World Health Organization

Annex 1:

Report on WHO questionnaire for review of psychoactive substances

Expert Committee on Drug Dependence

Forty-sixth Meeting

Geneva, 16–20 October 2023

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

Bromazolam

Of the 70 countries that agreed to provide data, 29 reported that they had information on the use of bromazolam in their country for medical, scientific, industrial or other professional purposes, for non-medical consumption or recreational purposes or for any other purpose (Table A1).

Table A1. Numbers of countries that provided information on bromazolam

Region	No. of countries with no information	No. of countries with information
African	9	2
Americas	7	2
South-East Asia	3	1
European	13	19
Eastern Mediterranean	7	0
Western Pacific	2	5
Total	41	29

Approved medical, scientific or industrial use

No country reported approved therapeutic indications for bromazolam, and none reported that bromazolam was currently used in medical or scientific research, such as in clinical trials for a human or veterinary indication (except as an analytical standard). None reported use for legitimate (legal) industrial purposes.

Epidemiology of non-medical use

Twenty-one countries (14 in the European, 4 in the Western Pacific, 2 in the Americas and 1 in the South-East Asia regions) reported evidence of use of bromazolam for non-medical purposes (i.e. outside the medical, industrial or scientific context). The evidence was derived mainly from data on seizures for law enforcement (n=17), customs (suggesting detection at international border points; n=10), toxicology reports after deaths (n=3), toxicology reports from emergency departments (n=3), drug checking (n=3) and poisons information calls (n=2). Other sources included reports submitted to or published by treatment providers, doctors and drug treatment centres and reports related to recreational use.

Routes of administration and formulations

The most common reported route of administration was oral (Table A2).

Table A2. Reported routes of bromazolam administration

Route of administration	No. of countries
Smoking	0
Oral	17
Inhalation	2 [a]
Sniffing	1
Injection	2

Other	0
Do not know	3

[a] "Inhalation route if consumed in combination with fentanyl", further described in the "Other" section.

The most common formulation of bromazolam reported was tablets (Fig. A1).

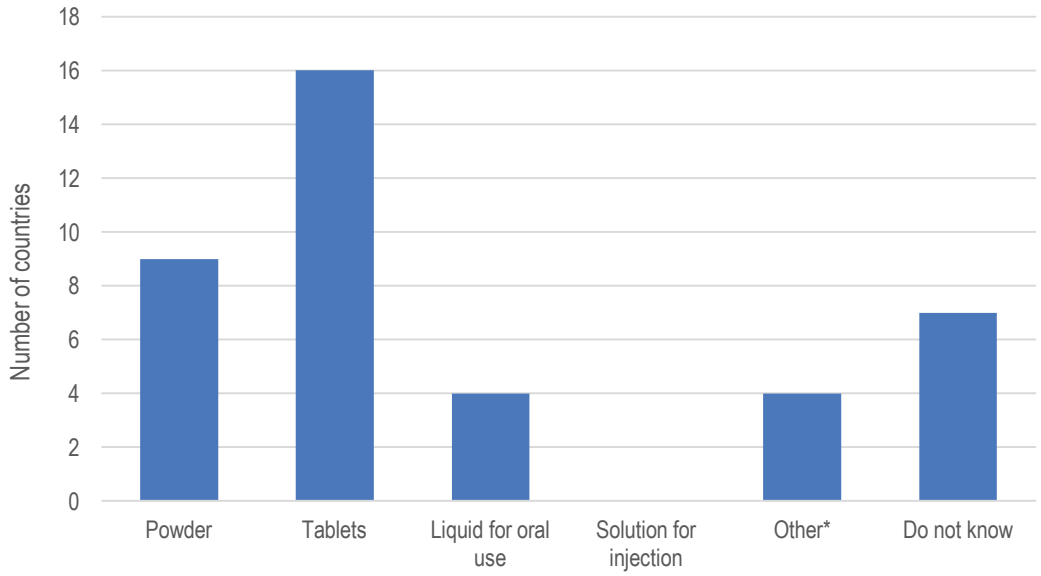

Fig. A1.P Formulations of bromazolam

*Other formulations included herbs or herbal products, blotting paper, chocolates, "residue", rock-like solid, crystalline substance, liquid, food, trips, capsule.

Perceived negative health impact

Twelve countries (6 in the European, 2 in the Americas, 2 in the Western Pacific, 1 in the African and 1 in the South-East Asia regions) reported that the negative health effect of non-medical consumption of bromazolam was "especially serious" or "substantial" (Fig. A2).

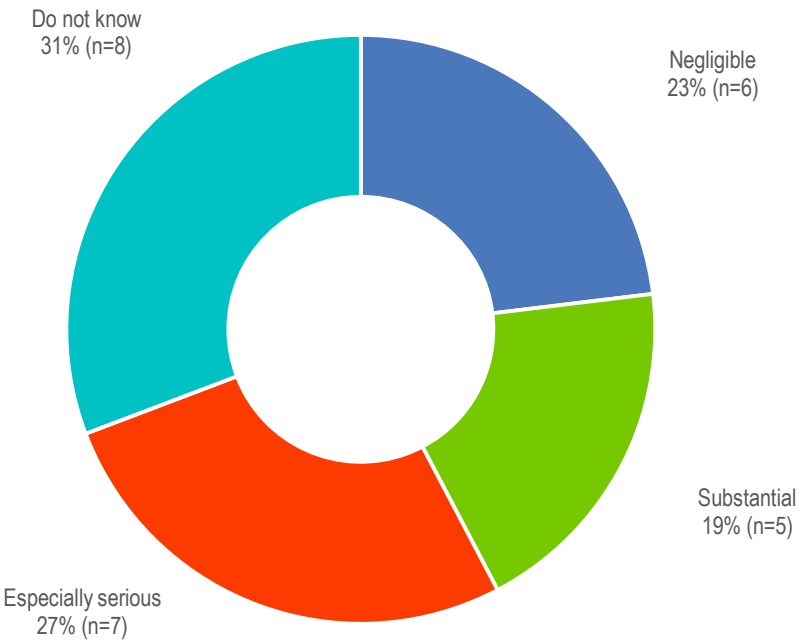

Fig. A2. Negative health impacts of non-medical consumption of bromazolam

Emergency department visits

Seven countries (5 in the European, 1 in the Western Pacific and 1 in the Americas regions) were aware of emergency department visits related to bromazolam. Five countries described emergency department presentations by people who had consumed bromazolam with other substances. Four reported the year in which the presentations occurred: 20 presentations in 2023 (16 in the Americas and 4 in the European regions), 7 presentations in 2022 (4 in the European and 3 in the Americas regions) and 1 presentation in 2021 (in the European Region).

The adverse effects (e.g. non-fatal intoxications) seen in patients who presented to emergency departments after use of bromazolam included dizziness, confusion, tachycardia, hallucinations, psychosis, depression, vomiting, unconsciousness, respiratory depression, memory loss, seizure, coma, delusional idea of persecution, addiction and psychiatric and psychotic disorders.

Deaths

Five countries (4 in the European and 1 in the Americas regions) reported bromazolam-related deaths between 2021 and 2023. In the four countries that reported the number of bromazolam-related deaths in 2021–2023 the number ranged from 1 to 53. One country in the European Region reported deaths in which bromazolam was the only drug involved and those in which another substance was involved, three countries (2 in the European and 1 in the Americas regions) reported deaths in which another substance was involved, and one country did not know whether other drugs had been involved.

Drug dependence

No country reported presentations for treatment of drug dependence due to use of bromazolam.

Current national controls

Twelve countries (9 in the European, 2 in the Western Pacific and 1 in the Africa regions) reported that the availability of bromazolam was controlled under substance-specific legislation, and five countries (2 in the European, 2 in the Americas and 1 in the Western Pacific regions) reported that the availability of bromazolam was controlled under legislation on analogue or generic drugs.

Illicit manufacture and trafficking

Table A3 shows the main reported activities involving bromazolam.

Table A3. Reported activities involving bromazolam for purposes other than medical, scientific or industrial use

Activity	No. of countries
Trafficking	9
Smuggling (from other countries)	6
Internet sales (other or location of sellers and website unknown)	6
Internet sales (from abroad to buyers in the respondent's country)	5
Internet sales (seller or website located in respondent's country)	4
Manufacture of the substance by chemical synthesis	1
Direct sales	1
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Diversion (from legal supply chain)	0
Do not know	11
Other	0

Detection in falsified medicines

Six countries (3 European, 2 Americas, 1 Western Pacific) indicated that bromazolam was falsely sold as Xanax or alprazolam.

Seizures

Ten countries (6 in the European, 2 in the Western Pacific, 1 in the Americas and 1 in the South-East Asia regions) reported seizures in 2023. The number of seizures per country ranged from 1 to 144, and the amounts seized ranged from 8 to 2306 g and 8 to 1518 tablets (Table A4).

Fourteen countries (14 in the European, 2 in the Western Pacific and 1 in the South-East Asia regions) reported seizures in 2022. The number of seizures per country ranged from 1 to 5168, and the amounts seized ranged from < 1 to 2119 g.

Nine countries (8 in the European and 1 in the Western Pacific regions) reported seizures in 2021. The number of seizures per country ranged from 1 to 1164, and the amounts seized were 3 to 2733 g.

Table A4. Reported seizures of bromazolam

Year	No. of countries that reported seizures	No. of seizures
2023	10	238
2022	14	5662
2021	9	1328

Laboratory capacity

Twenty-three of the 28 countries that provided information (16 in the European, 4 in the Western Pacific, 2 in the Americas and 1 in the South-East Asia regions) reported that they had the laboratory capacity to analyse bromazolam.

