Dr Christina Baxter, CEO of Emergency Response TIPS, and Dr Michael Logan, of the research and scientific branch, Queensland Fire and Emergency Services, Australia on Synthetic Opioids in Operational Environments – Part III: Protection

The drugs don't work

The first two papers in this series on responding to incidents involving synthetic opioids focused on detection and decontamination. This paper covers the selection of appropriate personal protective equipment (PPE). All three documents may be used together to formulate operational guidelines specific to your community.

Is your agency using an evidence-based approach to select the personal protective equipment for your team when responding to incidents involving synthetic opioids? Does this approach include both scientific evidence about the hazard and operational information regarding the risk? The opening section of this paper outlines the scientific evidence currently available for synthetic opioids, including fentanyl and fentanyl analogues pertinent to respiratory and skin exposure. The second part applies the risk associated with a variety of operational objectives along with the scientific evidence to recommend the appropriate protective posture for a variety of situations.

First, it is important to understand that synthetic opioids are inhalation, ingestion and dermal absorption hazards. Inhalation is the predominant hazard, but ingestion and dermal absorption contribute towards the total dose and therefore must be minimised or eliminated. Unfortunately, unlike many other hazards that we deal with in the operational environment, there are no published exposure standards or clean-up guidance telling us how much is safe. In the case of synthetic opioids, data is available from the pharmaceutical industry dating back to the invention of fentanyl by Dr Paul Janssen in 1959.[1] The industry has published occupational exposure limits (OELs) for fentanyl with the eight hour time weighted average (OEL-TWA) ranging from 0.1 to 0.7µg/m3 and a 15 minute short term exposure limit (OEL-STEL) of 2µg/m^3.[2,3]

In the case of fentanyl, for an average 165lb (75kg) person, the dose required for an analgesic effect is estimated to be 2.5µg, an anaesthetic effect ranges between 25 and 125µg, and the lethal dose is 2.5mg. While the analgesic effect is not lethal, it can cause symptoms (drowsiness, nausea, confusion, euphoria) that will reduce the emergency responder's ability to function properly. The anaesthetic effect can lead to respiratory depression and arrest if not properly monitored. Therefore, while the lethal dose is considered to be 2.5mg, it is imperative that the emergency responders never receive a dose of even 2.5µg so that they can continue to operate effectively.

Risk analysis for respiratory protection

To perform the risk analysis for a variety of scenarios in which an emergency responder might be exposed, several assumptions have to be made. These relate to: variations in product purity for different operational scenarios; variations in time for task execution; no other risk control measures being applied; a maximum airborne value of 7310ng/m^3 as measured in a pharmaceutical production facility[4]; the protection levels provided by different respiratory products; and, that standard breathing rates apply across a variety of operational tasks.[5]

First, let's determine the appropriate class of respiratory protection to provide the necessary level of safety using the assigned protection factor (APF). In the US, APFs can be found in OSHA 29 CFR 1910.14(d)(3)(i)(A). The table below provides a subset of APFs of interest to the emergency response community.

To determine the appropriate level of protection, we must first estimate the maximum concentration of threat material we expect to encounter for a given operational scenario. In the case of the pharmaceutical company[4] where the average maximum airborne concentration of fentanyl was measured at 7310ng/m^3, the required respiratory protection factor was 73, therefore a full-face piece PAPR or SCBA was needed. We would consider this similar to a moderate or high risk operational environment.

The next question is whether or not a half-mask APR would be suitable for situations where the risk was considered to be minimal (eg traffic stops). Using the protection factors and the OEL of 0.1µg/m^3, the maximum concentration allowable would be 1µg/m^3 of fentanyl in the air. Taking a midsize car with an average internal volume of 2.69m^3, the maximum amount of fentanyl in the air would only be 2.69µg. Even at a dilution factor of 1% fentanyl in the cut product, that still only allows for 269µg of cut product suspended in the air. This simple situation demonstrates the need to adopt respiratory protection even in minimal risk situations where there is uncontained product. However, caution should be used when employing half-mask respirators in the operational environment when the threat of opioid suspension in the air is viable.

