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August 14, 2017

To: All personnel In the EMS System for Metropolitan Oklahoma City and Tulsa

From: Jeffrey M. Goodloe, MD, NRP, FACEP, FAEMS, Medical Director

Re: Fentanyl exposure in the commission of public safety duties (EMS, Fire, Police)

There are many reports in the media about the potential dangers of fentanyl and its synthetic compounds (specifically, carfentanil). I will never take the personal safety of any EMS, Fire, or Police professional lightly. The work you do is critically important to the communities and citizens you serve and you always deserve to leave your shift safely, without medical illness or injury. Part of our medical oversight support is supplying you scientifically accurate information from highly credible sources.

Please find attached a medically evidence-based, carefully composed guidance document prepared by the United States' premier organizations in toxicology, the American College of Medical Toxicology and the American Academy of Clinical Toxicology. This document is the most evidence-based guidance available to date regarding fentanyl and synthetic fentanyl (for example, carfentanil) exposures that could be encountered in the commission of duties as an EMR, EMT, Advanced EMT, Paramedic, firefighter, and/or law enforcement officer. Its length should give you consideration of how detailed it has been designed to be. You will see at its conclusion many scientific studies cited in its creation.

Almost every media report of public safety professionals "nearly dying from fentanyl" that I have personally reviewed closely does not describe the symptoms associated with fentanyl or carfentanil, both opioid chemicals. Opioid chemicals in toxic amounts, as most of you are well aware, can and will cause drowsiness, lethargy, slowing of breathing, decreased amount of air movement with breathing, decreased heart rate (bradycardia), decreased pupil size in the eyes, and sometimes lowering of blood pressure (hypotension). Opioids do not cause agitation, anxiety, increasing of blood pressure (hypertension), increased heart rate (tachycardia), or air hunger. I encourage you if you do read any of these media reports about individual public safety professionals reportedly harmed by fentanyl or carfentanil to read the symptoms closely and better still, to look for actual outcomes, not subjective statements without evidence behind them. In no way am I ever saying that any of these public safety professionals involved in these media reports are purposefully spreading inaccurate information. They are most likely themselves dealing with incomplete information and you should considerably factor that reality.



You will find following my comments a news release from the National Association of EMS Physicians. This organization, comprised of EMS physician medical directors and EMS administrative and field professionals, does not endorse documents lightly. The attached guidance document has undergone thorough review. I would not share such otherwise.

I am pleased to report to you that as a representative of the American College of Emergency Physicians, I will be attending a key 2-day discussion on this very concern in Washington, DC in early September. A number of law enforcement organizations from the Department of Homeland Security and a number of first responder organizations (EMS, Fire, Police), including EMS physicians, will attend this meeting with a goal of reviewing and potentially developing further evidence-supported dialogue and resources for your safety. I will update you as those items become available.

Members of our Office of the Medical Director medical oversight team (Dr. Curtis Knoles, Assistant Medical Director; David Howerton, NRP, Director of Clinical Affairs - Western Division (metro OKC); Duffy McAnallen, NRP, Director of Clinical Affairs - Eastern Division (metro Tulsa) and I) are available collectively 24/7 to assist you real-time if you are worried about a suspected fentanyl or carfentanil related exposure. You can reach me directly via cell 918-704-3164 and I encourage you to program this into your cell for ease of access. Again, your safety matters and we are here to help protect you.

Dr. Goodloe

From: NAEMSP Executive Office [info-naemsp@naemsp.org]

## EMS PHYSICIANS ENDORSE TOXICOLOGY GROUPS' OPIOID SAFETY PRECAUTIONS GUIDANCE

### NAEMSP Votes to Support ACMT & AACT's Highly-Requested Guidance on Practical First Responder Opioid Safety Precautions

WASHINGTON, D.C. (August 9, 2017) - The National Association of EMS Physicians (NAEMSP) announces its endorsement of a new American College of Medical Toxicology (ACMT) and American Academy of Clinical Toxicology (AACT) document detailing pragmatic and actionable safety precautions for first responders in opioid overdose situations.

NAEMSP is an organization of physicians and other professionals partnering to provide leadership and foster excellence in the subspecialty of EMS medicine. In pursuing its mission to improve out-of-hospital emergency medical care, NAEMSP's Executive Board and Standards and Clinical Practice Committee voted unanimously to endorse the opioid safety guidance. This crucial document enables an appropriate and measured communication of risk, allowing first responders to understand their genuine risk of exposure and avoid unnecessary fear or over-preparing to a point where they're impaired in performing their job.

