UR-144

Critical Review Report

Agenda Item 4.11

Expert Committee on Drug Dependence

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World Health Organization

Contents

Acknowledgements 5

Summary 6

1. Substance identification 7

A. International Nonproprietary Name (INN) 7
B. Chemical Abstract Service (CAS) Registry Number 7
C. Other Chemical Names 7
D. Trade Names 7
E. Street Names 7
F. Physical Appearance 7
G. WHO Review History 7

2. Chemistry 7

A. Chemical Name 7
B. Chemical Structure 8
C. Stereoisomers 8
D. Methods and Ease of Illicit Manufacturing 8
E. Chemical Properties 8
F. Identification and Analysis 8

3. Ease of Convertibility into Controlled Substances 8

4. General Pharmacology 9

A. Routes of administration and dosage 9
B. Pharmacokinetics 9
C. Pharmacodynamics 9

5. Toxicology 11

6. Adverse Reactions in Humans 12

7. Dependence 13

A. Animal Studies 13
B. Human Studies 13

8. Abuse Potential 13

A. Animal Studies 13
B. Human Studies 14

9. Therapeutic Applications and Extent of Therapeutic Use and Epidemiology of Medical Use 14

10. Listing on the WHO Model List of Essential Medicines 14

11. Marketing Authorizations (as a Medicinal Product) 14

12. Industrial Use 14

13. Non-Medical Use, Abuse and Dependence 14

14. Nature and Magnitude of Public Health Problems Related to Misuse, Abuse and Dependence 14

15. Licit Production, Consumption and International Trade 15

16. Illicit Manufacture and Traffic and Related Information 15

17. Current International Controls and Their Impact 16

18. Current and Past National Controls 16

19. Other Medical and Scientific Matters Relevant for a Recommendation on the Scheduling of the Substance 17

References 18

Annex 1: Report on WHO Questionnaire for Review of Psychoactive Substances for the 39th ECDD: Evaluation of UR-144 21

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Summary

UR-144 is a synthetic cannabinoid receptor agonist (SCRA) which has been previously critically reviewed by the 36th meeting of the WHO Expert Committee on Drug Dependence in 2014. The Committee recommended that at that time UR-144 be kept under surveillance due to lack of scientific data on non-fatal and fatal intoxications involving solely UR-144.

UR-144 is a cannabinoid (CB) receptor agonist for both type 1 (CB_1) and type 2 (CB_2). It's selectivity for CB_2 is higher than CB_1. UR-144 is extensively metabolized by CYP3A4 at the tetramethylcyclopropyl moiety with minor contributions of CYP1A2.

The reported harmful effects of UR-144 include acute kidney injury (in combination with other SCRAs) and impairment of driving ability (slurred speech, poor coordination, etc.). UR-144 has been linked with a number of cases of driving under the influence of drugs (DUID).

In animal models, UR-144 has been shown to fully substitute for delta-9-tetrahydrocannabinol (THC) in THC-drug discrimination studies. Collectively, the effects of UR-144 on the central nervous system are similar to those of THC regarding dependence/abuse liability.

UR-144 was one of the most frequently seized synthetic cannabinoids in 2015.

The updated scientific literature on the adverse effects of UR-144 suggests that UR-144 could be comparable to the synthetic cannabinoids in Schedule II of the Convention on Psychotropic Substances of 1971.

1. Substance identification

A. International Nonproprietary Name (INN)

Not applicable.

B. Chemical Abstract Service (CAS) Registry Number

1199943-44-6

C. Other Chemical Names

(1-Pentylindol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone, (1-pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone, TMCP-018, KM-X1, MN-001, YX-17, UNII-1TYA7HVP1B

D. Trade Names

None

E. Street Names

There are many street names (K2, Spice, etc.) containing various synthetic cannabinoids mixed with dried herbs. No information available on the street names specific to UR-144.

F. Physical Appearance

In pure form, UR-144 is a white powder.

