THE EXPERT ADVISORY COMMITTEE ON DRUGS (EACD) ADVICE TO THE MINISTER ON:

3, 4 METHYLENEDIOXYMETHAMPHETAMINE (MDMA)

May 2004

CONTENTS

ADVICE TO THE ASSOCIATE MINISTER OF HEALTH ON MDMA

Executive Summary

This paper presents evidence on the risk of harm associated with 3,4, methylenedioxymethamphetamine [MDMA], an amphetamine-type stimulant with hallucinogenic qualities. The information presented addresses the criteria which the Expert Advisory Committee on Drugs [EACD] must take account of when considering the appropriate classification of a substance, under section 4B of the Misuse of Drugs Act 1975. MDMA is currently a controlled drug under Part 2 of the Second Schedule of the Act. The key issues that the EACD considered when assessing the current classification of MDMA included:

- Sharply rising prevalence of MDMA use and importation into New Zealand
- Mounting evidence that Ecstasy-type drugs have a neurotoxic effect
- No conclusive evidence that MDMA has any therapeutic application
- MDMA seems likely to be proven to be moderately dependence-producing
- Worrying links between New Zealand's MDMA market and organised crime
- Increasing number of cases of attempted MDMA manufacture in New Zealand
- MDMA is classified as a Schedule I or a Class A drug in other jurisdictions

Based on the evidence presented in this paper, the EACD recommends that presumption for supply of MDMA be set at 5 grams or more of MDMA, whether or not it is contained in a substance, preparation or mixture.

Recommendations

After considering all of the information put to the Committee and the classification criteria in the Misuse of Drugs Act 1975, the EACD makes the following recommendations to the Minister of Health:

(a) MDMA should be classified in Part 1 of the Second Schedule of the Misuse of Drugs Act 1975 (ie, B1).

(b) That the presumption for supply of MDMA be set at 5 grams or more of MDMA, whether or not contained in a substance, preparation, or mixture.

(c) This paper should be made publicly available (eg, posted on the National Drug Policy website www.ndp.govt.nz).

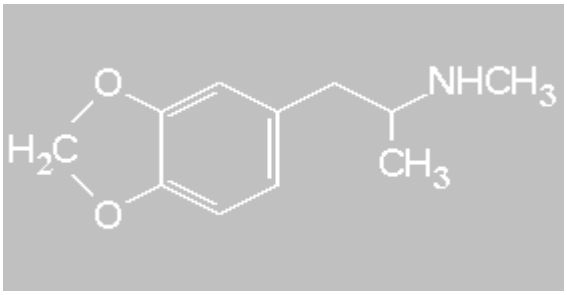
TERMINOLOGY

3. In this paper, the terms MDMA and "Ecstasy" will be used in different contexts. MDMA will be used when referring to studies in which it is known that MDMA was administered, or when referring to studies of Ecstasy users from the late 1980s and early 1990s, when it was highly likely that the tablets the users purchased contained MDMA. The term Ecstasy will be used to refer to the drug as it is sold on the street - often with the actual chemical composition unknown. (In addition to Ecstasy, other street names for MDMA include E, X, XTC, Adam, Eckie, Hug and The Love Drug.)

SUBSTANCE IDENTIFICATION

4. MDMA ($C_{11}H_{15}NO_2$) is an N-methyl analogue of the 'parent' compound MDA (3,4-methylenedixoyamphetamine). Its chemical structure is shown in Figure 1. In its base form, MDMA is a white, musty-smelling oil, with a searing, bitter taste.

FIGURE 1: Chemical structure of MDMA



5. MDMA production is a multistage process requiring a full laboratory set-up, which is considerably more complicated than methamphetamine production. Although there are more than 20 chemical recipes for MDMA, clandestine laboratory operators commonly use one of only seven methods (National Drug Intelligence Center 2000). Six of these seven common methods use safrole or isosafrole as precursor chemicals; the other uses piperonal.

6. In a successful production process, the resulting MDMA is a nearly 100 percent pure powder with a distinctive licorice scent (Marnell 2002). The powder is pressed into pills with identifying designs or symbols. These tablets often contain adulterants, diluents, and approximately 100 milligrams of MDMA. New Zealand testing of all Ecstasy seizures between July 1999 and June 2000 found that the majority of samples contained MDMA, however ketamine and cocaine were also found in some samples (ESR 2000). Of the 75 MDMA seizures analysed during this period, which yielded 8604 total doses, the average strength of the pills was 91.8 mg/dose (with a strength range of 30.2 mg/dose to 172.4 mg/dose). The average purity of the tablets was 36% (with a purity range of 12.7% to 97.3%).

SIMILARITY TO KNOWN SUBSTANCES

7. MDMA is related to both the amphetamine family of psychostimulants, and to the hallucinogen mescaline (Budavari et al. 1996). Although most often identified as an hallucinogenic stimulant, or amphetamine-type stimulant (ATS), some have argued that the drug's unique pharmacological profile justifies its own classification as an "entactogen" - meaning 'to touch within' (see Nichols 1986).

8. MDMA is sometimes confused with related chemical compounds, such as ethylenedioxymethamphetamine [EVE] and dioxymethylamphetamine [DMA] (Sweetman 2002). The *Australian Standard Classification of Drugs of Concern* also notes MDMA is closely related chemically to phenethylamines like 4-bromo-2,5-dimethoxyamphetamine [DOB], 2,5-dimethoxy-4-methylamphetamine [DOM], 3,4-methylenedioxyethylamphetamine [MDEA], paramethoxyamphetaminamine [PMA] and trimethoxyamphetamine [TMA] (refer to ABCI 2002).