"NAEMSP wholly endorses this impressive and highly-anticipated document and we will share it with our members and build on it with actionable guides that will be available for free to the public," said Dr. Brent Myers, President of NAEMSP. "It's important that our community act upon the most recent and best quality evidence available to us right now, as well as to stay vigilant and prepared to revise our procedures and advise our members as we continue to develop knowledge about dangerous substances."

Over the last year, ACMT and AACT, two key U.S. toxicology organizations, developed the document to satisfy a remarkable surge of first responder requests for fact-based opioid response safety guidance. The influx of such requests stemmed from the opioid crisis' dramatic rise in impact and publicity, punctuated by potentially disputable accidental contact overdose reports, and the sincere desire of first responders to be able to balance protecting themselves while being able to render life-saving care to victims of this epidemic. The American Association of Poison Control Centers (AAPCC) also endorses the document, solidifying support from all three major U.S. toxicology associations.

"A practical, fact-based guidance helps first responders maintain a proportional response to high-stress situations, such as responding to an emergency fentanyl overdose," said Dr. Charles McKay, President of ACMT. "We really wanted to provide scientific data that would balance the risk of exposure with any undue concern that would prevent first responders from performing their jobs."

Committed to the safety of first responders, NAEMSP will continue to ensure its members are informed on all pertinent safety measures. The association's Standards & Clinical Practice Committee has organized a task force to assist NAEMSP members by enhancing this position statement with actionable "how-to" guides and additional circumstance-specific guidances, such as for air transport EMS.

## **ACMT and AACT Position Statement: Preventing Occupational Fentanyl and Fentanyl Analog Exposure to Emergency Responders**

The position of the American College of Medical Toxicology (ACMT) and American Academy of Clinical Toxicology (AACT), is as follows:

Fentanyl and its analogs are potent opioid receptor agonists, but the risk of clinically significant exposure to emergency responders is extremely low. To date, we have not seen reports of emergency responders developing signs or symptoms consistent with opioid toxicity from incidental contact with opioids. Incidental dermal absorption is unlikely to cause opioid toxicity. For routine handling of drug, nitrile gloves provide sufficient dermal protection. In exceptional circumstances where there are drug particles or droplets suspended in the air, an N95 respirator provides sufficient protection. Workers who may encounter fentanyl or fentanyl analogs should be trained to recognize the signs and symptoms of opioid intoxication, have naloxone readily available, and be trained to administer naloxone and provide active medical assistance. In the unlikely event of poisoning, naloxone should be administered to those with objective signs of hypoventilation or a depressed level of consciousness, and not for vague concerns such as dizziness or anxiety. In the absence of prolonged hypoxia, no persistent effects are expected following fentanyl or fentanyl analog exposures. Those with small subclinical exposures and those who awaken normally following naloxone administration will not experience long-term effects. While individual practitioners may differ, these are the positions of American College of Medical Toxicology and American Academy of Clinical Toxicology at the time written, after a review of the issue and scientific literature.

### **Background**

Fentanyl and fentanyl analogs are potent opioid receptor agonists. Fentanyl and its analogs are increasingly implicated in overdose and death in North America among illicit opioid users. The reported mortality from synthetic opioids rose 72.2% (to 9,850) from 2014 to 2015 [1]. Due to limitations in identifying analogs, this figure likely underrepresents death from these drugs. Fentanyl analogs are distributed in North America both as substituted/adulterated powdered heroin and pressed into counterfeit tablet forms of opioids and other medications [2-4]. Authorities in the United States have reported seizures of a variety of these products including fentanyl, fentanyl precursors (e.g., N-phenyl-1-(2-phenylethyl) piperidin-4-amine), and different fentanyl analogs such as acetylfentanyl, butyrylfentanyl, and furanylfentanyl [4]. Other analogs, such as alfentanil, remifentanil, and sufentanil, are used in clinical practice.

Fentanyl is 50-100 times more potent than morphine at the mu-opioid receptor [5-8]. Carfentanil, an opioid developed for veterinary use, is 10,000 times more potent than morphine in animals, although it produces less apnea when dosed therapeutically [6, 9]. Despite its improved therapeutic index compared to morphine, very small errors in carfentanil dosing not unexpected with illicitly distributed drugs will result in lethal doses. There are limited pharmacological data on other analogs found in the illicit drug supply.

To date, there has been limited guidance for emergency responders. In June 2016, DEA published a warning to law enforcement on the dangers of fentanyl cautioning against field testing suspected fentanyl and recommending the use of gloves and a mask when such testing is conducted [10].

