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 (oxycodeone, 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, oxycodeone, oxycodone, hydrocodeone, 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, hydrocodeone, oxycodone.
- *Synthetic opioids*: Purely synthetic opioid drugs (e.g. fentanyl, fentanyl analogues, oxycodone, 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.
**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.
- **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 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.
**FACT SHEET – OPIOIDS & OPERATIONAL K9S**

- **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) / Buccal** 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.

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**IMPORTANT**

- The **HIGHEST** 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**

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**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 Q&A:

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 to; 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.

IMPORTANT: Naloxone has as a significantly shorter half-life (shorter duration of action) then 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.

NALOXONE VERSUS NARCAN®

Naloxone hydrochloride (HCL), 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 HCL is the main ingredient in the product Narcan®.

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 WITH 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 in OpK9s.

- Some IN naloxone products distributed for human use provide a single standardized 4 mg dose of naloxone per application; this is higher than the dose typically cited in the veterinary literature for K9s weighing 30 kg or less. Safety studies evaluating intravenous naloxone in canines revealed no demonstrable adverse effects with doses as high as 5 mg/kg. A DHS funded study (ref. HSHQDC-17-P-00112) recently demonstrated that 4 mg naloxone, administered intra-muscular or intranasal, was safe and effective in reversing clinical signs associated with IV fentanyl administration in K9s.

- Since OpK9s are not chronic opioid abusers, acute withdrawal syndrome that occurs in some people with abrupt cessation of opioid use is not an expected complication in the exposed and treated OpK9 patient.

- 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.
WHAT IS THE BEST ROUTE TO ADMINISTER NALOXONE?

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

- **Intravenous (IV) / Intraosseous (IO):**
  - **Advantage:** Direct injection of naloxone into the blood stream results in 100% bioavailability with the most rapid onset of action; when feasible, the IV and IO routes are the preferred routes for naloxone administration.
  - **Disadvantage:** Requires user to possess the training, skill proficiency and resources to administer the drug IV or to place an IV or IO catheter to facilitate administration. Time required to gain IV or IO access delays naloxone administration. Presents a needle stick hazard to the user.

- **Intramuscular (IM):**
  - **Advantage:** Possesses a relatively high absorption rate into the blood stream (bioavailability); successfully used to reverse opioid overdoses in people and K9s.
  - **Disadvantage:** Requires user to have the training, skill proficiency, and resources to administer IM. Presents a needle stick hazard to the user.

- **Intranasal (IN):**
  - **Advantage:** Possesses a relatively high absorption rate into the blood stream (bioavailability). Rapid acting. Eliminates needle stick hazard to the user. One study evaluating the pharmacokinetics of an IN naloxone spray (8mg/100uL) in healthy canines reported a bioavailability of 87.88%. A recent DHS-funded study in K9s demonstrated that 4 mg of naloxone administered either IM or IN (Narcan®) provided immediate and effective ‘reversal’ of clinical signs associated with intravenous administration of 0.3 mg fentanyl within 1 – 5 minutes. (Essler JL, et al. *Animals*, 2019)
  - **Disadvantage:** Abnormalities in nasal physiology (e.g. intranasal damage caused nasal trauma, the presence of excessive nasal mucus or other diseases involving the K9’s nasal cavity may impact the absorption and bioavailability of naloxone administered IN; Due to a lower bioavailability as compared to IV, IO or IM routes, IN naloxone may require higher doses to achieve similar results. (Barr et al.)
  - Pending the K9’s nasal conformation, the Narcan® nasal application may not fully seat into the nostril (See Figure 4).

- **Subcutaneous (SC):**
  - **Advantage:** Provides an alternative to IV, IO or IM administration that requires less user-skill and training to perform.
  - **Disadvantage:** Lower bioavailability, slower rate of absorption and slower onset of action as compared to other routes for administration. Although less technical than IV, IO or IM, it still requires user to have the training, experience and resources for administering a SC injection in a K9. Presents a needle stick hazard; Due to a lower bioavailability as compared to IV/IO or IM routes, SC naloxone may require higher doses to achieve similar results.

- **Per Rectum or Oral administration:**
  - Naloxone undergoes extensive first pass metabolism in the liver when administered orally, therefore, rendering much of the drug inactive prior to reaching the bloodstream.
  - In humans, reported bioavailability of oral ingested naloxone is ≤ 2% while per rectum (PR) is only 15%. No data is currently available evaluating the effectiveness of PR nor oral or oral transmucosal naloxone.
  - Neither are currently recommended as a route for naloxone administration in K9s.
**WHAT NALOXONE PRODUCTS ARE AVAILABLE ON THE MARKET?**

