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CCENDU Bulletin, June 2016

CCENDU Bulletin

Novel Synthetic Opioids in Counterfeit Pharmaceuticals and Other Illicit Street Drugs

Summary

- Counterfeit pharmaceuticals are fake products manufactured illegally in clandestine labs. They are designed to look like legitimate pharmaceuticals.
- Sale of counterfeit pharmaceuticals in the illicit market are becoming more frequent. In the United States and Canada there have been reports of counterfeit OxyContin® tablets, Percocet® tablets, Xanax® tablets, and Norco® tablets. These tablets often contain a synthetic opioid different from the active substance users believe is present.
- Novel synthetic opioids that have been used in these products are fentanyl and fentanyl analogues. Other substances that have been used or might be used include W-18,* U-47700, AH-7921 and MT-45.
- The presence of these synthetic opioids in tablets and powders dramatically increases the risk of overdose among people using them because they do not know what substances they are using or how much of the active substance or substances is included.
- Although the efficacy of naloxone has not been evaluated for all the novel synthetic opioids, in theory it should temporarily reverse the effects and so it should be administered immediately if an opioid overdose is suspected. For some of these opioids the overdose can return when the naloxone wears off, and repeated or higher doses of naloxone could be necessary. Individuals should call 911 immediately after administering naloxone.
- When warning people who use drugs about novel synthetic opioids, it should be made clear that it is the variability of the dose from one tablet or powder to the next that increases the risk of overdose, not simply the potency or toxicity of the individual substance in question.
- To confirm identification of a specific compound, laboratories require a sample of the substance. To test for new opioids as they emerge, toxicology laboratories must add them to their analytical methods. Ongoing issues include cost, availability and accessibility of analytical standards. Further, detection can be difficult due to the small quantity of the substance that might be present in a product or, because of their potency, their low concentration in blood or urine.

^{*} Emerging evidence suggests that W-18 is not an opioid. However, due to its analgesic effects and because it has been mixed in drugs sold illicitly as opioids, we have included it in this bulletin. For more information, see Health Canada's clarification of its position on W-18: healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2016/58866a-eng.php.

Fentanyl can be absorbed through the skin, which might also be possible with other synthetic opioids. Because of their potency and toxicity, and the chance of accidental exposure, law enforcement officers and others who encounter these substances in clandestine laboratories or pill pressing operations should immediately contact officers trained to deal with clandestine laboratories or chemists from Health Canada's Drug Analysis Service.

Background

Counterfeit pharmaceuticals are fake pharmaceutical products that can be contaminated or contain the wrong or no active ingredient.¹ These products are manufactured illegally in clandestine labs and designed to look like legitimate pharmaceuticals. In February, 2014, CCENDU released an alert advising that counterfeit oxycodone tablets containing fentanyl had been detected and become increasingly available in several Canadian communities.² The alert advised that the presence of fentanyl in these tablets dramatically increased the risk of overdose among people using them because they did not know what they were using (i.e., fentanyl or another active substance) and how much of the active ingredient was in them.

Since 2009, there have been numerous reports describing an increase in fentanyl-related deaths.³ In many of these cases, individuals were reportedly unaware they were consuming fentanyl, fentanyl analogues or other novel synthetic opioids. Recently, there have been scattered reports of novel synthetic opioids and substances other than fentanyl being included in tablets and powders for sale in the illicit market.

This bulletin describes some of the novel synthetic opioids that have appeared or might appear in counterfeit pharmaceuticals or be mixed into other illicit street drugs. These opioids include fentanyl and its analogues, W-18,⁺ U-47700, AH-7921 and MT-45. The bulletin also provides a brief overview of some of the counterfeit pharmaceuticals and other illicit street drugs that have been found to contain novel synthetic opioids as reported in the media and in other sources of information in Canada and the United States.

Finally, the bulletin includes a discussion of the implications of this phenomenon for those working in:

- Public health and harm reduction
- Emergency medical services and emergency response services
- Laboratories
- Poison control centres
- Law enforcement

Reports of Novel Synthetic Opioids in Counterfeit Pharmaceuticals and Other Illicit Street Drugs

The following table provides a non-comprehensive sample of recent reports of synthetic opioids appearing in counterfeit pharmaceuticals and other illicit street drugs. The purpose of this table is to illustrate the diversity of the products, their presence throughout North America, and the active substances that have been detected in them. This table is not an exhaustive listing of reports. (All reports were last accessed on June 2, 2016.)

