue to decrease.

Specifically, the GAO report that between 2010 and 2015, drug prices for Medicare part D declined by 59 percent. In January 2016, the Department of Health and Human Services released a comprehensive study which concluded, and I quote, "Our view of evidence strongly supports the conclusion that generic drug prices are not an important part of the drug cost problem facing the Nation." Taken with other important studies, these data show the competition in pharmaceutical markets is effective. The Drug Price Competition and Patent Term Restoration Act, commonly known as the Hatch-Waxman Act, created the abbreviated regulatory approval pathway for generics, while simultaneously providing lucrative incentives for brand manufactures to continue to bring new treatments to the market.

The overwhelming success of Hatch-Waxman led to the approval of over 14,000 generic applications. But, that incredible volume brought complications in the FDA's ability to effectively and effi-

ciently review them. By 2011, there where over 2.700 generic applications pending at the FDA and the average approval time for these products or these applications exceeded 30 months. To alleviate the burden on FDA and expedite generic approvals, the Generic Drug User Fee Program, or GDUFA, was improved and implemented in 2012.

Unfortunately, 4 years later the number of pending generic applications has ballooned to over 4,000 while the median approval time now exceeds over 45 months. Nonetheless, FDA has, under GDUFA, hired and trained over a 1,000 new employees and increased its efficiency in reviewing applications. As these are important steps forward, we will continue to work with the FDA to ensure it meets its GDUFA goals.

Generic manufacturers make complex and highly confidential analysis when selecting which products to pursue. This analysis can include assessing the complexity of reverse engineering, the state of the intellectual property, the size of the market, the likely number of competitors, the product development and manufacturing capabilities and costs.

Once the generic manufacturers make the decision to develop a product, they often face significant delay tactics from brand manufacturers, including the Risk Evaluation Mitigation Strategies or REMS program. And exempting themselves from scrutiny or their intellectual property covered by the U.S. Patent and Trade Office.

While current law forbids brand companies from using REMS to delay competition, they are nonetheless denying generic manufacturers access to samples of their products. These samples are required to conduct the bioequivalent studies necessary for FDA approval of the generic application. They have even begun applying restricted access programs to drugs for which FDA has not required a REMS program in order to delay generic entry.

Presently, two pieces of legislation are pending before Congress that would address this situation. The Fast Generic Act and the CREATES Act. The GPhA has encouraged that each of these addresses the barriers to success.

This Committee has also played a key role in recognizing The Interim Parties Review, the IPR, as a critical consumer protection against abusive patens. The IPR holds great promise in reducing anti-competitive evergreening practices that drive-up healthcare costs.

In conclusion, Mr. Chairman, GPhA believes that the best way to control drug costs, generally, whether in the drug addiction treatment market or otherwise is through policies that incentivize competition. Thank you very much.

[The prepared statement of Mr. Gaugh follows:]

TESTIMONY OF DAVID R. GAUGH, R.PH.

SENIOR VICE PRESIDENT FOR SCIENCES AND REGULATORY AFFAIRS

GENERIC PHARMACEUTICAL ASSOCIATION

TREATING THE OPIOID EPIDEMIC: THE STATE OF COMPETITION IN THE MARKETS FOR ADDICTION MEDICINE

BEFORE THE HOUSE JUDICIARY SUBCOMMITTEE ON REGULATORY REFORM, COMMERCIAL AND ANTITRUST LAW

UNITED STATES HOUSE OF REPRESENTATIVES

SEPTEMBER 22, 2016

I am David Gaugh, Senior Vice President for Sciences and Regulatory Affairs at the Generic Pharmaceutical Association and a licensed pharmacist. GPhA is the nation's leading trade association for manufacturers and distributors of generic medicines. GPhA's core mission is to improve the lives of patients and the U.S. healthcare system by advancing timely access to affordable generic medicines. Generic pharmaceuticals fill 88 percent of all prescriptions dispensed in the U.S., but consume just 28 percent of the total drug spending for prescription medicines.

Introduction

I would like to begin by commending the Committee for your continued focus on the important issues we will examine today. I have worked in and around the generic industry for more than three decades and have witnessed firsthand the industry's remarkable growth and the vital role it plays in the lives of Americans every day.

GPhA is strongly committed to addressing the misuse of prescription medication and improving treatment options for patients suffering from addiction. We understand that the current treatments for people with life-threatening addictions are nothing short of miraculous, and should be within reasonable financial reach of any patient suffering from addiction. We are committed to combating drug abuse at every level of the health system, including supporting community anti-drug coalitions, encouraging safe disposal of unused drugs, and through the development of abuse deterrent drug formulations.

A key part of this response includes ensuring the availability of high quality, low-cost generic drugs for the treatment of addiction; and I commend you for your attention to this issue.

As a representative of GPhA, I am here to discuss our organization's conviction that the best way of achieving the goal of providing patients access to these lifesaving treatments is through the development of policy that promotes robust, competitive markets. As GPhA is a trade association representing multiple competing generic manufacturers, we focus entirely on promoting the common interests of our members and the general welfare of the generics industry through policy processes. As such, we are not privy to member company information about their individual products or any pricing decisions around those products. Those decisions are made internally by each company, and GPhA has no knowledge about them beyond what is in the public domain.

We can however provide some insight to what we believe is the proven solution to rapidly inflating brand prices: competition. For more than three decades, the generics industry has demonstrated that direct competition in the pharmaceutical marketplace lowers costs and increases patient access. There are a number of ways policymakers can encourage competition and ensure that millions of patients will continue to have access to safe, effective, and affordable medicines.

In order to best illustrate that point, we believe the best way to show how access to generics is achieved is to explain the market and regulatory framework for generics, which differs significantly from the branded drug industry.

Savings From Competition

Competition from and among generic drugs drives savings and access, not costs. As drug cost issues recently have been at the forefront of policy issues, a variety of healthcare stakeholders have examined the role of generics and found a trend of overall price decreases. Before addressing the specific mechanisms that have been developed to create competition in the pharmaceutical marketplace, it is worth noting that it is not just GPhA calling for greater competition. Stakeholders throughout the healthcare environment recognize the value generics and biosimilars bring to patients. Competition works, and voices throughout the patient community, drug supply chain, and federal government are recognizing it.

- Just last week, the Government Accountability Office (GAO) published a report examining generic drug pricing in Medicare Part D. The report echoes the findings of multiple previous independent reports – that generic drug prices continue to decrease. Specifically, the GAO reports that between 2010 and 2015 generic drug prices in Medicare Part D declined by 59%.[1]

- In January 2016, the Department of Health and Human Services (HHS) Office of the Assistant Secretary for Planning and Evaluation (ASPE) released a comprehensive report, Understanding Recent Trends in Generic Drug Prices, which concluded, "Our review of evidence strongly supports the conclusion that generic drug prices are not an important part of the drug cost problem facing the nation." The report also found that "about two-thirds of generic products appear to have experienced price declines in 2014."[2]

- The Seventh Annual Generic Drug Savings in the United States report compiled by the IMS Institute for Healthcare Informatics on behalf of GPhA, generic drugs accounted for 88% of all prescriptions dispensed in the U.S., but equaled only 28% of total drug spending.[3]

- Express Script's 2015 Drug Trend Report[4] found that generic drug prices were 19.9% lower than a year earlier whereas brand drug prices were 16.2% higher. An index of commonly used generic drugs shows prices decreased by

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[1] *Generic Drugs Under Medicare: Part D Generic Drug Prices Declined Overall, but Some Had Extraordinary Price Increases.* GAO-16-706: Published: Aug 12, 2016. Publicly Released: Sep 12, 2016. http://www.gao.gov/products/GAO-16-706

[2] *Understanding Recent Trends in Generic Drug Pricing*. Office of the Assistant Secretary for Planning and Evaluation, January 2016. https://aspe.hhs.gov/sites/default/files/pdf/175071/GenericsDrugpaperr.pdf

[3] *Generic Drug Savings in the U.S. Seventh Annual Edition: 2015*. Generic Pharmaceutical Association, October 2015. http://www.gphaonline.org/media/wysiwyg/PDF/GPhA_Savings_Report_2015.pdf

[4] *Drug Trend Report*. Express Scripts, 2016. http://lab.express-scripts.com/lab/drug-trend-report

more than 70% from January 2008 through December 2015. During that same period, a brand drug price index increased in price by 164%.

- Another recent report[5] from AARP found that retail prices for generic drugs fell an average of 4% in 2013, marking nearly a decade of consecutive years of decreasing generic drug costs. The annual retail price decreased for 203 (73 percent) of the 280 most widely used generic drug products.

Looking forward, biosimilars present the same opportunity for high-cost specialty medicines. As more biosimilar drug applications are reviewed and approved by FDA, such products have the potential to save patients, insurers and the government billions of dollars each year in treatment costs. Estimates from various economic impact studies pin the projected savings from $42 billion on the low end to as high as $250 billion over the first 10 years of biosimilar market formation.

Taken together, and with other important studies, these data show that competition in pharmaceutical markets is effective, and that competition is fueled by the legal and regulatory framework that shapes the market.

The Hatch-Waxman and BPCIA Framework

For over 30 years, the foundation that has allowed the competitive market to work has been the Drug Price Competition and Patent Term Restoration Act, commonly referred to as "Hatch-Waxman," which was signed into law in 1984.[6] The law effectively established the modern generics industry by creating the abbreviated regulatory approval pathway for generic products, while simultaneously providing lucrative incentives for brand manufactures to continue to bring new treatments to the market.

Prior to enactment, manufacturers who wanted to compete with a brand product were forced to prove the safety and efficacy of their product in a very similar manner to the original brand product. Hatch-Waxman created a new "abbreviated" pathway that allows generics to instead demonstrate that they are the "same" as their branded reference product. By demonstrating sameness, generic drugs become eligible for automatic substitution at the pharmacy level, ensuring patients receive the most affordable treatment while also guaranteeing equivalent safety and effectiveness.

The law also created opportunities for generic manufacturers to challenge brand patents that they believed were improperly granted, artificially extending brand monopolies and costing patients. Generics are incentivized to invalidate those patents by receiving a short period of statutorily allowed time as the sole

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[5] *Trends in Retail Prices of Prescription Drugs Widely Used by Older Americans, 2006 to 2013*. February 2016. http://www.aarp.org/content/dam/aarp/ppi/2016-02/RX-Price-Watch-Trends-in-Retail-Prices-Prescription-Drugs-Widely-Used-by-Older-Americans.pdf

[6] 21 U.S.C. §355

competitor to the brand. As a counterbalance to that system, brands are also given valuable protections such as patent life extensions and guaranteed periods of market exclusivity in order to ensure that true innovation is properly rewarded.

In 2010, Congress passed the Biologics Price Competition and Innovation Act (BPCIA), which codified a new abbreviated pathway for new innovative medicines that were too complex to easily function under the old Hatch-Waxman framework. The new law provides biosimilar manufacturers and the FDA with a new standard of "biosimilarity" which requires biosimilar developers to show that they are highly similar to their reference product and that they have the same safety, purity, and potency as the original. While this initial biosimilarity determination does not allow for automatic substitution as expected in the generic industry, manufacturers can pursue an interchangeability designation by demonstrating the product has the same clinical effects in all patients and would not change outcomes in the event of switching between manufacturers. Interchangeable biosimilars are eligible for substitution by the pharmacist, in line with their state pharmacy practice laws.

The Generic Drug and Biosimilar User Fee Agreements

The overwhelming success of Hatch-Waxman in promoting a robust generics industry ultimately led to the approval of over 14,000 generic applications. With that incredible volume, however, came complications in FDA's ability to efficiently and effectively review the numerous generic applications being submitted every month. By 2011 there were over 2,700 generic applications pending at FDA and average approval times had begun to exceed 30 months, while Hatch-Waxman had never envisioned reviews taking longer than six.

In order to alleviate the burden on FDA, and begin to expedite generic approvals, the generic industry negotiated and agreed to the first-ever Generic Drug User Fee Program (GDUFA) in 2012. Since the approval of GDUFA, generic manufacturers have paid over one billion dollars in user fees to the FDA for the purposes of hiring and training new staff, updating outdated IT systems, increasing the manufacturing facility inspections necessary to grant approvals, improving the technical specifications of FDA's quality standards, and many other vital agency initiatives. Unfortunately, four years later, the number of pending generic applications has now ballooned to over 4,000 while median approval times exceed 45 months.

Nonetheless, there have been significant achievements under the GDUFA program. FDA has hired and begun to train over 1,000 new employees intended to increase its efficiency in reviewing generic applications, and it has issued a number of critical guidances providing insight into the data necessary in the approval of an applications. These are important steps forward, and we intend to continue to work with FDA to ensure it has the resources it needs to meet the GDUFA goals. We also will continue to seek sufficient clarity into the agency's approval process to ensure that generic manufacturers can submit applications that they reliably know meet the standards set.

Also included in the 2012 law was the inaugural Biosimilar User Fee Act (BSUFA), which provided biosimilar developers with the opportunity to engage FDA early in the development process to develop individualized applications that would meet the newly developing FDA standards. That process has led to 3 approvals thus far and over 50 biosimilar development programs being monitored at FDA.

Both GDUFA and BSUFA play an important role in giving follow-on manufacturers the opportunity to engaged with their regulatory overseer, and create accountability within the agency for meeting performance metrics that assure timely review of applications that leads to the earliest possible availability of affordable products for patients.

Portfolio Selection

The process by which generic and biosimilar manufacturers select which products they wish to pursue regulatory approval is a complex and highly confidential analysis. This calculation can include any number of variables that may come into play, including the complexity in reverse engineering the original product, the state of the intellectual property claimed by the brand manufacturer over the product, the size of the patient population served, the number of likely competitors for that product, the product development and manufacturing capabilities and costs.

Many of the largest generic manufacturers maintain portfolios of hundreds of different products that they manufacture and distribute throughout the country. Unlike brand manufacturers, who focus on a smaller number of high-margin products at any given time, generic manufacturers engage in a different type of portfolio management that is more similar to that of many other commodity markets.

Brand Abuses Delaying Patient Access to Generic Drugs

Generic and biosimilar manufacturers often face significant delay tactics from brand manufacturers looking to game the system in order prevent the massive loss of market share that follows the introduction of a competitive product.

Specifically, there are two major policy areas that directly impact generic manufacturers' ability to get through the initial development stages and reach the market at the earliest possible date:

1.) Abuses of patient safety programs, like the Risk Evaluation and Mitigation Strategies (REMS) programs to delay the development and approval of generic drugs; and
2.) Attempts by brand manufacturers to exempt themselves from scrutiny of their Intellectual Property (IP) by the US Patent and Trademark Office.

The Growing Use of Abusive, Anticompetitive Barriers to Generic Drug Development

In spite of current law that clearly forbids the use of a REMS program to block or

delay approval of a generic drug application, certain brand companies continue to use REMS and other restricted access programs to delay competition. They delay the development of generic drugs by denying generic and biosimilars manufacturers access to samples of branded drug products, which are required to conduct the bioequivalence studies necessary for FDA approval. They have even begun applying restricted access programs to drugs for which the FDA has not required a REMS program in order to delay generic entry.

According to a July 2014 study conducted by Matrix Global Advisors, the ongoing abuse of REMS and REMS-like programs costs the U.S. health system $5.4 billion annually – $1.8 billion to the federal government[7]. But such abusive practices affect more than just payers – they have a direct impact on the costs borne by patients.

These abuses are clearly anticompetitive, and have attracted the interest of the Federal Trade Commission, which argued in one case: "If successful, conduct of the type alleged in this case threatens to undermine the careful balance created by the Hatch-Waxman Act and potentially preserve a brand firm's monopoly indefinitely".[8]

FDA has also expressed its concerns. FDA Office of New Drugs Director Dr. John Jenkins called the abuse a "growing major problem" for FDA. He went on to say, "I think companies have really gone to the extent of kind of abusing the system, because the system was designed to try to ensure the safe use of the drug and now it's become an evergreening system for avoiding generic competition." He added, "The problem is use of REMS to block generic competition and the innovators have really become very aggressive in using that strategy and hiring the best lawyers to back up that strategy."[9]

Presently, two pieces of legislation are pending before Congress that would address these abuses. Congressmen Stivers (R-OH) and Welch (D-VT) have introduced H.R.2481, the FAST Generics Act; and Senators Leahy (D-VT), Grassley (R-IA), Klobuchar (D-MN) and Lee (R-UT) have introduced S.3056, the CREATES Act. While the two bills take different approaches, GPhA is encouraged that each of them directly tackle this growing barrier to generic drug competition and the success of the Hatch-Waxman Act. GPhA encourages the Committee to closely examine these bills and support legislation that would reform pre-approval restrictions on generic and biosimilar drug development. Such legislation must:

1. Ensure that generic and biosimilar drug developers have timely access to brand samples on market-based terms

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[7] Brill, Alex, *Lost Prescription Drug Savings from Use of REMS Programs to Delay Generic Market Entry*, Matrix Global Advisors, July, 2014.
http://www.gphaonline.org/media/cms/REMS_Studyfinal_July2014.pdf

[8] Brief of Federal Trade Commission on Actelion Pharmaceuticals v. Apotex, Inc., No. 1:12-cv-05743 (New Jersey District Court, Mar. 11, 2013).

[9] Gingery, Derrick. REMS That Block Generics Are 'Major' Problem For FDA, Jenkins Says. "The Pink Sheet" Daily. January 8, 2015.

2. Ensure that generic and biosimilar drug developers can enter into a brand's REMS program on fair and equitable terms without unnecessary delay or automatically be allowed to create a comparable (approved by FDA) REMS after a designated time
3. Ensure that the bill applies to REMS-covered drugs as well as brand drug manufacturers who self-impose restrictions on the sale or distribution of their product absent a direct FDA mandate.

Ensuring Appropriate Oversight of Intellectual Property

This Committee has also played a key role in recognizing the *Inter Partes Review* (IPR) process as a critical consumer protection against abusive patent activity in the prescription drug market. The IPR process is an important consumer protection against abusive patent extensions. It plays a vital role in quickly, efficiently and accurately clearing the system of weak patents -- including those that artificially prolong drug exclusivity provisions in order to delay competition from generics. The IPR holds great promise in reducing anticompetitive "evergreening" practices that drive up health care costs for consumers.

Unfortunately, brand manufacturers have sought to delay generic competition and extend their patent life by limiting the opportunity for the appropriate review and challenge of patents. These tactics run counter to the goals of promoting a viable and competitive health care market for consumers, small and large businesses, and taxpayers. As branded specialty drug costs continue to increase and outpace overall health care cost growth, any attempt to weaken a viable, administrative process that helps expedite patient access to more affordable medicines should be rejected.

The ability of generic and biosimilar manufacturers to utilize the IPR process to challenge patents plays a critical role in weeding out weak branded drug patents and bringing generics to market quickly. Proposals to carve out pharmaceuticals from the IPR process have been estimated to cost the federal government $1.4 billion over the course of the next decade.

The FDA Approval Process

Once a manufacturer has acquired the necessary product samples and navigated the various IP claims on any given product, it is still subject to regulatory review processes by FDA in order to ensure patient safety and outcomes. The process used by FDA for evaluating generic products is notably different from that of brand products. Generic and biosimilar manufacturers typically provide very different evidence to demonstrate their bioequivalence than the safety and efficacy studies conducted by brands.

In order to obtain approval, generics are required to provide bioequivalence studies to demonstrate sameness to the reference product. These products typically do not require any clinical trials like the ones used by brands as the drug has already been proven to be safe and effective. Certain "complex" products (I.E., inhalation, extended release, drug-device combinations, etc.) and biosimilars use

technologically advanced analytical analyses that provide in depth characterizations of the drug substance demonstrating their sameness to the original brand product. In addition to the analytical analyses package provided, complex generic and biosimilar manufacturers are required to provide clinical data to demonstrate that patients taking either the reference product or the follow-on product demonstrate the types of similar clinical outcomes that should be expected from the innovator products. Similar to brands, generic manufacturers are also subject to stringent regulatory standards and inspections to ensure their products are safe and effective.

Ultimately, the approval process leads to the issuance of a final generic label from the FDA that is identical to that of the original brand drug. The ability to maintain the same label between all generic products is a fundamental part of the system that promotes such high generic utilization rates among product classes that have seen generic entry. It assures patients and providers that the generic product they are getting will not produce any different result than the products they have grown accustomed to.

For that reason, we have significant concerns regarding a 2013 proposal from FDA to change the process for updating generic labels with new safety information. The proposal would allow for different labels among equivalent products, and likely cause significant confusion among patients and providers. Fortunately, the agency has to date been mindful of the wide range of stakeholders who have expressed similar concerns, including a number of members of this committee. We appreciate the committee's continued engagement on this issue, and hope that FDA will soon abandon this harmful proposal that will only harm competitive markets.

Conclusion

In conclusion, Mr. Chairman, and in light of the extremely complex competitive and regulatory forces that shape generic manufacturer behavior, GPhA continues to believe that the best way to control drug costs generally, whether that be in the drug addiction treatment market or otherwise, is through the promotion of policies that incentivize competition. There are clear opportunities for Congress to support greater development and availability of generic drugs. Specifically, Congress should act quickly to:

- Ensure a fully-resourced Food and Drug Administration (FDA) that can address the backlog of more than 4,000 generic drug applications and shorten FDA median generic drug approval timelines.
- Pass the bipartisan CREATES Act or the FAST Generics Act to curb some brand drug company abuses of FDA safety programs such as Risk Evaluation and Mitigation Strategies (REMS) used to keep generics off the market, an estimated savings of $2.4 billion - 3.2 billion over 10 years.

