Acetylfentanyl
Critical Review Report

Agenda item 5.2

Expert Committee on Drug Dependence
Thirty-seventh Meeting
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Summary

Acetylfentanyl is in the phenylpiperidine class of synthetic opioids that includes fentanyl, which is itself a Schedule I substance under the U.N. 1961 Single Convention on Narcotic Drugs. Desmethyl fentanyl is a synonym for acetylfentanyl, likely due to the removal of a methyl group from the structure of fentanyl. Acetylfentanyl is convertible into fentanyl and is identified as an impurity during the production of fentanyl. It has no known approved medical or industrial applications.

Acetylfentanyl is clearly being used for non-medical purposes, although the incidence and prevalence of its abuse cannot be accurately estimated because, in part, it is not routinely tested for in forensic toxicology. It has been identified in confiscated material being trafficked illicitly in the United States, Europe and Japan. It is sold over the Internet where it is sometimes promoted as a "research chemical", and its use is discussed on drug-user websites. Acetylfentanyl has been associated with at least 52 deaths in the United States (where it has been emergency scheduled under the Controlled Substances Act) and with deaths in Europe as well.

Users have reported using acetylfentanyl via insufflation, smoking, and through the intravenous routes of administration. Actual doses are thought to be in the microgram range. Effects reported by users appear indicative of heroin/fentanyl-like effects.

Controlled preclinical pharmacology and toxicology studies on acetylfentanyl are few, and such clinical studies are non-existent. Preclinically, acetylfentanyl has many characteristics of a mu opioid receptor agonist. It displaces $^3$H-endorphin binding (EC$_{50}$ of 676 nM) at the mu opioid receptor, completely inhibits the mouse vas deferens stimulated twitch (EC$_{50}$ of 4.42 x 10$^{-7}$ M), and has antinociceptive effects in several rodent models. Acetylfentanyl can relieve signs of withdrawal in the morphine dependent rhesus monkey and thus demonstrating cross-dependency to morphine. Other preclinical tests directly pertinent to its abuse potential such as self-administration, drug discrimination, intra-cranial self-stimulation or conditioned place preference, appear not to have been reported if conducted.

Acetylfentanyl is being controlled as an abused substance in some member states. Its use as an abused substance is unequivocal, and has resulted in several deaths. Precise estimates of the incidence and prevalence of acetylfentanyl's abuse, however, are difficult at present.
1. Substance identification

A. International Nonproprietary Name (INN)
   Not applicable.

B. Chemical Abstract Service (CAS) Registry Number
   3258-84-2 (base); 117332-89-5 (HCl)

C. Other Names
   Acetylfentanyl, desmethyl fentanyl, fentanyl acetyl analog, N-(1-phenethyl-4-piperidyl)-acetonilide, acetamide, N-phenyl-N-[1-(2-phenylethyl)-4-piperidinyl]-, NIH 10485; desmethyl fentanyl; MCV 4848; ‘China White’ (erroneously)

D. Trade Names
   None.

E. Street Names
   "fake heroin", acetyl fentanyl

F. Physical properties
   Pale purple powder (HCl)\(^1\) or light yellow oil immediately following synthesis.\(^2\)

G. WHO Review History
   Not previously reviewed.

2. Chemistry

A. Chemical Name
   IUPAC Name: N-[1-(2-phenylethyl)-4-piperidyl]-N-phenylacetamide
   CA Index Name: Acetamide, N-phenyl-N-[1-(2-phenylethyl)-4-piperidinyl]-

B. Chemical Structure
   Free base:
Molecular Formula: $C_{21}H_{26}N_2O$; $C_{21}H_{26}N_2O \cdot HCl$ (for the HCl salt)
Molecular Weight: 322.205 (base); 358 (HCl)
Melting point: 256.6 °C (HCl)
Boiling point: 453.8±38.0°C

C. **Stereoisomers**

None.