⁺ Emerging evidence suggests that W-18 is not an opioid. However, it can be mixed in drugs that are claimed to be opioids.



Title of Report	URL	Location	Date of report	Appearance	Active substances
A toxic drug, more powerful than fentanyl, hits Alberta	www.macleans.ca/ news/canada/a-new-drug- more-toxic-that-fentanyl- hits-the-streets-in-alberta/	Calgary, Alberta, Canada	Feb., 2016	Oxycodone tablets (CDN 80)	W-18
Warning Issued About Counterfeit Prescription Pills	www.chattanoogan.com/ 2016/2/8/317632/Warni ng-Issued-About- Counterfeit.aspx	Tennessee, USA	Feb., 2016	Oxycodone tablets (A215) Percocet tablets	Fentanyl
RCMP Bust Fentanyl Pill Operation in West Kelowna	www.kelownanow.com/wat ercooler/news/news/Kelo wna/16/03/04/RCMP_Bu st_Fentanyl_Pill_Operation _in_West_Kelowna	Kelowna, British Columbia, Canada	March, 2016	Oxycodone tablets Percocet tablets	Fentanyl
Fentanyl-Contaminated Street Norco	www.dhhs.saccounty.net/ PUB/Documents/AZ- Health-Info/ME- 20160325-Health+Alert+- +Contaminated+Norco.pdf #search=norco	Sacramento, California, USA	March, 2016	Norco‡ tablets	Fentanyl
Sheriff: Blend of Xanax, fentanyl has killed nine people in Pinellas ⁴	www.tbo.com/pinellas- county/sheriff-blend-of- xanax-fentanyl-has-killed- nine-people-in-pinellas- 20160322/	Tampa Bay, Florida, USA	March, 2016	Xanax tablets (G3722 inscribed along with 3 score marks) Oxycodone tablets (A215, V 4812)	Fentanyl or fentanyl and alprazolam
Broward man who smuggled synthetic heroin also had new lethal, but legal, street drug	www.sun-sentinel.com/ local/broward/fl-fentanyl- broward-sentencing- 20160318-story.html	Broward County, Florida, USA	March, 2016	2.5 lbs of white powder	W-18
Quebec City police seize \$1.5M worth of fentanyl	www.cbc.ca/news/canada/ montreal/fentanyl-quebec- city-police-seized- 1.3541118	Quebec, Canada	April, 2016	Oxycodone tablets (CDN100, A215)	Fentanyl
Health Department Alert: Counterfeit Street Pills and Fentanyl-Related Overdoses	ccgovernment.carr.org/ccg/ releases/Counterfeit%20 pill%200verdose%20 Alert.pdf	Westminster, Maryland, USA	April, 2016	Xanax tablets, Oxycodone tablets, Percocet tablets, Norco tablets	Fentanyl
Counterfeit Norco Poisoning Outbreak — San Francisco Bay Area, California, March 25– April 5, 2016	www.cdc.gov/mmwr/ volumes/65/wr/ mm6516e1.htm	San Francisco Bay Area, California, USA	April, 2016	Norco tablets	Fentanyl, promethazine, acetaminophen, trace amounts of cocaine
W-18 Seized in Edmonton (seizure, Dec. 2015; confirmed by testing, April, 2016)	www.alert-ab.ca/w-18- seized-in-edmonton/	Edmonton, Alberta, Canada	April, 2016	4 kg of white powder	W-18

Reports of Novel Synthetic Opioids

[‡] Norco tablets, when manufactured and sold legitimately, contain acetaminophen and hydrocodone (325 mg/10 mg). They are not sold commercially in Canada.



Novel Synthetic Opioids

The following substances are novel synthetic opioids that have been detected in seized tablets or powder or are suspected to be involved in drug-related deaths in North America. The list of compounds included is not meant to be exhaustive and the following descriptions are not meant to be comprehensive. Where possible, readers are referred to more comprehensive information.[§]

Fentanyl



Figure 1. Chemical structure of fentanyl (PubChem CID 3345; C₂₂H₂₈N₂O)

In June 2013, CCENDU first detected and issued an alert on the appearance of and potential for harms associated with fentanyl or fentanyl analogues that were for sale in the illegal marketplace.⁵ Since this time, information about fentanyl as an active ingredient in fake OxyContin tablets and other powders has become widely available.

