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Implementation of the international drug control treaties: changes in the scope of control of substances

Changes in the scope of control of substances: proposed scheduling recommendations by the World Health Organization on new psychoactive substances and medicines

Note by the Secretariat

Summary

The present document contains recommendations for action to be taken by the Commission on Narcotic Drugs pursuant to the international drug control treaties.

In accordance with article 3 of the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol, the Commission will have before it for consideration a recommendation by the World Health Organization (WHO) to place crotonylfentanyl and valerylfentanyl in Schedule I of that Convention.

In accordance with article 2 of the Convention on Psychotropic Substances of 1971, the Commission will have before it for consideration a recommendation by WHO to place DOC in Schedule I of that Convention, a recommendation to place AB-FUBINACA, 5F-AMB-PINACA (5F-AMB, 5F-MMB-PINACA), 5F-MDMB-PICA (5F-MDMB-2201), 4-F-MDMB-BINACA, 4-CMC (4-chloromethcathinone; clephedrone), *N*-ethylhexedrone and *alpha*-PHP in Schedule II of that Convention and a recommendation to place flualprazolam and etizolam in Schedule IV of that Convention.

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I. Consideration of the notification from the World Health Organization concerning scheduling under the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol

1. Pursuant to article 3, paragraphs 1 and 3, of the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol, the Director-General of the World Health Organization (WHO), in correspondence dated 15 November 2019, notified the Secretary-General of the United Nations that WHO recommended that crotonylfentanyl and valerylfentanyl be added to Schedule I of that Convention (see annex for the relevant extract of that notification).

2. In accordance with the provisions of article 3, paragraph 2, of the 1961 Convention, on 2 December 2019, the Secretary-General transmitted to all Governments a note verbale to which the notification and the information submitted by WHO in support of its recommendations were annexed. The recommendations had been presented to the Commission on Narcotic Drugs by the representative of WHO at the reconvened sixty-second session of the Commission, held in Vienna on 12 and 13 December 2019.

Action to be taken by the Commission on Narcotic Drugs

3. The notification from the Director-General of WHO is before the Commission on Narcotic Drugs for its consideration, in accordance with the provisions of article 3, paragraph 3 (iii), of the 1961 Convention, which reads as follows:

> If the World Health Organization finds that the substance is liable to similar abuse and productive of similar ill-effects as the drugs in Schedule I or Schedule II or is convertible into a drug, it shall communicate that finding to the Commission which may, in accordance with the recommendation of the World Health Organization, decide that the substance shall be added to Schedule I or Schedule II.

4. With regard to the decision-making process, the attention of the Commission is drawn to rule 58 of the rules of procedure of the functional commissions of the Economic and Social Council, which stipulates that decisions are to be made by a majority of the members present and casting an affirmative or negative vote. Members who abstain from voting are considered as not voting.

5. The Commission should therefore decide:

(a) Whether or not it wishes to include crotonylfentanyl in Schedule I of the 1961 Convention;

(b) Whether or not it wishes to include valerylfentanyl in Schedule I of the 1961 Convention.

II. Consideration of a notification from the World Health Organization concerning scheduling under the Convention on Psychotropic Substances of 1971

6. Pursuant to article 2, paragraphs 1 and 4, of the Convention on Psychotropic Substances of 1971, the Director-General of WHO, in correspondence dated 15 November 2019, notified the Secretary-General that WHO recommended placing DOC in Schedule I of that Convention, AB-FUBINACA, 5F-AMB-PINACA (5F-AMB, 5F-MMB-PINACA), 5F-MDMB-PICA (5F-MDMB-2201), 4-F-MDMB-BINACA, 4-CMC (4-chloromethcathinone; clephedrone), *N*-ethylhexedrone and *alpha*-PHP in Schedule II of that Convention and flualprazolam and etizolam in Schedule IV of that Convention (see annex for the relevant extract of that notification).

7. In accordance with the provisions of article 2, paragraph 2, of the 1971 Convention, on 2 December 2019, the Secretary-General transmitted to all Governments a note verbale to which the notification and the information submitted by WHO in support of its recommendations were annexed. The recommendations had been presented to the Commission on Narcotic Drugs by the representative of WHO at the reconvened sixty-second session of the Commission, held in Vienna on 12 and 13 December 2019.

