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Effect of Contaminant Form on the Contact Transfer of an Opioid to Latex and Army Combat Uniform Cloth

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The scoping studies presented here were designed to probe for answers to questions about the potential for hazards due to contact with opioid contaminants. Does decontamination by soapy water rinse reduce the potential for contact transfer of an opioid from contaminated protective equipment to other surfaces including skin and clothing? Does the form of the contaminant, such as the free base, salt, or a solution thereof, affect the potential for contact transfer? Using carfentanil free base and citrate salt as representative contaminants on butyl and nitrile gloves, this study confirms that contaminant form is a key factor in determining risk due to contact transfer following decontamination processes. The enhanced solubility of the citrate salt over the free base resulted in about 75% less residual citrate salt than free base on the glove coupons following soapy water treatment; however, enough residual contaminant remained to pose a contact hazard. On average, between 40 and 80% of the residual contaminant on the gloves was transferred to latex and Army combat uniform (ACU) contact samplers.

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PREFACE

The work described in this report was started in June 2018 and completed in December 2018. At the time this work was performed, the U.S. Army Combat Capabilities Development Command Chemical Biological Center (DEVCOM CBC; Aberdeen Proving Ground, MD) was known as the U.S. Army Edgewood Chemical Biological Center (ECBC).

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EFFECT OF CONTAMINANT FORM ON THE CONTACT TRANSFER OF AN OPIOID TO LATEX AND ARMY COMBAT UNIFORM CLOTH

1. INTRODUCTION

Similar to traditional chemical weapons agents (CWAs), pharmaceutical based agents (PBAs) can be used to cause great harm, incapacitation, and death to the Warfighter and general public. The use of synthetic opioids in the 2002 Moscow theater crisis raised awareness of this new threat across the world. Furthermore, the illicit drug trade has reinforced the threat by making many PBAs, such as fentanyl and carfentanil, readily available to those who either knowingly or unknowingly seek them. With a lethality on the same level as the nerve agent VX, opioids present a very real hazard to any unprotected person who comes in contact with them. Furthermore, the potential for secondary exposure due to contact transfer from gloves to skin or other materials may also be a matter of grave concern.

In late spring of 2018, the U.S. Army Edgewood Chemical Biological Center (ECBC) (now known as the Combat Capabilities Development Command Chemical Biological Center (DEVCOM CBC)) was contacted by the Product Director for Cross-Commodity Advanced Threats & Test Infrastructure (PDCATTI) with a request to probe for answers to questions about the potential hazards faced by military personnel such as the National Guard Bureau when encountering PBAs. For example, what happens when gloves that are contaminated with an opioid touch other surfaces, such as skin and clothing? Does rinsing with soapy water remove all of the contaminant from a surface? Does the form of the contaminant, such as the salt or a solution thereof, or the free base affect the potential for contact transfer?

From an experimental and modeling standpoint, numerous research challenges need to be addressed before a meaningful effort can be launched to answer specific questions associated with contact transfer. The primary objective of this effort is to evaluate whether contaminant form plays a significant role in the outcome of a decontamination effort. The contamination event itself, whether free base versus salt, neat versus in solution, must be considered when evaluating the potential for contact transfer from contaminated surfaces to secondary surfaces such as skin and clothing.

Carfentanil was used as a representative opioid for the experiments conducted as part of this effort, which were designed to demonstrate the effect of contaminant form on the contact transfer of synthetic opioids under two decontamination conditions: no treatment, and soapy water immersion followed by water rinse. The materials selected for surface contamination and contact transfer were representative of military relevant personal protective equipment (PPE) that would likely come into contact with PBAs in the field. Test coupons made from butyl rubber and nitrile gloves served as primary contamination sources, while coupons made of latex and unlaundered Army combat uniform (ACU) pants served as contact samplers. Latex was chosen as a skin simulant based on earlier contact transfer studies.[1]

The experimental outcomes include a qualitative and quantitative assessment of the data captured. While residual contaminant mass was accurately measured for both the contaminated surface materials and contact samplers, a wide margin of error exists for the mass of the starting challenge, particularly in the case of the free base contaminant. Wherever possible, photographic and video documentation was collected to provide additional insight into the complexities involved in accurately assessing contact transfer. One of the main conclusions drawn from this study is the need for enhancements in laboratory infrastructure and test methodology to support the study of non-liquid contaminant forms.

2. CONTACT TRANSFER – EXPERIMENTAL PROCEDURES

The goal of these contact transfer experiments was to accurately measure the amount of contaminant that is transferred from a contaminated surface to a secondary surface such as skin or clothing under a set of defined conditions. Lalain et al. provide the chemical biological defense community with robust, customizable test methodologies to enable evaluation of decontaminant performance on various materials of interest in Chemical Contaminant and Decontaminant Test Methodology Source Document: Second Edition (SD2ED).[2] The SD2ED defines panel treatment as a series of actions that are performed on a material as part of the test; while post-treatment evaluation involves destructive sampling where the analysis procedure modifies the contaminant in the material being studied. The major panel treatment actions involved in this study included environmental conditioning, contamination, contaminant-material aging, decontamination and post-decontamination rinse. The post-treatment contact transfer process was utilized to determine the amount of contaminant transferred to a second surface. The procedures described by Lalain et al. for panel treatment, post-treatment, and analysis used in this research are summarized in the following sections. The contaminants, carfentanil citrate and carfentanil free base, were synthesized at ECBC (Aberdeen Proving Ground, MD).

