Annex 1: Report on WHO Questionnaire for Review of Psychoactive Substances for the 42nd ECDD: Evaluation of Synthetic Stimulants (4-CMC (4-chloromethcathinone; clefedrone), N-ethylhexedrone (NEH, Hexen, Ethyl-Hex), Alpha-PHP (PV-7, α-pyrrolidinohexanophenone), DOC (2,5-Dimethoxy-4-chloroamfetamine)

Data was obtained from 75 Member States (10 AFR, 5 EMR, 32 EUR, 10 PAH, 5 SEAR and 13 WPR) for the WHO Questionnaires for the Review of Psychoactive Substances.

A total of 72 Member States started the questionnaire regarding synthetic stimulants. Of these, 35 respondents had information on the substances.

Region	Number of countries responded	Number of countries with information on each substance			
		DOC (2,5-Dimethoxy-4-chloroamfetamine)	4-CMC (4-chloromethcathinone; clefedrone)	Alpha-PHP (PV-7, α-pyrrolidino hexanophenone)	N-ethylhexedrone (NEH, Hexen, Ethyl-Hex)
AFR	1	0	0	0	0
EMR	2	2	0	2	0
EUR	24	18	20	21	15
PAH	2	2	1	0	1
SEAR	1	1	1	0	1
WPR	5	4	5	3	4
TOTAL	35	27	27	26	21

LEGITIMATE USE

No Member States reported any approved human medical or veterinary products containing synthetic stimulants.

Two Member States (Australia and France) reported that the synthetic stimulants are used for industrial or other non-medical/ non-scientific purposes:

"Forensic laboratories, university research, law enforcement standards and reference materials"

"usage récréatif".

No Member States reported the use of synthetic stimulants for any cultural, religious or ceremonial purposes.

EPIDEMIOLOGY OF NON-MEDICAL/NON-SCIENTIFIC USE – USE FOR PSYCHOACTIVE PURPOSES OR RECREATIONAL DRUG USE

Twenty-seven Member States reported that synthetic stimulants under consideration are being misused for their psychoactive properties (as a recreational drug).

The most common route of administration reported was oral administration, followed by injecting and sniffing (Table 1), with "sublingual" and "rectal" both cited by Japan and Sweden, and with "stamps (DOC)", "powder" and "ocular" each mentioned by Colombia.

Route of administration	Number of countries
Oral	18
Injection	9
Sniffing	9
Smoking	4
Inhalation	3
Other (please specify)	7
Do not know	6
Total	27

Table 1: Common routes of administration

Regarding 4-CMC, seven Member States specify "oral" as the most common route of administration, and five saying "sniffing".

For N-ethylhexedrone, five Member States specify "oral" as the most common route of administration, followed by three saying "sniffing" and two saying "injection".

For Alpha-PHP, eight Member States mention "oral" as the most common route of administration, followed by five Member States referring to "intravenous", "IV" or "injection", Five Member States refer to "sniffing".

For DOC, it was more clear-cut, with twelve Member States cite "oral" as the most common route of administration, followed by three saying "sniffing".

The most common formulation of synthetic stimulants reported was powder, followed by tablets/capsules (refer to Table 2). Nine Member States also reported "blotters" as a formulation (specifically for DOC on two occasions), three countries reported crystals as another formulation and there was a reference each to "stamps" and "plant material".

Formulation	Number of countries reporting formulations
Powder	24
Tablets/Capsules	11
Liquid or solution for oral administration/use	5
Solution for injection	1
Other (please specify)	13
Total	27

Table 2: Common formulations reported by countries

Smuggling (from other countries) was the main source of the synthetic stimulants for non-medical/non-scientific use, cited by fifteen of the eighteen Member States who could give an answer (refer to Table 3), with "post", "internet sales" and "personal use" each cited by one Member State.

Source	Number of countries reporting sources
Smuggling (from other countries)	15
Illegal manufacturing	3
Diversion (from legal supply chain)	1
Legal manufacturing	0
Legal trade	0
Other (please specify)	3
Do not know	9
Total	27

Table 3: Sources of substance for non-medical or non-scientific use

Six Member States indicated that there are specific subpopulations known to misuse any of the synthetic stimulants, mainly younger people in social settings:

"Dance parties and festival goers"
"chemsex/gay scene"
"Party goers"
"Homeless injecting Drugs users injecting this substance."
"Yakuza (the Japanese Mafia)"
"young of average class"

The extent and magnitude of public health problems or social harm caused by the use of the synthetic stimulants is either not known or considered to be low (at least for now), as illustrated by the following comments from different Member States:

"Very limited"
"The prevalence is low, harms cumulate to those already vulnerable"
"Small magnitude of the problem, extent increasing over the last years"
"The social harm caused by the use of 4-CMC and NEH maybe substantial (based on the animal experiments)".

