METHAMPHETAMINE ADDICTION: USING SCIENCE TO EXPLORE SOLUTIONS

HEARING

BEFORE THE

SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY

COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY

HOUSE OF REPRESENTATIVES

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September 18, 2013

METHAMPHETAMINE ADDICTION: USING SCIENCE TO EXPLORE SOLUTIONS

TUESDAY, SEPTEMBER 18, 2013

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY,
Washington, D.C.

The Subcommittee met, pursuant to call, at 10:09 a.m., in Room 2318 of the Rayburn House Office Building, Hon. Larry Bucshon [Chairman of the Subcommittee] presiding.

LAMAR S. SMITH, Texas
CHAIRMAN

EDDIE BERNICE JOHNSON, Texas
RANKING MEMBER

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Subcommittee on Research and Technology

Methamphetamine Addiction: Using Science to Explore Solutions

Wednesday, September 18, 2013
10:00 a.m. to 12:00 p.m.
2318 Rayburn House Office Building

Witnesses

First Sergeant Niki Crawford, Indiana State Police, Meth Suppression Section Commander

Dr. Edythe London, The Thomas and Katherine Pike Professor of Addiction Studies, Director of the UCLA Laboratory of Molecular Neuroimaging at the David Geffen School of Medicine, University of California at Los Angeles

Dr. Jane Maxwell, Senior Research Scientist, School of Social Work, University of Texas at Austin

Dr. T. Celeste Napier, Professor, Departments of Pharmacology and Psychiatry and Director, Center for Compulsive Behavior and Addiction, Rush University Medical Center

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
SUBCOMMITTEE ON RESEARCH

HEARING CHARTER

Methamphetamine Addiction: Using Science to Explore Solutions

Wednesday, September 18, 2013
10:00 a.m. - 12:00 p.m.
2318 Rayburn House Office Building

Purpose

On Wednesday, September 18th, the Research and Technology Subcommittee will hold a hearing to understand the methamphetamine (commonly known as "meth") addiction problem, and how science can inform and provide possible solutions. Witnesses will give a general background to this growing problem, and then discuss the latest research on meth addiction including prospective technologies to prevent large-scale unauthorized purchases of pseudoephedrine (PSE). They will also discuss the latest social science research to inform both prevention and treatment for meth addiction. The Science, Space, and Technology Committee has a legislative and hearing record over several Congresses on this problem, resulting in the Methamphetamine Remediation Research Act of 2007 (P.L. 110-143).

Witnesses

First Sergeant Niki Crawford, Indiana State Police, Meth Suppression Section Commander

Dr. Edythe London, The Thomas and Katherine Pike Professor of Addiction Studies, Director of the UCLA Laboratory of Molecular Neuroimaging at the David Geffen School of Medicine, University of California at Los Angeles

Dr. Jane Maxwell, Senior Research Scientist, School of Social Work, University of Texas at Austin

Dr. T. Celeste Napier, Professor, Departments of Pharmacology and Psychiatry and Director, Center for Compulsive Behavior and Addiction, Rush University Medical Center

Hearing Overview

Methamphetamine (or "meth") is a highly addictive stimulant that affects the central nervous system. Meth can be easily made in small clandestine laboratories, with relatively inexpensive over-the-counter ingredients, making it a drug with high potential for widespread abuse. Meth is a Schedule II stimulant, meaning that it has high potential for abuse and may lead to severe psychological or physical dependence. Meth is available only through a prescription. While it has some limited medical use, the dosage for meth used in medical treatments is much lower than those typically used by drug abusers.

The method of meth production depends primarily on the availability of the chemical ingredients and creating a laboratory (commonly referred to as "meth lab") to produce it. The meth "cooking" process continues to adapt as producers find ways to work around the constraints in getting the necessary chemical ingredients. Meth is relatively easy to make today, and individuals with little formal knowledge of chemistry, laboratory skills or equipment can start a meth lab. The number of meth labs has increased significantly, due to growth in the "one pot" or "shake and bake" method in which it can be manufactured in a small containers.

Scientific research to understand the relation between the brain and meth would be informative towards treatment. Long-term effects of meth abuse include addiction, which is a chronic relapsing disease; this disease is characterized by compulsive drug seeking and use, accompanied by changes in brain function and chemistry. Other symptoms include insomnia, mood disturbances, violent behavior, and psychotic episodes including hallucinations and delusions.[1]

National Institute for Drug Abuse (NIDA) funded research aims to apply the basic science of meth research to develop new treatments in addition to enhancing existing approaches, with the goal of bringing these treatments to the communities that need them. Chronic meth abuse has been shown to significantly change brain chemistry. Medical imaging studies have shown significant changes in the neurological areas responsible for motor skills and verbal learning. These changes are also the cause of many of the emotional and memory problems observed in meth abusers.[2] Various research approaches to understanding the role of meth in brain addiction are ongoing. In 2012, NIDA spent $64.5M on meth related research, while the overall NIH budget for meth research was $68.4M.

Meth abuse leads to devastating medical and social consequences, infusing whole communities with new waves of crime, unemployment, child neglect or abuse, increased incidences of infectious diseases (e.g., HIV and hepatitis) due to the re-use of contaminated syringes and needles, and other negative social consequences. Children raised in households where meth labs are operated are at increased risk to physical and sexual abuse by their own family, or other adults. In addition, children exposed to residences with meth labs increase the likelihood of exposure to toxic chemicals and contaminated food; they may also inhale the secondhand smoke of adults who are smoking meth. During a four-year period from 2007 to 2011, the state of Tennessee spent over $70 million to place 1,625 children removed from meth lab homes into foster care. [3]

Scientific research could also better inform law enforcement on how to clean up the hazardous materials found in meth labs that may result in propane tank explosions. In addition to the negative medical and social consequence, meth labs also pose a serious health risk to law enforcement officers who come across or respond to them. Since 2002, the Drug Enforcement Administration (DEA) has spent over $142 million to help state and local agencies with meth lab cleanup.

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[1] Meth Drug Fact Sheet found at http://www.justice.gov/dea/druginfo/factsheets.shtml
[2] http://www.drugabuse.gov/publications/research-reports/methamphetamine-abuse-addiction
[3] http://www.gao.gov/products/GAO-13-204

Recent Legislation

In 2005, Congress passed *The Combat Methamphetamine Epidemic Act* (CMEA) which requires retailers of non-prescription products containing pseudoephedrine (PSE) and associated derivatives to place these products behind the counter or in a secure location. Furthermore, consumers must show identification and sign into a logbook for each purchase. However, these restrictions led to a rise in the use of *smurfing*, which refers to the practice of hiring individuals to purchase PSE in multiple locations in order to exceed legal purchase limits. Some state legislatures have passed even more stringent laws to regulate the sale of PSE. In particular, Mississippi, Oregon and 63 Missouri cities and counties now only allow the obtaining of PSE by prescription only. Comparisons between those states that have legislatively instituted PSE blocking and tracking systems versus those states that have returned PSE to a prescription-only drug are now underway.

Congress then passed *The Methamphetamine Production Prevention Act* in 2008 to enable electronic data collection. This act allows retailers to use an electronic logbook to comply with the requirements of CMEA. The act aimed to monitor the sale of over-the-counter PSE related medication, and to stop purchases by individuals who exceeded the federal limits. Thirty states have now enacted laws to implement real-time stop sales systems, in an effort to move to a nationwide electronic system to enforce illegal purchases of PSE product; such a system allows retailers to block illegal sales that exceed daily and monthly limits. The National Precursor Log Exchange (NPLEx) is a real-time electronic logging system used by pharmacies and law enforcement in 29 of the 30 states to track sales of over-the-counter (OTC) cold and allergy medications containing precursors to the illegal drug, methamphetamine. According to a 2013 GAO report, the NPLEx system was used to block the sale of more than 576,000 boxes and 1,412,000 grams of PSE products in 17 states last year.[4]

The Methamphetamine Remediation Research Act of 2007 provided for a research program for the remediation of closed meth production laboratories. This act also required the Environmental Protection Agency (EPA) to develop guidelines for decontaminating and remediating meth labs, based on the best currently available research.

Issues for Consideration

This hearing aims to build on the July 31st, 2013 "Frontiers of Human Brain Research" Research and Technology Subcommittee Hearing by discussing the brain's role in meth addiction. The hearing also will emphasize the importance of inter-disciplinary research towards understanding the meth addiction problem. In addition, the role and application of sound social science research to understand the spread of this drug, in addition to informing public policy to address this problem, will be discussed by the witnesses.

[4] http://www.gao.gov/products/GAO-13-204

Chairman BUCSHON. The Subcommittee on Research and Technology will come to order. Good afternoon. Good morning. Welcome to today's hearing titled "Methamphetamine Addiction: Using Science to Explore Solutions." In front of you are packets containing the written testimony, biographies, and truth-in-testimony disclosures for today's witnesses. I recognize myself for five minutes now for an opening statement.

I would like to welcome everyone to today's Research and Technology Subcommittee hearing titled, "Methamphetamine Addiction: Using Science to Explore Solutions."

The problem of methamphetamine, or meth, abuse is a serious problem facing our country today. The main compound from which meth derives is pseudoephedrine, known as PSE, which is also a common drug used to treat nasal and sinus congestion. Unfortunately, criminal dealers have discovered new, easier ways to make more potent forms of meth that require the use of chemicals such as PSE.

As our witnesses will testify today, meth poses significant public safety and health risks, in addition to financial burdens to local communities where these toxic and dangerous labs are found.

According to a 2013 Government Accountability Office report titled "State Approaches Taken to Control Access to Key Methamphetamine Ingredient Show Varied Impact on Domestic Drug Labs," the number of meth lab incidents declined significantly after 2004, when state and Federal regulations on PSE product sales were implemented. Since 2007, however, these numbers have significantly increased, reflecting the emergence of smaller-scale production facilities by a new method called smurfing, where individuals purchase the legal limits of PSE at multiple stores that are then combined for meth drug production. They also buy it from multiple other people, including in some reports college students are—who are getting extra money by selling these products at a higher cost than they can buy them for.

But more than figures and statistics, meth addiction is a problem that personally hits home for many Americans. As a medical doctor, I personally know the devastation that addiction can cause and even after meth addicts kick the habit, some research shows these addicts experience permanent damage, similar to what LSD may have caused back in the '60s and '70s.

From January to July of this year, over 65 meth labs have been dismantled in the biggest county in my district, Vanderburgh County, making it the number one county for meth labs in the state of Indiana. This is extremely close to my home next door in Warrick County where we have had two meth lab explosions within a two-mile radius of my house. In November 2011, a meth lab exploded down the street from my house in a middle-class neighborhood burning down that house and causing over $25,000 in damage to surrounding middle-class homes. This is not a problem that is only isolated to certain areas of our communities.

Despite the grim realities of meth addiction, science can provide valuable insights to this problem. Basic science agencies like the National Institutes of Health have spent over $68 million in Fiscal Year 2013 to understand the neurological basis of meth addiction. The National Science Foundation also supports fundamental non-

medical basic science research, in particular behavioral research, behind the psychology of addiction.

Our witnesses today reflect the wide spectrum of work and research regarding the various facets of the meth problem. Witnesses will introduce the extent of the meth problem and will discuss a wide range of topics on how science can help us understand the prevention and treatment of meth, as well as how technology can be used to stop unauthorized purchases of PSE.

I would like to thank all of our witnesses for being here today and taking the time to offer their perspectives on this critical topic for our communities. I would also thank Ranking Member Lipinski and everyone else for participating in today's hearing.

[The prepared statement of Mr. Bucshon follows:]

PREPARED STATEMENT OF SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY CHAIRMAN LARRY BUCSHON

I would like to welcome everyone to today's Research and Technology Subcommittee hearing titled "Methamphetamine Addiction: Using Science to Explore Solutions."

The problem of methamphetamine, or meth, abuse is a serious problem facing our country today. The main compound from which meth derives is pseudoephedrine, known as PSE, which is also a common drug used to treat nasal and sinus congestion. Unfortunately, criminal dealers have discovered new, easier ways to make more potent forms of meth that require the use of chemicals such as PSE. As our witnesses will testify today, meth poses significant public safety and health risks, in addition to financial burdens to local communities where these toxic and dangerous labs are found.

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But more than figures and statistics, meth addiction is a problem that personally hits home for many Americans. As a medical doctor and physician, I personally know the devastation that addiction can cause and even after meth addicts kick their habit, research shows these addicts experience permanent damage. From January to July of this year, over 65 meth labs have been dismantled in the biggest county in my district, Vanderburgh County, making it the number one county for meth labs in the state. This is extremely close to my home next door in Warrick County and where we have had two meth lab explosions within a 2-mile radius of my house. In November of 2011, a meth lab exploded down the street from my house burning a house to the ground and causing over $25,000 in damage to houses around it.

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I would like to thank the witnesses for being here today and taking time to offer their perspectives on this critical topic for our communities. I'd also like to thank Ranking Member Lipinski and everyone else participating in today's hearing.

Chairman BUCSHON. At this point I will now recognize the Ranking Member of the Subcommittee, the gentleman from Illinois, Mr. Lipinski, for his opening statement.

Mr. LIPINSKI. Thank you. I want to thank you, Mr. Chairman, for holding this hearing and thank our witnesses for being here this morning.

As a Representative from the state of Illinois, I am very interested in this topic because my state experienced some of the same meth abuse problems as Chairman Bucshon's district and state. Geographically, Illinois sits right in the center of the top five states in the country for number of clandestine meth lab incidents reported in 2012. With 801, it had the 5th-highest number of lab incidents.

My colleagues in districts affected by heavy meth abuse, as well as my colleagues in districts affected by other illegal drugs, understand the heavy burden placed not only on families but also the local economy, hospitals, law enforcement, and the court system. Unfortunately, if the sequester continues, Illinois will lose about $3.5 million in grants to help prevent and treat substance abuse resulting in around 3,900 fewer admissions to substance abuse programs.

Congress and individual states have developed laws aimed at making the precursor chemicals for methamphetamine harder to purchase, as the Chairman stated, but there is still more work to be done. In order to do our jobs and craft effective policies to combat meth addiction, we need to know more about the science behind addiction and effective prevention and treatment programs.

Much of the research you will hear about this morning is funded by the National Institute on Drug Abuse at the National Institutes of Health, which unfortunately is not in our Committee's jurisdiction. But, I hope today we also have the opportunity to explore the types of foundational social and behavioral research, as well as the neuroscience research, that underlies much of the more application-driven research that is the purview of several of our witnesses today. As Dr. Gene Robinson testified at the BRAIN Initiative hearing in July, it is necessary to understand how healthy brains work from both a functional and behavioral perspective in order to cure the main devastating brain disorders that afflict our society. This is the type of science championed by NSF. Because of the important work already supported by both NSF and NIDA, our society is starting to accept addiction as a disease of the brain influenced by environmental factors.

Many people addicted to drugs trace their problem back to their school years and acting out teenage curiosity. Thus, to meaningfully change this trend, our conversation must also include teen behavior and drug use and how we might use the education system and public education campaigns as vehicles for prevention. Unless we apply what we know about a teenager's brain and behavior to design such education efforts, and change course as we learn more, we may be setting ourselves up to fail.

I look forward to Dr. Napier's testimony on her work studying the adolescent brain and supporting school-based curricula to help kids build good decision-making skills. These are the very skills they need to keep themselves out of the penal system where they are often introduced to a network of drug dealers within their communities, making the likelihood of relapse after release from jail very high.

Social networks and markets for meth are also important topics for research that can inform the development of more effective prevention policies. For example, we know that meth abuse often circulates within families among close acquaintances. Additionally, as I understand it, whereas meth labs used to be typically in a room or basement of a home, a 2-liter shake-and-bake bottle can now be quickly improvised in the backseat of a car or behind a dumpster in the schoolyard.

We also know that meth is more successful in penetrating some markets than others. Identifying and understanding the factors behind the meth market and how meth abuse spreads in social networks is a challenge that requires collaboration among social scientists and law enforcement officials.

Finally, evidence-based policymaking is essential for effective treatment. If meth addicts are only fixated on their next high as the research has shown, then the standard 12-step program will not be an effective treatment tool for them. Treatment programs for meth addiction have evolved based on our increased understanding of what works and what doesn't, but more progress is still needed. As a social scientist myself, I find all of these to be interesting, compelling research challenges.

Before I close, I would like to mention that a bipartisan law was passed through our Committee in 2007 that addressed meth, specifically with a focus on a lack of national standards for remediation of meth labs. For every pound of meth produced, five to six pounds of toxic byproducts remain in walls and carpets, as well as ventilation and wastewater systems. Perhaps it is worth this Subcommittee, through its jurisdiction over NIST, reviewing where we now stand with respect to remediation standards. I think this is an area in which we can work again on a bipartisan basis for the health of our first responders who investigate meth labs and citizens in those communities.

Again, I look forward to hearing testimony from the witnesses and hope the testimony can get us thinking about how research can help us better tackle the increasing meth addiction problem plaguing our communities.

I yield back the balance of my time.

[The prepared statement of Mr. Lipinski follows:]

PREPARED STATEMENT OF SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY
RANKING MINORITY MEMBER DANIEL LIPINSKI

Mr. Chairman, thank you for holding this hearing and thank you to our witnesses for being here this morning.

As a Representative from the state of Illinois, I am very interested in this topic because my state is experiencing some of the same meth abuse problems as Chairman Bucshon's district and state. Geographically, Illinois sits right in the center of the top five states in the country for number of clandestine meth lab incidents reported in 2012. With 801, it had the fifth highest number of lab incidents. My colleagues in districts affected by heavy meth abuse, as well as my colleagues in districts affected by other illegal drugs, understand the heavy burden placed not only on families, but also the local economy, hospitals, law enforcement, and the court system. Unfortunately, if the sequester continues Illinois will lose about $3.5 million in grants to help prevent and treat substance abuse, resulting in around 3,900 fewer admissions to substance abuse programs.

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I look forward to Dr. Napier's testimony on her work studying the adolescent brain and supporting school-based curricula to help kids build good decision-making skills. These are the very skills they need to keep themselves out of the penal system where they are often introduced to a network of drug dealers within their communities making the likelihood of a relapse after release from jail very high.

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Again, I look forward to hearing from the witnesses and hope that the testimony can get us thinking about how research can help us better tackle the increasing meth addiction problem plaguing our communities.

Thank you Mr. Chairman. I yield back the balance of my time.

Chairman BUCSHON. Thank you, Mr. Lipinski.

I now recognize the Chairman of the full Committee, Mr. Smith, for his opening statement.

Chairman SMITH. Thank you, Mr. Chairman.

Six weeks ago, this Subcommittee held a hearing on the frontiers of human brain research. During that hearing, our witnesses discussed many different neurological disorders, including Alzheimer's disease, autism, epilepsy, Parkinson's disease, and traumatic brain injury. However, witnesses did not have the opportunity to discuss

another important disorder, namely addiction, which affects millions of Americans and their families.

Our witnesses this morning will testify about how meth addiction leads to severe medical and social consequences, and why this drug is particularly destructive to the addict. The meth problem is an example of a clear societal need where science can yield potential solutions that will benefit the American public. Progress on this problem, like many other complex medical issues, will require an interdisciplinary approach that will inform the scientific basis of meth addiction and treatment.

The National Science Foundation will play an integral role in achieving a more complete understanding of this problem. Hypothesis-based data-driven social science research can be used to understand the behavioral science behind addiction.

Scientists should work with health officials to develop predictive models and algorithms that could aid law enforcement. Applied mathematicians should work with neuroscientists to develop the mathematical tools necessary to build a quantitative model that could help explain the neurological factors behind addiction. These are just a few examples where NSF money can be effectively spent to help solve an important societal problem.

I look forward to the witnesses' testimony and the questions, and I would especially like to thank a constituent of mine, Dr. Jane Maxwell from the University of Texas, for being here this morning and for her participation.

Mr. Chairman, finally, I explained to the witnesses a few minutes ago that, unfortunately, I have another Committee that is holding a classified briefing that I have to attend, that began 20 minutes ago so I am going to have to excuse myself. I do want to reassure the witnesses that I have seen their testimony and we appreciate, again, their contributions.

Thank you, Mr. Chairman, and I yield back.

[The prepared statement of Mr. Smith follows:]

PREPARED STATEMENT OF FULL COMMITTEE CHAIRMAN
LAMAR S. SMITH

Thank you Chairman Bucshon for holding today's hearing.

On July 31st, this Subcommittee held a hearing on the frontiers of human brain research. During that hearing, our witnesses discussed many different neurological disorders, including Alzheimer's disease, autism, epilepsy, Parkinson's disease and traumatic brain injury.

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just a couple of examples where NSF money can be effectively spent towards an important societal problem.

I look forward to the witnesses' testimony and questions and I would especially like to thank a constituent of mine, Dr. Jane Maxwell from the University of Texas, School of Social Work, for her participation this morning. And I yield back.

Chairman BUCSHON. Thank you, Chairman Smith.

If there are Members who wish to submit additional opening statements, your statements will be added to the record at this point.

[The prepared statement of Ms. Johnson follows:]

PREPARED STATEMENT OF FULL COMMITTEE RANKING MEMBER EDDIE BERNICE JOHNSON

Good morning, I would like to thank Chairman Bucshon for holding today's hearing to explore solutions to meth addiction using scientific research.

Methamphetamine and other drug addictions wreak havoc on so many of our communities. The Office of National Drug Control Policy reports that North Texas is a national distribution center for the crystal form of methamphetamine and other illicit drugs because of its transportation and financial infrastructures and its proximity to Mexico. But meth addiction knows no bounds. Meth use crosses most demographics including gender, age, and race, and may include parents, teens, the unemployed, the homeless, and veterans. With 15 years of experience as a Chief Psychiatric Nurse at the Dallas VA, I recognize the challenges faced by soldiers returning home and the unfortunate battle many of them face with addiction and substance abuse.

Research shows that the brain is substantially changed after heavy meth abuse. Our witnesses today will be testifying about the chemical changes that take place in the brain and that describe the chronic, relapsing disease that is addiction. They will also discuss some of the behavioral changes associated with addiction and the long-term injury to the brain. Meth abuse leads to depression, aggressive behavior, paranoia and hallucinations. Contributing to meth's formidable effects is the exponentially more potent methamphetamine coming out of Mexico.

These degenerative changes to the brain, and associated behavioral changes, have some similarities to findings in people with schizophrenia, bipolar disorder and Parkinson's disease. These similarities reinforce the need to bring many different kinds of experts together to solve this problem. We must encourage and support interdisciplinary work between neurobiologists who study the science of the brain and behavioral scientists who study the actions and reactions of humans. But we cannot make a dent in finding solutions to the meth problem unless these groups of researchers share the findings from their research with clinicians, prevention and treatment specialists, and law enforcement. And for the sake of the children, we must make more than a dent. As I said in July at this Subcommittee's hearing on the BRAIN Initiative, I am so proud of this kind of interdisciplinary and translational research being done on brain disorders, including addiction, at the University of Texas at Dallas' Center for Brain Health.

We must find better ways to treat addicts, but prevention is our best hope. In September 2011, the Greater Dallas Council on Alcohol & Drug Abuse received a $125,000 grant from the White House Office of National Drug Control Policy's Drug Free Communities Support Program. The Drug Free Communities program has already proven to be an effective tool in reducing substance abuse and providing children with the necessary tools to make more informed decisions about their future. I look forward to hearing about the latest prevention programs targeted to school-aged kids and based on scientific studies of adolescent behavior. A recent study reports that in 2012, 1.6 percent of seventh graders and 3.4 percent of twelfth graders in Texas had used meth. The fact we even have drug statistics for 12-year olds is truly disheartening. We must stop this steady and sad trajectory. We need more educational programs in place supported by the type of research done by our witnesses today.

