

ACMD Technical Committee:

Report on Ketamine

Spring 2004

1. Introduction

- 1.1 Ketamine is a synthetic drug that is commonly used in medical and veterinary practice. It is known as a dissociative anaesthetic and is also used as an analgesic. Ketamine use as a recreational drug was first reported soon after its release to the market in 1965. In the UK this use was at a very low level until the 1990s when it started to be used by young people involved in the dance music scene. It is used orally in tablet form, intra-nasally as a powder, or intravenously and intramuscularly as a liquid.
- 1.2 The traditional source of recreationally used ketamine has been diversion from legitimate medical supply. More recently HM Customs and Excise have noted bulk importation of ketamine from developing countries disguised as various gift products (see appendix 4). Although ketamine is not included in the British Crime Survey of abused drugs, other sources of epidemiological data demonstrate increasing rates of recreational use throughout the 1990s, although data from the last 4 years points to use levelling off or decreasing (see appendix 1).
- 1.3 At present ketamine is not controlled under the 1971 Misuse of Drugs Act and so its sole control is under the 1968 Medicines Act (see appendix 5). This means that a possession of ketamine for personal use is not an offence.
- 1.4 This Report considers the most appropriate way to control ketamine based on its harmfulness. As ketamine is widely used in medicinal and veterinary practice the impact of control on this use is considered. If more restrictions are decided upon, its Scheduling under the Misuse of Drugs Regulations 2001 should be carefully considered in light of this.
- 1.5 The Report itself is based on a detailed scrutiny of the relevant scientific literature including a recent risk assessment of ketamine by the European Monitoring Centre for Drugs and Drug Addiction¹ as well as an update commissioned by the Home Office and completed in March 2004².

2. Background

- 2.1 In 2003 the Advisory Council on the Misuse of Drugs (the “Council”) set out to review the use of ketamine as a drug of abuse in the light of current scientific evidence.
- 2.2 The Council is established under the 1971 Misuse of Drugs Act to keep under review the drug situation in the United Kingdom and to advise government ministers on the measures to be taken for preventing the misuse of drugs or

¹ EMCDDA (2002) – Report on the risk assessment of ketamine in the framework of the joint action on new synthetic drugs. Luxembourg: Office for official publications of the European Communities 2002

² Nutt and Williams (2004) – see appendix 1

for dealing with the social problems connected with their misuse. In particular, the Council is required to advise on the appropriate classification of substances being specified under Part I, Part II, and Part III of Schedule 2 of the Act.

- 2.3 The classification of drugs, in Schedule 2 of the 1971 Misuse of Drugs Act, is based on the harm they may cause:-

Class A (the most harmful) includes morphine and diamorphine (heroin).

Class B (an intermediate category) includes amphetamines, and barbiturates.

Class C (the least harmful) includes cannabis, anabolic steroids, benzodiazepines and growth hormones.

- 2.4 When advising on the harmfulness of drugs, the Council takes account of the physical harm that they may cause, their pleasurable effects, any associated withdrawal reactions after chronic use, and the harm that misuse may bring to families and society at large.

- 2.5 The Misuse of Drugs Regulations 2001 defines the categories of people authorised to supply and possess drugs controlled under the Act. In these Regulations, drugs are categorised under 5 schedules:-

Schedule 1 includes drugs such cannabis that are not, conventionally, used for medical purposes. Possession and supply are prohibited without specific Home Office approval.

Schedule 2 includes morphine and diamorphine and are subject to special requirements relating to their prescription, safe custody, and the need to maintain registers.

Schedule 3 includes the barbiturates and are subject to special prescription, though not safe custody requirements.

Schedule 4 includes the benzodiazepines and are neither subject to special prescription nor safe custody requirements.

Schedule 5 includes preparations that, because of their strength, are exempt from most of the controlled drug requirements.

3. Epidemiology

- 3.1 Information about the use of ketamine, in the UK, comes from two main sources; information of police and customs seizures and self-reported surveys often commissioned by dance music magazines. The largest epidemiological evidence of drug misuse in England and Wales, the British Crime Survey, does

not include ketamine as one of its reference drugs. Although the available data are not ideal, they provide a reasonable indication of the present scale of use in certain populations, and of changes that have occurred over the past 10 years.