Flubromazepam

Of the 70 countries that agreed to provide data, 26 had information on use of flubromazepam in their country for medical, scientific, industrial or other professional purposes or for non-medical consumption, recreational or any other purpose (Table A5).

Table A5. Numbers of countries that provided information on flubromazepam

Region	No. of countries with no information	No. of countries with information
African	7	1
Americas	7	2
South-East Asia	3	1
European	12	18
Eastern Mediterranean	5	0
Western Pacific	2	4
Total	36	26

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for flubromazepam, and none reported that flubromazepam was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard). None reported use for industrial purposes.

Epidemiology of non-medical use

Eighteen countries (12 in the European, 3 in the Western Pacific, 2 in the Americas and 1 in the South-East Asia regions) reported use of flubromazepam for non-medical purposes (i.e. outside the medical, industrial or scientific context). The evidence was derived from data on seizures from law enforcement (n=11) , seizures from customs (suggesting detection at international border points; n=9), toxicology reports from death (n=5), toxicology reports from emergency departments (n=3), poisons information calls (n=2), drug checking (n=2), hospitalization (n=1), presence of dark web cryptomarket listings that deliver to the country (n=1) and published reports of recreational use (n=1).

Routes of administration and formulations

The most commonly reported route of administration of flubromazepam was oral (Table A6).

Table A6. Reported routes of flubromazepam administration

Route of administration	No. of countries
Oral	13
Injection	2
Inhalation	1
Sniffing	0
Smoking	0

Do not know	6

The most common reported formulations of flubromazepam were tablets and a powder (Fig. A3).

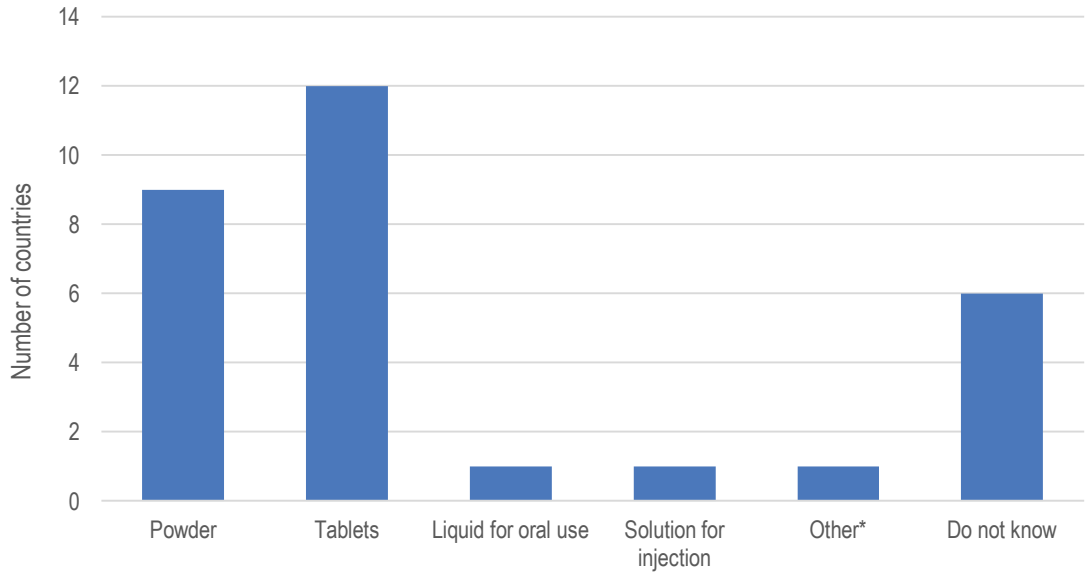

Fig. A3. Formulations of flubromazepam

* Other formulation descriptions included "rock-like solid, liquid, crystalline substance, syringe, capsule"

Perceived negative health impact

Eight countries (6 in the European, 1 in the Western Pacific and 1 in the South-East Asia regions) reported that the negative health impact of non-medical consumption of flubromazepam was “especially serious” or “substantial” (Fig. A4).

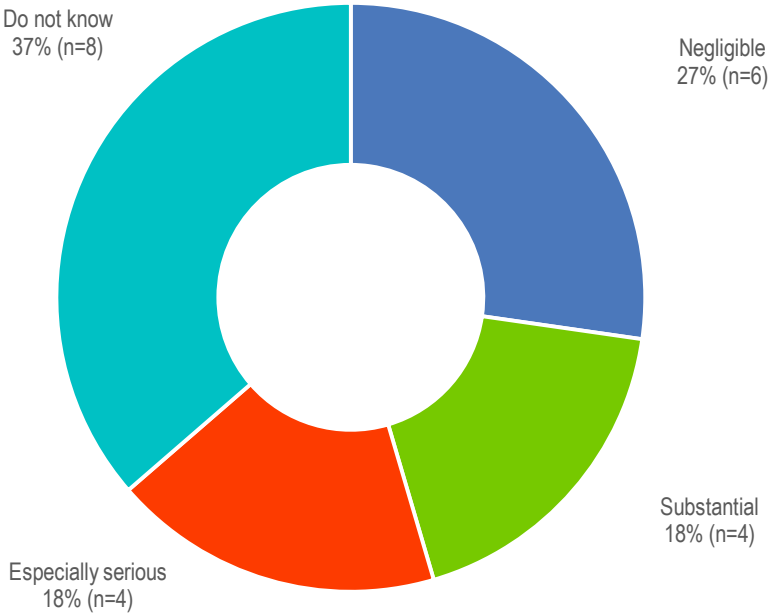

Fig. A4. Negative health impacts of non-medical consumption of flubromazepam

Emergency department visits

Five countries (4 in the European and 1 in the Americas regions) were aware of emergency department visits related to flubromazepam. Three countries described emergency department presentations by people who had consumed flubromazepam with other substances and also reported the year in which the presentations occurred, with 1 in 2023 (in the Americas Region), 1 in 2022 (in the European Region) and 1 in 2021 (in the European Region). One country in the European Region reported 38 flubromazepam-related emergency department presentations in the years before 2021.

Adverse effects (e.g. non-fatal intoxications) in patients who presented to emergency departments after use of flubromazepam were reported by three countries in the European Region. They included hypotension, tachycardia, hallucinations, chest pain, drug dependence, persecution delusion, psychotic and psychiatric disorders, coma with a Glasgow Coma Scale score from 8 to 3, mydriasis, cramp, rhabdomyolysis, impaired renal function, unrousable or difficult to wake, tired and lethargic, somnolent, lethargic, slowed heart rhythm, slurred speech and fluctuating or reduced consciousness.

Deaths

Three countries (2 in the European and 1 in the Americas regions) reported nine flubromazepam-related deaths in which other substances were also involved between 2021 and 2023. Two countries (1 in the European and 1 in the Americas regions) reported three flubromazepam-related deaths in 2023 in which other substances were also involved. Three countries (2 in the European and 1 in the Americas regions) reported five flubromazepam-related deaths in 2022 in which other substances

were also involved. One country in the Americas Region reported one flubromazepam-related death in 2021 in which other substances were also involved. One country in the European Region reported 24 flubromazepam-related deaths that occurred before 2021, in which flubromazepam was the only substance involved and 23 in which other substances were involved.

Drug dependence

One country in the European Region reported that people presented for treatment for drug dependence due to use of flubromazepam.

Current national controls

Twelve countries (9 in the European and 3 in the Western Pacific regions) reported that flubromazepam was controlled under substance-specific legislation, and 2 countries (1 in the European and 1 in the Americas regions) reported that the availability of flubromazepam was controlled under analogue or generic legislation.

Illicit manufacture and trafficking-related information

Table A7 lists the main reported activities involving flubromazepam.

Table A7. Reported activities involving flubromazepam for purposes other than medical, scientific or industrial use

Activity	No. of countries
Smuggling (from other countries)	2
Trafficking	4
Internet sales (from abroad to buyers in the respondent's country)	8
Internet sales (other or location of sellers and website unknown)	4
Internet sales (seller or website located in respondent's country)	3
Direct sales	1
Manufacture of the substance by chemical synthesis	0
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Diversion	0
Do not know	9

Detection in falsified medicines

Three countries (2 in the European and 1 in the Americas regions) were aware that flubromazepam had been detected in falsified medicines or other products. These countries indicated that flubromazepam was falsely sold as Xanax, alprazolam and hydromorphone.

Seizures

Seven countries (4 in the European, 1 in the Western Pacific, 1 in the Americas and 1 in the South-East Asia regions) reported seizures in 2023. The number of seizures per country in 2023 ranged from 1 to 144, and the amounts seized ranged from 1 to 1074 g (Table A8).

Eleven countries (9 in the European, 1 in the Americas and 1 in the Western Pacific regions) reported seizures in 2022. The number of seizures per country in 2022 ranged from 1 to 1798, and the amounts seized ranged from < 1 to 1707 g and from 10 to 415 tablets.

Six countries (5 in the European and 1 in the Americas regions) reported seizures in 2021. The number of seizures per country ranged from 1 to 235, and the amounts seized ranged from 1 to 2733 g.

Table A8. Reported seizures of flubromazepam

Year	No. of countries that reported seizures	No. of seizures
2023	7	160
2022	11	2205
2021	6	384

Laboratory capacity

Twenty of the 24 countries (15 European, 2 Western Pacific, 2 Americas, 1 South-East Asia) reported that they had the laboratory capacity to analyse flubromazepam

Butonitazene

Of the 70 countries that agreed to provide data, 15 provided information on butonitazene (Table A9).

Table A9. Numbers of countries that provided information on butonitazene

Region	No. of countries with no information	No. of countries with information
African	7	0
Americas	7	2
South-East Asia	4	0
European	19	11
Eastern Mediterranean	4	0
Western Pacific	4	2
Total	45	15

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for butonitazene, and none reported that butonitazene was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard). None reported use for industrial purposes.