D. **Synthesis**

Methods of manufacturing:
Several methods of syntheses of acetylfentanyl have been disclosed beginning with Janssen who had synthesized fentanyl from $N$-benzyl-4-piperidone.\(^3\)\(^,\)\(^4\) More recently, a three-step strategy was disclosed resulting in high-yielding transformations.\(^2\) $N$-[1-(2-phenylethyl)-4-piperidinyl]aniline was dissolved in methylene chloride and was treated with diisopropylethylamine. The solution was cooled and treated with acetic anhydride. The mixture was then partitioned (CH\(_2\)Cl\(_2\)/H\(_2\)O). The organic phase was washed with brine and saturated with NaHCO\(_3\), dried over anhydrous Na\(_2\)SO\(_4\) and evaporated in vacuo to furnish acetylfentanyl as a light yellow oil.\(^5\)

E. **Chemical description.**

Acetylfentanyl is in the phenylpiperidine class of synthetic opioids that includes fentanyl. Acetylfentanyl contains a phenylacetamide group (CH\(_3\)CONH\(_2\)) whereas fentanyl, which is a Schedule I drug under the U.N. 1961 Single Convention on Narcotic Drugs, has a phenylpropanamide (CH\(_3\)CH\(_2\)C=O(NH\(_2\))) group at the corresponding position (see figure below). Desmethyl fentanyl is a synonym for acetylfentanyl, due to the removal of a methyl group from the structure of fentanyl. Acetylfentanyl can be identified as an impurity during the production or degradation of fentanyl.\(^5\)

\[
\text{Acetyl fentanyl} \quad \text{Fentanyl}
\]

F. **Chemical properties**

Many details are provided in Section 2 above. In addition, and regarding solubility, the base has limited solubility in DMSO at 5 mg/mL when warmed.
G. **Chemical identification**

Acetylfentanyl is not a part of most illicit drug screens and may remain undetected in many of these cases. Immunoassays (e.g. ELISA) for fentanyl do not differentiate fentanyl and acetylfentanyl; confirmatory analysis such as gas chromatography/mass spectrometry (GC/MS) is required to confirm the presence of acetylfentanyl. General forensic analytical guidelines for detection of acetylfentanyl have been provided in a U.S. Center for Disease Control and Prevention Health Advisory alert, in which suggested extraction to be by routine n-butyl chloride liquid: liquid basic drug extraction, including an acid back extraction, using detection parameters of GC/MS EI Scan Ions 231, 146, 188 m/z and earlier eluter metabolite/breakdown 4-anilino-n-phenethylpiperidine (ANPP), a compound believed to be a precursor of acetylfentanyl 146, 189 m/z. Typical elution order occurring includes citalopram, ANPP, paroxetine, acetylfentanyl, fentanyl, zolpidem. Other approaches have been reported, including an assay that coupled solid phase extraction (SPE) with liquid chromatography-tandem mass spectrometry (LC-MS/MS) for detecting acetylfentanyl and its metabolite, acetyl norfentanyl, in urine.

3. **Ease of convertibility into controlled substances**

Acetylfentanyl is a de-methylated fentanyl, which is a Schedule I drug under the U.N. 1961 Single Convention on Narcotic Drugs. Thus, acetylfentanyl needs methylation to convert to fentanyl that could be done via deprotonation, followed by methylation (this route would be difficult as a strong base would be required - may be possible with NaH or KOrBu, but probably need lithium diisopropylamide). An easier synthetic route would be hydrolysis of the amide (with strong acid, e.g., HCl), followed by treatment with propionic anhydride to give fentanyl.

4. **General pharmacology**

A. **Pharmacodynamics**

Controlled, clinical reports evaluating the pharmacological effects of acetylfentanyl could not be found in the scientific literature, and were also reported not to be found in a recent report by the U.S. Drug Enforcement Administration during their 2015 review of the acetylfentanyl.

**Receptor binding and in vitro functional activity:** Acetylfentanyl displaced $^3$H-etorphine binding in rat cerebral membrane in the presence of NaCl with an EC$_{50}$ of 676 nM. By comparison, morphine's EC$_{50}$ was 23.6. Acetylfentanyl completely inhibited the mouse vas deferens stimulated twitch with an EC$_{50}$ of 4.42 x 10$^{-7}$ M. This inhibition was unaffected by the delta-opioid antagonist, ICI-17864, but was reduced to 29.3 (±2.1)% levels by the mu-opioid receptor antagonist, beta-funaltrexamine, and reverse by an equimolar concentration of naltrexone. Overall these results indicated that acetylfentanyl is a mu opioid receptor agonist similar to morphine.

