World Health Organization

Critical Review Report: 3-FLUOROPHENMETRAZINE

Expert Committee on Drug Dependence

Forty-third Meeting

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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

Executive summary

The patent describing the synthesis of 3-fluorophenmetrazine (3-FPM) was first filed in 2011 *(1)* and it was identified as a new psychoactive substance in the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) Early Warning System in 2014 *(2)*. It was purportedly identified in the illegal drug market for the first time in 2014 in Hungary, Sweden and the United Kingdom, and in 2015 in Croatia, the Czech Republic, Denmark, France, Germany, Lithuania, Norway, Romania, Slovenia and Spain *(3)*. It is structurally similar to phenmetrazine (trade name Preludin), a stimulant that was used in Europe in the 1950s as an anorectic agent until it was withdrawn from the market because of its high abuse potential *(4)*.

3-FPM is a fully efficacious releaser at monoamine transporters (MAT) where it acts as a substrate rather than a blocker. It is potent at releasing dopamine (DA) and norepinephrine (NE), with half maximal effective concentration (EC_{50}) values of 43 and 30 nM, respectively, and less potent at releasing serotonin (5-hydroxytryptamine (5-HT); 2558 nM *(1)*). These data are consistent with the activity of the parent compound, phenmetrazine *(5)*. The activity of 3-FPM is therefore more similar to amphetamine-like "releasers" than to cocaine-like "blockers" *(6)*.

Few fatalities have been attributed to 3-FPM although several case reports from around the world have identified the substance in human blood and urine samples. It appears to be used most often in combination with other psychoactive substances, the most common being benzodiazepines. It currently has no legitimate medical or veterinary uses and is only available commercially for research and industrial purposes.

1. Substance identification

A. International Nonproprietary Name (INN)

3-fluorophenmetrazine

B. Chemical Abstract Service (CAS) Registry Number

1350768-28-3

1803562-83-5 (HCl salt)

C. Other chemical names

2-(3-fluorophenyl)-3-methylmorpholine

2-(3-fluoro-phenyl)-3-methyl-morpholine

morpholine, 2-(3-fluorophenyl)-3-methyl-

D. Trade names

3-fluorophenmetrazine

PAL-593 or PAL593

1350768-28-3

UNII-BEV6RF569G

BEV6RF569G

SCHEMBL2599533

BCP18587

NS00017993

Q20707008

Z2379802370

E. Street names

3-FPM or 3-Fpm

3-FPH

PAL-593 or PAL593

F. Physical appearance

3-Fluorophenmetrazine is a white, solid, crystalline powder. It was also identified in yellow, blue or green pellets (tablets).

G. WHO review history

3-Fluorophenmetrazine has not previously been reviewed by the WHO Expert Committee on Drug Dependence.

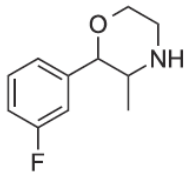
2. Chemistry

A. Chemical name

IUPAC name: 2-(3-fluorophenyl)-3-methylmorpholine; hydrochloride

CA Index Name: Not found

B. Chemical structure



3-Fluorophenmetrazine
(3-FPM)

Molecular formula: $C_{11}H_{14}FNO$

Molecular weight: 195.23 g/mol

C. Stereoisomers

3-FPM is a derivative of phenmetrazine. As described by McLaughlin and colleagues *(7)*, "the fluorinated analogs of phenmetrazine contain two chiral centers which yield the potential for four stereoisomers and two racemic mixtures (i.e., *cis*- and *trans*-racemates)" (See Fig. 1 in McLaughlin et al).

D. Methods and ease of illicit manufacturing

As described by McLaughlin and colleagues *(7)*, "The synthesis employed for preparations of 2-, 3- and 4-FPM was adapted from Blough et al (1). The synthesis involved bromination of the fluoropropiophenone starting material (a), yielding α-bromo-fluoropropiophenone (b). This was reacted with ethanolamine to give the intermediate 1-(3-flurophenyl)-2-((2-hydroxyethyl)amino)propan-1-one (c). Reduction to the alcohol (d) was achieved by reaction with sodium borohydride followed by reaction with concentrated sulfuric acid to aid cyclization and formation of the morpholine ring (e)" (See Fig. 2 in McLaughlin et al).