Epidemiology of non-medical use

Six countries (3 in the European, 2 in the Americas and 1 in the Western Pacific regions) reported evidence of the use of butonitazene for non-medical purposes (outside the medical, industrial or scientific context). This evidence was derived primarily from data on seizures from law enforcement (n=5) and customs (n=2) agencies. Toxicology reports on deaths (n=2), toxicology reports from emergency departments (n=1), a published report on emergency department presentations (n=1) and lists of dark web cryptomarkets that deliver to the country (n=1).

Routes of administration and formulations

The most common reported route of administration was injection, followed by smoking, oral, sniffing and nasal spray (Table A10).

Table A10. Reported routes of butonitazene administration

Route of administration	No. of countries
Smoking	1
Oral	1
Inhalation	0
Sniffing	1
Injection	2
Other[a]	1
Do not know	7

[a] Nasal spray (n=1)

The most common formulation of butonitazene reported was as a powder (Fig. A5).

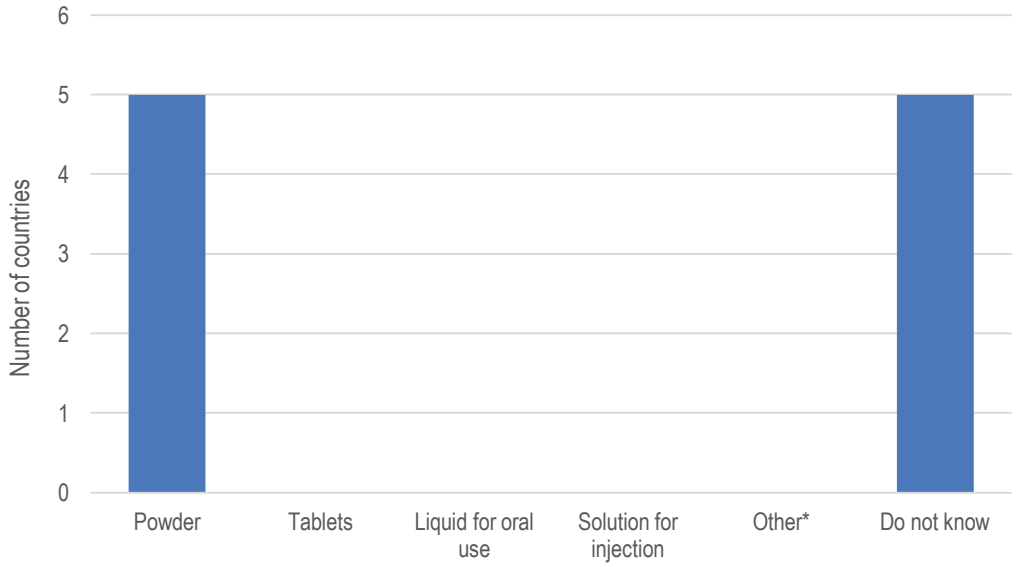

Fig. A5. Formulations of butonitazene

[a] Other formulations were not specified.

Perceived negative health impact

Four countries (3 in the European and 1 in the Americas regions) reported that the negative health impact of non-medical consumption of butonitazene was “especially serious” or “substantial” (Fig. A6).

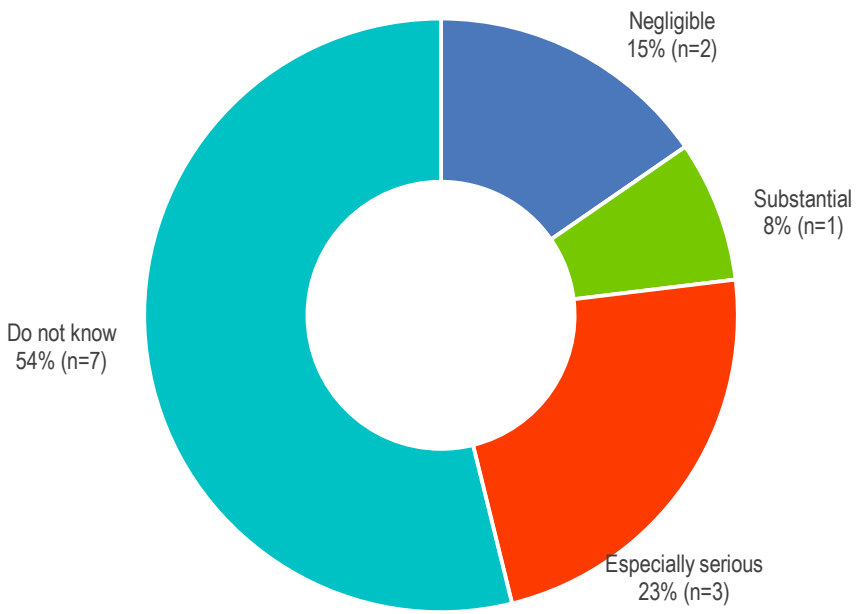

Fig. A6. Negative health impacts of non-medical consumption of butonitazene

Emergency department visits

Two countries (1 in the Western Pacific and 1 in the European regions) were aware of emergency department visits related to butonitazene. The country in the Western Pacific Region cited published reports on use of butonitazene by patients presenting to hospital emergency departments.

Deaths

One country (in the Americas Region) reported one death in 2021 in which butonitazene was identified post mortem; it was not known whether other substances were involved.

Drug dependence

No countries reported presentations for treatment of drug dependence due to use of butonitazene.

Current national controls

Seven countries (6 in the European and 1 in the Americas regions) responded that butonitazene was currently regulated under substance-specific legislation, and seven countries (3 in the European, 3 in the Western Pacific and 1 in the Americas regions) reported the availability of butonitazene was controlled under analogue or generic legislation.

Illicit manufacture and trafficking-related information

Table A11 shows the main reported activities involving butonitazene.

Table A11. Reported activities involving butonitazene for purposes other than medical, scientific or industrial use

Activity	No. of countries
Smuggling (from other countries)	1
Trafficking	2
Internet sales (from abroad to buyers in respondent's country)	2
Internet sales (other or location of sellers and website unknown)	1
Internet sales (seller or website located in respondent's country)	0
Manufacture of the substance by chemical synthesis	0
Direct sales	0
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Diversion	0
Do not know	7
Other	0

Detection in falsified medicines

One Western Pacific country reported that butonitazene was detected in falsified medicines.

Seizures

Two countries (1 in the Americas Region and 1 European) reported seizures in 2023. The amounts seized in 2023 ranged from 0 to 58 g (Table A12). Two countries (1 in the Americas Region and 1 European) reported seizures in 2022. The amounts seized ranged from 0 to 944 g in 2022 (Table A4). Four countries (3 in the European and 1 in the Americas regions) reported seizures in 2021. The number of seizures per country ranged from 1 to 12 and the amounts seized from 0.1 to 8 g. One country (Western Pacific) reported seizures (number and year were not specified).

Table A12. Reported seizures of butonitazene[a]

Year	No. of countries that reported seizures	No. of seizures
2023	2	4
2022	2	49
2021	4	14

[a] Data to August 2023

Laboratory capacity

Thirteen countries (9 in the European, 2 in the Western Pacific and 2 in the Americas regions) reported that they had the laboratory capacity to analyse butonitazene.

3-CMC

Of the 62 countries that agreed to provide data, 27 had information on 3-CMC (Table A13).

Table A13. Numbers of countries that provided information on 3-CMC

Region	No. of countries with no information	No. of countries with information
African	8	0
Americas	7	2
European	7	22
Eastern Mediterranean	4	0
South-East Asia	4	0
Western Pacific	3	3
Total	33	27

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for 3-CMC, and none reported that 3-CMC was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard). None reported use for industrial purposes.

Epidemiology of non-medical use

Nineteen countries (15 in the European, 2 in the Americas and 2 in the Western Pacific regions) reported evidence of the use of 3-CMC for non-medical purposes (outside the medical, industrial or scientific context). The evidence was derived primarily from data on seizures by law enforcement (n = 13) and customs agencies (n = 9), post-mortem reports (n=4), toxicology reports from emergency departments (n= 2) and poison information calls (n = 2). Other sources included drug checking (n = 2), driving under the influence of drugs, declarations to drug monitoring centres and listing of the drug on the dark web. One country in the European Region reported that 3-CMC had been detected as a replacement for 3-MMC.

Routes of administration and formulations

The most common reported route of administration was oral, followed by sniffing and smoking or injection (Table A14).

Table A14. Reported routes of 3-CMC administration

Route of administration	No. of countries
Oral	8
Sniffing	5
Injection	3
Smoking	3
Inhalation	2
Other[a]	1

Do not know	15

[a] Rectal use (with syringe without needle)

The most common known formulations of 3-CMC reported were powders and crystals or a crystalline substance (Fig. A7).