**Analgesia:** Acetylfentanyl demonstrated antinociceptive activity in the acetic acid writhing test in ddY-mice with an ED$_{50}$ of 0.021 mg/kg p.o. Acetylfentanyl was 15.7x more potent in this test than morphine that had an ED$_{50}$ of 0.33 mg/kg, but with 0.29x
the potency of fentanyl that had an ED50 of 0.0061 mg/kg. The ratio of acetylfentanyl's LD50/ED50 was 442.9x, and far less than morphine's at 1424.2x or fentanyl's at 10163.9x, suggesting a far narrower safety index for acetylfentanyl than for these other opioids.

Aceto and colleagues reported antinociceptive effects of acetylfentanyl in mice using the tail flick and the phenylquinone writhing tests. The ED50 (95% C.L.) for acetylfentanyl in the tail flick test was 0.3 (0.2-0.5) mg/kg s.c. As a comparator, morphine was 19x less potent at 5.8 (5.7-5.9) mg/kg s.c. In the phenylquinone writhing test, acetylfentanyl had an ED50 of 0.05 (0.03-0.1) mg/kg s.c., and again morphine was less potent when compared at an ED50 of 0.23 (0.2-0.25) mg/kg s.c. Acetylfentanyl was inactive up to 30 mg/kg s.c. as an antagonist against morphine's antinociceptive effects in the mouse tail flick test.

B. Routes of administration and dosage

In the Russian Federation, acetylfentanyl apparently first appeared in the market of smoking mixtures known as "spices" in 2012. Commonly, it appears on the illicit market as a powder or in tablet form. Often the powder form is mixed in with heroin. The actual dose needed to produce a behavioral effect is thought to be in the microgram range. One user website suggested, "If using iv then do 100-250 micros as starting iv, roughly 6-8mg of morphine IV." A user at another site apparently had tried several routes of administration with acetylfentanyl. This user reported insufflating 10 mg and reporting, "Effects were not immediate and took a good 5-10 minutes to fully kick in. The effects were typical of this class of drugs, mildly sedating, nothing crazy. No real euphoria present, as is typical with Fentanyl itself, so this wasn't surprising. All in all, 10mg produced a pleasant buzz that lasted around 90 minutes before a decline in effects was noticed." The user subsequently apparently insufflated 15 mg of acetylfentanyl and reported that reminded him/her of heroin's effects. This user also reported a lack of effect using 10 mg acetylfentanyl in his/her vaporizer. The user subsequently tried 10 mg acetylfentanyl intravenously and reported, "... 10mg produced very enjoyable, relaxing effects. And with the aid of two delicious beers (one chocolate stout and one pumpkin ale, both with slightly above average alcohol content) the effects could be felt the rest of the night without any inclination to redose."

C. Pharmacokinetics

Using gas chromatography and high performance liquid chromatography (HPLC) with mass spectrometry detection (GC–MS and HPLC–MS), Melent’ev and colleagues identified major metabolites of acetylfentanyl in urine from consumers of the drug and proposed a main path of its biotransformation. The main pathway of the biotransformation of acetylfentanyl is hydroxylation by the phenylethyl moiety, and not n-dealkylation as in fentanyl. In the second phase of acetylfentanyl metabolism, metabolites hydroxylated by the phenylethyl moiety form some conjugates and also methylation by one of hydroxyls proceeds. The degree of conjugation to all of the identified hydroxylated metabolites varies in the range from 74 ± 10% (n = 3) for monohydroxylated ones to 100% (n = 3) for the dihydroxylated metabolite. In an assay that coupled solid phase extraction (SPE) with liquid chromatography-tandem mass spectrometry (LC-MS/MS), Patton and colleagues reported that hepatic cytochrome P450s catalyzed the production of acetyl norfentanyl as the major metabolite from acetylfentanyl using pooled human liver microsomes. These authors
also reported that acetyl norfentanyl was also the major metabolite from in rat urine when acetylfentanyl was administered intravenously at 3 mg/kg.\textsuperscript{12}

5. **Toxicology**

There appear to be no published controlled studies on safety of acetylfentanyl for human use. Several adverse reactions in humans have been reported, however, including mortality (see Section 6 below).

