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From:	EMCDDA
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Subject:	Risk assessment report on a new psychoactive substance: *N*-phenyl-*N*-[1-(2-phenylethyl)piperidin-4-yl]-furan-2-carboxamide (furanylfentanyl)

Following the Council's request to conduct a Risk Assessment on a new psychoactive substance, Risk assessment report on a new psychoactive substance: *N*-phenyl-*N*-[1-(2-phenylethyl)piperidin-4-yl]-furan-2-carboxamide (furanylfentanyl), the EMCDDA hereby presents the above-mentioned Risk Assessment Report drawn up by its Scientific Committee pursuant to Article 6 of Council Decision 2005/387/JHA on information exchange, risk assessment and control of new psychoactive substances.

European Monitoring Centre
for Drugs and Drug Addiction

Risk assessment report on a new psychoactive substance:
***N*-phenyl-*N*-[1-(2-phenylethyl)piperidin-4-yl]furan-2-carboxamide (furanylfentanyl)**

In accordance with Article 6 of Council Decision 2005/387/JHA on the information exchange, risk assessment and control of new psychoactive substances

Contents

Furanylfentanyl is known from the scientific literature. Fentanyl is a fast but short-acting synthetic opioid that has been widely used in clinical practice including as an adjunct to general anaesthesia during surgery and for postoperative pain management. Furanylfentanyl is also structurally related to acetylfentanyl and acryloylfentanyl (Figure 1), both of which were the subject of an EMCDDA–Europol Joint Report in December 2015 and December 2016 following more than 30 deaths and more than 40 deaths, respectively.

Pharmacologically, furanylfentanyl is an opioid receptor agonist.

(5) Note that although 'furanylfentanyl' can refer to 2- and to 3-furanylfentanyl, in this report it will reference the 2- isomer

formulations, such as liquids for injection, tablets, transdermal patches, lozenges and nasal sprays. Some are also used in veterinary medicine as general anaesthetics, for pain management, and, in the case of carfentanil and thiafentanil, to immobilise large animals.

Fentanyl analogues first emerged on the illicit drug market in the United States of America in 1979. At the time they were not controlled under drug legislation. They were manufactured in clandestine laboratories and sold on the heroin market as heroin or 'synthetic heroin'.

A total of fifteen fentanils are controlled under the United Nations Single Convention on Narcotic Drugs, 1961, as amended by the 1972 Protocol.

The major pharmacological effects of the fentanils, including their analgesic activity, are due to their activation of opioid receptors, and, in particular, the μ-opioid receptor. Besides their analgesic properties, a notable feature associated with μ-opioid receptor agonists is that they cause dose-dependent respiratory depression, in which overdose can be life-threatening. Other additional pharmacological effects include miosis, sedation, bradycardia, hypothermia, constipation, physical dependence, and changes in mood such as euphoria.

Furanylfentanyl as free base or as its hydrochloride salt may occur as solids. There is no solubility data on furanylfentanyl or its hydrochloride salt; however due to its close similarity to fentanyl, the free base is expected to be poorly soluble in water and highly lipophilic.

In the acute intoxications suspected to involve furanylfentanyl that were reported to the EMCDDA, the routes of administration were: nasally (using a nasal spray), by intramuscular injection, snorted as a powder, inhaled or administered orally.

In the deaths associated with furanylfentanyl, the routes of administration included intravenous injection, snorting, and mixed routes of oral and injection.

From the limited data available it is not possible to discern the 'typical' dosages administered by users. While a range of doses have been reported, these appear to differ depending on factors such as the route of administration, the tolerance of the users, the use of other drugs, and the desired effects.

Analysis of the concentration of nasal spray solutions of furanylfentanyl seized in Finland found that they contain between 1.1 and 3.2 mg/ml of the substance.