2.1 Panel Treatment

Material test coupons consisted of standard 2 in. circular panels cut from the palms of 7 mil butyl rubber gloves and single use purple nitrile gloves. The butyl gloves were manufactured in accordance with MIL-DTL-43976D[3] and obtained from Mask Issue at ECBC, and the nitrile gloves were Kimberly-Clark (Irving, TX) purple nitrile powder-free exam gloves. Contact transfer coupons were also cut from 10 mil latex sheeting and unlaundered ACU pants. The latex sheeting was purchased from The Hygenic Corporation (Akron, OH), and the ACU pants were purchased through Propper International (St. Charles, MO).

2.1.1 Environmental Conditioning, Contamination, and Contaminant Material Aging

Test coupons were equilibrated to ambient temperature and passed through a Mettler Toledo/Haug anti-static system with U-electrode just before use to eliminate static electricity. The coupons were placed in plastic petri dishes and imaged before and after contamination. Two sets of both butyl and nitrile glove materials and corresponding control samples were prepared. One set was contaminated with neat carfentanil free base, while the

second set was dosed with a solution of carfentanil citrate dissolved in methanol. The experimental parameters targeted a contaminant mass of 2 mg of carfentanil parent molecule, not including the salt adduct. Unless otherwise noted, all contaminated coupons were aged at ambient conditions for 30 min before decontamination or contact transfer studies.

2.1.2 Substrate Contamination with Free Base

Contamination of test coupons is typically done by delivery of a known, reproducible volume (routinely 2 µL) of liquid chemical contaminant from a positive displacement pipette to the center of a test substrate. Due to the extremely viscous, glue-like consistency of the free base and its resistance to being stirred or pipetted at ambient temperature, alternative methods of contaminant delivery had to be considered. While attempts at stirring the free base at room temperature with a stir bar and magnetic stir plate were unsuccessful, gentle heating to 80 °C with stirring was sufficient to allow the free base to be drawn up into a positive displacement pipet.

The neat material also appeared to get thicker with subsequent uses and heating, and began to form string-like projections from the pipet tip as soon as it was removed from the warm vial and hit the cooler surrounding air. The hypothesis was that residual solvent left over from the synthesis was being driven off during the heating process and that the free base was actually becoming more pure and viscous with each subsequent use.

Several attempts were made to design a method to volumetrically deliver ~2 µL amounts of the carfentanil free base. Even though positive displacement pipet tips were used, the free base material formed a bead at the end of the plastic tip (Figure 1a), then clung to the sides of the pipet tip without dropping off. To transfer the free base, the pipet tip was gently scraped across the surface of the glove. As a result, the amount of free base and pattern of contamination delivered to each coupon was unique for each sample, requiring that the initial mass be determined gravimetrically (Figure 1b and Figure 2).

An analytical balance capable of measuring tenths of milligrams was used; however, the mass of the coupon with a secondary containment vessel far outweighed the miniscule amounts of carfentanil applied to the coupon. The requisite measurement of milligram-level contaminant amounts approached the limitations of the analytical balance and introduced a wide margin of error in the accuracy of the recorded starting challenge for those samples.

Corresponding positive dose control samples (DCSs) were prepared gravimetrically in glass vials with stir bars and diluted with 10 mL of methanol. The same dosing challenges were experienced in preparing the control samples as with the test samples (Figure 1c).

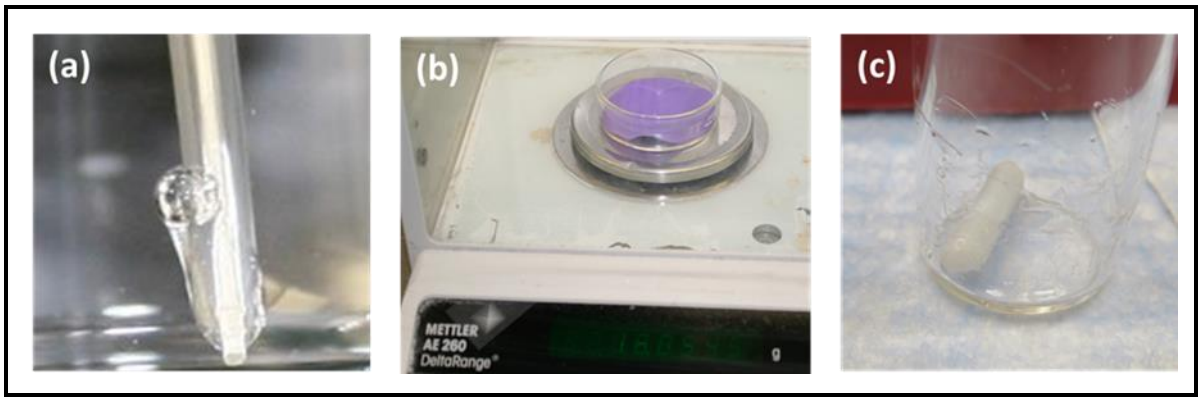

Figure 1. Challenges of substrate contamination with free base. (a) Bead of carfentanil free base clinging to sides of plastic positive displacement pipet tip. (b) Carfentanil contaminated 2 in. nitrile coupon on analytical balance. (c) Free base contaminant adhering to walls of a 7 mL glass vial used for DCS.