We must all continue to work tirelessly to ensure that we create effective public policies addressing drug prevention and effective treatment programs.

Thank you Mr. Chairman. I yield back.

Chairman BUSCHON. At this time I will introduce our witnesses. The first witness today is First Sergeant Niki Crawford from the

Indiana State Police. She is also the Commander of the Methamphetamines Suppression Section. Sergeant Crawford received her bachelor's degree from Indiana University in secondary education, and since 1993, she has been with the Indiana State Police and has served in various capacities in a variety of locations around the state. Her responsibilities with the Methamphetamine Suppression Section include overseeing all operations of the 125-member Indiana State Police clandestine lab team and supervising 18 full-time personnel assigned to the Methamphetamines Suppression Section.

Our second witness is Professor Edythe London from UCLA. Professor London is an internationally recognized expert in the study of drug addiction. At UCLA she is the Thomas P. and Katherine K. Pike Chair of Addiction Studies and is a Professor in the Departments of Psychiatry and Biobehavioral Sciences in addition to the Department of Molecular and Medical Pharmacology. She received her doctoral degree in pharmacology and toxicology from the University of Maryland. Before joining UCLA faculty in 2001 she worked at the National Institutes of Health for two decades conducting independent research at the National Institute on Drug Abuse. In 2008 she received the Marian Fischman award from the college on problems of drug dependence.

Our third witness today is Professor Jane Maxwell, who is a Senior Research Scientist in the Social Work School at the University of Texas Austin. Her research specialties include trends and patterns of substance abuse both nationally and internationally. She is a principal investigator on a grant from the National Institutes of Drug Abuse to study patterns of methamphetamine use in the Central Texas area. She has been a Fulbright Senior Specialist and a member of the National Institute on Drug Abuse's Epidemiology Work Group for 25 years.

Our fourth and final witness is Professor T. Celeste Napier, who is the Director of the Center for Compulsive Behavior and Addiction and a Professor in the Departments of Pharmacology and Psychiatry at Rush University Medical Center in Chicago. Dr. Napier has over 30 years of research related to brain and behavioral effects of abused substances and impulse control disorders that have been supported by grants from the National Institutes of Health and other private research foundations. She is the author of over 200 scientific publications, special issues, and books.

Thanks again to our witnesses for being here this afternoon. As our witnesses should know, spoken testimony is limited to five minutes, after which the Members of the Committee will each have five minutes to ask questions.

I now recognize First Sergeant Crawford for five minutes to present her testimony. Welcome.

TESTIMONY OF Sgt. NIKI CRAWFORD,
FIRST SERGEANT,
METH SUPPRESSION SECTION COMMANDER,
INDIANA STATE POLICE

Sgt. CRAWFORD. Chairman Bucshon, Ranking Member Lipinski, and distinguished Subcommittee Members, thank you for allowing

the Indiana State Police to be here to present to you on our meth lab epidemic.

As you can see in Table 1 and Appendix A of the written testimony submitted, Indiana has seen the problem of local manufacture of meth rise over the past two decades, and the problem exists in every corner of our state.

We have seen a variety of cook processes over the years, but the most significant change came around 2006 when we began to see the one-pot or the shake-and-bake labs where the entire meth cook is completed in a plastic bottle, glass jar, or other homemade reaction vessel. Because the one-pot labs are used with noncompatible chemicals, more injuries to both meth cooks as well as law enforcement officers are occurring. The corresponding data can be found in Table 2. One-pot labs are a much quicker, easier, and smaller way to manufacture meth.

Everyone asks the question why are meth labs so pervasive? What is the difference between meth and other drugs? From a law-enforcement perspective the difference that we see is that the vast majority of the meth labs in Indiana are not money-driven operations. They are addiction-based labs fueled by the need for a drug whose chemical precursor pseudoephedrine and the other chemical reagents used are readily available in local stores. Drug addicts are in a position where they can completely control their own destiny in terms of easy access to the chemicals and the ability to manufacture the drug—their drug of choice.

On January 16 of 2006 the Indiana State Police launched the Methamphetamine Suppression Section, which consisted of personnel assigned full-time to investigate meth crimes. The State Police personnel historically and currently respond to 97 percent of all labs seized in the state. At about the same time we launched the Meth Watch program, it focused on deterring meth cooks by educating retailers and citizens and putting smurfs on notice that we were watching purchases of certain chemicals. Smurfs by definition are those people who purchase pseudoephedrine products and other reagent chemicals to be diverted to the meth cooks.

Meth Watch kits consist of posters, signage, employee training materials, and brochures. The program was expanded to include stickers to warn thieves and tamper tags to track the thefts from anhydrous ammonia tanks. The success of the program was in the building of investigative relationships between law enforcement and retailers and citizens who sell and also use the products. However, the disappointment of the program was it did little to deter the smurfs and meth cooks. A sampling of the Indiana Meth Watch items have been provided to the Committee for your review.

Following the launch of the Meth Watch, the state police also launched the Indiana Meth Investigation System, also known as IMIS. The front end of IMIS is an informational website and the link is in your packet. The backside of IMIS was a secure meth investigation database for law enforcement to use. Although the state police knew IMIS would not be a preventive measure, it did allow more—excuse me—more efficient investigations and lab reporting both on the state and Federal level.

In 2011 Indiana, as well as many other states across the country, were mandated by law to use the National Precursor Log Exchange

or NPLEX. NPLEX is a national electronic tracking system of pseudoephedrine products. NPLEX was lobbied for under the pretext that it would prevent the illegal purchase of pseudoephedrine products by blocking sales that exceeded the legal limits, and therefore, it would prevent meth labs. Unfortunately, this has not been the case. The meth cooks response has been to double and triple their smurf groups to accommodate the law changes that have been made.

As stated earlier, the GAO did a study where they studied the results of tracking states versus controlled substance states, and in the country, Mississippi and Oregon are two states that returned pseudoephedrine to a prescription-only status.

There are a few pseudoephedrine products that are being marketed as meth-resistant. The technology focuses on the prevention of the extraction of pseudoephedrine from the tablet and impeding the conversion of pseudoephedrine to meth directly from the tablet. It is exciting to see companies working on this technology and in that direction, but of all the samples provided to DEA, their chemists have been able unfortunately to defeat the technology to some extent.

Ladies and gentlemen of the Committee, the word for the day is smurf. Most meth cooks and smurfs are also involved in other property crimes such as burglary and theft. However, the newest and most pervasive crime growth has been smurfing itself. With the establishment of the NPLEX system and mandated block sales, the black market for pseudoephedrine products has significantly expanded. Meth cooks are soliciting the services of family, friends, coworkers, college students, homeless people, and most commonly, other meth addicts to purchase their pseudoephedrine projects.

Bottom line, PSE products have become currency to meth cooks. The meth cooks pay between $20 and $100 for every box of pseudoephedrine or they trade a box for a half a gram of meth, which has a street value of $50.

There is rampant child neglect, endangerment, physical, and sexual abuse among the children being raised in these meth lab homes. Table 6 illustrates the growing number of children that are being identified in homes and locations where we have seized meth labs. As the parents' addiction grows, the lack of supervision of their children also grows.

The meth lab crisis is not an easy problem to solve but this particular drug problem causes much deeper damage to people and communities than other drug crimes. Those of us in law enforcement who have chosen this route in our career know that we will deal with drug-endangered and abused children, theft, burglary, and violence. Communities are dealing with contaminated homes that lead to innocent illness of parties, abandoned properties reducing property values, and fewer employable citizens to contribute to the economy.

As federal, state, and local leaders determine if additional steps are necessary to combat this problem, rest assured that we in law enforcement will remain on the front lines enforcing the applicable laws and fighting for the safety of our children and communities.

[The prepared statement of Sgt. Crawford follows:]

STATE OF INDIANA
INDIANA STATE POLICE
INDIANA GOVERNMENT CENTER NORTH
100 NORTH SENATE AVENUE
INDIANAPOLIS, INDIANA 46204-2259
www.in.gov/isp

Statement for the record of
Niki Crawford
First Sergeant
Indiana State Police
Methamphetamine Suppression Section Commander

Before the
Subcommittee on Research and Technology
House Committee on Science, Space and Technology
United States House of Representatives

Meth Addiction: Using Science to Explore Solutions

September 18, 2013

Written Statement of Niki Crawford
First Sergeant
Indiana State Police
Methamphetamine Suppression Section Commander

Before the
Subcommittee on Research and Technology
House Committee on Science, Space and Technology
United States House of Representatives

Meth Addiction: Using Science to Explore Solutions

September 18, 2013

Chairman Bucshon, Ranking member Lipinski and distinguished subcommittee members, thank you for allowing the Indiana State Police to be here to present to you on exploring solutions to the manufacture of methamphetamine epidemic from a law enforcement perspective.

How has the meth manufacturing problem evolved in your state over the past 20 years? Has the number of meth users in your state declined? Where is the problem most serious in your state, and what efforts are being used to combat the problem?

Indiana, like most Midwestern states, has seen the methamphetamine manufacture problem grow over the years. Along with the rise in meth labs, meth use has also risen. As shown in Table 1, meth lab seizures in Indiana doubled each year from 1995 to 2000. The state initially reached a high of 1,137 labs in 2004. With the passage of Indiana Senate Enrolled act 444, which placed pseudoephedrine (PSE) products behind the counter and required an ID and log for its purchase, Indiana, like most other states, saw an initial drop in meth labs. However, it did not take long for those who intended to divert PSE from its legitimate use to the manufacture of meth, widely known as "smurfs," to catch on to the weaknesses and loopholes of this law, and labs quickly began to rise again. The overall highest year for lab seizures was 2012 with 1,726 labs seized. 2013 is on track to surpass that number. With an average of 5 ½ labs per day, seizure numbers will likely exceed 1,900 labs in Indiana in 2013. One basic fact that is needed to understand the meth lab problem in Indiana is that our meth labs are fueled by addiction to the drug, not the quest for money. This dynamic makes the meth lab issue in most Midwestern states a unique problem where drug manufacturers and addicts have access to everything they need to feed their own addiction.

Labs have continued to rise due to the easy access to PSE products as well as evolving cook processes. Initially, Indiana saw many labs that utilized the red phosphorus and iodine method, which is a lengthier and more cumbersome process to manufacture the drug. However, because of the easy access to anhydrous ammonia in Indiana's farming communities, the Birch Reduction method, which utilizes this common and inexpensive farm fertilizer, took over. In roughly 2005-2006, law enforcement in Indiana as well as other parts of the country began to see a modification to the Birch Reduction method. This modification has become widely known as the One Pot or Shake and Bake method of manufacturing where the entire meth "cook" is completed in a 20 ounce pop bottle, 2 liter pop bottle, glass jar or other homemade reaction vessel. As the cook processes that are most seen have evolved, the dangers associated with those labs have also evolved resulting in more injuries to both meth cooks and law enforcement officers (see Table 2). One pot labs now constitute nearly 90% of all labs seized in the state of Indiana (see

Table 3). Because this process is a much quicker, easier and smaller way to manufacture meth, it appeals to the meth addict in a way most other cook processes do not because they obtain the finished product much quicker, needing less PSE product to produce the methamphetamine and continuing to have easy access to all reagent chemicals utilized in the one pot cook process.

There is no one area of the state that has a more significant problem than another. Indiana's top ten counties are geographically located on the Kentucky border, the Michigan border, rural counties, urban counties, and various locations in between (see Appendix A for 2010-2012 lab seizure maps).

A variety of efforts across many disciplines have been utilized to combat the problem in Indiana. The Indiana Criminal Justice Institute started the Meth Free Indiana Coalition where various agencies involved in justice, prevention, and treatment all came together to share information and programs. This coalition is now part of Drug Free Indiana. The Indiana Department of Corrections started Clean Living is Freedom Forever (CLIFF), a treatment and counseling program for inmates preparing to transition back to society from incarceration for meth crimes. Indiana won a State Prevention Framework State Incentive Grant. In 2006 a working group was organized for this grant to better focus the resources in areas with the most need. Although the initial granting period is over, the working group continues its data gathering and focused prevention efforts to help allocate and request additional funding to continue its prevention programs.

In 2005 the Indiana State Police began the process of creating the Methamphetamine Suppression Section (MSS) to proactively combat meth crimes. While the ISP had always taken the lead in responding to and processing drug lab crime scenes, until that time, the personnel assigned to the clandestine lab team were specialty team members with other work responsibilities within the ISP. On January 16, 2006, MSS began operations with 23 personnel assigned full time to combat the growing meth problem in our state. Currently, MSS has 19 full time personnel and over one hundred additional clan lab certified sworn and civilian agency members who respond to clandestine lab crime scenes. While there are many local officers certified to process clandestine labs, the ISP responds to 97% of all labs seized in the state. ISP also provides the safety equipment and processing supplies needed to appropriately process these crime scenes in a manner compliant with OSHA, EPA, DOT and ISP policies and guidelines. MSS was formed with the focus of education, partnerships and enforcement. Education and partnerships are listed first because we know our enforcement efforts to combat this problem would be lacking the outcomes desired if we didn't educate the public and other public safety organizations as well as build partnerships with the stakeholders in our communities.

What are the specific technical tools that have been developed to monitor or limit the sale of over-the-counter PSE? What are some impediments that are making this problem difficult to solve? What are some ongoing efforts to make PSE tamper resistant, in order to prevent it from being made into meth?

As you can see in Table 1, labs have continued to grow at significant rates, even with additional restrictions placed on the sale and purchase of PSE products. In 2006 the Indiana State Police launched the Meth Watch program. This program was already operational in other Midwestern states that also had high instances of methamphetamine labs. This program focused on deterring meth cooks by educating retailers about the tracking requirements for PSE and the reagent chemicals used in the manufacturing process. Meth Watch kits consist of posters, signage, employee training materials and the required paper logs that were to be completed for each PSE sale. In 2008, the program

was expanded to include stickers and tamper tags for anhydrous ammonia tanks. These tags are used by farmers and Co-Ops for the purpose of tracking thefts of the fertilizer from nurse tanks. Delivering these kits and making contact with retailers, farmers and Co-Ops has created lasting partnerships that still exist today and are one of our greatest assets in obtaining information on the local manufacture of meth. However, the disappointment of the program is that the signs did not deter the smurfs and meth cooks from continuing to purchase the products necessary to manufacture meth.

In June of 2009 the Indiana State Police Meth Suppression Section launched the Indiana Meth Investigation System (IMIS). The front end of IMIS is an informational website designed to educate and provide information on items related to the clandestine production of methamphetamine, as well as give a reporting mechanism for meth lab tips directly to law enforcement from the public (www.meth.in.gov). On the back side of IMIS is a secure database that includes all clandestine lab seizure reports submitted to the system and provided to the Drug Enforcement Administration's National Seizure System at the El Paso Intelligence Center. IMIS also contains all of the PSE sales, blocks, inquiries, smurf groups and tips and leads received on meth production. The system came to Indiana and more than a dozen other states free of charge from the Tennessee Methamphetamine Task Force which developed the program with Federal grant dollars. The system was not mandatory for the reporting of the PSE sales; however, approximately 50% of all Indiana pharmacies voluntarily reported their PSE sales to IMIS. Although the ISP knew IMIS would not be a preventive measure, it did allow for a more efficient manner to report meth labs and investigate the illegal purchase of PSE products.

During the state legislative session in 2010, a bill was passed that required all Indiana retailers selling PSE products to submit their sales to the National Precursor Log Exchange (NPLEx). NPLEx became fully operational in Indiana January 1, 2011. NPLEx was lobbied for under the pretext that it would prevent the illegal purchase of PSE products and, therefore, prevent meth labs. Unfortunately, this has not been the case, as labs have continued to rise. What investigators have found is that the electronic tracking of PSE purchases and the blocking of sales that would have put the purchaser over the legal limit actually hinders the investigative process. The meth cooks have simply expanded their smurf groups to include family, friends, co-workers, college students, the homeless and, most commonly, other meth addicts. The meth cooks pay between $20 and $100 for every box of PSE provided to them or they trade boxes of PSE for ½ gram of meth, which has a street value of $50. The smurfs purchase the PSE products at legal levels, thus making it more difficult to parse out the suspicious sales from the legitimate sales.

At the request of the Caucus on International Narcotics Control in the US Senate, the strengths and weaknesses of various state laws regarding the sale of pseudoephedrine products (tracking versus controlled substance) were studied by the Government Accountability Office (GAO) and the official report was released in January of 2013 (http://www.gao.gov/products/GAO-13-204).

There are a few PSE products being marketed as meth resistant. The technology focuses on the prevention of the extraction of PSE from the tablet and impeding the conversion of PSE to meth directly from the tablet. It is exciting to see pharmaceutical companies working on this technology, but there is still room for improvement. Of all of the samples provided to DEA, the chemists have been able to defeat the technology to some extent. To this point, no waivers to federal or state law have been granted for these products to exempt them from the tracking requirements.

How has meth contributed to a new wave in crime? Give some examples and trends that you have witnessed in your state.

Meth has contributed to a variety of different crimes. Many meth cooks and smurfs are also involved in other property crimes such as burglary and theft. However, the newest and most pervasive crime growth has been smurfing. In Indiana some meth cooks have very sophisticated criminal organizations centered on the purchase of PSE products. The meth cooks have "captains," "lieutenants," and "sergeants" that occupy a level within the organization to purchase and/or deliver the products from the bottom of the chain up to the top. Other meth cooks have solicited the services of family members to purchase their PSE products. Many use threats to persuade their elderly grandparents, parents, aunts and uncles to purchase PSE. We have had numerous reports from family members threatened with physical harm or property damage if they did not purchase certain products for the cook.

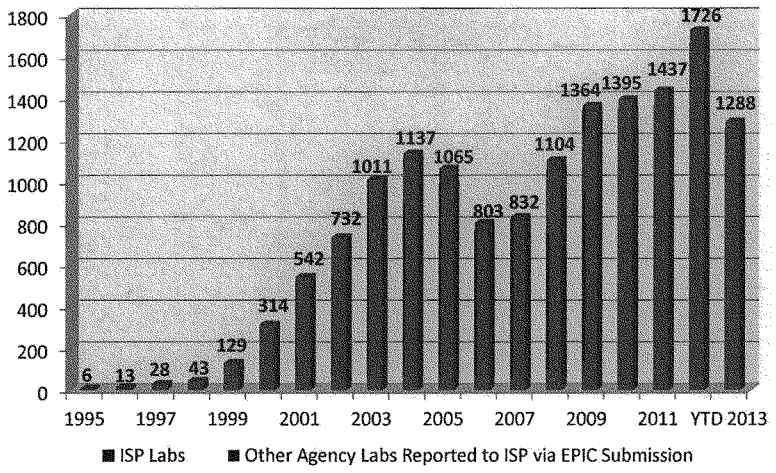
Table 4 shows that rates of arrest continue to increase. It is not uncommon for ISP personnel to document two to eight suspects at a clandestine meth lab crime scene. As shown in Table 5, not all identified suspects are arrested at the time of the lab, so it is important to show the difference between arrests reported and suspects who were identified. We believe this arrest data is a very good picture of the smurfing problem and how pervasive it is in Indiana: 1,529 suspects arrested or identified in 1,252 labs.

Smurfing also extends from PSE to the other reagent chemicals. As discussed earlier, boxes of pseudoephedrine products have become currency for meth cooks. They trade boxes for the drug or get cash in return. Undercover police officers working these cases know they cannot approach a meth cook and offer cash to buy meth. They must have boxes of PSE or other chemicals to trade, which puts law enforcement and prosecutors in a difficult position of providing precursors and chemicals to a meth cook that can turn those into more meth within an hour. Anyone at that location has now been placed in harm's way with exposure to chemical vapors, fires and explosions.

In addition, there is rampant child neglect, endangerment and abuse among the children being raise in these meth lab homes. Table 6 illustrates the growing number of children identified in homes or locations where meth labs have been seized. As the parents' addiction grows, the lack of supervision of their children also grows. Methamphetamine is a stimulant, and it is a sexual stimulant. Children are being sexually abused by both their parents as well as their parents' associates. Protecting children is a priority of Meth Suppression personnel who are trained each year on the Indiana Drug Endangered Child protocol and the reporting requirements of our state statute for children under the age of 18 found in meth labs.

The meth lab crisis is not an easy problem to solve, but this particular drug problem causes much deeper damage to people and communities than other drug crimes. Those of us in law enforcement who have chosen this route in our career know we will deal with drug endangered and abused children, theft, burglary, and violence. Communities are dealing with contaminated homes that can lead to illness of innocent parties, abandoned properties reducing property values, and fewer employable citizens to contribute to the economy. Until federal, state, and local leaders determine what steps are necessary to combat this problem, rest assured that law enforcement will remain on the front lines enforcing applicable laws and fighting for the safety of our children and communities.