In ddY-mice, the LD\textsubscript{50} for acetylfentanyl was reported to be 9.3 mg/kg p.o., and about seven times lower than fentanyl and about 50 times lower than morphine. The ratio between the LD\textsubscript{50} to the ED\textsubscript{50} as an analgesic in the acetic acid writhing test was over 3x lower than that of morphine and nearly 23x that of fentanyl,\textsuperscript{15} and these data led Melent’ev to comment, "... acetylfentanyl ... is one of the most dangerous fentanyl analogues because of the narrow range of harmless doses."\textsuperscript{17}

Germ cell mutagenicity, carcinogenicity, and reproductive toxicity reports appear to be lacking.\textsuperscript{21} Acetylfentanyl is not considered to be a carcinogen by IARC, NTP, or OSHA.\textsuperscript{21}

6. **Adverse reactions in humans**

The United States Drug Enforcement Administration reported in July of 2015 that at least 52 confirmed fatalities involving acetylfentanyl in the United States had occurred between 2013-2015. Amongst the earliest fatalities reported in the United States involving acetylfentanyl occurred in the state of Rhode Island between March-May of 2013.\textsuperscript{10, 22} Ten fatalities attributed to acetylfentanyl overdose were reported during March of 2013 alone in Rhode Island. Subsequently between March-May of 2013, four additional deaths attributed to acetylfentanyl overdose were reported in Rhode Island.\textsuperscript{10, 22} Among these 14 deaths attributed to acetylfentanyl overdose in Rhode Island, ages ranged from 19-59 years old, with 10 of the 14 decedents being male.\textsuperscript{10} Eight decedents tested positive for both acetylfentanyl and 4-anilino-n-phenethylpiperdine (ANPP; a compound believed to be a precursor of acetylfentanyl), five tested positive for acetylfentanyl and no ANPP, and one tested positive for ANPP without acetylfentanyl.\textsuperscript{10}

Other drugs of abuse found in the toxicology testing were cocaine (57%), morphine (a potential indication of heroin use) (36%), ethanol (36%), and benzodiazepines (21%). One decedent tested positive for acetylfentanyl and none of these other drugs.\textsuperscript{10} Fatalities associated with acetylfentanyl use have also been confirmed in several other states including: Arizona, Florida, Massachusetts, New Hampshire, Vermont, New Jersey, California, Louisiana, Maryland, North Carolina, Oregon, Pennsylvania, and Wisconsin.\textsuperscript{6, 23} In one report that reviewed 18 of these fatalities, the average acetylfentanyl whole blood concentration was 160 ng/mL (range: 0.58-730 ng/mL).\textsuperscript{23} All of these 18 decedents were male except one female (and one not reported) and the average age was 33 years (15 reporting with a range of 19-54 years). For the cases where full toxicology was performed, both designer drugs and more vintage drugs were also identified including phenazepam (2), 4- methylethcathinone (4-MEC) (1), methylone (1), cannabinoids (6), benzodiazepines (5), alprazolam (2), antidepressants / antipsychotics (5), opiates (2), cocaine (2), diphenhydramine (1) and methamphetamine (1). Additionally 2 cases were also positive for fentanyl, one at a high (22 ng/mL) and one at a low (0.67 ng/mL) concentration.\textsuperscript{23} As mentioned above for the deaths in Rhode
Island, there have been other reports from states where the only drug that could be detected in a fatality was acetylfentanyl.

The first serious adverse events associated with acetylfentanyl reported by the EU Early Warning System occurred in June of 2015 in which two death were reported in the United Kingdom. One death involved a 56 year old male in which 1.2 mg/L of acetylfentanyl was detected in post mortem blood, along with alcohol 11mg/dL (GC-FID) that was thought to be likely postmortem production, mirtazapine 0.15mg/L (GCMS) prescribed, pregabalin 3.7 mg/L (LCMS) prescribed, sertraline 0.39 mg/L (GCMS) unknown, olanzapine <0.05 mg/L (LCMS) prescribed. Cause of death was reported as acute heart failure, along with acetylfentanyl overdose and ischemic heart disease. The other death involved a 37 year old male in which acetylfentanyl (level not measured), phenazepam (trace), loperamide (low), methamphetamine (low), and buprenorphine (<1.6 ng/mL) were detected. In the case of this death, the suspected route of administration was intravenous, and the decedent presumably self-medicated with acetylfentanyl to "get off heroin". Beyond the EU on the continent, Melent’ev and colleagues reported detecting acetylfentanyl associated with 12 deaths in the Russian Federation, sometimes occurring with morphine, but in the absence of other narcotic or psychotropic substances.