- 3.2 Ketamine use remains at a low level; it is likely that it is used by less than 0.5% of the adult population. This is much lower than rates for ecstasy; reported to be used by 2.2% of adults aged 16-59 in the British Crime Survey 2001/2002. Data collected by the London Centre of the National Poisons Information Service (NPIS) shows that calls requiring information on ketamine intoxication rose steadily from 10 per year in 1995 to over 100 in 2001. Ketamine related calls accounted for less than 0.02% of calls in 1995 and rose to 0.1% of calls in 2002.
- 3.3 Epidemiological information is available from face to face interview at dance club venues. Such surveys sample a young population with high rates of polydrug use. The first study from 1997 reports that 31% of all respondents had tried ketamine at some time compared with 85% who had tried ecstasy. However only 4% of those who had tried ketamine were intending to use it again which contrasts with 53% for ecstasy. More recent surveys have demonstrated lifetime use of ketamine amongst clubbers at between 10-17% compared with 73-82% for ecstasy use.
- 3.4 Annual self-reported postal surveys of ketamine use amongst clubbers have shown a rise in regular users between 1999-2003 from 4% to 16%. Many people who use ketamine find the experience aversive and do not want to use again. One study found that 87% of those surveyed who had tried ketamine said they would never use it again.
- 3.5 A distinct epidemiological group of people also uses ketamine. These people tend to be older, use ketamine more by intravenous and intramuscular routes and use to achieve greater understanding of the self or universe. This group has been dubbed 'psychonauts' as distinct from 'party-goers' and represents a more long term, steady using group.
- 3.6 Seizures of ketamine in England and Wales were first reported in 1990. They increased during the early 90's reaching a peak of over 250 seizures in 1998. Seizures have been relatively constant since with 195 reported seizures in 2003, which approximates to 150,000 doses in the last 5 years. This is dwarfed by the amount and quantity of ecstasy seizures, 5000 of which were reported for 2002, accounting for over 1 million tablets.
- 3.7 HM Customs and Excise reported an emerging trend of ketamine importation in 2001. Ketamine brought in bulk in India was being covertly imported as a variety of products including rosewater and massage oils. Although this importation route seems to have slowed in the last year, the potential for criminal groups to make substantial profits for little risk remains.

4. Risks to Human Health

4.1 Drugs of abuse can affect health in a number of different ways. Some can produce immediate adverse medical effects (such as death from respiratory depression with heroin) or can damage health over a period of time (such as lung and heart disease from smoking tobacco). Some drugs injure health as a secondary consequence of the way in which they are used: the sharing of needles to inject heroin, leading to infections such as HIV and hepatitis, are obvious examples. Furthermore, some drugs cause physical or mental dependence which can distort the life of the user so that they endanger themselves (eg through prostitution) or others (e.g. through violent crime) in their attempts to obtain supplies of their drug.

4.2 Acute health risks

4.2.1 Acute health risks are those due to the direct effects of ketamine, on the body, after its immediate use. They include actions on brain, the heart and lungs, as well as other organs.

4.2.2 Ketamine produces stimulation of the cardiovascular system. There is an increase in heart rate, cardiac output and blood pressure. Ketamine may produce some increase in salivation and lacrimation. Ketamine has a bronchodilatory effect but pharyngeal and laryngeal reflexes are maintained

4.2.3 The cardiovascular actions of ketamine are similar to the effects of exercise. It produces stimulation of the cardiovascular system that leads to an increase in heart rate, cardiac output and blood pressure. This could potentially be dangerous to people with diseases of the cardiovascular system including those with coronary artery disease, irregularities of heart rhythm, high blood pressure, and in individuals at risk of stroke.

4.2.4 The respiratory effects of ketamine are a property beneficial to its use as an anaesthetic agent. Under ketamine anaesthesia subjects are able to maintain their own airway which means it can be used safely in less than ideal environments e.g. in the 'field'. These properties also reduce the potential risks for the recreational user.

4.2.5 Ketamine may produce some increase in salivation and tear production but coughing and swallowing reflexes are maintained. This again is a feature which protects recreational users from harm; because there is no suppression of the gag reflex even when extremely intoxicated, unlike sedative intoxicants such as alcohol, a user is less likely to choke and aspirate.