RATIONALE FOR RECLASSIFICATION

Likelihood or evidence of abuse

New Zealand prevalence data

11. New Zealand drug surveys indicate an increase in ATS use. The latest survey undertaken by the former Alcohol and Public Health Research Unit attached to the University of Auckland (Wilkins et al. 2002) found a significant increase in the number of respondents trying and using ATS [see Table 1]. The largest increases in the use of stimulants was in the 15-17 year old age group (increased from 2% to 6%) and 20-24 year old age group (increased from 6% to 11%). This data reflects a continuing trend of increased stimulant use that was also seen in the previous regional comparison survey (Field and Casswell 1999), where stimulant use increased from 2% in 1990 to 4% of respondents in 1998.

TABLE 1: Use of amphetamine/methamphetamine, 1998 and 2001

	Ever used		Used Last Year		Current User	
	1998	2001	1998	2001	1998	2001
Amphetamine / Methamphetamine	7.6%	11.0%	2.9%	5.0%	2.2%	3.5%

Source: Wilkins et al. 2002

12. The surveys also indicate an increase in the use of MDMA, with the rates of MDMA experimentation increasing from 3% to 5.4% between 1998 and 2001 [see Table 2]. Significantly, in the 20-24 year age group of survey

respondents, MDMA use during the previous 12 months rose from 3% in 1998 to 10% in 2001.

TABLE 2: Use of MDMA, 1998 and 2001

	Ever used		Used Last Year		Current User	
	1998	2001	1998	2001	1998	2001
MDMA	3.0%	5.4%	1.5%	3.4%	1.0%	2.3%

Source: Wilkins et al. 2002

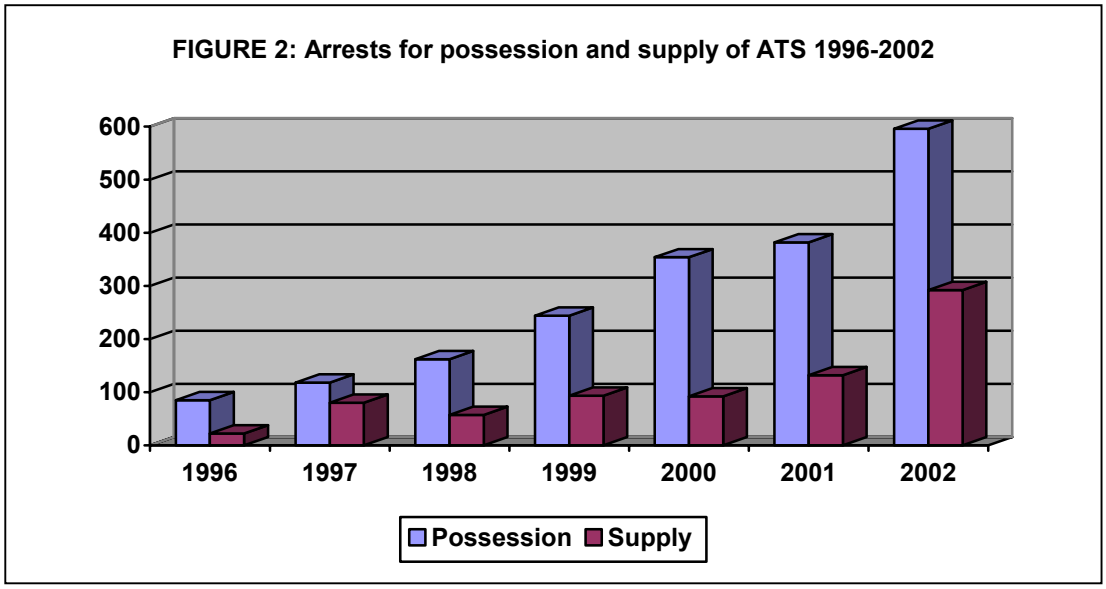
New Zealand MDMA-related mortality and morbidity

13. Hospital data is unable to provide definitive information about the health-related impact of MDMA. There are some problems associated with the data, including the fact that the data does not differentiate between MDMA-related admissions and those relating to the use of other ATS drugs. Nevertheless, there were 109 publicly funded stimulant-related hospitalisations between 1996 and 1998 (NZHIS 2001). These hospitalisations were for non-dependent abuse, dependence, and poisoning either as the presenting condition or as a secondary diagnosis. There was a rise in the total numbers of hospitalisations each year (18 in 1996, 46 in 1998), however, due to the small number and short timeframe it is difficult to describe this as a clear trend.

14. The New Zealand Health Information Service reports that there were no deaths associated with stimulant use in New Zealand between 1990 and 1996 (NZHIS 2001). Three MDMA-related deaths have been recorded by coroners since 1998.