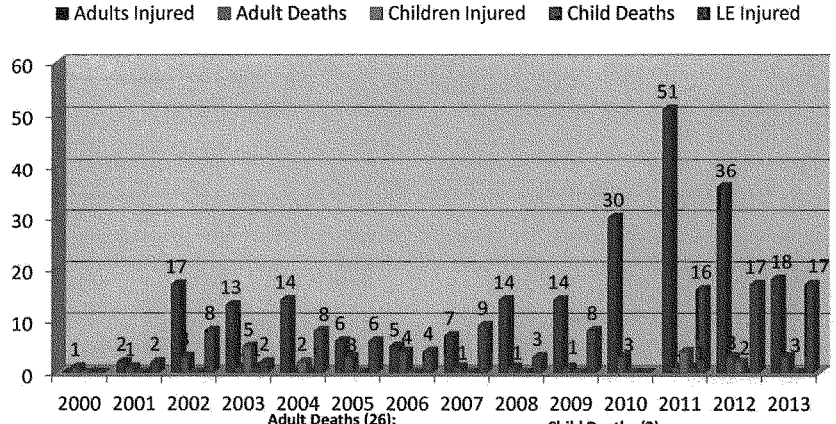
Indiana Law Enforcement Clandestine Lab Incidents 1995 - YTD 2013



All Agencies' lab seizures

Table 1

Indiana Meth Lab Injuries and Deaths 2000 - 2013



Adult Injuries:
227 total

Law Enforcement Injuries:
100 total

Adult Deaths (26):
Police Action Shooting: 3
Pursuit Crash: 2
Car Crash: 1
Suicide: 2
Fire/Explosion: 10
Homicide: 3
One Pot Explosion(no fire): 1
Overdose: 1
Other: 3

Child Deaths (2):
Fire: 1
Medical/Health: 1

Child Injuries (13):
Fire: 7
Chemical Burns: 1
Exposure to Chemical Vapors: 4
Swallowed Chemical: 1

All Agencies' lab seizures

Table 2

Indiana State Police Lab Seizure Type 2013

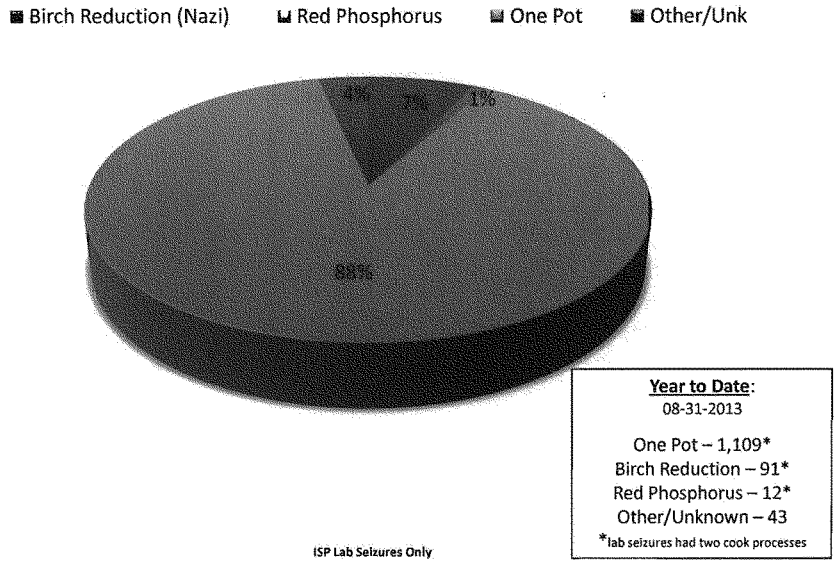


Table 3

Indiana Law Enforcement Clandestine Lab Arrests 1995-2012

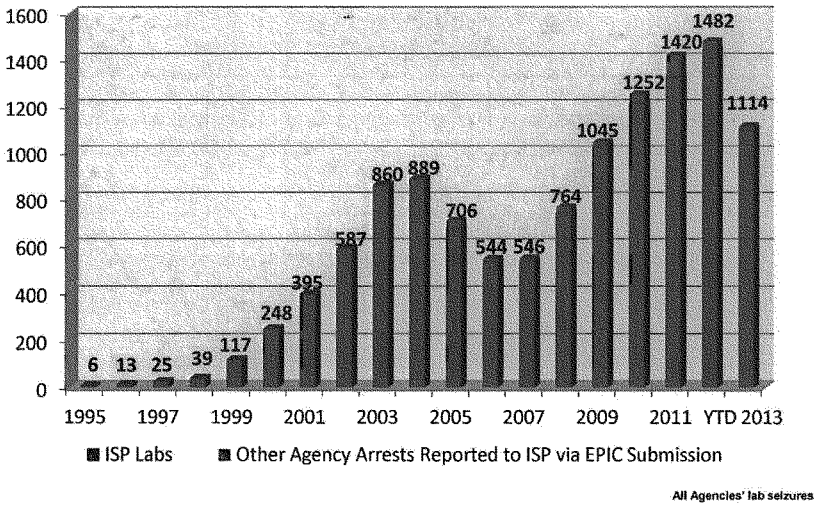
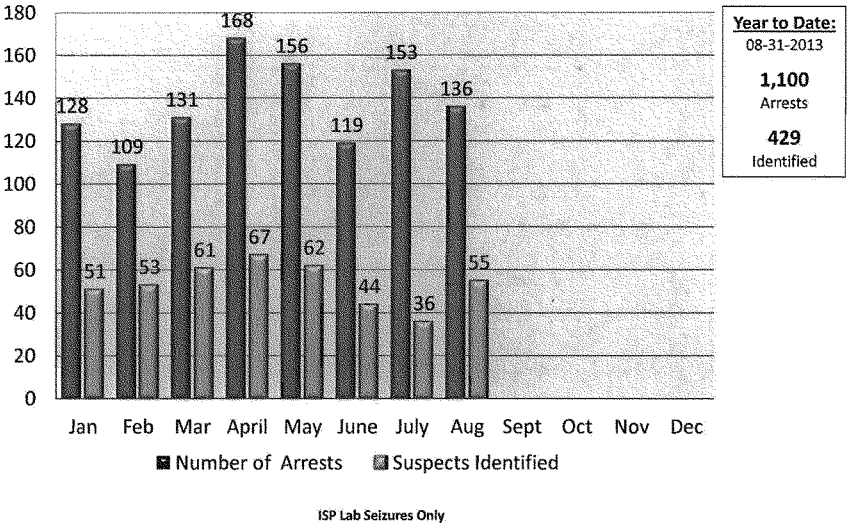


Table 4

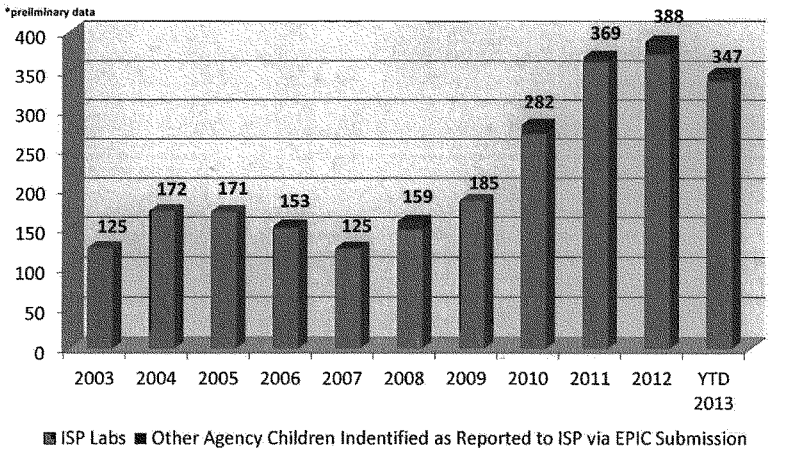
Indiana State Police Clandestine Lab Arrests & Suspects Identified But Not Arrested at Time of Lab - 2013



ISP Lab Seizures Only

Table 5

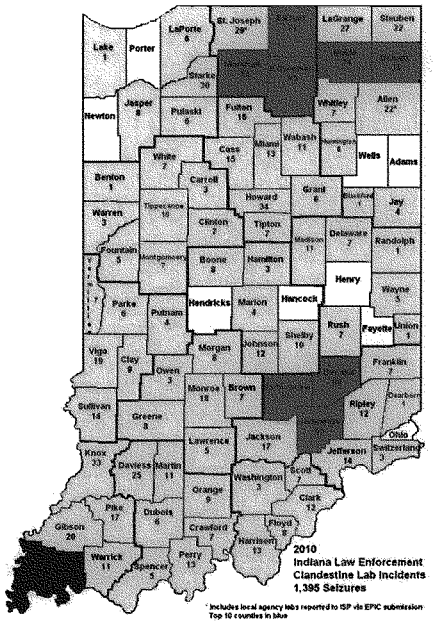
Indiana Law Enforcement Children Identified in Clandestine Lab Environments 2003 - 2012

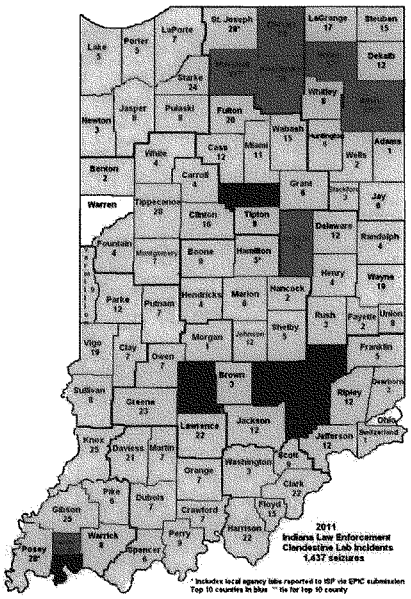


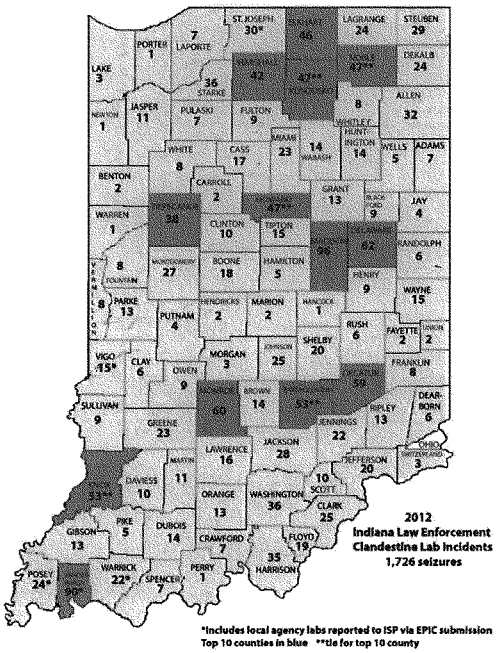
All Agencies' lab seizures

Table 6

Appendix A


2010
Indiana Law Enforcement
Clandestine Lab Incidents
1,395 Seizures
* Includes local agency labs reported to ISP via EPIC submission
Top 10 counties in blue


2011
Indiana Law Enforcement
Clandestine Lab Incidents
1,437 seizures
* Includes local agency labs reported to ISP via EPIC submission
Top 10 counties in blue **tie for top 10 county


2012
Indiana Law Enforcement
Clandestine Lab Incidents
1,726 seizures
*Includes local agency labs reported to ISP via EPIC submission
Top 10 counties in blue **tie for top 10 county

Biography
Nicole Crawford, First Sergeant
Indiana State Police
Methamphetamine Suppression Section Commander

Nicole (Niki) Crawford started her law enforcement career with the Indiana University Police Department in 1991. She was hired by the Indiana State Police in 1993. She has served in numerous capacities in a variety of locations around the state. She served as a road Trooper in the Bremen, Putnamville, and Fort Wayne Districts. She was assigned to the Problem Oriented Policing Section in the Northeast part of the state covering LaGrange, Noble, Steuben and DeKalb Counties. She has served as a recruit school counselor, interview committee member for the Department Chaplain vacancy and for personnel competing for Trooper appointments. She served on the committee that set the physical standards for police applicants. F/Sgt. Crawford was assigned as an undercover drug investigator from 2001 to 2004, and was promoted to Sergeant (squad leader) in the Drug Enforcement Section in December 2004. In the fall of 2005 she was asked to assist with creating and organizing the new Methamphetamine Suppression Section (MSS). She worked directly for the Commander of the section until she was promoted into that position as a First Sergeant in December of 2008. Her responsibilities with MSS include overseeing all operations of the 125 member ISP clandestine lab team and supervising the eighteen full-time personnel assigned to MSS. She coordinates the work of the MSS Safety Committee, writes and manages grants, purchases all equipment and supplies for MSS, maintains and updates the ISP MSS Policy Manual, and assists with coordinating clandestine lab annual refresher training for nearly 300 clan lab certified police officers around the state of Indiana. She has provided numerous briefings, programs and legislative testimony on clandestine methamphetamine labs in Indiana and around the country. Since 2008 Niki has served as a voting board member for the National Methamphetamine and Pharmaceuticals Initiative Advisory Board (NMPI), which is a High Intensity Drug Trafficking Area (HIDTA) Initiative in the Office of National Drug Control Policy. Niki has a bachelor's degree in secondary education from Indiana University.

Chairman BUCSHON. Thank you very much.
I now recognize Dr. London for her testimony.

**TESTIMONY OF DR. EDYTHE LONDON,
THE THOMAS AND KATHERINE PIKE PROFESSOR
OF ADDICTION STUDIES,
DIRECTOR OF THE UCLA LABORATORY OF
MOLECULAR NEUROIMAGING AT THE
DAVID GEFFEN SCHOOL OF MEDICINE,
UNIVERSITY OF CALIFORNIA AT LOS ANGELES**

Dr. LONDON. Chairman Bucshon, Ranking Member Lipinski, and Members of the Subcommittee, thank you for the opportunity to testify on the problem of methamphetamine addiction. My name is Edythe London, and I direct the Laboratory of Molecular Neuroimaging of the David Geffen School of Medicine at UCLA.

I would like to note at the outset that strong support from Congress to the National Institutes of Health and its grantees over the past two decades has enabled research that is driving the development of new treatments for this problem, which needs your continued support.

Among illicit substances, methamphetamine and amphetamines in general are second only to marijuana in prevalence of use worldwide. Methamphetamine abuse is associated with crime, premature mortality, lost productivity, and a host of medical problems. Illegal methamphetamine use in our country is now reduced from the levels in 2006, but the problem is still very severe where there are established cores of users and supply connections set up with the Mexican cartels.

In California, for example, admissions to treatment for methamphetamine use disorders in recent years exceeded those for all other substances, including alcohol. Like cocaine, methamphetamine augments the action of dopamine, but it is a more effective stimulant, has a longer duration of action, and is more potent, addictive, and toxic than cocaine. It also is relatively easy to manufacture and has, as you just heard, a low street cost.

Methamphetamine users stay under the influence for extended periods with sleep deprivation and poor health maintenance, leading to medical and psychiatric problems such as prolonged psychosis and suicide attempts. Methamphetamine use also is highly associated with HIV infection and in men who have sex with men.

Brain imaging techniques such as magnetic resonance imaging and positron emission tomography, MRI and PET, have helped clarify the effects of methamphetamine use on brain structure, chemistry, and function.

[Slide]

This slide shows the difference-maps of the lateral surface of the brain obtained with high-resolution MRI in a group of methamphetamine users and healthy controls. Red indicates a gray matter deficit in the methamphetamine group, especially in the prefrontal cortex on the right lateral surface in a region important for inhibitory control. Deficits are also seen in medial aspects of the brain, and volume loss in the hippocampus is related to memory deficits. Unexpectedly, white matter shows hypertrophy. The findings suggest a pattern of deterioration that promotes cognitive im-

pairment. The white matter hypertrophy may reflect reactive gliosis secondary to neuronal damage. These abnormalities accompany deficits in the brain's dopamine system, which functions in reward processing, motivation, self-control, and decision-making.

PET scans have revealed low levels of dopamine receptors and dopamine transporters and hypofunction of dopamine neurons. Notably, markers for dopamine system integrity predict the outcome of behavioral treatments for methamphetamine use disorders.

Functional MRI, which measures brain activity during cognitive processing, has shown that methamphetamine users recruit less neural activity in the prefrontal cortex than healthy controls while learning, paying attention, and being engaged in emotion processing. Functional MRI also can help evaluate the effects of potential treatments.

These fMRI brain activation maps show the response to modafinil in cortical regions while methamphetamine users are performing a task that requires inhibitory control. The activation corresponds to improvements in learning, and modafinil is an agent that improves dopaminergic activity and has cognitive benefits.

At this time, behavioral treatments are the most effective ones for methamphetamine dependence, but they don't help everyone. Efforts to identify a broadly effective medication for methamphetamine dependence have not been successful, but there are some promising leads such as bupropion, which reduces use in a subgroup of patients. Studies from animal models and PET scans of humans have also identified other potential medications, buspirone and microglial activation inhibitors, such as ibudilast.

This work has required collaboration of physicists, mathematicians who developed and improved the instrumentation and algorithms for data acquisition and analysis, as well as psychologists and clinicians. The field would be advanced with the development of new and more sensitive probes, but we need multidisciplinary teams. Such collaboration, for example, has proven that deep brain stimulation can be an effective treatment for depression. This advance required the confluence of several fields, including bioengineering, electrical engineering, materials science, neurosurgery, MRI physics, psychology, and neuroscience. Optimizing therapeutics for methamphetamine addiction requires this type of multidisciplinary effort.

[The prepared statement of Dr. London follows:]

SEMEL INSTITUTE
UCLA

Testimony and Statement for the Record of

Edythe D. London, Ph.D.
Thomas and Katherine Pike Professor of Addiction Studies
Director of the Laboratory of Molecular Neuroimaging

David Geffen School of Medicine, UCLA

Hearing: "Methamphetamine Addiction: Using Science to Explore Solutions"

Before the

Subcommittee on Research and Technology,
Committee on Science, Space, and Technology
House of Representatives

September 18, 3013
2321 Rayburn House Office Building
Washington, D.C.

Chairman Bucshon, Ranking Member Lipinski and Members of the Subcommittee, thank you for the opportunity to testify today concerning the use of science to address the problem of methamphetamine addiction in the United States. My name is Edythe London, and I am Director of the Laboratory of Molecular Neuroimaging of the David Geffen School of Medicine at the University of California at Los Angeles (UCLA).

Our program of research at UCLA began in 1999 with the generous support from the Office of National Drug Control Policy (ONDCP) and was one of the first major research efforts in the nation to address the growing problem of methamphetamine addiction. Here I would like to note at the outset that the strong support from the Congress to the National Institutes of Health and its research recipients over the past two decades have enabled both basic research as well as the development of new medications and treatment modalities. This critical area continues to be important, affects many lives in our nation, and needs your continued support.

Why is methamphetamine such a critical problem? Unlike other drugs of abuse, methamphetamine is relatively easy to manufacture; the street cost to the use is low compared to other drugs; and it produces a "high" that is long-lasting. At the same time there are very significant mental and physical effects from its use, and in far too many cases, it is a cause of early death.

1. Methamphetamine Abuse and the Scope of the Problem in the U.S.

Methamphetamine use disorders (classified as methamphetamine abuse and dependence in DSM-V) are major public health problems [1-3], with >14.3 million adults estimated to be using amphetamine-type stimulants for non-medical purposes worldwide. Among illicit substances, amphetamines are second only to marijuana in prevalence of use, exceeding heroin and cocaine combined [4]. In the United States, admissions to publicly funded drug treatment programs for amphetamine-related problems peaked at 8.1% in 2005 and increased from 3.7% to 5.7% between 2000 and 2010 [3]. The cost of MA abuse in the US in 2005 was estimated at $23.4 billion [5], and was associated with crime, premature mortality, lost productivity, and medical conditions, such as infectious disease and cardiovascular insults [6-8].

The illegal use of methamphetamine in our country is not as widespread as it was in the early to mid-2000s [9], now reduced to 50% of the levels of 2006; however, the problem is still severe in the communities where there still are established cores of users and supply connections set up with the Mexican cartels. In California, for example, admissions to treatment for methamphetamine use disorders in 2009 and 2010 exceeded admission rates for all other substances, including alcohol [10, 11].

2. How is Methamphetamine Different from Other Stimulants?

Among stimulants, methamphetamine is unique in its pharmacokinetic and pharmacodynamic properties, which render it more effective as a stimulant, more addictive, and more toxic. Methamphetamine is structurally very similar to amphetamine and related agents, such as MDMA (3,4-methylenedioxy-*N*-methylamphetamine), which is widely known as "ecstasy", and

designer drugs, such as cathinone derivatives (including "bath salts"). The amphetamines, including methamphetamine, are similar to cocaine in causing an increase of dopamine and other neurotransmitter levels in the synapse, augmenting their actions. Along with cocaine, the amphetamines have similar stimulant and euphorigenic properties. The amphetamines, however, have long durations of action (half-life of 9-12 hours for methamphetamine) [12] and, therefore, longer stimulant effects than cocaine, which has a half-life of 1 hour and behavioral effects that last up to an hour, depending on the dose and route of administration [13]. Methamphetamine also is well absorbed following administration by various routes, including inhalation; and it is highly lipophilic, entering the brain faster than other stimulants (including amphetamine), and is more stable to enzymatic degradation in the brain [14]. Finally, methamphetamine is more potent than other stimulants [15], leading to much higher concentrations of synaptic dopamine than cocaine, producing toxic effects on nerve terminals. These pharmacokinetic considerations, along with the lower cost as compared with cocaine, likely contribute to a more chronic and continuous use pattern of methamphetamine as compared with cocaine, which is used more in binges. They also may contribute to differences in addiction potential, with only 16-20% of cocaine abusers progressing from regular use to dependence [16, 17]. A corresponding figure for methamphetamine is not available.

Methamphetamine users stay under the influence for longer stretches of days and weeks, with extensive sleep deprivation, possibly contributing to the greater incidence of associated psychosis than with cocaine, along with poor health maintenance and hence more medical consequences (e.g., cardiovascular, neurological) than with cocaine. One notable problem involves dental problems, referred to as "meth mouth", due to diminished saliva production and other putative mechanisms; this problem is most commonly seen in intravenous users of the drug [18]. Other problems are the potential for prolonged psychosis [19, 20] and high rates of suicide attempts [21].

Finally, methamphetamine is used heavily in the community of men who have sex with men worldwide, and its use is connected to risky sexual behavior among these individuals more than cocaine abuse. Methamphetamine use is highly associated with HIV infection in gay men [22], and is the only drug whose use has shown significant correlation with the incidence of HIV infection among gay and bisexual men who are methamphetamine users [23]. No other drug has shown consistent and significant correlations with HIV transmission. Moreover, metabolic abnormalities in the brain due to HIV and chronic methamphetamine use are additive [24].

3. How have Basic Science Studies Advanced Knowledge about Addiction to Methamphetamine?

Building on a large body of preclinical research, controlled laboratory studies of human volunteers have provided critical insights into the factors that influence methamphetamine use, and the maladaptive consequences of chronic exposure. Noninvasive brain imaging techniques, such as positron emission tomography (PET) and magnetic resonance imaging (MRI), have proven to be particularly valuable for this purpose, clarifying the effects of methamphetamine use on brain chemistry, structure, and function. In related studies, neuroimaging procedures have assisted in the elucidation of the neural mechanisms underlying key behavioral abnormalities thought to promote compulsive drug use and predict poor treatment response. A

synthesis of the findings indicate that chronic use of methamphetamine is associated with deficits in the cerebral cortex and striatum, which accompany and appear to contribute to cognitive deficits, including impaired inhibitory control [25 review].

Molecular Neuroimaging. Human molecular neuroimaging studies suggest that, in addition to effects on other neurotransmitter systems [e.g., 26-28, 29 review], chronic methamphetamine use causes a down-regulation of dopamine neurotransmission in the striatum, which can disrupt cognitive processes in ways that may undermine the user's ability to remain abstinent. Dopamine signaling in the brain is critically involved in reward processing and motivation [30 review], and is linked to activity in the prefrontal cortex, with bi-directional influences guiding reward-related behavior and decision-making [31]. Dopamine signaling in the brain is influenced by the integrity of receptors for the neurotransmitter (D_1 and D_2 subtypes), by activity-dependent release of the transmitter from the neuronal terminals into to the synapse, by its reuptake to the presynaptic terminal, and by metabolic enzymes.

These studies have revealed that chronic methamphetamine abuse is associated with deficits in several markers of dopamine signaling in the striatum, including dopamine D_2-type receptor availability [32-35], dopamine transporter availability [36-40], and activity of the presynaptic dopaminergic terminal, indexed by dopamine release [34]. These deficits may contribute to a "Reward Deficiency Syndrome", characterized by anhedonia and a dysfunctional "impulsive-addictive-compulsive" trajectory of behaviors, in which one rewarding substance or activity is substituted for another. During early abstinence, methamphetamine addicts exhibit unusually high caloric intake, presumably reflecting the substitution of food for methamphetamine, and caloric intake is negatively correlated with striatal D_2-type dopamine receptor availability [35]. Moreover, low striatal D_2-type receptor availability has been linked with greater self-reported impulsivity in abstinent methamphetamine users [33], and along with reduced striatal dopamine release, with greater likelihood of relapse during treatment [34]. Although there is evidence for recovery of the dopamine transporter protracted abstinence [39], this is not true for D_2-type dopamine receptors. A direct relationship between the recovery of dopamine transporters and duration of abstinence from methamphetamine [37] suggests that reductions in the striatal dopamine transporter associated with methamphetamine dependence may reflect short-term, drug-induced neuroadaptations.