4.2.6 Nevertheless ketamine impairs the performance of complex tasks that require sustained attention and muscle control. When these involve risks to self or others (such as driving or operating machinery) ketamine has the potential to be dangerous. As ketamine produces a profound dissociation from one's

environment, individuals using ketamine are unlikely to attempt complex tasks such as driving.

- 4.2.7 There are few reports of fatal accidents where users put themselves at risk due to loss of consciousness while undertaking activities, such as taking a bath or going for a walk, in isolation. This is similar to the risks of intoxication with alcohol or benzodiazepines in such situations. There are very few recorded fatalities as a direct result of ketamine use alone. When ketamine-related deaths are reported the usual co-intoxicants are opiates and alcohol.
- 4.2.8 It is unlikely that acute use of ketamine increases risk-taking behaviour in the same way as with alcohol. Ketamine intoxication tends to produce relaxation and social withdrawal rather than the aggressive and disinhibited behaviour commonly found under the influence of alcohol. This means that ketamine does not appear to contribute to violence either to others or to oneself.

4.3 Long term health risks

- 4.3.1 Ketamine has been used safely in medical and veterinary practice since the 1970's and there are no reported adverse medical effects of long-term use. However its medical use is typically only for short time periods and so the possibility of long term harm for recreation users cannot be ruled out. Ketamine has some effects on mental health and functioning and these are detailed below. Ketamine is misused orally and intranasally as a tablet and powder respectively. However, it can also be used in solution intramuscularly and intravenously and this route carries the risk of infection blood borne viruses (especially hepatitis and HIV).
- 4.3.2 Dependence is a complex condition whose nature differs from drug to drug. This is reflected both by the presence of symptoms of withdrawal and the loss of the positive aspects of drug use. There are some case reports of individuals who have used ketamine in a compulsive manner. However, it appears that ketamine dependence is a relatively rare phenomenon.
- 4.3.3 Intoxication with ketamine produces profound effects on memory. There is now some evidence to show that subtle memory deficits persist for longer than 3 days after use and that these deficits are worse for regular users of ketamine. These memory problems have the potential to disrupt users personal and working life.
- 4.3.4 Ketamine causes hallucinations and experiences of alternate realities, often called the 'K-hole'. These symptoms are similar to those found in schizophrenia. There has been concern that use of ketamine can lead to psychotic relapse or precipitation of schizophrenia.
- 4.3.5 Ketamine has been given to schizophrenics in research to study relapse. Although ketamine does produce psychotic symptoms in these patients, the experiences are short lived and caused little anxiety to the patients. A review

of the adverse events from many of these studies reported that very few patients developed relapse that required treatment or re-admission to hospital. Nevertheless ketamine use by a schizophrenic patient can unquestionably worsen their symptoms and its use should be avoided by these individuals.

- 4.3.6 In research studies recreational doses of ketamine have been given to normal volunteers as a model of psychosis. There have been no reports of any volunteers developing a psychotic illness during these studies. However, usually only single doses are given and the subjects are supported by the investigators. This finding serves to reduce the impact and negative consequences of any experiences suffered. It would be wrong to surmise that ketamine could not precipitate psychosis as the conditions in research studies do not duplicate the conditions of recreational use.
- 4.3.7 There is evidence that high doses of ketamine in rats can cause localised neurotoxic changes. There are no data suggesting that ketamine causes long-term brain changes in humans or primates.

4.4 Ketamine and pregnancy

- 4.4.1 As ketamine use is still on a small scale there is very little information about its use in pregnancy. Most of the studies published are animal research.
- 4.4.2 Work in rats has shown that cocaine and a combination of cocaine and ketamine reduced foetal birth weight. However these results were not replicated with ketamine alone. Studies in several mammalian species has shown that ketamine does not cause birth defects and foetal abnormalities in these animals.
- 4.4.3 No evidence has come to light of brain damage in humans despite the use of ketamine as an anaesthetic agent during pregnancy and for young children.