The US National Institute for Occupational Safety and Health (NIOSH, Centers for Disease Control) published a bulletin addressing potential danger to law enforcement, public health workers, and first responders who may be exposed to fentanyl or its analogs [11]. Citing an absence of empirical evidence, the NIOSH bulletin recommended use of a P100-rated respirator, nitrile gloves, and eye protection. For personnel performing tasks that may aerosolize fentanyl, the NIOSH bulletin recommended dermal protection such as coveralls or protective sleeves.

Given the prevalence of synthetic opioids, law enforcement and emergency medical services (EMS) agencies have become increasingly concerned about potential exposures while responding to medical calls, crime scenes, or during drug raids [10, 12, 13]. Reports of emergency responders developing symptoms after contact with these substances have described nonspecific findings such as “dizziness” or “feeling like body shutting down”, “dying” without objective signs of opioid toxicity such as respiratory depression [10]. Law enforcement and EMS must balance safety with mobility and efficiency when entering and securing potential scenes where drugs are used, distributed, or produced. We aim to address the risks of occupational exposures to ultra-potent opioids and the role of various types of personal protective equipment to reduce those risks.

## **Methodology**

Our initial recommendations are based on the opinion and clinical experience of a task force of our members. In addition, the authors performed a literature search and drafted this position statement. This document was reviewed and approved by the ACMT Position Statement and Guidelines Committee, was sent to the ACMT Board of Directors, and then sent to the entire College membership for review. After revision by the task force, final approval was made by the ACMT Board of Directors and AACT Board of Trustees.

## **Inhalation Exposure Risk for Fentanyl and Fentanyl Analogs**

Inhalation is an exposure route of concern if drug particles are suspended in the air. Fentanyl has potentially high bioavailability (12-100%) by inhalation [14, 15]. It is highly suspected that a weaponized aerosolized containing carfentanil and remifentanil were used to subdue hostage-takers of a Moscow theater in 2002. One hundred and twenty-five died as a result of this weaponized aerosolized exposure [16]. Although an optimized airborne dispersal device is unlikely to be encountered in a local event, we considered such a scenario for respiratory protection.

Industrial producers of fentanyl use time-weighted average occupational exposure limits (OEL-TWA) for alfentanil (1 mcg/m<sup>3</sup>), fentanyl (0.1 mcg/m<sup>3</sup>), and sufentanil (0.032 mcg/m<sup>3</sup>) to limit exposure [17]. At the highest airborne concentration encountered by workers, an unprotected individual would require nearly 200 minutes of exposure to reach a dose of 100 mcg of fentanyl.

The vapor pressure of fentanyl is very low ( $4.6 \times 10^{-6}$  Pa) suggesting that evaporation of standing product into a gaseous phase is not a practical concern [18].

## **Dermal Exposure Risk for Fentanyl and Fentanyl Analogs**

Fentanyl is amenable to transdermal absorption because of its low molecular weight and lipophilicity [19, 20]. Depending on the specific product, transdermal delivery systems (“patches”) take 3-13 hours to produce a therapeutic serum fentanyl concentration and 35 hours to reach peak concentration [21-24]. Absorption of liquid or aqueous fentanyl increases with larger surface area of application, duration of application, broken skin, and heat. The physical properties of fentanyl analogs are similar to fentanyl, suggesting potential for dermal absorption. In a small volunteer study, sufentanil citrate applied to the forearm and covered in an occlusive dressing was absorbed comparably to fentanyl, although exact bioavailability was not determined [25].

However, incidental dermal absorption is unlikely to cause opioid toxicity. If bilateral palmar surfaces were covered with fentanyl patches, it would take approximately 14 minutes to receive 100 mcg of fentanyl [using a body surface area of 17,000 cm<sup>2</sup>, palm surface area of 0.5% [26], and fentanyl absorption of 2.5 mcg/cm<sup>2</sup>/h [24]. This extreme example illustrates that even a high dose of fentanyl prepared for transdermal administration cannot rapidly deliver a high dose.