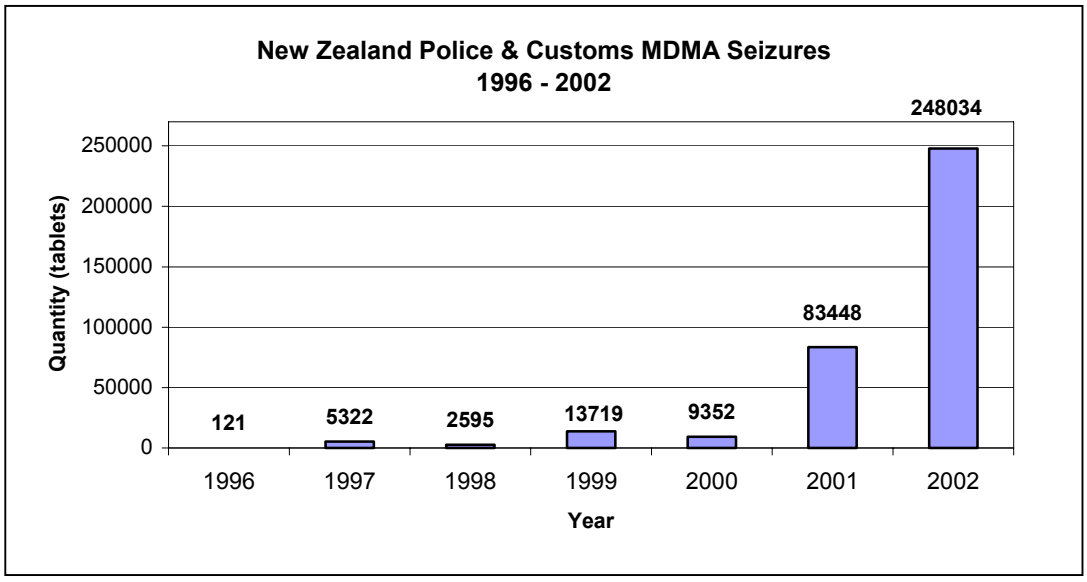
New Zealand arrest and interdiction data

15. New Zealand law enforcement data indicates growing ATS availability, however, some data systems do not currently distinguish between MDMA and other ATS. The number of people arrested for ATS possession has increased approximately 650 percent between 1996 and 2002 [see Figure 2]. Increasing numbers of people have also been charged with supply offences for ATS in recent years. In 2002, 596 people were arrested for possession of ATS and 292 for importation, supply and manufacture offences.



Source: Police data

16. There has also been a steep rise in MDMA seizures by Police and the Customs Service. Prior to 1998, seizures of MDMA were sporadic and small in quantity (NDIB 1999). However, since that time there has been a significant rise in interdiction rates and the size of MDMA seizures as outlined in Figure 3 [below]. In fact, provisional seizure figures for the year ended 31 December 2002 put the total quantity of MDMA interdicted at approximately 248,034 tablets (NDIB 2003).



Source: Police and Customs Service data

17. Finally, there has been a decline in the street price of MDMA. In its annual report for 1998, the National Drug Intelligence Bureau [NDIB] reported that MDMA sold for between $80 and $100 a tablet; in its most recent overview report, the NDIB states the current street price for MDMA is consistently

between $60 and $80 a tablet (NDIB 1999; 2003). This could be interpreted as a sign of increasing levels of supply, however, the relationship between price and availability is not explicit.

Specific effects of MDMA

Pharmacological effects

18. Animal research has indicated that MDMA has a high affinity for serotonin receptors and transport sites in the brain (eg. Battaglia and De Souza 1989; Pierce and Peroutka 1988). Serotonergic neural pathways regulate sleep, sexual activity, aggression, mood, and pain sensitivity, and are also important in the regulation of temperature and in memory function. MDMA initially enhances serotonergic function by binding to serotonin receptor sites. However, eventually this will lead to a depletion of the neurotransmitter and thus a decrease in serotonin levels. MDMA also stimulates the release of dopamine into the synaptic cleft (Daws et al. 2000). Dopamine is involved in control of movement, cognition, motivation and reward or pleasure.

19. In the rat, administration of MDMA results in increases in metabolic rate, evaporative water loss, heart rate, blood pressure, body temperature and locomotor activity (eg. Gordon 1991). The effects in the rat are influenced by ambient temperature (Malberg and Seiden 1988). Depending on the ambient temperature, either hypothermia or hyperthermia may be observed, such that the effect of the drug is best characterized as a loss of normal control of body temperature. On the basis of an established relationship between serotonin and hyperthermia, Loscher and colleagues (1990) hypothesized that the MDMA-mediated release of serotonin may underlie these temperature control problems.

20. In humans, common short-term physical effects of MDMA/Ecstasy are similar to those of ATS, including papillary dilation, increased jaw tension and grinding of teeth, loss of appetite, dry mouth, nausea and vomiting, tachycardia, hot and cold flushes and sweating (see, further, Greer and Tolbert 1986, 1990; Peroutka et al. 1990; Solowij et al. 1992; Vollenweider et al. 1998). Longer term effects perceived by users as being Ecstasy-related include insomnia, depression, headaches and muscle stiffness (see, for instance, Cohen 1995; Peroutka et al. 1990; Siegel 1986; Topp et al. 1999).

Psychoactive effects

21. Consistent results on psychoactive effects of MDMA have been demonstrated in surveys of MDMA/Ecstasy users (eg. Siegel 1986; Peroutka 1990; Solowij et al. 1992; Cohen 1995; Topp et al. 1999) and studies using controlled administration of MDMA (eg. Greer and Tolbert 1986, 1990; Vollenweider et al. 1998; Cami et al. 2000). They indicate that the immediate positive psychoactive effects of MDMA include euphoria and a sense of well-being, increased energy, and feelings of warmth, empathy and closeness with others. Less commonly, negative psychological effects may include anxiety, paranoia, and depression.

Neurotoxic effects

22. MDMA has been shown to be neurotoxic to serotonergic pathways in animals and in humans. However, the type and severity of this neurotoxicity is influenced by many factors, including ambient temperature, exercise, polydrug use and levels of hydration. These variables, when combined with the heterogeneity of compounds contained in tablets sold as Ecstasy, make it difficult to determine under which circumstances MDMA may have a neurotoxic effect in human users (Gowing et al. 2001).