Doses reported on user websites range from 0.3 to 1.6 mg (oral administration) and from 0.2 to 0.8 mg and above (insufflation). The assessment of such reports is problematic not least because the purity, amount and/or composition of the substance ingested are typically not

7

metabolites. Due to its lipophilicity, furanylfentanyl, like fentanyl, is expected to readily cross the blood-brain barrier and also diffuse into fat and other tissues and is thus likely to have a large volume of distribution.

The pharmacokinetics and the metabolic pathway of furanylfentanyl are expected to share some similarities with other fentanils. As such, furanylfentanyl could be predicted to undergo metabolism by hepatic CYP450 isoenzymes, including CYP2C19, CYP2D6, CYP3A4, and CYP3A5.

A recent study using human post-mortem urine samples suggested the identification of nine metabolites including 4-ANPP. While 4-ANPP might also be present as a synthesis by-product, this substance does exert some biological activity, although at several orders of magnitude lower than morphine. Further studies are required to assess the metabolism of furanylfentanyl and whether the other metabolites exert biological activity of pharmacological and toxicological relevance.

8

including the use of other CNS depressants such as benzodiazepines, pregabalin, gabapentin and ethanol.

The use of fentanyl with serotonergic agents, such as selective serotonin re-uptake inhibitors (SSRIs) (the most commonly prescribed antidepressants) or serotonin norepinephrine re-uptake inhibitors (SNRIs) or monoamine oxidase inhibitors (MAOIs) has been associated with serotonin syndrome, a potentially life-threatening condition. This association is likely to extend to illicit drugs which act on the serotonergic system. It is not known if this association is also seen with furanylfentanyl.

Similar to fentanyl, the use of partial opioid agonists/antagonists (such as buprenorphine, nalbuphine, pentazocine) which have high affinity to opioid receptors but relatively low intrinsic activity could partially antagonise the effects of furanylfentanyl and may induce withdrawal symptoms in people who are opioid dependent. It is unknown if such effects are possibly protective in individuals poisoned with furanylfentanyl or other fentanils.

carboxylic acid, which would be consistent with hydrolysed reagents used in the acylation step. In addition, two countries reported powdered samples containing 'synthesis by-products' although these were not specified.

The manufacture of furanylfentanyl most likely relies on precursors and synthetic methods similar to those used for the manufacture of pharmaceutical fentanyl. Accordingly, methods developed for the synthesis of fentanyl are applicable to furanylfentanyl. Most of these are straightforward, make use of common laboratory equipment and precursors, and require only basic knowledge of chemistry. A one-step method uses 4-ANPP and furanoyl chloride for the manufacture of the substance. Use of a different acylating agent in the first acylation step could provide other fentanils.

Two potential precursors of fentanyl and other fentanils, *N*-phenyl-1-(2-phenylethyl)piperidin-4-amine (4-ANPP) as well as *N*-phenethyl-4-piperidone (NPP, a pre-precursor), have been recently scheduled ([5]).

([5]) Table I of the United Nations Convention against Traffic in Narcotic Drugs and Psychotropic Substances, 1988

medicines (such as nasal decongestants) with fentanils. The lack of labelling increases the potential for accidental use by others and therefore poses a serious risk of poisoning.

Furanylfentanyl may be used in combination with other drugs (intentionally or unintentionally).

Limited data from seizures and collected samples have shown that furanylfentanyl has been detected in mixtures containing other opioids such as heroin, U-47,700, fentanyl, 2-fluorofentanyl, 4-fluorobutyrylfentanyl and carfentanil; as well as cocaine, caffeine, paracetamol, and sugars/sugar alcohols (lactose, mannitol, inositol). The overall significance of these seizures is unclear; however, the identification of carfentanil is of serious concern given its potency. In addition, the identification of heroin and fentanyl in the seizures suggests that furanylfentanyl is being supplied through the illicit heroin/opioid market.

Acute toxicity

No studies were identified that have investigated the acute effects of furanylfentanyl and/or its metabolites in animal or humans. For fentanyl the estimated lethal dose in humans could be as low as 2 mg by intravenous injection.