GPhA looks forward to continuing its work with Congress, the Food and Drug Administration (FDA) and others to accelerate access to safe, effective and more affordable generic drugs. Thank you and I look forward to taking your questions.

Mr. MARINO. Thank you. Mr. Merritt.

TESTIMONY OF MARK MERRITT, PRESIDENT AND CHIEF EXECUTIVE OFFICER, PHARMACEUTICAL CARE MANAGEMENT ASSOCIATION

Mr. MERRITT. Good afternoon Chairman Marino, Ranking Member Johnson, other Members of the Subcommittee. My name is Mark Merritt, president and CEO of the Pharmaceutical Care Management Association. I appreciate this opportunity to appear before the Committee examining sudden price spikes in opioid antagonists.

PCMA is a national trade association representing America's Pharmacy benefits managers which administer prescription drug plans for more than 266 million Americans with health care provided by Fortune 500 companies, health insurers, labor unions, Medicare part D, Medicaid, FEHPB, ACA, and other arenas. PBM's offer a wide variety of services aimed at making prescription drug benefit programs offered safely, efficiently, and affordably for their clients. PBM's are projected to save $654 billion on drug benefit costs over the next decade alone.

For today's discussion, we have seen far too many heartbreaking stories come out of nearly every corner of America about the destruction of lives due to opioid addiction. According to the Centers for Disease Control and Prevention overdose deaths involving prescription opioids have quadrupled since 1999. Over the last 15 years, more than a 165,000 people have died in the U.S. from overdoses related to opioids. The same period has seen a quadrupling of deaths due to overdoses specifically of illicit heroin including over 10,500 deaths in 2014 alone.

Addiction treatments and recovery medications are critical, but an important first step is overall prevention. That is why we commend Congress for passing the Comprehensive Addiction and Recovery Act, CARA. PCMA and its member company supported this legislation which among other provisions created a Medicare part D Lock in Program to curb substance abuse at the pharmacy counter.

The legislation will help stop drugstore shopping by allowing Medicare part D Plans to restrict known abusers to select pharmacies for certain medications, such as opioids. The law also expands the availability of Naloxone to law enforcement agencies and other first responders to reverse overdoses and save lives.

Unfortunately, as opioid antagonists have gotten more widely available, there have also been unprecedented price spikes. We encourage policy makers to consider the following recommendations to stem the rising tide of abuse and reduce cost.

First, we think it should be mandatory that prescribers use E-prescribing for controlled substances. Second, State governments should make their prescription drug management program databases more easily accessible, more user friendly, and better integrated across the country to make that data accurate and in real time. Medicare part D Plans should be allowed to suspend payments of suspicious claims just as is allowed throughout the rest of Medicare. This would effectively eliminate pay and chase activities which increase cost and make fraud detection more difficult.

We also recommend the following policy changes to enhance competition and reduce drug costs. First, address the generic drug backlog at FDA. As has been mentioned before me, improvements have been made but much more needs to be done.

Second, accelerate FDA approval of drugs with little or no competition. Third, limit delaying tactics and patent abuses that prevent competitors from coming to market. Fourth, unlock more innovative value based pricing arrangements by removing the existing barriers such as the Medicaid best price requirement. While this is certainly well intended, it acts as an artificial price war that discourages drug companies from steeper discounts in a commercial market. And finally, eliminate any or all Medicare part D protective classes which significantly weakens the power of PBM's to negotiate rebates and lower prices. Again, I appreciate this opportunity to be here today and look forward to answering any questions you might have.

[The prepared statement of Mr. Merritt follows:]

Testimony of Mark Merritt

Pharmaceutical Care Management Association

Before the

UNITED STATES HOUSE OF REPRESENTATIVES

JUDICIARY SUBCOMMITTEE ON REGULATORY REFORM, COMMERICAL AND ANTITRUST LAW

Treating the Opioid Epidemic:

The State of Competition in the Markets for Addiction Medicine

September 22, 2016

Introduction

Good afternoon. Chairman Marino and Ranking Member Johnson, members of the Subcommittee, ladies and gentlemen, my name is Mark Merritt, President and CEO of the Pharmaceutical Care Management Association (PCMA). I appreciate this opportunity to appear before the Committee for this hearing examining sudden price spikes in opioid antagonists. PCMA is the national association representing America's pharmacy benefit managers (PBMs), which administer prescription drug plans for more than 266 million Americans with health coverage provided through Fortune 500 employers, health insurers, labor unions, Medicare, Medicaid, the Federal Employees Health Benefits Program (FEHBP), and the ACA Exchanges.

PBMs offer a wide variety of services aimed at making prescription drug benefit programs operate safely, efficiently, and affordably for their clients, including health plans, employers, unions, and governments. PBMs are projected to save employers, unions, government programs, and consumers $654 billion — up to 30 percent — on drug benefit costs over the next decade.

America's Opioid Crisis

Too often we have seen the heartbreaking stories coming out of nearly every corner of America about the destruction of lives due to opioid addiction. According to the Centers for Disease Control and Prevention, overdose deaths involving prescription opioids have quadrupled since 1999, commensurate with sales of these prescription drugs.[i] From 1999 to 2014, more than 165,000 people have died in the U.S. from overdoses related to prescription opioids.[ii] The same period has seen a quadrupling of deaths due to overdoses of illicit heroin, including over 10,500 deaths in 2014 alone.[iii]

CARA: A Good First Step to Addressing the Problem

As a first step to address these problems, we commend the Congress for passing the Comprehensive Addiction and Recovery Act (CARA). My organization and our member companies strongly supported this legislation, which, among many provisions, created a Part D "lock-in" program to curb substance abuse in the Medicare Part D Program and expanded the availability of naloxone to law enforcement agencies and other first responders to reverse overdoses and save lives.

Opioid Antagonists and Addiction Treatment Price Increases

Along with efforts to make opioid antagonists more widely available, we are seeing unprecedented increases in the price of products to deliver the drugs. On the market since 1971, naloxone works by blocking opioid drugs from interacting with the brain's receptors, counteracting both the high and the drugs' dangerous side effects, like slow respiration, coma,

and death, during an overdose. The drugs almost instantly pull an overdose victim back to sobriety.

For decades, naloxone was typically administered in a hospital or similar setting via hypodermic needle. However, naloxone in self-contained, nasal-spray delivery packaging (branded as Narcan from Adapt Pharma) was approved by FDA last year. The new mechanism makes it easier for users without medical training to administer the drug, since the drug is increasingly being provided to laypeople.

In addition to the Narcan nasal spray product and the traditional injectable version, there is also an auto-injector version approved in 2014 (Evzio, from kaléo) as well as kits that combine the syringe (from several manufacturers) with a twist-on atomizer to create a nasal spray (assembled into kits by pharmacists) that have been used by first responders for years and now by family members and friends but are not specifically FDA approved.[iv]

Given the high demand and limited sourcing of auto-injectable and nasal-spray delivery versions of naloxone, it appears their manufacturers saw the opportunity to raise prices in a market with limited competition. As many have observed, naloxone has seen drastic price increases in recent years[v]. A popular injectable version of the drug has gone from $0.92 a dose to more than $15 a dose over the last decade. An auto-injector version is up to more than $2,000 a dose.[vi] Observers have noted that prices have risen in part because a field with fewer competitors has reduced pressure on companies to keep prices down. The drug has been made at one time or another by as many as a dozen companies since Endo International Plc received FDA approval for the brand-name version, Narcan, in 1971.[vii]

Unfortunately, this is a story we have seen before—certain manufacturers raising prices on previously affordable drugs once competition recedes or disappears. Just a few months ago, I testified before the House Government Reform Committee on the widely-reported practices of Turing Pharmaceuticals, which raised the price of Daraprim 5,000 percent after acquiring the rights to produce that medication. In this case, Turing acquired the rights to the drug from its sole manufacturer. In the face of no competition, it was able to set any price it wanted.

It is also important to look at the landscape of opioid treatments beyond naloxone. While that drug can save lives as it arrests an overdose, it does little to treat a patient's addiction to opioids. Indeed, patients may immediately feel symptoms of withdrawal as the opioid intoxication recedes. Many people seek treatment for opioid addiction through medication-assisted therapy (MAT) programs. Combining counseling and other services with drugs such as methadone, naltrexone, and buprenorphine, MAT has proven to be clinically effective and to significantly reduce the need for inpatient detoxification services.[viii] The Administration recently nearly tripled the cap on the number of patients a practitioner may treat with buprenorphine to 275. We encourage policymakers to monitor the effects of this change to see if it might be increased

further—the U.S. Substance Abuse and Mental Health Services Administration (SAMHSA) states that MAT services are "greatly underused."[ix]

Of course, treatment of opioid addiction is also subject to changes in the drug market just like drugs for any other condition. While once-daily buprenorphine pills, for example, can reportedly cost $130 to $190 a month, a newly approved six-month implanted version of the drug is priced at the equivalent of $800 a month. One study showed the subcutaneous implant version was somewhat more successful in preventing relapse, but the marginal improvement in adherence comes at a significantly higher cost.[x]

PBMs' Role

The key to making prescription drugs affordable is competition. It is PBMs who help bring down the prices of prescription drugs across the market by harnessing competition among manufacturers. PBMs aggregate the buying clout of millions of enrollees through their client health plans, employers and government payers, enabling plan sponsors and individuals to obtain lower prices for their prescription drugs through price discounts from retail pharmacies, rebates from pharmaceutical manufacturers, and the efficiencies of mail-service pharmacies.

Lack of competition and the presence of coverage mandates reduce PBMs' ability to negotiate lower drug costs. For example, the State of New York recently enacted legislation that requires insurance coverage of naloxone when prescribed to a person who is addicted to opioids and to her family members on the same insurance plan.[xi] While well-intentioned, such actions tie the hands of PBMs to negotiate discounts and rebates, since the drug manufacturers know the drug must be covered no matter the price set.

Given the immediate need to stop an overdose, today 43 states allow purchase of naloxone without a prescription, or will soon operationalize plans to do so. A person who is at risk of overdose, his or her caregiver, or a family member can now walk in to a retail pharmacy and obtain naloxone. Many first responders such as police, fire fighters, paramedics, and others keep naloxone on hand or nearby at all times. The ready availability of the drug has saved many lives. However, as dozens of states have passed laws to make naloxone injectors and/or inhalers available without a prescription, prices have gone up. Given consumers' ability to obtain naloxone, without a physician's prescription, directly at the pharmacy counter, naloxone is increasingly being dispensed to people other than the intended end-user. This raises questions about individuals' medical records as well as presents challenges to insurers.

Policy Changes Could Improve the Opioid Crisis

While the focus of this hearing has been on naloxone, I think it is important to note that opioid reversal drug is but one tool we have to fight the opioid epidemic. Indeed, even if a patient's overdose is stopped, he or she may still remain addicted to the opioid. A comprehensive, multi-

faceted solution is the only way to stop and reverse the alarming trends seen in the past few years.

We believe a number of practical steps can be taken to ameliorate the rising tide of abuse. At least in the case of abuse of prescription opioids, we recommend:

- **Mandatory eRx for Controlled substances**: Although adoption of e-prescribing has been shown to dramatically reduce medication errors and fraud, challenges to efficient processes and errors still persist, hindering the wider adoption of e-prescribing for controlled substances (EPCS).

- **Improving/Integrating PDMPs:** State governments should make their PDMP databases more easily accessible, more user-friendly, and better integrated across the country, and to make the data accurate in real-time. The goal would be to create prescriber, pharmacist, and insurer access to real-time information, or come as close as possible to real-time information.

- **Provider Check of PDMP for Controlled Substance Prescriptions:** Prescribers should be required to check state Prescription Drug Management Program (PDMP) databases when prescribing a schedule II opioid, such as oxycodone or morphine.

- **Allow Stronger Measures to Remove or Discipline Rogue Pharmacies from Plan Networks.** Today, any-willing-provider and other pharmacy network laws make it difficult for plans and PBMs to remove pharmacies that engage in fraudulent practices from plan- and provider-contracted networks. There should be common-sense measures to allow rogue pharmacies to be excluded from such networks and to allow plans to suspend payments for suspect claims.

- **Engage the Public on the Dangers of Controlled Substances:** Given clear evidence of past malfeasance by certain drug manufacturers on downplaying the risks of opioids to prescribers, the drug industry should fund a campaign to warn prescribers and consumers about the inappropriate use of opioids and other controlled substances.

- **Expand Drug Take-back Programs**: The Drug Enforcement Administration (DEA) coordinates a nationwide program with neighborhood pharmacies, local law enforcement, and other community activists to offer a means of prescription drug disposal. However, regulatory hurdles may be preventing more pharmacies from taking advantage of this opportunity. Senators Joni Ernst and Chuck Grassley have requested that the Government Accountability Office report on the DEA's regulations that pose barriers to voluntary participation.

Policy Changes Could Enhance Competition to Manage Drug Spending

We have specifically discussed the price of naloxone in this hearing, but news reports have shown again and again that manufacturers of any drugs not subject to competition can exploit their position in the market. Recent examples, including the high initial launch prices of hepatitis C drugs and PCSK9 cholesterol drugs, show that where competition exists, PBMs can leverage it to bring prices down. A number of policy changes to enhance competition could lower the cost of drugs generally or lessen the ability to exploit loopholes in the law that have allowed some manufacturers to implement price gouging and anticompetitive distribution regimes.

- **Removing the Generic Drug Backlog:** PBMs could bring additional competition to the market for other drugs, but FDA prioritizes breakthrough therapies, leaving generic and "me-too" brand drugs languishing on the approval sidelines. While the FDA has argued it has cleared the generic backlog, in actuality it has merely given the applications an initial look. The generic approval backlog, at 36 months, is down slightly from recent years, but still lengthy.[xii]

- **Bringing Speedier Approval of Drugs Based on Economic Need:** A number of recently approved drug and biologic therapies have entered the market with historically high manufacturer prices. Rather than directly intervening in manufacturer pricing, policymakers could better encourage price competition in the marketplace by accelerating FDA approval of drugs in development for conditions where the cost of existing medications is a barrier to treatment and where manufacturers of current therapies have little incentive to compete on price, e.g., where there are only one or two drugs in the class and no generics.

- **Eliminating Any or All of Medicare Part D's Protected Classes:** Part D requires that "all or substantially all" drugs in six different classes be covered by Part D plans. This requirement significantly weakens the power of PBMs to negotiate rebates and lower prices. The Medicare Payment Advisory Commission (MedPAC) has recommended lifting the requirement for antidepressants and immunosuppressants.

- **Unlocking More Innovative Pricing Arrangements:** The rapid increase in the cost of specialty drugs is driving the market to begin to consider alternative ways of paying for these expensive therapies. For PBMs and drug manufacturers, these trends will demand innovative approaches to pricing. To enable more creative value-based arrangements, however, our laws and regulations will need to be updated. For example, Medicaid best-price rules make drug manufacturers reluctant to offer pricing schedules that could, in theory, result in very low unit prices for some groups of patients, because manufacturers must then give that price to all Medicaid enrollees.[xiii]

PBMs exist because they increase the quality and affordability of prescription drug benefits. PCMA's member companies harness market forces and competition to corral drugs costs and deliver high-quality benefits and services to their health plan clients and enrollees. PCMA appreciates the opportunity to testify on the market for addiction medications, and looks forward to working with the Congress on ways to address the opioid crisis.

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[xi] New York State Bill S. 8137 as passed June 22, 2016.
[xii] HHS, "Department of Health and Human Services, Fiscal Year 2017 Justification of Estimates for Appropriations Committees, Food and Drug Administration." http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/BudgetReports/UCM485237.pdf
[xiii] Dana Goldman and Darius Lakdawalla, "Moving Beyond Price-Per-Dose In The Pharmaceutical Industry," Health Affairs Blog, September 30, 2015.

Mr. MARINO. Thank you. Dr. Ketcham.

TESTIMONY OF ERIC KETCHAM, M.D., AMERICAN COLLEGE OF EMERGENCY PHYSICIANS (ACEP), MEDICAL DIRECTOR, EMERGENCY DEPARTMENT AND URGENT CARE, CO-MEDICAL DIRECTOR, EMS SAN JUAN REGIONAL MEDICAL CENTER

Dr. KETCHAM. Thank you, Mr. Chairman. My name is Dr. Eric Ketcham. I am an emergency department medical director and EMS Medical Director and a medical director for an Opioid Addiction Treatment Clinic. On behalf of the 37,000 members of the American College of Emergency Physicians, I would like to thank you for this opportunity to testify today about this important issue.

The unnecessarily high price of these medications obstructs access to treatment for opioid addiction and overdose in America. And thus prolongs the scourge of heroin prescription opioid addiction and puts American lives at risk. Access to Buprenorphine, which should be a low cost medication, must be expanded so that more Americans can be successfully treated for the affliction of opioid dependence.

Secondly, access to Naloxone which also should be a low cost medication, must be increased. This is truly a lifesaving drug that when used properly can reverse opioid overdoses and save lives. In its current, most commonly used form, Buprenorphine has been FDA approved for 30 years. Because of its unique properties it produces much less euphoria and respiratory depression than traditional opioids, such as oxycodone, heroin, and methadone.

When properly prescribed, this medication is a very safe alternative to Methadone and thus can be effectively utilized to treat opioid abuse and addiction by a variety of physicians in a variety of settings, as opposed to Methadone which must be administered in a licensed opioid addiction treatment clinic, such as one that I run.

One would think that a lifesaving and life transforming medication such as Buprenorphine, which has a well-established safety profile, would be accessible to hundreds of thousands more opioid dependent patients. Unfortunately, that is not the case. In my written testimony, I provide specific examples of the rising prices associated with Buprenorphine and the related Buprenorphine Naloxone combination medications, including their generic counterparts.

For example, based on surveys I have conducted of local pharmacies affiliated with national chains in my region, the cost for a 30-day supply of Buprenorphine—that is two 8 mg tablets per day, the usual dose, is now $334 compared to a $142 just 6 months ago. And a month of the Suboxone brand name Buprenorphine Naloxone combination filmstrips, is $532. Shockingly, the generic version of the combination tablets is even more than the brand name prescription film strips this week and cost $625 for a 30-day supply.

The critical medication we use to treat acute opioid overdose is Naloxone. It has been utilized in hospitals and by fire EMS personal for decades. More recently, there has been an organized effort expand direct access to Naloxone and in some regions it can al-

ready be purchased from a pharmacy even without a prescription. However, these efforts to expand availability of Naloxone have surprisingly not caused the price of this medication to decrease. In fact, the price of Naloxone in nearly all forms of packaging has been steadily climbing.

In my community, the cost of a one-millimeter syringe of 0.4 milligrams of Naloxone went from about $12 in 2012 to $30 in 2016. Without a hospital or municipal volume discount for fire or EMS service, the preloaded two milligram syringe used by many first responders is now priced at approximately $49 a dose. That same dose was $17 in 2014 and reportedly as low as a $1 in 2001.

The consequence of these rising prices may force Naloxone out of the budget for the rural fire or EMS service that does not have the buying power of a hospital or a larger municipal agency. Furthermore, in my region, Naloxone products designed for the layperson are the most expensive of all.

For example, the cash price for the four-milligram nasal spray has increased to a $150 for the package of two doses. This simple device does not present a form of revolutionary technology, and it includes a generic, and until recently, very inexpensive medication. What is truly astounding is the price for the single dose Naloxone autoinjector, which can be more than $2,200 and is often not a sufficient rescue dose.

Another topic not yet addressed on this greater topic is the expanding Good Samaritan Laws are an important aspect of increasing Naloxone availability. These efforts must be paired with legislation that would make healthcare providers and lay users immune from liability for failure or misuse of the product by bystanders.

Moreover, administration of Naloxone is often not as simple as providing a single dose for various reasons. That is why ASEP strongly recommends that whenever Naloxone is administered by a bystander, to treat an opioid overdose, EMS must be called, and ideally, that patient would then be transported to the nearest emergency department for evaluation.

In conclusion, we urge Congress to help make Buprenorphine and Naloxone more readily available to those suffering from opioid addiction. These critical drugs cannot only save countless lives, but help alleviate a great burden on society by reducing crime, incarceration, and healthcare expenses including complications from intravenous drug use such as spreading HIV and Hepatitis C. Most important, access to Buprenorphine and Naloxone means potentially deadly overdose deaths could be avoided.

If Congress wants to help increase access to these drugs, then something must be done to curtail the cost of these lifesaving medications. Thank you, and I look forward to answering any questions you may have.