G. WHO Review History

UR-144 was previously critically reviewed in the 36th ECDD in 2014. The Committee recommended that UR-144 not be placed under international control at that time but be kept under surveillance. Of particular significance to the Committee was the lack of analytically confirmed cases of non-fatal and fatal intoxications involving solely UR-144.

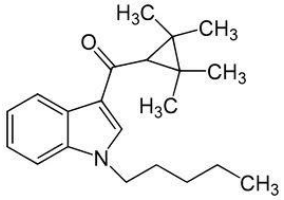
2. Chemistry

A. Chemical Name

IUPAC Name:
(1-Pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone
CA Index Name:
(1-Pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone

B. Chemical Structure

Free base:



Molecular Formula: $C_{21}H_{29}NO$
Molecular Weight: 311.5

C. Stereoisomers

No stereoisomers exist.

D. Methods and Ease of Illicit Manufacturing

The synthesis of UR-144 has been described by N-alkylation of 1*H*-indol-3-yl(2,2,3,3-tetramethylcyclopropyl)methanone with 1-bromopentane.[1;2]

E. Chemical Properties

Properties include: [3;4]

Melting point: 68 °C
Boiling point: 426.6 ± 18.0°C at 760 mmHg according to predicted data generated by the ACD/Labs Percepta Platform – PhysChem Module.
Solubility: 30 mg/mL in ethanol, DMSO, and dimethylformamide

F. Identification and Analysis

A forensic standard of UR-144 is available. UR-144 can be identified using nuclear magnetic resonance spectroscopy (NMR), gas chromatography–mass spectrometry (GC-MS) or infrared (IR) spectroscopy.[5] A commercial ELISA (enzyme-linked immunosorbent assay) to detect UR-144 in urine is available (Tulip Biolabs, Inc.) and an immunoassay that detects several UR-related synthetic cannabinoids has been developed by Immunalysis Inc. (Pomona, USA), however it is unclear whether cross reactivity is an issue. A new method for identifications of UR-144 based on use of attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR) has been developed in 2017. The limits of quantification are 14 to 79 mg/L with this method.[4]

3. Ease of Convertibility into Controlled Substances

Based on its structure, it is unlikely that UR-144 can be converted into a controlled substance.

4. General Pharmacology

A. Routes of administration and dosage

UR-144 is mostly smoked and mixed with tobacco or herbs. It can also be ingested orally, vaporized or inhaled.[6] The starting dose range is reported by users as 0.5-2 mg[6]. According to a website which provides various characteristics of new psychoactive substances, the tentative dose range of UR-144 is from 2.5 to 20 mg for inhalation. [7]

B. Pharmacokinetics

To date, the systemic data on the ADME (absorption, distribution, metabolism, and elimination) of UR-144 are not available. However, some data does exist on the metabolism of UR-144. Mono-hydroxylated metabolites seem to be most abundant *in vitro* and *in vivo*.[8] Analysis of urine from mice treated with UR-144 revealed that UR-144 is extensively metabolized and predominantly excreted in the urine as glucuronide conjugates. In one study, the involvement of cytochrome P450 (CYP) enzymes (CYP1A2, 2B6, 2C8, 2C9, 2C18, 2C19, 2D6, 3A4, and 2E1) in the metabolism of UR-144 was investigated using human liver microsomes. This study revealed that UR-144 was extensively metabolized by CYP3A4 at the tetramethylcyclopropyl moiety with minor contributions of CYP1A2.[10] It has been reported that the binding affinity of UR-144 to CYP3A4, in an *in-silico* docking modeling, was not influenced by single nucleotide polymorphism (SNP).[11]

An interesting study on the metabolism of UR-144 has been performed using a species of fungus (*Cunninghamella elegans*). The metabolites analyzed by liquid chromatography-quadrupole time-of-flight mass spectrometry (LC/QTOF-MS) were hydroxylation, dihydroxylation, trihydroxylation, aldehyde, carboxylation, *N*-dealkylation, aldehyde-, and ketone-formation (with/without combinations).[12]

C. Pharmacodynamics

UR-144 belongs to the category of synthetic cannabinoid receptor agonists (SCRAs). SCRAs mimic the effects of delta-9-tetrahydrocannabinol (THC) by binding to the CB_1 and CB_2 cannabinoid receptors.