4.5 Ketamine and the health of society

- 4.5.1 Drug use can affect the health of others, as well as users. For example, driving a car under the influence of a drug can lead to the injury of bystanders. Ketamine therefore might make a small contribution to road traffic accidents and other accidents involving the general public. Its use does not produce the mental states leading to violence against others. There is little evidence that the sale of ketamine contributes to the dangers from the illicit drugs market.
- 4.5.2 Drugs such as heroin, which are used intravenously, are amongst the most important causes of the spread of blood borne infections such as HIV or hepatitis B and C. Most ketamine use in the UK is intranasal or oral, however,

a small proportion of users inject. The pattern and frequency of use is different to that of heroin and so the impact of ketamine in the spread of blood borne viruses is likely to be small. Users of ketamine tend to be well educated and use in familiar surroundings further reducing this level of risk.

- 4.5.3 Although concern has been raised that ketamine may be used as a 'date-rape' drug, this has not been proven. Ketamine has a very unpleasant taste and a person unknowingly intoxicated with ketamine is likely to be disturbed by its effects, which means it is unlikely to be effective if misused in this way.

5. Discussion

- 5.1 Existing evidence suggests that ketamine use is relatively low and currently stable. However its use has increased amongst certain sub-populations, particularly young people who frequent dance-music night-clubs.
- 5.2 Ketamine is a relatively safe medical drug due to a wide therapeutic window of safety. It does not suppress respiration or the gag reflex and therefore even high doses cause few medical problems. It is these properties that make ketamine an ideal anaesthetic agent for veterinarians and in battle-field situations. Similarly, recreational users are unlikely to come to harm from any medical consequences. There is some evidence that it does increase the risks from taking other drugs, its dissociative effects making an individual less aware of warning signs of other drug use.
- 5.3 Use of ketamine, however, poses risks for people with disorders of the heart and circulation, and for those with schizophrenia and other psychotic disorders. Ketamine users and their health-care workers should be made aware of the potential risks of ketamine use in these disorders. However, in public health terms, both groups are at much more significant risk from stimulant drugs such as cocaine and amphetamines.
- 5.4 Regular use of ketamine can result in dependence, but its dependence potential is substantially less than that of drugs such as amphetamine, nicotine or cannabis.
- 5.5 Ketamine use poses potential individual and societal risks if taken by drivers, pilots and those operating machinery. It is more likely that ketamine would lead to an accident of neglect that could lead to injury or even death of the using individual.
- 5.6 Importation of ketamine currently falls between two pieces of legislation, the Misuse of Drugs Act and the Medicines Act. This means that criminal groups can potentially import and distribute ketamine for large profits and very little risk.

6. Recommendations of the Advisory Council on the Misuse of Drugs:

- 6.1 Based on the assessment of the risks undertaken by its Technical Committee, ketamine should be controlled under the Misuse of Drugs Act 1971.
- 6.2 Ketamine should be placed in Class C of the Misuse of Drugs Act 1971 and in Schedule 4 Part 1 of the Misuse of Drugs Regulations 2001.
- 6.3 Coroners and procurators fiscal should be encouraged to consider more routine screening for ketamine in unexpected deaths and road traffic accidents.
- 6.4 Ketamine should be included in the British Crime Survey in order to obtain more robust epidemiological data.

Members and officials of the ACMD Ketamine Sub-committee

Members

Professor David Nutt (Chairman), ACMD Member, Psychopharmacology Unit, University of Bristol

Mr Duncan Burrage, Mr Paul Sadler, Mr Chris Smith*, National Crime Intelligence Service, London

Mr John Corkery, Honorary Research Fellow, St. George's Hospital Medical School, London

Mr Joe Onofrio, HM Customs and Excise, London

Professor Geoffrey Phillips, retired Chemist and Advisor to the Home Office

Professor Ian Power, Anaesthesia, Critical Care and Pain Management, University of Edinburgh

Mrs Kay Roberts, Pharmacist, Glasgow

Mr David Robinson, Medicines and Healthcare products Regulatory Agency

Dr Polly Taylor, Veterinary Surgeon, Cambridgeshire

Mr Ric Treble, Laboratory Government Chemist, London

Dr Tim Williams, Psychopharmacology Unit, University of Bristol

Dr Mike White, Forensic Science Service, London

Officials

Mr Tony Hall, Legislation Team, DLEU, Home Office

Mr Jacob Hawkins, Communities Team, DLEU, Home Office

Mr Jeremy Sare, Legislation Team, DLEU, Home Office

Mr. Stuart Harwood, ACMD Secretariat, DLEU, Home Office

Mr Saleah Ahmed, ACMD Secretariat, DLEU, Home Office

* Duncan Burrage was originally invited, however, he was unable to attend therefore Paul Sadler attended in his place. Chris Smith attended meetings when Paul Sadler was unable to attend.