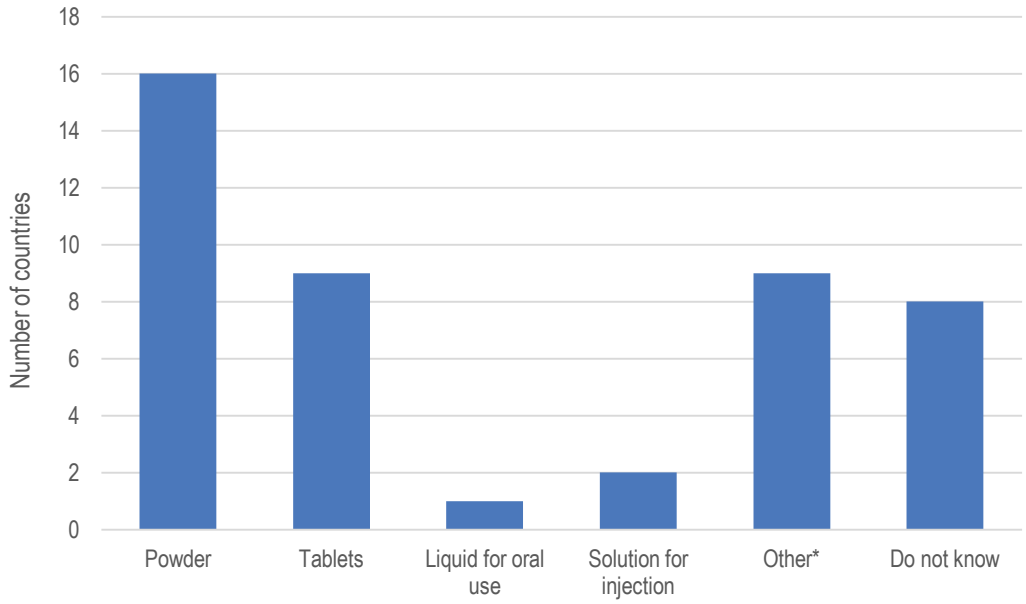

Fig. A7. Formulations of 3-CMC

[a] Other formulations referred to most commonly were crystals or crystalline substance (n=8), capsule (n = 1), rocks (n=1) and whitish substance (n = 1).

Perceived negative health impact

Eight countries in the European Region reported that the negative health impact of non-medical consumption of 3-CMC was “especially serious” or “substantial” (Fig. A8).

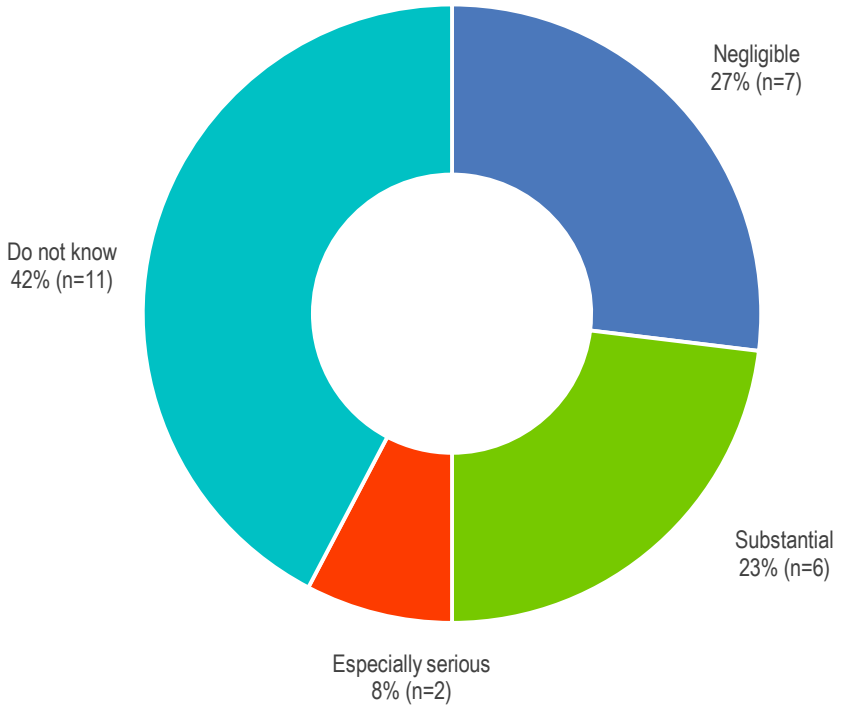

Fig. A8. Negative health impacts of non-medical consumption of 3-CMC

Emergency department visits

Five countries in the European Region were aware of emergency department visits related to 3-CMC. One country described 3-CMC as the only substance involved in five presentations in 2023, 12 presentations in 2022, 1 presentation in 2021 and 2 presentations in 2019. Two countries reported presentations for 3-CMC and other substances involved, comprising 12 presentations in 2023, 31 presentations in 2022, 4 presentations in 2021, 1 presentation in 2020 and 1 in 2019. One country reported the number of presentations in which it was not known whether 3-CMC was involved: 53 presentations in 2023, 53 presentations in 2022, 16 presentations in 2021 and 37 presentations between 2015 and 2018.

A wide range of adverse effects was described in non-fatal intoxications for which patients presented to an emergency department after use of 3-CMC. They included headache, dizziness, confusion, both hypertension and hypotension, agitation, tachycardia, hallucinations, psychosis, anxiety, vomiting, unconsciousness, nausea and chest pain. Other adverse effects were palpitations, hyperthermia, mydriasis, cramp, restlessness, cold sweats, itching, discomfort in breathing, feeling strange, redness, swelling, numbness in arm, anaphylactic reaction, difficulty in waking up, hyperventilation, slurred speech, elevated transaminases, haematuria, shaking, tired, restless leg syndrome, eye tics, hypokalaemia, burning in the throat, tongue, lips, intoxication, weight loss, dyskinesia, mydriasis and coma. The presentations included intentional poisonings and those in which 3-CMC dependence was involved.

Deaths

One country in the European Region reported three 3-CMC-related deaths in which it was the only substance involved. Two countries reported 2 deaths in which 3-CMC and other substances were involved in 2023. Two countries reported 13 deaths between 2023 and 2021 in which it was not known whether other substances were involved and 2 further deaths for which the year was not specified.

Drug dependence

Two countries in the European Region reported that people presented for treatment of drug dependence in their country associated with use of 3-CMC. One country reported that increased numbers had been reported in their local news media.

Extent and magnitude of public health problems or social harm

One country in the European Region reported public health problems or social harm due to use of 3-CMC, as reported in news media, increased numbers of seizures and calls to poison information centres, cases of driving under the influence of drugs, two deaths, minor drug offences and detection at drug treatment clinics.

One country reported that 3-CMC was used in the context of sexual activity (chemsex, mainly via injection), sometimes with very high consumption over several days and with other stimulating substances. The administration routes reported include nasal, oral and injection and also the rectal route with a pump (without needle). Risk was associated with intravenous injection, repeated consumption over short periods and combining use with other stimulants. An increase in the occurrence of serious cases was reported since 2019 in one country in the European Region, where increased presentations related to addiction or dependence were noted.

Current national controls

Sixteen countries (15 in the European and 1 in the Western Pacific regions) responded that 3-CMC was currently regulated under substance-specific legislation. Seven countries (4 in the European, 2 in the Western Pacific and 1 in the Americas regions) responded that the availability of 3-CMC was currently regulated under analogue or generic legislation. Four countries (3 in the European and 1 in the Americas regions) responded that 3-CMC was not controlled under any legislation.

Illicit manufacture and trafficking-related information

Table A15 shows the main reported activities involving 3-CMC.

Table A15. Reported activities involving 3-CMC for purposes other than medical, scientific or industrial use

Activity	No. of countries
Smuggling (from other countries)	7
Internet sales (from abroad to buyers in respondent's country)	7
Internet sales (other or location of sellers and website unknown)	7
Trafficking	6
Internet sales (seller or website located in respondent's country)	3
Direct sale	3
Manufacture of the substance by chemical synthesis	1
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Diversion	0
Do not know	9
Other[a]	1

[a] Includes street dealing and dealing via social media

Detection in falsified medicines

No countries reported that 3-CMC had been detected in falsified medicines.

Seizures

Six countries in the European Region reported seizures in 2023 involving 3-CMC. The number of seizures ranged from 3 to 689, and the amounts seized ranged from 2.16 to 150 kg (Table A16).

Fourteen countries (12 in the European and 2 in the Western Pacific regions) reported seizures in 2022 involving 3-CMC. The number of seizures ranged from 1 to 1017, and the amounts seized ranged from 0.1 g to 192 kg. One country reported that several tonnes of 3-CMC were seized in 2022.

Eight countries (7 in the European and 1 in the Americas regions) reported seizures in 2021 involving 3-CMC. The number of seizures ranged from 1 to 479 and the amounts seized from 28.8 g to 115 kg. One country specified that several tonnes of 3-CMC were seized in 2021.

Table A16. Reported seizures of 3-CMC

Year	No. of countries that reported seizures	No. of seizures
2023	6	1088
2022	13	1362
2021	7	514

Laboratory capacity

Twenty-six countries (22 in the European, 2 in the Western Pacific and 2 in the Americas regions) reported that they had the laboratory capacity to analyse 3-CMC.

Dipentylone

Of the 58 countries that agreed to provide data, 28 had information on dipentylone (Table A17).

Table A17. Numbers of countries that provided information on dipentylone

Region	No. of countries with no information	No. of countries with information
African	5	1
Americas	6	3
South-East Asia	2	1
European	10	19
Eastern Mediterranean	4	0
Western Pacific	2	4
Total	29	28

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for dipentylone, and none reported that dipentylone was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard). None reported use for industrial purposes.

Epidemiology of non-medical use

Nineteen countries (11 in the European, 3 in the Americas, 4 in the Western Pacific and 1 in the South-East Asia regions) reported evidence of use of dipentylone for non-medical purposes (outside the medical, industrial or scientific context). The evidence was derived from data on seizures for law enforcement (n=14), customs (n=7), drug checking or harm reduction services (n=5), post-mortem reports (n=3), toxicology reports from emergency departments (n=1), poisons information calls (n=1), drug treatment centres (n=1) and reports from police or service users (n=1).

Routes of administration and formulations

The most common reported route of administration was oral, followed by sniffing and smoking (Table A18).

Table A18. Reported routes of dipentylone administration

Route of administration	No. of countries
Oral	9
Sniffing	3
Smoking	2
Inhalation	0
Injection	0
Other	0

Do not know	15

The most common formulations of dipentylone reported were as a powder and as a tablet (Fig. A9).

