

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

“Ecstasy Abuse and Control”

Statement for the Record

**Alan I. Leshner, Ph.D.
Director, National Institute on Drug Abuse**

**Before the
Senate Committee on Governmental Affairs**

**Monday, July 30, 2001
Washington, D.C.**

Mr. Chairman, and Members of the Committee, thank you for inviting me to participate in this important and timely hearing on MDMA. I am pleased with the Committee's interest in this topic and for providing the National Institute on Drug Abuse (NIDA) this opportunity to share what the scientific community has come to learn about this illegal drug, commonly referred to as "Ecstasy" or "E." It is particularly timely, given that a little over a week ago, NIDA sponsored the first major international scientific conference on this topic on the NIH campus, to discuss the latest findings and to have the world's leading drug abuse researchers help identify future research directions. There is now tremendous interest in this topic. Over 500 people attended the event.

I would like to start out by providing you with a brief overview of MDMA. 3,4-methylenedioxymethamphetamine, which is commonly abbreviated and referred to as MDMA or "Ecstasy," is an illegal drug that has characteristics of both stimulants and hallucinogens. While MDMA does not cause overt hallucinations, many people have reported distorted time and perception while under the influence of the drug. It causes an amphetamine-like hyperactivity in people and animals and like other stimulants, it appears to have the ability to cause addiction. It increases heart rate, blood pressure and can disable the body's ability to regulate its own temperature. Because of its stimulant properties, when it is used in club or dance settings, it can enable users to dance vigorously for extended periods, but can also lead to severe rises in body temperature, what is referred to as hyperthermia, as well as dehydration, hypertension, and even heart or kidney failure in particularly susceptible people.

MDMA is a synthetic drug, meaning it is manufactured, in this case illegally. It is typically produced in capsule or tablet form and is usually taken orally, although there are some documented cases that it is being administered by other routes, including injection and snorting. MDMA's acute effects typically last from three to six hours depending on the dosage, with the reported average dose of MDMA being between one and two tablets, with each containing approximately 60-120 mg of MDMA. Importantly, in many situations Ecstasy tablets contain not only MDMA, but a number of other drugs or drug combinations that can be harmful as well. MDMA appears to be well absorbed from the gastrointestinal tract, and peak levels are reached in about an hour.

MDMA works in the brain by increasing the activity levels of at least three neurotransmitters: serotonin, dopamine, and norepinephrine. Much like the way amphetamines work, MDMA causes these neurotransmitters to be released from their storage sites in neurons resulting in increased brain activity. Compared to the very potent stimulant, methamphetamine, MDMA causes greater serotonin release and somewhat lesser dopamine release. Serotonin is the neurotransmitter that plays an important role in regulation of mood, sleep, pain, emotion, appetite and other behaviors. By releasing large amounts of serotonin and also interfering with its synthesis, MDMA causes the brain to become significantly depleted of this important neurotransmitter. As a result, it takes the human brain time to rebuild its serotonin levels. For people who take MDMA at moderate to high doses, depletion of serotonin may be long-term. These persistent deficits in serotonin are likely responsible for many of the long-lasting behavioral effects that the user experiences and what concerns us most about this drug.

MDMA is not a benign drug. In fact, all of the studies conducted to date in both animals and more recently in humans, confirm that club drugs, particularly MDMA, are not harmless “fun party drugs” as they are often portrayed. While users of club drugs often take them simply for energy to keep on dancing or partying, research shows these drugs can have long-lasting negative effects on the brain that can alter memory and other behaviors. There is substantial evidence to show that MDMA damages brain cells. Within the scientific community we can not say with absolute certainty how and to what extent the damage it can actually cause, but there is across-the-board agreement that brain damage does occur.

We know that even one dose of MDMA (10 mg in rats) has the ability to decrease serotonin levels for up to 2 weeks. Research in animals has unequivocally shown that MDMA is neurotoxic, meaning it literally damages brain cells. It is only recently with the advent of new brain imaging technologies that we are now beginning to see and understand the potential neurotoxic effects of MDMA in humans.

Essentially there are two ways that researchers are able to measure the effects of MDMA in humans. One is by looking at neurofunctional measures, which tell us how the brain is working. The other is to look at neurocognitive measures, which demonstrates the output of the brain, or how the brain is performing.

Using brain imaging and other state-of-the art equipment, researchers are able to show us in intricate detail how the brains of MDMA users differ from those that have not used this drug. We know from imaging that cerebral blood flow (CBF) is affected by

MDMA use (see FIGURE 1). We also have evidence from brain images that MDMA abusers may have fewer serotonin producing neuronal processes in the brain than non-users. In fact this is such a powerful and true-to-life example that we have developed an education campaign around these brain images. Individuals are able to literally see that the brain has changed from MDMA use.

The other way researchers are determining the effects of MDMA in humans is by looking at neurocognitive measures, such as standardized tests of mental abilities. A number of studies have consistently shown that repeated MDMA exposure is associated with significant impairments in visual and verbal memory.

In short, there is now a large body of evidence that links heavy and prolonged MDMA use to confusion, depression, sleep problems, persistent elevation of anxiety, aggressive and impulsive behavior and selective impairment of some working memory and attention processes.