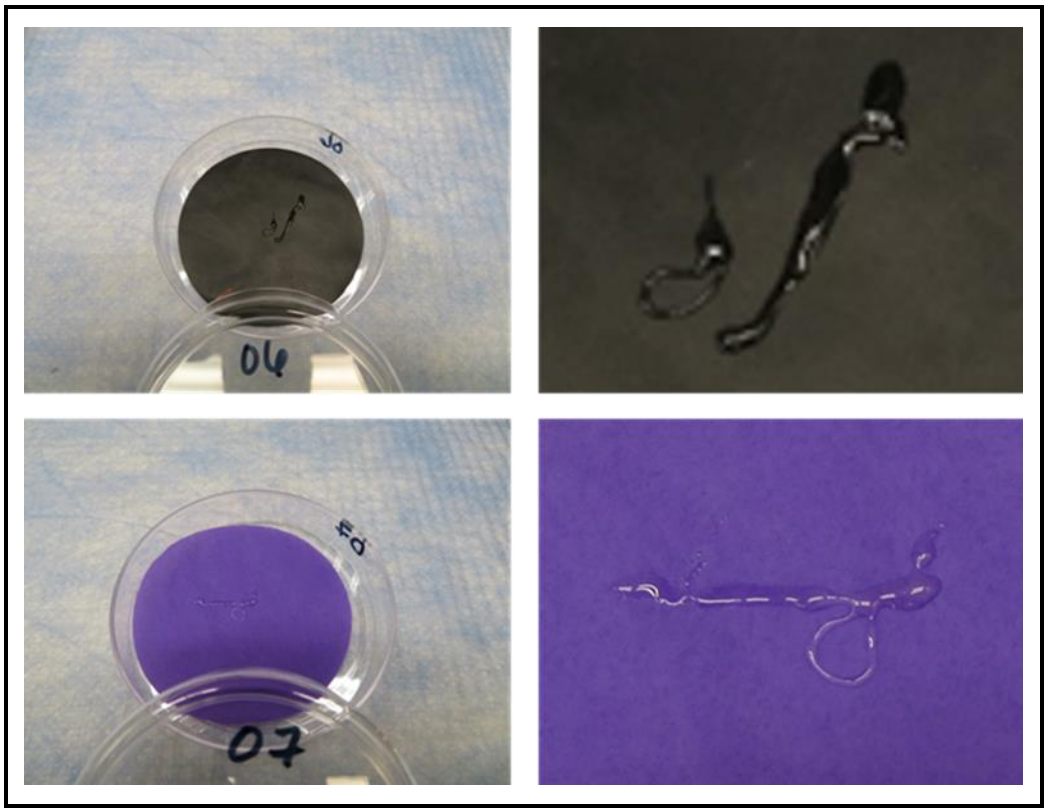

Figure 2. Butyl rubber and purple nitrile glove coupons contaminated with neat carfentanil free base. Images on the right were enlarged to show detail.

2.1.3 Substrate Contamination with Citrate Salt

Carfentanil citrate exists as a solid salt with an ultra-high potency and dangerously significant potential for aerosolization. Safe manipulation of the solid material presents a significant research challenge, as all experiments must be conducted inside a glove box, limiting the number of test samples that can be evaluated. As with the free base, the ability to accurately dose milligram amounts of solid material onto test coupons is limited by the sensitivity of the analytical balance coupled with the maximum tare weight tolerance.

As an alternative to working with the solid form, a high concentration solution (148 mg/mL) of carfentanil citrate in methanol was used to contaminate the butyl and nitrile gloves. The intended outcome from this type of contamination was that the methanol solvent would rapidly evaporate from the coupon, leaving the carfentanil salt behind. The coupons were spiked with 20 µL of the salt solution to yield an equivalent dose of 2 mg of carfentanil free base (after correction for salt content). The solution was dosed in a single bolus with a positive displacement pipet; however, a small drop of solution adhered to the end of the pipet, which was then touched off on the surface of each coupon (Figure 3).

Corresponding DCSs were also prepared by delivering 20 µL of the carfentanil solution into 10 mL of methanol in glass vials.

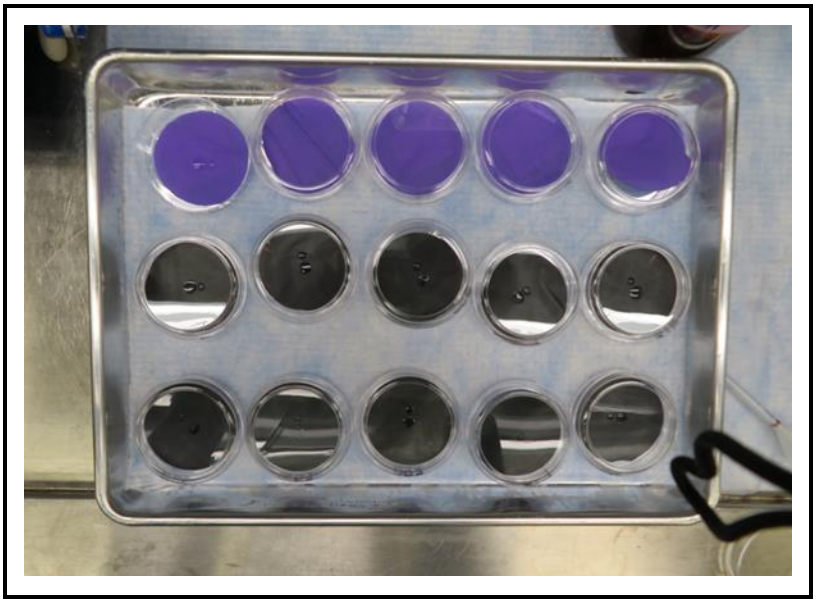

Figure 3. Butyl and nitrile glove coupons being contaminated with carfentanil citrate in methanol solution.

2.1.4 Decontamination and Post-Decontamination Rinse

Decontamination conditions included a no treatment scenario and a soapy water treatment scenario. In the no treatment scenario, the contaminated coupons were evaluated for

contact transfer immediately following the aging period using the method described in the following section. The second decontamination condition involved a 15 s immersion in 8 mL of soapy water, followed by a triple rinse with 20 mL of deionized water prior to the contact transfer study (Figure 4). These conditions were chosen to demonstrate the extreme between no treatment and the commonly recommended soapy water wash for physical removal.[4] It should be noted that, while the immersed coupon was gently swirled in the soapy water, no strong agitation, scrubbing, or rubbing was applied to aid in surface removal.