23. Animal studies have shown that administration of MDMA produces damage to serotonergic axons and axon terminal fibres in various brain regions (including the cortex, hippocampus and striatum), reduced density of serotonin reuptake sites, and reduced concentrations of the serotonin metabolite 5-HIAA, but without laterations in the major metabolites of dopamine and noradrenaline (McCann et al. 2000). Decreases in the density of brain serotonin axons have been seen in squirrel monkeys more than seven years after MDMA administration (Hatzidimitriou et al. 1999). While some regrowth of axons occurs, it appears abnormal and incomplete (Boot et al. 2000).

24. Such findings in animals have led to concerns regarding neurotoxicity of MDMA. Although animal studies are indicative of effects in humans, there remains a degree of uncertainty about the generalisability of animal research findings to human drug users. However, a series of studies using sophisticated brain imaging techniques, such as PET, SPECT and MRI, to assess different aspects of the human brain have found persisting abnormalities in the brain morphology in ex-users of Ecstasy, even with moderate use (eg. Chang et al. 1999, 2000; McCann et al. 1998; Obrocki et al. 1999; Reneman et al. 2000a; Semple et al. 1999). For example, Kish and co-researchers (2000) obtained autopsied brain from 11 neurologically normal subjects and one male MDMA user. They found that striatal levels of serotonin and 5-HIAA (but not dopamine) were depleted by 50% to 80% in the brain of the MDMA user.

25. The studies cited above have tended to include only small numbers of subjects, and many are confounded by uncertain histories of MDMA and other drug use. Although consistent with animal research in providing additional evidence of neurotoxicity, the imaging and coronial studies in particular do not indicate the functional significance of changes in brain morphology.

26. The functional significance of the neurotoxic effects of Ecstasy has been explored in a number of recent studies, which have used psychological tests to assess cognitive function, memory, and aspects of mood in current and former Ecstasy users compared to non-using controls. Again, these studies are confounded to some extent by small subject numbers, difficulties in determining history of Ecstasy use, concomitant use of other drugs such as cannabis, and the lack of baseline data from periods prior to Ecstasy use (in order to tease out pre-existing differences between users and non-users from the effects of Ecstasy itself). Despite these limitations, and despite some

variability between studies, an impairment in short-term memory function has consistently been observed in Ecstasy users (eg. Curran and Travill 1997; Parrott and Lasky 1998; Klugman et al. 1999), that appears to be mediated via the serotonin neurotransmitter system (eg. McCann et al. 1994, 1999; Bolla et al. 1998; Reneman et al. 2000b).

27. The results of the majority of these studies demonstrating memory impairment suggest that the deficits are not attributable to the concomitant use of other drugs, particularly cannabis. However, results of two studies that attempted to rigorously control for cannabis use (Gouzoulis-Mayfrank et al. 2000; Rodgers 2000) both suggest that although cannabis use is unlikely to fully account for the cognitive deficits observed in Ecstasy users, it may contribute to impairment above and beyond any Ecstasy-related deficits. A more recent study conducted in Sydney, Australia (Simon and Mattick 2002) found that Ecstasy users showed no impairment relative to cannabis using controls, which is suggestive that cannabis may have confounded earlier results demonstrating an association between memory impairment and lifetime exposure to Ecstasy.

28. In summary, the combination of evidence from animal and human research provides mounting evidence for a neurotoxic effect of Ecstasy. However, the long term functional consequences of Ecstasy use in humans remain uncertain. Only large-scale, community-based and prospective longitudinal research will be able to definitively address these issues. The exact mechanism of MDMA's neurotoxicity is also unclear, and is an area that is continuing to be researched.

The risks that MDMA poses to public health

29. As a preliminary remark, it is important to acknowledge that quantifying the risk to public health of any substance is a difficult task. The ability to do so for MDMA is further complicated by the lack of large-scale, longitudinal and epidemiological studies. For MDMA, we must rely on an analysis of case reports to examine the risks to public health. An analysis of case reports of adverse health effects of Ecstasy will inevitably be biased, however. More serious effects, particularly cases with fatal outcomes, are more likely to be published. It is also impossible from case reports to make a meaningful estimate of how likely these adverse effects are, due to the inability to relate the number of case reports to a population base (see, further, Gowing et al. 2001). However, in the absence of epidemiological and population-based studies, case reports constitute the best available evidence of the risks, if any, that MDMA poses to public health.

30. Case reports of Ecstasy-related death, as well as other sorts of outcomes, such as psychiatric sequelae, have been comprehensively reviewed by Gowing and associates (2002). It is not necessary to traverse the ground covered by Gowing et al. here; suffice it to note that at the conclusion of their review, the authors state: "The incidence of serious acute adverse events related to Ecstasy is low" (Gowing et al. 2002: 53).

31. Intense media scrutiny of a small number of Ecstasy-related deaths may well have led to the impression that the drug is more likely to be associated with adverse outcomes than may actually be the case. This should not be taken to imply that the use of the drug is free of risk; clearly, use of Ecstasy is associated with a risk of mortality and significant morbidity. However, in the absence of rigorous evidence suggesting otherwise, those risks should not be overstated. The most significant risk for health is that of hyperthermia and hyponatraemia (disturbed salt-water balance). Other problems are reported by Ecstasy users, including physical, psychological, social, relationship and occupational problems (see Topp et al. 1999), but most of these are relatively minor, and only a very small minority constitute significant disruptions to functioning.

32. One way to simplify and contextualise the task of quantifying MDMA's risk to public health is to compare the risk it poses with the risk posed by another drug. To this end, when the United States Sentencing Commission proposed to change the penalties applied to MDMA-related offences, the Federation of American Scientists, spearheaded by a large group of respected researchers and academics from the United States and Australia, argued that "the damage done by heroin to its users, and the damage done by its users and dealers to others, vastly outweighs the damage done by MDMA. Whether we look at death, addiction, infectious disease transmission, crime by users or violence among dealers, the damage from heroin is orders of magnitude greater" (Schuster et al. 2001: 2). Similarly, the relative risks associated with MDMA have convinced the United Kingdom's Association of Chief Police Officers [ACPO] and a recent independent Police Foundation inquiry team to recommend that Ecstasy be reclassified from a Class A to a Class B controlled drug (Runciman 2000: 50).