Studies of the vesicular monoamine transporter (VMAT2), which is present in all monoaminergic neurons, also have pointed to a transient neuroadaptation in response to methamphetamine exposure. Lower striatal VMAT2 was seen in postmortem brain tissue from former methamphetamine abusers [41], and PET studies of striatal VMAT2 in vivo showed lower levels in methamphetamine users even after 3 months of abstinence [40]. In another study, however, recently abstinent methamphetamine-dependent individuals had greater VMAT2 binding availability than controls [42], but increases relative to control subjects were seen only in those who had most recently used methamphetamine (<12 days) [42]. Collectively, these findings suggest that increased VMAT2 may be a transient response to drug exposure and the reduction in VMAT2 binding observed after longer abstinence may indicate lasting damage to neuronal terminals as a consequence of drug use.

With respect to D_2-type dopamine receptor deficits, methamphetamine abusers are not unique, as chronic users of cocaine [43], alcohol [44], opiates [45], or nicotine [46, 47] all

display below normal levels of striatal D_2-type receptor availability. This commonality across several addictive disorders raises questions regarding the extent to which low D2/D3 receptor availability predates drug abuse, or is an effect of chronic drug exposure. For ethical reasons, this question could be answered only by measuring D_2-type receptor availability before any drug use and performing a longitudinal study in which individuals naturalistically self-administer the drug, or by animal studies in which the agent is administered under controlled conditions. In this regard, Vervet monkeys exposed to a methamphetamine dosing regimen designed to mimic human consumption of the drug showed significant decreases in striatal D_2-type receptor availability after 2 weeks of methamphetamine exposure. These deficits persisted for at least 7 weeks following cessation of treatment [48], indicating deleterious effects that are long lasting. Taken together, these findings indicate that while D_2-type receptor deficiencies in methamphetamine users may, to some extent reflect a vulnerability to drug abuse, chronic methamphetamine abuse negatively impacts the dopamine system in the brain.

Other relevant data center on the D_3 receptor, a member of the D_2-type receptor family. The PET studies showing low striatal D_2-type receptor availability in methamphetamine users employed radiotracers that do not distinguish between D_2 and D_3 receptors (both in the D_2-type family). Development of a D_3-preferring radiotracer, [^{11}C]-(+)-propyl-hexahydro-naphtho-oxazin [49], now allows assessment of D_3 receptors in the living human brain. D2 dopamine receptors are distributed uniformly throughout the striatum [50], but D3 receptors are localized primarily to the ventral striatum, which functions in reward processing and motivation [50, 51], making them of special interest with respect to addiction. A recent study has shown higher binding of the D_3-preferring tracer in D_3-rich regions of the brain in methamphetamine users than in healthy controls, with D_3 receptor binding in the midbrain (*substantia nigra*) related to self-reports of "drug wanting" [52]. Therefore, unlike the D_2 receptor, the D_3 receptor may be upregulated in those who use methamphetamine chronically.

In addition to the dopamine system, another subject of interest with respect to the effects of methamphetamine in the human brain is the serotonin system. For example, PET was used to show that compared with healthy controls, methamphetamine users had lower density of the serotonin transporter in the midbrain, thalamus, caudate, putamen, cerebral cortex, and cerebellum [28]. This reduction was inversely correlated with the duration of methamphetamine use; and the density in the orbitofrontal, temporal, and anterior cingulate areas was associated with aggression in the methamphetamine abusers.

Microglial cells are activated in associated with neurodegenerative processes, and there is evidence that reactive microgliosis accompanies methamphetamine toxicity in animals [53-55]. Using PET, and a radiotracer for activated microglia, [^{11}C](*R*)-(1-[2-chlorophenyl]-N-methyl-N-[1-methylpropyl]-3-isoquinoline carboxamide) ([^{11}C](*R*)-PK11195), an elevation in activated microglia was shown in methamphetamine users, suggesting that chronic self-administration of methamphetamine can cause reactive microgliosis in the human brain [56].

Functional Brain Imaging. Brain function can be evaluated using PET imaging and the radiotracer [^{18}F]fluorodeoxyglucose, which can provide maps of how fast glucose is utilized throughout the brain. PET studies of cerebral glucose metabolism in meth-amphetamine users, who had remained abstinent for periods varying from weeks to over 2 years, showed elevated

activity relative to control in cortical areas but apparently reduced glucose metabolism in subcortical regions [57]. When participants were studied in early abstinence (4-7 days) corresponding to the time that many clients would approach a treatment episode, there was clear evidence for corticolimbic dysregulation, with reduced activity in prefrontal and limbic cortex, but elevated activity in ventral striatum and amygdala (Figure 1); hyperactivity in the amygdala was associated with depression and anxiety [58]. Among a variety of cognitive deficits [59], the early-abstinent methamphetamine users had higher error rates than control subjects on a vigilance task and abnormal relationships between task performance and activity in the cingulate cortex and the insula, brain regions important for cognitive control, error-monitoring and decision-making [60]. Over the course of a month of abstinence, cortical activity, especially in parietal cortex, increased [61], consistent with an umasking of reactive gliosis [56]. With protracted abstinence (12-17 months), glucose metabolism in thalamus but not the striatum recovered to control levels [62].

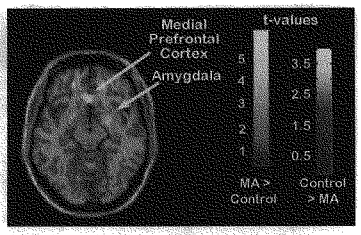


Figure 1. Methamphetamine users (MA) in early abstinence have dysregulated glucose metabolism. Warmer values (reds/yellows) indicate higher activity in MA users than in control subjects especially in the amygdala. Cooler values (blues) indicate lower activity in MA users than in control subjects (from London et al., 2004 [53]).

In addition to PET, functional MRI (fMRI) provides valuable information about brain function. With substantially greater time resolution than available with functional studies that use PET, fMRI allows measurement of brain activation while participants perform tasks that invoke cognitive and/or emotional processing. Such studies have shown that when abstinent, methamphetamine users exhibit less activation in prefrontal cortex than healthy controls during learning, attention, and emotion processing, consistent with deficits in cortical information processing [63-65]. Functional MRI studies also have also indicated that methamphetamine abusers have abnormalities in cortical activation when abstinent methamphetamine users choose between smaller, more immediate monetary rewards (which they favor) over larger, more delayed rewards [66]. While performing a task to test their temporal discounting of rewards, methamphetamine users exhibit as much recruitment in prefrontal and parietal areas of cortex when making an easy choice as when making a hard choice, suggesting an inefficiency of cortical function [66]. Defective prefrontal cortical control may also contribute to heightened aggression, a common feature of methamphetamine abuse [67], by limiting emotional insight. Functional MRI data have suggested that emotional insight relies on activity of the ventral inferior frontal gyrus, but that in methamphetamine-dependent participants exposed to an emotional probe, activity is low bilaterally in this area [68].

Broadly consistent with these findings and the view that a deficit in "top-down" cortical control is an important feature of methamphetamine abuse is the observation that cortical activation during a simple decision-making task can predict relapse risk in methamphetamine-dependent individuals [69]. The regions involved include components of the prefrontal cortex and the insula. These and other studies have shown the usefulness of fMRI for determining which brain regions under specific behavioral conditions are affected by prolonged methamphetamine use. They also point to fMRI as a valuable technique to evaluate the effects

of potential treatments for methamphetamine dependence. For example, medications, such as modafinil, which improve cognition, in part by promoting greater dopamine function, enhance brain function in the prefrontal cortical regions affected by methamphetamine abuse (Figure 2) [63].

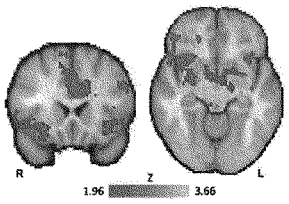


Figure 2. fMRI brain activation maps showing response to Modafinil in prefrontal cortex during learning in methamphetamine users that corresponded with improvements in learning. Prefrontal regions include the anterior cingulate cortex and bilateral anterior insula/ventrolateral prefrontal cortex, orbito-frontal cortex. No difference in activation was observed in healthy individuals (from Ghahremani et al,, 2011 [63]).

Structural Brain Imaging. In keeping with the observations of brain function and biochemistry as related to methamphetamine abuse, abnormalities in components of frontostriatal circuitry have been demonstrated by structural brain imaging as well. Structural MRI studies have generally yielded the unexpected finding that methamphetamine abuse is associated with greater gray-matter volume in the basal ganglia (including the striatum) than in healthy control subjects [70, 71]. Until recently, however, it was unknown whether these differences in gray matter were caused by methamphetamine or if they reflected vulnerability factors that predated substance abuse. One study revealed that stimulant abusers and their unaffected siblings have greater volume in the putamen than healthy control participants, suggesting that the difference reflects familial risk for drug dependence [72]. Animal studies, however, have also shown that monkeys exposed to methamphetamine, using a regimen that simulates human patterns of drug use, have increases in putamen gray matter [73] (Figure 3). The structural change is correlated with impaired performance on a three-choice visual discrimination task that evaluates inhibitory control/cognitive flexibility.

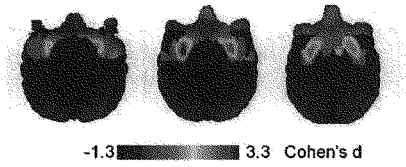


Figure 3. Exposure to methamphetamine is associated with structural differences in the brain. Warmer values (reds) indicate increases in gray matter in the putamen. Cooler values (blues) indicate trends toward losses of gray matter in the prefrontal cortex (from Groman et al., 2013 [73]).

With respect to the cerebral cortex, it was unexpectedly found that in addition to larger striatal volumes, research participants who had used methamphetamine but had maintained abstinence for an average of three months, exhibited larger volumes of the parietal cortex [70]. This effect was not seen in a study of participants who had used methamphetamine for most of the 30 days before enrolling in a brain imaging study and then maintaining abstinence for about 1-2 weeks [74]. Cortical maps of the MRI data revealed severe gray-matter deficits in medial aspects of the brain, including the cingulate, limbic, and paralimbic cortices as compared to control values, deficits in hippocampal volumes, which were related to verbal memory

performance, and an unexpected observation of white-matter hypertrophy. The findings suggested that chronic methamphetamine abuse causes a selective pattern of deterioration that contributes to impaired cognitive performance, and white-matter hypertrophy that may reflect adaptive glial changes, including gliosis secondary to neuronal damage. Although not as dramatic, the same study found a gray-matter deficit in lateral prefrontal cortex [74], including a region (right inferior frontal gyrus) that is important for several forms of self-control [75].

Given the prominence of self-control deficiencies in methamphetamine addiction as well as other substance use disorders, it is important to understand the etiology of this structural abnormality and the extent to which it may be reversed with abstinence from drug of abuse. Therefore, methamphetamine-dependent subjects underwent structural MRI before and after approximately 3 weeks of abstinence from the drug [76]. Gray matter volume increased over time in the prefrontal cortex and other brain regions in methamphetamine-dependent participants, but not in members of a healthy control group that were scanned at a similar time interval (Figure 4, from Morales et al., 2012 [76]). Lack of full recovery may indicate the need for prolonged abstinence, some permanent damage, or the influence of a factor other than methamphetamine use. For example, approximately 87-92% of individuals who abuse methamphetamine also smoke cigarettes [77], and research suggests that some of the of the gray matter deficits in prefrontal cortex detected in MA-dependent individuals may be attributable to cigarette smoking or premorbid factors that promote it [76]. More research is necessary to determine how smoking and other factors may interact to influence gray matter in stimulant abusers as these interactions may have important implications for treatment.

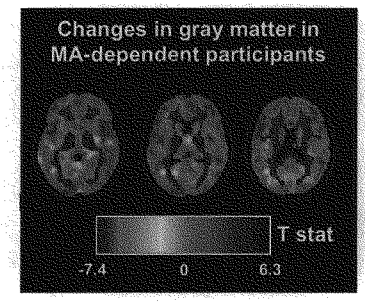


Figure 4. Abstinence from methamphetamine increases gray matter in the brain. Cooler values (blues) indicate increases in gray matter in over the course of the first month of abstinence from methamphetamine, while warmer values (yellows and reds) indicate losses of gray matter (from Morales et al., 2012 [76]).

4. What Promising Treatments have been Developed as a Result of Basic Science Research?

At this time, behavioral treatments are the most effective ones for methamphetamine dependence [78-81]. These include cognitive behavioral therapy and contingency management, but both are associated with high dropout rates early in treatment [82] and more than 50% relapse in the first 6-19 months after treatment ends [83, 84]. After more than two decades of concerted effort to develop a broadly effective medication for MA dependence, clinical trials have yielded no such agent [85 review]. One potentially very important consideration is the heterogeneity among methamphetamine users and the need to personalize treatment. In this

regard, promising findings have been observed with a handful of agents that reduce stimulant use in subgroups of patients. The approaches include opiate receptor antagonism, augmentation of dopamine action with medications that have relatively low abuse potential, antagonism of dopamine D3 receptors, and reducing glial cell activation.

Naltrexone, an opiate receptor antagonist drug has been considered as a medication for stimulant abuse, in part, because of its potential to antagonize stimulant-induced augmentation of dopaminergic neurotransmission indirectly [86]. To date, clinical trials with naltrexone for treatment of amphetamine dependence have shown stronger effects than those of placebo on drug abstinence [86, 87] and retention in treatment [87]. These findings suggest that naltrexone may be useful for the treatment of methamphetamine dependence.

The "agonist medication" approach, used successfully for treatment of opiate and nicotine use disorders, involves using a medication that mimics some of the actions of the abused drug without the same high addiction potential. In this regard, methylphenidate reduced amphetamine-positive urines in intravenous amphetamine users [88]. A phase II clinical trial involving methamphetamine users is now underway at UCLA, directed by Walter Ling.

Some positive findings were obtained with modafinil, a non-amphetamine stimulant that has cognitive enhancing properties, and augments synaptic dopamine and norepinephrine [89, 90]. In a randomised, double-blind, placebo-controlled trial with methamphetamine users, the medication was no more effective than placebo in improving retention in the trial or in reducing methamphetamine use in the full sample, but there was an indication of reduced stimulant use among participants who were compliant with their medication [91]. Negative findings were obtained in subsequent trials [92, 93], but compliance in one of these trials was cited as a problem [93]. Nonetheless, preliminary findings from the human laboratory indicate that modafinil reduces the rewarding effects of intravenous methamphetamine [94], and further studies are warranted, especially with the active enantiomer, R-modafinil [95].

Another medication that augments dopamine transmission is bupropion, which inhibits the dopamine transporter [96] and shows promise as a medication in subgroups of methamphetamine abusers. One placebo-controlled double-blind trial indicated that sustained-release bupropion did not outperform placebo in enhancing retention in the trail or in increasing methamphetamine-free urine samples, but participants who used methamphetamine 18 or fewer days in the month before randomisation exhibited a positive response to bupropion [97]. This finding was supported in a subsequent trial [98]. Finally, a small, randomised, placebo-controlled trial with high-risk men who have sex with men lacked the statistical power to detect differences in treatment outcome, but the findings were in the direction of efficacy of bupropion [99].

Another promising pharmacotherapy is buspirone, which has antagonist properties at the dopamine D_3 and D_4 receptor subtypes [100 review]. Buspirone (Buspar®) is approved by the US Food and Drug Administration for treating anxiety, and its anxiolytic effect is thought to be mediated by a partial agonist action at a serotonin receptor ($5HT_{1A}$) subtype [101-103]. Buspirone also exhibits antagonist properties at dopamine D_3 and D_4 receptors [100, 104-106]. The affinities of buspirone for D_3 and D_4 receptors are an order of magnitude higher than for D_2 receptors, but are similar to the affinity for $5HT_{1A}$ receptors [100]. Thus, any behavioral effects of buspirone are attributable to activity at D3, D4 or $5HT_{1A}$ receptors.

D_3 receptor antagonists reduce the reinforcing and reward-facilitating properties of methamphetamine in rats. For example, administration of the D_3 receptor antagonist SB-277011A [107] or PG01097 [108, 109] attenuate methamphetamine self-administration under a progressive ratio schedule of reinforcement, suggesting that the reinforcing efficacy or the incentive motivational properties of methamphetamine are counteracted. Notably, D_3 receptor blockade appears to diminish reinstatement of extinguished MA-seeking behavior [107, 108, 110]. Combined with the demonstration of D_3 receptor upregulation in methamphetamine users [52], these findings from animal studies identify buspirone as a potential medication for methamphetamine use disorders.

Finally, given substantial evidence from studies of animal models of methamphetamine toxicity [53-55] and PET studies of human methamphetamine users [56], it is reasonable to believe that reactive gliosis and inflammation may contribute to the neuropathology of methamphetamine dependence. For this reason, there is interest in the potential for medications that reduce microglial activation as medications for methamphetamine use disorders. One candidate is ibudilast, which is approved for treatment of bronchial asthma, post-stroke dizziness and ocular allergies in Asia. Ibudilast reduced methamphetamine self-administration in the rat [111] as well as methamphetamine prime-induced reinstatement of methamphetamine-seeking behavior in rats [112]. A phase Ib clinical trial of ibudilast for the treatment of methamphetamine dependence is now being conducted by Steven Shoptaw at UCLA.

5. How Can the Scientific Disciplines Complement Ongoing Research Efforts in Methamphetamine Addiction?

An interdisciplinary approach is needed for basic science to facilitate rapid progress in treatment for methamphetamine addiction. We have made great progress in understanding how methamphetamine alters brain function and behavior through the use of noninvasive brain imaging. This effort has required the collaborative effort of physicists and mathematicians to develop and improve the instrumentation for data collection as well as the algorithms for data analysis. Moreover, this research was linked to the efforts of cognitive neuroscientists to develop appropriate behavioral probes and clinicians to integrate this work in a way that targeted the problems of the addict.

Certainly, the field would be advanced with the development of new probes and more sensitive instruments. For example, there is still a substantive need for new radiotracers that can be used in molecular imaging to assess the complexities of brain chemistry, how it changes with the progression of addiction and how it responds to treatment. However, the greatest advances require a strong collaboration involving a multi-disciplinary team.

Such collaboration has been undertaken using cutting-edge neurotechnology in other areas of mental health, and can be used as models of success for addiction. For example, deep brain stimulation of neurocircuitry for the treatment of depressive illness has proven to be effective in mitigating relapse [113]. The work leading to this development comprised the confluence of several fields, including bioengineering, electrical engineering, materials science, neurosurgery, MRI physics, psychology, and neuroscience, to determine the optimal methods

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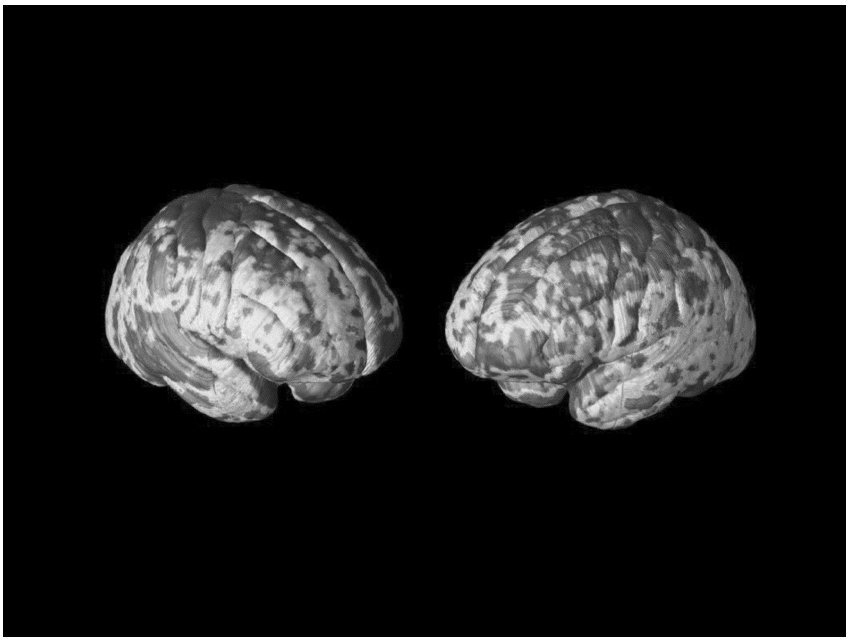

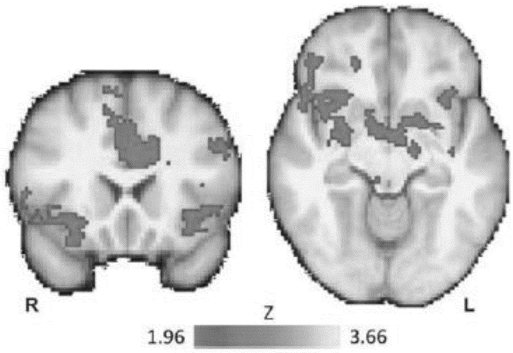
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EDYTHE D. LONDON, PH.D.

Dr. Edythe London holds the Thomas P. and Katherine K. Pike Chair of Addiction Studies, and is a Professor in the Departments of Psychiatry and Biobehavioral Sciences, and Molecular and Medical Pharmacology at UCLA. Dr. London is an internationally recognized expert in the study of drug addiction.

Dr. London received a doctoral degree in pharmacology and toxicology at the University of Maryland and postdoctoral training in neuropsychopharmacology at the Johns Hopkins School of Medicine. Before joining the UCLA faculty in 2001, she worked at the National Institutes of Health for two decades, where she directed the Neuropharmacology Research Laboratory and the Neuroimaging Research Center of the National Institute on Drug Abuse.

Dr. London pioneered the application of brain imaging to the study of substance abuse. She has authored 313 original research articles and 86 chapters and reviews, edited three books, and has delivered hundreds of invited lectures within the United States and internationally. Dr. London's work has been recognized by numerous awards, including the 2008 Marian Fischman Award from the College on Problems of Drug Dependence and the 2011 Scientific Freedom and Responsibility Award from the American Association for the Advancement of Science.

Dr. Edythe London's research uses a translational approach to develop a better understanding of addictive disorders and further the rational design of therapeutics. Her laboratory was the first to show a relationship between drug craving and activity in brain regions that underlie episodic memory and link memory with emotion. Her research also has contributed to the development of new approaches and probes for noninvasive brain imaging. Dr. London's laboratory now focuses on stimulant and nicotine addiction.

Chairman BUCSHON. Thank you very much.
Dr. Maxwell.

TESTIMONY OF DR. JANE MAXWELL,
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Dr. MAXWELL. Thank you. My thanks to you and to the Vice Chair for inviting me and I hope maybe I can shed some light on looking at this problem from an epidemiological standpoint or historically.

We know that until 1970 we really didn't have a methamphetamine problem because amphetamine was available over the counter. Amphetamine was scheduled in 1970 and that is when we first began to see problems with methamphetamine. They were using the P2P or the phenyl propanone, a precursor that we are now seeing used in Mexico. And for the first ten years it was the bikers, and remember the "crankcase" meth where they were carrying it in crankcases producing the meth.

In 1980 phenyl propanone was forbidden in the United States and that is when they started using pseudoephedrine.

[Exhibit 1]

And this slide is very busy but there is an easy message in it. If you look at the red lines, vertical lines, that is every time either the United States or Canada had passed a precursor. And you can see that we—the first precursor, the purity of methamphetamine drops, then it goes back up again; another precursor ban, it drops, it goes back up again. So this is a drug that is very cyclical. We do one thing to it and think maybe we are making progress and then it rebounds.