CB_1 is primarily localized in the central nervous system (CNS), and CB_2 in cells mainly associated with the immune system, such as macrophages, lymph nodes, spleen, and microglia cells.[13;14;15;16] CB_1 receptors are mainly found in the CNS-regions involved in cognition, short-term memory, movement and motor function.[17] Activation of the CB_1 receptor by THC or SCRAs modulates, amongst others, neurotransmitter release in many inhibitory and excitatory synapses in the brain. These effects are mediated through CB_1 receptor coupled G-protein activation and finally result in decreased activity of cAMP-dependent protein kinases.

Receptor binding studies

In 2006, a variety of UR-144 analogues showing selectivity to bind to CB_2-receptors was patented by Abbott Laboratories.[2] UR-144 showed a high binding affinity to both CB_1 and CB_2 receptors (Table 1).[9] The binding affinity of UR-144 (compound no.

46) within a series of 70 indole ligands was evaluated at human recombinant CB_1 (hCB_1) and CB_2 (hCB2) receptors using [^{3}H]CP-55,940 as the radioligand.[1] In this study, UR-144 showed 83-fold selectivity to bind to CB_2-receptors[1]. Using the same radioligand, Wiley et al. (2013) found a 6-fold selectivity for the CB_2-receptor.[9] UR-144 also displaced the radiolabeled agonist [^{3}H]CP-55,940 much more readily from the CB_1 receptor than the radiolabeled CB_1-selective antagonist [^{3}H]rimonabant (apparent K_i was 29 and 368 nM, respectively).[9] The US Drug Enforcement Administration (DEA) reported a K_i-value for UR-144 at CB_1 receptors of 28.9 nM.[18]

Although the selectivity to the CB_2 receptor for UR-144 was at least 6-fold greater, the binding affinity to the CB_1 receptor of UR-144 was 1.4 times higher than that of THC.[19] However, the CB_1 K_i value of UR-144 (1.4 nM) was relatively low, compared to that of JWH-018 (4.6 nM) and AM-2201 (40 nM),[19] the cannabinoid compounds listed in Schedule II of the Convention on Psychotropic Substances, 1971.

Table 1. Binding affinity of UR-144 and THC (mean ± SEM) to CB_1 and CB_2 receptors

Compound	K_i value (nM)		Ratio*	Method	Ref. No.
	CB_1	CB_2			
UR-144	29 ± 0.9	4.5 1.7	6.4	a	9
UR-144**	368			b	9
UR-144	150	1.8	83	a	1
UR-144	28.9	-			18
THC	40.7	36.4			20
THC	67	36	1.86	a	9
THC	15.3	25.1			21

* Ratio: K_i CB_1/K_i CB_2; ** K_i of THC in this study was 764 nM; ***method a: displacement of [^{3}H]CP-55,940, b: displacement of [^{3}H]rimonabant (SR 141716)

[Cited from the Critical Review Report for the 36th ECDD meeting]

Functional studies

In mice, UR-144 produced dose-dependent effects as a full agonist, which were blocked by the cannabinoid antagonist/inverse agonist rimonabant. The effects (Table 2) included antinociception, catalepsy, hypothermia and inhibition of locomotor activity.[9] In another study, UR-144 (10 and 30 mg/kg) depressed locomotor activity in mice in a time and dose-dependent manner and with an ID_{50}-value of 7.8 mg/kg.[18]

In a human embryonic kidney (HEK-293) cell line expressing CB_2 receptors, UR-144 behaved as a full agonist using a calcium mobilization assay, considering its almost maximal response (93%). Compared to other ligands in this series, the potency of UR-144 to mobilize calcium (EC_{50}-value of 29-43 nM) was relatively high.[1] In a functional assay mediated by CB_1-receptors (not specified, but presumably the GTPγ[^{35}S] binding assay), UR-144 showed agonistic activity with an IC_{50}-value of 1295 nM.[18]