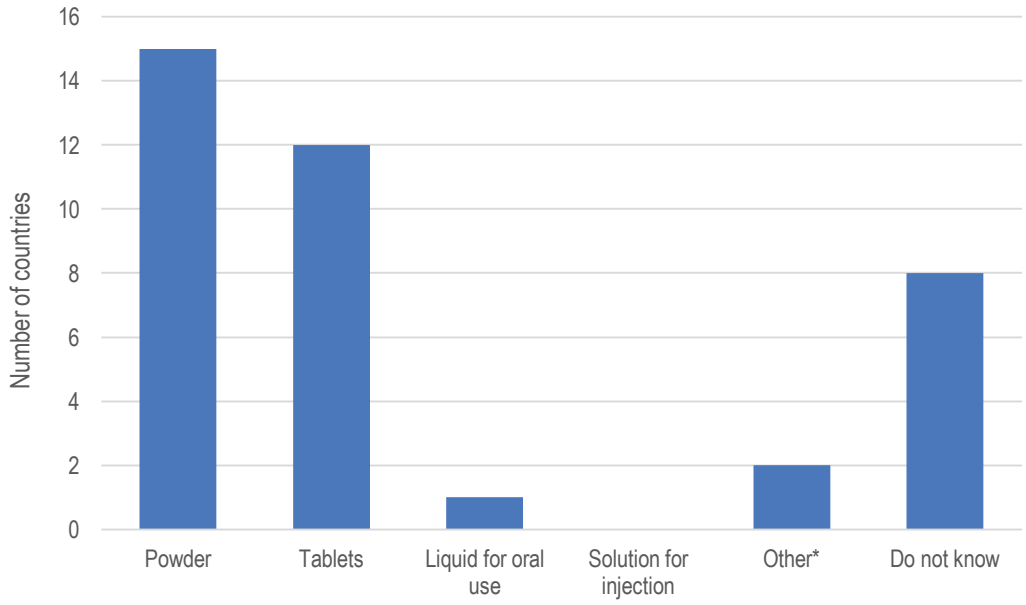

Fig. A9. Formulations of dipentylone

[a] Other formulations referred to were crystals or pieces.

Perceived negative health impact

Five countries (2 in the Americas and 1 each in the European, South-East Asia and Western Pacific regions) reported that the negative health impact of non-medical consumption of dipentylone was "especially serious" or "substantial" (Fig. A10).

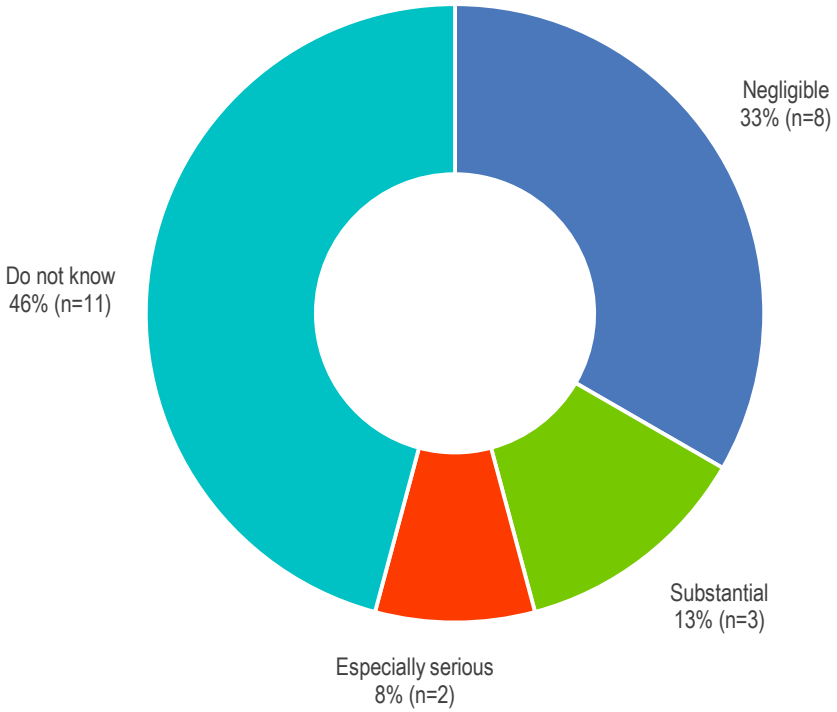

Fig. A10. Negative health impacts of non-medical consumption of dipentylone

Emergency department visits

Two countries in the European Region were aware of emergency department visits related to dipentylone. One country described an emergency visit in 2023 in which other substances were involved. Another country described one emergency visit in which other substances were involved, but the year was not given.

The reported adverse effects (e.g. non-fatal intoxications) in patients who presented to emergency departments after use of dipentylone include agitation, tachycardia and falls.

Deaths

Two countries (1 in the Americas and 1 in the Western Pacific regions) reported a total of 11 deaths involving dipentylone between 2023 and 2022. One country in the Americas region reported 1 dipentylone-related death in 2023 in which no other substance was involved; 8 deaths in which dipentylone and other substances were involved were reported in 2023. One country in the Western Pacific Region reported 2 deaths involving dipentylone in 2022 in which other substances were involved.

Drug dependence

No country reported that people had presented for treatment of drug dependence in their country due to use of dipentylone.

Extent and magnitude of public health problems or social harm

Five countries (3 in the European, 1 in the South-East Asia and 1 in the Western Pacific regions) reported on public health problems associated with dipentylone. Four countries (2 in the European, 1 in the South-East Asia and 1 in the Western Pacific regions) reported that dipentylone had been detected in seizures identified in laboratories or at drug checking sites. One country reported that dipentylone was not a drug of choice and sometimes occurred as an adulterant in other stimulants in 2022.

Current national controls

Nine countries (5 in the European, 3 in the Western Pacific and 1 in the Americas regions) reported that dipentylone was controlled under analogue or generic legislation. Nine countries (7 in the European, 1 the Americas and 1 the South-East Asia regions) reported that dipentylone was controlled under substance-specific legislation. Nine countries (in the 6 European, 2 in the Western Pacific and 1 in the Americas regions) reported that dipentylone was not controlled under any legislation.

Illicit manufacture and trafficking-related information

Table A19 shows the main reported activities involving dipentylone.

Table A19. Reported activities involving dipentylone for purposes other than medical, scientific or industrial use

Activity	No. of countries
Trafficking	5
Internet sales (other or location of sellers and website unknown)	6
Internet sales (from abroad to buyers in respondent's country)	3
Smuggling (from other countries)	3
Internet sales (seller or website located in respondent's country)	1
Manufacture of the substance by chemical synthesis	1
Direct sales	0
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Diversion	0
Do not know	13
Other	0

Detection in falsified medicines

No country reported that dipentylone had been detected in falsified medicines. One country

(Americas) reported that dipentylone had been sold as “tusi” and in the form of ecstasy-type tablets.

Seizures

Nine countries (5 in the European, 2 in the Western Pacific, 1 in the Americas and 1 in the South-East Asia regions) reported seizures in 2023. The number of seizures per country ranged from 1 to 2591, and the amounts seized ranged from 0.12 g to 33 kg (Table A20). In addition, one country (South-East Asia) reported that 3200 tablets were seized in 2023. Eleven countries (7 in the European, 2 in the Western Pacific, 1 in the South-East Asia and 1 in the Americas regions) reported seizures in 2022. The number of seizures per country ranged from 1 to 5381 and the amounts seized from 2.9 g to 73.8 kg. In addition, one country (South-East Asia) reported that 393 tablets containing dipentylone were seized in 2022. Two countries (1 in the Americas and 1 in the Western Pacific regions) reported seizures in 2021. The number of seizures ranged from 2 to 396, and the total amount seized was 3347 g.

Table A20. Reported seizures of dipentylone

Year	No. of countries that reported seizures	No. of seizures
2023	8	2687
2022	11	5461
2021	2	398

Laboratory capacity

Twenty-five countries (16 in the European, 5 in the Western Pacific, 3 in the Americas 1 in the South-East Asia regions) reported that they had the laboratory capacity to analyse dipentylone.

2-Fluorodeschloroketamine

Of the 70 countries that agreed to provide data, 28 provided information on 2-fluorodeschloroketamine (Table A21).

Table A21. Numbers of countries that provided information on 2-fluorodeschloroketamine

Region	No. of countries with no information	No. of countries with information
African	6	1
Americas	6	3
South-East Asia	2	1
European	11	18
Eastern Mediterranean	4	0
Western Pacific	1	5
Total	30	28

Approved medical, scientific or industrial use

No countries reported approved therapeutic indications for 2-fluorodeschloroketamine, and none reported that 2-fluorodeschloroketamine was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard). None reported use for industrial purposes.

Epidemiology of non-medical use

Twenty countries (13 in the European, 1 in the South-East Asian, 2 in the Americas and 4 in the Western Pacific regions) reported evidence of the use of 2-fluorodeschloroketamine for non-medical purposes (outside the medical, industrial or scientific context). The evidence was derived primarily from data on seizures by law enforcement (n=14) and customs (n=10). Toxicology reports from post-mortems (n=8) and from emergency departments (n=3), poisons information calls (n=1), drug checking (n=4), driving under the influence of drugs (n=1), drug monitoring centres (n=1), drug testing programmes (n=1), an online survey of new psychoactive substances (n=1) and lists of dark web cryptomarkets that deliver to the country (n=1).

Routes of administration and formulations

The most common reported route of administration was oral, followed by sniffing and injection (Table A22).