[Exhibit 2]

This slide shows what the market looked like right after the law was passed limiting the ability to buy pseudoephedrine. The far left is the price and purity right after the law goes into effect. Then you see the price going—skyrocketing and then dropping off. You see the purity, the blue line dropping and then going up. And the intersection of interest is the one with the second green area. This is the middle of 2008. This is when the Mexicans first really started distributing the P2P meth in the United States. And since then the prices dropped dramatically. And we are now up to about 94 percent purity of the meth that is being tested by DEA.

[Exhibit 3]

Two other data sets that are of use, the blue line is showing the proportion of all the methamphetamine that is tested that is now made from the P2P process. So it is about 93 percent; about another two to three percent is made from the pseudoephedrine. Now, one of the things that is not shown in this is a DEA-only test where the seizure is more than six grams, so a lot of the small amounts of meth that are made in the shake-and-bakes would not be tested.

Basically, the market really in terms of the massive quantities is now the P2P. The red is the drop-off in the last two years in the number of precursor clandestine labs as reported to DEA. I am not sure what is going on but we may be seeing the Mexican meth be-

ginning to move in other areas and perhaps overtaking some of these small labs.

[Exhibit 4]

This is the Texas data and I put it up there because it is 15 years of data, and the red line is 2006 so you can see after we get the precursor, whether it is the deaths or poison center exposures or treatment admissions or tox lab incidents, they all drop after 2006 in Texas. They are now going upwards again. So another cycle.

And besides using the quantitative data, I always get out on the street and ask people who are working out on the street what is going on. They are telling me now they are seeing more psychosis now than they saw six months ago among the users. The meth is very, very pure. The high is very, very intense, more use of needles, syphilis is up. DEA is reporting more and more seizures in the Dallas area of 100 pounds or more, and the reporting availability of meth is higher than it has ever been. So more bad news.

[Exhibit 5]

This is a map of the tox lab data from DEA, and basically it is showing, yes, meth is a problem in the West. But there was something else that really bothered me and I went and looked at the data. This is 2010 and there are seven states in the Northeast that are white. They don't show—so they had—they reported no meth in 2010. When I ran the data last night, we are down to only three states that didn't report meth in 2013.

[Exhibit 6]

And this is a report. I am a member of NIDA's Community Epidemiology Work Group, the members reporting no diminution in meth. It is not decreasing. It is increasing or staying stable.

You asked for information on data and methodologies and I put this in here for the—your assistance to use. So with that, I thank you.

[Exhibit 7]

[The prepared statement of Dr. Maxwell follows:]

SUMMARY OF TESTIMONY
Of
Jane Carlisle Maxwell, Ph.D.
Senior Research Scientist
School of Social Work
The University of Texas at Austin

To the

Committee on Science, Space, and Technology
Subcommittee on Research and Technology
U. S. House of Representatives
September 18, 2013

This presentation discusses the history of methamphetamine abuse in the U.S. and its cyclical nature based on the use of precursor regulations to limit the use of various chemicals and methods to produce methamphetamine. Currently methamphetamine is more dominant in the Western U.S. but it is an increasing problem in other parts of the country. There are two sources of the drug: large-scale production in Mexico using the phenyl-2-propanone (P2P) method and the use of pseudoephedrine cold tablets to produce small amounts using the "shake and bake" method. DEA estimates that 85% of the methamphetamine consumed in the U.S. comes from Mexico, and the potency of the P2P methamphetamine has now reached 93%. Traditional demand indicators such as human exposure calls to poison centers, treatment admissions, and deaths, which dropped after the 2006 precursor ban, are now rising and the high potency is resulting in more psychosis and problems seen in users, as well as reports from the DEA Field Divisions in Texas about the increased availability and lower price.

There are a number of data sources which can inform public policy about changes in the spread of the drug, including surveys, data from poison control centers, emergency room cases, treatment admissions, forensic test results, price and purity, reports from DEA field divisions, studies of users, and reports from street outreach workers and other qualitative information. Techniques such as time series analysis and capture-recapture methods can be used, and there is a need to be able to access some of these data sources in a more timely manner and to post non-sensitive data on the web to encourage use of these data by researchers. It is suggested that the confidentiality requirements be re-examined to weigh the benefit of the proposed research against limiting access to certain variables when it would be virtually impossible to identify an individual because of lack of specific information in the dataset.

Lastly, additional treatment resources are needed for these more impaired users, including treatment resources in the rural and semi-rural areas as well as therapy for trauma, gender-focused counseling for sexual abuse, motivational enhancement, and social-cognitive training.

TESTIMONY
Of
Jane Carlisle Maxwell, Ph.D.
Senior Research Scientist
School of Social Work
The University of Texas at Austin

To the

Committee on Science, Space, and Technology
Subcommittee on Research and Technology
U. S. House of Representatives
September 18, 2013

Good morning, Chairman Bucshon, Ranking Member Lipiski, and members of the Subcommittee. Thank you for the opportunity to provide testimony on the methamphetamine problem in the US and the data sources that can inform public policy.

I am an epidemiologist studying trends in substance abuse and have been a member of the National Institute on Drug Abuse's Community Epidemiology Work Group of the National Institute on Drug Abuse for nearly 25 years. The Workgroup is composed of researchers from some 20 different areas around the U.S. who meet twice a year to present detailed information on the drug trends in their areas, and I will be presenting some of their findings.

In addition to my epidemiology work, I have recently completed a study funded by the National Institute on Drug Abuse on methamphetamine users who entered treatment facilities in the Central Texas area and found that these users were troubled on many issues, including high scores on the Severity of Dependence Scale and high rates of abuse and neglect experienced by both male and female patients as children and adults.[1] Given the expertise of the other witnesses, I will defer discussion on the findings of my project to their presentations and focus on how sound social science research can be used to understand the spread of methamphetamine and how it can inform public policy. As I go through my presentation I am going to show you some of the data that have been analyzed and then point out trends of concern.

First, methamphetamine can be characterized as a cyclical drug in terms of increases and decreases in both supply and demand over time. Supply means not only the quantity of the drug available and seized, but also purity, price, and formulation. Demand indicators are those which show the effects of using the drug, such as prevalence findings from surveys, emergency room episodes, treatment admissions, and deaths where a drug is involved.

[1] Maxwell, JC. (2013). A new survey of methamphetamine users in treatment: Who they are, why they like "meth," and why they need additional services. *Substance Use and Misuse*, in press.

The cyclical nature of the increases and decreases in use after various methamphetamine precursor bans is shown in Exhibit 1, which uses time series analysis to track changes in purity of methamphetamine after each precursor ban (shown as red vertical lines).[2] Notice that after a precursor ban occurs, the purity of methamphetamine drops but then rises again later.

Our problems with methamphetamine go back to when amphetamine tablets were available in the U.S. without a prescription until they were scheduled in 1970.[3] After the scheduling, illicit manufacturers began making methamphetamine using phenyl-2-propanone (P2P). Motorcycle gangs and small-scale local producers dominated the manufacturing and distribution process. The term "crank" referred to the practice of transporting the methamphetamine in the crank cases of the motorcycles. After P2P became Schedule II in the U.S. in 1980, operators of clandestine laboratories shifted to using ephedrine and pseudoephedrine to make methamphetamine.

Large quantities of ephedrine and pseudoephedrine were then smuggled in from Mexico for use in super labs in the southern California desert. At the same time, a smokeable and highly pure form of d-methamphetamine hydrochloride, known as Ice, Crystal, or "Tina," was imported from Far Eastern sources into Hawaii and then into the west coast of the US with a gradual movement eastward towards the end of the 1990s.

As methamphetamine use and the demand for it grew, there was a parallel increase in small-time local producers in the U.S. who used over-the-counter cold medications and readily available chemicals to produce methamphetamine using the so-called "Nazi" and "cold" methods.

Federal regulations targeting ephedrine and pseudoephedrine in forms used by large-scale producers in the U.S. were implemented in 1989, 1995, and 1997 and precursors in forms used by small-scale producers (e.g., over-the-counter medications) were implemented in 1996 and 2001. During 2004, in response to the increase in the number of local laboratories, various states began to limit access to over-the-counter pseudoephedrine products and in March, 2006, U.S. federal legislation (P. L. 109-177) imposed limits nationwide. The supply of pseudoephedrine also decreased after Mexico arrested the head of a commercial chemical company that was alleged to have illicitly imported over 60+ tons of pseudoephedrine. Mexico banned pseudoephedrine in 2008.

Exhibit 2 shows the impact of P. L. 109-177. The left side of the graph shows the situation just as the ban became effective in January 2007 with higher prices and lower purity. But by July-September 2008, the pattern had reversed as prices began dropping and purity began

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[2] Cunningham JK, Liu L-M, Callaghan R. (2009). Impact of US and Canadian precursor regulation on methamphetamine purity in the United States. *Addiction*, 104, 441-453.

[3] Maxwell, JC & Brecht ML. (2011). Methamphetamine: Here we go again? *Addictive Behaviors,* 36, 1168-1173.

increasing as methamphetamine "cooks" found ways to circumvent the legislation by shifting to other precursors. The primary precursor became phenyl-2-propanone (P2P), which while banned in the US, was still available in Mexico. The P2P method normally produces a methamphetamine which has a potency of 50%, but the Mexican chemists have continued to refine their methods and now are producing methamphetamine which is 93% potent as of July, 2013. At the same time, local cooks in the US are using the "shake and bake" or "one pot" method to produce small amounts of methamphetamine using packages of cold medicine.

Exhibit 3 combines two different datasets, DEA's Methamphetamine Profiling Program and reports from DEA's Methamphetamine Clandestine Laboratory Incidents. This exhibit compares the increases in the proportion of methamphetamine made using the P2P process (blue line) with the number of U.S. clandestine methamphetamine laboratory incidents reported (red line). Notice the decrease in methamphetamine laboratory incidents since 2010. This may be an indication that the Mexican P2P methamphetamine is spreading across the U.S. and replacing the product of the "one-pot" or "shake and bake" methods, but more data will be needed to verify this trend. Also note that the data showing the increase in P2P methamphetamine does not reflect all the source information because it does not include small seizures (less than 6 grams), and those smaller seizures are more likely to come from the "shake and bake" forms of methamphetamine, which Exhibit 3 shows are decreasing. However, DEA estimates that 85% of the methamphetamine consumed in the US is produced outside the US.

Exhibit 4 shows the impact of the 2006 ban on pseudoephedrine and the subsequent decrease and then increase in Texas of stimulant deaths, human exposure calls to poison control center calls, and treatment admissions.

Exhibit 5 shows the percentage of drug items identified as methamphetamine by forensic laboratories. This slide is based on 2010 data, and it shows methamphetamine is more prevalent in the Western U.S. The 2013 statistics report that of the top 25 drugs identified in the laboratories in each state, methamphetamine is the number 1 or number 2 drug in 22 states. In addition, most of my colleagues on the Community Epidemiology Work Group report increasing patterns in methamphetamine use as of June 2013, with no reports of decreasing use (Exhibit 6).

Lastly, I want to emphasize that my research is showing not only the spread of the drug, but the need for more treatment. With the increases in the more potent Mexican methamphetamine, the 2013 Texas Drug Trends reported more psychosis, more intense "highs," more use of needles, mentions that methamphetamine is now more popular than alcohol or cocaine on the street, increased use among the homeless, as well as increased syphilis cases among those using crystal methamphetamine. At the same time, the DEA Field Divisions in Texas were reporting increases in methamphetamine availability and decreases in price, with multiple seizures of methamphetamine in excess of 100 pounds and the appearance of liquid

methamphetamine, which is easier to smuggle across the border before turning it into crystal methamphetamine.[4]

In response to your questions about data, please refer to Exhibit 7. There are a number of data sources which can inform public policy about changes in the spread of a drug and the treatment needs, and I would urge that attention be focused on getting these datasets out more quickly and making them available to researchers for immediate analysis rather than only releasing the data after the "official" reports are published in hard copy. Another change which could help policy analysis would be to place data sets which are not "sensitive" on the web so researchers can access them without having to file Freedom of Information requests. It would also be helpful if the confidentiality requirements for some datasets were revisited. We need to protect confidentiality, but some of the interpretations seem overly restrictive and prevent analysis of very important issues because key variables are not available to researchers. Perhaps the confidentiality restrictions should weigh the value of the proposed research against the need to prohibit the use of certain variables.[5] And, yes, an interdisciplinary approach is necessary. Policy-makers should not only look at the datasets in their own agencies or in their own geographic areas, but should look at supply and demand data to determine trends across these data. The interdisciplinary approach can provide a broader and more accurate view than can be obtained from one data source.

Exhibit 7 also lists a few of the analytical techniques which have been very useful in analyzing drug trend data. Exhibit 1 has shown the value of using time-series techniques, and I have used capture-recapture methods which originated in wildlife biology to estimate the number of individuals in need of treatment. I applaud the Committee's interest in encouraging use of such techniques.

In terms of interventions, I would cite this drug as an example of how rogue chemists have successfully worked around bans on various chemicals. In other research, Cunningham et al. analyzed clandestine laboratory data to study the impact of requiring prescriptions for pseudoephedrine and found that the impact of such a proposal was related to whether or not the state had a number of small laboratories. It resulted in a reduction of clandestine laboratory seizures in Mississippi, as compared to Oregon, but the effects of such regulations need to be

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[4] Maxwell, JC. Substance Abuse Trends in Texas, in *Epidemiologic Trends in Drug Abuse, Proceedings of the Community Epidemiology Work Group.* Rockville, MD: National Institute on Drug Abuse, 2013. On-line at http://www.utexas.edu/research/cswr/gcattc/documents/CurrentTrendsJune2013.pdf

[5] The Center for Behavioral Health Statistics and Quality of the Substance Abuse and Mental Health Services Administration has attempted to solve this problem through a system through which qualified research organizations may apply for access to confidential data for important research and policy analyses while still conforming to Federal law and protecting identifiable data from disclosure.

considered in terms of other hardships for the population.[6] So, again, the need to weigh supply vs. demand in terms of burdens and benefits. In addition, we know that rogue chemists are searching for other precursor chemicals in other regions of the world, so we should not limit our concerns to only controlling pseudoephedrine and phenyl-2-propanone.

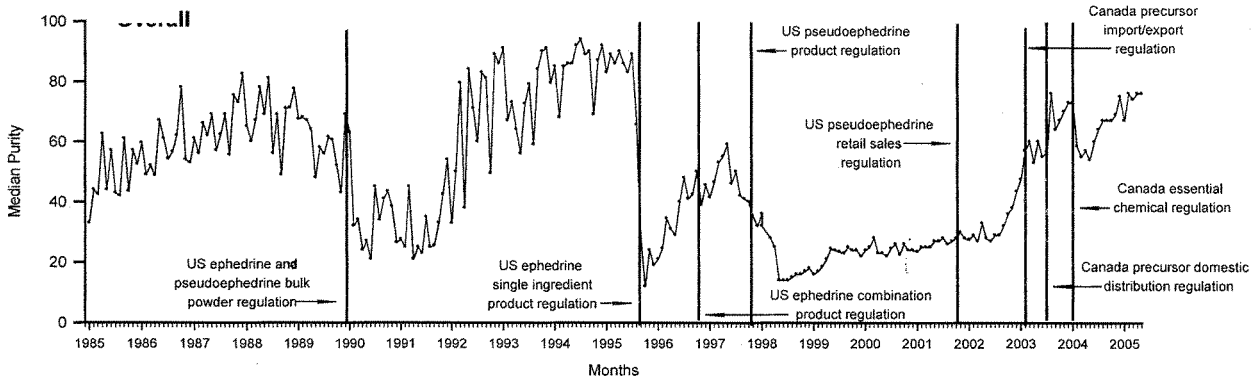
In closing, methamphetamine is a serious problem that continues to wreck our lives and communities and we need intensive treatment to heal not only the bodies, but also the minds of the users. Before the 2006 intervention limiting the sales of pseudoephedrine, there was an initiative to provide more treatment, but some of this effort was diminished because of the erroneous belief that the 2006 ban had "cured" the problem. Unfortunately, the methamphetamine problem has not been solved; the numbers are increasing and we need many more treatment programs. We need treatment in areas with both the more potent Mexican product and also in the rural and semi-rural areas. There is also a need for training for counselors who may have not developed the skill sets needed to successfully work with methamphetamine users who may still be cognitively impaired from their methamphetamine use. Many of these methamphetamine abusers need trauma therapy, gender-focused counseling for sexual abuse, motivational enhancement therapy, and social-cognitive skills training

Together, we have a lot of work to do on this problem. Thank you for your attention.

[6] Cunningham, JK, Callaghan, RC, Tong, D., Liu, L-M, LI, H-Y, Lattyak, WJ. (2012). Changing over-the-counter ephedrine and pseudoephedrine products to prescription only: Impacts on methamphetamine clandestine laboratory seizures. *Drug and Alcohol Dependence* 126: 55-64.

Exhibits for the Testimony of
Jane Carlisle Maxwell, Ph.D. to the Committee on Science, Space, and Technology
September 18, 2013

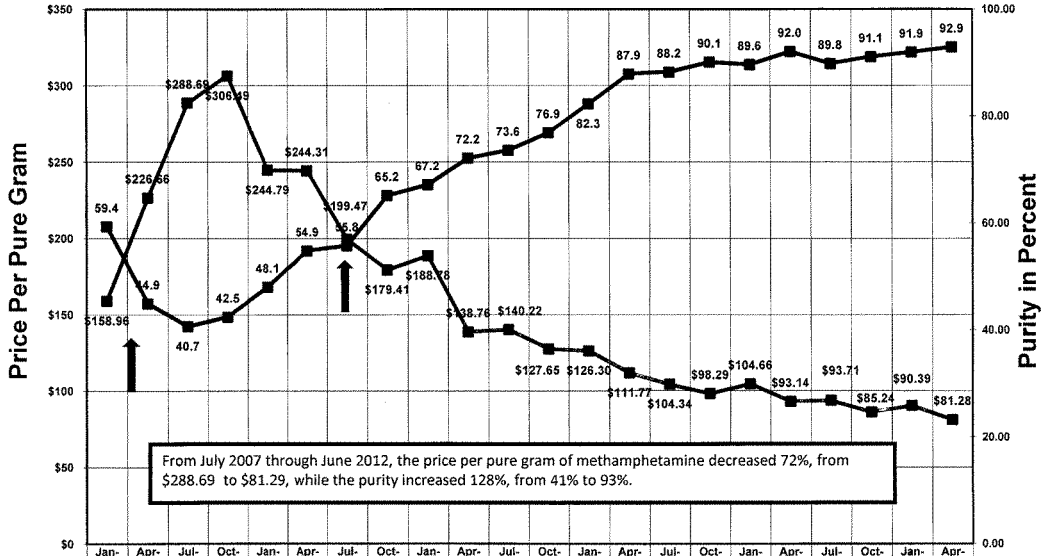
Exhibit 1. Median Methamphetamine Purity in the Continental United States (1985-2005)



Source: Cunningham JK, Liu L-M, Callaghan R. Impact of US and Canadian precursor regulation on methamphetamine purity in the United States. (2009) *Addiction*; 104, 441-453.

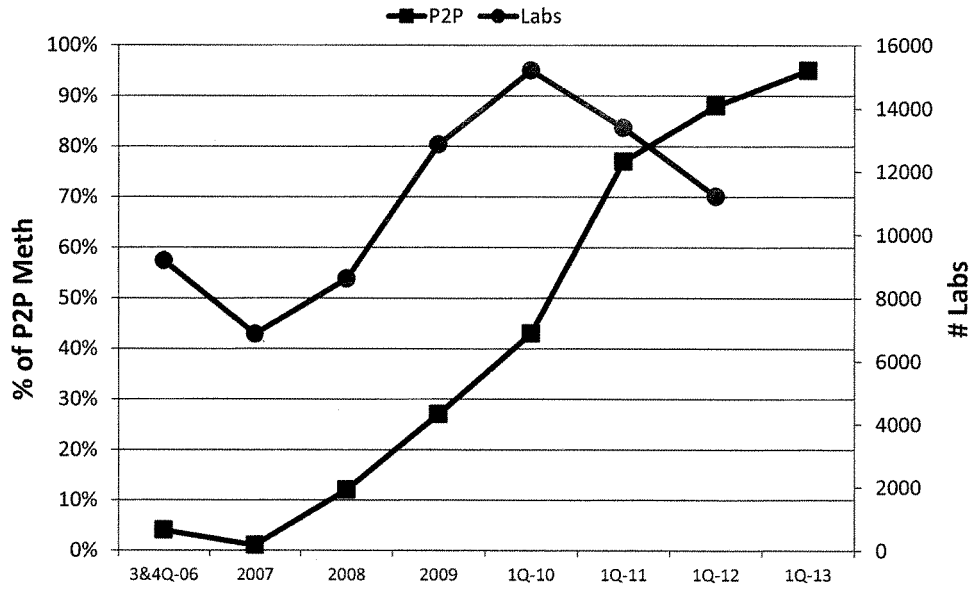
Exhibit 2. All Methamphetamine Purchases
Domestic STRIDE Data
January 2007 – June 2012

* * STRIDE is a database of drug exhibits sent to DEA laboratories from the DEA, FBI, CBP, ICE, USCG, and Washington MPD. STRIDE is not a representative sample of drugs available in the United States, but reflects all evidence submitted to DEA laboratories for analysis. STRIDE data are not collected to reflect national market trends. Nonetheless, STRIDE data reflect the best information currently available on changes in methamphetamine price and purity.