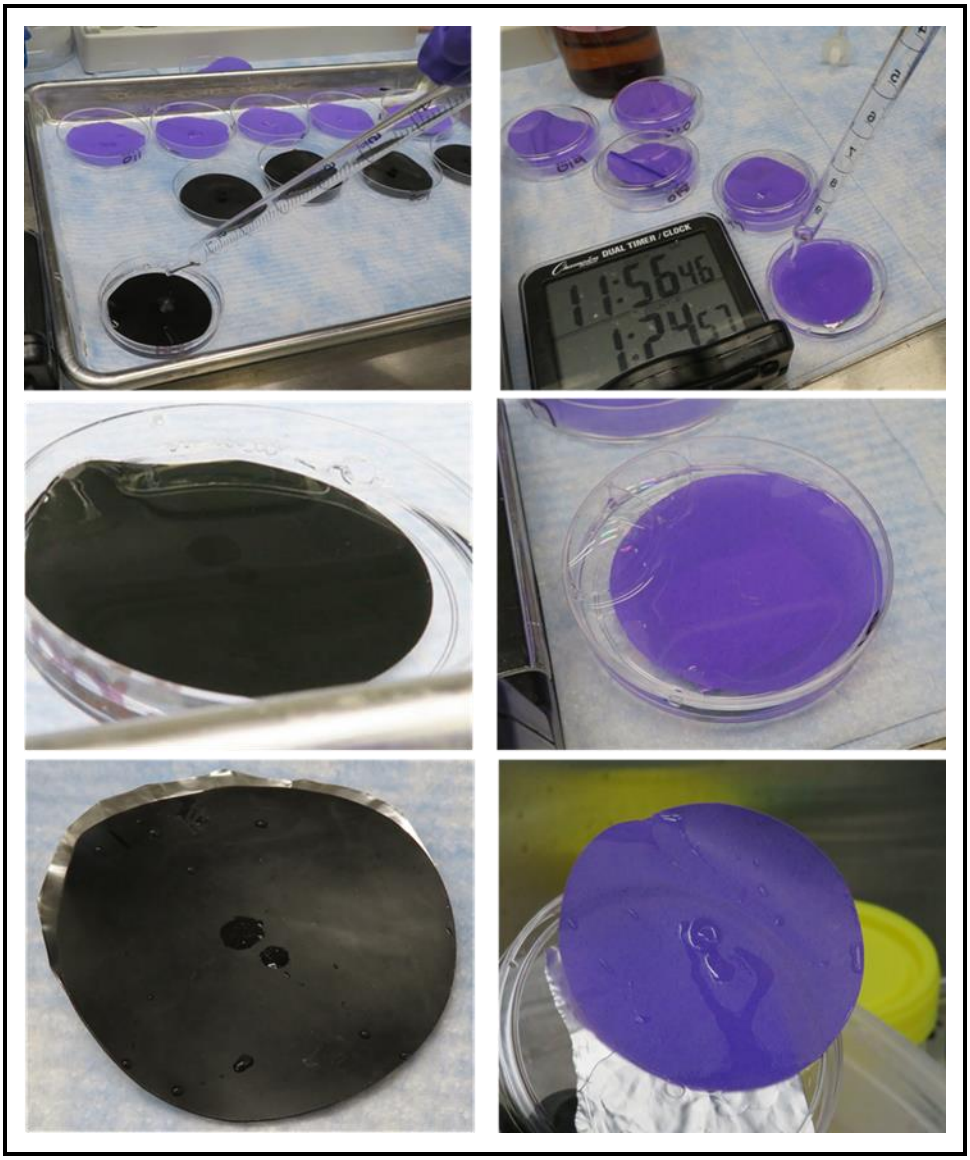

Figure 4. Soapy water immersion and rinse process as applied to butyl rubber and nitrile glove coupons contaminated with carfentanil citrate. The top row shows the addition of 8 mL of soapy water, the middle row shows the 15 s immersion process, and the bottom row shows the coupons after water rinses.

2.2 Post-Treatment Evaluation: Contact Transfer and Residual Contaminant Extraction

The contact transfer test measures the amount of contaminant present on a surface after a treatment process that could pose a risk to unprotected personnel through transfer to skin or other surfaces, such as clothing. The SD2ED defines a contact test event as a touch, which is characterized by the contact area, pressure, duration, and skin condition (wet versus dry). The contact test is the process of applying a contact sampler to a panel surface for a specific duration of time. The number of contact sampling periods is referred to as the number of touches. The standard contact test used in hazard mitigation evaluations utilizes a two-touch pattern, each touch lasting 15 min. Due to the scoping nature of the current study, only a single 15 min touch was employed.

For this study, post-treatment contaminated glove coupons (including those with the no treatment condition) were placed on aluminum foil discs on a 30 °C temperature controlled flat surface with the contaminated side facing up. A contact sampler, either latex or ACU material backed by an aluminum foil disc, was placed on the coupon, followed by a 1 kg contact mass. After the 15 min touch, the weight was lifted, and the contact sampler with the aluminum foil backing was removed from the contaminated coupon (Figure 5).