Guest Speakers

The following experts were invited to present their opinions on ketamine to the Ketamine Working Group.

Dr. Karl Jansen

Dr. Karl Jansen is a Psychiatrist and a member of the Royal College of Psychiatrists. He has a specific interest in ketamine and has published several papers on the topic.

Date attended: **10 September 2003.**
Title of presentation: **Ketamine: Further Observations on Use, Users and Consequences**
Accompanying paper(s): **Ketamine: Further Observations on Use, Users and Consequences, Jansen, K.L.R, Addiciones, 2003.**

Professor John Henry

Professor John Henry is a Professor of Accident and Emergency Medicine. He is currently working for the Academic Department of Accident and Emergency Medicine at St. Mary's Hospital, London.

Date attended: **13 November 2003.**
Title of presentation: **'Ketamine: An Emergency Department Viewpoint'.**
Accompanying papers: **None.**

Professor Val Curran

Professor Val. Curran is a Professor of Psychopharmacology at University College London. She has a special interest on the affects of ketamine especially in relation to its affect on memory and has published several papers on the topic.

Date attended: **13 November 2003.**
Title of presentation: **'Ketamine Abuse'.**
Accompanying papers: (a) Draft copy of a yet to be published paper titled, **'Acute Effects of Ketamine on Memory Systems and Psychotic Symptoms in Healthy Volunteers'.**

James Barratt

James Barratt is a Barrister representing Furnival Chambers. He attended on behalf of the prosecuting counsel in the case of R v. Veiga and others – the first prosecution for the importation of ketamine in the UK.

Date attended: **13 November 2003.**
Title of presentation: **'The Prosecution of Ketamine'.**
Accompanying papers: **'Submission to the Advisory Council on the Misuse of Drugs: The Prosecution of Ketamine'.**

Dr Paolo Deluca

Dr. Deluca has a doctorate in Psychology and is also an expert of Internet technologies. He has worked in the drug addiction field for a number of years and is currently the Co-ordinator of the European Union funded Psychonaut 2002 Project. The project is undertaking research into the promotion of illicit substances on the Internet.

Date attended: **27 January 2004.**
Title of presentation: **'The Psychonaut 2002 Project'.**
Accompanying papers: **None.**

Abbreviations

ACMD	Advisory Council on the Misuse of Drugs
BVA	British Veterinary Association
CNS	Central Nervous System
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
fMRI	Functional Magnetic Resonance Imaging
EEG	Electroencephalogram
FSS	Forensic Science Service
GABA	Gamma-aminobutyric acid
GHB	Gamma-hydroxybutyrate, a drug of misuse
HIV	Human Immunodeficiency Virus
HMC&E	Her Majesty's Customs and Excise
5-HT	5-Hydroxytryptophan, or serotonin
IMDU	Independent Drug Monitoring Unit
LSD	Lysergic Acid Diethylamide, a synthetic drug of misuse
MDMA	3,4-methylenedioxy-methamphetamine, or 'ecstasy'
MHRA	Medicines and Healthcare Regulatory Authority
MRL	Minimum Residue Limits
NCIS	National Criminal Intelligence Service
NMDA	N-methyl-D-aspartate
NPIS	National Poisons Information Service
PET	Positron Imaging Tomography
PCP	Phencyclidine, a synthetic drug of misuse
POM	Prescription Only Medicine

rCBF	Regional Cerebral Blood Flow
rCBV	Regional Cerebral Blood Volume
RCVS	Royal College of Veterinary Surgeons
SPECT	Single Photon Emission Computed Tomography
UK	United Kingdom
USA	United States of America