[The prepared statement of Dr. Ketcham follows:]

Statement of

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Before the
Judiciary Subcommittee on Regulatory Reform, Commercial and Antitrust Law
U.S. House of Representatives

Hearing on

"Treating the Opioid Epidemic:
The State of Competition in the Markets for Addiction Medicine"

Presented
September 22, 2016

I. Introduction

Thank you Mr. Chairman. My name is Eric Ketcham, M.D., F.A.C.E.P., and I am an Emergency Department Medical Director, an EMS Medical Director, a Medical Director for an Opioid Addiction Treatment Clinic, and the Immediate Past-President of the New Mexico Chapter of the American College of Emergency Physicians (ACEP). On behalf of the 37,000 members of ACEP, I would like to thank you for this opportunity to testify today about the high and rising prices of two medications, buprenorphine and naloxone, critical to the treatment of opioid addiction and overdose, respectively. The unnecessarily high price attached to these medications increases the cost of healthcare, and reduces patient access to these medications. The pricing of these medications by several pharmaceutical companies obstructs access to treatment for opioid addiction and overdose in America, and thus prolongs the scourge of heroin and prescription opioid addiction, and puts American lives at risk.

The United States currently faces a steadily growing crisis of opioid abuse and addiction that has reached epidemic proportions. According to the CDC, for the year 2013:

> "The total economic burden is estimated to be $78.5 billion. Over one third of this amount is due to increased health care and substance abuse treatment costs ($28.9 billion). Approximately one quarter of the cost is borne by the public sector in health care, substance abuse treatment, and criminal justice costs."[1]

Furthermore, more Americans have died each year during the past decade from drug overdoses than motor vehicle accidents.[2] In 2014, more than 28,000 Americans died of opioid overdoses alone.[3] This opioid abuse epidemic claims the lives of more than 78 Americans every day.[3]

We could endlessly debate the factors that have contributed to the rise of this widespread and deadly epidemic in America, and how best to curb its growth. However, today we must focus on two unique, specific treatments for this epidemic.

First, use of buprenorphine, which should be a low-cost medication, ought to be expanded so that more Americans could be successfully treated for the affliction of opioid dependence. These treatments would help alleviate a great burden on society by ameliorating crime, incarceration and healthcare expenses, including complications from intravenous drug use (HIV, Hepatitis C, infections, etc.), but most important, access to buprenorphine means more potentially deadly overdose deaths could be avoided.

Second, access to naloxone, which also should be a low-cost medication, must be increased. This is truly a life-saving drug that when used properly can reverse opioid overdoses and save lives.

Congress must ensure that buprenorphine, and buprenorphine/naloxone combination medications are affordable as prescriptions. Congress must also act to ensure naloxone is widely available and affordable for EMS and law enforcement agencies, as well as for patients and their caregivers.

II. Buprenorphine

Buprenorphine was developed in 1966 for the purpose of treating opioid dependence, but was first licensed, however, as an effective analgesic for severe pain.[4] The injectable form was licensed in Europe in 1978 and the oral dissolvable (sublingual) form followed in 1982.[4] By 1985, buprenorphine was licensed in 29 countries and was approved by the U.S. Food and Drug

Administration (FDA) the same year.[4] Although this medication was originally researched and developed for the purpose of treating opioid addiction, it was not successfully brought to market for this indication until 1996 when France implemented an off-label program of medication assisted treatment (MAT) for heroin addiction.[4,5] The results in France were astounding:

- The incidence of deaths from heroin overdoses dropped dramatically (by 2004, deaths from heroin overdoses had dropped over 80%) and
- The rate of HIV transmission through injection drug use (IDU) dropped by 50%.[5]

This dramatic success inspired the original developer of the medication, Reckitts Benckiser Pharmaceuticals, to return to its pursuit of licensing buprenorphine for the treatment of opioid addiction.[4] In 2002, the manufacturer obtained FDA approval for both the mono-agent buprenorphine (*Subutex*) and the combination medication buprenorphine/naloxone (*Suboxone*).[4]

Buprenorphine is an opioid medication known as a "partial agonist" and as an "agonist-antagonist." Essentially, this means that, similar to opioids, buprenorphine produces effects such as euphoria or respiratory depression. However, with this medication these effects are weaker than those of normal opioids such as heroin and methadone.[6]

Because of these properties, and even though it has an analgesic potency 25 times greater than morphine, there is a ceiling limit to its adverse effects.[4,7,8,9] With the exception of small children, buprenorphine causes only limited respiratory and central nervous system depression. When properly prescribed, this medication is a very safe alternative to methadone and thus can be effectively utilized to treat opioid abuse and addiction by a variety of physicians in a variety of

settings, as opposed to methadone, which must be administered in a licensed opioid addiction treatment clinic.[4,10,11,12]

One would think that a life-saving and life-transforming medication such as buprenorphine, which has a well-established safety profile as well as generic equivalents, would be accessible by hundreds of thousands more opioid dependent patients. Unfortunately, that is not the case.

Although access to buprenorphine can be diminished due to a shortage of properly trained physicians, many patients are unable to access this medication simply based on cost. Even more distressing, the cost of the generic version has more than doubled during the last six months, even though there are now multiple generic producers of buprenorphine.

Surveying local pharmacies in northwest New Mexico (all from national pharmacy chains), the wholesale price paid by the pharmacy for generic 8mg buprenorphine sublingual tablets recently increased from $2.37/tablet to $5.57/tablet. Most opioid dependent patients are treated with two tablets daily, and thus a 30-day supply costs $334.20. Although the pharmacies are providing this medication to the patients at near cost, with a margin of less than 2% (to cover the cost of packaging), if the uninsured or underinsured must also pay to see the prescribing physician, then for many this becomes unaffordable and many prescriptions go unfilled.

For Medicaid beneficiaries, that program is paying the full retail price and state Medicaid budgets are bearing a substantial burden trying to cover each patient's regular monthly supply of buprenorphine at an annual cost of more than $4,000 each. Many opioid addicted patients truly are safer if prescribed the combination medication of buprenorphine/naloxone (e.g. Suboxone,

Zubsolv, Bunavail) because it reduces the likelihood of injecting the medication rather than taking it sublingually. This is concerning, because, as of this week, in northwest New Mexico pharmacies, the average wholesale price (AWP), which is similar to the average retail price, for 8mg/2mg buprenorphine/naloxone (Suboxone) oral film strips is now up to $8.67 each, or $532.08 for 60 tablets (a 30-day supply). There are, however, "manufacturer coupons" sometimes available on-line, or from the pharmacy, to reduce this price by $50. Interestingly, however, the prices of the three brand names (Suboxone, Zubsolv, and Bunavail) at equipotent doses are all about the same, and after coupons, end up at roughly $470 (30-day supply).

Shockingly, the generic versions of Suboxone (buprenorphine/naloxone) tablets cost even more than the brand name prescriptions, despite the fact that it's a generic formulation and there are multiple manufacturers; this week they cost approximately $10.42 a tablet ($625.28 for a 30-day supply).

The high cost of buprenorphine, combined with the shortage of licensed prescribing physicians and the high rate of uninsured or underinsured individuals who are in need of this medication, has led many to turn to the "secondary market" for illegally diverted opioid addiction medications.[13,14] For the vast majority of opioid-dependent patients, whether addicted to heroin or prescription opioids (whose chronic pain and/or dependence is not managed by a physician or other healthcare provider), much of their life is spent securing the next supply, which might only be for the day, of heroin, oxycodone, etc. Rarely do these patients experience a "high," or state of euphoria.[13] The need to continue using heroin or other opioids is to avoid the extremely miserable condition of acute opioid withdrawal (abdominal pains, vomiting, diarrhea, severe

muscle cramps, tremor, twitching, headaches, dysphoria, and sometimes seizures).[12] Acute opioid withdrawal puts patients with certain underlying medical conditions (e.g. insulin dependent diabetes, epilepsy, heart failure) at particular risk of critical illness or death.

However, buprenorphine does not provide any significant euphoria even for those individuals who have never taken it before. As most addiction medicine physicians will attest and recent research supports, most patients who obtain buprenorphine on the secondary market do so simply for the purpose of self-managing their addiction.[12,13] Currently, in northwest New Mexico, the street price of buprenorphine is similar to the retail prices described earlier, usually marked up 50% or less above these current prescription prices.

III. Naloxone

Naloxone was patented over 55 years ago and approved for the treatment of opioid overdose by the FDA in 1971. Naloxone is on the World Health Organization's list of essential medicines, and thus is regarded as a medication necessary to the most basic health system. This medication can be administered intravenously, intramuscularly or intranasally and is effective within minutes. The response can be profound, literally producing a "Lazarus-like" effect. Victims of opioid overdose often completely stop breathing and without respiratory support death is imminent. However, after the prompt injection of naloxone, the victim begins to breathe again and may quickly become fully conscious, rescued from the edge of death.

Naloxone has been utilized in hospitals and by fire and EMS personnel for decades. In some communities where there has been a particularly high rate of opioid overdoses, law enforcement personnel carry naloxone in order to administer the medication while waiting for EMS to arrive, thus saving minutes and saving lives.

Recognizing the steady growth of opioid abuse and addiction in many communities around the country, there has been a movement, supported by the medical community, to further expand patient access to naloxone directly.[15] Some hospitals and clinics have begun to dispense naloxone kits to patients at risk of overdose and more physicians are writing prescriptions for at-risk patients to have naloxone kits available at home. In some regions, it is now legal for patients to purchase naloxone directly from a pharmacy, even without a prescription.[16]

While there has been a movement to increase prompt access to naloxone for opioid overdose victims over the last several years, the price of naloxone in nearly all forms of packaging has been steadily climbing in this country. Although the price of a pre-loaded 1 ml syringe of 0.4mg/ml of naloxone in India has risen to 78 Rupees (roughly $1.17 U.S.), the price of the same dose and concentration of naloxone in a single dose syringe device (carpuject) in northwest New Mexico has risen from approximately $12 in 2012 to ~$30 in 2016.[17] Without a hospital or municipal volume discount for a fire or EMS service, the Amphastar Inc. produced preloaded 2mg in 2ml syringe product (requires a fairly basic three-part assembly) used by many fire and EMS services is now priced at approximately $49/dose and has risen incrementally from approximately $17/dose in 2014 (and was reportedly about $1/dose in 2001).[18]

Given the increasing incidence of opioid overdoses, some of which are massive overdoses (e.g. from heroin contaminated with fentanyl or other drugs that are much more powerful than standard opioids) that require much more than 0.4mg, or even more than 2mg, of naloxone to successfully resuscitate an opioid overdose victim, fire and EMS services are now having to pay much closer attention to naloxone in their pharmaceutical budget. The consequence of these rising prices may force naloxone out of the budget for the rural fire or EMS service that doesn't have the buying power of a hospital or larger municipal agency.

Furthermore, while lawmakers and the medical community have been making progress in expanding access to naloxone through education and focused naloxone program implementation, much of this targeted access remains significantly theoretical as naloxone products designed for the layperson are the most expensive of all naloxone formulations. For example, the cash price for the 4mg nasal spray product produced by Adapt Pharma has increased to $150 for the package of two nasal sprays in northwest New Mexico.[17,19] The device certainly doesn't present any form of revolutionary technology and it includes a generic, and until recently, very inexpensive medication.

While the price of the Adapt Pharma product is cost prohibitive for individuals and outreach programs alike, it is the *Evzio* naloxone auto-injector product (built on the same basic technology of the *Epi-Pen* epinephrine auto injector), produced by Kaleo, Inc. that is truly astounding.[17,20] This product only includes 0.4mg per dose, which again may be insufficient as a rescue dose for many opioid overdoses, yet a two-pack of these devices is currently priced at $4,500.[17,19] It has

been reported that the cost of this device for EMS and law enforcement agencies is around $250 per two-pack, but this rate is significantly subsidized by federal grants.

There are also reportedly "patient-assistance programs" to help make the product affordable with commercial health insurance.[17,19] However, when I attempted to fill a prescription for this product; I was denied coverage even though I have a premium level employer-provided health insurance plan, with robust pharmaceutical coverage.

It must be noted that while ACEP applauds the great efforts to move naloxone closer to more patients at risk of overdose, with the concept of making naloxone an over-the-counter medication, we must acknowledge that there are several additional concerns and potential consequences related to this course of action, which must be carefully considered. First, unlike using an epinephrine auto-injector, almost no one ever saves his/her own life with naloxone. If not administered by EMS or law enforcement personnel, then naloxone must be administered by a bystander who could be a complete stranger, but who is more likely to be a friend, family member, or an off-duty EMT, nurse or physician. To rescue someone from a potential deadly opioid overdose, one must take action quickly and decisively, often with incomplete information.

For this reason, it is imperative that any directives or legislative efforts to expand naloxone to the public are accompanied by robust public education programs to improve the chances of correct patient selection and proper naloxone administration. Likewise, to encourage and ensure bystanders are not penalized for making a good faith effort to save someone's life, there must be an expansion of Good Samaritan laws because there are many other conditions that could cause

someone, including individuals who are opioid dependent, to be unconscious that are unrelated to an opioid overdose. If an opioid-dependent patient is not suffering from an acute overdose, but rather another condition, a dose of naloxone could force that patient into a state of acute opioid withdrawal and actually make the patient sicker despite the good intentions of the bystander administering the naloxone. The potential associated liability for placing individuals at risk for such an adverse event could certainly cause many physicians to be hesitant to prescribe naloxone kits for their patients.

Lastly, it cannot be emphasized often enough that the administration of a patient's naloxone auto injector or nasal spray empties the device and the device cannot be reused. The potential danger is that the opioids the patient overdosed on may have a much longer half-life than the naloxone administered to the patient. Thus, as the naloxone wears off, the patient may be at the same risk of relapsing into a deadly overdose. As advocates of patient safety, ACEP strongly recommends that whenever naloxone is administered by a bystander to treat an opioid overdose, EMS must be called. Ideally, any patient suffering from an opioid overdose should be evaluated in an emergency department.

IV. Conclusion

We are in the midst of an epidemic of opioid abuse and addiction that will take the lives of more than 28,000 Americans this year and keep many more Americans disabled. To help avert this tragedy, Congress first must act to ensure that buprenorphine, and buprenorphine/naloxone combination medications are affordable as prescriptions. Congress must also act to ensure access to naloxone is affordable and widely available to EMS and law enforcement agencies, as well as to patients and their caregivers who receive appropriate education and training. Finally, as we

push forward to make naloxone more readily available to patients, Congress must address the need for more robust patient and public education along with liability limitations for Good Samaritans and the prescribing physicians seeking to contain this disease. Thank you again for this opportunity to testify before your committee on these important issues.

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Mr. MARINO. Thank you. Professor Feldman.

TESTIMONY OF ROBIN FELDMAN, ESQ., HARRY AND LILLIAN HASTINGS PROFESSOR OF LAW, DIRECTOR OF THE INSTITUTE FOR INNOVATION LAW, UC HASTINGS COLLEGE OF THE LAW

Ms. FELDMAN. Mr. Chairman and esteemed Subcommittee members, I am honored to address competition issues in the market for addiction medicine. Open and vigorous competition is the backbone of U.S. markets, but we are not seeing that in the market for addiction medicine. Rather, drug companies are engaging in regulatory games, stringing these out one after another while competition languishes on the sidelines.

These games come in two baskets. One set involves manipulating Hatch-Waxman, which is the system for quick approval of generic drugs when the patents on the main drug expires. The other basket of games relates to the system for non-patent exclusivities known as regulatory exclusivities.

Some of these games just blatantly delay entry of competition. With addiction medicine, for example, we have seen petitions asking the FDA to deny approval of any generic versions. Among many of the demands, one addiction medicine company asked the FDA to require things for generic Suboxone that the FDA did not have the authority to do and that we would not want them to do in the first place. Now, the agency denies 80 percent of these petitions, as it denied this one, but the process takes time, even for silly petitions. In the case of the Suboxone petition, the FDA was so disturbed by the petitioning behavior that it referred the company's behavior to the Federal Trade Commission.

In other games, companies block competitors from getting access to the samples they need to get approval. Generics have to show that their drug is the same as the branded, and some brand companies just flatly refuse to sell samples to generic companies or to cooperate with generic companies to write safety plans. With addiction medicine, the FDA so despaired of getting one brand name company to cooperate that it took the unprecedented step of granting a waiver so that the generic company could just go forward on its own. Again, competition languished for another stretch in the addiction medicine market.

In other games, companies make slight modifications to the dosage or the delivery systems, and then encourage doctors to prescribe the new version, or even withdraw the old version completely. If that is successful, there is no market for the old version. There is just a new market for the new version that is protected by shiny new patents. We have seen this in the addiction medicine market as well where a company switched from tablets to meltaways just before the patents expired.

Now these modification patents are quite weak. And in fact, when generics challenge these patents, they win three quarters of the time. But again, these challenges can take years and competition is thwarted, and prices stay high.

In addition to gaming, Hatch-Waxman companies carve out competition free zones in ways that have nothing to do with patents. There are 13 forms of regulatory exclusivities that companies can

obtain by doing things like new clinical studies or pediatric studies. And with these, companies can keep competitors out even if the patent has expired.

Now these zones were created for very appealing reasons, but they are being exploited now to block competition in ways that were never intended. As a side note, the key drug in the addiction medicine market came through the most powerful of these, the orphan drug exclusivity.

The spotlight today is on the market for addiction medicine, but the game playing is epidemic throughout the pharmaceutical industry. Companies pile these games on, one after another, exploiting the laws and regulations that are in place. As always, society pays the price with higher taxes to pay for soaring Medicare costs, higher insurance premiums, higher treatment costs, and more suffering for those who cannot afford treatment. Nowhere is this terrible combination more apparent than in the market for addiction medicine. Thank you very much.

[The prepared statement of Ms. Feldman follows:]

Written Statement of Professor Robin Feldman, Director of the Institute for Innovation Law, University of California Hastings College of the Law

House of Representatives, Judiciary Subcommittee on Regulatory Reform, Commercial & Antitrust Law

Hearing on Treating the Opioid Epidemic: The State of Competition in the Markets for Addiction Medicine

September 22, 2016

Mr. Chairman and esteemed members of the Committee, I am Professor Robin Feldman of the University of California Hastings, and it is an honor to testify before you today on competition issues in the addiction treatment market. Open and vigorous competition is the backbone of the U.S. market, but that is not what we are seeing in the market for treating opioid addiction. Instead of vigorous competition, drug companies have engaged in legal and regulatory games to block entry into the market, stringing these games out, one after another, while competition languishes on the sidelines. The games come in two baskets: one set involves manipulating the Hatch-Waxman system for expedited entry of generic drugs when the patent expires; and the other set involves manipulating the system of non-patent exclusivities.

I have studied both areas in depth, including conducting an empirical study using more than a decade of FDA data. Below are three papers that identify and describe the games pharmaceutical companies are currently playing:

- *Drug Wars: A New Generation of Generic Pharmaceutical Delay*, Harvard Journal on Legislation (Summer 2016), available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2659308

  This article presents a comprehensive overview of three generations of games pharmaceutical companies play to keep generics off the market and maintain monopoly pricing. The first two generations were dominated by anticompetitive collusion. With the third generation, the industry has moved toward obstruction, using administrative processes, regulatory schemes and drug modifications to prevent generics from entering the market. The paper describes behavior in the opioid addiction treatment market in key examples throughout.

- *Regulatory Property: The New IP*, Columbia Journal of Law & the Arts (forthcoming), available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2815667

  This article describes a sprawling system of regulatory property which has developed alongside traditional intellectual property over the past thirty

years, and which pharmaceutical companies have been relying on to gain market advantage. Appendix A, a chart aggregating all thirteen regulatory regimes in one place, may be particularly helpful.

- *Empirical Evidence of Drug Pricing Games: A Citizen's Pathway Gone Astray*, Stanford Technology Law Review (forthcoming), available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2833151

  This article presents an empirical study we conducted using more than a decade of FDA data. The study found that pharmaceutical companies are systemically using the FDA's citizen petition process to delay approval of generic competitors. The timing of citizen petition filings suggests that companies are using them as a last-ditch effort to maintain market monopoly.

While the spotlight today is on the market for treating opioid abuse, the behavior is endemic to the pharmaceutical industry. One sees the same baskets of behavior throughout, including manipulation of the Hatch-Waxman system and manipulation of non-patent exclusivities. It is critical to understand all of these systems as single, unified organism. Only if we analyze them as a coherent whole can we hope to understand how all of the pieces fit together and address the places where systemic dysfunctions are arising. Without that, society will continue to pay the cost in the form of higher taxes (to compensate for soaring Medicare costs), higher insurance premiums, higher treatment costs, and more suffering for those who cannot afford to pay. Nowhere is this more apparent than in the opioid addiction treatment market.

Mr. MARINO. Thank you. Now, as I stated earlier, the Chair now recognizes the Chairman of the full Judiciary Committee, Mr. Bob Goodlatte from Virginia.

Mr. GOODLATTE. Thank you Mr. Chairman, and I apologize for stepping out of turn. It has been a very busy day, and I was held up in the last meeting; also I am going to have to leave for another one pretty soon. But I do want to offer some thoughts on this important subject. Today's preceding marks the fourth in our series of hearings focused on competition in the healthcare marketplace. Now, the Committee turns its attention to the pharmaceutical industry and the drugs that are used in the treatment of opioid overdose and addiction.