Table A22. Reported routes of 2-fluorodeschloroketamine administration

Route of administration	No. of countries
Smoking	0
Oral	10
Inhalation	0

Sniffing	7
Injection	2
Other[a]	1
Do not know	13

[a] Rectal

The most common known formulations of 2-fluorodeschloroketamine reported were a powder, tablets and a crystalline substance (Fig. A11).

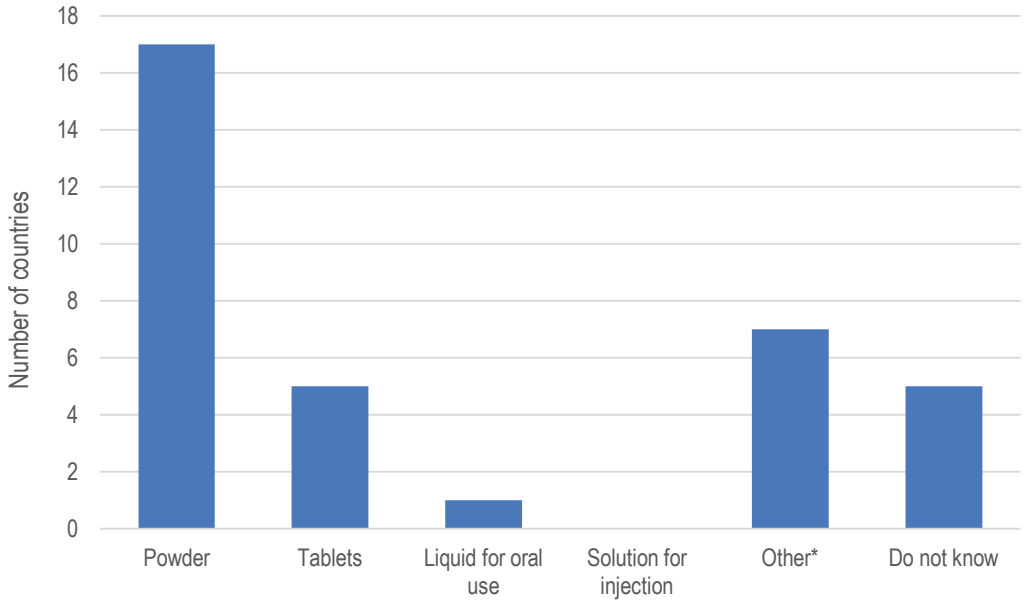

Fig. A11. Formulations of 2-fluorodeschloroketamine

[a] Other formulations most commonly referred to were crystalline substance (n=5), chocolate (n=1) and spray (n=1).

Perceived negative health impact

Eight countries (4 in the European, 2 in the Western Pacific, 1 in the Americas and 1 the South-East Asia regions) reported that the negative health impact of non-medical consumption of 2-fluorodeschloroketamine was “especially serious” or “substantial” (Fig. A12).

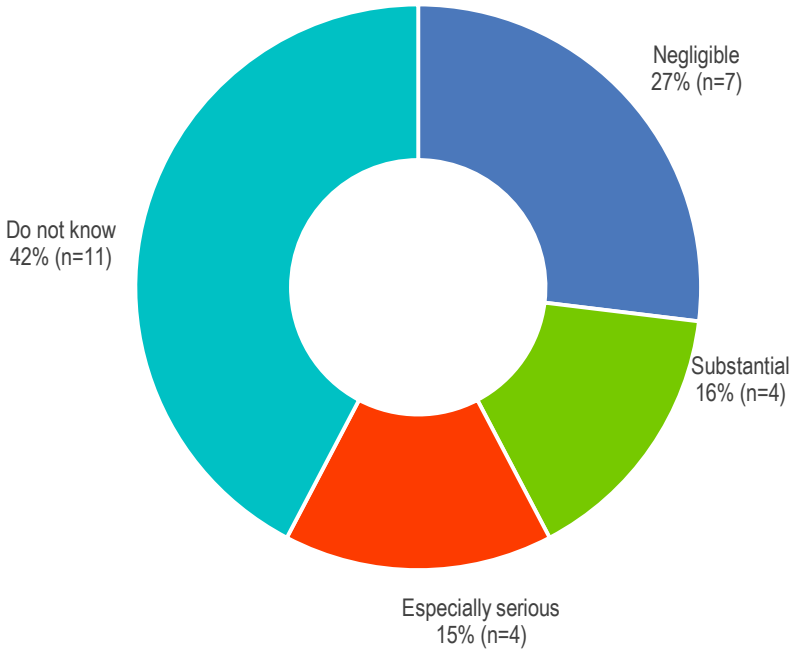

Fig. A12. Negative health impacts of non-medical consumption of 2-fluorodeschloroketamine

Emergency department visits

Four countries (3 in the European and 1 in the Americas regions) were aware of emergency department visits related to 2-fluorodeschloroketamine. One country in the European Region reported the occurrence of dizziness, confusion, agitation, anxiety and memory loss.

Three emergency presentations involved 2-fluorodeschloroketamine alone between 2021 and 2022, and 15 emergency presentations involving people who had consumed 2-fluorodeschloroketamine with other substances between 2021 and 2023. One country in the European Region reported that it was not known whether other substances were involved.

One country in the Americas described effects such as unconsciousness after 2-fluorodeschloroketamine was taken with other substances.

Deaths

At least 6 deaths were related to 2-fluorodeschloroketamine. Two countries (1 in the European and 1 in the Americas regions) reported three 2-fluorodeschloroketamine-related deaths between 2021 and 2022 in which other substances were involved. One country in the European Region reported deaths in which other substances were involved but did not specify the number of deaths. Three countries in the European Region also reported three deaths related to 2-fluorodeschloroketamine before 2021 in which other substances were involved.

Drug dependence

Two countries (1 in the European and 1 in the Western Pacific regions) reported that people presented for treatment of drug dependence in their country due to use of 2-fluorodeschloroketamine.

Current national controls

Eight countries (6 in the European, 1 in the Western Pacific and 1 in the South-East Asia regions) responded that the availability of 2-fluorodeschloroketamine was currently regulated under substance-specific legislation, and nine countries (4 in the European, 4 in the Western Pacific and 1 in the Americas regions) reported 2 -fluorodeschloroketamine was controlled under analogue or generic legislation.

Illicit manufacture and trafficking-related information

Table A23 shows the main reported activities involving 2-fluorodeschloroketamine.

Table A23. Reported activities involving 2-fluorodeschloroketamine for purposes other than medical, scientific or industrial use

Activity	No. of countries
Smuggling (from other countries)	3
Trafficking	8
Internet sales (from abroad to buyers in respondent's country)	6
Internet sales (other or location of sellers and website unknown)	9
Internet sales (seller or website located in respondent's country)	2
Manufacture of the substance by chemical synthesis	1
Direct sales	2
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Diversion	0
Do not know	8
Other	0

Detection in falsified medicines

No country reported that 2-fluorodeschloroketamine was detected in falsified medicines.

Seizures

Six countries (5 in the European and 1 in the Western Pacific regions) reported seizures in 2023. The number of seizures per country ranged from 1 to 8 and the amounts seized from 2 to 441 g (Table A24). Fourteen countries (11 in the European, 2 in the Western Pacific and 1 in the Americas regions) reported seizures in 2022. The number of seizures per country ranged from 1 to 26 and the amounts seized from 0.01 to 1354.55 g. Ten countries (7 in the European, 2 in the Western Pacific and 1 in the Americas regions) reported seizures in 2021. The number of seizures per country ranged from 1 to 54 and the amounts seized from 0.08 to 1503 g. One country (Western Pacific) reported seizures (number of seizures and year not specified). One country (European) reported 99 seizures pre 2021.

Table A24. Reported seizures of 2-fluorodeschloroketamine[a]

Year	No. of countries that reported seizures	No. of seizures

2023	6	29
2022	14	92
2021	10	126

[a] Data up to August 2023.

Laboratory capacity

Twenty-five countries (16 in the European, 5 in the Western Pacific, 3 in the Americas and 1 in the South-East Asia regions) reported that they had the laboratory capacity to analyse 2-fluorodeschloroketamine.

Nitrous oxide

Of the 70 countries that agreed to provide data, 38 provided information on nitrous oxide (Table A25).

Table A25. Numbers of countries that provided information on nitrous oxide

Region	No. of countries with no information	No. of countries with information
African	5	2
Americas	5	4
South-East Asia	2	1
European	5	23
Eastern Mediterranean	1	3
Western Pacific	1	5
Total	18	38

Approved medical, scientific or industrial use

Thirty countries reported approved therapeutic indications for nitrous oxide. Ten countries reported that nitrous oxide was currently used in medical or scientific research, such as in clinical trials for any human or veterinary indication (except as an analytical standard). Twenty countries reported use for industrial purposes.

Epidemiology of non-medical use

Twenty-six countries (18 European, 3 in the Western Pacific, 2 in the Americas, 1 in the African, 1 in the Eastern Mediterranean and 1 in the South-East Asian regions) reported evidence of use of nitrous oxide for non-medical purposes (outside the medical, industrial or scientific context). The evidence was derived primarily from data on seizures by law enforcement (n=13) and customs (suggesting detection at international border points; n=3), toxicology reports after deaths (n=1), toxicology reports from emergency departments (n=6) and poisons information calls (n=8). Additional sources of evidence included surveys (n=3), a variety of reports (n=4), drug treatment service data (n=1), media (n=1), drug monitoring centres (n=1), sales data (n=1) and reports of discarded portable cylinders (n=1).

Routes of administration and formulations

The most common reported route of administration was inhalation, followed by sniffing (Table A26).

Table A26. Reported routes of nitrous oxide administration

Route of administration	No. of countries
Smoking	0
Oral	0
Inhalation	26
Sniffing	3
Injection	0

Other	0
Do not know	8

The most common known formulations of nitrous oxide reported were a gas and as part of a liquid or solution for oral administration (Fig. A13).

