

## Ketamine's medical usage, abuse prevalence and control status

1. Ketamine belongs chemically to the phenyl cyclohexamine class, and like other drugs in its class, functions as a dissociative anaesthetic.<sup>1</sup> First synthesized in 1962,<sup>2</sup> ketamine has been used as a general anaesthetic in human and veterinary medicine<sup>3</sup> for some fifty years. At sub-anaesthetic doses, it is also used in select conditions for the management of pain<sup>4</sup> and depression.<sup>5</sup> However, aside from relieving pain, ketamine induces schizophrenia-like symptoms, such as hallucinations, social withdrawal and memory impairment.<sup>6</sup> Consequently, it is abused recreationally to produce feelings of unreality and bodily detachment.

2. Ketamine, some experts argue, should be under international control because of its potential for misuse. Its misuse was first reported amongst medicinal chemists in the United States in 1967,<sup>7</sup> and became more widespread in Europe in the 1990s, where it gained popularity as an adulterant in ecstasy tablets.<sup>8-9</sup> Today, recreational ketamine is geographically widespread, but its use is still mostly limited to nightclub and rave scenes.<sup>10-11</sup> Its prevalence in the general population is unknown, although it is estimated to be low (0.1 to 4%) in some countries.<sup>12</sup> For instance, 1.5% of twelfth grade students (ages 17-18) in the United States self-reported past-year ketamine use in 2014.<sup>13</sup> Global ketamine seizures may also provide an estimate of the substance's abuse prevalence. Seizures have increased significantly in recent years, almost all of which is attributable to East and South-East Asia, where seizures doubled from 6 tons in 2012 to more than 12 tons in 2014.<sup>13</sup> A rise in the non-medical use of ketamine in these regions<sup>13</sup> has prompted some countries to raise concerns about ketamine abuse<sup>14</sup> and a number of countries have placed the substance under national control.

3. Preventing misuse and diversion of ketamine into illicit traffic would be the key goal of putting ketamine under international control. Because of the difficulty in synthesizing ketamine, past reports observed only diversion from licit markets, such as veterinary clinics, hospitals and pharmacies.<sup>15</sup> However, in recent years, hundreds of illicit ketamine manufacture cases have been reportedly discovered in East and South-East Asia, and the clandestine laboratories dismantled.<sup>13</sup>

4. In 2014, the World Health Organization (WHO) recommended for the third time since 2006 that ketamine not be placed under international control. This recommendation was reconfirmed in 2015.<sup>14</sup> In its various reports (2006, 2012, 2014 and 2015), the WHO concluded that the threat of ketamine abuse to global public health did not appear to be a sufficient enough reason to warrant

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<sup>1</sup> R Quibell, M Fallon, M Mihalyo, R Twicross, A Wilcock (2015) "Therapeutic Reviews: Ketamine," *Journal of Pain and Symptom Management* 50(2): 268-278

<sup>2</sup> EF Domino, P Chodoff, G Corssen (1965) "Pharmacologic effects of Ci-581, a new dissociative anesthetic, in man," *Clinical Pharmacology and Therapeutics* 6(3):279-291

<sup>3</sup> J Carter, DA Story (2013) "Veterinary and human anaesthesia: an overview of some parallels and contrasts," *Anaesthesia and Intensive Care; Edgecliff* 41(6):710-718

<sup>4</sup> E Visser, S Schug (2006) "The role of ketamine in pain management," *Biomedicine and Pharmacotherapy* 60(7):341-348

<sup>5</sup> RM Berman, A Cappiello, A Anand, DA Oren, GR Heninger, DS Charney, JH Krystal (2000) "Antidepressant effects of ketamine in depressed patients," *Biological Psychiatry* 47(4):351-354

<sup>6</sup> A Lahti, M Weiler, T Michaelidis, A Parwani, C Tamminga (2001) Effects of ketamine in normal and schizophrenic volunteers," *Neuropsychopharmacology* 25(4):455-467

<sup>7</sup> K Jansen (2004) "Ketamine: Dreams and Realities," *Multidisciplinary Association for Psychedelic Studies: Sarasota, US*, 24

<sup>8</sup> PJ Dalgarno, D Shewan (1996) "Illicit use of ketamine in Scotland," *Journal of Psychoactive Drugs* 28(2): 191-199

<sup>9</sup> J Arditti (2000) "Ketamine, déviation d'usage en France," *Centre d'Evaluation et d'Information sur la Pharmacodépendance: Marseille, France*

<sup>10</sup> D Wood, M Nicolaou, P Dargan (2009) "Epidemiology of recreational drug toxicity in a nightclub environment," *Substance Use and Misuse* 44(11):1495-1502

<sup>11</sup> AS Kalsi, D Wood, P Dargan (2011) "The epidemiology and patterns of acute and chronic toxicity associated with recreational ketamine use," *Emerging health threats journal* (4):7107

<sup>12</sup> See estimates from Australia, Canada, United Kingdom and United States in Kalsi et al (2011)

<sup>13</sup> Report of the International Narcotics Control Board for 2015 (2016) E/INCB/2015/1

<sup>14</sup> The WHO Expert Committee on Drug Dependence presented "Ketamine (INN): update review report" at its 37th meeting, Geneva, 16-20 November 2015

<sup>15</sup> WHO Expert Committee on Drug Dependence's (2006) 34<sup>th</sup> report, "Critical Review of Ketamine," Geneva

scheduling. Moreover, because of ketamine's good safety profile, good efficacy and easy use,<sup>16</sup> it is frequently used worldwide. For example, ketamine exerts its anaesthetic effects while preserving the patient's cardiovascular stability, respiratory drive and airway reflexes.<sup>17</sup> Thus, in some low-resourced settings (e.g., without respiratory supports), it is often the only anaesthetic available for emergency or surgical procedures.<sup>14</sup> In fact, because of its medical utility, ketamine has been on the WHO List of Essential Medicines since 1985.<sup>18</sup>

5. To date, ketamine has not been placed under international control. The INCB, pursuant to resolutions 49/6, 50/3 and 57/10 of the Commission on Narcotic Drugs, calls upon Governments to pay particular attention to the misuse and diversion of ketamine. The INCB invites Governments to consider controlling ketamine under national legislation, where such measures are required, while ensuring its access for medical and scientific purposes. The INCB further encourages Governments to consider adopting an import-export authorizations system. A list of the countries and territories requiring import and/or export authorization for ketamine is updated regularly, and is available to all Governments in the Secure Area for Governments of the INCB.org website.<sup>19</sup>

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INCB is the independent, quasi-judicial body charged with promoting and monitoring Government compliance with the three international drug control conventions: the 1961 Single Convention on Narcotic Drugs, the 1971 Convention on Psychotropic Substances, and the 1988 Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances.

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<sup>16</sup> SM Green, NE Johnson (1990) "Ketamine sedation for pediatric procedures: Part 2, review and implications." *Annals of Emergency Medicine* 19(9):1033-1046

<sup>17</sup> G Dolansky, A Shah, G Mosdosy, MJ Rieder (2008) "What is the evidence for the safety and efficacy of using ketamine in children?" *Paediatrics and Child Health* 13(4):307-308

<sup>18</sup> WHO (2017) "WHO model list of essential medications," 20th edition

<sup>19</sup> See INCB Secure Area for Governments: [https://www.incb.org/incb/gov\\_secure/index.html?lf\\_id=](https://www.incb.org/incb/gov_secure/index.html?lf_id=)