The level of negative health-impact originating from these substances' non-medical consumption was reported as:

Serious	Substantial	Negligible	Don't Know
5	4	8	10

Five Member States indicate a serious negative health-impact from these substances (Colombia, Indonesia, Ireland, Italy, Sweden). Another four Member States report a substantial negative health-impact (Estonia, Finland, Germany and one other Member State which did not wish to be named). Among the Member States that reported a serious or substantial level of negative health-impact, all four synthetic stimulants were cited, led by Alpha-PHP (5 countries) and 4-CMC (4 countries):

"Alpha-PHP. Associated with increase in HIV in Homeless PWID"
"All substances have caused intoxications. All substances except DOC have been identified in deceased."
"4-CMC marketed in liquid form named snow white, blue safir as recreational drug."
,,DOC Alguna literatura indica que el uso de esta sustancia esta asociado con graves daños a la salud."
"NEH - increased (small) seizures. 4-CMC seen for several years; also 3-CMC - scale small. alpha-PHP is being used by the same population than alpha-PVP which has stayed in our market since the beginning. DOC has been around the longest, however the harms reported have not triggered the national scheduling process for control as a narcotic substance."
"The substances played a major role in Germany particularly in the years 2014 and 2015. Since their placement under the narcotics law and the introduction of provisions on substance groups they have notably lost importance."

Eight Member States reported emergency room/department visits related to the non-medical use of synthetic stimulants (Belgium, France, Germany, Ireland, Italy, Russian Federation, Sweden, United Kingdom of Great Britain and Northern Ireland). All four synthetic stimulants were mentioned:

"In June 2007 the NFP reported a collected sample of paper recovered from attendees at a dance from which three people were taken to hospital. Two were seriously ill requiring intensive care. They said they had taken a drug called 'DOI' or 'DO9'. Analysis by NMR and GC/MS and comparison with an authentic sample provided by the Swedish Forensic

Science Laboratory, Linköping, confirmed DOC. It was collected by the Toxicology Unit, St. George's Hospital Medical School on February."
"4-CMC: 5 visits (2015, 2017) N-etylhexedron: 5 visits (2016) Alpha-PHP: 43 visits (2014-2018) DOC: 1 visit (2016)"
"Emergency room for one case of intoxication by DOC."
"Attempted suicide of a 22 years old man in 2015 after the consumption of a-PBP und a-PHP."

Reported adverse effects are mainly psychological or neurological or metabolic: aggressive behaviour, agitation, anxiety, fever, hallucinations, hypertension, mydriasis, nausea, paranoia, paraesthesia, psychosis, seizures, tachycardia and vomiting (among others) were listed.

Six Member States (Finland, France, Germany, Spain, Sweden and one other Member State which did not wish to be named) reported a total of 53 deaths where the 4 synthetic stimulants were involved, of these only two where the synthetic stimulant was known to be the only substance involved. Among these reporting Member States, Sweden cites 40 deaths (22 where other substances were involved, and 18 where it was not known if other substances were involved or not), along with the following breakdown:

"DOC: None Alpha-PHP: 25 (2014-2018) 4-CMC: 2 (2015, 2018) N-ethylhexedrone: 13 (2016-2017) Information on cause of death is currently not available but can be retrieved upon request."

Only two Member States (Ireland, Republic of Moldova) report their awareness of people presenting to drug dependence treatment centres due to the use of synthetic stimulants, and provided the following details:

"4-CMC"
"Alpha-PHP use as part of a polydrug use pattern as opposed to single use of the substance".

STATUS OF NATIONAL CONTROL AND POTENTIAL IMPACT OF INTERNATIONAL CONTROL

Twenty-seven Member States report that at least one of the synthetic stimulants was under national control. The legislation that the control is based upon included the Controlled Substances Act (21 Member States), Criminal Law Act (5 Member States), Medicines Act (2 Member States), and other legislation (5 Member States).

The scope of the controls includes distribution (27 out of 27 Member States), importing (26 out of 27 Member States), manufacturing (25 out of 27 Member States), possession (24 out of 27 Member States), production (23 out of 27 Member States), and exporting and use (22 out of 27 Member States). None of the twenty-eight Member States report that the provisions are temporary.

Two Member States (Indonesia and another Member State which did not wish to be named) report challenges to implementing national controls, citing:

"analytical challenge posed by the New Psychoactive Substances"
"lack of reference standard material".

Reported illicit activities involving synthetic stimulants were (Table 4):

Illicit Activities	Number of countries reporting
Trafficking	19
Sales to people who use synthetic stimulants	9
Internet sales (from abroad to buyers in your country)	8
Internet sales (other or location of sellers and website unknown)	8
Internet sales (seller or website located in your country)	4
Diversion	3
Manufacture of the substance by chemical synthesis	1
Production of consumer products (dosage forms, packaging)	2
Manufacture of the substance by extraction from other products	0
Other (please specify)	1
Do not know	6
Total	27

Table 4: Reported illicit activities involving synthetic stimulants

Seventeen Member States gave answers re: the number of seizures of the synthetic stimulants, but the responses range from 1 to 6740). Overall Even so, seizures of DOC are low and have remained so, while seizures of the other three have all increased notably over time.

If any of the synthetic stimulants were placed under international control, thirty-two (out of thirty-four) Member States confirm that they would have the capacity to enforce the control at the national level; of these, thirty-one Member States indicate that they would have the forensic laboratory capacity to analyse the substance (with only Colombia indicating that they would not have this capacity):

,,A pesar de que los laboratorios cuentan con la tecnología para la identificación de estas sustancias, no se cuenta con material de referencia certificados o estándares y no se han desarrollado los métodos analíticos para la identificación de este tipo de drogas."