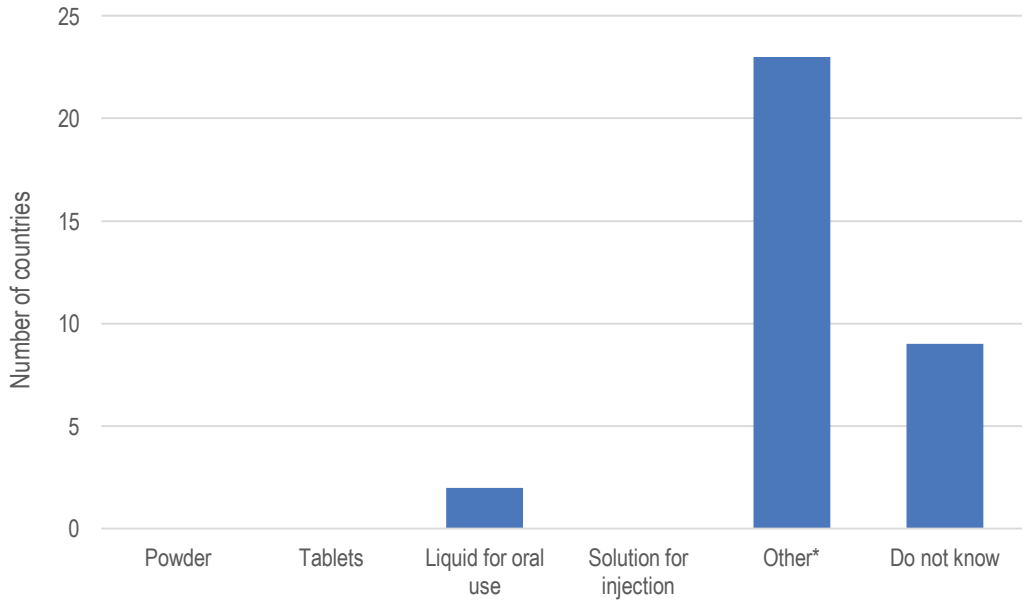

Fig. A13. Formulations of nitrous oxide

[a] The other formulation most commonly referred to was gas.

Perceived negative health impact

Fifteen countries (10 in the European, 2 in the Western Pacific, 1 in the Americas, 1 in the African and 1 in the Eastern Mediterranean regions) reported that the negative health impact of non-medical consumption of nitrous oxide was “especially serious” or “substantial” (Fig. A14).

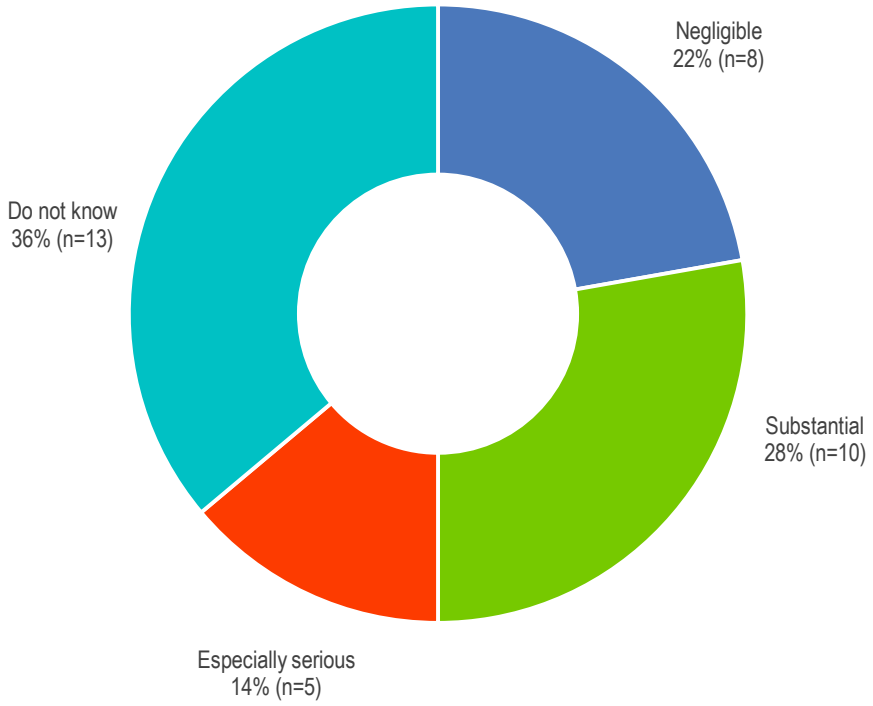

Fig. A14. Negative health impacts of non-medical consumption of nitrous oxide

Emergency department visits

Fourteen countries (8 in the European, 3 in the Western Pacific, 2 in the Americas and 1 in the African regions) were aware of emergency department visits related to nitrous oxide. Four countries (3 in the European and 1 in the Americas) reported emergency presentations by people who had consumed nitrous oxide with other substances.

Six countries (5 in the European and 1 in the Western Pacific regions) reported the occurrence of headache, and seven (5 in the European, 1 in the Americas and 1 in the Western Pacific regions) described effects such as dizziness and confusion. Unconsciousness was reported by ten countries (6 in the European, 2 in the Western Pacific, 1 in the African and 1 in the Americas regions). Various cardiovascular effects were reported, including hypertension (1 in the Americas and 1 in the European regions), hypotension (1 in the European Region), tachycardia (2 in the European and 1 in the Western Pacific regions), bradycardia (1 in the European Region) and chest pain (2 in the European and 1 in the Western Pacific regions). Gastrointestinal effects included nausea (3 in the European and 1 in the Western Pacific regions) and vomiting (2 in the European Region). Other effects included agitation (3 in the European and 1 in the Americas regions), hallucinations (4 in the European and 1 in the Western Pacific regions), psychosis (4 in the European, 1 in the Americas and 1 in the Western Pacific regions), anxiety (3 in the European Region), depression (1 in the European Region), sweating (1 in the European Region) and memory loss (2 in the European and 1 in the Western Pacific regions) in emergency department patients.

Deaths

One country in the European Region reported 9 deaths related only to nitrous oxide between 2021 and 2022. Two countries in the European Region reported three deaths in 2021 and seven deaths in 2022 in which another substance was also involved. One country in the European Region reported 1 nitrous oxide-related death in which another substance was involved in 2023. Two countries in the European Region also reported three deaths related to nitrous oxide before 2021 in which other substances were involved.

Drug dependence

Six countries (4 in the European, 1 in the Eastern Mediterranean and 1 in the Western Pacific regions) reported that people presented for treatment of drug dependence due to use of nitrous oxide.

Current national controls

Thirteen countries (8 in the European, 4 in the Western Pacific and 1 in the Eastern Mediterranean regions) responded that the availability of nitrous oxide was currently regulated under substance-specific legislation, and five countries (2 in the European, 1 in the Eastern Mediterranean, 1 in the South-East Asian and 1 in the African regions) reported that nitrous oxide was controlled under analogue or generic legislation.

Illicit manufacture and trafficking-related information

Table A27 shows the main reported activities involving nitrous oxide.

Table A27. Reported activities involving nitrous oxide for purposes other than medical, scientific or industrial use

Activity	No. of countries
Smuggling (from other countries)	1
Trafficking	7
Internet sales (from abroad to buyers in respondent's country)	6
Internet sales (other or location of sellers and website unknown)	6
Internet sales (seller or website located in respondent's country)	8
Manufacture of the substance by chemical synthesis	0
Direct sales	9
Production of consumer products containing the substance	3
Manufacture of the substance by extraction from other products	0
Diversion	4
Do not know	16
Other[a]	1

[a] Includes Internet sale.

Detection in falsified medicines

No country reported that nitrous oxide was detected in falsified medicines.

Seizures

Four countries (2 in the European, 1 in the Americas and 1 in the Western Pacific regions) reported seizures in 2023. The number of seizures per country ranged from 2 to 17. Although the amounts seized were reported in various units, they included large quantities, such as 1900 kg in one country (European) and 23315 ampoules and balloons in another (European) (Table A28). Seven countries (5 in the European, 1 in the Americas and 1 in the Western Pacific regions) reported seizures in 2022. The number of seizures per country ranged from 1 to 1155. The amounts seized were reported in various units. One country reported seizure of 8640 cylinders, another country reported 7 kg, and a third country reported 11 252 L (European). Six countries (4 in the European, 1 in the Americas and 1 in the Western Pacific regions) reported seizures in 2021. The number of seizures ranged from 1 to 1005, and the amounts seized were 300 and 400 capsules and bottles and 9791 L in another country.

Table A28. Reported seizures of nitrous oxide

Year	No. of countries that reported seizures	No. of seizures
2023	4	28
2022	7	1214
2021	6	1141

Laboratory capacity

Twenty-two countries (17 in the European, 3 in the Western Pacific, 1 in the South-East Asia and 1 in the Eastern Mediterranean regions) reported that they had the laboratory capacity to analyse samples for nitrous oxide.

Carisoprodol

Of the 58 countries that agreed to provide data, 22 provided information on carisoprodol (Table A29).

Table A29. Numbers of countries that provided information on carisoprodol

Region	No. of countries with no information	No. of countries with information
African	5	2
Americas	4	4
South-East Asia	1	2
European	21	7
Eastern Mediterranean	3	2
Western Pacific	1	5
Total	35	22

Approved medical, scientific or industrial use

Eight countries (3 in the Americas, 2 in the Eastern Mediterranean, 1 in the African and 1 in the Western Pacific regions) reported approved human therapeutic indications for carisoprodol. One country in the Americas reported approved veterinary therapeutic indications for the drug.