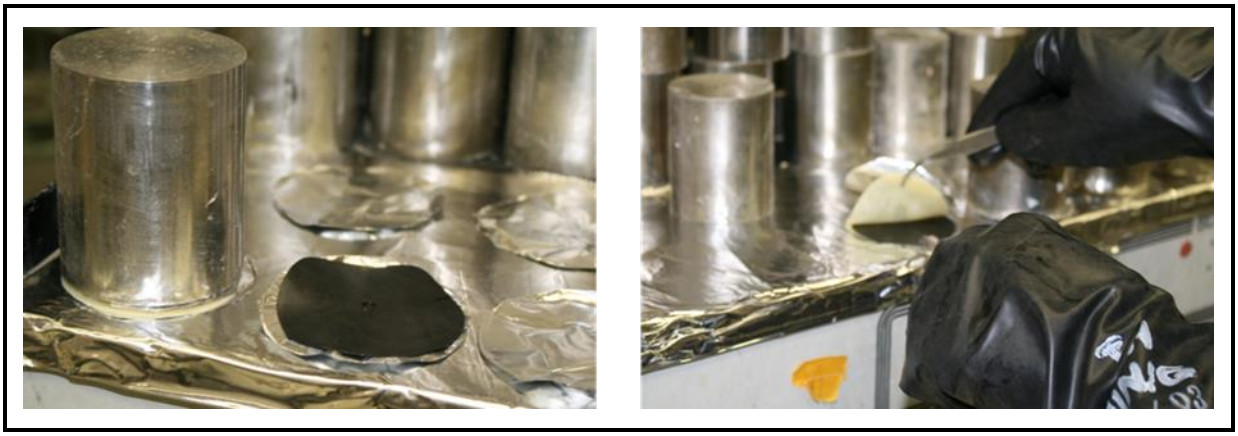

Figure 5. Contact sampling setup. The image on the left shows an in progress sample (left) and a contaminated butyl coupon about to be treated with a latex sampler. The image on the right shows the latex sampler being removed from the rubber coupon following the 15 min touch.

As illustrated in Figure 6, the contaminated glove coupon and associated foil backing was transferred to a 4 oz jar. The contact sampler with its associated foil backing was transferred to a separate 4 oz jar for extraction. The samples were extracted with 10 mL of methanol for 60 min with stirring. Following the extraction period, an aliquot of the extraction fluid from each jar was removed and diluted for analysis by liquid chromatography/mass spectrometry (LC/MS).

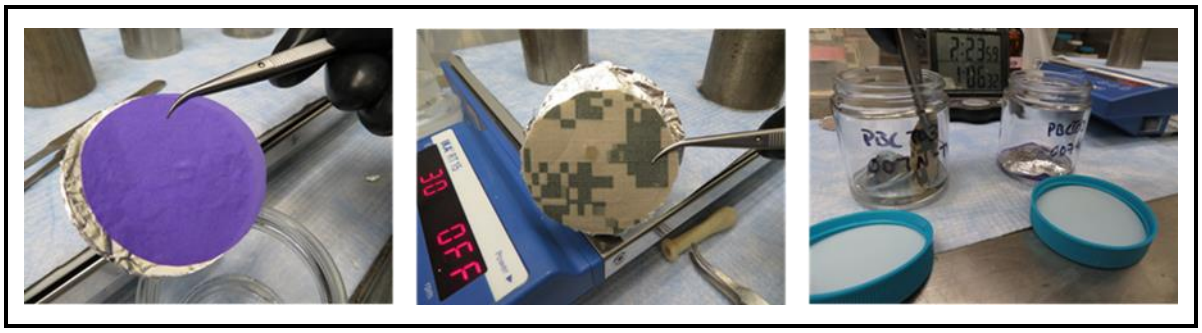

Figure 6. Coupon extraction process. Contaminated nitrile coupon (left) and ACU contact sampler (middle) being prepared for methanol extraction (right) following post-treatment contact transfer.

Carfentanil was quantified using an Applied Biosystems (Foster City, CA) API5500 QTrap Triple-Quadrupole MS, equipped with the TurboV Ion Source. Sample introduction and chromatography were performed with an Agilent (Santa Clara, CA) 1290 Infinity series ultra-high performance liquid chromatography (UHPLC) system, which included the Agilent Infinity binary pump, degasser, thermal column compartment, high performance automatic liquid sampler, and the ALS thermostat. Sample effluent was directed from the liquid chromatograph directly to the TurboV ion source of the API5500MS. The instrument operation and data analysis were performed with the Applied Biosystems Analyst software package (v. 1.5.1.). Details on the use of the chromatography platforms are published elsewhere.[5] Analysis conditions are summarized in Table 1.

Table 1. Summary of Instrumental Parameters

LC Parameters		
Mobile Phase A: 0.1% formic acid in deionized water		
Mobile Phase B: 0.1% formic acid in acetonitrile		
Gradient:		
Time (min):	%A	%B
0.00	70.0	30.0
0.50	70.0	30.0
1.25	20.0	80.0
1.50	20.0	80.0
1.60	70.0	30.0
2.25	70.0	30.0
Flow Rate: 0.5 mL/min		
Analytical Column: Waters Acquity HSS T3, 1.8 µm, 2.1 x 50 mm		
Typical Column Pressure: 330 bar		
Analytical Column Temperature: 40 ºC		
Injection Volume: 1 µL		
Autosampler Temperature: 5 ºC		
Post-injection Needle Wash: 10 s of mobile phase B		

Table 1. Summary of Instrumental Parameters (Continued)

Mass Spectrometer Parameters
Scan Type: multiple reaction monitoring (MRM)
Polarity: positive mode
Curtain Gas: 30
Collisionally Activated Dissociation (CAD) Gas: medium
Source Temperature: 500 ºC
GS1: 45
GS2: 55
Declustering Potential: 100
Exit Potential: 10
Collision Energy: 25 (for all analytes)
MRM for Carfentanil: 395.2 > 335.2 MRM for Norcarfentanil: 291.2 > 142.1 MRM for Carfentanil-d5 (Internal Standard): 400.2 > 340.2

3. RESULTS AND DISCUSSION

The results of these scoping experiments demonstrate that contaminant form is a key factor in determining the risk associated with contact transfer of residual carfentanil following decontamination processes. For liquid form contaminants, time is a key variable that can affect the mass transport of a contaminant in a material and; therefore, the efficacy of a decontamination process.[4] For this reason, immediate physical removal of the contaminant is a primary factor in reducing the residual vapor and contact hazard. The results of these scoping studies demonstrated that the physical removal process was less effective with the free base than with the solvated citrate form of the contaminant, resulting in more of the free base than the citrate form available for transfer. The actual transfer efficiency, the percent of available contaminant transferred to the contact sampler; however, was not significantly different between the two forms.