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>INJECTABLE</th>
<th>INJECTABLE CARPUJECT OR INTRANASAL (w/ M.A.D)</th>
<th>COMMERCIAL INTRANASAL</th>
<th>EVZIO AUTO-INJECTOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Requires technical experience</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Assembly required</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Titrate Dose</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Concentration</td>
<td>0.4 mg / mL</td>
<td>1 mg / mL</td>
<td>4 mg / 0.1 mL</td>
<td>2 mg / 0.4 mL</td>
</tr>
<tr>
<td>Total volume per kit / package</td>
<td>0.8 mg / 2 mL or 4 mg / 10 mL</td>
<td>4 mg / mL</td>
<td>8 mg / 0.2 mL</td>
<td>4 mg / 0.8 mL</td>
</tr>
<tr>
<td>Cost per kit</td>
<td>Cost variance per kit varies significantly between available products. Visit manufacturer websites for more information.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manufacturer Website</td>
<td>Hospira.com</td>
<td>Amphastar.com</td>
<td>Teleflex.com (L.N. adapter)</td>
<td><a href="http://www.narcan.com/evzio.com">www.narcan.com/evzio.com</a></td>
</tr>
</tbody>
</table>

**Narcan®** ([https://www.narcan.com](https://www.narcan.com)) is a naloxone nasal spray. It is designed to be easy to use by non-medically trained persons to include use by first responders, family, friends, and caregivers. It does not present a needle stick hazard and does not require any pre-assembly prior to application. A recent DHS-funded study in K9s demonstrated that 4 mg of naloxone administered either IM or IN (Narcan®) provided immediate and effective ‘reversal’ of clinical signs associated with intravenous administration of 0.3 mg fentanyl within 1 – 5 minutes.

*D* *Discount pricing is available for the first responders $37.50 per 4 mg dose ($75 per carton of 2 doses), for more information call 1-844-4-NARCAN (844) 462-7226*


**EVZIO®** is a naloxone auto-injector currently available on the market that provides a single standardized 2 mg dose of naloxone per application. It possesses an automatically retracting needle that reduces the risk of needle stick and results in a 15% greater maximum concentration delivered as compared to naloxone delivered using a standard needle and syringe. The auto-injector “provides simple, on-the-spot voice and visual guidance to help those with no medical training administer naloxone during an opioid overdose.” ([https://www.evzio.com/patient/](https://www.evzio.com/patient/))

*D* *Discount pricing is available for the first responders, visit: [https://www.evzio.com/patient/public-access-pricing/](https://www.evzio.com/patient/public-access-pricing/)*
**What is the Onset and Duration of Action of Naloxone in K9s?**

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, in some cases up to a few hours.

**Is there an Exposure Risk if the K9 Sneezes after Administering Intranasal Naloxone?**

It is possible that administering IN naloxone to an OpK9 may trigger a sneeze reflex. This may cause some opioid residue from within the nasal cavity and/or around the K9’s nares and muzzle to aerosolize resulting in an exposure hazard to anyone in the immediate vicinity. The actual risk this truly presents to a first responder remains uncertain; however, it seems unlikely that it would result in a life-threatening situation for any person, and no more so, than the risk associated with handling a contaminated OpK9 in general. In part, the exposure risk it depends upon the amount of drug residue remaining on the K9’s muzzle and remaining within the nasal cavity.

Mitigating the Exposure Risk from an OpK9 Sneezing Post-IN administration:
- When a K9 sneezes, this may cause desiccated (dry) drug powder residue on a K9’s hair coat and/or around its muzzle to aerosolize and dissipate over a large area (similar to that of a K9 shaking); again, this potential risk is no greater, and probably less so, than the cross-contamination that has been to occur from simply handling an OpK9 contaminated with a dry powder.
- Also consider that moisture traps drug powder residue preventing aerosolization; hence, why we recommend to dampen or wet any OpK9 contaminated with a dry illicit drug powder with water prior to handling. The nasal cavity has a moist mucus lining; subsequently, this mucus traps much of the inhaled opioid molecules reducing the free drug powder available for re-aerosolization.
- Since the mucus traps the powder molecules, then any exposure subsequent to an OpK9 sneezing is more likely a transdermal exposure due to contact with any nasal spray droplets projected from the sneeze.

What is a Sneeze Safe-Zone?
- Sneezes have a projected “Spray-Zone” relating to both the distance and direction the nasal spray will travel. Ideally, we want to stay out of the Spray-Zone to avoid any risk of contamination.
- Researchers in humans have shown that large droplets from a sneeze may travel a distance of 3 to 6 feet away from the person before settling, while smaller, mist-like, evaporative droplets can travel much farther. If any transdermal exposure occurs from contact with opioid contaminated nasal-spray droplets, then it seems reasonable that it would occur subsequent to exposure to the larger droplets.
- Also consider that sneezes are directional. Think of the K9 sneezing similar to that of the Directional Claymore Mine that has the words, “Front, Towards Enemy” printed on the side the mine is designed to project its payload towards. In that regard, you always want to remain behind the mine (the K9 nose) to avoid the directional Spray Zone from a sneeze:

Additionally, consider that a proportion of inhaled drug molecules are rapidly absorbed across the nasal mucosa into the K9’s circulation or inhaled into the lungs. Both events further reduce the amount of actual drug residue a person is exposed too when a K9 sneezes.