E. Chemical properties

Boiling point
280.6 °C ± 35.0 °C at 760 mmHg

(Obtained from an online chemical structure database *(8)*.)

F. Identification and analysis

A number of analytical tests have been used to differentiate 3-FPM from its positional isomers, 2- and 4-FPM, including gas chromatography-mass spectrometry, liquid chromatography-mass spectrometry, and thin-layer chromatography *(7).* All of the methods successfully differentiated 3-FPM from its

isomers. X-ray crystallography further revealed that the 3-FPM cation existed in the chair conformation, which is consistent with the conformation of phenmetrazine hydrochloride.

3. Ease of convertibility into controlled substances

No reports of conversion of 3-fluorophenmetrazine into other controlled substances were found.

4. General pharmacology

A. Routes of administration and dosage

Information from drug user forums indicates that 3-FPM is used orally and by insufflation *(9, 10)*. Oral doses purportedly range between 10 mg and 90 mg or more, with common doses being 30–60 mg and strong doses 60–90 mg. Insufflated doses range between 5 mg and 50 mg or more, with common doses being 20–35 mg and strong doses being 35–50 mg. The oral route of administration is reportedly preferred by some users because insufflation of the powder produces a burning sensation *(3)*.

Intravenous use and smoking of 3-FPM have also been reported but the amounts used by these routes were not specified *(3, 11).*

B. Pharmacokinetics

One study described both the in vivo metabolism of 3-FPM in rats and humans and in vitro metabolism of 3-FPM in wastewater and wastewater-isolated *Pseudomonas Putida (12)*. In humans, most of the 3-FPM was excreted unchanged and in the *N*-oxide form in urine. In rat urine, aryl hydroxylated metabolites were found, with CYP2A6, CYP2B6 and CYP3A4 being the main CYP isoenzymes involved. The authors concluded that "urinary excretion is assumed to be the main route of excretion for 3-FPM" *(12).*

Information from drug user forums indicates that the duration of action of 3-FPM is 4–8 hours when used orally with an onset of action between 20 and 40 minutes *(9, 10)*. When used via insufflation, the duration of action of 3-FPM is 3–6 hours with an onset of action within 5 minutes.

C. Pharmacodynamics

3-FPM is potent at releasing dopamine (DA) and norepinephrine (NE), with half maximal effective concentration (EC_{50}) values of 43 and 30 nM, respectively, and less potent at releasing serotonin (5-HT; 2558 nM *(1)*). In monoamine release assays using rat brain homogenates, 3-FPM was 100%, 95%, and 93% effective at DA, 5-HT and NE receptors, respectively, with little activity at 5-HT_{2B} receptors *(1)*.

Radiotracer uptake experiments in human embryonic kidney (HEK293) cells demonstrated that 3-FPM potently inhibited transporter-mediated uptake of dopamine (DAT) and norepinephrine (NET) but its potency was much lower for inhibiting uptake of serotonin (SERT *(13)*). The DAT/SERT and NET/SERT ratios

progressively decreased whereas the DAT/NET ratio stayed relatively constant as the fluorine moved from position 2-, to 3- to 4-.

Rat brain synaptosome assays further revealed that 3-FPM is a fully efficacious releaser at monoamine transporters (MAT) where it acts as a substrate rather than a blocker and, consistent with the data collected in HEK293 cells, is equipotent at DAT and NET and less potent at SERT *(13)*. These data are consistent with the activity of the parent compound, phenmetrazine *(14)*. The activity of 3-FPM is therefore more similar to amphetamine-like "releasers" than to cocaine-like "blockers" *(6)*.

5. Toxicology

No formal toxicology studies have been performed with 3-FPM.