Using a functional assay that determines the change in the intracellular levels of the radiolabeled CB_1 ([^{3}H]Win55-212-2) and CB_2 agonists ([^{3}H]CP55-940), it was shown that UR-144 inhibited the internalization of CB_1 and CB_2 receptors. The IC_{50} values (nM ± standard error) for UR-144 were 27.2 ± 6.6 (CB_1) and 83.6 ± 22 (CB_2).[22] This indicates a selectivity of only 3 for CB_1, whereas others have previously shown a 83-fold selectivity in binding to the two receptors.[1]
UR-144 stimulated GTPγ[^{35}S] turnover through both the hCB_1 receptor and the hCB_2 receptor at nanomolar concentrations, indicating that UR-144 acts as an agonist at both receptor subtypes. The mean EC_{50} values ± SEM for stimulation by UR-144 at the CB_1 receptor was 98 ± 20.4 nM, and 334 ± 171 nM at the CB_2 receptor. At both receptors UR-144 acted as full agonist.[9;23]

Table 2. ED_{50} values in µmol/kg in the mouse tetrad test

Compound	SA	% MPE	RT	RI	AP	Ref. No.
UR-144	1.0 (0.55-2.25)	2.6 (1.83-4.05)	0.6 (0.51-0.74)	1.0 (0.64-1.66)	1.3	9
THC	15 (4.8-41.9)	12 (9.3-16.8)	4 (2.8-6.5)	3 (1.9-5.2)	8.5	9
THC	0.92	2.7	2.5	NT	2.0	25

Abbreviation: ED_{50} (dose at which half maximal effect occurred); SA (spontaneous activity); % MPE (% maximum possible anti-nociceptive effect); RT (rectal temperature); RI (ring immobility); NT (not tested); AP (averaged potency)
95% confidence intervals are given in parentheses.
[cited from the Critical Review Report for the 36th ECDD meeting]

Table 2 shows UR-144 effect on spontaneous activity (SA), anti-nociceptive effects (%MPE), rectal temperature (RT) and ring immobility (RI) with 3 to 15-fold greater potency relative to THC.[9]

In summary, these results demonstrate that *in vitro* and *in vivo* UR-144 shares the pharmacological properties of THC.[9] However, compared to THC, UR-144 is a highly selective CB_2-agonist.

According to a recent study, the cyclopropyl ring moiety undergoes thermal rearrangement possibly during smoking. The pyrolyzed form of UR-144 showed four times higher agonistic activity for the CB_1 receptor (locomotor activity and body temperature) compared to UR-144 itself, indicating heating synthetic cannabinoids possessing cyclopropyl moiety by smoking may lead to more profound pharmacological effects on the central nervous system than expected.[24]

5. Toxicology

A study which tested the genotoxicity of synthetic cannabinoids using various *in vitro* assays such as SCGE assay (comet assay), micronucleus assay, and *Salmonella*/microsome assay indicated that UR-144 induced DNA-damage at the chromosomal level without gene

mutations in human lymphocytes.[26] The authors concluded that the tested synthetic cannabinoids including UR-144 may cause adverse health effects in users, due to induction of DNA damage.[26]

6. Adverse Reactions in Humans

In general, toxic effects of SCRAs include tachycardia, nausea/vomiting, somnolence, mydriasis, and hypokalemia.[27] Less frequent are reduced or missing pupillary light reflex, agitation, vertigo, paraesthesia, aphasia, dysphasia, generalised seizures, myoclonia or muscle jerking, hypopnoea with hypoxemia and aspiration with respiratory insufficiency. Most symptoms cease within a few hours.[27]