Competition in the addiction medicine markets, like the pharmaceutical market as a whole, involves a delicate balance. On the one hand, we want to encourage pharmaceutical companies to invest in expensive research and development in order to bring innovative and life-saving drugs to market. On the other hand, we also want to encourage sufficient competition to ensure that there is an appropriate check on consumer prices. Today's hearing will explore what polices help to maintain this balance and whether it has been upset.

Like other drugs in the market, addiction medicine has been the subject of media reports detailing steady and sometimes dramatic price increases. Oftentimes, however, these reports can be misleading, glossing over nuance to achieve a sensational headline. Today's hearing will allow us to explore whether prices have indeed increased material, and what competitive factors impact the ultimate cost to consumers.

The issues that have been raised in connection with the addiction medicine market parallel the issues facing the pharmaceutical market at large. For example, two of the most predominant drugs used in the treatment of the opioid epidemic have existed for over 50 years. Yet, new variations of these old drugs and increasingly inventive applications to administer the drugs continue to come to market often accompanied by high prices tags. Persistent innovation is one of the hallmarks of a free market and should be celebrated.

However, there have been allegations that some companies may be using this innovation as a disguise to cover-up the manipulation of regulations to preclude competitors from coming to market. Clearly, this is anti-competitive conduct that should be swiftly and harshly punished. I look forward to hearing the witnesses' views on this issue and whether our existing antitrust laws are equipped to address any such behavior.

I also look forward to hearing what policies influence competition in the addiction medicine market including the impact on competition on regulatory oversight by the Drug Enforcement Agency, the Food and Drug Administration, and the Department of Health and Human Services. To the extent regulation is necessary, we should ensure that the addiction medicine market and the entire pharmaceutical market includes proper incentives that foster a competitive environment.

No one wishes for a friend, family member, or a loved one to succumb to addiction. For those that are forced to face the opioid epi-

demic head on, we should strive to encourage a competitive market for the drugs that can help them back on the path toward recovery.

I also want to mention that I think the government plays a role in this that needs to be examined more closely. We, I think, invited the Drug Enforcement Administration to participate in this hearing, and for various reasons they are not here today. But a number of issues related to their work need to be addressed as a part of making sure that our consumers, our physicians, and our first pharmaceutical companies, are able to operate in a manner that effectively brings the drugs to the right people at the right time and I think sometimes government regulations are interfering with that.

Therefore, we should continue to expect further public examination of this, and have the DEA here before us in the future to address this and some other of their regulatory issues.

So, thank you Mr. Chairman for your forbearance, and I look forward to hearing the questions of the other Members of the Committee.

Mr. MARINO. Thank you. We will now move into the questioning of the panel. The panel did such a good job in keeping within their 5 minutes, now we will see how well we Congress Members do.

Dr. Pritchett, I am especially interested in innovative new options to treat overdose. As an 18-year prosecutor, I have seen hundreds if not thousands. When I think of this space, I look to the loved ones and first responders who are often the first to address addiction and potential overdose. Your testimony mentions that there are innovative drugs in new therapeutic areas.

My two questions are, would you expand on this and explain how branded pharmaceuticals are investing and researching new ways to address increase need in recent years, as well as different applications that would be used by first responders, emergency medical personal, and family? And anytime you want me to repeat these, please ask me.

Ms. PRITCHETT. In terms of looking at the Naloxone space, yes, there has been a substantial range of generic products available for a long period of time. As I mentioned in my testimony, what we have seen change in the past couple of years is the market has sent different signals to our industry. So what we have seen is a need for expanded options in terms of convenient delivery forms, and we have seen a substantial change in State laws, making Naloxone more widely available.

One of the key dynamics here is that now most States have changed their laws allowing Naloxone to be available at the retail level via standing orders, meaning without a prescription. So, it is hard to say in terms of the pricing issues, what is occurring there in terms of whether in different elements as a supply chain how that is affecting pricing at the retail level. But, in terms of the fact that these products are being made more readily available to first responders and others, that speaks to the increased demand for convenient delivery systems.

And what we have seen over the past few years, we have seen the introduction of an autoinjector but we have also seen most recently the approval of a nasal spray. At the same time, another nasal spray was in development that was not approved by the

FDA. But in terms of our review of the pipeline, there are about 35 drugs in development to treat addiction treatment. Some of them are in this space, some of them are in the Buprenorphine space, but I think what is critically important though is that the market has to send signals that there is an incentive to enter this market.

So, when a company is looking at entering this space, they are looking at is there going to be demand, are they going to be able to make a significant benefit to patients compared to existing therapies? And, in this case, that is what driving the introduction of new brand competition in this area.

Mr. MARINO. Thank you. Mr. Gaugh, Dr. Ketcham states in his written testimony that the cost of the generic version of Buprenorphine had doubled despite a number of competitors in the market. Can you explain why that is the case concerning the BUP market, and why prices increase generally in the market with a number of generic competitors?0

Mr. GAUGH. Thank you. So, to your question, there are a number of different situations that a company has to look at and face when they are in a market, and I am assuming in this case these companies are already in the market. So, you have API sources that can change and go up in price. You have mergers and acquisitions that occur, as I think you well know throughout the supply chain.

So, when API companies merge, a lot of times that takes one or two of the players out of the market and that may increase the price of the API. The components that the products use whether it is an injectable, tablet, capsule, inhalation, or autoinjector, those components have a price point to them as well. And so these many factors are taken into account into what causes the price to go up. Why a specific company made that decision, I do not know the answer to that.

Mr. MARINO. Then in 35 seconds, Dr. Ketcham, your testimony lays out that there are many barriers experienced by first responders and medical professionals in an effort to respond to these overdoses. Can you speak to the belief within the medical community as the best methods and science to approach?

Dr. KETCHAM. I want to make sure I understand your question. So, barriers to getting addiction treatment or treatment for overdose?

Mr. MARINO. Treatment for overdose.

Dr. KETCHAM. So, right now, the issue with getting a timely treatment for overdose is really having access to Naloxone and the people who are around the patient. Just remember that a patient never treats himself for an overdose. So, unlike an autoinjector such as an EpiPen, where somebody will treat themselves for their allergic reaction, getting treatment for your opioid overdose requires there is a bystander who is ready to administer that medication and or a prompt response from law enforcement who hopefully can be able to carry that medication which is not necessarily done by all law enforcement agencies. This is becoming a bigger part of law enforcement's budgets now, as well, of course traditional EMS and fire agencies.

Mr. MARINO. Thank you. Time is expired. The Chair now recognizes the Ranking Member, Mr. Johnson.

Mr. JOHNSON. Thank you, Dr. Pritchett. Professor Feldman testified that drug companies have engaged in legal and regulatory games to block entry into the market for opioid addiction treatments, including the practice of evergreening and product hopping, brand products whose patents are about to expire. What is your response?

Ms. PRITCHETT. I do not particularly care for the terms "product hopping" or "evergreening." I think when we are looking particularly at the addiction medications base and we look at the new delivery reforms that have been introduced, these are significant medical advances in this very challenging area. One of the most challenging aspects of successfully treating addiction is compliant patient compliance. And it is not a minimal tweak to develop a new delivery system to conduct a relevant clinical trials and make the case to the FDA that this is a significant benefit and that this should be approved and that it can be easily used.

So, I think that the innovations that we have seen have been incredibly valuable in increasing our arsenal in the treatment of addiction. If you think about these two spaces what we have seen is, we have had standard care in Naloxone has been in vial form for decades. And we have had standard treatments in Buprenorphine in pill form for decades. But what we are seeing now is a great expansion in the use of the delivery methods.

Mr. JOHNSON. Okay, all right, thank you. Mr. Gaugh, in your written testimony you state that Senate bill 3056, The CREATES Act would address abuses of patient safety programs like the Risk, Evaluation, and Mitigation Strategies Program. And in a letter opposing the CREATES Act, PhRMA president, Stephen Ubl, recently argued that it provides considerable incentives for generic manufactures to litigate, rather than arrive at agreements with innovators. What is your response?

Mr. GAUGH. Under the current situation, as a company comes to the market dynamic and the market decision, when they come to market, the first thing they have to do is get samples so they can develop that product. The only way they can get that sample in a REM situation is from the company, directly. So, we do this all the time but in a non-REM situation you go to a wholesaler distributor to buy that product. Under REMs, it is in a strict distribution and you cannot do that.

So you have to go to the company and once we supply a letter to the FDA saying that we want to develop this product, the FDA has to determine that we are a company in good standing, they will present a letter to us on that, we present that letter to the innovator company and they are to sale the products. But there is no factor today that requires them to do that. Other than, we can take them to court under antitrust laws.

Mr. JOHNSON. All right, I understand. Thank you. Mr. Merritt, in your written testimony you state that the generic approval backlog is currently at 36 months, undermining competition in the brand drug market. What recommendations do you have for reducing the backlog?

Mr. MERRITT. Well, we would ask for better staffing, better resources there; not better staffing because of quality, but more staffing and so forth. It is a very serious issue and if there is a backlog

there needs to be maybe better capacity there. We would also ask for the FDA to look at situations where for instance there is a generic that does not have competition or an off patent brand that does not have competition and accelerate approvals for drugs that can compete in those spaces too.

Representing the payers for these medicines, the unions, lawyers, insurers, and so forth, obviously we just want lower costs. But, lower costs only happen when there is competition. And the more competition there is, the lower the costs that there are. And the FDA, I think, is doing a good job they have a lot of volume but they need to do more. And I think the situation in America is changing where they may need to ramp things up maybe than they anticipated.

Mr. JOHNSON. Thank you. Dr. Ketcham, have other areas of treatment suffered as the result of the necessary response and the expense associated with that response to opioid overdoses and addiction treatment?

Dr. KETCHAM. I am trying to make sure I understand the question.

Mr. JOHNSON. Yeah, because of the costs associated or the increased costs associated with opioid overdoses and addiction treatment, have other areas of treatment suffered?

Dr. KETCHAM. So, specifically, many patients that I would see in the emergency department who are wanting to get started on treatment for their addiction: Their single most common barrier is being able to afford the medication; the same thing upon release of prisoners, of those incarcerated upon reentry into society, which is a very important time to begin treatment. The cost of medication is the single biggest barrier.

Therefore, it is the process, even when working with social workers in the emergency department, to try to help the patient now get onto Medicaid. There is a time delay between when they can get Medicaid acceptance, then to submit and get preapproval for Buprenorphine. I can give them a dose in the emergency department to get them started, but really getting a prescription filled and then have a place for them to follow up, that is the significant barrier for addiction.

Mr. JOHNSON. All right, thank you. Mr. Chairman, I would ask that a letter dated September 22, 2016 from Consumers Union on this issue be admitted into the record, without objection.

Mr. MARINO. Without objection, so ordered.

[The information referred to follows:]

ConsumersUnion
POLICY & ACTION FROM CONSUMER REPORTS

September 22, 2016

The Honorable Tom Marino, Chairman
The Honorable Hank Johnson, Ranking Member
Subcommittee on Regulatory Reform, Commercial and Antitrust Law
Committee on the Judiciary
U.S. House of Representatives
Washington, DC 20515

RE: Treating the Opioid Epidemic: The State of Competition in the Markets for Addiction Medicine

Dear Chairman Marino and Ranking Member Johnson:

Consumers Union, the policy and mobilization arm of Consumer Reports,[1] appreciates your Subcommittee's continuing work to protect and promote competition and the benefits it provides consumers in greater choices, lower prices, and improved quality and innovation. We appreciate your holding this hearing today on the availability and affordability of medicines relied on to free people from the grip of opioid addiction, and to save those still in that grip from fatal overdoses.

The escalating cost of prescription drugs is a top concern for many consumers. And nowhere is that concern more acute than in regard to drugs used to address opioid addiction, where the drugs are critical to the survival and recovery of a population that is extremely vulnerable and often, because of their addiction, with limited financial means.

So it is particularly troubling that in just the last two years, the price of Evzio's auto-injectors for the emergency overdose rescue treatment Naloxone has shot up from $625 to nearly $4000 for a 2-pack – a more than six-fold increase.[2]

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[1] Founded in 1936, Consumer Reports is an expert, independent, nonprofit organization whose mission is to work for a fair, just, and safe marketplace for all consumers, and to empower consumers to protect themselves. Using its more than 50 labs, auto test center, and survey research center, the nonprofit rates thousands of products and services annually. Consumer Reports has over 7 million subscribers to its magazine, website, and other publications. Its policy and mobilization arm, Consumers Union, works for health reform, food and product safety, financial reform, and other consumer issues in Washington, D.C., the states, and the marketplace. It employs a dedicated staff of policy analysts, lobbyists, grassroots organizers, and outreach specialists who work with the organization's more than 1 million online activists to change legislation and the marketplace in favor of the consumer interest.

[2] *See* GoodRx, Opioid Antagonists, Price Trends, http://www.goodrx.com/opioid-antagonists. Although Evzio's marketing strategy, for consumers who have insurance coverage, is to adjust the price so that the net cost to the consumer is zero, the insurance companies are absorbing the inflated price. Consumer Reports phone interviews.

Opioid addiction touches every community and many families. And the broader problem of soaring drug costs touches many more. High drug costs impose a significant burden on the health and financial security of millions of Americans – nearly 60% of adults regularly take a prescription drug.[3]

Consumer Reports is an expert, independent, nonprofit organization whose mission is to work for a fair, just, and safe marketplace for all consumers. From our founding 80 years ago, one of our top priorities has been to make health care available and affordable for all Americans. One area of particular focus has been the prescription drug marketplace.

As part of our work to help consumers find the best value when purchasing prescription drugs, in 2004 we launched Consumer Reports Best Buy Drugs. This program uses evidence-based, systematic reviews of prescription drugs to clearly demonstrate the efficacy and safety of commonly used medicines in over 30 categories.[4] We combine this information with reliable cost information, enabling consumers to truly identify the "best buy" for many drugs.

As part of our work to help consumers find the best value when purchasing prescription drugs, in 2004 we launched Consumer Reports Best Buy Drugs. This program uses evidence-based, systematic reviews of prescription drugs to clearly demonstrate the efficacy and safety of commonly used medicines in over 30 categories.[5] We combine this information with reliable cost information, enabling consumers to identify the "best buy."

One of the key ways consumers often find the best buy for the drugs they need is through the availability of generic alternatives to the original brand-name version of a drug. That can make a dramatic difference in whether a drug is affordable or not.

A feature article in the August issue of Consumer Reports, now available on our website, asks in its title: "Is There a Cure for High Drug Prices?"

The article reports on the results of a nationally representative telephone poll of more than 2,000 consumers who take a prescription medication, conducted by Best Buy Drugs in March, finding that high drug prices are taking a serious toll on consumers.

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[3] As of 2011-12, nearly 3 in 5 Americans over age 20 take at least one prescription drug. As of 2012, those taking five or more drugs has doubled since 1999-2000 to 15% of all Americans. Elizabeth D. Kantor et al., *Trends in Prescription Drug Use Among Adults in the United States From 1999-2012, JAMA. 2015;314(17):1818-1830.*

[4] http://www.consumerreports.org/health/best-buy-drugs/index.htm. Note: Best Buy Drugs does not do cost-effectiveness analysis. Instead, we present price data alongside the effectiveness, safety, and side-effect data. And then we let consumers—in consultation with their doctors—interpret and adapt these data according to individual preferences, clinical circumstances, and priorities (including budgetary).

[5] http://www.consumerreports.org/health/best-buy-drugs/index.htm. Note: We do not do cost-effectiveness analysis. Instead, we present price and cost data alongside the effectiveness, safety, and side-effect data. And then we let consumers – in consultation with their doctors – interpret and adapt these data according to individual preferences, clinical circumstances, and priorities – including their budgets.

We found that 45 percent of people regularly take a prescription drug, and on average take between four and five medications. Three in ten people told us their out-of-pocket costs for one of their prescriptions has gone up in the past 12 months, costing them an average of $63 more for a drug they routinely take – with a few being hit with increases of $500 or more. And for those consumers:

- 47 percent took less of the drug than the prescription called for, to save money, with 17 percent skipping or splitting doses, and 30 percent not filling the prescription at all.
- 28 percent put off a doctor's visit.
- 19 percent took an expired medication.
- 19 percent postponed paying other bills to pay for their medications.

Our investigation found recent price hikes on everything from longtime generics used to treat common conditions such as diabetes, high blood pressure, and high cholesterol to new treatments for diseases such as hepatitis C.

As we noted in our article, one principal reason drug manufacturers are charging high, even exorbitant, prices is "because they can." In other words, because there is a lack of competition – and a resulting lack of consumer choice.

The case of Turing Pharmaceuticals jacking up the price of Daraprim – the best treatment for toxoplasmosis, an infection to which those with HIV/AIDs or cancer are susceptible – from $13.50 per tablet to $750, is a notorious example. So is Mylan's five-fold hike in the price charged to consumers for its life-saving EpiPen, relied on as a life-saving anti-allergy delivery system by millions of consumers, including families and children dealing with serious allergies and the possibility of life-threatening anaphylaxis.

And as mentioned above, the Evzio auto-injector, which works similarly to Mylan's EpiPen, is another glaring example.

As this Committee knows, a company's exploitation of monopoly power that it finds itself in possession of, at the expense of consumers who depend on its product, however objectionable we may all regard it, may not by itself violate the antitrust laws. But it *is* a violation for a company to *maintain* monopoly power by sabotaging or undercutting efforts by competitors to provide consumers more choice. That is an important and proper focus for this Subcommittee, and for the antitrust enforcement agencies.

The workings of the pharmaceutical industry, and the way the development and introduction of new drugs is regulated, creates special opportunities for restricting competition. To begin with,

there is a rigorous application process in the Food and Drug Administration for new drugs, designed to ensure their safety and effectiveness before they are approved for the market. And to encourage brand-name drug makers to invest in research and development, including the expenses of the FDA application and approval process, the government grants the new drug a patent, which is a legal monopoly. That patent is not intended to last forever, but the brand-name drug maker gets used to the monopoly profits, and has a natural business incentive to look for ways to prolong them.

Three decades ago, in the Hatch-Waxman Act, Congress established a national policy of encouraging competition from affordable generic alternatives, consistent with patent laws. But enacting that law didn't change that underlying business incentive of the brand-name drug makers. And so we have had to continue fighting roadblocks thrown up against availability of generics, such as "pay for delay" schemes to buy off generic drug makers, and "ever-greening" strategies, also called "product-hopping," using minor alterations to the way a drug is packaged or delivered as a basis for getting a new patent, prolonging the patent beyond its natural life. These schemes and strategies block generic entry for a further extended period of time, restricting access to lower-cost generic alternatives of the drug.

In the Mylan case, there are a number of troubling reports that Mylan may have engaged in a range of anticompetitive conduct to maintain its monopoly. These include:

- Reports that Mylan attempted to influence the FDA to derail approval of Teva's competing delivery system.[6]

- Reports that Mylan had earlier persuaded the same competitor, Teva, to delay its application for FDA approval, perhaps in an anticompetitive "pay for delay" scheme. In fact, Mylan reportedly began its campaign to derail the application only as this delay was set to expire.[7]

- Reports that Mylan included restrictions in its contracts with schools purchasing the EpiPen at a discount under its EpiPen4Schools program, requiring these schools to agree not to purchase competing delivery systems.[8]

Engaging in any of these practices to maintain a monopoly by blocking competition could very well run afoul of the antitrust laws. Accordingly, we have asked the Federal Trade Commission to investigate, and to take appropriate enforcement action as supported by the facts.

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[6] *See, e.g.*, I-Team: Company Behind EpiPen Fought to Keep Cheaper Generic off Market, http://www.nbcnewyork.com/investigations/EpiPen-Cheap-Generic-Teva-Product-Mylan-Investigation-Drug-Cost-391758871.html.

[7] *See, e.g., id.*

[8] *See, e.g.*, Mylan May Have Violated Antitrust Law in Its EpiPen Sales to Schools, Legal Experts Say, http://www.pbs.org/newshour/rundown/mylan-may-violated-antitrust-law-epipen-sales-schools-legal-experts-say/.

After more than a decade of sustained effort on the part of the Federal Trade Commission and private parties to establish the basic principle that brand-name drug companies could be held accountable under antitrust law for "pay for delay" deals, the Supreme Court definitively ruled in the 2013 *Actavis* decision that the antitrust laws *do* apply to "pay for delay." Now brand-name drug makers have tried shifting to other, more subtle forms of pay-off, claiming that the Supreme Court's decision only applies to pay-offs in cold, hard cash. And they have turned to product-hopping.

Both these kinds of schemes are now the subject of government enforcement actions and private challenges wending their way through the courts.

Another roadblock some brand-name drug makers are now throwing up involves using an FDA-approved Risk Evaluation and Mitigation Strategy (REMS) to deny generic and biosimilar drug makers access to a sufficient supply of the brand-name drug, or to the established testing processes, that the generic needs in order to be able to do the necessary testing to satisfy the FDA's bio-equivalency requirements and ensure that the generic is safe and effective. Like pay for delay and product hopping, this kind of restrictive roadblock could very well be a violation of the antitrust laws.[9]

Daraprim's astronomical price hike by Turing Pharmaceuticals is propped up by this kind of restricted distribution. The drug went off-patent about 40 years ago. And until recently, it was available on ordinary distribution channels to wholesalers and retail pharmacies. But it was taken off those ordinary channels two months before Turing acquired it, reportedly as a condition of the deal.[10] As a result of that change, Turing only distributes the drug through a "closed" pharmacy system, and obtaining samples of Daraprim in order to make and market a lower-cost alternative has become difficult.