6. Adverse reactions in humans

No controlled clinical studies have been conducted with 3-FPM. Adverse reactions to 3-FPM are expected to be similar to those associated with phenmetrazine, however, because they have similar chemical structures and mechanisms of action. Some case reports describing adverse reactions associated with 3-FPM are available.

A 2016 report from Poland describes the presence of 3-FPM in the blood of a 20-year-old man who was involved in a motor vehicle accident *(3)*. Twenty-four bags of white powder, which he admitted to using the previous evening, were found in his possession. No other drugs were detected in his blood and no symptoms were reported on the blood collection form other than a suspicion that he was under the influence of psychotropic drugs. In the introduction to the paper, the authors describe short-acting psychoactive effects of 3-FPM that result in "repetition of doses" that can occur over hours or days, with a rapid development of tolerance to its effects. Adverse reactions reportedly include anxiety and sweating, as well as jaw clenching and bruxism while positive effects include "euphoria, stimulation, empathy, increased libido, improvement of concentration and mood, increase of motivation and energy, talkativeness, insomnia and a different perception of music" *(3).* During the "comedown" period after the drug effects have dissipated, the authors describe a series of unpleasant reactions including "anxiety, fatigue, depression and irritability" which "appear 9–72 h after the last dose and may persist for up to a week" *(3).* Benzodiazepines purportedly are taken by users to treat these symptoms. How this information was obtained, however, is not clearly described in the paper.

A 2016 report from Sweden using data from the STRIDA project describes a case-series involving 3-FPM *(11).* Between November 2014 and October 2015, eight consultations at the Poison Information Center were recorded as involving 3-FPM or "phenmetrazine" intoxications. Of the seven blood and/or urine samples collected from these individuals, six were positive for 3-FPM and none for phenmetrazine. Thirteen additional cases were identified through the STRIDA project. Blood samples were obtained from the 19 total cases, and additional urine samples from 14 of these cases. 3-FPM was identified in 15 of the 19 blood samples and in all 14 urine samples. Other psychoactive substances were present in all of these samples, including central nervous system depressants, stimulants and dissociatives, with the most common co-occurring substances being benzodiazepines.

Symptoms commonly associated with the acute polysubstance intoxications involving 3-FPM include tachycardia, reduced level of consciousness, agitation/anxiety and delirium, and less common symptoms include miosis, seizures and hypertension *(11)*; all of the individuals survived the intoxication.

A 2017 report from Poland described one confirmed fatality associated with 3-FPM *(15)*. Both 3-FPM (9 ng/ml) and *N*-ethylhexedrone (37 ng/ml) were measured in the blood of a 27-year-old man who died following a motor vehicle accident, but whether and/or how 3-FPM contributed to the death is unclear. The article did not specify the country in which the motor vehicle accident occurred or when the blood was collected.

A 2017 paper from the United Kingdom described the clinical course of a 52-year-old man who reportedly injected 3-FPM intravenously *(16)*. The patient denied recent use of any other non-prescription drugs but blood or urine drug tests for 3-FPM or any other substances were not described. Symptoms were characterized as follows: "On the same day, after injecting the drug he started to develop flu-like symptoms feeling feverish with general malaise and tachycardia. Over the next 2 days the symptoms worsened, he started to develop symptoms of shortness of breath, a productive cough of white sputum, central chest pain, fever with rigors and multiple episodes of diarrhea and vomiting. He also complained of cold lower limbs with reduced sensation in both legs". He developed widespread livedo reticularis and acute kidney injury. All four limbs became ischaemic and he ultimately required amputation of both legs below the knees.

A 2017 report from the USA described the case of a 34-year-old man who had apparently had a fatal overdose. He was found dead with hypodermic needles and a plastic bag labelled "5582 mg 3-FPM" nearby *(17)*. Postmortem samples of body fluids, including blood and urine, revealed the presence of 3-FPM, U-47700, amitriptyline, nortriptyline, diazepam, nordiazepam, temazepam, delorazepam, flubromazolam and amphetamine. The cause and manner of death were characterized as "multiple drug-toxicity; accident" *(17)*.

