

FACT SHEET – OPIOIDS & OPERATIONAL K9S

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THE PROBLEM

The increasing prevalence of using potent opioids (e.g. fentanyl, carfentanil) for illicit drug manufacturing poses a life-threatening hazard to law enforcement (LE) and first responders (e.g. EMS, Fire and Rescue) that may unknowingly come into contact with these drugs during the course of their routine, daily activities. Similarly, Operational K9s (OpK9s) of all disciplines i.e. detection (drug, explosive, accelerant), patrol, tracking, Search and Rescue, and others remain at risk for accidental illicit opioid exposure. The most immediate and life threatening adverse effect of an accidental opioid exposure is marked respiratory depression (slow, shallow breathing) or complete cessation of voluntary breathing (respiratory arrest). This informational fact sheet will describe the potential risks of opioid exposure and the use of naloxone as it pertains to the OpK9.

WHICH OPIOIDS ARE INVOLVED?

Although heroin is the prototypical manufactured illicit opioid known by society, all types of prescription and non-prescription opioids (natural, semi-synthetic, and synthetic) are being manufactured and sold for illicit, recreational use. The diversion of pharmaceutical fentanyl along with the clandestine manufacturing of illicit fentanyl and fentanyl-related substances (e.g. carfentanil, 4-Fluorobutyrylfentanyl, furanylfentanyl, acrylfentanyl, and 3-methylfentanyl, etc.) has dramatically increased over the past few years. These compounds are used in place of or to adulterate (“cut”) other illicit substances (e.g. heroin, methamphetamines, cocaine, etc.) as well as to produce counterfeit prescription tablets of other semi-synthetic opioids (oxycodone, hydrocodone, and others). It is impossible to know in the field what exact compound(s) make up these illicit drug cocktails without performing Gas Chromatography/ Mass Spectrometry (GC/MS) in a forensic laboratory. In fact, most drug users and sellers are completely unaware that their substance/product may contain fentanyl or fentanyl-related substances.

WHAT ARE OPIOIDS?

Opioids are a class of naturally-occurring, semi-synthetic and synthetic drugs that include the illegal drug heroin as well as prescription drugs such as fentanyl, morphine, methadone, oxycodone, oxycontin, hydrocodone, hydromorphone, codeine, and many others. Opium is the archetypal natural compound for which all medicinal and illicit opioid drugs are either derived from or synthesized to mimic.

- *Opium alkaloids*: Morphine, thebaine and codeine are the major psychoactive, naturally-occurring alkaloids derived directly from the sap of the opium poppy plant.
- *Semi-synthetic opioids*: Medicinal drugs produced by combining an opium alkaloid with a synthetic compound. These include drugs such as hydromorphone, oxymorphone, hydrocodone, oxycodone.
- *Synthetic opioids*: Purely synthetic opioid drugs (e.g. fentanyl, fentanyl analogues, oxycontin, the U-series opioids, methadone, and others) are synthesized in a laboratory setting solely from chemicals (no natural compounds).
- *Narcotic*: Drugs or agents that produce insensibility or state of stupor, drowsiness, or unconsciousness (i.e. narcosis). This term is applicable to any illicit (heroin, cocaine, cannabis) or controlled psychoactive drug (e.g. opioids).

OPIOID RECEPTOR (OR) PHYSIOLOGY

Opioids are *agonist* drugs (bind to and elicit a pharmacodynamic or physiological response) for opioid receptors (OR) located throughout the body. The three main ORs include: mu (μ), kappa (κ), and delta (δ). The psychoactive effects of opioids result primarily from their binding and activation of **mu (μ) opioid receptors** (MOP) located on nerve cells scattered throughout the brain. MOP receptors are also located in other parts of the body such as the spinal cord and digestive tract. Activation of MOP receptors by opioid agonist drugs primarily results in analgesia (pain relief); however, their activation also produces sedation, euphoria, respiratory depression, bradycardia (slow heart rate), nausea, vomiting and decreased digestive motility.