11

In 2 cases it was reported that the patient recovered; in the remaining 9 cases the outcome was unknown.

Reported clinical features included: miosis, unconsciousness, and respiratory depression; however, the lack of analytically confirmed drugs in the majority of cases hinders the interpretation of this as other drugs may have caused or contributed to the features observed. Nevertheless, such clinical features would be consistent with poisoning from an opioid, including fentanils.

Recently, a group of cocaine users in Canada were treated for opioid overdose symptoms in a hospital emergency department after they had smoked what they believed to have been crack cocaine. Analysis of samples of the drug used by the patients identified furanylfentanyl and cocaine in a mixture. Of particular note is that community members, first responders, and emergency department staff reported that patients required high doses of naloxone, in some cases up to 3.0 mg.

depressants and antipsychotics. In 11 cases, furanylfentanyl was the sole opioid present. In the remaining 12 cases, other opioids detected were: fentanyl (6 deaths), acetylfentanyl (2), buprenorphine (2), tilidine (2), methadone (1), 4-chloroisobutyrylfentanyl (1), and tramadol (1).

No information was available regarding symptoms experienced by the decedents prior to death.

Sufficient data was available in 19 of the 23 deaths to allow an analysis to evaluate the toxicological significance of furanylfentanyl. Of these, furanylfentanyl was either the cause of death or is likely to have contributed to death (even in presence of other substances) in 17 cases. Whilst other drugs may have contributed some toxicity, a synergistic and/or additive effect with furanylfentanyl would have been likely (e.g. other central nervous system depressants such as ethanol, benzodiazepines, other opioids, etc.). Nevertheless, the pharmacological opioid nature of furanylfentanyl means the primary toxic contribution could be attributed to the drug and death may not have occurred if furanylfentanyl had not been used. In 2 cases, furanylfentanyl may have contributed to toxicity/death but other drugs were present that may be also toxicologically significant and contributed. Overall, there is no defined 'fatal' concentration that can be assigned to furanylfentanyl but in 17 cases where measured, post-mortem blood concentrations between 0.2 to 1.54 µg/L and between 0.33 to 2.74 mg/g blood were recorded (the latter somewhat but not exactly equivalent to µg/L).

13

furanylfentanyl. Given what is currently known about the pharmacology of furanylfentanyl, including some similarities to other fentanils and opioid narcotic analgesics, it is reasonable to assume that the substance has both a potential for abuse and dependence. Further research will be required in order to determine such effects.

Public health risks

The public health risks associated with furanylfentanyl may be categorised in terms of patterns of use (extent, frequency, route of administration, etc.); availability and quality of the drug; information, availability and levels of knowledge amongst users; and, negative health consequences. Detailed information, including data on sporadic versus chronic use, that allow for a determination of public health risks associated with furanylfentanyl are not available. In addition, risk of accidental exposure needs to be considered.

Extent, frequency, and patterns of use

There are no prevalence data on the use of furanylfentanyl in the European Union or elsewhere, but the available information does not suggest wide use of the substance.

14

Furanylfentanyl was typically offered in powder form and listed as a 'research chemical, not fit for human consumption'. The amounts offered ranged from 1 g (EUR 54) up to 5 kg (corresponding to EUR 5.9 per 1 g).

One site offered furanylfentanyl as a ready-to-use nasal spray and also liquid intended for vaping in electronic cigarettes. This site also offered furanylfentanyl in powder form mixed with either mannitol (ratio of 1:10) or caffeine (ratio of 1:25).

Furanylfentanyl has also been sold on darknet marketplaces.