3.1 Physical Removal Decontamination Process – Effect of Contaminant Form

The active decontamination process (soapy water immersion with water rinse) was compared with the no treatment scenario using the residual contaminant found following the process. The residual contaminant was determined by adding the amounts of carfentanil found on the individual glove and contact sampler coupon pairs for each of the material-contaminant-decontamination process configurations studied.

3.1.1 Carfentanil Free Base

The wide margin of error associated with the delivery of carfentanil free base, as discussed in section 2.1.2, is reflected in the recoveries of the control samples (Table 2) as well as the contaminated material coupon-contact sampler pairs (Table 3). In most cases, the total recovered contaminant exceeds the starting challenge that was measured gravimetrically. A graphical depiction of these results is shown in Figure 7a.

The poor aqueous solubility of the free base was observed both empirically and quantitatively. Following the soapy water immersion and water rinse, the free base remained readily visible, adhering to the surface of the glove coupon with little evidence of physical removal. The free base "sandwiched" between the contaminated coupon and the contact sampler acted as an adhesive to hold the two materials together. Regardless of the treatment process, the contact samplers had to be peeled away from the glove coupons using two sets of tweezers. The residual contaminant measurements confirmed that the soapy water immersion followed by water rinsing had little effect on the removal of the carfentanil free base from either the butyl or nitrile glove material, as shown in Figure 7b.

Table 2. Summary of Contaminant Recovered in the Free Base DCSs

DCS References	Contaminant Dosed (mg)	Contaminant Recovered (mg)	Recovered (%)	Average Recovery (%)	Standard Deviation (%)
Latex Sampler	1.3	2.21	170	131	38.1
	1.7	2.19	129		
	2.3	2.16	94		
ACU Sampler	2.9	6.77	232	145	49.7
	2.8	3.63	128		
	3.0	3.50	118		
	1.0	1.35	140		
	1.2	1.31	109		

Note: Replicates for samplers were different, with latex (*n*=3) and ACU (*n*=5).

Table 3. Total Recovered Free Base Following Contact Transfer Studies

Material Pair	Contaminant Dosed (mg)	Contaminant Recovered (mg)	Recovered (%)	Average Recovery (%)	Standard Deviation (%)
No Treatment Controls					
Butyl and Latex	1.70	2.79	164	125.0	63.5
	1.60	2.54	159		
	4.00	2.07	52		
Butyl and ACU	3.88	4.95	128	157.4	30.1
	2.56	4.81	188		
	2.16	3.39	157		
Nitrile and Latex	1.30	2.12	163	167.8	64.4
	1.00	2.34	234		
	2.30	2.44	106		

Table 3. Total Recovered Free Base Following Contact Transfer Studies (Continued)

Material Pair	Contaminant Dosed (mg)	Contaminant Recovered (mg)	Recovered (%)	Average Recovery (%)	Standard Deviation (%)
Nitrile and ACU	5.14	5.34	104	110.0	5.3
	6.16	7.01	114		
	6.00	6.73	112		
Soapy Water Rinse Treatment					
Butyl and Latex	2.00	1.83	91	97.9	6.1
	2.10	2.07	98		
	2.10	2.18	104		
Butyl and ACU	2.35	4.19	178	168.3	8.9
	3.35	5.51	165		
	4.49	7.27	162		
Nitrile and Latex	2.40	2.05	86	78.5	6.1
	3.10	2.35	76		
	2.50	1.85	74		
Nitrile and ACU	4.92	4.55	92	110.4	16.9
	10.6	11.91	113		
	4.89	6.16	126		

Note: In all cases, *n*=3.