And particularly pertinent to today's hearing, there are indications that Reckit Benckiser may have used a number of the anticompetitive practices described above to delay entry by a competing generic, and thereby extend its lucrative monopoly, for Suboxone, a leading drug used for treatment of opioid addiction. Specifically, Reckit Benkiser reportedly secured FDA approval for a required joint REMS program, then refused to cooperate with the affected generics, thus blocking their participation;[11] filed a questionable petition urging the FDA not to approve generic substitutes for Suboxone;[12] obtained extended patent life for a "new" drug by switching its packaging of Suboxone from tablets to film strips, with no changes to the clinical formula, claiming

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[9] *See* Carrier, Michael A., Levidow, Nicole, and Kesselheim, Aaron S., *Using Antitrust Law to Challenge Turings' Daraprim Price Increase*, 31 Berkeley Tech. L.J. ____ (forthcoming 2016), http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2724604.

[10] Andrew Pollack and Julie Creswell, *Martin Shkreli, the Mercurial Man Behind the Drug Price Increase That Went Viral* , N.Y. Times, Sept. 22, 2015, http://www.nytimes.com/2015/09/23/business/big-price-increase-for-an-old-drug-will-be-rolled-back-turing-chief-says.html.

[11] *See* In re Suboxone (Buprenorphine Hydrochloride and Naloxone) Antitrust Litigation, 64 F. Supp. 3d 665 (E.D. Pa. 2014).

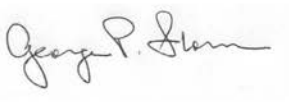
[12] *Id.*

that the tablets were unsafe, while continuing to sell the tablets in other markets around the world;[13] and waged a massive fraudulent sales and marketing campaign, with doctors and the public, to disparage as the tablets that generics were preparing to introduce as unsafe, and discourage their use.[14]

In addition to supporting vigorous antitrust enforcement, we are also open to practical legislative solutions. For example, we expressed our support for the Creating and Restoring Equal Access to Equivalent Samples Act, or CREATES Act, legislation introduced in the Senate that would clarify that abuse of REMS restrictions to impede generic testing and entry are unlawful and would give the affected generics a way to stop them, enabling new choices to get to consumers more quickly.

Our health care system is multifaceted, and the solutions go beyond antitrust. Competition will not solve every marketplace problem. But the lack of competition makes marketplace problems harder to solve. We appreciate your commitment to seeing that competition is protected and promoted in this critical marketplace.

Respectfully,



George P. Slover
Senior Policy Counsel
Consumers Union

cc: Members Subcommittee on Regulatory Reform, Commercial and Antitrust Law

[13] *Id.*
[14] *Id.*

Mr. JOHNSON. Thank you.

Mr. MARINO. The Chair now recognizes the Chairman, Mr. Goodlatte.

Mr. GOODLATTE. Thank you, Mr. Chairman. Dr. Ketcham, there have been allegations that threats by the Drug Enforcement Administration, the DEA, have resulted in pharmacies removing Buprenorphine products from their inventory. Are you familiar with these allegations, and can you comment on the alleged conduct?

Dr. KETCHAM. I cannot verify that that is necessarily the case. I do know that pharmacies in my region try to keep only a limited amount of Buprenorphine in stock, try to preserve that for when a patient shows up with a prescription in hand.

I will say, however, that, regarding the DEA, and I think their general view of treating addiction with Buprenorphine and office-based practice; that after you have been a licensed Buprenorphine prescriber for 3 years, at some point you are supposed to have a random meeting with the DEA, in which they are going to interview you, go over your patient logs, your prescriptions, et cetera.

When they do this, they do interrogate you and make you feel like you are a criminal, and this really is a significant factor that causes physicians not to want to participate in addiction treatment.

Let me also add that there is, however, a significant amount of diversion of Buprenorphine, you know, in almost every community, and I believe that the DEA has a very founded interest in why there is such a tremendous amount of diversion of Buprenorphine in most communities.

Mr. GOODLATTE. But do you think that if that is indeed leading to local pharmacies carrying limited supplies, is that leading to the inconsistency that patients are finding? They will get a prescription. They will go get it filled, and then the next month or whenever they go back again, that pharmacy does not honor their prescription?

Dr. KETCHAM. I think the issue is that the cost of the medication is high, and in pharmacies that I have spoken to, when working with Medicaid, for example, they are selling the Buprenorphine to patients at the same cost for which they are paying for the medication, and usually they pay through a wholesaler such as McKesson, let's say.

So, if your pharmacy is buying it at that price, that is exactly the price they are turning around and selling it to patients for, with usually a minimal fee of about a dollar or so for packaging. So there is no market. There is no, you know, profit for them anywhere in this.

Mr. GOODLATTE. I get the profit side of it.

Dr. KETCHAM. Yeah.

Mr. GOODLATTE. We definitely want to hear more about why these prices cannot be lowered through competition, but I also would suspect that if you are treating a patient for addiction, consistency and being able to stay on the regimen prescribed by the physician would be extremely important, and the inconsistency with which that physician can rely on local pharmacies to have the product available would make a big difference in the success of treating the patients.

Dr. KETCHAM. I completely agree, and that is definitely a problem that our patients face. I will also add to that that there appears to be varying quality amongst the generic product, and when the generic product changes within a pharmacy, patients then are often trying to look for a different pharmacy that carries a different generic version of the drug.

Mr. GOODLATTE. So the physician wants them to take a specific formulation, and expect that it is going to be at the same place where that patient is used to going. This consistency of carrying the same product over a period of time is very important, and pharmacies should work with the DEA and work with their suppliers to make sure that they can be more consistent than they are in some areas.

Dr. KETCHAM. Absolutely.

Mr. GOODLATTE. Thank you. Dr. Pritchett, your testimony outlines what appears to be a relatively competitive market for both Buprenorphine and Naloxone products. Given its competitive state, can you explain the media accounts and testimony today that suggests rising prices in each of these markets?

Ms. PRITCHETT. So I would just say that I represent a trade association. My representative from GPhA is not privy to actual pricing information of any of these products. We did have IMS just take a look at the overall trends and, for example, for Buprenorphine related medications IMS data shows that pricing for both the generic and innovator products have similar pricing; that it has remained generally stable since 2011.

Now, one of the challenges related to Naloxone, as I mentioned in my testimony, is that we have had a shift in that now many States are having standing orders where Naloxone products are available without a prescription at the pharmacy level. We do not have insight into what pricing may be occurring at the retail level. So, that is one of the challenges inherent there.

But I would say what we have seen in terms of—not looking at sales, but looking at volume, is that in both of these spaces that you have substantial generic competition. We have recently had an influx of innovative products. If you look at Naloxone, we have had an autoinjector form that has been introduced, and then we have had a nasal form introduced, and I think now you have two brands competing on the delivery system method, so that is a sign of positive competition and, given what we are seeing in the pipeline, we expect to see more competition there. But, again, I cannot speak to the price reports that have been reported in the media.

Mr. GOODLATTE. Let me just say——

Ms. PRITCHETT. IMS data just does not seem to be bearing that out.

Mr. GOODLATTE [continuing]. As a member of the trade association that many pharmaceutical companies belong to, I hope you will convey back to them our concern, that the Congress has just passed CARA legislation, designed to try to deal with the addiction epidemic in our country, and that one of the aspects of being successful—we passed about 17 bills, some out of this Committee, some out of the Energy and Commerce Committee, that are going to help, I think, a lot in this area, but they are not going to help as much as they could unless the product, for people who obviously

are not, taken as a whole, the most likely to be able to pay whatever the market demands.

They are going to need to be able to have an affordable product; that that is an important thing for your industry to consider, as we take on this national challenge of dealing with addiction.

Ms. PRITCHETT. Thank you for that. One thing I would note, IMS just released a report this morning that found that the annual growth rates in the number of prescriptions for Buprenorphine medicines slowed from 22 percent in 2012 to about 6.4 percent in 2016, and IMS found that the states with the highest rates of heroin and other opioid use had below average levels of Buprenorphine use and public funding, suggesting a disconnect between the need for treatment and access and coverage of treatment. And what we have seen is that a lot of these medications require, as mentioned by Dr. Ketcham, require a step therapy. So, you have to fail on multiple other options before you get to some of these medications.

Some of these are not even covered. For example, Vivitrol, which is an innovative medication in terms of it is a once monthly injectable that just does not just treat withdrawal symptoms, but treats opioid dependence; that you have three State Medicaid programs that require substantial step therapy and prior auth before you can even have an opportunity for that. And the Arkansas State Medicaid program does not even allow access to it.

So, agree that we need more competition, but we also need to ensure that, as we are introducing competition, that there is the potential that there is going to be uptake of these products. As innovators are looking at entering a market, they do need to know that this is going to be valued by payers and patients. So that is an important dynamic as well, but appreciate the thoughts.

Mr. GOODLATTE. Well, thank you, and if you would submit that study to the Committee, we would be more than anxious to have the benefit of it.

Ms. PRITCHETT. Certainly, will do so.

Mr. GOODLATTE. Thank you. Mr. Chairman, my time has long since expired.

Mr. MARINO. Thank you. The Chair now recognizes Mr. Conyers, the Ranking Member of the full Judiciary Committee.

Mr. CONYERS. Thank you very much. I thank the witnesses. Professor Feldman, what are some of the ways that drug manufacturers manipulate the existing patent and regulatory schemes to extend their monopolies on brand drugs?

Ms. FELDMAN. Understanding the life cycle in the pharmaceutical industry is a matter of understanding how the games get piled on one after each other. With each of them, they got a small amount of additional exclusivity; 5 months here, 6 months there, a couple of years. But you add them together and they add up. So, a 5-month extension in a blockbuster drug can be worth half a billion dollars or more. You add a billion here, a billion there, that adds up to real money, and the taxpayers are paying. So it is not the individual game. It is the way that games are strung out, one after another.

Mr. CONYERS. Is this true of generic manufacturers as well?

Ms. FELDMAN. The best and most competitive market is when you have lots of competitors directly in that market. When there

is only one generic competitor, the price generally drops by only about 15 percent. When you have multiple generics, you often see price drops in the 85 to 90 percent. So there are definitely incentives for first generics, also who wish to keep others out as well.

Mr. CONYERS. Thank you. Do you support S3056, the CREATES Act, which, as you know, among other things, allows a generic drug developer to sue a brand manufacturer to obtain the necessary samples to create a bio-equivalent product?

Ms. FELDMAN. I had the honor of testifying on the Senate side about the CREATES Act a couple of months ago. I do support that type of approach, particularly taking the competition policing out of the FDA, and into agencies and courts that are better at doing that. The FDA is great at policing safety; not so great at policing competition.

Mr. CONYERS. Thank you. Mr. Merritt, you suggest that one of the factors keeping the price of the Naloxone high is the fact that many States require insurance coverage for it, hampering the ability of pharmacy benefit managers to negotiate discounts and rebates. Do you support that?

Mr. MERRITT. Well, insurance does cover that, just to clarify that, sir. Insurance and insurers generally cover these products. The challenge is when there is a mandate to cover one particular generic, if there are competitors available, or one particular brand, for that matter. Because when there is a mandate to cover that, it gives all the pricing power back to PhRMA because they do not need to compete on price to get on a formulary or to get on a formulary with a lower co-pay.

So that was the intent of that particular statement, but these are broadly covered, although I will add that many, many times, although I do not have the percentage in front of me, these are not processed through insurance. They are products that have been given away. Different drugs have been given away. People come and sometimes they do not want to process it through insurance, sometimes they are uninsured themselves, and so that is just another clarifying factor.

Mr. CONYERS. Dr. Ketcham, what is the impact of the spiking price of opioid addiction treatments on the ability of healthcare providers to address addiction long term?

Dr. KETCHAM. Sir, the rising price essentially means that patients will not fill their prescriptions, and without filling the prescription, it means they discontinue getting their addiction treatment. What invariably often happens in this situation, which is very unfortunate, is that patients, when they cannot afford the medication, will often do their own sort of self-tapering.

Many patients are self-managing with Buprenorphine; either that they have been prescribed for that they are running out of, or that they are obtaining in a secondary market, and very often when we see them tapering very quickly, much faster than we would recommend that they do, there is a very high rate of relapse, and then proceeding back to using heroin or other black-market opiates.

Mr. CONYERS. Thank you, Mr. Chairman, for permitting me to ask these questions.

Mr. MARINO. Mr. Ranking Member, you came under everyone else today. So, kudos. The Chair now recognizes the gentleman from Georgia, Congressman Collins.

Mr. COLLINS. Thank you Mr. Chairman, and the Ranking Member said I could have his time, his extra. There you go. We will split it; that is what we will do. No, I appreciate the time, Mr. Chairman. We will be submitting questions for four of the witnesses today on different wells, but I have some other issues that I would like to address because I do not get the opportunity often to do so. Mr. Merritt, thank you for being here today.

I have an opportunity to say something here that, for many in this room, is going to find they may fall out of their chairs because I am going to agree with you on some parts of your testimony. I agree that opioid epidemic and opioid addiction is heartbreaking. I have seen it tragically up close and personal, and agree that the Comprehensive Addiction Recovery Act was a good first step toward combating this problem. That is why I was a part of that act.

I think we can agree there needs to be competition in the addiction medication market, but when we talk about general pricing, there are some points that I want to raise that concern me, and I think you know we have a different opinion on the value of PBMs to the healthcare marketplace. You say in your written testimony that PBMs help bring down prices of prescription drugs across the market by harnessing competition and among manufacturers. You go on to say that the one way the PBM lower prices for prescription drugs is through taking advantage of all the efficiency of mail service pharmacies.

Mr. Merritt, is there not an inherent conflict of interest when a PBM mandates or heavily incentivizes patients to use their own specialty or mail order pharmacy? Can you please explain how steering patients to a PBM owned specialty or mail channel allows for greater competition in the marketplace?

Also, help me understand how it is beneficial for a patient to obtain expensive, complex medications, some of which need to be self-injected, in the mail, where they have zero opportunity to show in-person how to properly use the medication for maximum benefit?

Mr. MERRITT. Sure, well, first of all, the Federal Trade Commission has looked into this, in terms of the mail and if there is a conflict of interest, and found that there is not. And I think probably the way to think about it——

Mr. COLLINS. That is not a real helpful analogy, given their track record in some of the trade.

Mr. MERRITT. No, I have——

Mr. COLLINS. We are going down a wrong road to start with here.

Mr. MERRITT. Okay, well, I think the FTC is a respected agency, but we can disagree on that. I would say this. Maybe a simpler way to think about it, because all this is so complex, with so many different layers, even for people who really know a lot about health care. Think about it like Amazon.com. They have Prime, which a lot of us use for home delivery. Amazon is its own deliverer.

Would it be smart to force them to use Federal Express or UPS or some other higher cost carrier to deliver their goods? Would that be better for consumers? Would that take advantage of scale? No, I think it would cost more. It would not add any value to con-

sumers, and the fact that we work with mail service pharmacies often that we partner with or own adds value because we can deliver those products cheaply and more effectively to consumers.

Mr. COLLINS. Well, I think that is even under question because even a study was done from TRICARE says that you are 83 percent higher than most community pharmacies serving through mail order. So I mean, these are the problems that I have. I understand the PBMs will usually pay the pharmacy one amount for dispensing a drug, but charge a payer a different amount, referring to this as the spread.

CMS is aware of this and have changed part of the rules to account for this practice, which is inflating patient costs. Can you explain to me, and the rest, the often large differential in the spread between what PBMs reimburse pharmacies, versus what you charge health plans, and could you not save the system dollars, which is actually what your own website says that you supposedly do by lowering that spread?

Mr. MERRITT. Well, first of all, we do not work for the pharmacies. We work for the employers and the consumers who go there, right?

Mr. COLLINS. Most of your members own pharmacies.

Mr. MERRITT. No, but we do not work——

Mr. COLLINS. Let's at least get this straight.

Mr. MERRITT. We do not work for drugstores. Our job is negotiating——

Mr. COLLINS. No, you own them.

Mr. MERRITT. No, that is a different story. We——

Mr. COLLINS. Yeah, we do not want to talk about that story. It is vertical integration that is a problem here.

Mr. MERRITT. Well, if you give me just a second, I will talk about it and answer your question. PBMs are hired by employers to negotiate against and with drug companies and drugstores to make sure that people get access to the medications and drugstores they need, but that we also use the competition in those spaces, for instance, where there are numerous brands or brands and generics that treat the same conditions. We want to encourage people to use the least expensive one. The same is true with drugstores. Some local drugstores are more expensive than others. We want to encourage people to use the more affordable drugstores.

In terms of spread pricing and so forth, that is something that the plan designs. That is something that the employer decides. They are fully aware of that, and if they want to provide incentives for us to get better deals with drugstores by doing that, they will go ahead and do that but, as you said, Medicare and a lot of other programs and payers do not want that. That is fine too. It is totally up to the payer.

Mr. COLLINS. Look, TRICARE's own study said if they got rid of PBMs, they would save $1.3 billion in 2013. You cannot tell me, and sit here and tell me that your groups, which you represent, many of which have testified before this Committee and been untruthful with this Committee can say——

Mr. MERRITT. No.

Mr. COLLINS [continuing]. No, I would not go there with me on that one. You did not testify. One of your members did.

Mr. MERRITT. Okay.

Mr. COLLINS. And this is the problem we have. And do you want to look at it over all, not only the opioid addiction issues we have got here, but the pharmacy prescription. I have one more Mr. Chairman, because this is out of his own testimony. It says, "Allow them stronger measures to remove disciplined or rogue pharmacies from plan networks," as one of your solutions.

I do not think you need any more power because right now you are removing pharmacies that actually try to compete in their marketplace and serve on regular means. You do not need more power to go after them. You have got plenty right now, controlling 83 percent of the market. Your business model that suffers and forces customers to have problems; not the other way around. The last thing we need to do is give PBMs more power. Thank you, Mr. Chairman, I yield back.

Mr. MARINO. Mr. Merritt, you can respond if you choose to.

Mr. MERRITT. Well, I would just say that, as Dr. Ketcham pointed out, there is a problem with diversion. There is a problem with fraud in health care, in general. We see it at the pharmacies. We see it in other places in health care as well. Some drugstores are better than others, and so we want to make sure the highest quality, most affordable drugstores are ones that people are encouraged to go to. We may have a disagreement on this, but this is the way that we see it, and I think facts back that up.

Mr. COLLINS. Mr. Chairman, all that is in these pharmacies were actually doing something——

Mr. MARINO. Gentleman——

Mr. COLLINS. Are we going to get a second round, because that statement right there is false.

Mr. MARINO. No, we are not, because before I got here because of votes and not keeping this panel, you certainly can submit written questions too. This the business to be answered. The Chair now recognizes the gentlelady from the State of Washington, Congresswoman DelBene.

Ms. DELBENE. Thank you, Mr. Chairman, and thanks to all the witnesses for being with us today. Today, we are considering the intersection of two important policy priorities; addressing the cost of prescription drugs, and combatting the opioid crisis. As everyone knows, the epidemic of opioid abuse is having a devastating effect on Americans' health and safety, both in my home State of Washington, and across the country. With more than 120 deaths occurring from drug overdoses every day, more than half from prescription drugs, it is clearer than ever that Congress must take action to treat addiction and save lives.

Addressing this epidemic will require a multi-pronged approach, and one piece of the solution must be ensuring access to addiction treatment medicines, and overdose reversal drugs. That is why the Comprehensive Addiction and Recovery Act, or CARA, authorized important new funding for the expansion of medication assisted treatment. But that support could be severely diminished if our constituents cannot afford the cost of these medications, not to mention law enforcement agencies and State, local, and tribal governments. And CARA cannot solve this crisis alone. We are also

going to depend on the manufacturers of addiction medicines, and the regulatory structure that governs them.

So, as someone who started her career in the life sciences, I know how important it is to strike the right balance between incentivizing medical innovation, and ensuring access to affordable medicines. But some companies have rightfully drawn criticism for increasing drug prices to generate profits, rather than support the development of life-saving therapies, and I have heard from hundreds of constituents who are outraged by what they have heard on the news.

So, as we work together to fight the opioid crisis, it is appropriate to examine the state of this marketplace, and ensure that it is working as it was intended.

Dr. Ketcham, in negotiations over CARA, Congress failed to provide the President's request for $1.1 billion in emergency funding to immediately fund new addiction treatment efforts. Instead, funding decisions were left to the annual appropriations process, and now we hear there might be $37 million in a continuing resolution.

So, do you believe that emergency funding would have helped Americans with the substance use disorder; help them to seek treatment, complete treatment, or sustain their recovery?

Dr. KETCHAM. Well, absolutely. In any way that funding filters down to the patient being able to obtain that medication, as well as in any path that funding proceeds to help keep open and open more addiction treatment centers or other mental health centers, where addiction medicine is handled.

Ms. DELBENE. How do you believe those funds would best be used to help first responders and healthcare providers fight the opioid epidemic. I mean, you have talked a little bit about keeping treatment centers open, but where do you think those funds are most critically needed?