A 2018 report from Canada described the clinical course of an unresponsive 33-year-old man who presented at an emergency room *(18)*. Family members found him in his bedroom after an hour of "yelling and thrashing". Empty packages labelled "etizolam 50 mg" and "3-FPM 500 mg" were found on the floor next to him. "A rapid 7-drug urine drug screen was positive for benzodiazepines and indeterminate for amphetamines" *(18)*. During intensive care monitoring on the first day after admission to hospital, abnormal four-limb movements were observed, even after propofol infusion. These abated, however, after administration of lorazepam. Naloxone was ineffective in altering any of these responses. A fever of 38.9 °C was recorded on day 1 after admission and, on day 5, new but asymptomatic widespread T-wave inversions were noted on the electrocardiogram. All symptoms ultimately resolved before he was discharged on day 7.

7. Dependence potential

A. Animal studies

No preclinical studies of the dependence potential of 3-FPM in animals were found in the published scientific literature.

B. Human studies

No clinical studies of the dependence potential of 3-FPM in humans were found in the published scientific literature.

8. Abuse potential

A. Animal studies

No preclinical studies of the abuse potential of 3-FPM in animals were found in the published scientific literature.

B. Human studies

No studies of the clinical abuse potential of 3-FPM in humans were found in the published scientific literature.

9. Therapeutic applications and extent of therapeutic use and epidemiology of medical use

3-FPM is not approved for therapeutic use in any country.

10. Listing on the WHO Model List of Essential Medicines

3-FPM is not included in the WHO Model List of Essential Medicines.

11. Marketing authorizations (as a medicinal product)

3-FPM is not approved as a medicinal product in any country.

12. Industrial use

3-FPM is available for use in research and for industrial purposes.

13. Nonmedical use, abuse and dependence

Information obtained from drug user forums described 3-FPM as being “habit forming”, “causing psychological dependence”, and “tolerance…with prolonged and repeated use” *(9, 19)*. but the magnitude of misuse and abuse of 3-FPM is unknown. Given the structural similarity between 3-FPM and phenmetrazine, as well as its pharmacology, it is expected that 3-FPM has high potential for nonmedical use.

The Welsh Emerging Drugs and Identification of Novel Substances Project reported on 30 samples that were either intended to be purchased as 3-FPM and/or positively identified as 3-FPM *(20)*.

14. Nature and magnitude of public health problems related to misuse, abuse and dependence

Only one study reported the confirmed presence of 3-FPM alone *(3)* in an individual who was suspected of being under the influence of psychoactive drugs, so the nature and magnitude of public health problems related to misuse of 3-FPM is unclear.

15. Licit production, consumption and international trade

3-FPM does not appear to have a licit medicinal or veterinary use in any country.

16. Illicit manufacture and traffic and related information

No information was found about the illicit manufacture and trafficking of 3-FPM.

17. Current international controls and their impact

3-FPM has not been subject to international control under the 1971 United Nations Convention on Psychotropic Substances or the 1961 Single Convention on Narcotic Drugs.

18. Current and past national controls

As described on a drug user website *(9)*, 3-FPM is controlled in several countries, including the following:

"Germany: 3-FPM is controlled under the NpSG (New Psychoactive Substances Act)[6] as of November 26, 2016.[7] Production and import with the aim to place it on the market, administration to another person and trading is punishable. Possession is illegal but not penalized.[8]

Israel: 3-FPM is illegal to buy, sell or possess in Israel as of 2017.[9]

Sweden: The public health agency suggested the classification of the drug as an illegal narcotic on June 1, 2015.[10]

Switzerland: 3-FPM was added to the list of controlled substances in December 2015.[11]

United Kingdom: 3-FPM is illegal to produce, supply or import under the Psychoactive Substance Act, which came into effect on May 26th, 2016.[12]

United States: 3-FPM may be considered to be an analogue of phenmetrazine, a Schedule II drug[13], under the Federal Analogue Act if it is intended for human consumption.[14]"[1]

In the USA, 3-FPM is not explicitly controlled at the national level but it was designated as a Schedule 1 controlled substance in Virginia on 16 November 2016, which was to be effective until 10 May 2018. During the 2019 legislative session, the Virginia state legislature was set to vote on a bill that would permanently schedule 3-fluorophenmetrazine as a Schedule 1 substance, but it is unclear whether that occurred.