The above calculation is based on fentanyl patch data, which overestimates the potential exposure from drug in tablet or powder form in several ways. Drug must have sufficient surface area and moisture to be efficiently absorbed. Medicinal transdermal fentanyl utilizes a matrix designed to optimize delivery, whereas tablets and powder require dissolution for absorption. Relatedly, powdered drug sits on the skin, whereas patches have adhesive to hold drug in close proximity to the skin allowing both to remain moist. Finally, the above quoted figure 2.5 mcg/cm<sup>2</sup>/h represents delivery at steady state after drug has penetrated the dermis, which overestimates the amount of absorption in the first few minutes of dermal exposure. This initial period is of most relevance in unintentional exposure, because fentanyl that is observed on skin can be rapidly removed by mechanical (brushing) means or cleansing with water. Therefore, based on our current understanding of the absorption of fentanyl and its analogs, it is very unlikely that small, unintentional skin exposures to tablets or powder would cause significant opioid toxicity, and if toxicity were to occur it would not develop rapidly, allowing time for removal.

### **Ocular-Facial Exposure Risk for Fentanyl and Fentanyl Analogs**

Mucous membranes present opportunity for absorption of fentanyl and its analogs. Fentanyl, for example, exhibits greater than 30-fold absorption across mucous membranes when compared to skin, and is available in a formulation that utilizes transmucosal administration [27]. A healthy male veterinarian was splashed in the eyes and mouth with contents of a dart containing 1.5 mg of carfentanil and 50 mg xylazine. Despite immediately washing his face with water, he became drowsy within two minutes; he responded promptly to the administration of naloxone [28]. It is not clear to what extent these effects were a result of carfentanil exposure. Although facial contact with liquid or powder opioids is unlikely, OSHA rated splash protection would be sufficient to prevent mucous membrane exposure.

### **Naloxone**

Naloxone, a mu-opioid receptor antagonist, administered by parenteral, or intranasal routes, reverses opioid-related respiratory depression. The effective dose of naloxone depends on the patient's weight, amount of opioid to be reversed, and relative binding affinities at the mu receptor [8, 29]. There is scant information on human and animal naloxone reversal of fentanyl analogs. Despite anecdotal reports that higher-than-usual doses may be necessary [30], animal data suggest that standard doses of naloxone should be sufficient to reverse carfentanil [31]. While a detailed discussion of dosing and administration of naloxone is beyond the scope of this guideline, if a patient does not respond to 10 mg of naloxone, it is unlikely additional naloxone will be of value [29]. For patients who are hypoventilating and unresponsive to initial doses of naloxone, promptly assisting ventilation and oxygenation are recommended.

### **Recommendations**

The American College of Medical Toxicology and American Academy of Clinical Toxicology recognize the challenges in issuing recommendations where available data are incomplete. We believe that recommendations should be protective of emergency responders, but not result in unnecessary delays in care to patients with time-sensitive conditions. We also recognize that PPE can interfere with task performance by emergency responders and law enforcement officials. Due to the limited available data, the following recommendations primarily represent consensus expert opinion.

The position of ACMT and AACT, is as follows:

#### **General Precautions and Management of Exposure**

- Workers who may encounter fentanyl or fentanyl analogs should be trained to recognize the symptoms and objective signs of opioid intoxication, have naloxone readily available, and be trained to administer naloxone.
- For opioid toxicity to occur the drug must enter the blood and brain from the environment. Toxicity cannot occur from simply being in proximity to the drug.

- Toxicity may occur in canines utilized to detect drug. The risks are not equivalent to those in humans given the distinct contact that dogs, and not humans, have with the local environment.

#### Dermal precautions

- For routine handling of these drugs, nitrile gloves provide sufficient protection.
- In situations where an enclosed space is heavily contaminated with a potential highly potent opioid, water resistant coveralls should be worn.
- Incidental dermal exposures should immediately be washed with copious amounts of water. Alcohol based hand sanitizers should not be used for decontamination as they do not wash opioids off the skin and may increase dermal drug absorption.

#### Respiratory precautions

- In the unusual circumstance of significant airborne suspension of powdered opioids, a properly fitted N95 respirator or P100 mask is likely to provide reasonable respiratory protection.

#### Mucous Membrane/Splash Exposure

- OSHA-approved protection for eyes and face should be used during tasks where there exists possibility of splash to the face.

#### Naloxone Administration and Airway Management

- Naloxone should be administered to those with objective signs of hypoventilation from opioid intoxication.
- If hypoventilation persists following initial naloxone dose and personnel with advanced airway training are not available, repeat naloxone until reversal is seen or 10 mg is administered.
- Personnel with advanced airway training should provide airway support for patients who are in extremis or those who do not improve with naloxone.

#### Long-term Sequelae of Exposure

- In the absence of prolonged hypoxia, no persistent effects are expected following fentanyl or fentanyl analog exposures. Those with small subclinical exposures and those who awaken normally following naloxone administration will not experience long-term effects.

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