Critical Review Report:

4F-MDMB-BINACA

Expert Committee on Drug Dependence

Forty-second Meeting

Geneva, 21-25 October 2019

This report contains the views of an international group of experts, and does not necessarily represent the decisions or the stated policy of the World Health Organization

Contents

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Executive Summary

Substance identification

The identification of 4F-MDMB-BINACA (4F-MDMB-BUTINACA) (IUPAC name: methyl (2*S*)-2-{[1-(4-fluorobutyl)-1*H*-indazole-3-carbonyl]amino}-3,3-dimethylbutanoate) has been described first in 2018. Information obtained from seizures and collections suggests that it has been encountered in powdered form, in liquids used for vaping, and as a synthetic constituent in herbal plant mixtures most commonly distributed for the purpose of smoking. It is a homologue of 5F-ADB (5F-MDMB-PINACA) that is listed in Schedule II of the Convention on Psychotropic Substances of 1971.

WHO Review History

4F-MDMB-BINACA has not been previously pre-reviewed or critically reviewed.

Chemistry

There is no specific information available about the routes of synthesis employed for seized 4F-MDMB-BINACA products circulating on the drug market but straightforward methods for its preparation exist without requiring access to precursors that are controlled internationally. The presence of an asymmetric carbon atom gives rise to the (*R*)- and (*S*)-enantiomer and it seems likely for 4F-MDMB-BINACA to be most commonly available as the (*S*)-enantiomer.

Ease of convertibility into controlled substances

There is no specific information available but it appears unlikely that 4F-MDMB-BINACA is converted into a substance currently listed in any of the international drug conventions.

Similarity to known substances / Effects on the central nervous system

The information currently available suggests that 4F-MDMB-BINACA functions as a synthetic cannabinoid receptor agonist (SCRA). Information about effects induced *in vivo* is currently not available but the existing data suggest that 4F-MDMB-PICA will likely exhibit a profile shared by other SCRAs controlled internationally (potent full agonists at cannabinoid receptors) such as 5F-ADB.

General pharmacology

4F-MDMB-BINACA, in its pure form but mostly as a synthetic constituent added to a plant matrix, is primarily smoked (or vaped) although reliable data about dosage are unavailable. Results obtained from one *in vitro* study suggest that 4F-MDMB-BINACA binds to and activates human CB_1 receptors at low nanomolar concentrations. Similar to other SCRAs listed in the Convention on Psychotropic Substances of 1971, 4F-MDMB-BINACA was more potent than Δ^9-THC although it displayed lower efficacy under the experimental conditions used. Data collected from *in vitro* metabolism studies and detections in biological specimens revealed that the biotransformation steps observed included cleavage of the methyl ester, hydrolytic defluorination of the alkyl chain, oxidation to a butanoic acid metabolite, hydroxylation of aromatic and alkyl structures, dehydrogenation, and combinations thereof. Detections of the *N*-dealkylated species and the *N*-dealkylated ester hydrolysis product were also reported.

Toxicology
Information could not be identified.

Adverse reactions in humans
Detailed information about the clinical features associated with the consumption of 4F-MDMB-BINACA specifically is not available. Aggregated data have been reported that featured the detection of 4F-MDMB-BINACA in biological specimen obtained from cases involving deaths and impaired driving. It appeared that at least in some cases, other substances including SCRAs were also detected. SCRA-like effects for 4F-MDMB-BINACA were documented based on self-reports, which included auditory and visual hallucinations, vomiting, paranoia, euphoria, relaxation, irregular heartbeat, agitation, confusion, insomnia, and chest pain. Data collected from intoxication cases with other SCRAs suggest that clinical features might include a range of adverse effects on gastrointestinal, neurological, and cardiovascular systems.

Dependence potential
No studies carried out in humans or animals could be identified.

Abuse potential
Studies specifically linked to 4F-MDMB-BINACA could not be identified.