A previously healthy 26-year-old male was presented to the emergency department with one day of abdominal pain, nausea, vomiting and lower back pain. He had smoked "Mr. Happy", a product which contained 61 mg/g of UR-144 and 69 mg/g of its fluorinated analogue XLR-11. He stated that he had used this product two or three times a day for approximately one year and that he had used the product on the morning of his presentation. In his blood, 6 ng/ml of UR-144 and 35 ng/ml of XLR-11 were detected. The man had elevated serum creatinine values and was diagnosed with acute kidney injury of unknown etiology. Twenty-three days later his serum creatinine had normalized. It is unclear whether and how UR-144 and/or XLR-11 contributed to the kidney injury.[29;30] Right after smoking of a joint, a 36-year old man collapsed and was transferred to the hospital. Upon arrival, the man suffered seizures and died several hours later. Amphetamine and five SCRAs, including UR-144, were detected in the femoral blood post mortem.[31]. Concentrations were 0.39 ng/ml JWH-122; 1.5 ng/ml MAM-2201; 1.4 ng/ml AM-2201; 6.0 ng/ml UR-144; 0.1 ng/ml JWH-018; and 250 ng/ml amphetamine. The amphetamine level is not indicative for the fatal amphetamine intoxication and, presumably, the combination of amphetamine with SCRAs was the probable cause of death.

In a series (closely similar and probably overlapping with the previously reported series of the same group[27;32]), UR-144 was one of the twelve different SCRAs detected in serum samples of 25 emergency department (ED) patients with analytically verified consumption of synthetic cannabinoids. UR-144 was found in three serum samples.[33] In 65% of the cases, more than one SCRA was identified and at maximum 8 different SCRAs were identified in one patient. Symptoms of intoxication were similar to those reported by this group before.[27]

In another study of this group, the cases of four additional ED patients were presented.[28] In these four cases, six SCRAs (JWH-122, JWH-018, JWH-210, MAM-2201, UR-144, and JWH-081) were detected in the blood or the urine. In the serum of case 2 (a 17-year-old male), UR-144 (0.24 ng/ml) together with MAM-2201 (0.15 ng/ml) was detected. In the urine of this patient (case 2) the N-(5-OH-pentyl) metabolite of JWH- 122 (1.6 ng/ml) and the N-(5-carboxypentyl) metabolite of JWH-018 (0.11 ng/ml) along with two metabolites of UR-144 were detected. Clinical symptoms in this patient were pronounced sinus tachycardia (160 beats/min), mydriasis, anisocoria, retrograde amnesia, and a mild somnolence which resolved within 12 h of admission. According to the authors, it is unlikely that the clinical symptoms seen were evoked by UR-144, because UR-144 possesses relatively low affinity for the CB1 receptor.[28]

More recently, the adverse effects of UR-144 have been reviewed through 39 individual cases in Poland from 2012 to 2015.[6] In 26 cases out of the 39 cases, UR-144 was the sole substance detected. In the remaining 13 cases, the authors claimed that the observed effects could be regarded as UR-144 effects because the concentration of other substances was negligible. The most characteristic symptoms observed were slurred speech and dilated pupils, other observations include poor coordination, unsteady gait and difficulty standing, as well as abnormal pupillary reaction.[6]

Acute kidney injury requiring hemodialysis from SCRA use, particularly XLR-11, UR-144, and AM-2201 has been described in a book edited by Smith et al. (2014).[34] The CDC has also described several clinical effects of synthetic cannabinoids including seizures, agitation, anxiety, irritability, sedation, confusion, paranoia, psychosis, tachycardia, dysrhythmia, chest pain, myocardial infarction, elevated blood pressure, nausea, vomiting, acute kidney injury, hypokalemia, hyperglysemia, mydriasis, conjunctivitis, hyperthermia, tolerance, withdrawal, and dependence.[29] These are also covered in reviews by Nelson et al. and Debruyne et al. [35]

Additionally, there has been a report of over 200 people being hospitalized after using "MOCARZ" ("the Mighty One") containing UR-144, BB-22, 5F-PB-22, XLR-144, and AB-CHMINACA. Some individuals were in a serious condition, and one died. However, it should be noted that UR-144 was not the sole cause of these events.[36]

It has been suggested that abusers of UR-144 might increase the dose resulting in unexpected toxic side effects, due to the low psychotropic effect of UR-144.[37]

7. Dependence

A. Animal Studies

No animal studies on the dependence potential of UR-144 have been performed.