33. In summary, although some commentators would undoubtedly disagree, many well-respected researchers, academics and practitioners suggest that the risk to public health of MDMA is relatively low.

The therapeutic value of MDMA

34. Although MDMA was first patented in 1914, voluntary human experimentation with the drug can only be traced back to the 1970s (Shulgin 1990). Prior to the criminalisation of MDMA in the United States during the mid-1980s, the drug had been used since the mid-1970s in a therapeutic context by psychotherapists on both the East and West Coasts of America. These therapists, including psychiatrists and physicians, considered the drug an invaluable therapeutic adjunct when used in strictly controlled environments under medical supervision (Beck and Rosenbaum 1994). They believed that the relatively short duration of MDMA's action, along with its ability to facilitate self-insight and an openness of emotional expression in which a patient was not fearful or inhibited, positioned the drug as an ideal tool in standard psychotherapeutic processes (eg. Grinspoon and Bakalar 1986; Adamson and Metzner 1988). Despite their belief in its efficacy, the therapists were wary of drawing too much attention to MDMA, fearing that this would only hasten its criminalisation and block further research (Eisner 1989; Seymour 1986). For this reason, although those familiar with the drug

firmly believed in its therapeutic value (Beck 1986), very little research, and no rigorously controlled trials, were ever conducted to examine MDMA's therapeutic potential before it was criminalised.

35. In 1985, the United States Drug Enforcement Administration [DEA] proposed that MDMA be classified as a Schedule 1 drug under the Controlled Substances Act. For this to occur, three criteria had to be met: MDMA must be deemed to have a high potential for abuse, no currently accepted medical use, and a lack of safety for use even under medical supervision. The DEA was unaware that MDMA was being administered to patients in a therapeutic context (Beck and Rosenbaum 1994); enforcement officials considered Ecstasy a dangerous drug devoid of therapeutic value. The controversy continued through three federal administrative law hearings to determine the scheduling of MDMA. Although the main finding of each of the three hearings was the lack of research assessing the potential benefits and/or harms arising from MDMA use, the continued spread in the recreational use of the drug led to its emergency scheduling in 1985, and subsequent permanent classification in Schedule 1 the following year.
36. Under United States law, therefore, MDMA has been classified for more than 15 years as having no currently accepted medical use. This scheduling has meant that it is virtually impossible to obtain research funding to examine the question of whether MDMA has true therapeutic potential. For this reason, the therapeutic potential, or otherwise, of MDMA has never been examined through rigorous research. Moreover, because the drug was patented and the patent has lapsed, there are no financial incentives for a pharmaceutical company to invest in research into the benefits and risks of MDMA; the drug is in the public domain and any company could now market the same product with minimal investment.

37. It is prudent to emphasise that the absence of evidence relating to therapeutic value of MDMA does not mean that the drug has no such value. Rather, the absence of evidence reflects the fact that the research that could definitively answer this question has never been conducted. Alongwith the numerous testimonials provided by patients and users whose motivations for MDMA use were therapeutic or spiritual (eg. Watson and Beck 1991), it bears noting that many of the therapists who administered MDMA to their patients in the United States in the late 1970s and early 1980s were highly respected clinicians and academics (eg. Adamson and Metzner 1988; Greer and Tolbert 1986, 1990; Grinspoon and Bakalar 1986; 1987; Wolfson 1986). These therapists, despite MDMA's Schedule 1 status, appear to have remained committed to their belief in the therapeutic efficacy of the drug (eg. Greer and Tolbert 1998).

38. In summary, there is no conclusive evidence to either prove or disprove the contention that MDMA has therapeutic value. Furthermore, at least in the near future, research that could comment more authoritatively on this issue is unlikely to be conducted.

The potential for MDMA to cause death

39. As noted earlier, there is a lack of large-scale, longitudinal and epidemiological studies that could provide robust measures of the risk of death related to MDMA. Instead, we must rely on an analysis of case reports to examine the risks to public health of Ecstasy – which, inevitably, will be biased; simply because more serious effects, particularly cases with fatal outcomes, are more likely to be publicised than non-serious or benign effects. It is also impossible from case reports to make a meaningful estimate of how likely adverse effects are, due to the inability to relate the number of case reports to a population base (Gowing et al. 2001). However, in the absence of epidemiological and population-based studies, case reports constitute the best available evidence we have in this area.

40. MDMA/Ecstasy undoubtedly has the potential to cause death, with hyperthermia the most common cause of fatalities (Gowing et al. 2002). Some studies have suggested that the risk of using Ecstasy ranges from between one death in 2000 first time users to one death in 50,000 first time users (Gore 1999). Moreover, although users tend to believe that only 'fake pills' (that is, those not containing MDMA) are likely to be associated with death, some studies that report on toxicological analyses show that MDMA alone (with no other drugs or contaminants) has been implicated in deaths. For example, a very recent study of Ecstasy-related deaths in England and Wales found that, although typically the deceased had taken several different (prescribed and non-prescribed) drugs with Ecstasy, a small proportion of fatalities (6 out of 81, or 7% of the sample) died after only taking Ecstasy (Schifano et al. 2003).