Therapeutic applications / usefulness
4F-MDMB-BINACA is not known to have any therapeutic uses.

Listing on WHO Model List of Essential Medicines
4F-MDMB-BINACA is not listed.

Marketing authorizations
4F-MDMB-BINACA is not known to have any marketing authorisations.

Industrial use
4F-MDMB-BINACA is not known to have any agricultural, industrial or cosmetic uses.

Non-medical use
The mode of use may involve the combinational use (intentionally or unintentionally) of other drugs and users may be unaware of the exact dose or compound being ingested (by whatever route). Household or subpopulation surveys that specifically probe for prevalence of 4F-MDMB-BINACA could not be identified. People who use SCRAs in general include recreational users, high-risk substance users but also individuals who are subject to drug testing such as people in drug treatment, prisoners, abstinence control programs and drivers.

Nature and magnitude of public health problems
Products sold as herbal smoking mixtures frequently change in drug composition and quantity, often without indications on product labels, which results in challenges to unambiguously correlate harms to public health with a specific drug such as 4F-MDMB-BINACA. People who use these drugs are most likely not aware of the identity of the constituent and the quantity. The

consumption of these products might be attractive to a variety of users, such as regular users of cannabis and those who believe that SCRA use might help with avoiding a positive finding in drug-testing procedures. There are indications that socially vulnerable and stigmatised substance users, for example found in homeless and prison populations, are increasingly associated with problematic use of SCRA products. Heavy use of SCRAs has been associated with problematic withdrawal symptoms and further research is needed to evaluate the underlying mechanisms.

Licit production, consumption, and international trade

4F-MDMB-BINACA is available as standard reference material and produced for scientific research by a number of commercial suppliers. Other uses could not be identified.

Illicit manufacture and traffic

4F-MDMB-BINACA began to emerge in 2018 both in Europe and the United States of America. SCRAs are often imported in their pure form and converted into herbal forms on the domestic level. In recent years it has emerged that SCRAs have been smuggled into prisons in the form of impregnated papers (e.g. letters) and textiles and this extended to the detection of 4F-MDMB-BINACA.

Current international controls and their impact

4F-MDMB-BINACA is not controlled under the 1961, 1971 or 1988 United Nations Conventions.

Current and past national controls

4F-MDMB-BINACA is controlled in some UN Member States.

1. Substance identification

A. International Nonproprietary Name (INN)

Not available.

B. Chemical Abstract Service (CAS) Registry Number

Not yet assigned at the time of this writing.

C. Other Chemical Names

Methyl (*S*)-2-(1-(4-fluorobutyl)-1*H*-indazole-3-carboxamido)-3,3-dimethylbutanoate

Methyl (2*S*)-2-{[1-(4-fluorobutyl)-1*H*-indazole-3-carbonyl]amino}-3,3-dimethylbutanoate

N-[[1-(4-Fluorobutyl)-1*H*-indazole-3-yl]carbonyl]-3-methyl-L-valine, methyl ester

D. Trade Names

Not available.

E. Street Names

4F-MDMB-BINACA
4F-MDMB-BUTINACA

4F-MDMB-BINACA has also been detected in a collected sample in Wales (United Kingdom) labelled as "Black Mamba Anihilation" *(1)*. However, products associated with the sale of synthetic cannabinoid receptor agonists (SCRAs) rarely retain the same composition and will frequently change over time.

F. Physical Appearance

4F-MDMB-BINACA has been described as a neat solid *(2)*, an off-white solid material *(3)*, and as a white solid *(4)*.

G. WHO Review History

4F-MDMB-BINACA has not been previously pre-reviewed or critically reviewed. A direct critical review is proposed based on information brought to WHO's attention that 4F-MDMB-BINACA clandestinely manufactured, of especially serious risk to public health and society, and of no recognized therapeutic use by any party. Preliminary data collected from literature and different countries indicated that this substance may cause substantial harm and that it has no medical use.