Recommended resources

- Know your source? Retrieved from www.knowyoursource.ca
- Canadian Community Epidemiology Network on Drug Use. (2015). CCENDU Bulletin: Deaths Involving Fentanyl in Canada (2009–2014) Ottawa, Ont.: Canadian Centre on Substance Abuse. Retrieved from www.ccsa.ca/Resource%20Library/CCSA-CCENDU-Fentanyl-Deaths-Canada-Bulletin-2015-en.pdf.
- Young, M. M., Pirie, T., Buxton, J. A., & Hosein, F. S. (2015). The rise of overdose deaths involving fentanyl and the value of early warning. *Canadian Journal of Addiction*, 6(3), 13–17. Retrieved from www.csam-smca.org/wpcontent/uploads/2016/01/CSAM-December2015.pdf

Fentanyl Analogues

Sometimes referred to as designer fentanyls or non-pharmaceutical fentanyls, these compounds include acetylfentanyl,⁶ butyrfentanyl and 3-methylfentanyl. All three have been detected in drug-related fatalities in Canada, although no specific numbers are available. In the United States, the Drug Enforcement Agency reported that there have been at least 52 confirmed fatalities involving acetylfentanyl between 2013 and 2015.⁷

A newer fentanyl, furanylfentanyl has appeared in Canada in the last six months. In the United States, since mid-December, at least seven deaths were caused, at least in part, by furanylfentanyl, according to toxicology tests results received this year.⁸ In March 2016, there was a report that furanylfentanyl might have been used as an active ingredient in heroin in Illinois, resulting in the death of a 30 year old male.⁹ Similar to fentanyl, the fentanyl analogues are noteworthy due to their toxicity, many being significantly more toxic than fentanyl.^{**}

[§] All chemical structures included in this bulletin come from the National Center for Biotechnology Information, PubChem Compound Database: pubchem.ncbi.nlm.nih.gov/. All resources were last accessed on June 2, 2016.

^{**} For the purposes of this bulletin, the terms toxicity and potency are used interchangeably as there is evidence that use of the term potency can increase interest in the substance. Though potency and toxicity are highly correlated, it is acknowledged that potency and toxicity are measured using different methods and can differ depending on the substance.



Recommended resources

• European Monitoring Centre for Drugs and Drug Addiction. (2015). *Fentanyl drug profile*. Retrieved from www.emcdda.europa.eu/publications/drug-profiles/fentanyl



Figure 2. Chemical structure of acetyl fentanyl (PubChem CID 527015 ; $C_{21}H_{26}N_{2}O)$

W-18



Figure 5. Chemical structure of W-18 (PubChem CID 13373555, 223436564; $C_{19}H_{20}\text{CIN}_3\text{O}_4\text{S})$

Figure 3. Chemical structure of butyrfentanyl (PubChem CID 621174; C₂₃H₃₀N₂O) Figure 4. Chemical structure of 3-methylfentanyl (PubChem CID 61996; $C_{23}H_{30}N_2O$)

W-18 was developed in 1981 at the University of Alberta as a possible analgesic drug. It is part of a class of compounds, W-1 to W-32, referred to as the W-series. Although W-18 is included in this bulletin on synthetic opioids, researchers have recently stated there is no evidence that it is an opioid.¹⁰,¹¹ As a precaution, however, and until the appropriate pharmacological testing has been conducted, W-18 should be considered a potentially dangerous analgesic that can be sold as an opioid or mixed in drugs that are claimed to be opioids.