B. Human Studies

Although the possibility of showing withdrawal symptoms such as insomnia, anxiety, irritability, malaise, myalgias, shakiness, nausea, vomiting, and drug craving for one to two weeks after abrupt cessation of synthetic cannabinoids has been suggested[34], no human studies on the dependence potential of UR-144, specifically, have been performed.

8. Abuse Potential

A. Animal Studies

In mice, UR-144 substituted for THC in a THC discrimination study (ED_{50} value 7.1 to 7.4 μmol/kg i.p.).[30;18] This effect was antagonized by rimonabant. In rats, UR-144 (2.5 mg/kg) fully substituted for the discriminative stimulus effects of THC (3 mg/kg) at 15 and 60 minutes after administration, and the effect was diminished to less than 40% after 4 hours.[38]

B. Human Studies

No experimental studies were identified that have investigated the abuse potential of UR-144 in humans. However, it has been suggested on drug forums and in country responses to the 36th ECDD WHO questionnaire on UR-144 that tolerance to UR-144 may develop resulting in users consuming larger doses[6]

9. Therapeutic Applications and Extent of Therapeutic Use and Epidemiology of Medical Use

Pre-clinical studies of nociceptive and neuropathic pain models have shown that CB_2-selective ligands are analgesics without causing the adverse side effects linked with CB_1 receptor activation.[2] However, UR-144 has no therapeutic application. According to the FDA (US Food and Drug Administration) there are currently no approved or on-going drug applications for the medical use of UR-144.[18]

10. Listing on the WHO Model List of Essential Medicines

UR-144 is not listed on the WHO Model List of Essential Medicines (20th List) or the WHO Model List of Essential Medicines for Children (6th List).

11. Marketing Authorizations (as a Medicinal Product)

UR-144 is not marketed as a medicine.

12. Industrial Use

No commercial or industrial use known.

13. Non-Medical Use, Abuse and Dependence

Non-medical use of UR-144 is reported in Austria, Poland, Canada, Portugal, France, Romania, Germany, Singapore, Hungary, Ukraine, Lithuania, United States, and Norway. However, the extent of its use is largely unknown.[39] Also refer Annex 1: Report on WHO questionnaire for review of psychoactive substances.

14. Nature and Magnitude of Public Health Problems Related to Misuse, Abuse and Dependence

Kronstrand et al. (2013) presented eight cases of intoxications with SCRAs between 2011 and early 2013, where blood from subjects suspected of an innocent drug offence or driving under the influence of drugs (DUI) was analysed.[40] Of 3,078 blood samples analysed, 28% were found positive for one or more SCRAs. UR-144 could be detected in 181 samples; mean (median) concentration was 1.26 (0.34) ng/g blood.

Redwood Laboratories (California, USA) routinely test specimens of illicit drugs users. Following the addition of UR-144 and XLR11 to their toxicological panel, 300 randomly

selected samples from December 2012 were re-analyzed. The positivity of the 300 samples increased from 2.8% to 16% (39 additional samples positive for UR-144 and/or XLR11).[18] NMS Laboratories (PA, USA) had a similar experience when 46 samples (collected in July 2012) and 28 samples (collected in December 2012) that had been positive for a synthetic drug compound, were reanalyzed with a panel that included UR-144 and XLR11. In the total of 74 samples, 35 (47%) and 26 (35%) were positive for UR-144 and XLR11, respectively.[18] A third tests for SCRAs (collected between July 1, 2012 and December 20, 2012), 24 were positive for SCRAs, and 19 of these 24 were positive for UR-144.[18] Specific studies to the abuse potential of UR-144 in humans have not been performed. Considering the close pharmacological resemblance of UR-144 to THC, abuse of UR-144 is likely to occur.