2. Chemistry

A. Chemical Name

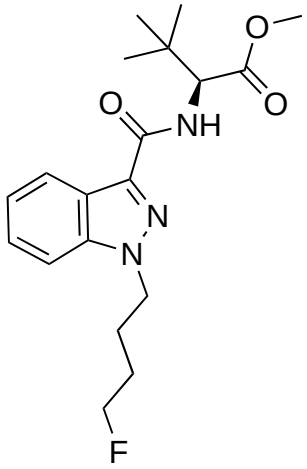
IUPAC Name: Methyl (2*S*)-2-{[1-(4-fluorobutyl)-1*H*-indazole-3-carbonyl]amino}-3,3-dimethylbutanoate

Methyl *N*-[1-(4-fluorobutyl)-1*H*-indazole-3-carbonyl]-3-methyl-L-valinate

CA Index Name: Not yet available at the time of this writing.

B. Chemical Structure

Free base:



Molecular Formula: $C_{19}H_{26}FN_3O_3$
Molecular Weight: 363.43 g/mol

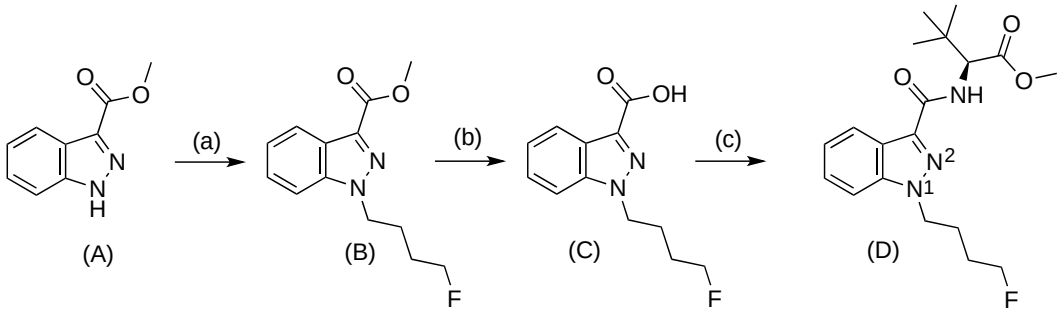
C. Stereoisomers

The presence of an asymmetric carbon atom gives rise to the (*R*)- and (*S*)-enantiomer of 4F-MDMB-BINACA. Historically, structurally related synthetic SCRAs that feature such chiral centres have typically shown the (*S*)-configuration. It is currently not known whether 4F-MDMB-BINACA has been exclusively found on the market with the absolute (*S*)-configuration although it appears likely to be the case. Similar to other closely related SCRAs, it seems conceivable that the (*R*)-enantiomer might be detectable as an impurity *(e.g. 5, 6)*.

D. *Methods and Ease of Illicit Manufacturing*

Information on the manufacturing of 4F-MDMB-BINACA seized or collected from the market is not available. The preparation of this substance is however straightforward and follows standard procedures using cheap reagents. One example could include the procedure outlined in the Scheme below which has also been employed for the synthesis of closely related SCRAs including 5F-ADB *(7)*.

Under these conditions, methyl 1*H*-indazole-3-carboxylate (A) could be subjected to selective alkylation with 1-bromo-4-fluorobutane to give the alkylated 1*H*-indazole-3-carboxylate methyl ester (B). Hydrolysis gives the carboxylic acid intermediate (C) followed by coupling with L-*tert*-Leucine methyl ester to afford 4F-MDMB-BINACA (D). Depending on the reaction conditions used during manufacturing it seems conceivable that the formation of the 2-alkyl-2*H*-indazole regioisomer of 4F-MDMB-BINACA might be detectable as an impurity *(8)*.



Reagents and conditions: (A) t-BuOK, 1-bromo-4-fluorobutane, 0 °C–rt; (B) 1 M aq. NaOH, MeOH, reflux; (C) methyl L-*tert*-leucinate, EDC·HCl, HOBt, DIPEA, DMSO, rt. Adapted from *(7)* on closely related compounds such as 5F-ADB.