41. As previously noted, ambient temperature influences MDMA's interruption to temperature control, and the fact that Ecstasy is commonly consumed in hot environments where users engage in sustained physical activity and may not adequately replace their fluids (eg. dance party venues), has undoubtedly contributed to the number of Ecstasy-related deaths reported in the literature.

42. However, it is important once again to emphasise that although Ecstasy/MDMA has been implicated in the deaths of some users, the number of reports is small. Given the extremely large number of Ecstasy/MDMA doses consumed globally each week, it seems reasonable to suggest that, although use of MDMA carries with it a potential to cause death, the risk of death from consuming MDMA is low in relative terms.

43. In summary, use of MDMA has been associated with a small number of deaths reported in the literature, including three deaths in New Zealand since 1998. There is no doubt that the drug has the potential to cause death. However, the available evidence suggests that the risk of death after using solely MDMA is low.

The ability of MDMA to cause physical or psychological dependence

44. Early studies of community samples of MDMA users in both Australia and the United States found generally self-limiting patterns of use, with low levels of injecting, few negative health effects, and use confined mainly to inner city areas (eg. Peroutka et al. 1988; Solowij et al. 1992; Moore 1993; Beck and Rosenbaum 1994). Such results seemed to confirm the prevailing view that MDMA was a relatively benign substance with few associated problems (eg. Nicohols and Glennon 1984; Downing 1986; Fromberg 1990). Dependence on MDMA, if addressed in the literature at all, was considered uncommon (eg. Peroutka 1989; Steele et al. 1994; Green et al. 1995). It was generally agreed that MDMA dependence was unlikely due to a rapid development of tolerance to the desired effects, along with the simultaneous intensification of unpleasant side-effects such as teeth grinding, anxiety and agitation (eg. Chesher 1990; Beck and Rosenbaum 1994). Even so, others cautioned that the self-limiting nature of MDMA use might change if the dominant pattern of use (infrequent oral consumption of small amounts of MDMA) were to change (Hall and Hando 1993).

45. Indeed, not long after in the United Kingdom, Merrill (1996) described a group of Ecstasy users who administered the drug repeatedly in increasing doses to overcome short-term tolerance. Similarly, Topp and others (1997) found that 83% of a sample of 185 regular Ecstasy users reported significant tolerance to the effects of the drug, and 56% reported that they used more than double the amount of Ecstasy that they first started with, in order to achieve similar effects. Although there are difficulties in assessing self-reported tolerance due to the variations in both the purity and contents of tablets sold as Ecstasy, these results are consistent with those of Frederick et al. (1998), who observed the development of tolerance in monkeys after exposure to high doses of MDMA.

46. Relatively few studies have examined self-reported abuse and dependence symptoms among MDMA users. In an early study done in Sydney that asked MDMA users about dependence, Solowij and co-investigators (1992) reported that only 2% of their sample of 100 people who had ever used the drug had “ever felt dependent on Ecstasy”, although 47% believed “addiction” to the drug was possible. Jansen (1999) described three case reports of individuals who met criteria for a diagnosis of dependence on Ecstasy. Although this report provided little detail as to how the diagnoses were derived, the individuals were described as feeling that they had lost control over their use of Ecstasy, neglecting alternative pleasures, and continuing to use the drug despite believing that it was causing them problems.

47. In a more rigorous study conducted in 1995, Schuster et al. (1998) interviewed a representative community sample of 3021 14-24 year olds in Munich, Germany. They found that 4% of the male and 2.3% of the female respondents reported having used Ecstasy at some time, and that about half of these lifetime users had used the drug more than five times. The most common pattern of Ecstasy use was between once per month and twice per

week, although 17% of users reported using Ecstasy on three or more days per week. Referencing to the clinical criteria for drug dependence in the *Diagnostic and Statistical Manual of Mental Disorders* [DSM] (American Psychiatric Association 1994), Schuster and colleagues found that the prevalence of DSM diagnoses of abuse/ dependence on Ecstasy and related drugs was about 1%. These results suggest that approximately 20% of young people who use Ecstasy at least once in their life are likely to subsequently meet diagnostic criteria for an Ecstasy use disorder.

48. A study by Topp et al. (1997) used the same structured diagnostic interview schedule as Schuster et al. (1998), but administered it to a sample of 185 respondents who reported having used Ecstasy at least five times in their lives. The mean age of the sample was 22.1 years (ranging from 15-42 years), with 77% aged 25 years or younger, and 54% female. Each of the DSM criteria for abuse and dependence were endorsed by at least 25% of this sample, with the most commonly reported criteria being the development of significant tolerance (endorsed by 62% of the sample), unsuccessful attempts to stop or reduce Ecstasy use (45%), and repeatedly using more or for longer than intended (41%). In total, 48% of their sample of regular Ecstasy users met the diagnostic criteria for dependence on the drug, and 36% met diagnostic criteria for abuse.

49. Also reporting high rates of Ecstasy use disorders was the study of Cottler et al. (2001). In order to examine the applicability of DSM diagnoses to Ecstasy, these authors twice administered a structured diagnostic interview schedule to 52 young people aged 13-27 years old, who reported having used Ecstasy more than five times in their lifetimes. (They found that when the same interview was administered to the same users a second time approximately five days after the first interview, the dependence criteria exhibited acceptable test-retest reliability.) The researchers reported that, of their sample, 43% met criteria for dependence on Ecstasy, and 34% met criteria for abuse.