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LEGITIMATE AND ILLICIT USE OF OPIOIDS

For centuries, opium had been used for its euphoric, analgesic, and anti-anxiety effects. Legitimately, opioids are primarily prescribed for acute and chronic pain management as well as perioperative anesthesia. When taken or administered as prescribed by a licensed medical or veterinary professional, opioids are considered a relatively safe and warranted medical treatment. Illicitly, people use opioids for their psychoactive euphoric effects and ability to cause an intense “high”. Both the legitimate and illicit use of opioids have led to the development of physical dependence and addiction. Carfentanil, one of the most potent commercially available synthetic opioids, has recently entered the illicit drug market; legally, it is prescribed for sedating large zoo animals (e.g. elephants). A myriad of novel synthetic opioids (e.g. W-series opioids, MT-45, AH-7921, U-47700) also continue to come in to the illicit drug trade. Many of these novel drugs have been associated with opioid-induced deaths in people. Since many of these novel synthetic opioids never reached the human market, the potency and potential adverse effects of these agents remains completely unknown in people and OpK9s. As such, the unregulated production and sale of these novel synthetic opioids represents a significant health risk to first responders and OpK9s.

COMPARATIVE POTENCY

Potency is the amount [concentration or dose (mg/kg, mcg/kg)] of drug required to produce an effect of given intensity. In a weight to weight comparison to the natural opiate morphine the following are reported comparative potencies:

- **Heroin** is 2 to 4 times as potent as morphine.
- **Fentanyl** is about 50 – 100 times more potent than morphine, and 30 – 50 times more potent than heroin. As little as **two milligrams (2,000 micrograms)**, about the size of 5 grains of salt, can cause adverse health effects and possible overdose.
- **Carfentanil** is 10,000 times more potent than morphine, and about 100 times more potent than fentanyl.

IMPORTANT NOTE: The above comparative potencies apply to drugs found in their purest form and when manufactured at their highest quality. Very rarely are illicit street drugs found in their purest form, instead, they are often ‘cut’ or laced with other drugs or compounds. Variations in the origin and quality of raw materials as well as processing methodologies used in clandestine drug laboratories also significantly influences the quality of the end-product. As such, the potency and clinical effects of illicitly manufactured opioids encountered in the field may vary greatly depending upon the purity and quality of the compound encountered. Novel synthetic opioids present a great risk to public health. The pharmacokinetics and pharmacodynamics of many of these novel compounds have not been evaluated in people or canines, therefore, estimates of their relative potency in humans or canines remains completely uncertain.

ROUTES OF EXPOSURE:

Illicit opioids are found as powders, liquids, nasal sprays, and pills. Accidental illicit opioid encounters in the field typically involve exposures to a dry powdered form of the drug; however, more recent evidence demonstrates an upsurge in trafficking of highly concentrated liquid opioid compounds. Powders possess a particulate size ranging from 0.2 to 2.0 mm; therefore, powders are easily aerosolized when disturbed (e.g. “burping” containers of potential narcotics or “brushing” powdered residues from surfaces or off an OpK9 hair coat).

Similar to people, unintentional exposure to opioids in OpK9s occur via one or more of the following routes: **inhalation, skin contact (transdermal), oral ingestion**, and / or **contact with a mucous membrane** (eyes, nose, gums).

- **Inhalation exposure**, via breathing in drug molecules through the mouth or nose, is probably the most significant exposure route for an OpK9. Drug absorption via this route may occur across the surface of the nasal cavity (intranasal) and / or across the alveolar barrier (intrapulmonary).
- **Transdermal exposure** is not expected to cause significant toxicity risk unless the integrity of the skin barrier is compromised (e.g. abrasion, cut, other open wound). The K9’s hair coat provides a protective barrier, particularly, when exposed to a powder or other non-liquid. When an OpK9 shakes or brushes up against surrounding objects, then any powder on their hair coat may disperse into the air presenting an inhalation risk to any person or K9 within the immediate vicinity. K9s lack functional sweat glands dispersed throughout their body (K9s don’t perspire). Although functional sweat glands are located in their paw pads, these glands represent a minutely small proportion of the OpK9’s total body surface; therefore, they are not considered to present a significant exposure risk.