Characteristics and behaviour of users

No studies were identified that have examined the characteristics and behaviours of users of furanylfentanyl. Nonetheless, information from police seizures as well as investigations into deaths indicates that furanylfentanyl is available to and being used by high-risk drug users, including opioid users. The available information, including from user websites, suggests that some may use furanylfentanyl as a substitute for illicit opioids and prescription opioids; this includes for self-medication, such as the alleviation of pain and/or opioid withdrawal. Finally, some users (such as psychonauts) may be experimenting with this opioid.

15

respiratory arrest, and death. This risk may be exacerbated given the difficulty of diluting fentanils; the lack of experience of users with this new substance (in terms of a lack of familiarity with how to use it, the effects and dose of the substance); the concomitant use of other CNS depressants (such as other opioids, benzodiazepines, gabapentinoids, and ethanol); in some cases no apparent tolerance to opioids; and, the environment in which the substance is used — typically in the home environment.

In the past few years, new dosage forms — such as ready-to-use nasal sprays, homemade transdermal patches and e-liquids for vaping — along with open sales on the surface web and darknet marketplaces add to the complexity of the problem caused by the fentanils. They have become easier to get hold of and easier to use. The Committee is concerned about whether the availability of 'novel' dosage forms has the potential to make the use of fentanils more socially acceptable.

An additional challenge in respect to reducing risk in users and potential users, is the balance between providing information to prevent harm and the unintended consequences of communicating the risks of opioids. There is evidence that using terms to describe them as 'potent', 'strong', 'deadly', and 'toxic' can lead some individuals to specifically seek out these

commonly used opioid analgesics and benzodiazepines), cocaine, and other illicit drugs. As users will be unaware of this, it increases the risk of severe and fatal poisoning in both opioid users and especially other groups who may have no existing tolerance to opioids. Non-opioid users are unlikely to be aware of these risks and are unlikely to have access to community opioid overdose prevention programmes, including take-home naloxone programmes.

Long-term consequences of use

There is no information on the long-term consequences of use of furanylfentanyl.

Conditions under which the substance is obtained and used

There is limited information on the conditions which furanylfentanyl is obtained and used. It appears furanylfentanyl has been sold on the surface web and darknet marketplaces, typically as powders but also as ready-to-use nasal sprays. A small number of e-liquids for use in electronic cigarettes have also been reported.

There is no information on the possible effects of furanylfentanyl on the direct social environment; however, they may have some similarities with those associated with the use of illicit opioids.

Possible effects on society as a whole (public order and safety, acquisitive crime)

There is no specific information on the possible effects of furanylfentanyl on society as a whole.

As discussed above, accidental exposure of furanylfentanyl and other fentanils — such as skin contact, inhalation, or ingestion — also poses a risk of poisoning to those who may come into contact with the substances. This includes the family and friends of users, law enforcement, emergency personnel, medical and forensic laboratory personnel as well as custodial settings and postal services. Where required, these risks should be assessed and appropriate procedures, training, and protective measures should be implemented. This may include training in resuscitation and adequate provision of naloxone to reverse poisoning.

14

Information from seizures in four Member States that were reported to Europol shows that some furanylfentanyl on the market in Europe has been produced by chemical companies based in China.

In addition to importation, the seizure of an illicit laboratory in Europe in 2013 that was producing fentanils, that may have included furanylfentanyl, suggests that the production in Europe cannot be excluded. This recent case demonstrates the capability to manufacture fentanils exists within the European Union.

In 7 seizures made by Belgian customs the country of destination of the seizure was: Spain (1), Germany (3), France (1), the Netherlands (1) and Slovenia (1).

7. Information on any assessment in the United Nations system

The World Health Organization (WHO) is the specialised United Nations agency designated for the evaluation of the medical, scientific and public health aspects of psychoactive substances under the Single Convention on Narcotic Drugs, 1961, and the Convention on Psychotropic Substances, 1971. At the time that the Joint Report was prepared (*), the WHO informed the

19

Application of the Criminal Law'.