**BLUF:** Although there is a potential risk of exposure from IN administration triggering a sneeze reflex, the risk is no greater (and actually less so) then that associated with disturbing any dried drug powder that occurs by simply handling a contaminated OpK9, which, was demonstrated in the DHS funded study that evaluated Narcan® nasal spray. Most importantly, since cross contamination from the K9 to First Responder is considered the highest health risk to anyone that handles the contaminated K9; it is paramount that any person handling the OpK9 don appropriate PPE (N95 mask or APR, gloves, long sleeves, and eye protection) before handling any K9; this alone will negate the exposure risk from a sneeze.
KEY POINTS to MITIGATE THE RISK OF EXPOSURE FROM A K9 Sneezing:

- **Stay to the rear of the K9’s head** and **Remain upwind** to prevent any contaminated nasal spray droplets from blowing back into your face or onto your body.
- Cover the nares loosely with a damp cloth, rag, towel, or similar item to absorb/’catch’ any powder or opioid-contaminated nasal spray that is sneezed out or aerosolized from the sneeze.
- Take a wet cloth, towelette or similar moistened material (non-alcohol based) or use a small volume of water to dampen / wet the K9’s external nares and muzzle prior to administering the IN naloxone; this will prevent aerosolization of any powder residue.
- IMPORTANT: PROTECT YOURSELF with appropriate PPE. Cross contamination from the K9 to First Responder is the highest health risk to anyone that handles the contaminated K9; therefore, donning appropriate PPE is a mandatory requirement before handling any K9. PPE required of ALL personnel includes, at minimal: N95 mask or APR, gloves, long sleeves, and eye protection (e.g. goggles, face mask).

DOES INTRANASAL NALOXONE AFFECT OLFACTION?

Current evidence does not support adverse effects on a K9’s ability to detect odor post-IN naloxone. The study published by Essler et al. in 2019, evaluating the 4 mg intranasal naloxone spray (Narcan®) in K9s exposed to 0.3 mg fentanyl IV, found no detectable influence from application of intranasal naloxone on the K9’s olfactory acuity. The same study also demonstrated that K9s were able to perform their searches for target odor at levels comparable to pre-sedation two-hours, 24 h, and 48 h post-sedation, irrespective of whether they received IN or IM naloxone for reversal.

HOW DO I USE THE NALOXONE AUTO-INJECTOR IN A K9?

The procedure for using the EVZIO® auto-injector (https://www.evzio.com/patient/) in humans is similar for an OpK9. Although naloxone is absorbed if injected subcutaneously, ideally, we want the needle to seat deep within a large muscle belly before injecting naloxone to promote rapid and maximal uptake in the K9’s circulation. In this regard, the **EVZIO® auto-injector** possesses a needle length of only 0.5 inches. This is a very short needle considering the combined thickness of OpK9’s hair coat, skin layers and fat overlying the muscle that the needle must traverse to penetrate adequately into a muscle belly.

NOTE: To overcome the potential limitation of a short needle length, then similar to using the auto-injector in pediatrics, considering pinching / squeezing up the middle of the intended muscle belly before you give EVZIO and continue to pinch while you give EVZIO.

**Use-errors when using the Auto-injector:**

Raffa et al. provided a detailed report evaluating the naloxone auto-injector in people which listed commonly reported use-errors during application. Some of those errors applicable to the OpK9 include (refer to article for full list of use errors):

- **Failure to hold the auto-injector in place for a full 5 seconds ... User moves device during the injection, leading to possibility of ineffective dose ... User never applies sufficient force to activate the injection ... User pulls the device away from the outer thigh prematurely or fails to hold the injector in place for recommended period of time ...**
  K9 implication: Above errors are potential complications in an OpK9 that is still alert, conscious and able to move.

- **User places the device in the wrong location (inappropriate muscle).**
  K9 implication: The recommended muscle belly locations for placement of the auto-injector in OpK9s include (in order or preference): **epaxial muscles** (along their back), quadriceps, and triceps. Avoid applying the auto-injector into the K9’s thigh/gluteal muscles do to the potential risk of Sciatic nerve injury.
  See accompanying pictures of appropriate muscle injection sites at the end of this paper.

Although the EVZIO® auto-injector tends to cost significantly greater than the other IN or IM products, the manufacturer, Kaléo, offers a discount pricing for government agencies, first responders, health departments, and other qualifying groups when they purchase directly from Kaléo or authorized distributors.