Seven countries (3 in the Americas, 2 in the Eastern Mediterranean, 1 in the African and 1 in the Western Pacific regions) reported that carisoprodol is used as an analgesic or muscle relaxant. Two countries (1 in the Americas and 1 in the South-East Asia regions) reported that carisoprodol had been used as a registered medicine but that it was no longer approved.

Epidemiology of non-medical use

Eight countries (2 in the Americas, 2 in the Eastern Mediterranean, 2 in the European, 1 in the South-East Asia and 1 in the Western Pacific regions) reported use of carisoprodol for non-medical purposes (outside the medical, industrial or scientific context). The evidence was derived primarily from data on seizures by law enforcement (n=6) and customs authorities (n=3), post-mortem reports (n=3), emergency departments (n=2), poisons information calls (n=2), clinical and medical data (n=2) and dark web cryptomarkets for sale (n=1).

Routes of administration and formulations

The most common reported route of administration was oral (Table A30).

Table A30. Reported routes of carisoprodol administration

Route of administration	No. of countries
Oral	9
Smoking	0

Inhalation	0
Sniffing	0
Injection	0
Other	0
Do not know	5

The most common known formulation of carisoprodol reported was a tablet (Fig. A15).

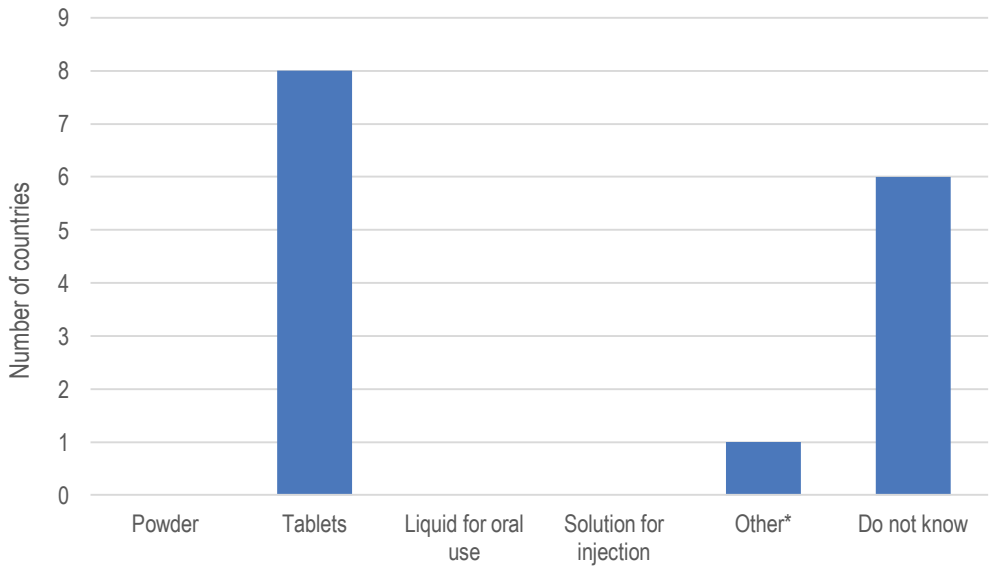

Fig. A15. Formulations of carisoprodol

[a] Another formulation referred to was a "whitish substance".

Perceived negative health impact

Five countries (1 in the African, 1 in the South-East Asia, 1 in the European, 1 in the Eastern Mediterranean and 1 in the Western Pacific regions) reported that the negative health impact of non-medical consumption of carisoprodol was "especially serious" or "substantial" (Fig. A16).

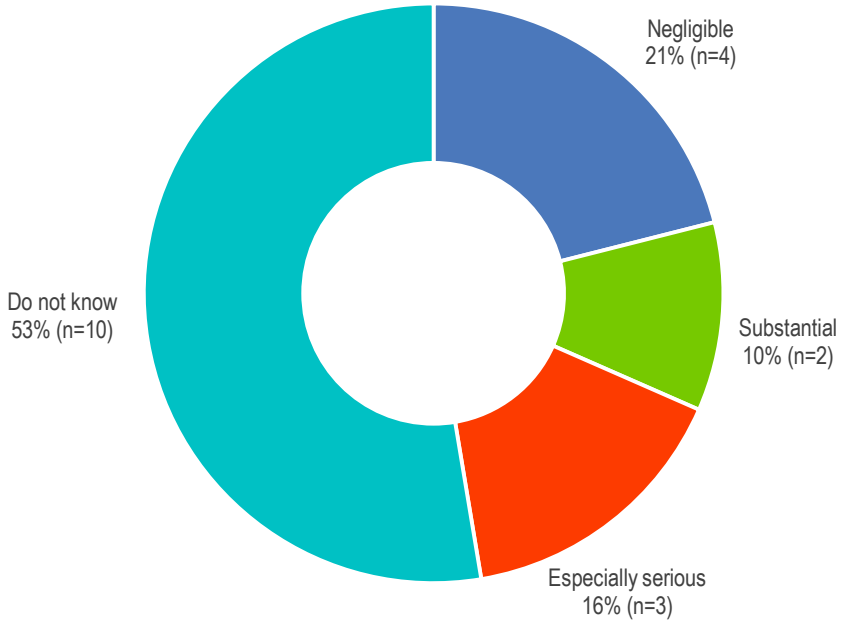

Fig. A16. Negative health impacts of non-medical consumption of carisoprodol

Emergency department visits

Three countries (1 in the Americas, 1 in the South-East Asia and 1 in the European regions) were aware of emergency department visits related to carisoprodol. One country in the South-East Asia Region reported 14 emergency presentations in 2022 in which carisoprodol was the only substance involved. The country also reported five emergency presentations in 2023 in which carisoprodol and other substances were detected.

One country in the European Region reported 1 emergency presentation in 2023, 6 emergency presentations in 2022 and 2 emergency presentations in 2021 involving carisoprodol. It was not known whether other substances were involved.

One country in the Americas reported a single emergency presentation but did not specify the year.

The adverse effects (such as non-fatal intoxications) of patients who presented to emergency departments after use of carisoprodol included headache, dizziness, confusion, hypotension, tachycardia, unconsciousness, nausea, seizures, limb paralysis, clonic movements, stupor, coma and respiratory depression.

Deaths

One country in the European Region reported two carisoprodol-related deaths in which other substances were involved in 2023. Two other countries (in the African and South-East Asia regions) noted that deaths had been reported but did not specify a number. One of the deaths occurred in 2017; the date of the other death was not specified.

Drug dependence

Three countries (1 in the Americas, 1 in the South-East Asia and 1 in the Eastern Mediterranean

regions) reported that people presented for treatment of drug dependence in their country due to use of carisoprodol. One country in the South-East Asia Region reported that specific treatment for carisoprodol was required after an assessment, which included a community intervention and outpatient and inpatient care.

Extent and magnitude of public health problems or social harm

Three countries reported public health problems linked to carisoprodol use. One country in the European Region reported two deaths linked to carisoprodol use. One country in the South-East Asia Region reported that carisoprodol was misused, usually for analgesia or relaxation. One country in the Eastern Mediterranean Region reported addiction to carisoprodol.

Current national controls

Fourteen countries (5 in the Western Pacific, 4 in the European, 2 in the South-East Asia, 2 in the Eastern Mediterranean and 1 in the Americas regions) reported that carisoprodol was currently controlled under substance-specific legislation. One country in the African Region responded that carisoprodol was currently controlled under analogue or generic legislation. Five countries (3 in the European and 2 in the Americas regions) reported that carisoprodol was not controlled under any legislation.

Illicit manufacture and trafficking-related information

Table A31 shows the main reported activities involving carisoprodol.

Table A31. Reported activities involving carisoprodol for purposes other than medical, scientific or industrial use

Activity	No. of countries
Trafficking	4
Smuggling (from other countries)	3
Internet sales (other or location of sellers and website unknown)	3
Internet sales (from abroad to buyers in respondent's country)	1
Diversion	1
Internet sales (seller or website located in respondent's country)	0
Manufacture of the substance by chemical synthesis	0
Production of consumer products containing the substance	0
Manufacture of the substance by extraction from other products	0
Direct sales	1
Do not know	9
Other	0

Detection in falsified medicines

Three countries (2 in the Western Pacific and 1 in the Americas regions) reported that carisoprodol had been detected in falsified medicines. One country in the Western Pacific Region reported that illegal tablets that were seized were labelled "carisoprodol tablets", and carisoprodol was also detected in unlabelled tablets and cough syrups. The country in the Americas Region reported that carisoprodol had been falsely sold as alprazolam tablets.

Seizures

Four countries (1 in the Americas, 1 in the South-East Asia, 1 in the European and 1 in the Western Pacific regions) reported seizures in 2023. The number of seizures per country ranged from 1 to 92, and the amounts seized were 1.9 kg, 5000 units, 8015 tablets and 12 617 tablets (Table A32). Five countries (2 in the Western Pacific, 1 in the Eastern Mediterranean, 1 in the Americas and 1 in the European regions) reported seizures in 2022. The number of seizures per country ranged from 1 to 404, and the amounts seized ranged from 20 to 28 323 tablets, with one total seizure of 58 kg. Four countries (2 in the Western Pacific, 1 in the Americas and 1 in the European regions) reported seizures in 2021. The number of seizures per country ranged from 1 to 608 and the amounts seized from 3.5 to 46 kg and 1333 to 9176 tablets.

Table A32. Reported seizures of carisoprodol

Year	No. of countries that reported seizures	No. of seizures
2023	4	95
2022	5	405
2021	4	610

Laboratory capacity

Fifteen countries (6 in the European, 3 in the Americas, 3 in the Western Pacific, 2 in the South-East Asia and 1 in the Eastern Mediterranean regions) reported that they had the laboratory capacity to analyse carisoprodol.