- In Lithuania, furanylfentanyl is subjected to control measures by The Republic of Lithuania Minister of Health Order No V-1511 (28/12/2015) 'On the amendment of the Ministry of Health of the Republic of Lithuania Order No. 5 of 6 January 2000'.

- In Slovenia, furanylfentanyl was classified as a 'category I illicit drug', which includes 'psychoactive substances that are extremely dangerous to health due to serious consequences that may result from abuse and that are not used for medicinal purposes'. The amended decree on the classification of illicit drugs was published in the Official Gazette of the Republic of Slovenia on 24 March 2017.

- In Sweden, furanylfentanyl is regulated as a narcotic, as of 25 January 2017.

- In the United Kingdom, furanylfentanyl is controlled under the Misuse of Drugs Act 1971 by way of a generic definition.

- In Turkey, furanylfentanyl is under control of Drug Law on Drugs numbered 2313 (Official Gazette 29790 of 3 August 2016).

Three Member States (Austria, Hungary and Poland) reported that furanylfentanyl is controlled under specific new psychoactive substances control legislation.

least delay the open manufacture and sale of this substance by chemical companies in this country, which are linked to the supply of the substance in Europe.

There are no studies on the possible consequences of such control measures on furanylfentanyl. If this option of control is pursued, the Committee considers that the following consequences are possible. Some of these may apply to any new psychoactive substance.

- This control option could be expected to limit the availability of furanylfentanyl and hence the further expansion of the current open trade in this substance.

- A health consequence that might result from this control option is the benefit brought about by the presumed reduction in availability and use.

(10) In addition, since 5 May 2017, furanylfentanyl has been controlled under the newly defined generic definition for a group of fentanyl analogues by ministerial decree No. 40/2017, (V. 2.) that amended decree No. 65/2014 (XII. 3.) on New Psychoactive Substances.

(11) There is a recommendation of the Risk Assessment Team to place furanylfentanyl on the list of controlled substances in schedules of acts of counteracting drug addiction.

(12) In February 2017, the National Institute of Health, following the formal request of the Ministry of Health, proposed the inclusion of furanylfentanyl in Table I of Presidential Decree 309/90 of illicit psychotropic substances.

Decision, other options for control may be available to Member States. These may include restricting the importation and supply of the substance as some Member States have already done.

16. Conclusion

N-Phenyl-*N*-[1-(2-phenylethyl)piperidin-4-yl]furan-2-carboxamide (furanylfentanyl) is a synthetic opioid and is structurally related to fentanyl, a controlled substance widely used in medicine as an adjunct to general anaesthesia during surgery and for pain management. Currently available information suggests that pharmacologically furanylfentanyl is a narcotic opioid analgesic broadly similar to fentanyl.

Furanylfentanyl has been available in Europe since at least June 2015 and has been detected in 16 Member States and Norway. The detected quantities are relatively small; however, they should be considered in the context of the potency of furanylfentanyl.

22

Due to the nature of furanylfentanyl both non-fatal intoxications and deaths are likely to be under-detected and under-reported.

Information from police seizures as well as investigations into deaths indicates that furanylfentanyl is available to and being used by high-risk drug users, including opioid users.

Accidental exposure to furanylfentanyl, as well as to other fentanils, poses a risk to law enforcement, emergency personnel, medical and forensic laboratory personnel, as well as to those in custodial settings and postal services. Specific risks and appropriate measures to reduce these risks should be identified and implemented. This may include appropriate protective equipment, training in resuscitation, and making naloxone readily available to relevant personnel in sufficient quantities in the event of poisonings.

There is no information to suggest the involvement of organised crime in the manufacture, distribution (trafficking) and supply within the European Union. There is limited information on the chemical precursors and the synthetic routes used to manufacture the furanylfentanyl detected within the European Union. Most of the synthetic routes are straightforward, make use

the potential interaction between furanylfentanyl and other substances, the dependence and abuse potential, and the public health risks associated with its use.