Dr. KETCHAM. I do think that a multi-pronged approach is necessary. I am worried that, particularly as I stated earlier, the smaller fire departments, EMS agencies that are starting to really look at the price of Naloxone as a significant budget item in their pharmaceuticals. I think this needs to be addressed, and this is one area where I think funding should be directed.

However, funding can be used to lower the overall price and evaluate the whole competition issue. That would, I think, go a long way as well. But also, again, we certainly need more access by patients, you know, to the mental health care so they can start getting their addiction treatment.

Ms. DELBENE. Thank you. Regarding competition, Professor Feldman, we talked a little bit about the competitive marketplace in this area. Are there other factors we have not talked about yet today that you think are critical that we should be aware of that are impacting pricing?

Ms. FELDMAN. I think I would put it this way. In a well-functioning market, if someone charges eye-popping prices, a bright young company will come in and compete and the price will come down. So if we are not seeing that—and we are not seeing that—then we have to ask, "What is going on, and what is functioning improperly in the market?" We have lots of carving out of little ter-

ritories there, but we do not have the type of robust competition that we would like to see in this market.

Ms. DELBENE. Thank you. Thank you, Mr. Chair, and I yield back.

Mr. MARINO. Thank you. Seeing no other Members, this concludes today's hearing. I really want to take the time to thank you for being here. I am glad we did not have to hold you over, nor would I have held you over, but I appreciate what you had to tell us today. We have learned from it, and all of us in this room, from the family members, to the businesses, to Congress. We have to pay particular attention to this and react, because it is only going to get worse. Without objection, all Members will have 5 legislative days to submit additional written questions for the witnesses or additional materials for the record. This hearing is adjourned.

[Whereupon, at 3:29 p.m., the Subcommittee adjourned subject to the call of the Chair.]

APPENDIX

Material Submitted for the Hearing Record

Response to Questions for the Record from Anne McDonald Pritchett, Ph.D, Vice President, Policy and Research, Pharmaceutical Research and Manufacturers of America (PhRMA)

Question: Testimony at our hearing stated the FDA often takes years to review a pending drug application. Can you comment on how that has affected the entry into the market for addiction medicine and other pharmaceutical markets?

There are several ways in which the FDA can result in more timely and efficient review of medicines and spur additional competition in areas of unmet medical need. Below I highlight several areas for consideration.

Until recently there have been long-standing delays in the reviews of generic drug applications at the FDA. The FDA's Office of Generic Drugs (OGD) is responsible for the timely review and approval of generic drug applications. Since the implementation of a pathway for the approval of generic drugs under Hatch-Waxman in 1984, abbreviated new drug application (ANDA) submissions have steadily increased. This has resulted in a significant backlog at OGD as annual submission rates have far outpaced annual approval rates. In addition to a growing backlog of applications, approval times have also increased over the years. According to the FDA's own data, OGD received over 1,400 ANDA submissions in FY2014 – up from about 360 per year in the mid-1990s and the highest number of receipts in a single year to date – but approved only 409 applications that same year.[1] In fact, the number of submissions has outpaced the number of approvals by multiples ranging from about 1.5:1 to about 3:1 each year between 2002 and 2014. This large discrepancy between the number of annual submissions and the number of annual approvals –led to a backlog of about 4,000 ANDAs, up from a consistent level of 400 ANDAs per year until 2002. In July 2016, the FDA announced it has reduced that backlog significantly and will eliminate the backlog prior to reauthorization of the generic drug user fee act. While the FDA should be applauded for addressing this critical issue, it is critically important that we ensure that FDA takes steps to ensure that this situation does not recur.

Innovative biopharmaceutical companies have made substantial R&D investments to develop abuse-deterrent formulations for some medicines that are susceptible to widespread abuse (e.g., opioids) as well as non-opioid pain medicines, medications to treat addictions, and opioid reversal agents. Given the public health importance of these medications, the FDA should prioritize the review and approval of these products. In the case of abuse deterrent formulations, for example, these formulations have characteristics that help prevent widespread abuse by impeding the delivery of their active ingredient or by making abuse of the drug more difficult or less rewarding ("abuse-deterrent formulations"). The reality is the science of abuse deterrence is challenging and both the formulation technologies and the analytical, clinical, and statistical methods for evaluating those technologies are rapidly evolving. Public policies should encourage the scientific and clinical research needed to advance the development and assessment of abuse-deterrent technologies. We would encourage the FDA to incentivize the development of abuse-deterrent formulations, which is in the best interest of patients. Specifically,

- When an innovator has developed, and FDA has approved, such a formulation, FDA should not approve a generic formulation of the medicine that does not incorporate comparable abuse deterrence. Permitting the approval of generic products that lack comparable abuse deterrence not only undermines the incentive for industry to invest in important new abuse-deterrent technologies, but also more importantly, fails to mitigate a public and societal health risk.

[1] http://www.lachmanconsultants.com/2015/07/the-backlog-at-ogd-a-historical-look/

- In addition, when an abuse deterrent formulation of a drug has been approved, PhRMA encourages FDA to exercise its authority to remove from the market non-abuse deterrent generic formulations of the same drug.
- Given more than 90% of the most frequently abused opioids are generic, we support swift finalization of FDA guidance to inform the development of generic ADFs.

In terms of opioid reversal agents, while the medication Naloxone has been around since the 1970s and is available in generic form, given the growing opioid crisis, there has been increased focus on drug-device combination products that allow the drug to be easily delivered and ensure accurate dosing. Naloxone is produced and sold by 8 different biopharmaceutical manufacturers. There are 6 generic manufacturers in a range of dosage forms and there are also 2 brand naloxone medications offering convenient delivery systems. Relative to the market in early 2015, the number of manufacturers in this space has close to doubled. In late 2016, a joint FDA advisory panel was split on whether dosing of injectable naloxone should remain the current standard. The lack of consensus around appropriate dosing has implications for the review of future products in this space. Given the continuing need for easy to use drug device combination products, there is a need to address the FDA regulatory framework that governs the development and review of combination products. Innovator and generic biopharmaceutical companies face a range of challenges in developing combination products. These include but are not limited to: additional dosing and other scientific studies that may be required for approved medicines being delivered through the use of a device; and different regulatory paradigms for medicines, biologics and devices that result in inefficiencies and make review processes more complex as companies must work with multiple FDA review centers. To address hurdles in bringing new combination products to market, there should be an independent third-party review to improve the FDA's combination product review process, FDA staff capacity needs to be enhanced and access provided to needed scientific expertise, and perhaps most importantly, improving coordination among FDA's review centers. These improvements will not only enhance the regulatory framework that governs the development and review of combination products, but could also increase competition.

In some therapeutic areas, there appear to be insufficient incentives to attract generic entrants. In the well-publicized situation involving the drug Daraprim, which was produced by Turing Pharmaceuticals, the drug treated a small patient population, the drug did not have intellectual property or regulatory exclusivities preventing market entry, but because the drug treated a small patient population, there appeared to be insufficient incentives for generics to enter the market. In cases such as this and where the drug is meeting a critical need, the FDA should prioritize the review of any generic applications when they meet these criteria. We also feel there is a need to explore additional incentives to encourage generic entry in these areas. One potential solution would be to provide regulatory incentives for more than one generic drug manufacturer to enter and require agreement to manufacture the product for a set period of time, including waiving the user fee for the drug intended to treat the patient population and expediting the ANDA/505(b)(2) review to the greatest extent possible.

Question: **Professor Feldman has detailed a number of practices that she believes inhibit competition in the addiction medicine markets as well as other pharmaceutical markets. Do you believe that "product hopping" is a practice that exists to preclude competition, and should Congress consider policies to prevent this type of conduct?**

Professor Feldman's testimony disparaged the value of incremental advances resulting from new formulation strategies that provide novel modes of delivery. The ideal delivery system seeks to provide the right amount of a medicine to the right part of the body at the right time and for the requisite

period. Advances in molecular biology, better understanding of the disease or condition, and the introduction of new technologies creates the potential for new indications (e.g., pediatric indications) and more efficient, effective, or convenient ways of delivering a medicine contributing to increased competition and improving patient outcomes.

To obtain FDA approval for new formulations, clinical trials are generally required to demonstrate safety and efficacy, as was needed in the testing phase of the original formulation. The company then must make the case to payers and prescribers of the value of the new formulation, which must compete with other therapeutic options in a class.

Contrary to Prof. Feldman's assertions, new formulations do not preclude competitors to earlier formulations and promote competition. Patents or exclusivity that may cover new formulations do not in any way extend the patents or exclusivity on existing formulations, or otherwise delay or block generic copies of the earlier formulations.[i] The introduction of new formulations also results in increased competition, which is further expanded when generics enter the market. As opioid reversal agents are being made more widely available in many states without a prescription, it is critically important that the delivery system be convenient and easy to use, but because receiving the right dosage at the right time can mean the different between life and death, we need to foster continued advances. Similarly, in terms of addiction medicines, having more rather than fewer treatment options is critically important.

Legal remedies exist to investigate and prosecute potentially anti-competitive behavior. To date, the FTC has not brought a case based on allegations described by Prof. Feldman. However, private litigants have brought several lawsuits alleging that some companies have violated anti-trust laws by seeking to thwart generic competition. The decisions to date have already established that the current antitrust laws are sufficient to address any conduct that may be considered by a court to be anti-competitive.[2]

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[i] A known compound may be reformulated with other substances to create a new composition of matter. Provided that the resulting composition is both new and not obvious, it can be patented. The new patent only covers the new formulation not any previously existing formulations nor the original formulation.

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[2] *See, for example, Mylan Pharmaceuticals Inc. v. Warner Chilcott PLC et al.*, No. 15-2236, 2016 WL 5403626 (3d Cir. Sept. 29, 2016) (granting summary judgment: "While product hopping under certain circumstances may be viewed as anticompetitive conduct, this is not one of those cases.... Mylan was not foreclosed from the market."); *Walgreen Co. v. AstraZeneca Pharm. L.P.*, 534 F. Supp. 2d 146, 151 (D.D.C. 2008) ("*Walgreen*") (granting motion to dismiss: "here, there is no allegation that AstraZeneca eliminated any consumer choices. Rather, AstraZeneca added choices.... Plaintiffs have also not identified any antitrust law that requires a product new on the market-with or without a patent-to be superior to existing products. Antitrust law holds, and has long held, to the contrary. Courts and juries are not tasked with determining which product among several is superior. Those determinations are left to the marketplace. New products are not capable of affecting competitors' market share unless consumers prefer the new product, regardless of whether that product is superior, equivalent, or inferior to existing products."); *Abbott Labs. v. Teva Pharm. USA, Inc.*, 432 F. Supp. 2d 408, 422 (D. Del. 2006) ("*Tricor*") (denying motion to dismiss because removal of prior drug formulations from the market "result[ed] in consumer coercion" and was "potentially anticompetitive": "If consumers are free to choose among products, then the success of a new product in the marketplace reflects consumer choice, and 'antitrust should not intervene when an invention pleases customers...."By contrast, when the introduction of a new product by a monopolist prevents consumer choice, greater scrutiny is appropriate.")

Response to Questions for the Record from David R. Gaugh, R.Ph., Senior Vice President for Science and Regulatory Affairs, Generic Pharmaceutical Association

David R. Gaugh, R.Ph.
Senior Vice President
Science and Regulatory Affairs
GPhA

Questions for the Record

September 22, 2016 House Judiciary Subcommittee on Regulatory Reform, Commercial and Antitrust Law hearing

"Treating the Opioid Epidemic: The State of Competition in the Markets for Addiction Medicine"

1. **Dr. Prichett's testimony states that generic competitors dominate most markets, including the addiction medicine market, and are coming to market quicker than ever. Do you agree with those statements and, if so, do you still believe that Congress should focus its attention on increasing the speed to market for generics?**

   Increased competition benefits patients and the U.S. healthcare system by increasing market access and lowering drug prices. The generic user fee program has improved the review and approval timelines of generic applications but more needs to be done to ensure that access and cost savings are available from multiple generics for approved innovator products.

2. **When a brand drug gets removed from the market, how does that impact the generic version of the brand product?**

   The impact on the generic industry depends on the reason why the brand product was removed from the market.

   A. If the brand product was removed due to safety and/or efficacy reasons, then the generic marketed products will be subject to a safety and efficacy assessment to determine if the generic product also poses a safety and/or efficacy threat because the safety and efficacy of the approved generic product is determined by establishing bioequivalence to the brand product.
   B. If the brand product was voluntarily withdrawn and the withdrawal was NOT due to safety and/or efficacy concerns than all approved generic versions of that product will remain on the market. The Office of Generic Drugs (OGD) will designate an approved generic which has the largest market share as the "new" reference listed drug (RLD) for that drug product for future drug application submissions.

David R. Gaugh, R.Ph.
Senior Vice President
Science and Regulatory Affairs
GPhA

3. In your testimony, you mentioned that over a billion dollars has been contributed to the FDA to improve the review process. Yet, it appears that the review time has increased. Can you explain how that can be the case?

FDA has used the generic drug user fee funds to restructure OGD and the Office of Pharmaceutical Quality to implement FDA's One Quality Voice plan to achieve its user fee commitments as well as its mission. According to FDA, the first several years of GDUFA I were focused on capacity building (as stated by the Agency, "building the foundation"), such as hiring, training, and improving its internal processes, IT included, to ensure FDA met its commitments. FDA also had to address and "tackle" all the pending backlog applications that were not touched for years. In the midst of all the internal FDA changes, industry experienced inconsistencies stemming from the lack of transparency and communication, which undoubtedly added unnecessary strain, pain and confusion to the successful implementation of the new GDUFA program. All of these reasons have increased the time FDA has taken to review applications.

Response to Questions for the Record from Mark Merritt, President and Chief Executive Officer, Pharmaceutical Care Management Association

PCMA

PCMA's Answers to Questions for the Record

United States House of Representatives Judiciary Subcommittee on Regulatory Reform, Commercial And Antitrust Law

Treating the Opioid Epidemic: The State of Competition in the Markets for Addiction Medicine

1. **Pharmacy benefit managers sit in the middle of the drug supply chain and arguably have the best visibility into pricing and competition. Are your members seeing price increases for Naloxone and buprenorphine products? If so, what do you believe are the drivers of these price increases?**

   PCMA is not privy to prices charged by manufacturers nor their negotiations with PCMA member companies, but public data suggests that the prices of many of these drugs continue to rise. Truven Health Analytics recently reported that the price of Kaleo's naloxone auto-injector Evzio went from $750 for two injectors last year to $3,700 this year.[i] That is almost a 400 percent increase.

   While naloxone has been on the market for decades, recent changes in forms of packaging and delivery have resulted in renewed patent protections for products that contain naloxone and are still branded, resulting in very limited competition. While these delivery changes have led to the drug being available for use under standing orders and administered by non-clinicians, the makers of these drugs apparently have exploited their market position created by an unprecedented spike in demand as America's opioid crisis unfolds.

   Additionally, a substantial portion of the newly packaged and administrable forms of these drugs is purchased directly by first responders, given away free of charge, or dispensed to cash paying customers who either have no insurance or prefer not to submit a claim to the insurer, leaving PBMs removed from many transactions, and so unable to negotiate lower prices. This is unusual in the drug marketplace.

2. **Are there instances in which competitors come into the market and you see prices increase rather than decrease? Can you explain why this occurs?**

   The PBMs competing in the marketplace, across all lines of business, represent total patient populations of approximately 266 million individuals,[ii] bringing significant negotiating leverage to the table with brand manufacturers.[iii] Recent

events demonstrate how head-to-head competition in the marketplace can drive significant savings on expensive drugs unrelated to treating opioid addiction. Recently, a drug manufacturer reported that PBMs were able to negotiate a 46 percent rebate discount for one new hepatitis C drug—saving billions—when a direct competitor drug was introduced into the market.[iv] Due to this competition, the resulting prices were below those in many other countries that employ price-setting policies.[v]

However, in some cases, it may be possible to see the price of drugs remain the same or even increase when a second competing brand drug or generic may enter the market. In this case, the manufacturers may be engaging in a tacit collusion of shadow pricing their competitors, meaning there may be little to no difference in the price of competing drugs, and the prices move closely together over time. However, once a third and subsequent competing brands or second and subsequent generics enters the market, the shadow pricing scheme is nearly impossible to maintain, as manufacturers are forced to compete for market share.

Policies such as awarding accelerated FDA review for second and third drugs in a class and taking steps to clear FDA's generic backlog would increase competition and reduce manufacturer opportunities to shadow price.

In some cases, a given class or category of drugs may have multiple brand entrants that nonetheless do not compete head-to-head; for instance, individual patients may respond to the drugs differently. In this situation, until multiple generics enter a market, PBMs are unable to use competition to incent manufacturers to give price concessions, and manufacturers are able to raise prices on their brand products as they see fit. This typically applies to brand cancer drugs and multiple sclerosis drugs[vi].

[i] Truven Health Analytics data reported in KARE News, "Naloxone Price Hike 'Shocks' Local Law Enforcement" November 22, 2016.
[ii] PR Newswire, "PBMs Provide Policy Solutions to Increase Competition, Reduce Rx Costs," February 4, 2016.
[iii] Health Strategies Group. "Pharmacy Benefit Manager Research Agenda 2015," http://www.healthstrategies.com/download/file/fid/1892
[iv] New York Times, "Costly Hepatitis C Drugs for Everyone?" September 2, 2015.
[v] Quintiles. IMS, "Comparison of Hepatitis C Treatment Costs." September 20, 2016.
http://www.imshealth.com/files/web/IMSH%20Institute/Healthcare%20Briefs/IIH1_Comparison_of_HepatitisC_Treatment_Costs.pdf
[vi] STATNews, "Insurers Pay More for Multiple Sclerosis Drug Because Rebates Don't Help, Report Says," October 13, 2016.
https://www.statnews.com/pharmalot/2016/10/13/multiple-sclerosis-drug-prices-teva/

Response to Questions for the Record from Robin Feldman, Esq., Harry and Lillian Hastings Professor of Law, Director of the Institute for Innovation Law, UC Hastings College of the Law

Robin Feldman
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January 9th, 2017

Dear Chairman Goodlatte,

It is with pleasure that I provide the following responses to the questions submitted for the record following the Committee on the Judiciary's Subcommittee on Regulatory Reform, Commercial and Antitrust Law's September 22, 2016, hearing titled, "Treating the Opioid Epidemic: The State of Competition in the Markets for Addiction Medicine."

1. *How can policymakers and others differentiate between "product hopping," by which a manufacturer is manipulating the system to retain exclusivity, and true innovation, through which a manufacturer is adding value to the market with a new product?*

Product hopping is characterized by three factors: 1) timing; 2) minor modifications, such as in dosage or delivery; and 3) market blocking. First, shifts to a new product are timed to coincide with expiration of the exclusivity. Second, the brand-name company makes minor modifications to the drug, such as modifications to dosage or delivery. Third, the brand-name company employs strategies to discourage generic substitution. These can include withdrawing the original medication, campaigns for doctors to insist that prescriptions be "dispensed as written," and various insurance formulary strategies.[1]

Behind these three identifying factors lies a general principle: The hallmark of competition is choice. Given open choice, markets are an excellent judge of whether a new product adds value. Behaviors that deter open choice—for patients, doctors, pharmacists, or insurers—should be suspect.

[1] For detailed examples of product hopping strategies, see Robin Feldman & Evan Frondorf, *Drug Wars: A New Generation of Generic Pharmaceutical Delay,* 53 HARV. J. ON LEGIS. 499, 527-533 (2016), *available at https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2659308*.

One should be cautious, however, in defining the behavior with too much precision, lest those definitions simply become lines to avoid. For example, modifications in dosage or delivery are a current, favored approach for product hopping, but new pathways could be chosen.

2. *Brand Drugs often take years and millions of dollars to develop. Shouldn't we encourage these companies to continue to innovate and bring life-saving drugs to market?*

It is important for innovative pharmaceutical companies to receive an appropriate return for their wonderful contributions to consumer health and to the American economy. The patent system, along with the extensions and benefits provided by the Hatch-Waxman legislation, is designed to ensure that pharmaceutical companies enjoy those returns. The system is designed as a quid pro quo, however, and at the end of the exclusivity period, society should receive the benefits of open competition. When the government grants a patent, it is a deal made for the benefit of society, and pharmaceutical companies should not be permitted to sidestep their end of the bargain.

Most important, the patent system creates a balance between providing rewards for past innovation and ensuring space for future innovators to enter the field. Attempts to expand patent exclusivity and avoid open competition threaten to upset that delicate balance.

3. *Are the antitrust laws properly equipped to address the type of conduct you detailed in your testimony that may be inhibiting competitors from coming to market and placing a check on drug prices?*

Providing effective antitrust pathways would require shifts in at least two areas of antitrust doctrines.[2] First, antitrust actions related to pharmaceutical behavior are likely to involve challenging actions related to patents or to activity at federal agencies such as the Food & Drug Administration (FDA). The *Noerr-Pennington* line of cases, dating back to the 1960s, establishes the general principle that one has the right to petition government without fear of antitrust liability. Although antitrust liability may still attach if one's petition to the government is judged to be a "sham," the bar for establishing a sham petition is extremely high, particularly where patents are concerned. That standard would need to be changed, if antitrust law is going to provide a consistent and effective approach.