E. Chemical Properties

Melting point: Information could not be identified.

Boiling point: Information could not be identified.

Solubility: A sample obtained from a test purchase was reported to be soluble in dichloromethane and methanol and partially soluble in water *(9)*.

F. Identification and Analysis

Data and analytical methodologies that facilitate the identification of 4F-MDMB-BINACA in various sample matrices have only recently emerged and include various chromatographic, spectroscopic and mass spectrometric methods *(3, 4, 9-12)*. Analytical reference standards are accessible to assist with the implementation of routine methods of analysis associated with forensic and clinical investigations. The analytical determination of synthetic cannabinoid receptor agonists such as 4F-MDMB-BINACA in biological fluids can be a challenge, for example in cases where analytical methodologies are not specifically designed to detect these substances. In some instances (e.g. analysis of urine), the detection of metabolites may be the preferred approach.

Challenges for its identification may also arise due to some analytical similarities with isomeric species, such as 5F-AMB-PINACA (5F-MMB-PINACA, 5F-AMB) and this extends to some of its metabolites as well (Section 4B) *(12)*. The explicit identification of the (*S*)-enantiomer has not been confirmed in the reports

associated with the identification of 4F-MDMB-BINACA but it would seem likely that the 4F-MDMB-BINACA available on the market exists as the (*S*)-enantiomer. Until further information is available, one cannot exclude the existence of the (*R*)-enantiomer (including its presence as an impurity). The differentiation between these two species might present challenges in routine forensic laboratories unless more specific approaches are employed to facilitate chiral analysis.

3. Ease of Convertibility Into Controlled Substances

No information could be identified.

4. General Pharmacology

A. Routes of administration and dosage

4F-MDMB-BINACA, in its pure form but mostly as a synthetic constituent added to a plant matrix, is primarily smoked (or vaped) although reliable data about dosage are unavailable. The variations in drug composition and quantities frequently observed with many smoking mixtures also make such estimations impossible for users despite the information that might be displayed on a product label (e.g. *(13, 14)*).

B. Pharmacokinetics

Information from clinical studies in humans is not available. However, a recent study investigated the metabolic fate of 4F-MDMB-BINACA in an *in vitro* assay using pooled human liver microsomes for comparison with phase I metabolites detected in 17 authentic human urine samples *(12)*. A total number of 13 metabolites were detected and associated with the following biotransformations: cleavage of the methyl ester, hydrolytic defluorination of the alkyl chain, oxidation to a butanoic acid metabolite, hydroxylation of aromatic and alkyl structures, dehydrogenation, and combinations thereof. Eleven of these metabolites were also detected in the *in vitro* assay which meant that two metabolites were not detectable under these conditions: M01 (ester hydrolysis and oxidation to the butanoic acid metabolite) and M04 (ester hydrolysis and hydroxylation).

The three most abundant metabolites detected in human urine were the products of ester hydrolysis, ester hydrolysis plus dehydrogenation, and hydrolytic defluorination. The first two were also recommended as suitable urinary markers. In addition, it was highlighted that some analytical features were similar to closely related SCRAs. For example, 4F-MDMB-BINACA is an isomer of 5F-AMB-PINACA (5F-MMB-PINACA, 5F-AMB). Furthermore, the main ester hydrolysis metabolite of 4F-MDMB-BINACA is also an isomer of other SCRA metabolites, for example, originating from 5F-AMB-PINACA (5F-MMB-PINACA, 5F-AMB, see above) but also 5F-AB-PINACA which could add additional challenges *(12)*. In another study, the analysis of 4 human blood and 4 human urine samples revealed the detection of 9 metabolites *(4)*. The ester hydrolysis product (also most abundant) and methyl 2-(1-(4-hydroxybutyl)-1*H*-indazole-3-carboxamido)-3,3-dimethylbutanoate were

considered suitable biomarkers. The detection of the *N*-dealkylated species and the *N*-dealkylated ester hydrolysis product were also reported *(4)* and these were not reported in the other study *(12)*, thus, providing complementary data.