The Committee notes that a decision to control furanylfentanyl has the potential to bring with it both intended and unintended consequences. Potential intended consequences include reduced levels of availability and ultimately use. This may reduce the health and social risks and consequences arising from the use of furanylfentanyl. It is important to recognise that a potential unintended consequence of control may be the manufacture and availability of other substances. Indeed, since furanylfentanyl was first detected at least eight new fentanils and a number of other new opioids that may replace furanylfentanyl have appeared / are already being sold on the drug market. The implementation of control measures may also lead to the criminalisation of those who continue to use this substance with the possible attendant risks of socio-economic stigmatisation and marginalisation.

Finally the Committee notes that it is important to continue to collect and disseminate accurate information on furanylfentanyl to users, practitioners, policy makers, decision makers and those who may be at risk of accidental exposure. An additional challenge in respect to reducing risk in users and potential users is the balance between providing information to prevent harm and the unintended consequences of communicating the risks of opioids. There is evidence that using terms to describe them as 'potent', 'strong', 'deadly', and 'toxic' can lead some individuals to

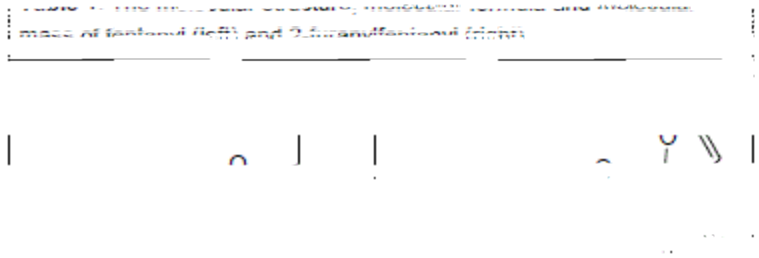
This technical report has been prepared for the risk assessment of *N*-phenyl-*N*-[1-(2-

(4) OJ L 127, 20.5.2005, p. 32.

Chemical structure-based searches were done in SciFinder® (American Chemical Society, Chemical

Chemical description and names

(*) Fentanyl is included in Schedule I of the United Nations Single Convention on Narcotic Drugs, 1961, as amended by the 1972 Protocol.



(5) The Chemical Abstract Service Registry Number (CAS RN) is a unique numeric identifier assigned by the Chemical Abstract Service Division of the American Chemical Society to a specific, single chemical substance.

[illegible]

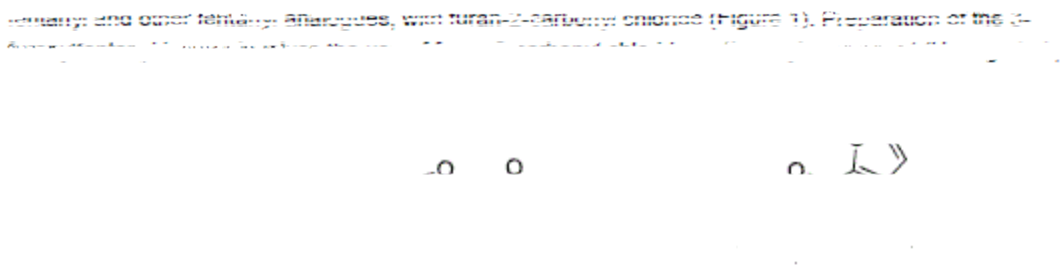
[illegible]

substances listed in electronic cigarettes.

([2]) Systematic name: *N*-phenyl-*N*-[1-(2-phenylethyl)piperidin-4-yl]furan-3-carboxamide. CAS RN (free amine): 101343-82-2; 101343-83-3 (oxalate).

GC-MS, ^{1}H-NMR	material.	