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[2] For a description of these problems, see ROBIN FELDMAN, RETHINKING PATENT LAW 166-170 (Harvard 2012); see also Robin Feldman, Evan Frondorf, and Andrew K. Cordova, *Empirical Evidence of Drug Pricing Games—A Citizen's Pathway Gone Astray,* (forthcoming 2017 in STANFORD TECHNOLOGY LAW REVIEW), *available at https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2833151.*

Second, behaviors related to obtaining samples from competitors would run up against the *Trinko* doctrine, as well. The Supreme Court in *Trinko* established that competitors generally are not required to sell to each other. As the Department of Justice has noted, "forced sharing" rarely helps consumers in the long run.[3] Providing samples for generic approval may be the rare exception to the rule, however, and *Trinko* would need to be adjusted as well, if antitrust law is to provide an effective approach to anticompetitive behavior involving samples of the branded drug.

In addition to antitrust, one could characterize these behaviors as forms of regulatory abuse. Thus, regulatory remedies that do not involve the antitrust system could be designed to deter the behavior.[4]

Whatever reforms are chosen, it will be critical to ensure that regulators, legislators, courts, and the public can see new schemes as they emerge. Although the FDA makes a wealth of information publicly available, there are significant gaps in the system that should be remedied, as noted in my study.[5] In addition, much behavior is hidden behind the murky world of pricing rebates, deals, and preferences organized through systems such as pharmacy benefit managers (PBMs) and dedicated pharmacies. Aspects of that information should be available to the public and to regulatory actors. A little sunshine goes a long way.

4. *In your testimony, you discuss companies using the FDA citizen petition process to delay the approval of competing drugs. Can you explain exactly how this works and how Congress should respond?*

The FDA's citizen petition process, and similar programs at other agencies, were created in the 1970s as part of an effort to fashion more participatory regimes in which ordinary citizens could access the administrative process. Recent evidence suggests that the process at the FDA has been diverted by those very companies it was meant to rein in. I recently completed a large-scale empirical study of twelve years of FDA data which confirms that the "concerned citizen" is frequently a large drug company raising frivolous or questionable claims in a last-ditch effort to

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[3] *See* Department of Justice, *Competition and Monopoly: Single-Firm Conduct Under Section 2 of the Sherman Act*, at Chapter 7, Unilateral, Unconditional Refusals to Deal with Rivals *available at* https://www.justice.gov/atr/competition-and-monopoly-single-firm-conduct-under-section-2-sherman-act-chapter-7.

[4] *See* Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act of 2016 S. 3056, *available at* https://www.congress.gov/bill/114th-congress/senate-bill/3056; Feldman et. al, *supra* note 2.

[5] *See* Feldman, et al. *supra* note 2 (final section, "The Road Ahead").

hold off competition.[6] The motivation is clear—delaying entry of generic competitors for just a few months can translate into hundreds of millions of dollars in revenue.

The study paints a picture of widespread, strategic exploitation of the citizen petition pathway by drug companies striving to hold off price competition. Nearly half of the petitions in the data set were filed within approximately a year of when the FDA approved the generic, and the most common timing for citizen petitions related to generics was within half a year or less before generic approval. If the brand-name company had legitimate concerns about the pending generic, it could raise those concerns much earlier in the approval process, as opposed to waiting until the FDA is nearly ready to grant approval.

Use of this delay strategy has proliferated over the past decade. The number of such petitions from competitor companies—branded and generics seeking to delay generics--has effectively doubled since 2003. In some years, out of all citizen petitions the FDA is tasked with reviewing (including those related to medical devices, food, dietary supplements, tobacco, etc.), one-in-five are filed by a drug company seeking obstruction of generic competition.

Such petitions do not appear to be based on legitimate concerns about consumer safety. The FDA denies approximately 80% of citizen petitions related to pharmaceuticals.[7] Even when petitions are granted, some represent pure delay tactics. For example, many petitions ask the FDA to stay approval of the generic until the applicant conducts a test that the FDA *already* requires for approval. The FDA is forced to grant the petition, even though its demands are redundant with the FDA's existing requirements.

Although Congress passed amendments in 2007 in an attempt to block potential avenues for citizen petition abuse, the study demonstrates that those amendments have been largely toothless.

The study describes in detail various approach that could be used to deter such behavior, including adjusting the antitrust laws as described in response to question 3 above. Regulatory remedies, such as the CREATES Act, could be helpful, as well.[8] Perhaps the most promising approach, however, would be to set up procedural blocks—such as requiring that drug companies file their citizen petitions within a year of when the generic files its application or

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[6] *See* Robin Feldman, Evan Frondorf, and Andrew K. Cordova, *Empirical Evidence of Drug Pricing Games—A Citizen's Pathway Gone Astray,* (forthcoming 2017 in STANFORD TECHNOLOGY LAW REVIEW (peer reviewed)), *available at* https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2833151; see also Michael A. Carrier & Carl Minniti, *Citizen Petitions: Long, Late-Filed, and At-Last Denied,* AM. U. L. REV. (forthcoming 2016) http://ssrn.com/abstract=2832319.

[7] Michael Carrier and Daryl Wander in *Citizen Petitions: An Empirical Study,* 34 CARDOZO L. REV. 249, 274 (2012).

[8] *See* Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act of 2016 S. 3056, *available at* https://www.congress.gov/bill/114th-congress/senate-bill/3056.

establishing that issues raised by the petition will be resolved on a timeline separate from that of generic approval.

Regardless of the policy approaches undertaken, greater transparency will be critical for exposing new schemes and inappropriate behaviors as they emerge. Please see my response to Question #3 for transparency recommendations.

Warmest regards,
Robin Feldman

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Review

From morphine clinics to buprenorphine: regulating opioid agonist treatment of addiction in the United States

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Abstract

The practice of prescribing opioid drugs for opioid dependent patients in the U.S. has been subjected to special government scrutiny for almost 100 years. From 1920 until 1964, doctors who used opioids to treat addicts risked federal and/or state criminal prosecution. Although that period ended when oral methadone maintenance was established as legitimate medical practice, public concern about methadone diversion and accidental overdose fatalities, combined with political pressure from both hostile bureaucracies and groups committed to drug-free treatments, led to the development of unprecedented and detailed Food and Drug Administration (FDA) regulations that specified the manner in which methadone (and later, levo-alpha-acetyl methadol, or levomethadyl acetate, (LAAM)) could be provided. In 1974, Congress gave the Drug Enforcement Administration (DEA) additional oversight of methadone treatment programs. Efforts to liberalize the FDA regulations over the past 30 years have been resisted by both the DEA and existing treatment providers. Additional flexibility for clinicians may evolve from the most recent effort to create an accreditation system to replace some of the FDA regulations. The development of buprenorphine, a partial opioid agonist, as an effective treatment for opioid addiction reopened the possibility for having a less burdensome oversight process, especially because of its reduced toxicity if ingested by non-tolerant individuals. New legislation, the Drug Addiction Treatment Act (DATA) of 2000, created an opportunity for clinicians with special training to be exempted from both federal methadone regulations and the requirement to obtain a special DEA license when using buprenorphine to treat addicts. Some details of how the DATA was developed, moved through Congress, and signed into law are described.
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1. Early history of opioid-addiction treatment

The federal regulation of medical prescribing of opioids in the U.S. began with the Harrison Act of 1914. While the Harrison Act did not actually prohibit physicians from prescribing opioids for addicted patients within a legitimate medical context, the Treasury officials who were empowered to implement the Act vigorously opposed the practice and were successful in deterring physicians from engaging in it. By 1920, the American Medical Association (AMA) also condemned prescribing opioids to addicts, thereby opening the door further to the prosecution and conviction of physicians who continued to do so. This difficult situation for people who were dependent on opioids and for the practitioners who wanted to help them did not begin to change until 1964. It was then that Vincent Dole and Marie Nyswander first described their work treating heroin addicts with orally administered methadone (Musto, 1987; Jonnes, 1996).

Some of the milestones of those 50 years between the Harrison Narcotic Act of 1914 and the studies of methadone maintenance in 1964 include the rise and fall of morphine clinics (the last of them closed in 1923); the successful federal prosecution of physicians who prescribed morphine to addicts; and, following a period of relative stability in the 1930s and 1940s, a post-World

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War II rise in heroin addiction that led to new federal legislation increasing the severity of penalties for the use and possession of illicit drugs. In 1961, a report issued by a joint committee of the American Bar Association and the AMA questioned those repressive drug policies and encouraged research on opioid maintenance (Musto, 1987).

Throughout most of this period, and until he retired in 1962, Harry J. Anslinger headed the Bureau of Narcotics. Anslinger believed strongly that addiction would disappear in the face of severe penalties for the possession, use, or sale of drugs, and that getting rid of drugs, drug users, and drug pushers would solve the drug problem. Under Anslinger's influence, demonizing the drugs, especially heroin, became a key element of federal drug policy, and addiction to opioid drugs was portrayed as an incurable disorder that condemned its victims to a life of degradation (Musto, 1987; Courtwright, 1992).

2. Evolution of methadone treatment

The current system of opioid treatment regulations, as well as American attitudes towards addicts, were influenced not only by this history, but also by other equally important elements and events. These included a heroin epidemic that accelerated in the early 1960s; the rise of the therapeutic community movement, which convincingly demonstrated that heroin addicts were not beyond redemption; the Narcotic Addict Rehabilitation Act (NARA) of 1966, which established a federal civil commitment program modeled partly on similar programs in California and New York; and the work of Dole, Nyswander, and their collaborators at the Rockefeller Institute. Their work, from the early 1960s and onward, showed that heroin addicts who were maintained on oral methadone could give up heroin and lead productive, law-abiding lives (Glasscote et al., 1972; Gerstein and Harwood, 1990).

The data reported by Dole, Nyswander, and coworkers, and soon confirmed by others, showed that treatment in methadone treatment programs sharply reduced heroin use and criminal activity, increased gainful work, and resulted in generally improved health. Equally important, patients found the treatment acceptable, and several treatment centers began operation. Most of the treatment centers using methadone operated under Investigational New Drug (IND) applications issued by the Food and Drug Administration (FDA), and thereby claimed exemption from the policies of the Bureau of Narcotics, which still viewed providing opioids to addicts as illegal. It is of historical interest that Dole and coworkers at Rockefeller did not seek or obtain an IND, since they took the position that methadone was an approved therapeutic agent and that off-label use did not require an IND. From 1967 to 1970, the FDA liberally issued INDs for methadone research. Beginning in 1968, INDs were also issued for the study of LAAM, (levo-alpha-acetyl methadol, or levomethadyl acetate). By 1969, several thousand patients were enrolled in methadone maintenance treatment research programs (Jaffe, 1975; Gerstein and Harwood, 1990; Jonnes, 1996; Kreek and Vocci, 2002).

Yet, methadone was not well received in the early 1970s. Most federal agencies were hostile towards it or were at least skeptical about it. The Departments of Justice and the Treasury, still influenced by Anslinger's vision, saw methadone treatment as wrongheaded. Advocates for psychosocial programs within the treatment community derided it as a 'magic bullet' that was likely to lessen concerns about unemployment, housing, and the psychological and sociological origins of addiction; vocal groups of recovering heroin addicts saw it as both an irrational treatment and a threat to the therapeutic community movement; some minority activists described it as a government effort to control the behavior of young black men.

Even the FDA did not find the data that were generated sufficient to approve methadone as a safe and effective treatment for heroin addiction. Further, there was no rationale for determining how many INDs to issue and no practical mechanism to prevent their misuse as a cover for profit oriented prescribing of methadone unaccompanied by rehabilitative services. No standards had been established for what constituted minimally acceptable treatment, and no rules governed the amount of opioids that could be prescribed, or taken home, or for whom the treatment was appropriate, giving the recipients of the methadone INDs large leeway in making those decisions. Newspapers published stories about physicians who prescribed methadone for patients who were not seriously dependent on opioids; about methadone being diverted from the clinics to the street; and about children being poisoned by drinking methadone that was brought home legitimately by household members who were in treatment. Methadone maintenance also drew criticism from advocates and providers of 'drug-free' treatment, who saw it as another form of addiction, from law enforcement groups, and from minority groups who denounced it as 'genocide' (Jaffe, 1975; Jonnes, 1996).

In June of 1970, the FDA proposed a new ruling on methadone IND applications. Largely a response to the numerous Congressional and community concerns about the issues of diversion of methadone, iatrogenic methadone addiction, and accidental overdoses, the new IND regulations imposed such strict requirements on entry into treatment, dosage, and duration of treatment that they discouraged methadone use. With this ruling, which became final in April, 1971, the FDA avoided making a decision on whether methadone treatment was

safe and effective, but allowed it to continue 'thinly disguised as research.' These stringent regulations were of no help to the many heroin addicts who were seeking treatment but could only be put on waiting lists. The status of methadone treatment as 'research' made government authorities at all levels reluctant to provide funds to support its expansion.

Nevertheless, in June of 1971, the Nixon administration's initiative on drug abuse included the decision to accept methadone maintenance as an effective treatment, to develop ways of minimizing the real and perceived problems with its use, and to expand access to treatment for those who wanted it. The White House Special Action Office for Drug Abuse Prevention (SAODAP) worked with the FDA to revise the overly stringent regulations in order to achieve those objectives. First proposed in April 1972, the new regulations established the basic framework that governed the use of methadone and similar opioid agonist drugs in the treatment of heroin addiction for the following 30 years. These regulations created a hybrid IND NDA (New Drug Application) that acknowledged the safety and efficacy of methadone maintenance as a treatment, but imposed a number of conditions on how it could be used. Those conditions represented a substantial and unprecedented departure from the usual practice of allowing licensed physicians to use their own professional judgment, guided by a drug's labeling, to determine how to prescribe a medication. Among other things, the 1972 regulations specified, according to various criteria including age and duration of drug dependence, who could be eligible for methadone treatment. They also specified the maximum initial dosages that could be used, the minimum amount of counseling that must be provided, and the factors to be considered when deciding on take home medication, such as how long a patient had been in treatment and whether drug tests showed any evidence of illicit drug use. The new regulations also created a closed system for methadone, restricting its availability to approved clinics and hospital pharmacies, with the aim of deterring those few individual physicians who, in violation of the 1971 regulations, continued prescribing methadone for substantial fees (Jaffe, 1975; Rettig and Yarmolinsky, 1995; Jaffe, 1997; Kreek and Vocci, 2002).

Each element in the 1972 regulations was intended to reduce or prevent problems that had been experienced under the largely informal pre-1971 IND system; or to correct the overly restrictive aspects of the 1971 regulations; or to assure concerned parties, including Congress, that methadone would be used in combination with, not as a substitute for, rehabilitation. In short, the 1972 regulations were designed to allow expansion of treatment while maintaining some control over quality of treatment. They described 'medication units' because they anticipated a time when clinics and individual practitioners would be linked to pharmacies and other sites that would be authorized to dispense drugs, such as methadone, for the treatment of addiction. The drafters of the regulations did not intend for medication dispensing to be forever limited to a few large clinics. Although they recognized that access to treatment by individual physicians might temporarily be limited, they believed that the regulations would be revised as knowledge expanded and as opioid maintenance treatment became less controversial (Jaffe, 1975, 1997). The regulations became fully effective in March, 1973. However, throughout 1972 and the beginning of 1973, some members of Congress and certain journalists continued to see methadone diversion as a serious problem. In June 1973, the Senate passed the Methadone Diversion Control Act of 1973, which became the Narcotic Addict Treatment Act of 1974 (NATA). This law, which was an amendment of the Controlled Substances Act (CSA), gave the newly created Drug Enforcement Agency (DEA) jurisdiction over the storage and security of drugs used in the treatment of addiction. It also required separate DEA registration annually of practitioners and treatment sites. The Secretary of Health, Education, and Welfare (now Health and Human Services [HHS]) retained the responsibility for setting standards for proper professional practice in the medical treatment of addiction.

Since 1970, clinicians have criticized the Federal regulations as a burdensome interference with the practice of medicine. Some claim that the paperwork burdens and constraints on take-home doses contribute to patients' dropping out of treatment (Dole, 1992). Although some of the criticism is valid, it often fails to distinguish between federal, state, and local regulatory burdens. State and local jurisdictions have also seen fit to enact legislation governing these programs, and some of those regulatory requirements are far more restrictive than federal ones. For example, some localities do not permit any take-home medication. Another criticism is that regulatory oversight is concerned exclusively with process, although actual treatment outcome can be measured. But regulations alone are not responsible for all of the problems methadone treatment providers encounter. Not to be overlooked is the impact of the more than 50% reduction (inflation-adjusted) in the level of financial support for methadone treatment programs in most parts of the country over the past 30 years (Gerstein and Harwood, 1990).

Alternatives to the current regulatory framework have been sought and proposed over the years. There is no federal legislation that requires the Secretary of HHS to issue *regulations* dealing with the medical treatment of 'narcotic addiction.' *Guidelines* could accomplish this task equally well. In 1984, Congress amended the NATA, and gave the DEA authority to withdraw registration from treatment programs or

individual practitioners for committing (in DEA's judgment) 'such acts as would render registration inconsistent with public interest.' Since one federal agency (DEA) already has the authority to revoke licensure, there may be no good reason to have any HHS *regulations*. However, if the use of opioid agonists in the treatment of opioid dependence were governed only by HHS guidelines or professional judgment, any oversight of the quality of treatment would be left to the discretion of the DEA and to the tort system (Molinari et al., 1994).

In summary, for most of the past 30 years the regulatory framework dealing with the use of opioids in the treatment of addiction in the U.S. has consisted of a dual oversight at the federal level (HHS and DEA), as well as various (and varying) regulatory requirements at the state and local levels. Although the FDA regulations were intended to be more flexible and responsive than legislation to changing conditions, prior to the major revision that was finalized in 2001 they had been revised only twice, in 1980 and 1989. Those changes were relatively minor, mostly having to do with urine testing, on-site services, and easing constraints on admissions. Despite complaints about over-regulation, when the FDA and the National Institute on Drug Abuse (NIDA) issued a proposal in 1983 to convert most regulations to 'guidelines', most of the treatment providers who responded to the proposal stated a preference for the existing regulatory system (Rettig and Yarmolinsky, 1995). In 1989, largely as a response to the spread of HIV among intravenous drug users, NIDA and the FDA published a rule regarding 'interim methadone maintenance'—the provision of methadone without rehabilitative services to addicts waiting to get into full service programs (Rettig and Yarmolinsky, 1995). The methadone treatment providers and some state authorities reacted unfavorably. Many treatment providers believed that interim maintenance would inevitably lead local, state, and federal governments to further reduce funding and to pay only for dispensing methadone (Rettig and Yarmolinsky, 1995).

3. Opioid-agonist treatment regulations—recent changes

The number of patients in methadone treatment programs has grown since the early 1970s, from about 20,000 to about 180,000 (Kreek and Vocci, 2002). Some states still do not permit methadone or other opioid agonist treatment regulated by the NATA. In 1993, when the FDA finally approved LAAM for the treatment of heroin addiction, multiple state and local legislative and regulatory barriers still prevented it from being used. Even where it was permitted its utility was compromised because the FDA regulations that prohibited take-home doses entirely. (New regulations that took effect in 2001 now permit take-home doses.)

In 1992, the Institute of Medicine (IOM) undertook a review of the Federal regulation of methadone and LAAM in the treatment of addiction. Their report, issued in 1995, concluded (among other things) that the current regulation by multiple agencies: (1) overemphasizes the dangers of methadone diversion; (2) burdens programs with unnecessary paperwork; (3) constrains clinical judgment; (4) reduces access to treatment; and (5) contributes to premature discontinuation of treatment. The IOM recommended that the current detailed regulations be replaced by practice guidelines and sharply reduced regulations (Rettig and Yarmolinsky, 1995).

In response to the IOM recommendations, the federal agencies that comprise the Interagency Narcotic Treatment Policy Review Board (FDA, NIDA, Substance Abuse and Mental Health Services Administration [SAMHSA], Department of Veterans Affairs [VA], DEA, and the Office of National Drug Control Policy [ONDCP]) undertook the work of substantially revising the HHS regulations. The DEA did not propose any changes in its authority to require special licensing and to oversee addiction treatment that uses opioid drugs. Originally, the new system was to have as its central feature a set of HHS regulations requiring programs or practitioners that use opioid agonists for addiction treatment to be accredited by an approved accrediting body, and establishing an upper limit on the amount of opioid medication that could be given to patients for use outside the clinic at any one time. Accrediting bodies would base their decisions on a set of treatment standards approved by the Secretary of HHS, and representing the best clinical thinking of experts in the field, subject to change as knowledge changes. It was recognized at the outset that value judgments and tradeoffs are implicit in how standards of care are set. Setting high standards that require competent initial assessments, good medical care, and some minimal level of psychosocial support will limit access for some addicts where states, localities, or insurance carriers are unwilling to pay for those services. If the standards are not met, neither programs nor individual practitioners can be accredited, and the power to accredit becomes the power to destroy. Conversely, if standards are set quite low, the cost of delivering care will be reduced and access may increase; but then it becomes likely that some programs would be no more than opioid dispensaries staffed by the lowest cost personnel, and with considerable risk of hazardous prescribing practices and drug diversion. Unless federal and state priorities were to be reordered so as to provide much greater financial support for opioid treatment, setting standards, whether by guideline or regulation, will involve difficult value judgments.