A. Pharmacodynamics

Data currently available from one *in vitro* study suggests that 4F-MDMB-BINACA functions like a synthetic cannabinoid receptor agonist (SCRA) as it has been found to bind and activate CB_1 receptors (Table 1). At the time of writing, information on the *in vivo* effects of 4F-MDMB-BINACA could not be identified.

Table 1. 5F-MDMB *in-vitro* data	Reference
Receptor binding: [a] 4F-MDMB-BINACA at CB_1: K_i = 14.3 nM (*R*)-(+)-WIN-55,212-2 at CB_1: K_i = 172 nM Δ^9-THC at hCB_1: K_i =22.5 nM Functional activity: [b] 4F-MDMB-BINACA, EC_{50} = 0.20 nM (E_{max} = 67.7%) (-)CP-55,940, EC_{50} = 0.40 nM (E_{max} = 95.6%) Δ^9-THC, EC_{50} = 14.2 nM (E_{max} = 82.9%)	*(15)*
[a] Ref *(15)*: HEK cells; [^{3}H]CP-55,940 (~1.3 nM) used as radioligand. [b] Ref *(15)*: Adenylate cyclase assay using cyclic AMP ELISA kit. Basal cAMP subtracted from all values; CB_1 receptor agonists inhibit forskolin-stimulated cAMP formation with maximal inhibition defined using 1 µM (-)CP-55,940.	

5. Toxicology

Information could not be identified.

6. Adverse Reactions in Humans

Reports associated with the detection of 4F-MDMB-BINACA in biological specimens have been published *(12, 16-18)* but further details about the clinical features were not documented. One of the scientific studies reporting the analysis of 4F-MDMB-BINACA in seized and biological specimens revealed that 4F-MDMB-BINACA was identified in 29 toxicology cases (November 2018–March 2019) *(4)*. The samples were obtained from 10 US States and were stated to have originated from post-mortem (n = 20, 69%) and

impaired driving (n = 6, 21%) investigations. Most cases involved male individuals (n = 24, 83%, average age 42.9 ± 16.4 yr, median 40 yr, range 14–76 yr). 4F-MDMB-BINACA was commonly found in conjunction with other SCRAs such as 5F-MDMB-PICA (n = 12, 41%) and APP-BINACA in four cases. Additional SCRAs were detected in some cases (not specified) and one case was also positive for heroin and fentanyl *(4)*. In a related document published in the form of a public alert, 4F-MDMB-BINACA reported as detectable in 8 blood specimens associated with post-mortem and driving under the influence of drugs investigations *(19)*.

Self-reported effects provided by people who use SCRAs and who submitted a variety of samples (herbal matrices and liquids) to a drug testing service (and found to contain 4F-MDMB-BINACA as the major constituent) indicated SCRA-like effects including auditory and visual hallucinations, vomiting, paranoia, euphoria, relaxation, irregular heartbeat, agitation, confusion, insomnia, and chest pain *(1)*.

A document published by the U.S. Drug Enforcement Administration (DEA) contains the statement that "multiple law enforcement encounters of 4F-MDMB-BINACA have been reported involving overdose deaths, illicit use, and seizures of drug evidence between December, 2018 and February, 2019" but without further details. It has also been stated that "serious adverse effects including death have been reported following the use of 4F-MDMB-BINACA" *(20)*. Background information documents normally associated with Factor Analysis for temporary scheduling considerations in the USA are not available in the case of 4F-MDMB-BINACA since it is considered as isomer of 5F-AMB-PINACA (5F-MMB-PINACA, 5F-AMB) which is already controlled under the Controlled Substances Act *(21)* and this would therefore extend to 4F-MDMB-BINACA.

