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Implementation of the international drug control treaties:**Changes in the scope of control of substances****Further information provided by the People's Republic of China on the proposed scheduling of ketamine**

On 8 March 2014, pursuant to article 2, paragraph 1, of the Convention on Psychotropic Substances of 1971, the Government of China notified the Secretary-General of the United Nations that China recommended that ketamine should be placed in Schedule I of the 1971 Convention (see E/CN.7/2015/7, annex III).

Following its thirty-sixth meeting, the World Health Organization's Expert Committee on Drug Dependence has recommended that ketamine not be placed under international control at this time (see E/CN.7/2015/7, annex IV).

On 4 March 2015, the Government of the People's Republic of China referring to its note verbale dated 8 March 2014, informed the Secretary-General of the United Nations, that China wished to change the proposal for scheduling ketamine from under Schedule I to under Schedule IV of the 1971 Convention, based on further consideration guided by the principle of a comprehensive and balanced approach with regard to the needs, on one side, to prevent the ever-growing and wide abuse, diversion and illicit trafficking of ketamine, and on the other side, to ensure its availability for therapeutic use.

The annex to this document contains further supporting information and rationales for considering the proposal to control ketamine under Schedule IV of the 1971 Convention on Psychotropic Substances, submitted by the People's Republic of China.

* E/CN.7/2015/1.



Annex

Further information and rationales for the proposal to list ketamine under Schedule IV of the 1971 Convention on Psychotropic Substances**

I. The abuse and illicit trafficking of ketamine is becoming a global trend

According to various reports and assessments of UNODC and INCB (including most recent ones: UNODC World Drug Report (2013, 2014), UNODC 2014 Global Synthetic Drugs Assessment and INCB Annual Report (2014, 2015)), the abuse, illicit manufacturing, illicit trafficking and flow of ketamine in recent years through illicit channels are no longer limited to certain countries in Asia. As ketamine begins to be a substance of abuse globally, manufacturing and trafficking has been worsening and becoming a global problem. Abuse of ketamine is also becoming a public health issue in many countries posing health risks and public-health concern. INCB “has noted with concern” that “diversion or trafficking of ketamine has been noted worldwide and that the abuse of ketamine has become a health risk in a number of countries” (E/CN.7/2014/CRP.2). Over the years, Member States have continuously expressed concern on this topic in meetings of the United Nations Commission on Narcotic Drugs (UNCND), and the UNCND has also passed several relevant resolutions by consensus (resolution 49/6 “Listing ketamine as a controlled substance” in 2006, resolution 50/3 “Responding to threats posed by the abuse and diversion of ketamine” in 2007 and resolution 57/10 “Preventing the diversion of ketamine from legal sources while ensuring its availability for medical use” in 2014).

Back in 2009, 48 countries had imposed national control on ketamine (E/CN.7/2014/1). By 2014, of the 105 countries and territories which responded to the UNCND’s report, 63 had already introduced import authorization requirements for ketamine, and 57 had introduced export authorization requirements (E/CN.7/2014/1). Those figures cover countries/territories from various regions. This also indicates that the trend of abuse and trafficking of ketamine has increasingly aroused concern among a considerable number of countries across various regions.

II. The abuse of ketamine constitutes a serious public health and social problem

The abuse of ketamine leads to various negative social and public health consequences.

Ketamine has clear drug abuse potential and drug dependency. Theoretically and clinically, it is observed that ketamine has the potential to be abused and cause

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dependency. According to researches, ketamine has strengthening effect. Animal experiments show that ketamine could produce self-administration and drug discrimination. Its euphoriant effect is similar to cocaine and cannabis.

In recent years, there are more researches on the damages of ketamine to humans and other aspects. For example, various research reports have indicated that prolonged and heavy dosage of abuse of ketamine will cause damages to the urinary system, brain, cognitive system and kidneys. It will also lead to relevant psychological and mental disorders. In particular, there is no lack of clinical cases and research reports which show that ketamine will cause irreversible damage to the urinary system. These symptoms of the urinary system suffered by long-term abusers still persist even after they cease abusing ketamine. The most common examples include painful urination, debilitating urinary frequency, incontinence and haematuria. These symptoms seriously disrupt the daily lives of the drug abusers. Some need to wear diapers. In severe cases, urinary bladders have to be removed and the patients have to wear an external urostomy bag to collect urine for the rest of their lives. Latest researches also show that long-term abuse of ketamine will lead to abnormal liver function. The damage of ketamine abuse is no longer limited to a few human organs.