Some changes have now been approved, but the effort to shift from federal regulations with their implied criminal penalties for violations to a system of peer review accreditation did not result in as much freedom for clinical judgment as those within HHS, who originally proposed the accreditation process, had hoped for. Pressures from already licensed methadone providers and the DEA left in place many of the regulatory constraints on clinical judgment, particularly with respect to the compliance burden placed on virtually all new patients regarding take-home medication and clinic attendance. While the new regulations eased considerably the maximum take-home dosages permitted for long term patients (in treatment for more than 2 years), new patients, regardless of level of stability or need for other treatment services, are still required to obtain nearly all their medication at the clinic for a period of several months. Furthermore, the burdens of meeting the accreditation requirements are likely to prevent individual physicians, no matter how well trained, from using opioid medications such as methadone or LAAM to treat opioid dependent patients in their offices, unless the physician is administratively linked to an existing opioid treatment program. In addition, the NATA still requires all physicians who might wish to treat opioid addicts with Schedule II opioid medications to obtain a separate registration for this purpose from the DEA, even if they intend to treat only a few patients.

Although these latest changes in the regulations, including the institution of accreditation, are far greater than those accomplished by the two previous revisions, their modesty and the time it took to bring them from initial proposal to reality gives testimony to the inertia in the system, the complexity of forces that influence it, and the power of the current stakeholders. The notion of a system of accreditation to replace the regulations was raised by Curtis Wright and Jerome Jaffe at a meeting of the Interagency Narcotic Treatment Policy Committee in 1995, shortly after the release of the IOM report on methadone regulation. It did not get final approval within HHS until some time in December of 2000. There were considerable reservations voiced at ONDCP. Following the Presidential elections of 2000 and the change in administration, a hold was placed on all regulatory change. The modifications of the methadone regulations did not go into effect until May 18, 2001 (N. Reuter, personal communication).

4. Buprenorphine: a new pharmacotherapy for opioid addiction

A major justification for the regulation, accreditation, and separate DEA registration was to minimize the diversion of opioid drugs from treatment programs. Among the most important concerns about diversion are the serious toxic consequences that ensue when non-tolerant individuals ingest dosages of methadone or LAAM typically used in treatment. As early as Jasinski et al. (1978) had noted the possible clinical utility of buprenorphine, a partial opioid agonist. By the early 1990s, it became clear that buprenorphine could be used effectively for the treatment of heroin addiction (Johnson et al., 1992; Ling et al., 1996) and that its partial agonist properties resulted in very substantially decreased toxicity even for non-tolerant individuals (Walsh et al., 1994, 1995). Under these circumstances, one major justification for maintaining the 'closed system' for medications used in opioid maintenance was largely eliminated. It was not so much that diversion of a partial agonist could be considered a trivial issue, but rather that with lethality from diversion of prescribed medication sharply reduced, a fresh look could be taken at the costs and benefits of making opioid treatment both more accessible and less stigmatizing by moving it from the clinics into the offices of individual physicians. It seemed possible that, under the right circumstances and once approved by the FDA for use in the treatment of opioid dependence, buprenorphine might be exempted from some of the burdens associated with the use of methadone and LAAM.

To achieve such an outcome, two major hurdles had to be overcome. First, buprenorphine would have to win FDA approval for the treatment of opioid addiction; second, some regulatory or legislative action was needed that would exempt it from the provisions of the CSA of 1970 and the NATA of 1974. It is important to point out here that from the perspective of Reckitt and Colman (now Reckitt Benckiser Pharmaceuticals), the company that originally developed buprenorphine as an analgesic and still controlled its use, the legislative effort to be described and the effort to develop and win FDA approval for its use in addiction treatment were seen as being inextricably intertwined. It was obvious from the experience with LAAM that winning FDA approval for a drug used in the treatment of addiction in no way assures its utilization if it also requires legislative changes in each of the 50 states. Also, from a corporate perspective it seemed unlikely that a drug confined to a limited number of clinics that were already comfortable using generic methadone would be used enough to justify the investment involved in taking buprenorphine through the regulatory process.

Reckitt and Colman knew it would be at least a 5-year project and that it would be committing millions of dollars to develop a product that had no patent protection remaining. The Board of Directors decided to approve the process nevertheless. It was apparent that, to recover any significant portion of corporate expenditures, two conditions would be needed. First, buprenorphine would need to reach the mainstream

practice of medicine a goal that certainly seemed achievable in light of the IOM report on methadone regulation. Second, a period of market exclusivity would be needed to protect the product once FDA approved it. The Company faced three challenges. To address the matter of market exclusivity they needed to seek Orphan Drug designation. This was accomplished fairly quickly in 1994. The next challenge was to somehow amend the CSA of 1970 to allow physicians to treat patients with buprenorphine in the normal course of the practice of medicine. This change would result in an exemption from the NATA, which is itself a modification of the CSA. The third was to submit an NDA to the FDA and gain its approval. What follows here is the story of how the legislation that largely exempts buprenorphine from certain provisions of the CSA made its way through Congress to the Oval Office.

5. A need for new legislation

Reckitt and Colman was convinced by the history of efforts to modify the methadone regulations that amending treatment program regulations through administrative change would be a long and cumbersome process unlikely to reach the goal of moving treatment into the mainstream of medicine and expanding access for new patients. The company therefore chose to seek a change in the law. The original aim of the proposed legislative solution seemed simple and straightforward: to change the law to waive the current requirements for physicians prescribing opioids to treat opioid dependence. The proposed legislation would leave the methadone system intact but expand the possibilities for treatment. The original draft of this legislation, called the Drug Maintenance and Detoxification Act, was written by Charles O'Keeffe and Robert Angarola in October, 1995. That first draft stated simply that the requirements of the CSA did not apply when a physician treated no more than 20 patients with a Schedule V narcotic. As it turned out, this proposed legislation went through many changes and was not finally passed by Congress until 2000. It took more than 5 years to enact a very minor amendment to the existing legislation.

The high points of that journey make an interesting lesson about the process of change in our democracy. In 1995, representatives of Reckitt and Colman approached Capitol Hill offices to explain the issue as they saw it: there is a new product which, when approved, will have the potential to bring a significant number of new patients into treatment. But there will be no market for it and the medical community will not be able to use it because of current legal requirements. In several offices, staff members were very receptive.

Senator Carl Levin, who has had a long standing personal interest in expanding and improving addiction treatment, became a supporter. Senator Orrin Hatch and his staff on the Senate Judiciary Committee, which has jurisdiction over the Controlled Substance Act, was also interested. Senator Joseph Biden, who had previously introduced legislation to encourage the development of new addiction treatment medication, was most interested. Strong allies in the House of Representatives included Congressman Thomas Bliley, who was then Chairman of the Commerce Committee, which shares jurisdiction over the CSA with the Judiciary Committee. With their efforts, several key members of the Judiciary Committee and others on both sides of the aisle became persuaded that the proposed legislative changes would be good policy. Despite this promising start, it was not until the end of the 1998 congressional year that the Company could rally enough support to get something going. But 1998 was an election year and the end of the 106th Congress. It was clear that the bill could not be enacted using the full legislative route. Senate staff suggested an alternate approach: using what is called a 'must-do' vehicle: that is, attaching it to a bill not necessarily related to the subject matter, but one such as an appropriation bill that must be signed into law. Senator Hatch's staff, with agreement from the offices of Senators Levin, Biden and Moynihan, arranged to have the proposed change to the CSA tucked into a multiagency appropriations bill for Senate action. This required negotiating with HHS, Justice, and the White House over provisions of the bill. The parties reached agreement in late October 1998, about 3 years after the original draft was written. Although Chairman Bliley of the House Commerce Committee was willing to let this amendment pass as part of the appropriations bill, the senior Democrat member of that committee, Congressman John Dingell, was not. He objected to the process, not the policy. He said the Committee had never held hearings on the matter and had never formally considered the legislation, and this, he said, deprived the members of the Committee of an opportunity to examine the policy, understand it, and either agree or disagree with it. He also noted that appropriations bills are not the place to change health care policy. The provision was removed from the bill.

Shortly thereafter the bill's supporters in the Senate produced a new draft of the legislation. This time the Company and the involved congressional staffers tried to follow everyone's rules. They worked with virtually all of the interested parties, including the Clinton administration, FDA, SAMHSA, NIDA, DEA, and the departments of HHS and Justice. FDA was concerned that the system could get out of hand unless limits were placed on the number of doctors and patients who initially could participate in the system. DEA worried that they would not be able to get a handle on whether physicians were appropriately registered. SAMHSA was concerned about the impact on

their resources and about the potential impact on current methadone clinics. The College on Problems of Drug Dependence (CPDD), the American Methadone Treatment Association (AMTA), the American Academy of Addiction Psychiatry (AAAP), the American Society of Addiction Medicine (ASAM), the American Psychiatric Association (APA), the AMA, the American Osteopathic Association (AOA), and others in the field, also had concerns and suggestions.

The new bill was introduced at the end of January, 1999, by Senators Hatch, Levin, and Biden. It provided that physicians who were qualified to treat opioid-dependent patients would be allowed to prescribe certain FDA approved opioids without being subject to current regulations, so long as they certified to their qualifications with the Secretary of HHS 30 days in advance of treating such patients and treated no more than 20 at a time. The bill also provided that the new federal paradigm would not be pre-empted by the states for at least a period of 3 years, but gave the Secretary of HHS and the Attorney General ample authority to stop the entire program if there was significant abuse. It was passed by the full Senate in November. Still needed was a House bill and agreement between the House and Senate, but some people on the Democrat side of the House were still irritated by the ill-fated effort to put the matter into an appropriations bill the year before. Congressman Dingell had written to the Secretary of HHS, Donna Shalala, raising questions and concerns about the buprenorphine bill that needed to be addressed before there could be further movement. Fortunately, Secretary Shalala responded in support of the policy change. She argued for changing the regulatory framework of drug treatment, for destigmatizing treatment, and for the promise of new treatment products such as buprenorphine. This was a positive development, but it was not until the end of July of 1999 that a bill was finally introduced into the House of Representatives. A hearing was held on July 30th, and although one witness raised concerns about the impact of new treatment arrangements on the current methadone system, and another raised the issue of whether insurance would cover new treatments, the witnesses were otherwise quite positive. Significantly, Senators Hatch and Levin testified in the House of Representatives in support of the bill. Dr Westley Clark, of the Center for Substance Abuse Treatment (CSAT), testifying for SAMHSA, noted the importance of ensuring that states would follow any new federal oversight arrangement from the outset to make certain it caught hold. He cited the LAAM experience as an example of how not to get new interventions broadly adopted. Another 3 months passed before the Commerce Committee acted and the bill was ready for House consideration. During that time various changes were made to the bill, including, for example, greater specificity about what makes a provider 'qualified'. Although state preemption remained a concern for some members, the final language was believed to provide sufficient opportunity after an initial transition period for states to make different rules.

Meanwhile, a bill aimed at shutting down illicit methamphetamine laboratories had been introduced into the Senate by Senator John Ashcroft and was arousing interest and support. This interest was shared by many House members as well, and it now gained priority in both the House and Senate Judiciary Committees. Thus, before the Drug Addiction Treatment Act (DATA) of 2000, or the 'Buprenorphine bill', as it came to be known, could be released, some activities on methamphetamine, including hearings in members' home districts, had to be undertaken. Furthermore, the members wanted to ensure that the methamphetamine bill would sail through the legislative process. This required a considerable amount of negotiation about both bills among interested parties. The House finally considered the buprenorphine bill on July 18, 2000 under 'Suspension of the Rules'. Under this procedure, only 1 h of debate is allowed and no amendments are accepted. While it is more predictable than a process where multiple amendments can be offered, under this procedure a two-thirds vote, rather than a simple majority, is needed to pass a bill, and for this reason the committee was concerned that the bill not be controversial. The debate was held, the bill was supported, and it seemed poised to be passed by the House on a voice vote, when Chairman Bliley made a motion to require a roll call vote to take place later that day. Then another glitch appeared: the version of the bill printed in the Congressional record was different from the version that had been considered on the House floor. This administrative error meant the bill would have to lay over until the next day at least.

Although the Secretary of HHS had been supportive, the DEA had serious reservations, and the 1-day layover gave them another opportunity to voice their concerns. They immediately contacted the House Judiciary Committee and attempted to add a requirement for physicians to register separately with the DEA or to get DEA approval before prescribing. The effort failed. The bill passed the House the next day with a vote of 412 to 1. It was then placed on the Senate calendar, but before it could come to consideration, the Senate Judiciary Committee passed the methamphetamine bill and attached to it their version of the buprenorphine bill. The Senate now had its own bill, quite different from the House version, a methamphetamine/buprenorphine bill, which it passed and sent to the House on January 27, 2000. Although the buprenorphine amendment to the CSA had now been passed by both House and Senate, there was still no law on the books that actually changed policy.

Throughout this process, staffers in the offices of Senators Hatch, Levin and Biden were seeking other vehicles for both the methamphetamine and buprenorphine bills. Ultimately, both bills were included in another 'must pass'—a huge bankruptcy reform bill. The House and Senate were in conference on this bill. Bankruptcy reform was hardly benign and the conference was not without some rancor. Senator Levin was determined to pass the buprenorphine bill, with or without the methamphetamine bill. As the ranking member of the Senate Armed Services Committee, and with the concurrence of the chairman of that committee, Senator John Warner, he had the buprenorphine bill placed in the Department of Defense Authorization conference, attached to another 'must pass' bill to allow the military to continue to function.

In the spring of 2000, there were six versions of the buprenorphine bill making their way through the legislative process: two versions of a stand-alone buprenorphine bill; two versions of a buprenorphine/methamphetamine bill; a buprenorphine/bankruptcy bill; and a buprenorphine/guns bill. Then events took another amazing turn. On May 9, 2000, the House passed a bill, H.R. 4365, to 'amend the Public Health Service Act with respect to children's health'. Without fuss or fanfare, this combination of several children's health bills was scheduled for action. It was now Chairman Bliley's chance to seize an opportunity; so H.R. 2634, Bliley's buprenorphine bill, became part of what came to be known as the 'Children's Health Act'. The House passed their bill and sent it to the Senate. After some behind the scenes negotiations, the bill passed the Senate on September 22, 2000, with an amendment that was, not surprisingly, the Senate version of the buprenorphine bill with the methamphetamine provisions. That amended bill, of course, had to be sent back over to the House and reconsidered. The House passed the bill exactly as the Senate had passed it, as Public Law 106–310, on September 27, 2000. On October 17th, President Clinton signed it into law. It is of some academic interest that the bankruptcy bill and the defense authorization conference were still in play, so at the last minute the buprenorphine provisions had to be snatched out of those bills. The President vetoed the bankruptcy bill on December 19, 2000.

6. The drug addiction treatment act of 2000

The new law, the DATA of 2000, offers an opportunity to make significant changes in the way addiction treatment is delivered. The change could be of benefit to hundreds of thousands of patients addicted to opioids. Perhaps as result of this legislation, other companies will see more opportunity in the development of new pharmaceuticals to treat addiction. The last hurdle was the final approval of the buprenorphine NDA by the FDA.

Buprenorphine for the treatment of opioid dependence was approved on October 8, 2002. This approval marks a new milestone in the evolution of the American response to opioid addiction, but it does not mark our crossing into therapeutic utopia. There will be problems. With FDA's approval of buprenorphine we will have, concurrently, two distinct oversight systems that deal with the use of opioid drugs in the treatment of opioid addicts. One is the modified set of regulations that emerged from the hybrid IND–NDA that developed and evolved over 30 years to provide a framework for oversight of methadone treatment. That system, which applies to all Schedule II opioids, such as methadone and LAAM, now incorporates a system of professional accreditation to oversee some aspects of treatment quality. It would not be inaccurate to describe this system as a hybrid–hybrid. And it still includes, by federal regulation, numerous constraints on the free exercise of judgment by treating clinicians. The other oversight system is the set of conditions that will govern the use of Schedule III–V opioid drugs, such as buprenorphine, that are approved for the treatment of addiction by the FDA. In this system, the judgment of the clinicians, who must attain certain qualifications or special training in order to be exempt from certain requirement of the NATA, is constrained by the requirement to limit the number of patients treated at any one time and the restriction on group practices.

7. Future challenges

It is not clear at this time how these two concurrent systems will interact and what the impact will be on patient access to treatment or the array of services provided. It is anticipated that the changes in the older system (the hybrid–hybrid) and the availability of buprenorphine in the offices of qualified physicians will serve both to increase access to treatment and to ease the compliance burdens on patients, and that both of these conditions will result in substantial benefits to the public and patients treated. But the law of unintended consequences has not been repealed, and it will remain for future commentators to judge what has been brought by these policy changes.

Undoubtedly, there will be some diversion of buprenorphine, and there will be some overdoses. We hope that few, if any, are fatal. Some young people will try buprenorphine and find it reinforcing. Somewhere, someplace, these events will be reported on by the media. It is difficult to predict the spin that such news will be given. The published articles and the television programs will probably not mention that in France the widespread therapeutic use of buprenorphine for the

treatment of 70,000 heroin addicts seems to have reduced significantly the opioids overdose death rate (Ling and Smith, 2002). What the coverage might underscore is that, other than peer pressure, neither government nor the medical profession will have mechanisms to deal with the individual rogue physician who prescribes inappropriately or too generously. If such behavior persists there is, at the federal level, only the extreme measure of reconsidering the status of buprenorphine as a Schedule III drug, or of the provisions of the Drug Abuse Treatment Act of 2000. What happens, of course, will reflect the peculiar American ambivalence about the opioid addict as not quite a patient and not quite a criminal. Thus, Americans seem willing to tolerate occasional untoward events and misuse of drugs for treatment of hyperactivity or anxiety, but not those associated with treatment of opioid addiction. The most optimistic scenario is that the use of buprenorphine in office based settings will simply increase access and lead the United States to a more pragmatic attitude towards dealing with the consequences of heroin addiction – and that such pragmatism will be long lasting and will demonstrate what can be achieved by easier and less stigmatizing access to treatment. With continued support from NIDA and CSAT, the new era of clinical freedom will be just another step in the long national effort to achieve the right balance between investing in supply control and demand reduction.

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STATEMENT OF PROPERTY CASUALTY INSURERS ASSOCIATION OF AMERICA

SUBCOMMITTEE ON REGULATORY REFORM, COMMERCIAL AND ANTITRUST LAW,
HOUSE JUDICIARY COMMITTEE
HEARING ON

"Treating the Opioid Epidemic: The State of Competition in the Markets for Addiction Medicine"

The Property Casualty Insurers Association of America is composed of nearly 1,000 member companies, representing the broadest cross section of insurers of any national trade association. PCI members write $202 billion in annual premium, 35 percent of the nation's property casualty insurance. We appreciate the efforts of the Permanent Subcommittee on Investigations to focus attention on combatting the opioid epidemic. Our members are deeply concerned about this problem. Unfortunately, the United States is suffering from an epidemic of accidental deaths and addiction resulting from the increased sale and use of powerful narcotic painkillers. The abuse of prescription painkillers is a serious public health and public safety problem. Three out of four prescription drug overdoses are caused by prescription painkillers—also called opioid pain relievers.

An opioid is defined as any morphine-like compound that produces pain relief. The American College on Occupational and Environmental Medicine indicates that opioids are appropriate in the treatment of acute musculoskeletal pain only on a short-term basis and for chronic pain only when other methods and medications have failed.

Opioid painkillers such as oxycodone, hydrocodone, and methadone have been identified as one of the primary reasons for the tragic increase in prescription drug overdose deaths, and they are being prescribed in the United States at an unprecedented rate.

From a workers compensation perspective, PCI has aggressively worked at the state level to advocate for solutions. *The primary goal of an individual state workers compensation system is to provide injured workers the best care available, so they can return to work as soon as they are able and continue to be productive members of our society*. There is significant evidence that long-term opioid use leads to longer workers compensation claim duration, long-term disability, higher costs, and higher medical expenses. Most importantly, long-term opioid use will significantly hinder an injured worker's chance to return to work.

To effectively address this epidemic, federal and state agencies need to continue to work together to address this public health crisis. At both the state and federal level, PCI has recommended a number of solutions to help control prescription painkiller abuse including the following:

- Educate providers so they can make better decisions and identify opioid-related problems in their patients;

- Reduce inappropriate access to opioids;
- Require providers to follow the CDC guidelines when prescribing opioids including the limiting of a prescription to a short period of time during the acute phase of recovery;
- Require providers to follow consistent, evidence-based treatment guidelines for acute and chronic pain;
- Require providers to check individual state prescription monitoring programs (PDMP) to help identify patients with addiction problems;
- Enhance interstate data sharing among PDMPS;
- Create a closed formulary to control costs and limit unnecessary use of opioids in the workers compensation system;
- Require providers to offer psychological evaluations to patients with long term opioid to determine appropriate psychological treatment; and
- Implement media and education programs regarding the safety of prescription painkillers.

We appreciate the opportunity to provide comments.

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