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- **Oral ingestion** is considered a low exposure risk for OpK9s. Most opioids have a very low oral bioavailability; only 20 – 30% of the ingested opioid is absorbed into the K9’s systemic circulation. Oral transmucosal (OTM) or absorption across the surface of the gums may also serve as an exposure route. OTM absorption depends upon: the compounds’ pH (acid-base balance), formulation (solid vs. liquid), and the dwell time the drug resides within the buccal (cheek) pouch. Interestingly, the pH of canine saliva is highly variable resulting in highly variable OTM absorption of various drugs.
- Dissimilar to people, exposure through a **needle stick** is an unlikely contact route for an OpK9.

IMPORTANT

- **HIGH** risk of toxicity exists for **anyone** (handler, first responder, veterinary staff) handling an exposed OpK9.
 - Opk9s covered in an illicit drug powder present a high risk for **inhalational exposure** and **cross-contamination** to personnel and other K9s located within the immediate vicinity.
 - Cross contamination occurs through:
 - **Direct contact** with the contaminated OpK9
 - **Dispersion** of the powder into the air [K9 shakes or brushes up against surrounding objects (to include people)].
- ALL** personnel involved with an exposed OpK9 **MUST DON** appropriate Personal Protective Equipment

CLINICAL SIGNS OF OPIOID TOXICITY IN OPK9S

The following concepts influence an OpK9’s relative risk for succumbing to Opioid Toxicity:

1. Opioids have a dose-dependent effect for invoking a physiological response (e.g. the greater amount of drug absorbed into the circulation, equates to greater manifestation of clinical effects).
2. Canines tend to have a higher tolerance (**less susceptible**) to opioid-induced respiratory depression as compared to humans. In other words, K9s require a greater exposure (weight-based) to opioids in order to induce the same clinical manifestation seen in a human at a significantly lower dose.

Clinical signs of opioid overdose in K9s include:

- **Dysphoria (vocalizing, agitation, appearing frantic, etc.)** - may be an early indicator of exposure.
- **Low heart rate (bradycardia)** [less than 50 beats per minute]
- **Low blood pressure (hypotension)** [< 90 mm Hg systolic BP and/or < 60 mm Hg Mean BP]
- **Pin-point pupils (miosis)**
- **Hypothermia** (body temperature < 97°F)
- **Progressive respiratory depression and hypoventilation** (slow to absent breathing)
- **Altered mental status** (continuum of mild sedation to comatose).

NALOXONE – WHAT IS IT?

Naloxone is the drug of choice for treating people and animals suffering from an opioid overdose or toxicity. Commonly known as the “antidote” or “reversal agent” for opioid overdoses, naloxone is a *competitive antagonist* for ORs. As an antagonist drug, naloxone competes for the same OR (mu, delta, kappa) sites that the opioid agonists (heroin, fentanyl, oxycodone) bind too, however, when bound to the receptor, naloxone does not activate the OR; therefore, it produces no pharmacodynamic or clinical effect. Due to its competitive nature for the OR, naloxone may either displace (‘kick off’) an already bound opioid agonist from the OR or block an opioid agonist from binding to an OR in the first place.

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NALOXONE VERSUS NARCAN®

Naloxone hydrochloride, or simply naloxone, is the *common* (or *generic*) drug name. Narcan® is a *brand* or *trade* name for naloxone that is specific to the manufacturer and protected by registered or trademark rights; therefore, naloxone hydrochloride is the main ingredient in Narcan®.

NALOXONE – THE FACTS

Naloxone has as a significantly shorter half-life (shorter duration of action) than many of the opioid agonists it is used to reverse. Clinically affected OpK9s are likely to require repeated doses of naloxone during transport to a Veterinary Hospital; particularly, if carfentanil is the culprit drug.

Routes of administration for naloxone include: intravenous (IV), intraosseous or into the bone marrow (IO), intramuscular (IM), intranasal (IN) and subcutaneous (SC).