The harm that MDMA may potentially cause is not limited to the user alone. Findings released in May of this year in the Journal of Neuroscience found the first evidence that prenatal use of MDMA may cause memory loss and other impairments in offspring. Rats that were exposed to MDMA during stages of brain development (similar to brain and central nervous system development time frames in humans) were found to have memory and learning deficiencies.

One encouraging thought to keep in mind as we unravel the effects of this drug on the human brain is not to underestimate the amazing capabilities of the brain and its ability to compensate and adjust to stressors. For example, there is some new research emerging on other drugs of abuse, such as methamphetamine, a drug structurally similar to MDMA, that is showing that neuronal functions and systems that have been damaged by chronic drug use can recover. This is a positive and hopeful note, though it is too soon to determine how functional the brain cells actually are after recovery and to determine if an individuals' cognitive deficits resulting from the initial damage are completely reversed.

One of the more alarming facts about this drug is that despite its known detrimental consequences, there are increasing numbers of students and young adults who continue to use MDMA in increasingly higher doses. Several of our Nation's top monitoring mechanisms, including NIDA's long-standing national survey of drug use among 8th, 10th and 12th graders, Monitoring the Future (MTF), and our Community Epidemiology Work Group (CEWG) are reporting that the use of club drugs, particularly MDMA, is increasing in popularity among high school and college students. There are also clear indicators that MDMA and other so called "Club Drugs" such as GHB, Rohypnol, and methamphetamine, are no longer just being used in "night clubs" and "rave settings."

Results from the 2000 MTF indicate that the use of MDMA increased among students in all three grades from 1999 to 2000. For 10th and 12th graders, this is the second consecutive year MDMA use has increased. But this year the drug has also

spread to 8th graders. Lifetime use of MDMA among 8th graders increased from 2.7% in 1999 to 4.3% in 2000. Among 12th graders, lifetime use increased from 8.0% to 11.0% -- one-in-nine seniors have tried ecstasy in their lifetime. In addition to the overall increases in use, perceived availability of MDMA increased among seniors from 40.1% to 51.4%. African Americans, however, show considerably lower rates of MDMA use than do either Whites or Hispanics (1.3 percent versus 7.6 percent and 10.6 percent, respectively, for past year use among seniors in 2000).

Ethnographic data from NIDA's Community Epidemiology Workgroup meeting in June of this year showed that MDMA use is spreading from raves and dance parties to high schools, colleges, and other social settings frequented by youth and young adults. Although, compared to other drugs, the number of cases of MDMA use remains relatively small, the group of epidemiologists, public health officials, and researchers who monitor emerging drug trends, found increases in MDMA abuse in 13 of the 21 CEWG areas looked at and easy availability in most other areas. Also it is increasingly presenting itself in emergency rooms across the country. According to SAMHSA's Drug Abuse Warning Network, emergency room mentions in the US increased significantly from 253 in 1994 to 4,511 in 2000.

Although to many, MDMA appears to be the new drug on the scene, it is not. In fact, it is a problem that Europe has been dealing with for quite a number of years. European scientists who participated in our MDMA meeting last week discussed the trends in their own countries and discussed approaches they have tried to curtail use and to develop treatments. It is also not a new problem in the US. MDMA's origins date

back to the early 1900s when MDMA was first synthesized, developed and patented in Germany. The drug remained somewhat dormant in the US until the 1970s when it began being used by some psychotherapists who claimed that it enhanced communication in patient sessions. It was in the mid 1980s that there were indications that MDMA was being used at all night dance parties or raves. For a variety of reasons, including the fact that there was a growing body of scientific evidence that MDMA was causing damaging effects on serotonergic axons in animals, the US Drug Enforcement Administration moved the drug to Schedule 1 status in 1985. Schedule 1 under the Controlled Substance Act means there is no accepted medical use for MDMA in the US.

Despite MDMA's status as a Schedule 1 drug, it continues to be used illegally. To ensure that the public is well informed about the harmful effects of this and other drugs, NIDA has undertaken a number of extraordinary steps to share the scientific findings about this drug. For example, we teamed with "In the Mix," this past Spring to develop a television show on Ecstasy for their award-winning PBS series for teens. The MDMA conference I mentioned earlier, "*The Advances, Challenges And Future Directions Of MDMA/Ecstasy Research*," is one other example of the type of international leadership NIDA is stewarding to combat this particular public health problem. We have learned a lot about the short and long-term consequences of this particular drug. Yet, there are many scientific questions that remain to be explored and answered. By bringing together leading researchers to candidly discuss their findings and the challenges they confronted, we are all in a better position to advance the science and make policy and other public health decisions that are based on a strong research base and not anecdotal evidence. We have and will continue to develop publications on

this topic for different audiences. We will continue to make all of these materials available on a specially-designed website - www.clubdrugs.org. As new findings become available, we will be able to alert the public immediately through this and other venues.

In closing, I would like to say there are at least two things that the research community has concluded about this drug. One is that MDMA is not a benign drug. It is a harmful drug that can damage brain cells. And secondly, like other areas of science, there is much more to be learned about this drug.

Thank you again for your interest in this subject. I will happy to answer any questions you might have.