The W-series compounds were patented by Edward Knaus, Brent Warren and Theodore Ondrus in 1984,¹² but were never pursued as pharmaceutical analgesics. There is little information available about W-18 and the other compounds in the series.¹³ Although there have been many reports about the potency and toxicity of W-18, lack of pharmacological data means that these reports are speculative. Based on the weak evidence in the patent, W-18 might be a potent analgesic that poses an unknown risk of overdose. However, there is no information

available that reliably describes the mechanism of action, or the potency or toxicity of W-18.14



On May 9, 2016, NMS Labs, a forensic toxicology testing laboratory in the United States, "confirmed W18 in two otherwise unrelated deaths in a Midwestern state. To the best of our knowledge, this is the first reported toxicological confirmation of deaths involving this drug."¹⁵ On May 20, the Office of the Chief Medical Examiner of Alberta issued a statement that W-18 was detected in a man who had died. However, because of the presence of other drugs, the Office could not confirm that W-18 was the cause of death.¹⁶

On June 1, 2016, the Government of Canada announced that it had, on the recommendations of Health Canada, published final amendments adding W-18 to Schedule 1 of the *Controlled Drugs and Substances Act* and Part I of the Schedule to Part J (Restricted Drugs) of the *Food and Drug Regulations*, rendering unauthorized activities such as its production, possession and trafficking illegal.¹⁷

Recommended resources

• ForensicToxGuy. (2016, April 24). What do we know about W-18? Retrieved from dosemakespoison.blogspot.ca/2016/04/what-do-we-know-about-w-18.html

AH-7921



AH-7921 is a synthetic opioid developed as a possible analgesic drug by the British pharmaceutical company Allen and Hanburys in 1974. AH-7921 is a μ -opioid receptor agonist and there have been no studies that have assessed its pharmacology in humans.¹⁸

As of 2015, 16 deaths have been associated with AH-7921 in Sweden, the United Kingdom, Norway and the United States.²⁰ AH-7921 has been associated with two deaths in Canada. However, in one case, although AH-7921 was detected, it was not considered to be the cause of death. The manner in which the substance was consumed intentionally, but inadvertently as an ingredient in a counterfeit pharmaceutical or inadvertently in powder form is not known.

Figure 6. Chemical structure of AH-7921 (PubChem CID 275055802; $C_{16}H_{22}CI_2N_2O$)

On June 1, 2016, the Government of Canada announced that it had, on the recommendations of Health Canada, published final amendments adding AH-7921 to Schedule 1 of the *Controlled Drugs and Substances Act* and Part I of the Schedule to Part J (Restricted Drugs) of the *Food and Drug Regulations*,

rendering unauthorized activities such as its production, possession and trafficking illegal. 17

Recommended resources

- Katselou, M., Papoutsis, I., Nikolaou, P., Spiliopoulou, C., & Athanaselis, S. (2015). AH-7921: the list of new psychoactive opioids is expanded. *Forensic Toxicolology*, 33(2), 195–201. Retrieved from www.ncbi.nlm.nih.gov/pmc/articles/PMC4525185/
- European Monitoring Centre for Drugs and Drug Addiction. (2014). EMCDDA-Europol Joint Report on a new psychoactive substance: AH-7921 3,4-dichloro-N-{[1-(dimethylamino)cyclohexyl]methyl}benzamide. Lisbon, Portugal: Author. Retrieved from www.emcdda.europa.eu/system/files/publications/816/AH-7921_465209.pdf

U-47700



Figure 6. Chemical structure of U-47700 (PubChem CID 223436571, 13544015; $C_{16}H_{22}Cl2N_2O$)

Recommended resources

MT-45

Another analgesic that has never been brought to market, U-47700 is a synthetic μ -opioid agonist that was developed in the 1970s by the pharmaceutical company Upjohn. It was derived from AH-7921. Its potency is estimated to be seven to eight times that of morphine. There are no published studies assessing the effects of U-47700 on humans.¹⁹

While there is at least one report indicating that this opioid has been detected in Canada, it has been suspected to have been involved in several deaths in the United States.⁴

- Cheney, B. V., Szmuszkovicz, J., Lahti, R. A., & Zichi, D. A. (1985). Factors affecting binding of trans-N-[2-(methylamino) cyclohexyl] benzamides at the primary morphine receptor. *Journal of Medicinal Chemistry*, 28(12), 1853–1864.
- Bluelight. (2014, November). 2014 Novel opioid, U-47700 [listserver message thread]. Retrieved from www.bluelight.org/vb/threads/739960-Novel-opioid-U-47700



Figure 7. 2D chemical structure of MT-45 (PubChem CID 431865; $C_{24}H_{32}N_2$)

MT-45 is a synthetic opioid patented in 1975 by the Japanese pharmaceutical company Dainippon Pharmaceutical.²⁰ There have been no human studies conducted to assess the pharmacological or behavioural effects of MT-45.^{21.} However, its potency for pain relief and withdrawal effects is estimated to be comparable to morphine and it has been associated with hearing loss among users.²². It is associated with at least 28 deaths in Sweden between 2013 and 2014 and two in the United States. We have not received any information about its presence in Canada.