[1] Citations from quote in Section 18. Current and past national controls:

6. "Anlage NpSG" (in German). Bundesministerium der Justiz und für Verbraucherschutz. Retrieved December 19, 2019.
7. "Gesetz zur Bekämpfung der Verbreitung neuer psychoaktiver Stoffe" (PDF) (in German). Bundesanzeiger Verlag. Retrieved December 19, 2019.
8. "§ 4 NpSG" (in German). Bundesministerium der Justiz und für Verbraucherschutz. Retrieved December 19, 2019.
9. https://www.nevo.co.il/law_html/Law01/P170_001.htm
10. http://www.folkhalsomyndigheten.se/nyheter-och-press/nyhetsarkiv/2015/juni/23-nya-amnen-kan-klassas-som-narkotika-eller-halsofarlig-vara
11. "Verordnung des EDI über die Verzeichnisse der Betäubungsmittel, psychotropen Stoffe, Vorläuferstoffe und Hilfschemikalien" (in German). Bundeskanzlei [Federal Chancellery of Switzerland]. Retrieved January 1, 2020.
12. Psychoactive Substances Act 2016 (Legislation.gov.uk) | http://www.legislation.gov.uk/ukpga/2016/2/contents/enacted
13. https://www.deadiversion.usdoj.gov/schedules/orangebook/c_cs_alpha.pdf
14. https://www.law.cornell.edu/uscode/text/21/813

19. Other medical and scientific matters relevant for a recommendation on the scheduling of the substance

None.

References

1. Blough BE, Rothman R, Landavazo A, Page KM, Decker AM. Phenylmorpholines and analogues thereof. Patent No. WO20111 46850 A1, Research Triangle Institute; 2011.

2. European Monitoring Centre for Drugs and Drug Addiction EMCDDA–Europol 2014 Annual Report on the implementation of Council Decision 2005/387/JHA, Implementation reports. Luxembourg: Publications Office of the European Union; 2015.

3. Adamowicz P, Gieroń J. 3-Fluorophenmetrazine - a new psychoactive substance on the Polish drug market. Probl Forensic Sci. 2016;105:418–27.

4. Beharry S, Gibbons S. An overview of emerging and new psychoactive substances in the United Kingdom. Forensic Sci Int. 2016;267:25–34.

5. Sitte HH, Freissmuth M. Amphetamines, new psychoactive drugs and the monoamine transporter cycle. Trends in Pharmacol Sci. 2015;36:41–50.

6. McLaughlin G, Morris N, Kavanagh PV, Dowling G, Power JD, Twamley B, et al. Test purchase, synthesis and characterization of 3-fluorophenmetrazine (3-FPM) and differentiation from its ortho- and Para-substituted isomers. Drug Test Anal. 2017;9:369–77. https://doi.org/10.1002/dta.1945

7. Chemspider [online chemical structure database]. (http://www.chemspider.com/Chemical-Structure.37509994.html?rid=a106afd4-a0e6-4a5f-bfff-7adf632524c5, accessed 21 July 2020).