Action to be taken by the Commission on Narcotic Drugs

8. The notification by the Director-General of WHO is before the Commission on Narcotic Drugs for its consideration, in accordance with the provisions of article 2, paragraph 5, of the 1971 Convention, which reads as follows:

> The Commission, taking into account the communication from the World Health Organization, whose assessments shall be determinative as to medical and scientific matters, and bearing in mind the economic, social, legal, administrative and other factors it may consider relevant, may add the substance to Schedule I, II, III or IV. The Commission may seek further information from the World Health Organization or from other appropriate sources.

9. With regard to the decision-making process, the attention of the Commission is drawn to article 17, paragraph 2, of the 1971 Convention, which stipulates that the decisions of the Commission provided for in articles 2 and 3 are to be taken by a two-thirds majority of the members of the Commission. From a practical point of view, this means that, for a decision to be adopted, an affirmative vote of at least 36 members of the Commission is required.

10. The Commission should therefore decide:

(a) Whether it wishes to place DOC in Schedule I of the 1971 Convention or, if not, what other action, if any, might be required;

(b) Whether it wishes to place AB-FUBINACA in Schedule II of the 1971 Convention or, if not, what other action, if any, might be required;

(c) Whether it wishes to place 5F-AMB-PINACA (5F-AMB, 5F-MMB-PINACA) in Schedule II of the 1971 Convention or, if not, what other action, if any, might be required;

(d) Whether it wishes to place 5F-MDMB-PICA (5F-MDMB-2201) in Schedule II of the 1971 Convention or, if not, what other action, if any, might be required;

(e) Whether it wishes to place 4-F-MDMB-BINACA in Schedule II of the 1971 Convention or, if not, what other action, if any, might be required;

(f) Whether it wishes to place 4-CMC (4-chloromethcathinone; clephedrone) in Schedule II of the 1971 Convention or, if not, what other action, if any, might be required;

(g) Whether it wishes to place *N*-ethylhexedrone in Schedule II of the 1971 Convention or, if not, what other action, if any, might be required;

(h) Whether it wishes to place *alpha*-PHP in Schedule II of the 1971 Convention or, if not, what other action, if any, might be required;

(i) Whether it wishes to place flualprazolam in Schedule IV of the 1971 Convention or, if not, what other action, if any, might be required;

(j) Whether it wishes to place etizolam in Schedule IV of the 1971 Convention or, if not, what other action, if any, might be required.

Annex

Extract of the notification from the Director-General of the World Health Organization to the Secretary-General dated 15 November 2019: scheduling of substances under the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol, and the Convention on Psychotropic Substances of 1971, including a summary of the rationale of the recommendations of the forty-second meeting of the Expert Committee on Drug Dependence

The forty-second meeting of the World Health Organization (WHO) Expert Committee on Drug Dependence was convened from 21 to 25 October 2019 at WHO headquarters in Geneva. The objective of the meeting was to carry out an in-depth evaluation of psychoactive substances in order to determine whether WHO should recommend that these substances be placed under international control or if their level of control should be changed.

At its forty-second meeting, the Committee reviewed 13 psychoactive substances, five of which are synthetic cannabinoids, four of which are synthetic stimulants, two of which are fentanyl analogues and two of which are benzodiazepines. In addition, the Committee carried out a pre-review of preparations of acetyldihydrocodeine, codeine, dihydrocodeine, ethylmorphine, nicocodine, nicodicodine, norcodeine and pholcodine that are listed in Schedule III of the 1961 Convention on Narcotic Drugs.

With reference to article 3, paragraphs 1 and 3, of the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol, and article 2, paragraphs 1 and 4, of the Convention on Psychotropic Substances of 1971, I am pleased to submit recommendations of the Expert Committee on Drug Dependence at its forty-second meeting, as follows:

To be added to Schedule I of the 1961 Convention

Crotonylfentanyl

Chemical name:
(2E)-*N*-phenyl-*N*-[1-(2-phenylethyl)piperidin-4-yl]but-2-enamide

Valerylfentanyl

Chemical name:
N-phenyl-*N*-[1-(2-phenylethyl)piperidin-4-yl]pentanamide

To be added to Schedule I of the 1971 Convention

DOC

Chemical name:
1-(4-chloro-2,5-dimethoxyphenyl)propan-2-amine

To be added to Schedule II of the 1971 Convention

AB-FUBINACA

Chemical name:
N-[1-amino-3-methyl-1-oxobutan-2-yl]-1-[(4-fluorophenyl)methyl]-1H-indazole-3-carboxamide