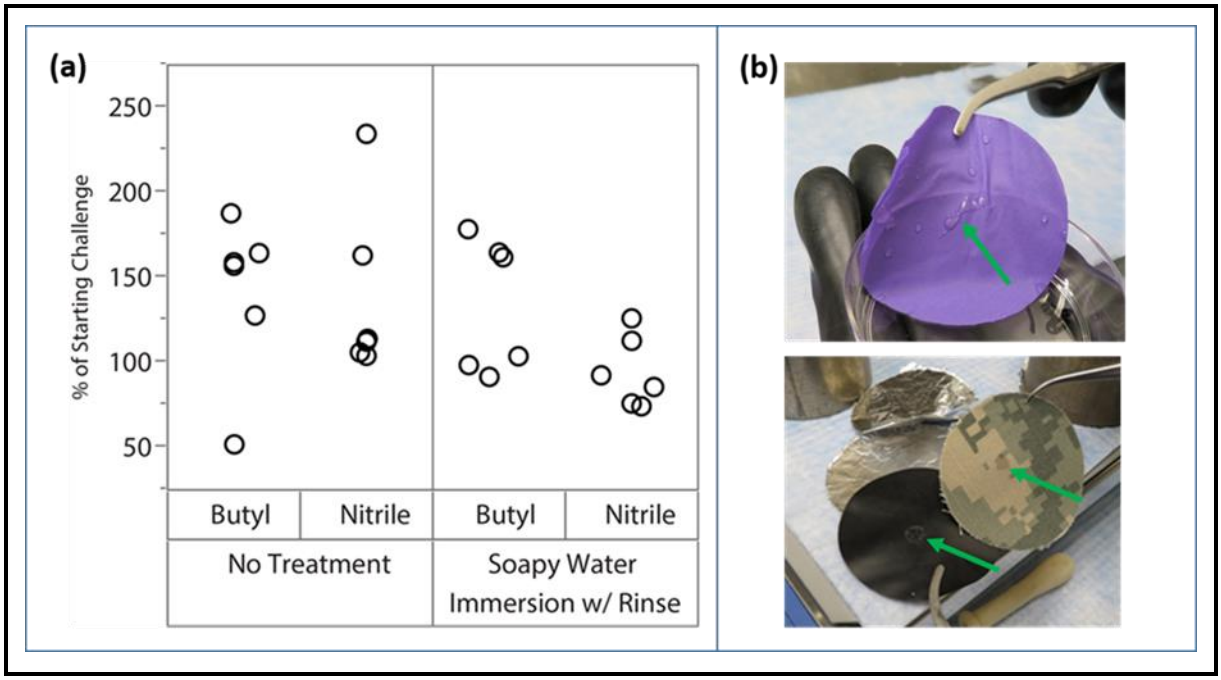

Figure 7. Graphical depiction of total free base recovered (coupon + contact sampler) during contact transfer studies (a). Free base adhering to nitrile glove coupon following the soapy water immersion and water rinse (b, top). Free base acting like an adhesive sandwiched between butyl rubber coupon and ACU sampler (b, bottom).

3.1.2 Carfentanil Citrate in Methanol

In contrast to the free base, the carfentanil citrate was dissolved in methanol prior to use. The solution was prepared at a concentration of 100 mg/mL (after correction for the weight of the citrate salt) and was refrigerated after the first use. When the solution was equilibrated to room temperature for the next use, salt crystals were noted on the inside of the glass wall of the vial. A fresh citrate solution was prepared and used for the next two studies. The mass of carfentanil dosed onto the coupons was test specific and estimated from the average contaminant mass recovered from the DCS for each test session. All samples in a test session, including the DCS, were dosed with 20 µL of the same citrate solution. DCS results are listed in Table **4**.

Table 4. Summary of Contaminant Recovered in the Citrate DCSs

DCS References	Contaminant Recovered (mg)	Average Recovered (mg)	Standard Deviation (mg)
Test One	1.62	1.99	0.35
	2.04		
	2.32		
Test Two	2.71	2.89	0.16
	2.99		
	2.97		
Test Three	2.64	2.38	0.23
	2.20		
	2.31		

Note: In all cases, *n*=3.

The improved precision due to the delivery of the contaminant in solvated form is evident in the recoveries listed from the “no treatment” condition in Table 5.

Table 5. Total Recovered Citrate Following Contact Transfer Studies

Material Pair	Contaminant Dosed (mg)	Contaminant Recovered (mg)	Recovered (%)	Average Recovery (%)	Standard Deviation (%)
No Treatment Controls					
Butyl and Latex	1.99	1.67	83.8	92.0	5.8
	1.99	1.80	90.3		
	1.99	1.81	90.8		
	1.99	1.92	96.2		
	1.99	1.97	98.9		
Butyl and ACU	2.89	2.72	94.2	94.6	10.4
	2.89	2.44	84.4		
	2.89	3.04	105.2		
Nitrile and Latex	2.38	2.51	105.5	95.6	6.7
	2.38	2.08	87.4		
	2.38	2.19	91.9		
	2.38	2.28	95.7		
	2.38	2.32	97.3		
Nitrile and ACU	2.89	2.81	97.3	93. 1	4.8
	2.89	2.54	87.8		
	2.89	2.72	94.1		
Soapy Water Rinse Treatment					
Butyl and Latex	1.99	0.44	22.2	19.6	7.1
	1.99	0.42	21.3		
	1.99	0.30	15.0		
	1.99	0.21	10.5		
	1.99	0.58	29.1		
Butyl and ACU	2.89	0.42	14.6	12.2	3.1
	2.89	0.25	8.7		
	2.89	0.39	13.4		
Nitrile and Latex	2.38	0.56	23.4	18.0	5.5
	2.38	0.58	24.3		
	2.38	0.38	15.9		
	2.38	0.31	13.1		
	2.38	0.31	13.1		
Nitrile and ACU	2.89	0.22	7.8	6.3	2.5
	2.89	0.22	7.6		
	2.89	0.10	3.4		

An average of 94% of carfentanil was recovered across the no treatment condition of all materials. An average of 15% of carfentanil, spanning a range of 3 to 29%, was recovered across the samples treated with the soapy water immersion and water rinse. The decrease in

residual carfentanil for these samples is attributed to the enhanced solubility of the citrate form, resulting in physical removal of the bulk contaminant by the soapy water treatment and wash.

It is interesting to note; however, that the evaporative residue of the citrate remaining on the coupons following the age time was similar in appearance to the free base. The expectation was that the residue left behind after the methanol evaporated would have a dry, crusty appearance and would be easily rinsed away. Instead, the carfentanil residue left behind on the glove coupon was thick and tacky like the free base and acted as an adhesive when topped with the contact sampler. Some of the residue was clearly visible on the contaminated coupons following the soapy water rinse treatment, as can be seen in Figure 8.