	Jan-Mar07	Apr-Jun07	Jul-Sep07	Oct-Dec07	Jan-Mar08	Apr-Jun08	Jul-Sep08	Oct-Dec08	Jan-Mar09	Apr-Jun09	Jul-Sep09	Oct-Dec09	Jan-Mar10	Apr-Jun10	Jul-Sep10	Oct-Dec10	Jan-Mar11	Apr-Jun11	Jul-Sep11	Oct-Dec11	Jan-Mar12	Apr-Jun12
PPG_mean	$158.9	$226.6	$288.6	$306.4	$244.7	$244.3	$199.4	$179.4	$188.7	$138.7	$140.2	$127.6	$126.3	$111.7	$104.3	$98.29	$104.6	$93.14	$93.71	$86.20	$90.39	81.28
Purity_mean	59.39	44.94	40.67	42.46	48.07	54.86	55.80	65.17	67.20	72.15	73.63	76.90	82.28	87.86	88.22	90.08	89.62	92.04	89.79	91.08	91.91	92.89

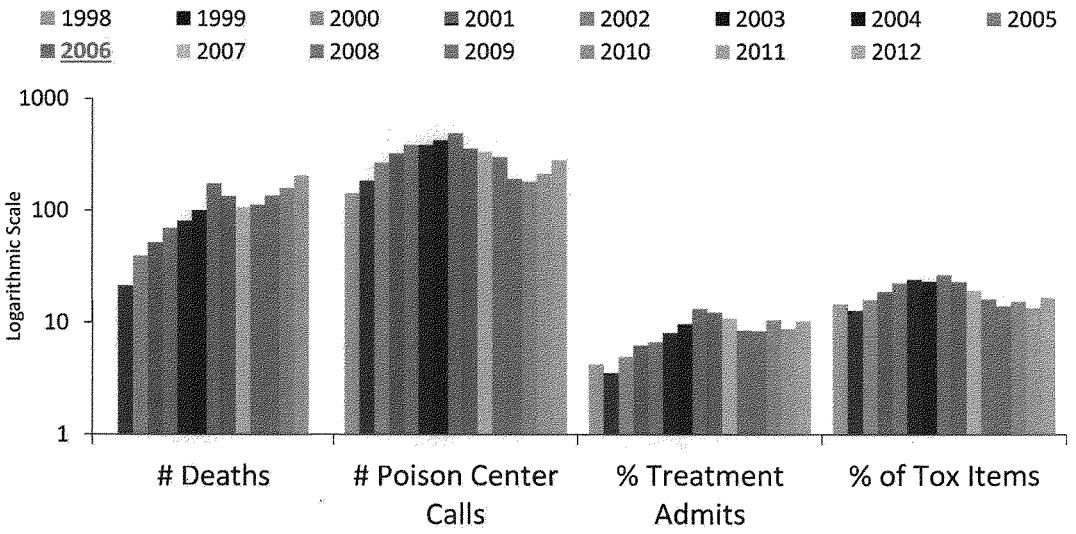
Exhibit 3: Production of P2P Methamphetamine* and Clandestine Methamphetamine Lab Incidents in the US: DEA



*Only P2P samples over 6g reported here

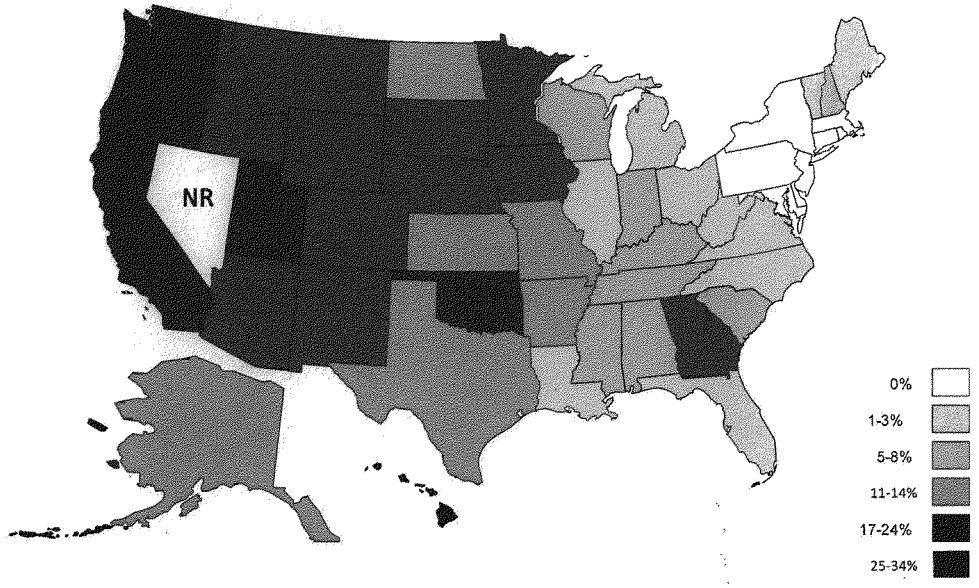
Source: National Forensic Laboratory Information System and DEA's Methamphetamine Clandestine Laboratory Incidents

Exhibit 4. Methamphetamine Indicators in Texas: 1997-2012



Source: Deaths, Poison Calls and Treatment Admissions from the Texas Department of State Health Services and Toxicology Items from National Forensic Laboratory Information System.

Exhibit 5. Percentage of Drug Items Identified as Methamphetamine by ForensicyLabs: NFLIS 2010



Source: National Forensic Laboratory Information System

Exhibit 6

Indicators of Methamphetamine Abuse 2012 vs. 2013					
Increasing		**Mixed Indicators**		**Stable**	
High Level	Low Level	High Level	Low Level	High level	Low Level
Los Angeles	Maine	San Diego		San Francisco	Boston
Albuquerque	Atlanta	Honolulu			New York City
Seattle	South Florida	Phoenix			Philadelphia
Texas	Cincinnati				Washington DC
St. Louis					Detroit
Minneapolis / St.Paul					Chicago

Source: Hall, JN. *Meeting Notes from the June 12-14, 2013 Community Epidemiology Work Group (CEWG) of the National Institute on Drug Abuse.*

Exhibit 7. Available Data Sources for Policy Analysis (Federal, State, Local) and Analytical Techniques

DATA SOURCES

- Surveys: National Household Survey on Drug Use and Health (NSDUH), Youth Risk Behavior Survey (YRBS), Monitoring the Future (MTF)
- Poison control centers
- Emergency room data (formerly Drug Abuse Warning Network) — will be consolidated into Centers for Disease Control and Prevention's National Center for Health Statistics (NCHS)
- Treatment Admissions & Discharges (TEDS)
- Forensic tests of seized drugs – National Forensic Laboratory Information System (NFLIS)
- Price and purity – System to Retrieve Information from Drug Evidence (STRIDE)
- Semi-annual Trends in Trafficking reports from DEA Field Divisions
- Automation of Reports and Consolidated Orders System (ARCOS) –sales of scheduled pharmaceuticals
- Sexually Transmitted Diseases, Hepatitis, HIV and AIDS data
- Studies of users
- Reports from street outreach workers and others who work with users in homeless shelters, drop-in centers, health care settings, syringe exchange programs, etc.

ESTIMATION TECHNIQUES

- Graph changes in drugs over the long-term (10-15 years)
- Compare different datasets to see changes in characteristics of users or to compare trends.
- Studies that merge different datasets
- Time series analysis of STRIDE or other longitudinal datasets.
- Capture-Recapture to estimate number of users.

NEEDS

- Quicker release of federal datasets, even if they are incomplete (title them as preliminary and release them).
- More access to federal data without having to file Freedom of Information requests when the data are not sensitive.
- Revisit confidentiality requirements to see if there are ways to protect confidentiality but make needed data elements accessible to qualified researchers.
- Training for counselors in trauma therapy, gender-focused counseling, motivational therapy, and social-cognitive skills training.
- **Additional treatment programs, including those in rural and semi-rural areas.**

Chairman BUCSHON. Thank you very much.
Dr. Napier.

TESTIMONY OF DR. CELESTE NAPIER, DIRECTOR, CENTER FOR COMPULSIVE BEHAVIOR AND ADDICTION, PROFESSOR OF PHARMACOLOGY AND PSYCHIATRY, RUSH UNIVERSITY MEDICAL CENTER, CHICAGO, ILLINOIS

Dr. NAPIER. Chairman Bucshon, Ranking Member Lipinski, and distinguished Members of the Subcommittee, thank you so much for the opportunity to testify on how science can provide solutions to the problems associated with methamphetamine abuse.

Methamphetamine is an insidious drug, and while the user initially experiences an incredible sense of euphoria, the brain's natural brake system is overridden, and the consequences of this overload can be devastating. Methamphetamine can cause brain abnormalities that occur even years after the addicted individual stops using the drug, and understanding these persistent abnormalities is an important topic for modern neuroscience.

Pilots of my own research can underscore this point. We studied the effects of methamphetamine in laboratory rats. These rats readily learned to press a lever in order to receive an infusion of methamphetamine into their bloodstream, and if we let rats self-administer methamphetamine for two weeks and then leave them alone for different periods of time, we find that by three weeks of abstinence, the rats' brains had degenerated and they looked similar to the brain of a human that has Parkinson's disease.

Such findings provide neurobiological explanations to recent reports that human methamphetamine addicts have a 75 percent greater risk to develop Parkinson's disease than do controls. An increasing prevalence for Parkinson's disease has enormous health and medical cost ramifications, and we are now working to identify viable biomarkers of Parkinson's-disease-like pathology in methamphetamine abusers with the hope that presymptomatic detection will allow early therapeutic interventions to avoid this outcome.

As suggested by these studies, effective treatments for methamphetamine abuse may be those that work after the drug-taking has stopped. Indeed, relapse by the withdrawn addict is as high as 70 percent and thus halting relapse is a high priority for medication development.

Basic research has identified treatments that reduce relapse-like behavior in laboratory rats, as Dr. London had indicated. We are using treatment protocols that are already used in humans to treat other diseases. Such a repurposing provides a rapid—a relatively rapid and cost-effective process to bring treatment to market.

To attract the interest of pharmaceutical industry to the patent opportunities of this endeavor, we are working with an innovative foundation named Cures within Reach. This foundation is stewarding fundraising for repurpose treatments that we think should reduce cocaine and methamphetamine use. We feel that teaching old drugs new tricks is a win-win model that should be explored to its greatest extent by academic biomedical researchers, government agencies, foundations, and pharmaceutical companies alike.

An example of the urgent need to develop effective treatments for addiction is in our Nation's jails and prisons where approximately 80 percent of the incarcerated have substance abuse problems. As drug courts mandate treatment, we are working with the continuing legal education programs to integrate the neuroscience of addiction in order to help inform sentencing decisions. I think that such knowledge base is especially important for methamphetamine cases for which coerced treatment is often the only way that the addict will access help.

Particularly vulnerable to the ravages of methamphetamine are the Nation's youth, as Mr. Lipinski mentioned. Each day in the United States more than 4,500 children try an illicit drug for the first time. As these striking data suggest, the traditional approach to drug education is largely ineffective. New strategies are critically needed and I believe there is a role for neuroscience in this endeavor.

Recent initiatives by the Robert Crown Center for Health Education, a not-for-profit organization based in a suburb of Chicago, in conjunction with our addiction center at Rush University, is providing what I believe to be an excellent template for this goal. The Robert Crown Center is developing a completely new educational framework that integrates knowledge and building strategies for middle school, high school students, school personnel, and parents. Our center provides access to cutting-edge brain research. Thus, the prevention program includes both the neuroscience-based knowledge of how abused drugs act on the adolescent brain, as well as the socioeconomic learning required to reduce drug abuse among our youth.

Understanding how the brain goes awry during methamphetamine abuse is a formidable challenge. The exciting advances that we made towards this challenge attest to the ingenuity and determination of the addiction neuroscientist. But to continue this trajectory we must carefully consider where to direct our resources. Successful templates should be supported and promising new paradigms should be considered. Education programs need to be promoted to translate the wealth of empirically derived neuroscience to our public.

However, with concerted teamwork from all sectors of our society, I am confident that we can meet the challenge of controlling the abuse of methamphetamine and reducing the suffering of those who struggle with addiction. Thank you.

[The prepared statement of Dr. Napier follows:]

TESTIMONY

of

T. Celeste Napier, Ph.D.
Director, Center for Compulsive Behavior and Addiction
Professor, Departments of Pharmacology and Psychiatry
Rush University Medical Center
Chicago, IL

to the

Committee on Science, Space, and Technology
Subcommittee on Research and Technology
U.S. House of Representatives
September 18, 2013

Chairman Buschon, Ranking Member Lipinski, and distinguished members of the Subcommittee, thank you for the opportunity to provide testimony on methamphetamine addiction and how we can use science to explore solutions to problems associated with the abuse of this drug.

My name is T. Celeste Napier, and I am the Director of the Center for Compulsive Behavior and Addiction, and a Professor in the Department of Pharmacology and the Department of Psychiatry, at Rush University Medical Center in Chicago. I also serve as the Scientific Advisor for the Robert Crown Center for Health Education in Hinsdale, IL.

I will address three topics related to the abuse of methamphetamine. First, how basic brain research has informed us about methamphetamine abuse and has led towards promising treatments for addiction. Second, what scientific gaps remain in our knowledge of methamphetamine abuse, and what is needed to enable neuroscience to fill these gaps. Third, examples of prevention programs and the role that educational institutions can have in prevention will be discussed.

Methamphetamine is an insidious drug. Indeed, no other abused drug has such profound effects on the brain as methamphetamine, and modern neuroscience has deciphered many of the mechanisms that underlie its effects. Dopamine is a key chemical in the brain that mediates the sensation of pleasure. Its biological purpose is to provide rewards for behaviors that keep the individual and its species alive. For example, when given food, laboratory rats show an increase in dopamine of about 50% in a brain region called the nucleus accumbens, one of the brain's 'pleasure centers'. Sexual activity in laboratory rats is associated with about a 100% increase in accumbens dopamine. Abused drugs produce their effects by hijacking this natural reward system; for example, cocaine causes a 200% increase in accumbens dopamine. Methamphetamine increases dopamine in the nucleus accumbens by over 1,000%, completely swamping the ability of the brain to control this neurotransmitter. So while the user initially experiences an incredible sense of pleasure and euphoria when taking methamphetamine, the brain's natural brake system is overridden, and the consequences of this dopamine overload can be devastating.

Modern neuroscience research has revealed that the brain effects of methamphetamine extend beyond these temporary, albeit extraordinary, increases in brain dopamine. Methamphetamine causes inflammation in the brain and elsewhere in the body, it causes the breakdown of the brain's protective barrier, and it damages neuronal projections. Modern imaging studies of the human brain show biochemical and functional abnormalities even years after the methamphetamine-addicted individual

stops using the drug. Because of the health ramifications and related costs to the abusing individual and society, understanding the driving mechanisms of methamphetamine-induced neuropathology is a critically important topic of neuroscience research.

Some highlights of my own research can underscore this point. One of the ways my laboratory studies the effects of methamphetamine on brain function is with laboratory rats. Laboratory rats can learn a task in which they can press a small lever in a test box in order to receive an infusion of methamphetamine into their blood stream. The rats will continue to press the lever sufficiently enough to maintain their desired dose for the duration of the test period. This illustrates that the feel-good sensations evoked by methamphetamine drive the rats to continue to use the drug for as long as it is available. If we let rats self-administer methamphetamine for a few hours each day for 2 weeks, and then leave them alone in their home cage for different periods of time, we find that by 3-4 weeks of abstinence, the rats' brain have degenerated to the point that the anatomy and neurobiology looks similar to the brain of a human with Parkinson's disease. These studies have helped identify the neurobiological constructs which support recent epidemiological studies showing that human methamphetamine abusers exhibit a 75% greater risk to develop Parkinson's disease than do non-abusing humans. Given that there are approximately a half a million methamphetamine-abusing individuals in the United States (National Survey on Drug Use and Health), the possibility that methamphetamine may promote such a devastating disease has enormous ramifications in terms of human suffering and medical costs required to treat Parkinson's disease. Consequently, our research is identifying viable biomarkers that hold promise as early detectors of Parkinson's disease-like pathology in the methamphetamine abuser, with the hope that presymptomatic detection will allow early therapeutic intervention to avoid developing Parkinson's disease. This example shows how basic neuroscience, using laboratory models of human methamphetamine abuse, can explain clinical observations about this condition, and in so doing, aid in identifying possible treatments.

The effects methamphetamine occur at all levels of neurobiology, including genes, proteins, cells, circuits and whole brain regions, and the profile of the damage changes with time. Such knowledge is informing modern day thinking about treatment, and this is critically important, as currently there are no FDA-approved treatments for methamphetamine addiction. Though dopamine plays a role in initiating the pathological effects of methamphetamine, we know that targeting treatments that act on the dopamine system is not clinically fruitful. Like the analogy that the train is already out of the station, treating addiction may have more to do with the progression of pathology that is subsequent to the excessive release of dopamine. This new view is directing current medication development where therapies being tested are better-suited to halt or slow down the chain of events that continue after drug-taking stops. For example, relapse to drug-taking by the withdrawn methamphetamine addict is hallmark to addiction, and identifying unique therapeutic targets that govern relapse has gained the spotlight in recent years. These endeavors span testing of vaccines for methamphetamine, as well as identification of targets that are involved in the intense urges for the drug that are thought to drive relapse. Research in our laboratory relates to this theoretical construct, and we have identified potential therapies that reduce relapse-like behaviors in laboratory rats that self-administer methamphetamine. Early clinical studies have indicated that these therapeutic agents may indeed be useful in humans. Embedded in this research endeavor are evaluations of therapies already used to treat humans for other diseases, and have pharmacological profiles we hold should also be useful in reducing relapse. As these therapies are already shown to be safe in humans, this should allow a more rapid translation of our laboratory findings with animal models back into humans. Moreover, as current estimates for developing clinically effective therapies from new chemical entities range from $4 to $11 billion (Forbes, March, 2012) and 12 years (US FDA) in the making, such rediscovery and repurposing of therapies provides a exceptionally expedited mechanism for developing effective, safe and affordable

treatment solutions for addiction. To attract the interest of the pharmaceutical industry to addiction therapy, we are working with a innovative, international foundation based in Chicago named 'Cures Within Reach' to steward fundraising for repurposed treatments that we have identified for cocaine and methamphetamine addiction that present patent opportunities. We feel this approach of 'teaching old drugs new tricks' is a win-win model that should be explored to its greatest extent by academic biomedical researchers, government agencies and foundations like Cures Within Reach to work with pharmaceutical companies in implementing treatments for those that suffer from addictions.

Several other new paradigms are being explored by medication development researchers with the objective of expediting the implementation of treatments for methamphetamine addiction. We are challenging old normatives on what constitutes successful treatment. Current FDA guidelines for approving addiction therapeutics require the treatment to provide complete abstinence from the abused drug. This rubric differs from that applied to alcohol or nicotine abuse, where a significant reduction in the use of the drugs is sufficient, as it is known that such reductions are associated with positive health benefits for the patient. Thus, it is necessary for current research to verify the health benefits of reducing methamphetamine intake for those addicted to the drug. Spearheaded by NIDA, such research is now underway. Basic neuroscience research predicts that positive outcomes will be obtained, and it is our hope such empirical evidence will redirect FDA guidelines so we can rapidly put in place therapies that can provide relief from the ravages of methamphetamine addiction.

While the aforementioned research illustrates the forward momentum of the neuroscience of methamphetamine abuse, and how this research has informed medication development, several critical pieces remain before the puzzle of addiction can be completely assembled. To do so, may take a more bird's eye view of addiction and how abused drugs change the brain in such profound and enduring ways. The brain is extremely complex, more complex than the internet, traffic flow on metropolitan highways, or the weather. Thus, all of the tools that are at the disposal of modern science need to be utilized to understand the brain complexities associated with addiction. Like most genetically linked diseases where more than one gene is involved, there will not be a single cause to methamphetamine addiction. To best elaborate the complexities of addictions, this area of neuroscience would benefit greatly by more incorporation of mathematical models of reward-motivated behaviors, and by linking molecular neurobiology to function at the circuit and behavioral levels by utilizing shared data sets. This is a great opportunity for hand-shaking of efforts from NSF, DARPA and NIH as was so exquisitely discussed by this Subcommittee in a Hearing on July 31st of this year on the BRAIN Initiative.

An important sector of our society that is in critical need of effective treatment, are those that are incarcerated. According to the Substance Abuse and Mental Health Services Administration, approximately 80% of incarcerated adults have a substance use problem. In recent years, I have had numerous opportunities to be involved in Continuing Legal Education for Criminal Defense Attorneys and Judges, speaking on the topic of the neuroscience of addiction and its impact on sentencing decisions. I am extremely impressed by the sincere desire of leaders within our judicial system to properly deal with substance abusing individuals. As Drug Courts mandate treatment, we need to do our best to assure that our judicial system has access to front line neuroscience. This is so important, particularly in methamphetamine cases, for which coerced treatment is often the only way an addict will access help. Studies show that coerced treatment yields the same, if not better treatment results, by motivating clients to stay in treatment longer. According to the National Association of Drug Court Professions, for methamphetamine-addicted people, Drug Courts increase treatment program graduation rates by nearly 80%. The savings offered by Drug Courts is substantial. The Office of National Drug Control Policy estimates that Drug Courts yield a savings of $21,000 per person annually, as the average cost per participant is $2000 and the cost of incarceration is $23,000. Clearly, a success.

However, our nation's courts are seeing an increase in the number of veterans with drug-related offenses, and this alarming trend deserves serious consideration. Substance use disorders are particularly high in returning warriors who have suffered traumatic brain injuries (TBI) and are experiencing post traumatic stress disorders (PTSD). We, as a nation, owe it to our warriors to figure out why this happens; therefore, this should be a topic of intense research efforts in the addiction field. I also believe that we need to establish clear educational links between scientists in the fields of TBI, PTSD and addiction with the nation's Drug Courts and do an even better job of informing our judicial system on the complexities of these disorders. Such efforts could be spearheaded by NSF, DARPA, and various institutes within NIH.

A particularly vulnerable population to the ravages of methamphetamine is our nation's youth. For example, according to the National Survey on Drug Use and Health, each day in the United States more than 4,500 children aged 12-17 years of age used an illicit drug for the first time. We must address this need, and I believe there is a role for neuroscience in this effort. Educational institutions typically include drug education in their health curriculum in grades 7 - 10th, and drug-related topics often focus on the legal consequences of illicit drug use, not health. As the striking epidemiological data suggest, the traditional approach to drug education is outdated and ineffective. New strategies that are initiated in earlier grades, involve yearly programming at regular intervals with up-to-date science-based curriculum and successful prevention methods, and include age-appropriate guidance are critically needed. Recent efforts by the Robert Crown Center for Health Education, a not-for-profit organization based in a suburb of Chicago, in conjunction with our Center for Compulsive Behavior and Addiction at Rush University Medical Center provides ,what I believe, is an excellent template for these goals. The Robert Crown Center is developing and implementing a completely new educational framework to interface with the school systems, based on what science tells us are the risk factors faced by youth and which contribute to experimenting with drugs. The primary prevention approach to this drug education program is a comprehensive, whole-school educational framework that integrates long-term, knowledge-building strategies for middle school and high school students, school personnel, and parents. The critical partnership with our Center for Compulsive Behavior and Addiction provides access to the cutting edge brain research that is then transferred to the classroom. The educational framework includes both the neuroscience-based knowledge of how abused drugs act on the adolescent brain as well as the social/emotional learning required to reverse the rising trends of drug abuse among our youth. Here again, is a critically important opportunity for active involvement of neuroscientists, both in terms of understanding how the adolescent brain differs from that of an adult, as well as, how drugs influence the brain. NSF and NIH have mechanisms to support these initiatives, and given the impact on the future of our nation's youth, new paradigms that expand these programs should be explored.

Understanding how the brain normally functions and how these functions go awry during methamphetamine abuse is a formidable challenge. The exciting advances we have made towards this challenge attests to the ingenuity and determination of addiction neuroscientists. To continue this trajectory, so that pharmacological treatments can be identified, will take careful consideration of where resources should be directed. Successful templates should be supported and promising new paradigms should be considered. Education programs need to be promoted to translate the wealth of empirically derived neuroscience to the public. By supporting the continuation of the impressive work in our academic research centers and government laboratories, in partnership with private foundations and the pharmaceutical industry, we will continue to make tremendous inroads into our nation's struggle with methamphetamine addiction. Funding from government agencies and leadership from our policy makers are critical components in the continued success of these initiatives. With concerted teamwork from all aspects of our society, I am confident that we can meet the challenge of controlling the abuse of methamphetamine, and reducing the suffering of those who suffer from its addiction.

T. Celeste Napier, Ph.D. is the Director of the Center for Compulsive Behavior and Addiction, and a Professor in the Departments of Pharmacology and Psychiatry at Rush University Medical Center, Chicago, IL. Dr. Napier has over 30 years of research related to brain and behavioral effects of abused substances and impulse control disorders that have been supported by grants from the National Institutes of Health and several private research foundations. She has authored over 200 scientific publications, special issues and books.

Chairman BUCSHON. Thank you all for your testimony.

I remind the Members of the Committee rules limit questioning to five minutes, and the Chair at this point will open the round of questions. I recognize myself for five minutes.

Dr. Maxwell, from an epidemiological viewpoint—urban versus rural communities, is there a difference in methamphetamine—because I am in a relatively rural area of Indiana—versus Chicago, for example?