5F-AMB-PINACA (5F-AMB, 5F-MMB-PINACA)

Chemical name:
methyl 2-{[1-(5-fluoropentyl)-1H-indazole-3-carbonyl]amino}-3-methylbutanoate

5F-MDMB-PICA (5F-MDMB-2201)

Chemical name:
methyl 2-{[1-(5-fluoropentyl)-1H-indole-3-carbonyl]amino}-3,3-dimethylbutanoate

4-F-MDMB-BINACA

Chemical name:
methyl 2-{[1-(4-fluorobutyl)-1H-indazole-3-carbonyl]amino}-3,3-dimethylbutanoate

4-CMC (4-chloromethcathinone; clephedrone)

Chemical name:
1-(4-chlorophenyl)-2-(methylamino)propan-1-one

N-ethylhexedrone

Chemical name:
2-(ethylamino)-1-phenylhexan-1-one

Alpha-PHP

Chemical name:
1-phenyl-2-(pyrrolidine-1-yl)hexan-1-one

To be added to Schedule IV of the 1971 Convention

Flualprazolam

Chemical name:
8-chloro-6-(2-fluorophenyl)-1-methyl-4*H*-benzo[*f*][1,2,4]triazolo[4,3-*a*][1,4]diazepine

Etizolam

Chemical name:
4-(2-chlorophenyl)-2-ethyl-9-methyl-6H-thieno[3,2f][1,2,4]triazolo[4,3-a][1,4]diazepine

To be kept under surveillance

APINACA (AKB-48)

Chemical name:
N-(adamantan-1-yl)-1-pentyl-1H-indazole-3-carboxamide

To proceed to critical review

Preparations of acetyldihydrocodeine, codeine, dihydrocodeine, ethylmorphine, nicocodine, nicodicodine, norcodeine and pholcodine listed in Schedule III of the 1961 Convention

Summary of the rationale for the recommendations of Expert Committee on Drug Dependence at its forty-second meeting

1. Substances recommended to be added to Schedule I of the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol

1.1 Crotonylfentanyl

The chemical name for crotonylfentanyl is (2E)-*N*-phenyl-*N*-[1-(2-phenylethyl) piperidin-4-yl]but-2-enamide.

Crotonylfentanyl binds to mu opioid receptors and acts as an opioid agonist. In animal models, crotonylfentanyl produces antinociception, actions predictive of oxycodone-like subjective effects and both central nervous system stimulation and depression. The opioid antagonist naltrexone blocks the effects of crotonylfentanyl. This pharmacological profile indicates that crotonylfentanyl is an opioid and comparative studies suggest that it has a potency intermediate between oxycodone and fentanyl.

Consistent with the results from animal studies, the effects of crotonylfentanyl were reversed by an opioid antagonist in a clinical admission due to overdose. Owing to its opioid mechanism of action, crotonylfentanyl has the potential to be associated with substantial harm.

Crotonylfentanyl has been found in seized material from countries across several regions. It has no veterinary or medical use.

Based on its opioid mechanism of action and similarity to drugs such as oxycodone and fentanyl that are controlled under Schedule I of the 1961 Convention, it is recommended that crotonylfentanyl also be controlled under Schedule I of the 1961 Convention.

1.2 Valerylfentanyl

The chemical name for valerylfentanyl is *N*-phenyl-*N*-[1-(2-phenylethyl)piperidin-4-yl]pentanamide.

Valerylfentanyl binds to mu opioid receptors and acts as an opioid agonist. In animal models, valerylfentanyl suppresses opioid withdrawal symptoms, produces antinociception and has actions predictive of oxycodone-like subjective effects. The opioid antagonist naltrexone blocks the effects of valerylfentanyl. This pharmacological profile indicates that valerylfentanyl is an opioid and comparative studies suggest that it has a potency less than that of fentanyl.

Valerylfentanyl has been detected in biological samples from a small number of deaths and cases of driving under the influence of drugs.

Valerylfentanyl has been detected in seizures from countries across several regions. It has no veterinary or medical use.

Based on the evidence of its opioid mechanism of action and similarity to drugs such as fentanyl that are controlled under Schedule I of the 1961 Convention, it is recommended that valerylfentanyl also be controlled under Schedule I of the 1961 Convention.