Long-term chronic users, short-term repeated users and simple high-dose users of ketamine are all susceptible to positive symptoms of schizophrenia like acoasm and delusion etc. and negative symptoms like lack of feeling or emotion, a loss in interest in social activities such as shrinking from others, fear and depression etc. Numerous clinical observations in recent years also confirm that the abuse of ketamine can damage the urinary system, liver and other important human organs. The memory quotient, vocal intelligence quotient, performance intelligence quotient and full intelligence quotient of ketamine abusers dropped obviously compared to the control group, showing obvious damages to the memory and intelligence of the abusers. When ceasing to take ketamine, they exhibit different levels of withdrawal syndromes, mainly drug-taking desire, drowsiness and exhaustion. One of the clinical conditions for the abuse of ketamine is abstinence syndrome, displaying an increase in drug tolerance, the appearance of withdrawal syndromes and compulsive drug-seeking behaviours etc.

Ketamine abuse may spread HIV and other infectious diseases. Ketamine is a synthetic drug with "Club Drug" features. Teenagers usually take ketamine in places of public entertainment. The effect of hallucination and stimulation generated by ketamine abuse could lead to sexual impulse. On one hand, abusers may commit sexual offences like rape etc. On the other hand, it could help spread HIV and other infectious diseases which impose serious public hygiene and social problems. Acts of sexual intercourse after abusing ketamine would also hamper the continuous usage rate of condoms will also decrease.

Abuses of ketamine result in substantial loss of wealth in the society, jeopardizing public security and hence resulting in serious social problems. The majority of ketamine abusers are young people. The need for resources to finance drug taking causes criminal activities like robberies and thefts. Some ketamine abusers suffer from drug-induced hallucinations and commit serious crimes like homicide or causing bodily harm to others. Apart from physical dependence, ketamine abusers also typically display mental and behavioural dependence symptoms. In addition, the increase in young abusers with irreversible health

damage inflicted by prolonged ketamine abuse also imposes a heavy burden on the medical and social welfare services in supporting them on a long-term basis, significant productivity loss and serious family problems (Survey Report on Ketamine Abuse in China submitted to the United Nations by China in March 2014).

III. Ketamine becomes less difficult to synthesize

While the report of the 36th meeting of ECDD suggests that it is difficult to synthesize ketamine, there is more and more evidence indicating another trend. The scale of illicit manufacture of ketamine in Asia has been increasing year by year. According to the law enforcement agencies of China, there were more than 105 cases of illicit manufacture of ketamine, with 501 clandestine laboratories dismantled nationwide in 2014 and a total of 7.85 tons of ketamine seized. These statistics account for an increase of 122 per cent as compared with 2013. In Asia, the majority of illicit ketamine were synthesized in clandestine laboratories instead of sourcing from licit channel. These clandestine laboratories are capable of synthesizing the precursor, 1-[(2-chlorophenyl)-*N*-(methylimino)methyl]cyclopentanol from various chemicals (1-[(2-chlorophenyl)-*N*-(methylimino)methyl]cyclopentanol is synthesized through bromination and amination from 2-chlorophenyl cyclopentyl ketone). Ketamine is finally synthesized from a rearrangement process by heating. Although the synthesis of the precursor is relatively complicated, the final step from 1-[(2-chlorophenyl)-*N*-(methylimino)methyl]cyclopentanol to ketamine requires electric ovens or stoves only instead of professional chemical equipment without major technical problems. Thus, there is a high risk of the spread of such technical knowledge to other countries or regions.

IV. The adverse drug reactions (ADR) of ketamine as a medicine and its being limited and decreasing in clinical use

Although ketamine is relatively cheap and easy to use clinically, it has adverse drug reactions (ADR), such as hallucination, agitation etc. With the availability of newer anaesthetic and sedative agents, the clinical usage of ketamine has therefore decreased in recent years and in most of the developed countries it is only for veterinary use. Ketamine is currently used mainly as a second line sedative agent, in particular for patients with cardiorespiratory instability, due to the lack of side effect on respiration and blood pressure.

Ketamine is relatively cheap for medical use. The increased potential of its manufacturing for abuse purposes also suggests that it is relatively more affordable than many other psychoactive substances, hence its rapid growth as a popular drug of abuse in countries or regions plagued by the problem.