Finally, the considerations for filtration efficiency must be addressed for those situations where half-face air

	Half-Mask	Full-Face Piece	Hood (Tight Fitting/Loose Fitting)
Air Purifying Respirator (APR)	10	50	--
Powered Air Purifying Respirator (PAPR)	50	1000	1000/25
Self-Contained Breathing Apparatus (SCBA)	–	10,000	--

purifying respirators are acceptable. Let's return to the situation above were 2.69µg of fentanyl was suspended in the air. If all of that material was in the respiratory zone and it were fentanyl, an N95 mask would be sufficient. But, what if it were carfentanil? Now, we are approaching the analgesic dose and a N100 would be more suitable. What if the purity of the material was 10% or 100%, versus 3%?

Recommendations for respiratory protection

As you can see, as the incident risk level escalates, the requirement for a minimum of a N100 respirator becomes clear. The results of the calculations above support the current recommendations set forth by the US InterAgency Board[6] and the National Institute for Occupational Safety and Health[7] (NIOSH), both of whom recommend the N100/P100/R100 filtering facepiece respirator as a minimum level of protection.

Exposure Risk	Operational Example	Minimum Recommended Respiratory Protection
Minimal	Traffic stop (no uncontained product)	Protection not required; Follow agency policy
Minimal	Traffic stop (up to 1g product uncontained)	Disposable N100, R100, or P100 filtering face piece respirator or half-face APR
Moderate	Trafficking search; cut fentanyl	Disposable N100, R100, or P100 filtering face piece respirator or half-face APR
Moderate	Trafficking search; uncut fentanyl	Full-face PAPR, tight-fitting hooded PAPR, or SCBA
High	Milling lab (initial entry)	Full-face PAPR, tight-fitting hooded PAPR, or SCBA
High	Milling lab (evidence recovery)	Full-face PAPR, tight-fitting hooded PAPR, or SCBA

For exposed tissue lacking the epidermis, such as mucosa (eyes, nose, and mouth), allow for a 30-fold increase in the rate of fentanyl absorption,[8] therefore, it is imperative that the eyes, nose and mouth are always protected. In addition to the recommended respiratory protection, goggles, preferably indirectly vented ones, should be employed unless a full-face respirator is used.

Risk analysis for dermal protection

It is important to understand the skin's substructure in order to appreciate how fentanyl permeates the skin. In its simplest form, skin comprises three layers, the epidermis (outermost), dermis (centre), and the hypodermis (inner). Many factors such as size and solubility in both the lipid (epidermis) and aqueous (dermis) layers of the skin affect a material's ability to penetrate the skin. Fentanyl is sufficiently small and is able to rapidly diffuse into the lipophilic epidermis due to its high lipid solubility, with the free base diffusing the fastest. Because fentanyl's water solubility is less than its lipid solubility, a 'depot' of fentanyl forms at the junction between the epidermis and the dermis. The time profile for a fentanyl patch, which has the added benefit of ethanol in its matrix to increase absorption, is one to two hours before detectable amounts are found in the blood serum, 12-16 hours to reach a therapeutic level, and 36 hours to reach the maximum serum concentration.[8]

In order to reach a lethal dose (2.5 mg) of fentanyl via the skin, calculations show that a subject would need to cover their entire body (approximately 17,000cm^2) with pure fentanyl and leave it there for longer than two hours (provided the respiratory tract and mucous membranes were protected) and then wait another hour before reaching the lethal dose. This is not operationally viable in an emergency response context. If, however, a 5cm^2 area of the skin on the palm of the hand was covered in fentanyl for 15 minutes, an estimated 75ng of fentanyl would be able to penetrate and reach the blood stream after about one to two hours. This is well below the 2.5µg required to exhibit symptoms in an average person. Therefore, while skin absorption is not a high-risk entry route by which responders would be adversely affected, opportunities for direct or indirect skin contact should be minimised as any skin absorbed opioid will contribute to the overall total dose received.