2. Substance recommended to be added to Schedule I of the Convention on Psychotropic Substances of 1971

2.1 DOC

DOC is also known as 4-chloro-2,5-DMA or 2,5-dimethoxy-4-chloroamphetamine. Its chemical name is 1-(4-chloro-2,5-dimethoxyphenyl)propan-2-amine.

DOC is an agonist at the serotonergic 5-HT2A receptor, a mechanism it shares with hallucinogens such as LSD.

In animal models, DOC has actions predictive of hallucinogenic subjective effects (similar to LSD and DOM) and shows evidence of rewarding effects. It can produce both central nervous system stimulation and depression.

Based on clinical admissions due to overdose, the adverse effects associated with use of DOC include agitation, aggression, hallucinations, tachycardia, hyperthermia and seizures.

DOC has been detected in 40 countries. It has no veterinary or medical use.

Based on its similarity in mechanism of action and effects to currently scheduled hallucinogens such as LSD and DOM, and the evidence that it is abused so as to constitute a public health and social problem, it is recommended that DOC be controlled under the 1971 Convention. As it has no medical use and its use constitutes a serious risk to public health, it is recommended that it be controlled under Schedule I of the 1971 Convention.

3. Substances recommended to be scheduled in Schedule II of the Convention on Psychotropic Substances of 1971

3.1 AB-FUBINACA

The chemical name for AB-FUBINACA is *N*-[1-amino-3-methyl-1-oxobutan-2-yl]-1-[(4-fluorophenyl)methyl]-1H-indazole-3-carboxamide.

In common with other synthetic cannabinoids, AB-FUBINACA is a full agonist at the cannabinoid CB1 receptor that mediates the psychoactive effects of cannabinoids. In animal studies, it produced central nervous system depression and other typical cannabinoid behavioural effects and had actions predictive of cannabinoid subjective effects.

AB-FUBINACA produces neurological signs in animals that are indicative of toxicity, including seizures, hyperreflexia and aggression. Based on its mechanism of action, it would be expected to produce a range of adverse effects in human users that include tachycardia, nausea, vomiting, confusion and hallucinations. There are a large number of cases of intoxication resulting from AB-FUBINACA, often in combination with other drugs, and at least one death has been reported that is attributable to the effects of AB-FUBINACA.

AB-FUBINACA use has been reported in over 30 countries across different regions. It has no veterinary or medical use.

Based on its capacity to produce a state of dependence, its ability to produce central nervous system depression and the evidence that it is abused so as to constitute a public health and social problem, it is recommended that AB-FUBINACA be controlled under the 1971 Convention. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of the 1971 Convention.

3.2 5F-AMB-PINACA

5F-AMB-PINACA is also known as 5F-AMB and 5F-MMB-PINACA. Its chemical name is methyl 2-{[1-(5-fluoropentyl)-1H-indazole-3-carbonyl]amino}-3-methylbutanoate.

In common with other synthetic cannabinoids, 5F-AMB-PINACA is a full agonist at the cannabinoid CB1 receptor that mediates the psychoactive effects of cannabinoids. In animal studies it produced central nervous system depression and had actions predictive of cannabinoid-like subjective effects. 5F-AMB-PINACA produces impairment of memory and seizures in animals.

5F-AMB-PINACA use has been associated with a number of cases of fatal and non-fatal intoxication often in combination with other drugs. In a case of non-fatal intoxication due to 5F-AMB-PINACA alone, the effects included cognitive impairment, slowed movement, slurred speech and poor coordination. Based on its mechanism of action, it would also be expected to produce a range of other effects in human users that include tachycardia, nausea, vomiting, confusion and hallucinations. 5F-AMB-PINACA has been identified as a causal factor in motor vehicle accidents, some of which were fatal.

5F-AMB-PINACA use has been reported in over 30 countries across different regions. It has no veterinary or medical use.

Based on its capacity to produce a state of dependence, its ability to produce central nervous system depression and the evidence that it is abused so as to constitute a public health and social problem, it is recommended that 5F-AMB-PINACA be controlled under the 1971 Convention. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of the 1971 Convention.

3.3 5F-MDMB-PICA

5F-MDMB-PICA is also known as 5F-MDMB-2201. Its chemical name is methyl 2-{[1-(5-fluoropentyl)-1H-indole-3-carbonyl]amino}-3,3-dimethylbutanoate.