7. **Dependence potential**

   **A. Animal Studies**

   Cross-dependency tests: Acetylfentanyl was tested for its ability to attenuate signs of spontaneous withdrawal in morphine dependent rhesus monkeys. Rhesus monkeys were made dependent upon morphine by four daily injections of 3 mg/kg s.c. morphine during several weeks of treatment. Morphine administration was then discontinued for 15 h and the monkeys would then begin to show signs of spontaneous withdrawal. Re-administering the 3 mg/kg morphine dose completely suppressed and prevented further signs of withdrawal from emerging during the 150 min test session. Acetylfentanyl was tested at 0.125 and 0.5 mg/kg, and at 0.5 mg/kg s.c. it completely, but briefly (90 min), substituted for morphine. At peak effect, the drug was considered to be 6x more potent than morphine. Demonstrating an ability to attenuate signs of morphine withdrawal indicates cross-dependency between morphine and acetylfentanyl that suggests opiate-dependent individuals, such as those dependent upon heroin, would find relief during withdrawal by administering acetylfentanyl and could subsequently seek it out if only for that effect.

   **B. Human Studies**

   Physical dependence tests in human subjects: There apparently have been no published reports with acetylfentanyl under controlled conditions reporting the primary physical dependence inducing effects, or the cross-dependency effects of acetylfentanyl.

8. **Abuse potential**

   **A. Animal Studies**

   Relevant pre-clinical abuse liability tests: Published reports involving controlled studies with acetylfentanyl in directly relevant abuse-liability procedures such as self-
administration, drug discrimination, intra-cranial self-stimulation, or conditioned place preference could not be found.

**B. Human Studies**

*Relevant clinical abuse liability tests:* Published reports involving controlled studies with acetylfentanyl in directly relevant abuse-liability procedures such as self-administration, drug discrimination, or using drug-liking inventories could not be found.

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

There are no known approved medical products containing acetylfentanyl.

10. **Listing on the WHO Model List of Essential Medicines**

Acetylfentanyl is not listed under the WHO Model List of Essential Medicines.

11. **Marketing authorizations (as a medicinal product)**

None known of.

12. **Industrial use**

None known of.

13. **Non-medical use, abuse and dependence**

Acetylfentanyl has been associated with several deaths in the United States and in Europe.\(^{10,22}\) It has been identified in confiscated material being trafficked illicitly and is sold over the Internet.\(^{6,25,26,27}\) Its use is discussed on drug-user websites.\(^{19,20,28}\) It is clearly being non-medically used and abused, although the extent of its abuse cannot be accurately estimated given, in part, it is not routinely tested for in forensic toxicology. Controlled, clinical evidence of it inducing or maintaining physical dependence is not available, although user and treatment websites suggest that it should have much the dependence-related effects of the controlled substance, fentanyl, of which acetylfentanyl is found as an "impurity" during fentanyl's synthesis and to which acetylfentanyl can be converted.

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

Scholarly epidemiological studies regarding the incidence and prevalence of acetylfentanyl have not been published. Some information can be gathered from seizure and other detection information as in Section 16 below. There have been several deaths associated with the use of acetylfentanyl in the United States in particular, but also in Europe that are discussed in section 6 above. What might be estimated of the abuse and mortality associated with acetylfentanyl is likely to be grossly underestimated because it is not included in most drug screens.\(^{18}\)

The National Forensic Laboratory Information System (NFLIS) is a program of the U.S. Drug Enforcement Administration Office of Diversion Control that collects drug identification results from cases analyzed by federal, state, and local laboratories. The NFLIS Data Query System (DQS) is an online database that provides users with the
ability to analyze NFLIS data at the national, regional, state, or local level. The NFLIS DQS database was accessed for information regarding the identification of acetylfentanyl (including the base and the hydrochloride salt) in samples analyzed by NLIS laboratories between 2013 to June, 2015 to provide an indication of incidence of its use in the United States.\textsuperscript{29} The incidence of samples identified as containing acetylfentanyl has grown in the U.S. from 2013 in which 8 were confirmed, to 59 confirmations in 2014, to 151 confirmations in just the first half of 2015 alone.\textsuperscript{29} The greatest incidence of acetylfentanyl samples came from the northeast, midwest, and southern regions of the U.S., and only low levels had been reported on the west coast and there appeared to be no trends in this distribution between 2014 and 2015. For instance, only two acetylfentanyl mentions occurred in the west in 2013 and all the other 57 mentions occurred elsewhere.\textsuperscript{29} Similarly, in the first half of 2015, only five mentions occurred in the west while the other 146 occurred in other regions.\textsuperscript{29}