In an updated report provided by the UNODC that includes data obtained from the UNODC's ToxPortal, a total number of two case reports involving the detection of 4F-MDMB-BINACA were recorded *(22)*. More detailed case level information was not provided (Table 2):

Table 2. Toxicology reports according to data provided by the UNODC's ToxPortal *(22)*

Case reports	Reporting country	Type of cases	Comments
2019 (2)	Singapore (1) Germany (1)	Clinical admission (1)	No other substances detected.
		Other cases (1)	–

More specific information related to 4F-MDMB-BINACA, however, could not be identified. Generally, however, reported adverse drug reactions associated with a range of other SCRAs frequently include gastrointestinal (e.g. nausea/hyperemesis), neurological (e.g. hallucination, agitation, anxiety, paranoia, confusion, delusions, catatonia, lethargy, psychosis (including susceptible individuals)), cardiovascular (e.g. tachycardia, hypertension) and renal (e.g. acute kidney failure) clinical features (e.g. *(23-26)*).

7. Dependence Potential

A. Animal Studies

Information could not be identified.

B. Human Studies

Information could not be identified.

8. Abuse Potential

A. Animal Studies

Information could not be identified.

B. Human Studies

Information could not be identified.

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

4F-MDMB-BINACA is not known to have any therapeutic applications.

10. Listing on the WHO Model List of Essential Medicines

4F-MDMB-BINACA is not listed on the WHO Model List of Essential Medicines.

11. Marketing Authorizations (as a Medicinal Product)

4F-MDMB-BINACA is not marketed as a medicinal product

12. Industrial Use

4F-MDMB-BINACA has no reported industrial use.

13. Non-Medical Use, Abuse and Dependence

Household or subpopulation surveys that specifically probe for prevalence of 4F-MDMB-BINACA could not be identified in the currently available literature. Epidemiological data, such as prevalence of use, abuse and dependence information, are not available specifically for 4F-MDMB-BINACA. The Monitoring the Future (MTF), a national cross-sectional survey in the United States of America that queries use of SCRAs among high-school attending adolescents revealed a decrease in past-year use from 11.86% in 2011 to 4.75% in 2015. It was however found that the decrease was slower for some subgroups, predominantly those with high socioeconomic status and those who are frequent marijuana users. Across time, risk factors for use also include older adolescents, adolescents who identify as Hispanic/mixed race, and cigarette/other substance users *(27)*.

Heavy use of synthetic cannabinoid receptor agonists has been associated with problematic withdrawal symptoms (e.g. *(28, 29)*) and further research is needed to investigate the underlying mechanisms. As highlighted by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), people who use SCRAs include recreational users, high-risk drug users but also individuals who are subject to drug testing such as people in drug treatment, prisoners and drivers *(30, 31)*.

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

The majority of available SCRA products (including those containing 4F-MDMB-BINACA) is sold in the form of herbal mixtures, and designed for smoking purposes and vaping. 4F-MDMB-BINACA has also been detected in samples sold as cannabidiol- and THC-containing liquids presumably used for smoking/vaping *(1)*. It is common for retailers to purchase bulk quantities of the synthetic substance and to add the synthetic material to a variety of vegetable matter as the plant base. Products sold as herbal smoking mixtures frequently change in drug composition and quantity, often without indications on product labels, which results in challenges to unambiguously correlate harms to public health with a specific drug such as 4F-MDMB-BINACA. The consumption of these products might be attractive to a variety of users, such as regular users of cannabis and those who believe that SCRA use might help with avoiding a positive finding in drug-testing procedures. Ease of access, and perceived lack of legislative control might equally be of interest to some users. However, people who use these drugs are most likely not aware of the constituent and the quantity. The high potency associated with many synthetic cannabinoids carries the risk of accidental overdose and potentially severe adverse events but information specific to 4F-MDMB-BINACA is limited (Section 6). Detections of 4F-MDMB-BINACA in biological specimens involving impaired driving cases have been published *(4)*. Impaired driving cases and motor vehicle collisions have been reported with closely related SCRAs such as 5F-ADB (5F-MDMB-PINACA) *(32)*. There are indications that socially vulnerable and stigmatised substance users, for example found in homeless and prison populations, are increasingly associated with problematic use of SCRA products *(33-36)*. SCRA use in prisons has been associated with increase in aggression, violence, bullying and debt but also serious threats to safety and security of the prison environment *(30, 31)*. The detections of 4F-MDMB-BINACA in biological specimens confirm that 4F-MDMB-BINACA is consumed either intentionally or unintentionally and that it appears to be associated with adverse effects though detailed information on the extent of use and circumstances are not available.