The manufacture of furanylfentanyl relies on precursors and synthetic methods similar to those used for the manufacture of pharmaceutical fentanyl. Accordingly, methods developed for the multistep synthesis of fentanyl are applicable to furanylfentanyl but use a different acylating agent in the final acylation step. Correspondingly, the synthesis method of furanylfentanyl reported in the literature employed the acylation



fentanyl. Two samples purchased as the synthetic opioid U-47,700 ( ) were confirmed to contain

samples obtained from 'darknet' vendors were reported to also contain glycerol (see section C).

([115]) https://www.youtube.com/watch?v=qDPE0EYe5Gs (last accessed 07 May 2017)

vaping (Reddit, 2017 ([19])), intravenous injection (Erowid, 2017 ([20])), and preparations of solutions for

Limited information is available regarding the dose and the dose regimens of furanylfentanyl. From this it

([19]) https://drugs-forum.com/threads/creating-a-fu-f-fent-analog-nasal-spray.281744/ (last accessed 07 May 2017)

([20]) http://drugs.tripsit.me/furanylfentanyl (last accessed 07 May 2017)

values of 39.2 nM and 54 nM, respectively (Table 21(**)) (DEA, 2017).

as a MOR agonist more potent than morphine (EC_{50} = 91.0 nM, [^{35}S]GTPγS binding assay, E_{max} = 85.3%) and fentanyl (EC_{50} = 17.9 nM, E_{max} = 81.2%) although it functioned less efficaciously than morphine or

(**) According to Von Voigtlander and Lewis (1982), U-50,488H refers to the methanesulfonate hydrate salt whereas U-50,488E refers to the monohydrochloride hemihydrate salt.

substance at various doses as compared to untreated control.

([25]) Systematic name: *N*-Phenyl-*N*-[1-(2-phenylethyl)piperidin-4-yl]prop-2-enamide.

detectability in human urine samples (Watanabe et al., 2017). A metabolism study involving butyrfentanyl

abundance of this; however, the detection of clarithromycin, a known potent CYP3A4 inhibitor, was also

([27]) Systematic name: *N*-Phenyl-*N*-[1-(2-phenylethyl)-4-piperidinyl]butanamide.

([28]) Systematic name: *N*-Phenyl-*N*-(piperidin-4-yl)butanamide.

vivo conditions.

There is some information on the biological activity of 4-ANPP using intact guinea pig ileum preparations

(*) For a more comprehensive list of drug interactions with fentanyl, see, for example, http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/epar_search.jsp&mid=WC0b01ac058001d124&source=homeMedSearch&keyword=fentanyl&category=human&isNewQuery=true

system. It is not known if this association is also seen with furanylfentanyl.

No studies of the effects of furanylfentanyl on the ability to drive and operate machines have been performed. However, it is well established that opioid analgesics, such as fentanyl, impair the mental and

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(31) https://fenxrid.org/buprenorphine.php?ID=100046 (last accessed 19 April 2017)

fluranylmethanyl in animal models.

purchases) for monitoring and research purposes. Biological samples are those from human body fluids (urine, blood, etc.) and/or specimens (tissues, hair, etc.)

Information reported to the EMCDDA and Europol indicates that 143 seizures of furanylfentanyl have

country level. Data is drawn from the Joint Report Questionnaires and data provided in the bi-annual data gathering (EU EWS progress and final reports) and from individual Reporting forms submitted on an ad hoc basis.

- [illegible] reported by Finland (4) and Belgium (1). Two of the samples from Finland were found to contain [illegible]

[illegible] iBF (1 to 5 parts).

(35) 'Talizman motocykllisty', 'Talizman 0,5g-Ziel', 'Talizman 1,0g – Ziel', 'Talizman GT 0,5g-Ziel' and 'Talizman GT 1,0g – Ziel'.

- 14 of the seizures were of powders, while the remaining 2 were in liquid form.

suggests that the production in Europe cannot be excluded.