V. Scheduling of ketamine will not substantively restrict its accessibility and availability for medical and use

In view of the fact that various substances to be under international control may have medical and pharmaceutical values in varying degrees, the 1971 Convention on Psychotropic Substances, based on the comprehensive and balanced consideration on the need to prevent risks posed by abuse of those substances and the other need to ensure their medical values, classifies schedules of control into Schedule I to Schedule IV. The listing of substances under different schedules aims to reaffirm the medical and pharmaceutical values of the relevant substances, while minimizing the negative risks that might be posed to human beings through their illicit abuse. In proposing to list ketamine under Schedule IV (the most lenient control measure) of the 1971 Convention on Psychotropic Substances, it is intended to curtail, even with the minimum degree international cooperation as the schedule IV dictates, the further worsening and spreading of the risks posed by its abuse, diversion and illicit trafficking, and at the same time, in acknowledging its medical and therapeutic values in developing countries, to ensure to the maximum extent its accessibility and availability for medical uses in developing countries to be protected from any substantive restriction.

Under Schedule IV, the manufacture, trade and distribution of substances need to be under licence or other similar control measure. And it would require medical prescriptions for its supply and dispensing. Quantities manufactured, as well as on total quantities exported and imported would be reported to INCB to furnish to the Board's annual statistical reports.

All the above-mentioned would not pose unreasonable burdens to its medical use and import and export trade.

Under the 1971 Convention on Psychotropic Substances, placing ketamine in Schedule IV would not substantively or unreasonably limit its availability and accessibility. A number of other substances considered to have medical value had been listed under Schedule IV (including diazepam, recognized as a core medicine in the WHO Model List of Essential Medicines), but their continued use for proper medical purposes has not been affected.

Considering the controlled measure of ketamine in China, scheduling even under Class I of Psychotropic Substances (the strictest controlling for psychotropic substance in China) doesn't prevent it from medical use.

In addition, under paragraph 3 of article 9 of the 1971 Convention, member States could still, if local circumstances so require, authorize, licensed pharmacists or relevant public health authorities to supply without prescriptions the substances in Schedule IV for medical uses by individuals in exceptional cases, which reflects the flexibility of scheduling of substances while preserving their medical use.

VI. The control of substances calls for international cooperation

Ketamine is a substance liable to abuse, diversion and illicit trafficking and has not yet been under international control despite the decade-long continued calls by a growing number of concerned countries to that effect. This is one major reason

for the worsening situation of its illicit production, manufacturing, smuggling and trafficking in Asia and beyond, and for the difficulties encountered by the affected countries or regions in taking effective anti-drug law enforcement actions.

The INCB shared the opinion of the Governments concerned on the growing risks posed by the continued abuse, diversion and illicit trafficking of ketamine that “national control measures alone may not be sufficient to enable law enforcement cooperation between the countries involved” (E/CN.7/2014/CRP.2).

As affirmed by the “Political Declaration and Plan of Action” in 2009, the world drug problem remains a common and shared responsibility that requires effective and increased international cooperation. It is far from sufficient to rely on regional or national measures and efforts alone in combating a newly emerged substance which poses health hazards. The preamble of the 1971 Convention on Psychotropic Substances clearly states that “Believing that effective measures against abuse of such substances require co-ordination and universal action”. This is the very purpose of the Convention in establishing a control regime offering a wide range of scheduling options for concerned substances proportionate to their abuse risks and medical values.

It is more strategic to make a balanced and integrated understanding on the necessity and cost-effectiveness assessment of scheduling from the worldwide point of view. It is far from sufficient to depend upon the internal control measures implemented by any single country or region to prevent risks posed by abuse of substances of dangerous properties like ketamine. It is only through bringing ketamine under some form of international control that there is a chance to call to a halt the burgeoning trend of risks posed by its abuse, diversion and illicit trafficking.

To conclude, in view of the fact that the abuse, illicit manufacturing and trafficking of ketamine have posed serious threats to public health and social cohesion in Asia and beyond, at the same time, taking full account of the medical value of ketamine, China proposes listing ketamine in Schedule IV of the 1971 Convention. Such proposal is in line with the basic principle of achieving an appropriate balance between the prevention of abuse, illicit manufacturing and trafficking of concerned substances, and ensuring its availability to the maximum extent for medical purposes, as promulgated by the 1971 Convention.