A number of trend reports published in the USA have also featured the detection of 4F-MDMB-BINACA in various biological samples or sample extracts. In total, cases were submitted from 24 US States and the District of Colombia (Table 3).

Table 3. Trend reports that feature the detection of 4F-MDMB-BINACA.[a]			
Time frame	Positive findings	5F-ADB	Reference
Oct–Dec 2018	1 out of 964 specimens Metabolites: NR[b] Combinations: 1	32 out of 964 specimens Metabolites: 31 Combinations: 11	*(16)*
Jan–Mar 2019	37 out of 1,533 specimens Metabolites: 8 Combinations: 16	8 out of 1,533 specimens Metabolites: 19 Combinations: 3	*(17)*
Apr–June 2019	32 out of 1,328 specimens Metabolites: 7 Combinations: 14	None reported.	*(18)*
[a] 5F-ADB (SCRA reviewed during 39th ECDD, *(32)*) results included for comparison. [b] NR: not reported.			

15. Licit Production, Consumption and International Trade

4F-MDMB-BINACA is available as standard reference material and produced for scientific research by a number of commercial suppliers. Other uses could not be identified.

16. Illicit Manufacture and Traffic and Related Information

EMCDDA received reports that 4F-MDMB-BINACA (detection first notified in November 2018 *(37)*) was encountered in seizures and collected specimens (herbal mixtures or powders) in France, Croatia, Slovakia, Estonia, Sweden, Finland, Slovenia, Lithuania, Germany, Romania, Hungary, Netherlands, and United Kingdom. SCRAs are typically imported from Chinese suppliers and prepared locally for distribution in their herbal form *(30)*.

Detections of 4F-MDMB-BINACA have also been reported to UNODC's Early Warning Advisory on New Psychoactive Substances *(38)*. Detections of 4F-MDMB-BINACA were reported by 2 countries in 2018, and 3 countries in 2019 (as of 02 August 2019).

In recent years it has emerged that SCRAs are smuggled into prisons in the form of impregnated papers (e.g. letters) and textiles *(31, 39, 40)* including 4F-MDMB-BINACA *(12, 41)*.

In a drug-monitoring pilot programme covering three Scottish prisons in the United Kingdom, suspected SCRA-infused paper samples were seized for analytical evaluation in the period between 01 June 2018 and 01 July 2019. In this period, 257 individual paper samples obtained from 116 seizures were analysed which revealed the detection of at least one SCRA in 108 samples (42%). 4F-MDMB-BINACA began to emerge in February 2019 and appeared to have become increasingly prevalent (16.5%, n = 106 in total). Its emergence (together with other SCRAs such as 5F-MDMB-PICA) was also seen to signal a replacement

of 5F-ADB, and FUB-AMB as the most commonly detected compounds in infused papers until the end of 2018 *(42)*.

17. Current International Controls and Their Impact

4F-MDMB-BINACA is not controlled under the 1961 (as amended by the 1972 Protocol), 1971 or 1988 United Nation Conventions.

18. Current and Past National Controls

Refer to 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

No further comments.

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Annex 1: Report on WHO Questionnaire for Review of Psychoactive Substances

Refer to separate Annex 1: Report on WHO questionnaire for review of psychoactive substances