50. Von Sydow et al. (2002) have reported perhaps the most rigorous examination to date of self-reported symptoms of dependence among Ecstasy users, using a prospective longitudinal design in which a representative sample of young people have been followed over time to examine the development of Ecstasy and other drug use disorders. The study found that, although about 1% of the sample of young people met criteria for an Ecstasy use disorder at baseline, the rates for spontaneous cessation of Ecstasy use were high at follow-up, even among those who had met criteria for a diagnosis at baseline. This finding led the study's authors to suggest that although Ecstasy use disorders do occur, they are a relatively transient and youth-specific phenomenon, and only a small proportion of regular users of the drug are likely to develop chronic problems controlling their use of the drug.

51. A major limitation of the literature relating to the assessment of abuse and dependence symptoms among self-reported Ecstasy users is that it is virtually impossible to obtain reliable and valid information about the specific chemical structure of the substances used, because of the extreme

heterogeneity and variability of active ingredients in tablets sold as Ecstasy. In other words, although a slowly growing body of evidence suggests that users will report symptoms of dependence on the use of tablets sold as Ecstasy, the extent to which these results are relevant to MDMA is extremely difficult to determine.

52. Having noted this limitation, it is also important to observe that, were MDMA shown in the future to be a drug that was not associated with a dependence potential, such a finding would be unique and highly counter-intuitive. This is because virtually all drugs that are repeatedly self-administered by humans who desire specific subjective effects have been shown, eventually, to be associated with a risk of dependence. In the absence of strong evidence to the contrary, it seems unlikely that MDMA would be a drug that followed a substantially different pattern to that of all other drugs that have been demonstrated to be voluntarily and repeatedly self-administered by human drug users. The facts that, under some circumstances, primates will engage in repeated self-injection of MDMA (eg. Beardsley et al. 1986; Lamb and Griffiths 1987), and MDMA is known to activate the dopaminergic reward pathways, which may underlie the rewarding effects of other drugs used illicitly by humans (Nichols and Oberlander 1989), are also consistent with the notion that MDMA use is associated with some risk of dependence (McCann and Ricaurte 2000).

53. In summary, a small but growing literature indicates that some users report symptoms of dependence on the use of tablets they purchase as Ecstasy, and that a proportion of these meet clinical criteria for a diagnosis of dependence on the drug. The extent to which these results are relevant to MDMA is impossible to determine, as a result of the heterogeneity and variability of the contents of tablets sold as Ecstasy. Although further research is required before a complete understanding of the nature of dependence on Ecstasy can be clarified, it seems reasonable to suggest that, in the future, MDMA is likely to be demonstrated to have moderate dependence liability, in that a substantial minority of those who use Ecstasy regularly are likely, at some point, to: (1) experience problems in controlling their use of the drug, (2) continue to use despite knowing that the drug is causing them physical, psychological or social problems, and (3) find that their Ecstasy use has assumed priority over other activities that were once considered important. The most recent and rigorous research in this area suggests that, although MDMA use disorders do occur, they are a relatively transient and youth-specific phenomenon, and only a small proportion of regular MDMA users are likely to develop chronic problems in controlling their drug use.

International classification and experience

United Nations drug control conventions

54. As a state party to the 1971 United Nations Convention on Psychotropic Substances, New Zealand has an international treaty obligation to implement a control regime for the drugs that are listed in the schedules to the Convention. Along with its ‘parent’ compound MDA, and the chemically

related substances DMA, DOB, DOM, PMA and TMA, MDMA is listed as a Schedule I substance under the 1971 Convention.

55. MDMA's Schedule I status under the 1971 Convention, while not requiring New Zealand to put in place any particular legal regime for the drug, does require that dealings with MDMA at a national level must be prohibited, except for scientific and very limited medical purposes. Schedule I status reflects an assessment by the World Health Organization Expert Committee on Drug Dependence that MDMA is a substance whose liability to abuse constitutes an especially serious risk to public health, and which has very limited (if any) therapeutic utility.

56. While the current classification of MDMA in Part 2 of the Second Schedule of the Misuse of Drugs Act technically fulfils New Zealand's international obligation to strictly control this substance, the EACD may feel that elevating MDMA to a higher classification better reflects the risk assessment that the drug has been given by the World Health Organization, and the wider United Nations system.

Other countries' classification of MDMA

57. In the United States, MDMA is a Schedule 1 substance under the Controlled Substances Act; and in the United Kingdom, MDMA is a Class A drug under the Misuse of Drugs Act.

58. MDMA is also a highly controlled substance in most Australian jurisdictions. For example, MDMA is a Schedule I substance under Queensland's Drugs Misuse Act Regulations 1987, Victoria's Drugs, Poisons and Controlled Substances Act 1981, and South Australia's Controlled Substances (Prohibited Substances) Regulations 2000. Similarly, in the Australian Capital Territory, MDMA is listed in the same category of substances as heroin and LSD, under that jurisdiction's Drugs of Dependence Act 1989 and Drugs of Dependence Regulations 1993.

59. The assessment and classification of MDMA by the World Health Organization and the United Nations drug control treaties, clearly recognises that MDMA's liability to abuse constitutes an especially serious risk to public health, and that it has very limited (if any) therapeutic utility. This assessment and classification is reflected in strict controls associated with MDMA in the legislation of several overseas jurisdictions.

RECOMMENDED PRESUMPTION FOR SUPPLY AND JUSTIFICATION

60. The EACD recommends that a presumption for supply of MDMA be set at:

- 5 grams or more of MDMA, whether or not contained in a substance, preparation, or mixture.

61. This figure is based on an assumption that the average active dose is between 30 mg and 170 mg, averaging to around 100 mg. Thus 5 grams of

pure MDMA would be the equivalent of approximately 50 doses and have a street level price of between $3000 and $4000. However, this figure does not account for groups of people buying in larger quantities to avoid detection. For example, current intelligence suggests that MDMA can be distributed at a wholesale level for around $18 a tablet, if the quantities purchased are between 10,000 and 20,000 tablets (NDIB 2003). Such issues will need to be taken into consideration during any vetting process for compliance with the New Zealand Bill of Rights Act 1990.