- IV and IO administration result in direct injection of naloxone into the blood stream and, therefore, are the preferred routes for administration;
- Intramuscular and IN administration have a relatively high absorption rate into the blood stream; both routes have successfully reversed narcotic overdoses in people and K9s. A recent DHS-funded study evaluating K9s receiving 0.3 mg fentanyl IV demonstrated that IM and IN naloxone administration provided immediate and effective ‘reversal’ of clinical signs associated with fentanyl administration.
- One small study evaluating the pharmacokinetics of an IN naloxone spray (8mg/100uL) in healthy canines reported a bioavailability of 87.88%.
- In humans, reported bioavailability of oral ingested naloxone is $\leq 2\%$ while per rectum (PR) is only 15%. No data is currently available evaluating the effectiveness of PR nor oral or oral transmucosal naloxone.

Intranasal naloxone is available to administer via:

- Non-FDA approved injectable formulation of naloxone administered through a nasal atomizer device
- Commercialized naloxone nasal spray (Narcan®, <https://www.narcan.com/>)

DOES NALOXONE WORK FOR DRUG OVERDOSES OTHER THAN OPIOIDS?

Naloxone only reverses the effects of opioids (e.g. heroin, methadone, morphine, opium, codeine, hydrocodone, fentanyl, carfentanil, others). It does not reverse the effect of other classes of narcotic drugs [e.g. marijuana, benzodiazepines (diazepam, midazolam, or alprazolam), barbiturates (phenobarbital) or stimulants (cocaine, methamphetamines)].

ARE THERE ADVERSE EFFECTS IN ADMINISTERING NALOXONE TO K9S?

Naloxone has a very wide margin of safety in K9s and is considered a relatively ‘safe’ intervention for treating opioid overdose. Administering the recommended dosages of naloxone (even when repeated based upon clinical signs) is very unlikely to result in any adverse effects. Some IN naloxone sprays distributed for humans contain a 4 mg naloxone dose. Although this is higher than the typically recommended naloxone dose for OpK9s weighing 30 kg or less, a DHS funded study demonstrated that a 4 mg dose of naloxone was safe and effective in reversing clinical signs associated with IV fentanyl administration in K9s.

Many illicit drug compounds are comprised of opioids mixed with other drugs (e.g. cocaine, methamphetamines, etc.). Even during situations when it is uncertain whether an OpK9’s clinical signs are the result of an opioid overdose or another illicit drug compound, it will not hurt to administer naloxone; worst case scenario, administering naloxone will have no effect, best case scenario it will save a life. **WHEN IN DOUBT ADMINISTER NALOXONE.**

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TREATMENT OF OPIOID OVERDOSE IN OPERATIONAL K9S

- **Activate EMS response system, perform a scene survey and ensure scene safety:**
 - Avoid self-exposure to opioids and cross-contamination while handling the OpK9.
 - Take appropriate Personal Protection Actions and don PPE (nitrile gloves, N-95 dust mask, eye protection, paper coveralls, and shoe covers, etc.).
- **After addressing the immediate health needs of any exposed humans at the scene, then consider providing care for any exposed OpK9s using the recommendations below.**
- **Contact one of the following for Emergency Veterinary Care Consultation:**
 - Primary veterinarian's or local 24/7 emergency veterinary hospital phone number
 - ASPCA Animal Poison Control Center (APCC): 1-888-426-4435
 - Pet Poison Hotline (PPH): 1-855-764-7661
- **Support ABC's (establish patent airway, support ventilation, provide oxygen supplementation as needed, initiate CPR if in cardiac arrest):**
 - **If rescue breathing is warranted, AVOID 'mouth-to-snout'**. Instead, use a BVM with a canine specific face mask.
 - OpK9s with no pulse may be in cardiac arrest or may have an undetected weak or slow pulse. Manage as cardiac arrest patients. See *Recommended Internet Resources* for veterinary CPR guidelines.
- **When feasible, thoroughly wash powder or agent off of OpK9s hair coat and skin.**
 - **Avoid interventions that may enhance transdermal absorption (e.g. alcohol-based hand sanitizers, alcohol, warm to hot water, etc.).**
 - After washing drug/agent off OpK9, take actions to dry and keep the OpK9 warm (cover with blanket, sheet).
 - If washing the K9 is not feasible, then consider wrapping the OpK9 in a sheet, blanket or other similar material to mitigate dispersion of powder off the OpK9's hair coat.
- **Administer naloxone (see dose recommendations listed below) when there is a known or highly suspect risk of exposure, and the OpK9 is displaying clinical signs such as:**
 - **Unresponsive or altered mental status**
 - Slow or absent breathing or gasping breaths
 - Slow (< 50 bpm) heart/pulse rate and weak femoral pulse quality
 - Weakness or staggering
 - Pinpoint pupils
 - Dysphoria (vocalizing, agitation, appearing frantic, etc.) may be an early indicator of exposure.