8. Psychonautwiki [online drug user forum]. (https://psychonautwiki.org/wiki/3-FPM; accessed 4 September 2020).

9. TripSit [drug-related harm reduction network] (http://drugs.tripsit.me/3-fpm, accessed 20 July 2020).

10. Bäckberg M, Westerbergh J, Beck O, Helander A. Adverse events related to the new psychoactive substance 3-fluorophenmetrazine - results from the Swedish STRIDA project. Clin Toxicol. 2016;54: 819–25. https://doi.org/10.1080/15563650.2016.1211288

11. Mardal M, Miserez B, Bade R, Portolés T, Bischoff M, Hernández F, et al. 3-Fluorophenmetrazine, a fluorinated analogue of phenmetrazine: studies on in vivo metabolism in rat and human, in vitro metabolism in human CYP isoenzymes and microbial biotransformation in Pseudomonas putida and wastewater using GC and LC coupled to (HR)-MS techniques. J Pharm Biomed Anal. 2016;128:485–95. https://doi.org/10.1016/j.jpba.2016.06.011

12. Mayer FP, Burchardt NV, Decker AM, et al. Fluorinated phenmetrazine "legal highs" act as substrates for high-affinity monoamine transporters of the SLC6 family. Neuropharmacology. 2018;134(Pt A):149-157. https://doi.org/10.1016/j.neuropharm.2017.10.006

13. Rothman RB, Katsnelson M, Vu N, Partilla JS, Dersch CM, Blough BE, et al. Interaction of the anorectic medication, phendimetrazine, and its metabolites with monoamine transporters in rat brain. Eur. J. Pharmacol. 2002;447, 51e57.

14. Mikołajczyk A, Adamowicz P, Tokarczyk B, Sekuła K, Gieroń J, Wrzesień W, Stanaszek R. Determination of N-ethylhexedrone, a new cathinone derivative, in blood collected from drivers – analysis of three cases. Prob Forensic Sci. 2017;109:53-63.

15. Fawzy M, Wong-Morrow WS, Beaumont A, et al. Acute kidney injury and critical limb ischaemia associated with the use of the so called "legal high" 3-fluorophenmetrazine. CEN Case Rep. 2017;6:152–5.

16. Ellefsen KN, Taylor EA, Simmons P, Willoughby V, Hall BJ. Multiple drug-toxicity involving novel psychoactive substances, 3-Fluorophenmetrazine and U-47700. J Anal Toxicol. 2017;41(9): 765–70. https://doi.org/10.1093/jat/bkx060

17. Benesch MGK, Iqbal SJ. Novel psychoactive substances: overdose of 3-fluorophenmetrazine (3-FPM) and etilozam in a 33-year-old man. BMJ Case Rep 2018. doi:10.1136/bcr-2018-224995

18. Erowid [online drug user forum] (https://www.erowid.org/experiences/exp.php?ID=112907, accessed 4 September 2020).

19. Welsh Emerging Drugs and Identification of Novel Substances Project [online publication of drug contents of samples submitted anonymously] (https://wedinos.org/db/samples/search/page:1, accessed on 4 September 2020).

Annex 1. Report on WHO Questionnaires for Review of Psychoactive Substances for the 43rd ECDD: evaluation of 3-FLUOROPHENMETRAZINE (3-FPM)

Data were obtained from 105 Member States (19 African Region, 13 Eastern Mediterranean Region, 40 European Region, 16 Region of the Americas, seven South-East Asia Region and 10 Western Pacific Region) for the WHO Questionnaires for the Review of Psychoactive Substances. The total number of countries opting out of participation in the questionnaire is 13 (three African Region, two Eastern Mediterranean Region, two European Region, three Region of the Americas, one South-East Asia Region and two Western Pacific Region), leaving 92 active countries. Of these, 31 countries had information on the substance (Table 1).).

Table 1. Number of countries providing information on 3-FLUOROPHENMETRAZINE (3-FPM)

Region	Number of countries without information	Number of countries with information on substance
Africa Region	15	1
Eastern Mediterranean Region	7	4
European Region	21	17
Region of the Americas	10	3
South-East Asia Region	5	1
Western Pacific Region	3	5
Total 92	**61**	**31**

LEGITIMATE USE

One country (South-East Asia Region) reported approved human medical products or veterinary products containing 3-FLUOROPHENMETRAZINE (3-FPM).