The pharmaceutical industry study referenced earlier reported an average of 30µg of fentanyl was deposited under the protective equipment used by operators during non-bulk operations with the highest areas of exposure being at the hands, arms, and neck. They were wearing disposable Tyvek coveralls, boot covers, nitrile gloves, and full-face air-purifying respirators. They found deposition occurred over the entire body, but the highest levels were at the interface regions of the protective ensemble (hands, arms, and neck). The Tyvek clothing also showed a residual contamination level on the outside of the garment of 800ng/cm^2.[4] What does this mean?

It tells us that we must select appropriate protective equipment for the task and ensure it is donned and used correctly. It also tells us we should decontaminate and doff correctly to avoid any further contamination.

Recommended protective clothing

For the reasons cited above, and the varied tasks and operational environments we encounter, it is recommended that particulate tight protective clothing be employed when dealing with milling lab operations to minimise exposure at interfaces and permeation of particles through the

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garment. In operations where there is minimal, if any, potential for contact with opioids or the dust, standard duty uniforms will provide the necessary protection. The table below highlights PPE to consider in various operational situations.

When choosing nitrile gloves, it is recommended that they are tested for liquid penetration in accordance with ASTM F1671/F1671M[9]. This requirement incorporates suspended particulate matter and is more stringent than the ASTM D5151 water leakage test used for a lot of examination gloves. Any nitrile gloves certified against NFPA 1999[10] as single use examination gloves are appropriate for use with fentanyl. NIOSH also recommends that the nitrile gloves have a minimum thickness of 5mm.

When choosing a particle tight ensemble for moderate to high exposure risks, it is recommended that the entire ensemble, as worn, is tested in accordance with the particle inward leakage test referenced in section 8.5 in NFPA 1994.[11] This test, modified from the US Department of Defense aerosol system test[12], challenges ensembles with 2.75µm particles which are similar in size to fentanyl particles. Any ensembles certified against NFPA 1994 Class 4 are appropriate for use with high hazard fentanyl milling laboratories. In addition, ensembles that are challenged with the man-in-simulant tests used in NFPA 1991[13] and NFPA 199411 are also suitable and provide the extra benefit of chemical vapour protection to varying levels.

In summary, the protective clothing and accessories should meet suitable standards and should be selected taking into account the task, task duration, location, situation, hazard, and potential for contact. The tables above provide a basis to support your PPE selection. Each country has its own sets of standards and test methods that should be applied in your site-specific risk assessment in place of the US standards mentioned above.

Exposure Risk	Operational Example	Recommended Protective Clothing
Minimal	Traffic stop (no OD)	Nitrile gloves, standard duty uniform
Minimal	Traffic stop (with OD)	Nitrile gloves, standard duty uniform
Moderate	Trafficking search; cut fentanyl	Nitrile gloves, standard duty uniform with long sleeves or sleeve covers
Moderate	Trafficking search; uncut fentanyl	Particle tight ensemble
High	Milling lab (initial entry)	Particle tight ensemble
High	Milling lab (evidence recovery)	Particle tight ensemble

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9. ASTM F1671/1671M. (2013) Standard Test Method for Resistance of Materials Used in Protective Clothing to Penetration by Blood-Borne Pathogens Using Phi-X174 Bacteriophage Penetration as a Test System.
10. NFPA 1999 (2018) Standard on Protective Clothing and Ensembles for Emergency Medical Operations.
11. NFPA 1994 (2018) Standard on Protective Ensembles for First Responders to Hazardous Materials Emergencies and CBRN Terrorism Incidents.
12. DoD (2013) Test Operating Procedure (TOP) 10-2-022A Chemical Vapor and Aerosol System-Level Testing of Chemical/Biological Protective Suits.
13. NFPA 1991 (2016) Standard on Vapor-Protective Ensembles for Hazardous Materials Emergencies and CBRN Terrorism Incidents.