On June 1, 2016, the Government of Canada announced that it had, on the recommendations of Health Canada, published final amendments adding MT-45 to Schedule 1 of the *Controlled Drugs and Substances Act* and Part I of the Schedule to Part J (Restricted Drugs) of the *Food and Drug Regulations*, rendering unauthorized activities such as its production, possession and trafficking illegal.¹⁷

Recommended resources

 Papsun, D., Krywanczyk, A., Vose, J.C., Bundock, E.A., & Logan, B.K. (2016). Analysis of MT-45, a novel synthetic opioid, in human whole blood by LC-MS-MS and its identification in a drug-related death. *Journal of Analytical Toxicology*, 40(4), 313–317.

Implications

The risks associated with any drug use is dramatically increased when people consume a tablet or powder they think is an opioid, but do not know:

- What psychoactive substance or substances are in it or their potency; or
- The quantity or dose of the substance or substances in it.

Some speculate²³ that the appearance of many novel synthetic opioids might be related to the scheduling of 116 compounds, including a number of fentanyl analogues, by the Chinese government in October 2015.²⁴ The implications of this trend for those working in public health and safety are discussed in the following sections.

Implications for Public Health and Harm Reduction

Communicating drug alerts among people who use drugs

The use of many and diverse active substances in counterfeit pharmaceuticals and other illicitly produced powders means that people using these products have little information about what or how much of the substance or substances they are taking, or their potency and toxicity. This places them at great risk of overdose. Information should be provided to people who use drugs (PWUDs) about what might be included in the tablets and powders they are consuming.

In 2015, Soukup-Baljak, Greer, Amlani, Sampson and Buxton conducted a series of focus groups with PWUDs.²⁵ Based on this research, they formulated guidelines to make drug alerts more effective:

- Flyers, posters or other advisories should avoid terms that might attract users, such as "potent," "strong" or "more powerful," which could inadvertently result in an increase in people seeking out the drug. Better alternatives are "toxic," "dangerous," or "lethal," terms that imply harm.
- Date information materials so that people know when something is a recent concern, not an ongoing issue.
- Include specific calls to action. If individuals decide to use substances regardless of the danger, advise them to:
 - Make a plan in case of overdose;
 - Make sure that someone with them is sober enough to call 911 if an overdose is suspected;
 - Use a small amount to start; and
 - If an overdose is suspected, perform rescue breathing, administer naloxone and call 911.
- Consider mentioning some of the signs of an overdose, so people know what to look out for:
- Early signs of opioid overdose include severe sleepiness; trouble breathing (can sound like laboured snoring); slow, shallow breathing; cold, clammy skin; and unresponsiveness to pain.
- An Ontario Harm Reduction Distribution Program poster communicates these signs.²⁶

Communicating the toxicity and potency of novel synthetic opioids

The inclusion of novel synthetic opioids in tablets and powders for sale in the illicit market raises several important considerations in communicating the risk of these substances. When describing the potency or toxicity of these synthetic opioids it is often asserted that these drugs are several times more toxic or potent than morphine.



In their pure form substances such as fentanyl and other synthetic opioids can be orders of magnitude more potent, and therefore possibly more toxic, than morphine. However, rarely do those purchasing these substances in the illicit market encounter them in their pure form. Instead, they purchase products mixed with bulking agents or diluents designed to increase the volume of the product without increasing the amount of active ingredient. However, clandestine labs or illicit pill pressing operations have difficulty distributing the active substance evenly across an entire batch of tablets or powders, particularly when the active dose is very small, as when using such potent substances as fentanyl. The result is an uneven distribution of active substance, while other tablets or powders might contain a small quantity of the active substance, while other tablets or powders might contain a lethal dose.

In media reports and other warnings aimed at PWUDs, this detail is often not communicated clearly. CCENDU partners working in harm reduction programs have anecdotal reports of people who, after consuming a fake OxyContin tablets containing fentanyl and not overdosing or experiencing a large subjective effect, dismiss media and public health warnings as nothing more than exaggeration or drug-related hysteria. Measured language should be used and it should be made clear that the variability of dose from one tablet or powder to the next increases the risk of overdose, not simply the potency or toxicity of the active substance.