One country (Region of the Americas) reported 3-FLUOROPHENMETRAZINE (3-FPM) being currently used in medical or scientific research (excluding use as an analytical reference standard), specifically in cell line studies (binding/functional assays) and animal studies.

One country (Region of the Americas) reported 3-FLUOROPHENMETRAZINE (3-FPM) being used in industrial or other non-medical or non-scientific use.

No countries reported approved therapeutic indications for 3-FLUOROPHENMETRAZINE (3-FPM).

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

Thirteen countries reported that 3-FLUOROPHENMETRAZINE (3-FPM) is being misused or abused for its psychoactive properties/recreational use.

The most common known route of administration reported was oral (Table 2).

Table 2. Common routes of administration

Route of administration	Number of countries
Oral	9
Injection	0
Inhalation	0
Sniffing	4
Smoking	4
Don't know	15

The most common known formulation of 3-FLUOROPHENMETRAZINE (3-FPM) reported was powder (Table 3).

Table 3. Common formulations reported by countries

Formulation	Number of countries
Powder	12
Tablets	4
Liquid for oral use	0
Solution for injection	0
Don't know	14

To the above, countries added:

- "trips, capsule"
- "herbal mixture".

Eight countries reported the level of negative health-impact due to 3-FLUOROPHENMETRAZINE (3-FPM)'s non-medical consumption as "serious" or "substantial" (Table 4).

Table 4. Level of negative health-impact

Serious	Substantial	Negligible	Don't know
4	4	10	11

One country (European Region) commented, "… there may be unknown cases of negative health impacts because … there is no reporting obligation by hospitals, poison centers, etc.". Another country (Region of the Americas) wrote, "3-FPM was involved in a multiple drug-toxicity fatal overdose (Ellefsen et al., 2017, J Anal Tox 41: 765)".

Three countries (three European Region) reported emergency room admissions related to the non-medical use of 3-FLUOROPHENMETRAZINE (3-FPM).

Concerning adverse effects one country (European Region) noted, "visual, auditory, coloured and moving hallucinations, respiratory distress, strong anxiety, dyspnoea, cyanosis of extremities, scalp pain, absence, paranoia". Another country (European Region) noted, "hallucinate quite strongly, did not sleep, relatively high heart rate".

No countries reported users of 3-FLUOROPHENMETRAZINE (3-FPM) presenting for drug dependence treatment.

Regarding mortality, only one country (Region of the Americas) reported deaths involving 3-FLUOROPHENMETRAZINE (3-FPM):

- one fatal case where other substances were also involved (2017).

STATUS OF NATIONAL CONTROL AND POTENTIAL IMPACT OF INTERNATIONAL CONTROL

Nine countries (seven European Region, two Western Pacific Region) responded that 3-FLUOROPHENMETRAZINE (3-FPM) is currently controlled under national legislation to regulate its availability.

Table 5 shows the main reported activities involving 3-FLUOROPHENMETRAZINE (3-FPM).

Table 5. Reported illicit activities involving 3-FLUOROPHENMETRAZINE (3-FPM)

Activities	Number of countries
Smuggling from other countries	4
Manufacture of substance by chemical synthesis	1
Manufacture of substance by extraction from other products	0
Production of consumer products containing the substance	0
Trafficking	6
Diversion from legal supply chain	0
Internet sales – seller or website located in country	1
Internet sales – from abroad to buyers in country	2
Internet sales – other, or location of sellers and website unknown	4
Direct sales to people who use the substance	0
Don't know	16

To the above, countries added:

- "trafficking through postal services"
- "Internet sales without other information".

Six countries (three European Region, one Region of the Americas, two Western Pacific Region) reported seizures (Table 6).

Table 6. Reported seizures of 3-FLUOROPHENMETRAZINE (3-FPM)

Year	Seizures
2020	21
2019	58
2018	103
Total	**182**

Twenty-two countries have the forensic laboratory capacity to analyse 3-FLUOROPHENMETRAZINE (3-FPM).

One country (European Region) commented, "Forensic laboratories have the capacity to analyse 3-FPM if reference material is available".