In common with other synthetic cannabinoids, 5F-MDMB-PICA is a full agonist at the cannabinoid CB1 receptor that mediates the psychoactive effects of cannabinoids.

Its use has been associated with a number of fatal and non-fatal intoxications that have been characterized by effects such as decreased mental status, agitated delirium and seizures. While 5F-MDMB-PICA has been present in biological samples mostly in combination with other drugs, in at least some of these cases 5F-MDMB-PICA has been assessed as having a high contribution to the effects produced. It has been used by victims of three apparent mass overdose events, but at least one other synthetic cannabinoid was also detected in biological fluids from the victims.

5F-MDMB-PICA has been detected in 20 countries. It has no veterinary or medical use.

Based on its mechanism of action, 5F-MDMB-PICA has the ability to produce a state of dependence and central nervous system depression. There is evidence that it is abused so as to constitute a public health and social problem. It is therefore recommended that 5F-MDMB-PICA be controlled under the 1971 Convention. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of the 1971 Convention.

3.4 4F-MDMB-BINACA

4F-MDMB-BINACA is also known as 4F-MDMB-BUTINACA. Its chemical name is methyl 2-{[1-(4-fluorobutyl)-1H-indazole-3-carbonyl]amino}-3,3-dimethylbutanoate.

In common with other synthetic cannabinoids, 4F-MDMB-BINACA is a full agonist at the CB1 receptor that mediates the psychoactive effects of cannabinoids.

Self-reported effects provided by individuals who had used cannabinoid products that included 4F-MDMB-BINACA as the major constituent, included auditory and visual hallucinations, vomiting, paranoia, euphoria, relaxation, irregular heartbeat, agitation, confusion, insomnia and chest pain. These effects are consistent with the cannabinoid full agonist mechanism of action of 4F-MDMB-BINACA. Its use has been associated with a number of fatal and non-fatal intoxications and of cases of driving under the influence of drugs. However, other synthetic cannabinoids have been detected in most of these cases.

4F-MDMB-BINACA has been detected in a small number of countries to date, but its use may be increasing. It has no veterinary or medical use.

Based on its mechanism of action, 4F-MDMB-BINACA has the ability to produce a state of dependence and central nervous system depression. There is evidence that it is abused so as to constitute a public health and social problem. It is therefore recommended that 4F-MDMB-BINACA be controlled under the 1971 Convention. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of the 1971 Convention.

3.5 4-CMC

4-CMC is also known as 4-chloromethcathinone and clephedrone. Its chemical name is 1-(4-chlorophenyl)-2-(methylamino)propan-1-one.

In common with other stimulants used non-medically, 4-CMC increases neuronal concentrations of the neurotransmitter dopamine. It also has effects on serotonin and, to a lesser extent, noradrenaline.

In animal models, 4-CMC has effects predictive of abuse potential, including actions predictive of MDMA-like subjective effects and stimulation of brain reward centres. It also produces central nervous system stimulation. Users of the drug report effects

similar to other stimulants, particularly MDMA-like effects, including increased energy, mood elevation and increased sociability.

4-CMC use has been associated with adverse effects typical of stimulant drugs, including tachycardia, agitation and impaired movement. Based on these effects and its mechanism of action, major risks associated with use of this drug will include cardiac failure and psychosis. In association with other drugs, 4-CMC has been involved in fatalities due to overdose, suicide and traffic accidents. It has been detected in used syringes, indicating the potential for injection-related health problems in association with its use.

4-CMC has been detected in many countries across different regions. It has no veterinary or medical use.

Based on its mechanism of action and effects, 4-CMC has the ability to produce a state of dependence and central nervous system stimulation. There is evidence that it is abused so as to constitute a public health and social problem. It is therefore recommended that 4-CMC be controlled under the 1971 Convention. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of the 1971 Convention.

3.6 *N*-ethylhexedrone

The chemical name for *N*-ethylhexedrone is 2-(ethylamino)-1-phenylhexan-1-one.

In common with other stimulants used non-medically, *N*-ethylhexedrone increases neuronal concentrations of the neurotransmitter dopamine. It also has effects on noradrenaline.

In preclinical models, *N*-ethylhexedrone has actions predictive of methamphetamine-like subjective effects and produces central nervous system stimulation. Users of the drug report effects similar to other stimulants, including increased energy, mood elevation, perceptual changes and increased sociability.