(Information provided by CCENDU members.)

Implications for Emergency Response Services

The classic triad of respiratory depression, miosis or excessive constriction of the pupil, and decreased level of consciousness triggers an emergency physician or paramedic to think of an opioid overdose. Novel synthetic opioids are expected to induce this toxidrome or group of symptoms constituting the basis for a diagnosis of poisoning, just like regular opioids do, and so should be treated as any other opioid or sedative toxidrome. Although urine drug tests are not yet designed to detect many of the novel synthetic opioids, this gap does not affect the emergent and acute management of the opioid toxic patient as patients are treated based on their clinical presentation and not the result of a drug test.

Treatment focuses on supportive care with airway protection and respiratory assistance, and on ruling out co-ingestions. Naloxone can be administered to treat novel synthetic opioid overdoses, but up to six times the usual 0.4 mg intravenous dose might be required for fentanyl analogues or other synthetic opioids because of its greater toxicity compared with other opioids and the unpredictable amount of substance in each tablet.²⁷

Until new information becomes available, it is advised that the treatment of synthetic opioid-induced toxicity should not differ greatly from that for other opioid toxicity, except for the fact that higher or repeated doses of naloxone might be required to reverse the toxidrome. With the increasing availability of synthetic opioids, paramedics and emergency physicians might be seeing an increase in the frequency and the severity of opioid overdoses because PWUDs might not know what substances are in them, or what quantity they are consuming.

(Information provided by an emergency physician from The Ottawa Hospital and the Canadian Association of Emergency Physicians.)

Implications for Laboratories

To test for new opioids as they emerge, toxicology laboratories have to add the newest ones appearing on the market to their analytical methods. To do so and to confirm the identification of a specific compound, they require an analytical standard (i.e., a sample of the substance that is compared to the sample being tested). Although this requirement seems simple, laboratories face challenges:

• **Cost:** Constantly updating a laboratory's analytical methods is costly and many laboratories lack the time, budget, technology and so on to keep up with the changing environment.



- Availability and accessibility of analytical standards: Laboratories face difficulties getting standards for new drugs when the drugs are not commercially available. Further, laboratories often encounter bureaucratic hurdles (e.g., requesting import or purchase exemptions from Health Canada) and delays when trying to acquire analytical standards of illegal drugs.
- Detection challenges: The detection of some substances, such as fentanyl, can be challenging because their higher potency can make their effective dose much lower than common opioids. The blood or urine concentration might be too low to be detected. Based on estimates of analgesic potency from rodent studies, concentrations about 100 times less than for fentanyl might be expected for W-18.
- Screening for metabolites: The metabolism of many of these substances is unknown, so screening for metabolites could be problematic. Also, analytical standards might not exist for metabolites. If extensive metabolism has occurred, the detection of the parent drug could be unlikely. For instance, it is possible that W-18 undergoes extensive metabolism to the amino analogue and probably other pathways, making detection of the parent drug more difficult.

Because of these challenges, exposure to new substances should not be ruled out solely based on negative laboratory results.

(Information provided by the Chief Toxicologist, Office of the Chief Medical Examiner of Alberta, and CCENDU members.)

Implications for Poison Control Centres

Specialists in poison control centres and medical toxicologists are concerned about the increasing availability of synthetic opioids such as the fentanyl analogues and, more recently, the seizure of several other novel synthetic opioids. More specifically, the medical toxicology community is concerned that there is limited knowledge about the pharmacology of the new opioids and whether naloxone can reverse their toxic effects.

(Information provided by the Canadian Association of Poison Control Centres.)