In 7 seizures made by Belgian customs at Bierset airport the country of destination of the seizure (all in powder form) was: Spain (1 seizure amounting to 101 grams), Germany (3), France (1), the Netherlands

furanylfentanyl' (searches in English, Swedish and Danish, including variations in spelling). The first 100 results were recorded and the sites reviewed. Each identified vendor site was then scored for information on geographical location, quantities and prices, and substance marketing.

vaping in electronic cigarettes. This site also offered fluranylfentanyl in powder form mixed

(n =5 sites) and 5,299 for 1 kg (n = 4 sites).

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(29) Prices listed in USD were converted to EUR according to the XE Currency Converter from the 11/01/2017 (USD 1 = EUR 0.95). The prices were then rounded up to the nearest EUR.

similarity might exist (Moffat et al., 2016).

(*2) In addition, Germany reported a non-fatal intoxication in which furanylfentanyl and lactose were identified in a sample of the drug that was apparently used by the patient (sample not quantified). However, insufficient information was available at the time of reporting to de-duplicate with other cases.

biological samples taken from the patient.

Clinical features

(*[1]*) Including a suspected case which involved cardio-respiratory arrest 10 minutes after inhalation of furanylfentanyl.

(*[2]*) Including the confirmed and probable case.

[illegible]

information was either unknown or not reported in the [illegible] remaining cases.

[illegible]

(49) The probable case and a suspected case.

two patients left without being seen by emergency department staff, and six patients were admitted to the

Deaths reported by the Member States

([50]) Seven of the deaths reported by Sweden are also reported in Guenieri et al., (2017).

furanylfentanyl. Of these, furanylfentanyl was either the cause of death or is likely to have contributed to

pharmacological opioid nature of furanylfentanyl means the primary toxic contribution could be attributed

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(51) Including the bathroom (2 cases) and the couch (2 cases).

and wholesale quantities. It has been sold as a "research chemical" in several physical forms, including as powders and ready-to-use nasal sprays.

Among other adverse effects, opioid analgesics, such as fentanyl, produce dose-dependent respiratory depression. This risk is greater in opioid-naïve persons. Similar to other fentanils in overdose, the most serious acute risk arising from the use of furanylfentanyl appears to be from profound and rapid respiratory depression, which can lead to apnoea, respiratory arrest, and death. This risk may be exacerbated given:

- [illegible]

- the concomitant use of other CNS depressants (such as other opioids, benzodiazepines,

of the substance present (de Boer et al., 2003).

(53) Including paramedics and hospital emergency room staff.

inhalation, or ingestion — pose a serious risk of poisoning to the public, law enforcement, emergency

that they are being sold to unsuspecting users in/as heroin or other illicit opioids, counterfeit medicines

E2. Possible effects on direct social environment

There is no information on the possible effects of furanylfentanyl on the direct social environment; however, they may have some similarities with those associated with the use of illicit opioids.

inhalation, or ingestion — also poses a serious risk of poisoning to those who may come into contact with

excluded. This case demonstrates the capability to manufacture fentanils exists within the European Union.

In 7 seizures made by Belgian customs the country of destination of the seizure was: Spain (1), Germany (3), France (1), the Netherlands (1) and Slovenia (1).

psychoactive substances as well as new psychoactive substances

F3. Evidence of the same groups of people being involved in different types of crime

Casale, J. F., Mallette, J. R. and Guest, E. M. (2017), 'Analysis of illicit carfentanil: emergence of the

Report on a new psychoactive substance: N-phenyl-N-[1-(2-phenylethyl)piperidin-4-yl] acetamide (acetylfentanyl). In accordance with Article 5 of Council Decision 2005/387/JHA on the information exchange, risk assessment and control of new psychoactive substances. EMCDDA, Lisbon. Available at: http://www.emcdda.europa.eu/system/files/publications/2693/TDAS16001ENN.PDF.

overdose deaths with take-home naloxone, Publications Office of the European Union, Luxembourg.

Report on a new psychoactive substance: *N*-(1-phenethylpiperidin-4-yl)-*N*-phenylacrylamide

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2