Dr. MAXWELL. The difference is that treatment resources aren't available in the rural areas. I don't see any difference in the patterns of urban versus rural but serious need for treatment facilities in the rural areas.

Chairman BUCSHON. Sergeant Crawford, in Indiana, do you notice a difference?

Sgt. CRAWFORD. We saw a big difference back in the late 1990s and early 2000s when meth labs really started to grow. The vast majority of them were in rural areas. But now, with the one-pot or the shake-and-bake labs coming in, we are getting more and more labs in urban areas. I think within Indiana, Allen County and even Vanderburgh County, while it has got some rural areas, it is second- or third-largest city, so if you look at those two counties and the growth that they have seen, that kind of shows you that with the one-pot labs, it is much easier to cook in an urban area.

Chairman BUCSHON. You were commenting on how it wasn't necessarily economically driven; it was addiction-driven. Dr. Napier, maybe you can comment on this? I have heard that in certain respects, you know, as methamphetamine tries to overtake cocaine, for example, or other drugs that are being sold by certain groups of individuals in urban areas, that in areas where there is a strong dealer in cocaine, and that is where the money is, that methamphetamine has a hard time breaking into that area. Is that true or not true? Is that perception? Dr. Maxwell and then Dr. Napier?

Dr. MAXWELL. No, cocaine is down. There is a shortage of cocaine because a lot of it is going to Europe now. And I am hearing more and more people who are shifting to methamphetamine because cocaine—what we are—the cocaine that we are getting is not very pure. It is not worth "paying for." No, they are going to methamphetamine now. Meth has far out-passed in most of the states cocaine in terms of prevalence.

Chairman BUCSHON. Dr. Napier, in Chicago?

Dr. NAPIER. By understanding what is happening in Chicago is two things. One is it is still a very rural problem. Southern Illinois, as Mr. Lipinski knows, has some clandestine labs that are really supplying the problem there. In Chicago there are certain subpopulations of people that abuse methamphetamine more than others. For example, men who have sex with men or the gay men community are one of the higher users of methamphetamine in the City of Chicago. In the south side of Chicago and the west side of Chicago, cocaine is still the preferred drug. But we are—I predict that we will be seeing more methamphetamine infiltrating the city as it becomes more readily available.

Chairman BUCSHON. Dr. London, in the area of research—and I know you do research on the effects of it, I have discussed with FDA about trying to find ways to make pseudoephedrine not usable

to produce meth. Are you aware of universities and other people—other in industry that are doing that type of work?

Dr. LONDON. I am not aware of that.

Chairman BUCSHON. Yes, and I think, Sergeant Crawford, you mentioned some of that, that tamper resistance and things like that, it is a very interesting subject because pseudoephedrine in and of itself isn't going to be a Schedule I drug because it is just not a Schedule I drug. So attacking it from the FDA standpoint and trying to schedule one drug based on the fact that it is used to produce another drug is not something that can be done at this point because of legal and other challenges.

So I am interested in the science of trying—of not only finding ways to treat people that are on it but trying to make it more preventable to make it in rural areas like in Indiana. I recognize the fact that a lot of this is going to come from Mexico and that is a different problem to attack. So we really have two separate problems here, I think as it relates to that.

And with that, I will yield to Mr. Lipinski.

Mr. LIPINSKI. Thank you. I want to thank all the witnesses for their testimony. This is fascinating to hear this and very troubling in many ways.

I want to start out with Sergeant Crawford. As I mentioned in my opening statement, the Methamphetamine Remediation Research Act passed through this committee in 2007. I was a cosponsor. I believe it was spearheaded by the then-Chairman of the committee Bart Gordon from Tennessee. In that bill, which became law, it established a research program on residue from methamphetamine production and developed voluntary guidelines for preliminary site assessment and remediation of meth labs. You know, at that time most meth was—that was cooked was cooked in drug houses. As you spoke about and others, you know, the new shake-and-bake method of cooking, seizures aren't restricted to collecting items in drug houses.

So if this committee were to revisit the law that I mentioned, we would need to take this into consideration. Is there anything you could say about the new kinds of immediate or long-term risks, if any, that are faced by law enforcement officials and surrounding communities giving the—given the prevalence of the new method?

Sgt. CRAWFORD. I think the biggest issue that we are having is really in terms of the dangers associated with the one-pot labs. When we first started to see them, we didn't really understand. We knew—we understood the chemistry but we didn't understand the long-term effects, and we didn't realize what an enormous amount of ammonia gas that the one-pot labs actually create. And so when you look at injuries, especially to law enforcement, that is our issue that we are dealing with right now is the exposure to the ammonia gas that comes off of the one-pots because it creates its own ammonia gas within the reaction vessel itself.

So in terms of the contamination that we are dealing with with these labs, whether it is a one-pot lab or other, is typically going to be your ammonia gas. But the bigger issue is in the last step of the process when they salt out or they solidify the meth and they introduce hydrochloric acid gas to the reaction vessel, those molecules bond with one another, and because it is a gas, it escapes

into the air. And that is typically the types of exposures that we are dealing with, both long-term exposures from facilities or homes or cars or whatever it is that have had cooks happen in them, especially long-term. Automobiles are a little bit less because you can roll the windows down. They are smaller. They are not going to hold in the contamination as much as others, such as a house or a hotel room would.

Mr. LIPINSKI. Thank you.

Dr. Napier, I wanted to ask you, you had talked about these new programs for—educational programs. Is there anything more that you would like to see us doing here in Washington that would help to—help the research that would feed into these programs or in the helping to disseminate the findings of research and get those—get this out to people?

Dr. NAPIER. There is always room to grow and help needed. From my perspective in working with these outstanding educators, one of the things that we really are trying to do is to determine if—outcomes. Are we really making a difference with our new curriculum? So we have several schools that have served as beta test sites in the Chicago metropolitan area, and we are just now getting feedback from our first year of implementing this curriculum in different schools.

What we need to be able to do is to customize this curriculum to the individual community schools and then determine if we are as effective in the different environments, because clearly, the way we are going to reach children, for example, in rural areas is going to be quite different than what we are going to be needing to use in the suburban parts of Chicago.

So this kind of epidemiology and this kind of validation of outcome-support takes money. We have to hire people to do this; we have to have researchers employed. And so this again is an area where grant support mechanisms could be very critical in driving the momentum to get this thing to the schools as quick as we can.

Mr. LIPINSKI. And is the—what about the funding for the research that is going on to learn more and to improve these educational programs? Is there—I know there is always a need for—you could say for more but is there anything that is missing, anything that can be done differently?

Dr. NAPIER. Well, there are mechanisms for this kind of educational directives if you will through both the NIH and at NIDA, as well as NSF. And I think that what we need to do is to take those vehicles and optimize them. One idea that we might explore actually, as you know, all of these programs have training grants, so we are putting young people in their Ph.D. programs on training grants that are being supported by NIH.

One of the things we might consider to do is that there would be a component required of these training grants to have these students volunteer, and this could be part and parcel to their training and part and parcel to the institutions getting the grant awarded. And I think that kind of infusion of these are young men and women who are going into the neurosciences who are right out of college, and having them work in these different high schools and junior highs would be a huge infusion of great knowledge and understanding that would be very useful in these kinds of programs.

So that is something that might not cost so much money that might be very effectual.

Mr. LIPINSKI. All right. Thank you.

Chairman BUCSHON. I now recognize Mr. Schweikert for his questioning.

Mr. SCHWEIKERT. Thank you, Mr. Chairman.

Professor London—and forgive me, some of my knowledge on this is a bit outdated, but walk me through methamphetamine and its attachment to the receptors. Is it different than other opiates in both the dopamine receptors and other parts in the brain?

Dr. LONDON. Methamphetamine interacts with the dopamine transporter.

Mr. SCHWEIKERT. Um-hum.

Dr. LONDON. It is taken up into neurons that use dopamine as a neurotransmitter. It gets into the vesicle where dopamine is stored, and reverses the activity of the transporter so that lots of dopamine is released into the synapse, and these very high concentrations that are released—much, much more than a release from the administration of cocaine—are toxic because dopamine itself in a high concentration will autooxidize.

Mr. SCHWEIKERT. Almost to that, wasn't there—and wasn't it even happening at a couple of the big southern California universities a couple years ago looking at abilities to almost block those receptors from absorption? Do you have any memory of what happened or where that research is?

Dr. LONDON. Yes. At this point with respect to interacting with the dopamine transporter, one of the best clues that we have for therapy is with bupropion, which has——

Mr. SCHWEIKERT. Okay.

Dr. LONDON. —as part of its action, the ability to enhance dopamine function by blocking the transporter. It is in a sense a type of agonist or mimic for the drugs of abuse but without the abuse potential.

Mr. SCHWEIKERT. Okay. So if I remember my little friend who is trying to explain this to me—she actually sort of drew with crayons so I would understand it; it is always amazing how, you know, two times in life you think you know everything: when you are 14 and when you become a Member of Congress—is it an actual block on the receptor or is it changing the—as you call it, the transporter?

Dr. LONDON. Methamphetamine interacts with the presynaptic element of the neurons. All of the transmission takes place at the gap in between neurons——

Mr. SCHWEIKERT. Um-hum.

Dr. LONDON. —which is called the synapse.

Mr. SCHWEIKERT. Yes.

Dr. LONDON. And methamphetamine acts at the first neuron in the sequence causing massive releases of dopamine. This massive release of dopamine really destroys the system over time in that the dopamine receptors that are needed for dopamine to have its normal activity are down-regulated, and in fact the presynaptic element doesn't function very well in terms of releasing dopamine in response to natural rewards.

Mr. SCHWEIKERT. Okay. The impossible-to-answer question—where do you think we are in the research of being able to have

a pharmaceutical sort of solution to at least either blocking those receptors and would it only be meth specific or would it be other types of opiates?

Dr. LONDON. Well, meth is not an opiate. It is an amphetamine, and so it has a different chemical structure. And the opiates interact directly with other kinds of receptors.

With respect to a treatment that will help all methamphetamine abusers globally I think we are not in good shape. But we do have treatments that help subgroups of methamphetamine users. For example, bupropion is effective in reducing stimulant use by individuals who use methamphetamine on fewer than 18 days a month, but not in the heavy users. There is also a positive signal with bupropion being effective in men who have sex with men.

There are clues from the recent PET literature and animal studies that there are other targets that haven't been used as therapeutic targets that might be useful.

Mr. SCHWEIKERT. Okay.

Dr. LONDON. One of them is the D3 receptor, which seems to be up-regulated in meth users, and blocking it in animals reduces methamphetamine self-administration.

Mr. SCHWEIKERT. All right. Thank you. And I know we are very short on time.

Dr. Maxwell, wonderful data you have put together. My quick question is let's say we had great success in strangling the supply of methamphetamine. When you have been looking at data particularly in the Texas environment, are there any other drugs that you see potentially in the upswing either because of their price or their potency?

Dr. MAXWELL. Okay. Two different things: DEA is telling me that the cause of the pseudoephedrine is not—we can't get enough of it to collect and the problems with the P2P if Mexico bans it. We know people are out all over the world in Africa and South America looking for other chemicals that can be used to make meth. And in terms of other drugs going up, methamphetamine continues to go up. I am worried about heroin among young users and the synthetic drugs, we are just beginning to understand what is going on with them. And a lot of them are actually related to methamphetamine. We like uppers. We like trippy uppers that you can—it is kind of like combining LSD and, you know——

Mr. SCHWEIKERT. See, I have always assumed——

Dr. MAXWELL. Yes.

Mr. SCHWEIKERT. —that is why the dear Lord created coffee for me.

Dr. MAXWELL. Exactly.

Mr. SCHWEIKERT. Mr. Chairman, I yield back. Thank you for your patience.

Chairman BUCSHON. You are welcome.

Dr. Bera.

Mr. BERA. Thank you, Mr. Chairman and Ranking Member Lipinski, and thank the witnesses.

I am a physician by training and I represent Sacramento County in the northern California area where we have got a huge methamphetamine challenge. The Sacramento Bee reported that 40 percent of the men arrested in Sacramento County have meth in their

system. And just as we think we are making some progress, as Dr. Maxwell showed, those that are supplying are staying one step ahead of us here.

Increasingly, more of the meth that does seem to be coming from Mexico does seem to be being smuggled in as liquid as well. And then I think Sergeant Crawford has talked about the ease of the shake-and-bake production. So if we focus on the back end, it looks like it is going to be a very difficult challenge for us to get a handle on.

On top of that, when I look at our law enforcement at one time most of our law enforcement agents had narcotics units. Now, a lot of our police departments have lost narcotic units. In Sacramento, the Sacramento PD shuttered their narcotics unit in 2011. So that also adds to the challenge here.

You know, we have seen the ability to provide treatment go down. In California in 2006 we had 78,000 patients admitted to meth addiction programs. Less than five years later, it is less than 44,000.

So I am not painting a rosy scenario here. This is a challenge. And then concomitant to that, you know, I was chief medical officer for Sacramento County. The number of folks that have dual diagnosis—mental illness and substance abuse—the number of folks that, you know, by not addressing the root-cause issues, we end up building more jails. We end up having to build these backend solutions.

The challenge that drug addiction—not just methamphetamine but cocaine—we are now seeing a huge uptick in prescription drug abuse and the impact that has on the family social structure, the impact it has on the foster care system, et cetera. So there are these huge sociological challenges. I haven't asked a question yet because these are real issues.

We have talked a lot about backend solutions, but if we were to look at the root-cause issues and try to shift towards prevention in some of the social science that it potentially leads to drug abuse and addiction, I guess I would ask Dr. Maxwell where would you like us to focus if we were to try to focus on frontend solutions and root-cause solutions?

Dr. MAXWELL. Thank you. We have tried a number of different approaches on—to prevent youngsters from using drugs. There have been some that have been proved to be quite effective, but it seems like we start doing something and then we drop it.

Mr. BERA. Right.

Dr. MAXWELL. I really wish we would go back to some of those prevention programs that have, through the follow-up tests, been shown to be effective.

Mr. BERA. Because it is probably making a commitment over a generation, right? I mean if——

Dr. MAXWELL. Exactly.

Mr. BERA. So——

Dr. MAXWELL. Um-hum.

Mr. BERA. —what would you say some of those programs are that you would like to see?

Dr. MAXWELL. They are up on the SAMHSA website and I can give your staff the links to it, but some very, very good ones. So

before we start over again, I think it is time to go back and look at which of those are the most effective and could we modify them to handle these new drugs?

Mr. BERA. Dr. Napier?

Dr. NAPIER. And to continue that dialogue, there is a couple things. One is we have to understand that the curriculums are regulated by criteria that have to be met, and so first to come in with a new curriculum adds a huge burden on our already-burdened teaching system, so we have to be very sensitive to that.

So what I think is a good approach is a more integrated approach and it needs to be over the course of the students' experience in junior high and high school. It can't be you have a speaker come in and you give a talk in the auditorium and leave. It needs to be integrated into health sciences, P.E., social sciences, and be science-driven. And I think that is where we have a lot more that we can do to make this better to where good decision-making is part and parcel to drug prevention.

And we all know that the adolescent brain is a different brain than the adult brain, and the capacity to make decisions is not the same. And we all know that the frontal cortex is not developed in children until they are 21 or 23. And so we need to have empirically based curriculum that will reach the adolescent in terms of these decision-making processes based on their neurobiology.

Mr. BERA. What would you say the right age for intervention is if we were to—elementary school?

Dr. NAPIER. Elementary school.

Mr. BERA. Yes. Okay.

Dr. NAPIER. Absolutely. And also I think it is important to think about in urban situations where students drop out of school, you want to reach those children before the dropout rate start to escalate. So again, that means starting them sooner.

Mr. BERA. I am out of time but I don't know if Sergeant Crawford or Dr. London——

Chairman BUCSHON. We are going to do another round of questioning if you have more questions if you can stay.

Mr. BERA. Okay. Fabulous, thank you.

Chairman BUCSHON. Yes. And so we are going to do a second round for those who can stay.

For whatever it is worth, I have four kids aged 20 to age 9, and Dr. Napier, maybe you can comment on this, but even though us as parents think we are the ones that have the most influence over the direction that our children take, in actual fact, their peer group has probably more overall effect on what they do every day than we do. And so I found it interesting when you are talking about having volunteer children or high school kids who, rather than having the county sheriff come out and talk about the Just Say No program and things like that, which also needs to be done, is working on designing programs that actually get people of the same age that are willing to interact at a peer-group level, to try to affect that. Do you think this something that would be effective?

Dr. NAPIER. Well, I think there are a couple points here that you made that are really important to bring home. Number one is the influence of peers. Now, we all know even in basic research, which is what I do, that people, places, and things influence the way an

animal—in my case, the rat—will make decisions about taking drugs and the cues associated or the things that are associated with the drug-taking has a huge influence on subsequent drug-taking. Now, you superimpose that on the brain of an adolescent, which is wired to be more sensitive to these environments and to their friends. That is the way their brain is made, and then they have hormones.

So all of these factors sort of escalate into this thing we call a teenager that greatly influences how they are making choices and who is going to inform them about the kind of choices they make. So that is why I do agree that getting younger people that may relate to the students in a more—level that they can sort of gear into is something that we could exploit more.

But I don't want it necessarily to be teenagers. My suggestion had to do—these would be graduate students and medical students, so they are in their mid-20s that would be able to come back to junior high and high schools, and they would have a science-based knowledge that then could be incorporated into whatever curriculum is being implemented by that particular school.

Chairman BUCSHON. I think that is just a fascinating subject because, like I said, have four kids, and like cigarette smoking, for example, there are studies on why almost every teenager at some point tries cigarettes but only a certain percentage of them actually become chronic smokers. And the reason they originally try it is because of peer pressure and peer group influence. Even in contrast to the factual data that shows that cigarette smoking in the long run is bad for your health, most people are not influenced by that when they try it. But why some people will become chronic cigarette smokers and others don't is fascinating.

And that in meth, my understanding is you don't have a second chance a lot of times. I mean once people start to get on meth with the changes Dr. London has described, you may have a higher percentage of chronic users of methamphetamine versus cigarettes, for example, and that is why peer group stuff, I think, may be important.

Dr. London, once these changes happen, are these permanent? I mean are these reversible?

Dr. LONDON. There have been studies with positron emission tomography on both the metabolic pattern in the brain, glucose metabolism, and also some of the dopamine receptor markers and structural markers. And in fact what we found is that decrease in the volume of the striatum, which is a part of the brain that is very important in reward and motor function, does recover to some extent. And there can be recovery in as early as a month of abstinence.

With respect to some of the chemical markers, it takes a very, very long time to reach recovery and it—at two and a half years after cessation of chronic methamphetamine use, one area of the brain that is affected, the thalamus, shows complete recovery where another area of the brain, the striatum, does not show complete recovery.

So it is a very long drawn-out process, and it can be very frustrating for the addict who is approaching a treatment episode because what happens is that these people, as a result of the struc-

tural and biochemical changes that are very long-term, are very frustrated when they are in treatment because the treatments are behavioral treatments, where they have to exercise some kind of self-control in thought-stopping, and they are really not very able.

So I think educating the client in addition to ultimately developing some medications that can help the cognitive therapy along would be useful.

Chairman BUCSHON. Yes, it seems to me from what you just said is that there will have be medication in addition to other therapy if we are going to fix this for people who are chronically addicted to methamphetamine. And so that is why ongoing research is so critical to try to solve this problem.

We will go to Mrs. Lummis for her questions.

Mrs. LUMMIS. Thank you, Mr. Chairman.

I sure appreciate the panel's attendance today, your knowledge, your information.

As you have testified, there was a wave of addiction going from the West Coast to the East Coast. It swept across my state of Wyoming into the Midwest leaving almost a lost generation where children of addicts are being raised by their grandparents. People in their 30s and early 40s are struggling with addiction. It was staggering and has affected every family, including my own. So the work you are doing is just critical to helping the recovery of this literal generation that was lost to this addiction that are now adults, young adults.

Dr. London, I believe it was you that mentioned that the striatum does not recover after two and a half years whereas the thalamus does. Can you tell me what the striatum does?

Dr. LONDON. Yes, the striatum has multiple functions. On the most superficial level we think about the striatum as being important in motor control. The striatum is the area—one of the areas that receives a very, very rich enervation of dopamine neurons from the mid-brain, and it is those neurons that degenerate in the pathology of Parkinson's disease.

Mrs. LUMMIS. Oh.

Dr. LONDON. The striatum has other functions as well, and dopamine signaling in the striatum is very important for decision-making. We have recently published a report showing that there is a very, very strong relationship between dopamine receptors in the striatum and the function of the prefrontal cortex when a person is deciding to take risk or not take risk. And so what you see with the damage to the dopamine system in the striatum is a situation in which the addict really has a difficult time making the right decision to go to sobriety. It is as if the drug—the effects of drug-taking reinforce the addiction.

Mrs. LUMMIS. So given that physiological understanding, is there some research that is being undertaken that can affect the dopamine receptors' ability to recover?

Dr. LONDON. We have some very exciting findings that are preliminary—strong but preliminary. What we have known is that even though the dopamine receptors show down-regulation in methamphetamine dependence, treatments that are aimed directly at the dopamine receptors, agonist drugs that would make the re-

ceptors work, don't really work very well for methamphetamine dependence.

Mrs. LUMMIS. Okay.

Dr. LONDON. Maybe that is because the receptors are down-regulated so much or the ones that remain are not functional. And what you really need are fresh dopamine receptors. Using a different approach, we have an ongoing study where exercise, moderate exercise in a very controlled study, has shown a very remarkable up-regulation of the dopamine receptors in—over the course of eight weeks. And this is very exciting and this might make that system more amenable to all kinds of therapy, be it cognitive, behavioral, or pharmacological.

Mrs. LUMMIS. Thank you, Dr. London.

Would anybody else in the last half-minute I have care to weigh in on the dialogue that I have been having with Dr. London?

Well, I am deeply grateful for your testimony here today, your work on this subject. It is enormously important to my state of Wyoming and to that wave of young people now in their 30s and 40s that were tremendously affected.

And I would just add that on the Indian reservations in Wyoming and elsewhere, the Mexican drug cartels chose to set up base camps, and between the grinding poverty on reservations and what may be some genetic component to the addiction, they have been tremendously devastating to our Native American population as well. So the work you are doing is just tremendously critical and I thank you very much.

And Mr. Chairman, I thank you and yield back.

Chairman BUCSHON. Since I missed that you came in during the first round, we have done a second round of questioning, so if you have other questions, I think it would be appropriate to allow you another five minutes for a second line if you have any other questions.

Mrs. LUMMIS. Well, Mr. Chairman, I would just use my time to ask the members of the panel, is there information that you would like to share with us that you haven't been able to convey yet in your testimony? I want to give you a very open opportunity to make some points that previously have not been made that you don't want to leave this room without making.

Dr. NAPIER. I can weigh in first here. I think this is an incredibly complex scenario and we are not going to find a resolution probably in my lifetime. But I do think what is really, really important is to consider this both on the supply and the demand side and both in terms of prevention and then adequate treatment, but to understand that treatment may have to do—have—will have to be highly individualized, because depending on if we catch someone early in their use and exploration of methamphetamine versus someone who has used it for a protracted period of time, that is a different brain state. That is a different individual.

If we catch them during early withdrawal periods versus someone like Dr. London was talking about two and a half years out when they are even motivated to quit using the drug and they are fighting against their own brain biology that is influencing their decision-making processes, it is tapping into the brain that actually—those brain regions that make decisions that succumb to

methamphetamine. So it is a double whammy. And I think we have to have an appreciation for that.