K9 Tactical Emergency Casualty Care Working Group  www.k9tecc.org  June 2019
**How does storing Naloxone at Extreme Temperatures Effect the Drug’s Efficacy?**

According to available data, naloxone shows heat-dependent degradation; meaning that it degrades more when exposed to higher temperatures for prolonged periods of time. One study revealed heat-dependent degradation occurred after 4 weeks when stored at a continuous temperature of 113°F (45°C).

- The current recommendation is to store at room temperature 59°F to 77°F (15°C to 25°C) with only brief excursions (short periods) permitted up to 104°F (40°C). The length of the ‘brief excursion’ is not absolutely defined and depends upon the temperature exposed to; however, one sources states the **EVZIO® auto-injector maintains stability at temperatures of up to 104°F for six months.** (Raffa et al., 2017)
- We recommend that providers/handlers store their naloxone in a climate controlled environment and away from direct sunlight at all times. When off-duty, do not leave the product in a vehicle or other non-climate controlled environment. Instead, store inside at the recommended 59°F to 77°F (15°C to 25°C).
- If stored in continuously in high-temperature environments for prolonged periods of time, consider routinely testing and / or replacing naloxone products to ensure optimum effectiveness.

**Can We Use Expired Naloxone for Operational K9s?**

The shelf-life of most naloxone products varies from 12 months up two year. Naloxone is a relatively stable compound when stored in accordance with manufacturer guidelines. In 2018, Pruyn et al. published a study demonstrating that, even after many years of storage, a significant portion of expired naloxone products tested still met USP standards containing more than 90% of the labeled naloxone; some of the tested products had been stored up to 30 years. Other resources report that the Narcan® nasal spray showed chemical stability for 10 months after its labeled expiration date while the EVZIO® auto-injector was chemically stable for at least one year after its expiration date; interestingly, neither product was kept in ideal storage conditions (https://www.cnn.com/2018/11/06/health/naloxone-expiration-date-potency-study/index.html). It is important to note that further pharmaceutical and clinical investigations are warranted for newer naloxone products and products with different formulations and routes of administration as those evaluated by Pruyn et al.

Unfortunately, without appropriate laboratory testing, it is relatively impossible to know the efficacy of an expired naloxone product. Ideally, you should always replace all expired products; however, if an expired naloxone product is all that is available for treating an exposed OpK9, then even though it may have lost some of its efficacy, it may still possess enough active naloxone to at least partly reverse an overdose. Additionally, there are no adverse effects associated with administering an OpK9 an expired naloxone product, as long as the integrity of the package/applicator remained uncompromised during storage.

Considering the current and future issues surrounding the lack of availability of naloxone products for humans and the OpK9, departments / agencies should consider taking appropriate steps to extend the shelf-life of their current naloxone products.

**Remember:**

**Protect Yourself First.**

**Always Don Appropriate PPE before Handling any Contaminated OpK9**
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.
  - **IMPORTANT:** 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 with copious water +/- mild soap.**
  - 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 garbage bag) 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.
RECOMMENDED K9 NALOXONE DOSING:

Routes and Initial Dose
- Intravenous (IV) / Intraosseous (IO): 2 mg per 25 kg (55 lbs)
- Intramuscular (IM): 4 mg per 25 kg (55 lbs)
- Intranasal (IN): 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. Consider that it is difficult to overdose a K9 on naloxone in the field.
- 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/](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:
   o Primary veterinarian’s or local 24/7 emergency veterinary hospital phone number
   o ASPCA Animal Poison Control Center (APCC): 1-888-426-4435
   o 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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https://www.interagencyboard.org/.


11. Barr, Ciara et al. Pharmacokinetics of intranasal or intramuscular naloxone in working dogs. Veterinary Anaesthesia and Analgesia, Volume 45, Issue 6, 885.e1 - 885.e2

12. HTTPS://BJATTA.BJA.OJP.GOV/NALOXONE/HOW-SHOULD-NALOXONE-BE-STORRED
The epaxial muscles are located dorsal to the line of transverse processes of the vertebrae and lateral to the dorsal spinous processes. They are best palpated between the last rib and wing of the pelvic ilium with the appropriate location for injection is at the level of the 3rd to 5th lumbar vertebrae (X).

To overcome the potential limitation of a short needle length associate with the EVZIO® auto-injector, then similar to using the auto-injector in pediatrics, consider pinching / squeezing up the middle of the intended muscle belly before you give EVZIO and continue to pinch while you give EVZIO.
**Figure 3: K9 Muscle Injection Sites**

![Diagram showing muscle injection sites on a K9: Epaxial, Quads, Triceps](image)

**Figure 4: Application Narcan® in K9**

![Application of Narcan to a K9](image)

Extracted from: Fig. 3, Essler JL et al. *Animals* 2019, 9(6), 385; https://doi.org/10.3390/ani9060385