In a study of 526 suspected cases of impaired driving in Washington, DC between 2012 and 2013, 19 cases were analytically confirmed positive for synthetic cannabinoids. Of which, UR-144 N-pentanoic acid was detected in 17 cases (87%).[41]

In 2015, a case of DUI of UR-144 was reported. The concentration of UR-144 in blood obtained 2h after the collision and 4.5h after self-reported dosing was 14.6 ng/mL. The authors concluded that the driver was under the influence of UR-144, and that UR-144 produced impairment similar to, or even more dangerous than, THC.[42]

There were several other DUI cases described by Karinen et al. (2015).[43] For two DUI cases, the blood concentration of UR-144 was 0.22 and 0.47 ng/mL and the concentration of the pyrolyzed form of UR-144 was 0.15 ng/mL in one of the two cases. However, whether UR-144 was the sole substance in the two cases is not clarified. An additional six DUI cases are described with observed symptoms including poor coordination, slurred speech, lack of convergence and tremor. This indicates that UR-144 has the potential to strongly and negatively impact a driver's ability to operate a motor vehicle safely. [44]

UR-144, similar to other SCRAs, has been used used as a substitute for cannabis. In general, adverse effects of SCRA intoxications are more intense than with cannabis, possibly because of their high activity and ease of overdosing.[39]

Also refer Annex 1: Report on WHO questionnaire for review of psychoactive substances.

15. Licit Production, Consumption and International Trade

No data available.

16. Illicit Manufacture and Traffic and Related Information

As reported to the EMCDDA, UR-144 has been encountered in seized products in Latvia, Croatia, Spain, Denmark, Belgium, Germany, France, Slovenia, Turkey, United Kingdom, Sweden, Hungary, Norway, Poland, and Finland.[45] According to the European Drug Report 2017, UR-144 was one of the most frequently seized synthetic cannabinoids in 2015.[46]

In Korea, UR-144 has been detected in seized herbal products (resin, herbals and powder).[37;47] In the USA, UR-144 has been seized as a pure substance and as a substance spiked on products that are marketed as herbal incense and promoted as legal alternatives to

marijuana under a variety of names.[18] Between January 2010 and April 2013, 5,356 reports from forensic laboratories were identified in the National Forensic Laboratory Information System (NFLIS) regarding UR-144. In addition, the System to Retrieve Information from Drug Evidence (STRIDE), a DEA program, 179 cases and 1,510 records were identified involving UR-144 between January 2009 and April 2013.6 Submissions to DEA laboratories from January 2012 through April 03 2013 have documented over 150 distinct packaging examples containing mixtures of UR-144, XLR11 and/or AKB-48.[18] In Japan, UR-144 has been identified in sold designer drugs.[48;49] The number of seizures world-wide containing UR-144 is not known.

No data about the manufacture is available. The global emergence retrieved from the UNODC Early Warning Advisory on NPS is listed in Table 3.[50]

Table 3. Global emergence of UR-144[50]

List of countries (13)	
Austria	Poland
Canada	Portugal
France	Romania
Germany	Singapore
Hungary	Ukraine
Lithuania	United States
Norway	

[cited from the Critical Review Report for the 36th ECDD meeting]

Also refer Annex 1: Report on WHO questionnaire for review of psychoactive substances.

17. Current International Controls and Their Impact

UR-144 is not controlled under the 1961, 1971 or 1988 United Nations Conventions.

18. Current and Past National Controls

Overall, UR-144 is controlled at a national level in many countries with some countries scheduling UR-144 as an individual substance while others control this compound as part of their analogue/derivative system.

UR-144 is a schedule I controlled substance under the US Federal Controlled Substances Act (2016)[51], and under national control in Germany (2012), Denmark, Hungary, Portugal, Slovakia, Slovenia, Turkey, and Russia. UR-144 has also been banned in the UK since 2013. It is also a controlled substance in China (2016), Japan (a designated substance, 2012), and Republic of Korea (an analogue of JWH-018, 2014).

Also refer Annex 1: Report on WHO questionnaire for review of psychoactive substances.

19. Other Medical and Scientific Matters Relevant for a Recommendation on the Scheduling of the Substance

None.

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Annex 1: Report on WHO Questionnaire for Review of Psychoactive Substances for the 39th ECDD: Evaluation of UR-144

Please refer to separate Annex 1 document published on ECDD website