When in doubt, administer naloxone.

- **Repeat naloxone as needed**
- **Seek immediate veterinary medical attention even if OpK9 responds to naloxone administration.**

WARNING:

After administering naloxone, expect the OpK9 to rapidly "awaken" from their state of drug-induced stupor; however, they may still be disoriented and be in a 'protective/defensive' mode.

- OpK9s may want to bite/attack anything in their immediate vicinity, to include their handler.
- OpK9s should be properly restrained +/- have an open basket muzzle secured in place prior to, or immediately after, administering naloxone.

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RECOMMENDED K9 NALOXONE DOSING:

Routes

- **Intravenous (IV) / Intraosseous (IO):** 0.01 to 0.04 mg/kg [**2 mg per 25 kg (55 lbs)**]
- **Intramuscular (IM):** 0.04 to 0.16 mg/kg [**2 to 4 mg per 25 kg (55 lbs)**]
- **Intranasal (IN):** **2 to 4 mg per 25 kg (55 lbs)**
- **Oral Transmucosal (OTM) (buccal pouch):** Use IN dosing recommendations. Consider as a last resort if no other route is available (e.g. cannot establish IV/IO access and IM or IN administration unavailable [blocked nasal cavity, excess nasal discharge, etc.]).
- **Repeat** as needed to effect.
- **Two doses** are most likely required as the duration of action of naloxone is often much shorter than that of the opioid it is being used to antagonize. Some exposures require 5 - 10x the typical dose of naloxone.

Onset of Action:

- **IV/IO:** rapid onset of action, usually within 1-2 minutes.
- **IM/IN:** onset of action within 5 minutes

Duration of action: 45-90 minutes, may last longer.

PREPARATION AND PREVENTATIVE MEASURES FOR OPK9 HANDLERS

1. Have appropriate Personal Protective Equipment on hand at all times

- a. The Interagency Board's "*Recommendations on Selection and Use of Personal Protective Equipment and Decontamination Products for First Responders Against Exposure Hazards to Synthetic Opioids, Including Fentanyl and Fentanyl Analogues*" (free downloadable .pdf at <https://www.interagencyboard.org/>).

2. Perform an OpK9 Medical Threat Assessment before training events and real-world missions:

- a. Identify local veterinary resources available in the area of operations.
 - i. Hours of operations
 - ii. Staffing resources
 - iii. Establish line of communications and rapport
- b. Identify evacuation and transport routes.
- c. Identify logistical evacuation assets (vehicle, air ambulance, etc.).

3. Receive training in the following:

- a. Identifying opioid toxicity in OpK9s,
- b. Proper use and administration of naloxone,
- c. Basic K9 life support measures (e.g. rescue breathing with BVM, Chest compressions, etc.).

4. Keep important veterinary contact information on hand:

- Primary veterinarian's or local 24/7 emergency veterinary hospital phone number
- ASPCA Animal Poison Control Center (APCC): 1-888-426-4435
- Pet Poison Hotline (PPH): 1-855-764-7661

NOTE: A nominal one-time fee may be charged when calling the above APCC and PPH helplines.

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