And I think that is why this multidisciplinary, highly integrative approach that is going to start young—and understand that we have got baby boomers now that are moving into retirement and they are going to be having drug abuse issues that we are going to have to deal with as a society as well.

So I do believe it is going to take a multidisciplinary across institutes, across states and an education end and a treatment end for us to really make a dent in this problem.

Mrs. LUMMIS. Dr. London?

Dr. LONDON. We haven't said much about the need for an integrated approach in pushing the technology with respect to this problem. And I think we are—especially with respect to the interest of this particular Subcommittee, science, technology, and mathematics can really be put into the arena to move the field forward.

Particularly, we could talk about the combination of nanotechnology with cutting-edge neuroscience methods. That combination could be very powerful with nanotechnology giving you dynamic chemical measurements in very, very discrete areas of the brain. Already there is cutting-edge electrophysiological recording that is being combined in animals with electrochemical detection of glutamate, dopamine, and other neurotransmitters that can give us a moment-to-moment readout of how neurotransmitter signaling can modulate coordinated neural activity.

And so I think that we need to keep in mind that we really need better tools, and some of these tools could be within our imaging area. We need to have better radio tracers that will selectively allow us to evaluate chemical changes in the brain.

Mrs. LUMMIS. May I interrupt you there?

Dr. LONDON. Of course.

Mrs. LUMMIS. Where is this research being done now and with regard to, for example, nanotechnology, radio transmitters? Is it being done? Where? And is Congress helping fund that?

Dr. LONDON. There is a California Nanotechnology Institute that is located at UCLA, and I believe it really was an initiative that has been helped by Congress, although I am not sure of the specifics there.

What we also really need are education programs for the specialist. For example, there is a dearth of radiochemists in the world, and it is a specialty that is really required to give us those molecules that would allow us to do these noninvasive measurements.

Mrs. LUMMIS. Where are they trained? Who trains radiochemists?

Dr. LONDON. There is a program at Johns Hopkins, there is a program at the University of Michigan, the Karolinska Institute, the National Institutes of Health Intramural programs.

Mrs. LUMMIS. Thank you. And I want to thank all of you for your testimony.

Chairman BUCSHON. I am going to allow the other two that didn't get a chance to give their final comments some time to follow up with what Mrs. Lummis asked to just comment on what you

might want to say to the Committee that you didn't get a chance in your testimony starting with Sergeant Crawford.

Sgt. CRAWFORD. At first when I saw the list of folks that were going to be here to testify, it was kind of one of those situations where I am really glad I slept at a Holiday Inn Express last night because doctor, doctor, doctor, sergeant.

But I will say one of the things that law enforcement, not only within our state but across the country, we're very cognizant that prevention programs are important. And having come from a background within the State Police where I worked in our problem-oriented policing section, which focused on community problems and what do we do to help solve those problems from our aspect, I think it is important that we have—you have heard interdisciplinary all morning this morning, and I think that is such an important thing that it is so important to get the medical community, the treatment community, the prevention community, and law enforcement together so that we can come in from an interdisciplinary.

Because I am pretty good at coming into your junior high class, the drug and alcohol or the health class and I can give them a good one-day program, but if we don't have something leading up to that and we don't have something after that to focus their attention, then I think it is not a waste of an hour but it is not as productive as it could be.

And so from our perspective, while we are big into the enforcement side obviously and do our job to enforce the laws that are on the books, we do also focus on—within our section our mission statement is about education, prevention, and enforcement. And we keep them in that order because we know with education and—I am sorry, education, partnerships, and enforcement. With the education and partnerships that we create in the communities that we work, our enforcement efforts are going to be so much better.

So the Meth Watch kits, even though we didn't get the turnaround necessarily from the meth cooks we did, we got great relationships that we built within the communities that offer us very good information about what is going on and where to focus our enforcement efforts. So I think those—the interdisciplinary is very important.

Chairman BUCSHON. Dr. Maxwell?

Dr. MAXWELL. Thank you. In listening to the testimony and in preparing my presentation, I think one of the things that is very, very important is we have a lot of data out there but it is accessing it and thinking about it and do things change as we do bring research? What does that mean for the user population or the statistics on what sources—are they shifting from methamphetamine to something else?

It is always looking at little pieces of data, but when I start pulling it together and I think particularly with the Committee's support for going much further in dealing with methamphetamine, we ought to be able to sit down and say we have made progress here, we are not making progress there.

One of the problems that we have now is that after the pseudoephedrine limitations started, everybody declared we had won the war and gone home and we don't need any more specialized methamphetamine treatment. They weren't looking at the

data. So I am a data nerd but I think it tells us often where we need to go and where we have missed the ball.

Chairman BUCSHON. Well, I would like to thank all the witnesses again for their testimony. This is been a fascinating hearing. And I think from my perspective I do think from a research perspective it is very important that we continue to make sure we have Federal support for basic research in all of these areas, as well as other—through National Science Foundation, which is under the purview of this Subcommittee and other agencies such as the NIH.

I also think it is important probably to have a national strategy on this type of work because in Indiana if you put laws in place for one thing, and the states around you don't, or if the States around you put a law in and you don't, it just gets transferred across the state, especially in Evansville where we have Illinois, Kentucky, and Indiana. So I do think it is appropriate to discuss the national strategy and attack this particular issue in my opinion.

With that, that ends the hearing and the hearing is adjourned.

[Whereupon, at 11:33 a.m., the Subcommittee was adjourned.]

Appendix I

Answers to Post-Hearing Questions

ANSWERS TO POST-HEARING QUESTIONS

Responses by Dr. Edythe London

HOUSE COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY

"Meth Addiction: Using Science to Explore Solutions"

Questions for the Record, Edythe D. London, Ph.D., the Thomas and Katherine Pike Professor of Addiction Studies, Director of the UCLA Laboratory of Molecular Neuroimaging, David Geffen School of Medicine, University of California at Los Angeles

Questions submitted by Rep. Larry Bucshon, Chairman
Subcommittee on Research and Technology

1. Individuals addicted to methamphetamines often have co-occurring dependence on other drugs such as prescription opioid pain killers or alcohol. According to the 2012 National Survey on Drug Use and Health by the Substance Abuse and Mental Health Services Administration (SAMHSA), 2.8 million individuals are addicted or abuse alcohol in combination with other addictive substances, such as methamphetamines. For individuals who are methamphetamine dependent, is it important to treat the other co-occurring addictions when they are present?

Co-occurring addictions can have notable effects on the success of addiction treatment. For example, comorbid alcohol use is a risk factor for relapse among cocaine dependent individuals (Mckay et al., 1999; Shah et al., 2006; Poling et al., 2007). The use of other addictive drugs, such as alcohol, can potentially reduce inhibitory control and increase risky behaviors, which may further erode the ability of the methamphetamine-dependent individual to maintain abstinence. Other drugs that are frequently taken alongside methamphetamine may also serve as potent triggers/cues that promote craving for methamphetamine (Volkow et al., 2009). Finally, there is evidence that methamphetamine abusers suffer from a "reward deficiency syndrome", in which one rewarding substance, such as food or another drug, is substituted when methamphetamine is not available (Zorick et al., 2011). Therefore, abstaining from methamphetamine during treatment may lead to an increased desire for alcohol or other drugs, exacerbating a co-occurring addiction. Accordingly, several lines of evidence indicate that the treatment of a co-occurring addiction is likely to improve the methamphetamine user's ability to achieve long-term abstinence.

2. Does the presence of a co-occurring addiction, such as alcohol dependence, make recovery from methamphetamine dependence more complex and challenging? Does the presence of co-occurring alcohol dependence increase the risk for dangerous behaviors, such as violent crime? Or suicide?

Research has suggested that multiple dependencies may present a barrier to successful treatment intervention (e.g., Downey et al., 2000; Bovasso et al., 2003; Williamson et al., 2006). Notably, primary methamphetamine users averaged 6.3 classes of other drugs in addition to meth (Brecht et al., 2005). Research results also support the clinical and treatment implications of polydrug use, in terms of greater psychopathology (Beswick et al., 2001; Sumnall et al., 2004; Booth et al., 2006; Malcolm et al., 2006; Medina et al., 2007), higher levels of health risk behaviors (Patterson et al., 2005), and difficulties in engaging in treatment (John et al., 2001). Among methamphetamine users, secondary use of cocaine or heroin is a predictor of failure in completing treatment (Brecht et al., 2005).

Methamphetamine abuse is associated with a propensity for irritability, hostility, and aggression, resulting in high rates of interpersonal violence, emergency department/ trauma center visits, assault, weapons charges, and ultimately, public health and safety burdens (reviewed in Payer et al., 2011). The use of alcohol, however, is more strongly associated with violence than methamphetamine use (Martin et al., 2009). In both methamphetamine-dependent and alcohol-dependent research participants, alexithymia is greater than in healthy control subjects, meaning that the addict participants are less conscious of their feelings and have more difficulties identifying and expressing their feelings than the control subjects (Bochand and Nandrino, 2010; Payer et al., 2011). Inasmuch as alexithymia scores are correlated with measures of aggression in methamphetamine users, a potentially exacerbated alexithymia due to alcohol dependence logically could lead to heightened violence. It therefore seems likely that methamphetamine abusers who are also dependent on alcohol are more likely than abusers of methamphetamine alone to commit violent crimes or suicide. However, to our knowledge, studies directly comparing rates of violent crime and suicidality among alcoholic methamphetamine-dependent individuals with those in individuals who abuse only methamphetamine (but are not alcohol-dependent) are lacking.

3. We understand that one of the challenges to successful addiction treatment is the willingness or ability of patients to take their medication as prescribed. How important is medication adherence in addiction treatment? Are there medications available for the treatment of addiction that helps address the issue of non-adherence?

Addiction is a chronic disease, and chronic illnesses commonly are treated with long-term pharmacotherapy. To their own detriment, however, approximately 50% of patients do not adhere to the medication regimens prescribed for them (Brown et al., 2011). Estimates of non-adherence are higher for some psychiatric disorders (Julius et al., 2009), and substance abuse is generally associated with poorer medication adherence among psychiatric patients (Sowers et al., 1999; Weiss, 2004).

While there are no approved medications for the treatment of stimulant dependence, there are approved medications for opioid dependence and alcohol dependence. Adherence to the medication regimen has proven to be effective, and non-adherence can be a reason for treatment failure. One of the available medications is naltrexone, and depot naltrexone is available to solve the problem of non-adherence to taking oral naltrexone. Depot naltrexone is approved for the treatment of both alcohol dependence and opioid dependence. Approval is now being sought from the FDA for an implantable form of buprenorphine, probuphine, for the treatment of opioid dependence. Probuphine as a 6-month duration of action, and probuphine implants offer the potential for enhanced delivery of effective opioid substitution treatment while minimizing risk for abuse of the medication (White et al., 2009). Injectable forms of buprenorphine with one-week and one-month durations are under development.

4. The recently published SAMHSA survey estimates that 2 million Americans are dependent on opioids, including heroin. Heroin dependence has more than doubled since 2002 to almost half a million heroin addicts. Are there medications that can successfully treat opioid dependence? Are these medications routinely incorporated into treatment of opioid dependence when it co-occurs with methamphetamine dependence? Would it be beneficial to do so?

There are medications that effectively treat opioid dependence. These include replacement therapy with methadone or buprenorphine, and antagonist treatment with naltrexone. While these medications, especially replacement therapy, are the mainstay for

treatment of opioid dependence, there is little documentation regarding whether they are incorporated in treatment of addicts who have dual dependencies on opioids and methamphetamine. This is because, while there is a high incidence of co-morbid methamphetamine and opioid abuse, methamphetamine abusers who use opioids typically do so to counteract the negative effects associated with a prolonged methamphetamine binge, and therefore are less likely to use opioids when not using methamphetamine. Opioid addicts typically use methamphetamine only to counteract the sedating effects of the opioids and generally do not come to treatment for methamphetamine dependence.

While physicians specializing in addiction medicine, would treat opioid dependence (most likely with preparations of buprenorphine or naltrexone) while treating co-occurring methamphetamine dependence, most patients with methamphetamine use disorders do not see addiction doctors, but are enrolled in non-medical programs. Often these are behavioral treatment programs that do not favor medical treatment; therefore, it is not routine to incorporate medications to treat opioid dependence into treatment for combined opioid + methamphetamine dependence. Nonetheless, as medications to treat opioid dependence are of benefit with or without co-occurring methamphetamine dependence, incorporating their use in a treatment program for patients with dual addictions would be helpful. Moreover, research suggests that both naltrexone and buprenorphine maybe helpful in treating methamphetamine use disorders (Cottencin et al., 2012; McCann, 2008).

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Responses by Dr. Jane Maxwell

HOUSE COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY

"Meth Addiction: Using Science to Explore Solutions"

Questions for the Record, Jane Maxwell, Ph.D., Senior Research Scientist, Center for Social Work Research, The University of Texas at Austin

Questions submitted by Rep. Larry Bucshon, Chairman, Subcommittee on Research and Technology

1. Individuals addicted to methamphetamines often have co-occurring dependence on other drugs such as prescription opioid pain killers or alcohol. According to the 2012 National Survey on Drug Use and Health by the Substance Abuse and Mental Health Services Administration (SAMHSA), 2.8 million individuals are addicted or abuse alcohol in combination with other addictive substances, such as methamphetamines. For individuals who are methamphetamine dependent, is it important to treat the other co-occurring addictions when they are present?

   Response: In my study of methamphetamine-dependent users in treatment in Central Texas, I found they had used many substances in their lifetimes. However, their favorite drugs to use with methamphetamine included alcohol (42%), cannabis (38%), powder cocaine (20%), crack cocaine (19%), heroin (19%), and alprazolam (18%). Powder and crack cocaine give similar "highs" as methamphetamine but do not last as long and are more expensive, but they would use it when they could afford it. The other drugs, including alcohol, were used to take "the edge" off the effects of methamphetamine and were particularly used to "come down" from a binge. In my study, 83% had binged for over 48 hours in the six months prior to the interviews, so the "downers" were used to calm them down and enable them to sleep.

   Clearly it is important to treat all of their drug problems, as they used all these drugs in combination, and if you took away methamphetamine and left the other drugs, they would become more addicted to some of them unless they entered treatment for addiction to all substances, not just methamphetamine. Treating all the drugs is the common approach.

2. Does the presence of a co-occurring addiction, such as alcohol dependence, make recovery from methamphetamine dependence more complex and challenging? Does the presence of co-occurring alcohol dependence increase the risk for dangerous behaviors such as violent crime? Or suicide?

   Response: Most of the individuals I interviewed were addicted to methamphetamine and alcohol was a drug they could use to lessen some of the effects of the methamphetamine. However, they had been exposed to alcohol use as youngsters. Ninety-five percent reported someone in their family had a drinking problem, 89%

reported someone in the family had a drug problem, and 91% reported someone had a psychiatric/emotional problem. As minors, 41% reported "serious drinking" with relatives and 34% "did drugs" with relatives.

I did not query about dangerous behaviors, but found that when asked about the biggest risks of methamphetamine use, 16% reported aggressive/violent behavior, 38% reported paranoia, 20% reported social/relationship problems, and 17% reported psychosis; so yes, they were worried about dangerous behaviors. The most common risks of methamphetamine use cited were in the areas of damage to their brains: mental health problems, such as anxiety, depression, paranoia, social relationships; and problems with other aspects of their lives that resulted from their drug use, including problems with social services, legal, and employment.

3. We understand that one of the challenges to successful addiction treatment is the willingness or ability of patients to take their medication as prescribed. How important is medication adherence in addiction treatment? Are there medications available for the treatment of addiction that helps address the issue of non-adherence?

   Response: While we have drugs that can treat opioid addiction and alcoholism, as the testimony from the panelists showed, we still are looking for drugs that will be effective for methamphetamine and cocaine. For opiates and alcohol, naltrexone is an antagonist that blocks opioid receptors, so an individual cannot get "high" after using and it reduces craving for alcohol and decreases motivation to drink and the amount drunk. Some of these drugs can be costly, which limits their availability either as private patients or as patients in publicly-funded programs. One of the advantages of naltrexone is that a dose can be injected every 30 days, so the craving is reduced and the heroin addict cannot get "high." The 30 day window provides time to work with the patient and counter the cravings that can drive them back to using drugs.

   In addition to the 30-day dose of naltrexone, there is a pill form that can be taken daily. Other mediations that are FDA-approved for opiates include buprenorphine, either as a daily pill or as a film like a breath film. The "duo" product is buprenorphine and naloxone, which is a partial agonist that will cause withdrawal if the patient tries to use heroin on top of the buprenorphine. There is also a "mono" form of buprenorphine which does not have the safety feature of the naloxone and it is subject to abuse since it can be injected. Buprenorphine's main strength is that any doctor who undergoes training that meets federal criteria can prescribe it and the patient can fill it at his or her own drug store and take the medication at home.

   Methadone, which, if properly titrated, will prevent withdrawal but also avoid letting the patient get high, has been well studied and used for many years. It requires a daily liquid dose and patients must start taking the medication in a licensed methadone program and if they do well in their treatment and make progress in building a drug-free life, they can receive some take-home doses. The

take-home doses are a strictly limited privilege for the most compliant patients.

FDA-approved drugs for alcohol include naltrexone (1 pill per day or the 30 day injection) or daily doses of acamprosate, topiramate, or disulfiram. So we have some medications for opioids and alcohol and more will be available for FDA approval as research continues.

4. The recently published SAMHSA survey estimates that 2 million Americans are dependent on opioids, including heroin. Heroin dependence has more than doubled since 2002 to almost half a million heroin addicts. Are there medications that can successfully treat opioid dependence? Are these medications routinely incorporated into treatment of opioid dependence when it co-occurs with methamphetamine dependence? Would it be beneficial to do so?

   Response: In response to your questions about successful medications to treat opiate dependence, see #3. These medications are very successful. I doubt the medications for opioids would routinely be used for patients whose primary problem is with methamphetamine unless they met the criteria for dual addiction. As the testimony showed, the new medications are successful in stopping craving for alcohol or heroin but they were not meant for methamphetamine. Drugs to help with methamphetamine craving are in development; they work on different parts of the brain.

   We are making progress, but not as quickly as I would like. As the efficacy of these medications becomes better known, we will see more and more programs adopt medication-assisted therapies.

Responses by Dr. Celeste Napier

HOUSE COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY

"Meth Addiction: Using Science to Explore Solutions"

Questions for the Record, T. Celeste Napier, Ph.D., Director, Center for Compulsive Behavior and Addiction, Professor, Departments of Pharmacology and Psychiatry, Rush University Medical Center

Questions submitted by Rep. Larry Bucshon, Chairman, Subcommittee on Research and Technology

1. Individuals addicted to methamphetamines often have co-occurring dependence on other drugs such as prescription opioid pain killers or alcohol. According to the 2012 National Survey on Drug Use and Health by the Substance Abuse and Mental Health Services Administration (SAMHSA), 2.8 million individuals are addicted or abuse alcohol in combination with other addictive substances, such as methamphetamines. For individuals who are methamphetamine dependent, is it important to treat the other co-occurring addictions when they are present?

Answer: Yes, methamphetamine addicts with co-occurring disorders need comprehensive treatment that addresses the physical and psychological disorders that may be uniquely associated with the drugs that are being abused. The changes that are imposed on the brain by co-occurring addictions are different from those imposed by any one of the individual drugs; therefore, individualized treatment programs that include a combination of behavioral therapy and pharmacological therapy is often required.

2. Does the presence of a co-occurring addiction, such as alcohol dependence, make recovery from methamphetamine dependence more complex and challenging? Does the presence of co-occurring alcohol dependence increase the risk for dangerous behaviors such as violent crime? Or suicide?

Answer: A co-occurring addiction can make recovery more complex and challenging. Alcohol dependence, itself, if untreated raises the risk of suicide and violence. When combined with methamphetamine that risk rises even further.

3. We understand that one of the challenges to successful addiction treatment is the willingness or ability of patients to take their medication as prescribed. How important is medication adherence in addiction treatment? Are there medications available for the treatment of addiction that helps address the issue of non-adherence?

Answer: Treatment does <u>not</u> have to be voluntary to be effective. While terms like "willingness" were once thought essential, we now have NIDA-outlined guidelines that help us understand addiction treatment based on scientific research. Excerpts from the NIDA website illustrate these points:

Principles of Effective Treatment

Scientific research since the mid–1970s shows that treatment can help patients addicted to drugs stop using, avoid relapse, and successfully recover their lives. Based on this research, key principles have emerged that should form the basis of any effective treatment programs:

- Addiction is a complex but treatable disease that affects brain function and behavior.
- No single treatment is appropriate for everyone.
- Treatment needs to be readily available.
- Effective treatment attends to multiple needs of the individual, not just his or her drug abuse.
- Remaining in treatment for an adequate period of time is critical.
- Counseling—individual and/or group—and other behavioral therapies are the most commonly used forms of drug abuse treatment.
- Medications are an important element of treatment for many patients, especially when combined with counseling and other behavioral therapies.
- An individual's treatment and services plan must be assessed continually and modified as necessary to ensure that it meets his or her changing needs.
- Many drug–addicted individuals also have other mental disorders.
- Medically assisted detoxification is only the first stage of addiction treatment and by itself does little to change long–term drug abuse.
- Treatment does not need to be voluntary to be effective.
- Drug use during treatment must be monitored continuously, as lapses during treatment do occur.
- Treatment programs should assess patients for the presence of HIV/AIDS, hepatitis B and C, tuberculosis, and other infectious diseases as well as provide targeted risk–reduction counseling to help patients modify or change behaviors that place them at risk of contracting or spreading infectious diseases.

4. The recently published SAMHSA survey estimates that 2 million Americans are dependent on opioids, including heroin. Heroin dependence has more than doubled since 2002 to almost half a million heroin addicts. Are there medications that can successfully treat opioid dependence? Are these medications routinely incorporated into treatment of opioid dependence when it co-occurs with methamphetamine dependence? Would it be beneficial to do so?

Answer: Co-occurring addictions complicate diagnoses and treatment designs, and often require more intense interventions. However, these interventions often do include those used for each drug, as overviewed below:
Current treatments for opioids include methadone, buprenorphine and, for some individuals, naltrexone are effective medications for the treatment of opiate addiction. Acting on the same targets in the brain as heroin and morphine, methadone and buprenorphine suppress withdrawal symptoms and relieve cravings. Naltrexone works by blocking the effects of heroin or other opioids at their receptor sites and should only be used in patients who have already been detoxified. Naltrexone is not as widely used as the other medications, due in large part to compliance issues. All medications help patients disengage from drug seeking and related criminal behavior and become more receptive to behavioral treatments.
According to NIDA, the most effective treatments for methamphetamine addiction are behavioral therapies, such as cognitive-behavioral and contingency-management interventions. For example, the Matrix Model, a 16-week comprehensive behavioral treatment approach that combines behavioral therapy, family education, individual counseling, 12-Step support, drug testing, and encouragement for non-drug-related

activities, has been shown to be effective in reducing methamphetamine abuse. Contingency management interventions, which provide tangible incentives in exchange for engaging in treatment and maintaining abstinence, have also been shown to be effective. Motivational Incentives for Enhancing Drug Abuse Recovery (MIEDAR), an incentive-based method for promoting cocaine and methamphetamine abstinence, has demonstrated efficacy in methamphetamine abusers through NIDA's National Drug Abuse Clinical Trials Network.

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