Implications for Law Enforcement

Exposure to fentanyl and fentanyl analogs has resulted in hospitalization of law enforcement members in both Canada and the United States. As fentanyl can be absorbed through the skin, ensuring that personal protective equipment and environmental controls to prevent contamination are present is imperative to prevent accidental exposure during investigations. Because of the toxicity of the novel synthetic opioids, any risk of exposure should be immediately referred to trained emergency medical services. Law enforcement officers who encounter clandestine laboratories or pill pressing operations should contact officers trained to deal with clandestine laboratories or chemists from Health Canada's Drug Analysis Service chemists to prevent accidental exposure or contamination. The RCMP can provide guidelines for handling suspected fentanyl and other novel synthetic opioids along with risk assessment guidelines. Samples must be transported in compliance with Transportation of Dangerous Goods regulations to ensure any persons involved in the transport are not placed at risk. Potential exposure to any synthetic opioid can lead to respiratory suppression and possible loss of consciousness. Though the efficacy of naloxone has not been assessed for all the novel synthetic opioids, in theory it should temporarily interrupt the effects of accidental exposure and so should be administered. Further information about transporting or destroying novel synthetic opioids can be obtained from the RCMP's Clandestine Laboratory Enforcement and Response Teams or Health Canada's Drug Analysis Service.

(Information paraphrased from documents prepared for the RCMP and reproduced with their permission.)

CCENDU will continue to monitor the situation regarding novel synthetic opioids and other substances in counterfeit pharmaceuticals and other illicit street drugs in Canada. If you have any questions, comments, information to contribute or corrections to the information contained in this bulletin or wish to subscribe and receive updates as new information becomes available, please contact CCENDU@ccsa.ca.

For information on CCENDU and to read previous CCENDU Alerts and Bulletins, visit www.CCENDU.ca.

Prepared by the CCSA in partnership with the Canadian Community Epidemiology Network on Drug Use (CCENDU)

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⁵ Canadian Community Epidemiology Network on Drug Use. (2013). CCENDU Drug Alert: Illicit Fentanyl. Ottawa, Ont.: Canadian Centre on Substance Abuse.

⁶ World Health Organization. (2015). Acetylfentanyl. Critical Review Report. Agenda item 5.2. Expert Committee on Drug Dependence Thirty-seventh Meeting. Geneva, 16-20 November 2015. Retrieved June 2, 2016, from www.who.int/medicines/access/controlledsubstances/5.2_Acetylfentanyl_CRev.pdf

⁷ Drug Enforcement Administration. (2015). Acetyl fentanyl (N-(1-phenethylpiperidin-4-yl)-N-phenylacetamide). Retrieved June 2, 2016, from www.deadiversion.usdoj.gov/drug_chem_info/acetylfentanyl.pdf

⁸ Cook County Government. (2016, April 18). Medical Examiner Reports Deaths from Powerful Opioids on the Rise [Blog post]. Retrieved June 2, 2016, from www.cookcountyil.gov/2016/04/18/medical-examiner-reports-deaths-from-powerful-opioids-on-the-rise/

⁹ Will County Illinois. (2016). 2016 Accidental Overdoses. Retrieved June 2, 2016, from www.willcountyillinois.com/County-Offices/Judicial-Services/Coroner/2016-Overdose-Statistics

¹⁰ Fournier, A. (2016, May 24). Edmonton doctor warns dangers of W-18 are still a mystery. *CBC News*. Retrieved June 2, 2016, from www.cbc.ca/news/canada/edmonton/edmonton-doctor-warns-dangers-of-w-18-are-still-a-mystery-1.3596971

¹¹ Southwick, R. (2016, June 2). Health Canada defends its position on W-18 in the face of rebuke. *Calgary Herald*. Retrieved June 2, 2016, calgaryherald.com/news/local-news/health-canada-defends-its-position-on-w-18-in-the-face-of-rebuke

¹² Knaus, E. E., Warren, B. K., & Ondrus, T. A. (1984). U.S. Patent No. 399,994. Washington, DC: U.S. Patent and Trademark Office.
¹³ ForensicToxGuy. (2016, April 24). What do we know about W-18? [blog post]. Retrieved June 2, 2016, from dosemakespoison.blogspot.ca/2016/04/what-do-we-know-about-w-18.html

¹⁴ Southwick, R. (2016, June 1). Health Canada statements on W-18 misleading, potentially wrong, experts warn. *Calgary Herald*. Retrieved June 2, 2016, calgaryherald.com/news/local-news/health-canada-statements-on-w-18-misleading-potentially-wrong-experts-warn

¹⁵ Logan, B. (2016, May 9). W18 Confirmed in two fatalities in Illinois. Email communication to the National Drug Early Warning System (NDEWS) Network Listserv.

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