Information on the adverse effects is limited, but the effects reported are consistent with the effects of stimulant drugs and include tachycardia, tremor, seizures and hyperthermia. *N*-ethylhexedrone has been implicated as the cause of at least one fatality and of cases of impaired driving. It has been detected in used syringes, indicating the potential for injection-related health problems in association with its use.

N-ethylhexedrone has been detected in 30 countries across different regions. It has no veterinary or medical use.

Based on its mechanism of action and effects, *N*-ethylhexedrone has the ability to produce a state of dependence and central nervous system stimulation. There is evidence that it is abused so as to constitute a public health and social problem. It is therefore recommended that *N*-ethylhexedrone be controlled under the 1971 Convention. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of the 1971 Convention.

3.7 *Alpha*-PHP

Alpha-PHP is also known as *alpha*-pyrrolidinohexanophenone. Its chemical name is 1-phenyl-2-(pyrrolidine-1-yl)hexan-1-one.

In common with other stimulants used non-medically, *alpha*-PHP increases neuronal concentrations of the neurotransmitter dopamine. It also has effects on noradrenaline.

In animal models, *alpha*-PHP has effects predictive of abuse and dependence potential, including actions predictive of methamphetamine-like subjective effects and reinforcing properties. It produces central nervous system stimulation in animals. Users of the drug report effects similar to other stimulants, including increased energy, mood elevation, perceptual changes and appetite suppression.

The adverse effects of the drug include tachycardia, paranoia and hallucinations. It has been identified as the cause of multiple deaths and clinical admissions.

Alpha-PHP has been detected in over 20 countries across different regions. It has no veterinary or medical use.

Based on its mechanism of action and effects, *alpha*-PHP has the ability to produce a state of dependence and central nervous system stimulation. There is evidence that it is abused so as to constitute a public health and social problem. It is therefore recommended that *alpha*-PHP be controlled under the 1971 Convention. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of the 1971 Convention.

4. Substances recommended to be scheduled in Schedule IV of the Convention on Psychotropic Substances of 1971

4.1 Flualprazolam

The chemical name for flualprazolam is 8-chloro-6-(2-fluorophenyl)-1-methyl-4*H*-benzo[*f*][1,2,4]triazolo[4,3-*a*][1,4] diazepine.

Flualprazolam is chemically similar to the benzodiazepines alprazolam and triazolam and in animal models it produces the typical benzodiazepine effects of sedation, muscle relaxation and anticonvulsant actions. Users have reported effects such as sedation, disinhibition and memory impairment that are common with benzodiazepines and have described it as similar to alprazolam and clonazepam.

In toxicology reports, flualprazolam has been documented as contributing to forensic and clinical events, including fatal and non-fatal intoxications and cases of driving under the influence. It has no medical use.

There is limited information on the extent of global use of flualprazolam with most reported identifications coming from two countries. There are numerous reports of its use on Internet forums.

Based on its capacity to produce a state of dependence and central nervous system depression similar to the controlled benzodiazepine alprazolam, which is controlled under Schedule IV of the1971 Convention, as well as evidence that it is likely to be abused so as to constitute a public health and social problem, it is recommended that flualprazolam be controlled under Schedule IV of the 1971 Convention.

4.2 Etizolam

The chemical name for etizolam is 4-(2-chlorophenyl)-2-ethyl-9-methyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine. It has been previously reviewed by the Expert Committee on Drug Dependence, most recently at its thirty-ninth meeting in 2017.

Etizolam is an agonist at the benzodiazepine site on the GABAA receptor, inducing central nervous system depression. It has typical benzodiazepine effects that include sedation and muscle relaxation as well as anxiolytic and anticonvulsant actions. Adverse effects include drowsiness, ataxia, slurred speech, cognitive impairment and loss of consciousness.

Etizolam use has been associated with a large number of deaths, generally along with another drug or drugs. Benzodiazepines such as etizolam pose a significant risk when combined with opioids as they can potentiate the respiratory depressant effects of opioids.

Etizolam has been used in a number of countries and in some of these countries has been associated with reports of fatal and non-fatal intoxication as well as cases of driving under the influence. It has marketing authorization for medical use in three countries.

Based on its capacity to produce a state of dependence and central nervous system depression similar to other controlled benzodiazepines, as well as evidence that it is abused so as to constitute a public health and social problem, it is recommended that etizolam be controlled under Schedule IV of the 1971 Convention.