OTHER RELEVANT INFORMATION

Organised crime links with importation of MDMA

62. National Drug Intelligence Bureau analysts are concerned that, despite the Netherlands remaining the main source of MDMA being illegally trafficked into the country, three clandestine laboratories capable of producing MDMA have recently been located and dismantled in New Zealand. This is a worrying trend, and reflects the fact that organised crime groups internationally and domestically recognise the potential to further exploit New Zealand's expanding market for Ecstasy.

63. In addition to Asian organised crime involvement in the New Zealand MDMA market, law enforcement officials have detected the emergence of Israeli and Dominican Republic trafficking syndicates in recent large-scale MDMA seizures. One of these successful Police and Customs operations in December 2002 resulted in New Zealand's largest ever seizures of MDMA (53,895 tablets).

64. Combined with the huge rise in MDMA seizures during the last two years (from some 10,000 tablets in 2000 to a provisional estimate of 248,034 tablets in 2002) law enforcement agencies are deeply concerned that New Zealand is being targeted by organised crime groups as a lucrative market for illegally trafficked or manufactured MDMA.

65. The high profitability and current Class B classification of MDMA may contribute to the readiness of persons to become involved in illicit manufacturing and/or trafficking of the drug.

Significant developments

New trafficking trends

66. Significant developments have included two importations (9 litres in total) of pure MDMA base oil (which are believed to be the first seizures of "trafficked" MDMA base product in the world). If MDMA manufacturers and traffickers in the Benelux nations move to utilise this liquid method as the norm, it represents a critical challenge to law enforcement.

67. Another significant development has been the importation of four litres of the precursor chemical Sassafras Oil using the Internet (which could potentially have yielded between 10,000 and 20,000 MDMA tablets, depending upon

the manufacturing process). In recent times, Police and Customs Service officials have also recorded New Zealand's first significant importations of MDMA powder by attempted internal concealment. The concealment method makes MDMA virtually impossible to detect at the border, and seizure must rely on effective intelligence and investigation.

Attempts at domestic manufacture

68. As noted earlier, the Netherlands as a source-country accounts for the overwhelming majority (some 99%) of MDMA seizures made by Police and Customs Service personnel. However, in the past year there has been evidence that MDMA is being manufactured domestically in clandestine drug laboratories.

69. The synthesis of MDMA requires high levels of chemistry and pharmaceutical knowledge and skills, as well as sophisticated apparatus (National Drug Intelligence Center 2000). The risk of explosion, chemical burns or poisoning associated with manufacture of MDMA is high due to the toxic, corrosive, volatile and extremely flammable chemicals used in the production process. These risks are often exacerbated by the fact that those involved in the manufacturing often have a very rudimentary knowledge of the chemical process they are completing, and also do not typically observe safe chemical handling and disposal practises.

70. There are also very real risks of environmental pollution associated with the illicit manufacture of MDMA in New Zealand. A number of clandestine laboratory operators, both nationally and internationally, have already been discovered dumping chemical waste into local water supplies, venting fumes near schools, and dumping volatile waste into natural waterways. In this context, it is notable that Dutch authorities have estimated that the manufacture of 1 kilogram of MDMA produces 12 kilograms of toxic waste (NDIB 2003).

'Passing off' other substances as MDMA

71. Concern that New Zealand is being targeted by organised crime groups as a lucrative market for MDMA also raises further issues about the potential for pills to be sold as Ecstasy, but actually containing other, more dangerous substances. This trend has been observed in several 'mature' Ecstasy markets, where tablets sold on the street as Ecstasy have contained more potent drugs like PMA. For instance, PMA tablets responsible for four deaths in Norway and Denmark since 2000 were marked with the "Mitsubishi" or "E" logo - well known Ecstasy tablet brands – in order to be passed off as pills containing MDMA. Likewise, 12 deaths have been recorded in Australia since 1994, as a result of users consuming what they thought was Ecstasy but was in fact PMA (see ABCI 2002).

72. The use of logos on Ecstasy tablets is a marketing tactic that can lead the user into thinking that it is the same, or will have the same effect, as a previously consumed tablet bearing the same logo. This is far from guaranteed, however, as the strength and composition of Ecstasy tablets can

vary widely, leading to the potential for different and unpredictable reactions to the pills by consumers. [The variability of tablets sold as “E” was borne out by New Zealand testing of all Ecstasy seizures in 1999/2000, which found MDA, MDEA, methamphetamine, amphetamine, and ketamine in some samples (ESR 2000). Of the 8604 doses of MDMA analysed during this period, the strength of the pills ranged from 30.2 mg/dose to 172.4 mg/dose, and the tablet purity ranged from 12.7% to 97.3%.]

Polydrug use by people who consume MDMA

73. One final significant development that is worthy of note is that Ecstasy users often tend to be polydrug users, who combine licit and illicit drugs to increase the pleasurable effects of the substance, as well as to soften the withdrawal effects. In particular, quantitative and qualitative studies of MDMA users indicate that alcohol and cannabis are often used to soften the ‘come down’ symptoms of having taken Ecstasy (see, for instance, Hammersley et al. 2002). There is also evidence of an emerging trend where Ecstasy is being used in conjunction with other drugs: in particular, LSD, ketamine, GHB and a variety of hallucinogenic substances. The health risks associated with MDMA can increase if other drugs are consumed at the same time, or shortly after taking MDMA, because of the uncertain chemical and idiosyncratic reactions that can result from mixing drugs.

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