In an April 2015 review of the actual and potential risks to public health of acetylfentanyl, conducted by the U.S. Department of Justice during its review of acetylfentanyl for emergency scheduling in the United States, it concluded...."Based on the ... pharmacological data, the abuse of acetyl fentanyl leads to the same qualitative public health risks as heroin, fentanyl and other opioid analgesics. The public health risks attendant to the abuse of heroine and other opioid analgesics are well-established.... The abuse of opioid analgesics has resulted in large numbers of treatment admissions, emergency department visits, and fatal overdoses. This indicates that acetyl fentanyl poses an imminent hazard to public safety."\textsuperscript{18}

15. **Licit production, consumption and international trade**

Other than as a reference standard or for scientific research purposes, acetylfentanyl is not licitly produced.

16. **Illicit manufacture and traffic and related information**

Acetylfentanyl was detected in tablets that mimic pharmaceutical opiate products, in powder form and spiked on blotter papers.\textsuperscript{6} The first laboratory submission of acetylfentanyl in the United States was recorded in Maine in April 2013 according to the National Forensic Laboratory Information System1 (NFLIS).\textsuperscript{18} According to DEA's STARLiMS (a web-based, commercial laboratory information management system) and National Forensic Laboratory Information System, federal, state and local forensic laboratories reported 10 exhibits identified as acetylfentanyl in 2013 and 40 exhibits identified as acetylfentanyl in 2014.

The EU Early Warning System Network reported that acetylfentanyl had been detected in 5 member states including Finland, France, Poland, Sweden and the United Kingdom.\textsuperscript{25} The first notification occurred in 2014 by Poland in which acetylfentanyl was identified in a 20.2 g seizure of white powder by Polish customs in 2014. Acetylfentanyl has been seized as a white or pale-beige powder (0.42 g–28 g) and in a nasal spray. In one case involving a seizure of 28 g of white powder made by customs, the acetylfentanyl had been shipped by express freight from China.\textsuperscript{25}

In late April 2013, Montreal police raided seven locations in Montreal seizing more than 300,000 tablets of illegally-produced synthetic prescription drugs.\textsuperscript{27} 11,000 of these pills contained acetylfentanyl.\textsuperscript{18} In addition, 3 kg of acetylfentanyl in powder form was confiscated.\textsuperscript{18} Given that a typical dose of acetylfentanyl is in the microgram range, a
three kilogram quantity could potentially produce millions of dosage units.\textsuperscript{18} It was the first time Montreal police had confiscated acetylfentanyl on the black market.\textsuperscript{27}

Acetylfentanyl has been sold on the Internet often as a "research chemical". For instance, from November of 2013 to May of 2014 acetylfentanyl was identified in herbal products obtained over the internet in Japan.\textsuperscript{26} The products appeared as alternatives to controlled substances such as narcotics and designated substances.\textsuperscript{26} In a recent search conducted by this reviewer, accessing the Internet on 2 September 2015, the apparently China-based companies Dharmachems.com (http://www.dharmachems.com/products/acetyl-fentanyl/) and Shouguang Huatian Co Ltd (http://small-order.hktdc.com/static/image/common/icon-pin.png) were offering acetylfentanyl, the former at a "negotiable price", and the later within a product identified as, "Product:W-15 W-18 Etizolam Diclazepam Flubromazepam Acetylfentanyl".

17. **Current international controls and their impact**
Acetylfentanyl is currently not controlled under the 1961, 1971 or 1988 United Nations Conventions.

18. **Current and past national controls**

   **United States:** Acetylfentanyl is a Schedule I substance under the federal Controlled Substances Act (temporary scheduling).

   **Japan:** Acetylfentanyl was expect to have been controlled as a designated substance in Japan beginning July 2014(27), but it was not found listed in the Chemical Risk Information Platform (CHRIP) on 7 September 2015.

19. **Other medical and scientific matters relevant for a recommendation on the scheduling of the substance**
None.
References

13. Coop A. Ease of convertibility of MT-45 and acetylfentanyl into a controlled substance. Personal communication to Patrick M. Beardsley, Ph.D.; Email: 16 August 2015. p. 1.