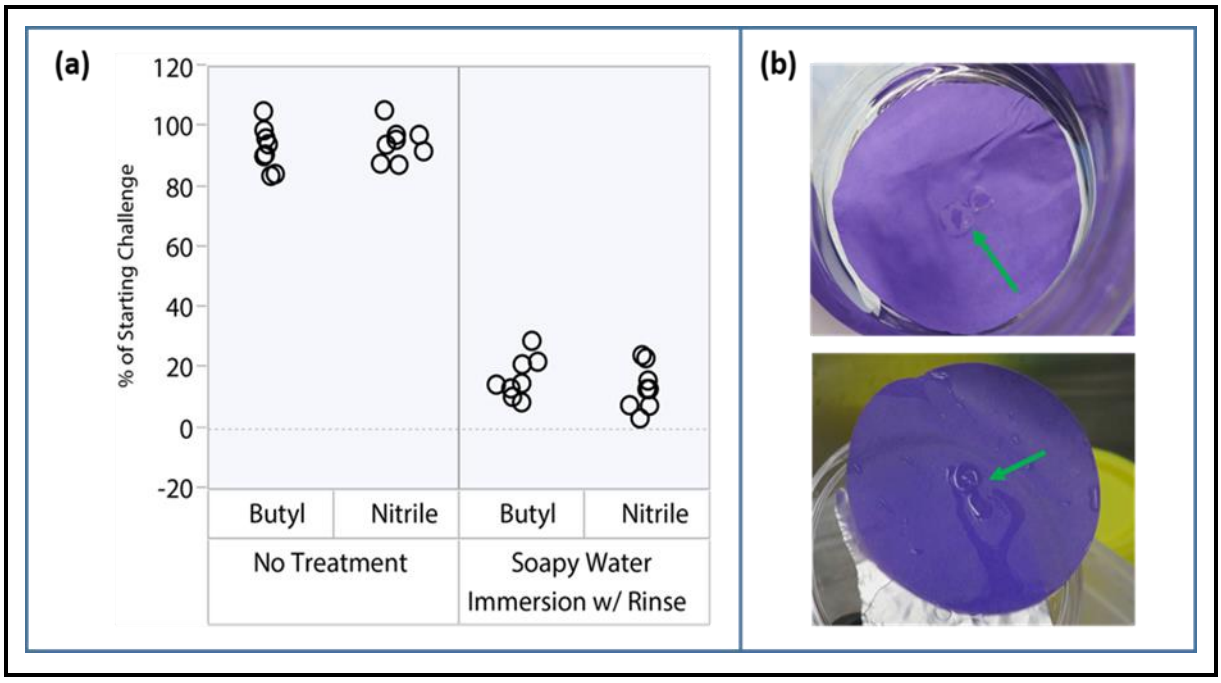

Figure 8. Graphical depiction of total carfentanil from citrate in methanol (coupon + contact sampler) recovered during contact transfer studies (a). Evaporative residue from the citrate in methanol remaining on a nitrile coupon following the 30 min age time (b, top) and following the soapy water immersion and rinse (b, bottom).

3.2 Contact Transfer – Effect of Contaminant Form

The results in the previous sections demonstrated that contaminant form is a key factor in decontamination via physical removal. The neat free base clearly presented the greater challenge in physical removal; however, both forms left behind a significant amount of contaminant on the surface of the glove materials. This residual contaminant is what translates into a potential hazard through transfer to skin or other surfaces.

This study also investigated the potential transfer of contaminant from two similar non-permeable smooth surfaces, butyl and nitrile gloves, to two potentially permeable surfaces, one smooth (latex) and the other rough (ACU). The exploratory studies performed here were intended to provide some insight into the effects of surface morphology on contact transfer of PBAs.

3.2.1 Contact Transfer of Citrate Form

The enhanced solubility of the citrate resulted in removal of contaminant from the surfaces of gloves during the soapy water treatment. Less contaminant was available for transfer with this condition than with the no treatment condition. To accommodate for the bias in transfer due to the disparate amounts of available contaminant, the mass of contaminant found on the glove coupon and its associated contact sampler was summed, then normalized to 100%. Transfer efficiency across conditions was compared based on the percent of total contaminant that was recovered on the contact sampler.

In the case of the latex samplers, both the contaminated gloves and the contact samplers had a similar surface smoothness. The results displayed in Table 6 and illustrated in Figure 9 show that, regardless of treatment, approximately 25 to 50% of the remaining citrate contaminant on the gloves was transferred to the latex samplers.

Table 6. Citrate Form Transferred to Latex from Glove Materials

Glove Material	Opioid (mg)			Opioid Transferred (%)	Average Opioid Transfer (%)*
	On Glove	On Latex Sampler	Total Recovered		
No Treatment Controls					
Butyl	1.03	0.64	1.67	38.5	47.2±6.5
	0.86	0.94	1.80	52.0	
	1.01	0.81	1.81	44.5	
	0.86	1.05	1.92	55.0	
	1.07	0.90	1.97	45.9	
Nitrile	2.32	0.19	2.51	7.7	26.6±11.8
	1.47	0.61	2.08	29.2	
	1.31	0.88	2.19	40.0	
	1.68	0.60	2.28	26.3	
	1.63	0.69	2.32	29.8	

Table 6. Citrate Form Transferred to Latex from Glove Materials (Continued)

Glove Material	Opioid (mg)			Opioid Transferred (%)	Average Opioid Transfer (%)*
	On Glove	On Latex Sampler	Total Recovered		
Soapy Water Rinse Treatment					
Butyl	0.23	0.22	0.44	48.9	44.4±8.7
	0.21	0.21	0.42	49.9	
	0.14	0.16	0.30	53.2	
	0.14	0.07	0.21	35.2	
	0.38	0.20	0.58	34.8	
Nitrile	0.30	0.25	0.56	45.8	40.0±5.8
	0.35	0.23	0.58	39.0	
	0.22	0.16	0.38	42.2	
	0.20	0.12	0.31	37.5	
	0.22	0.09	0.31	30.3	

Note: In all cases *n*=5.
*Reported as the mean ± standard deviation.

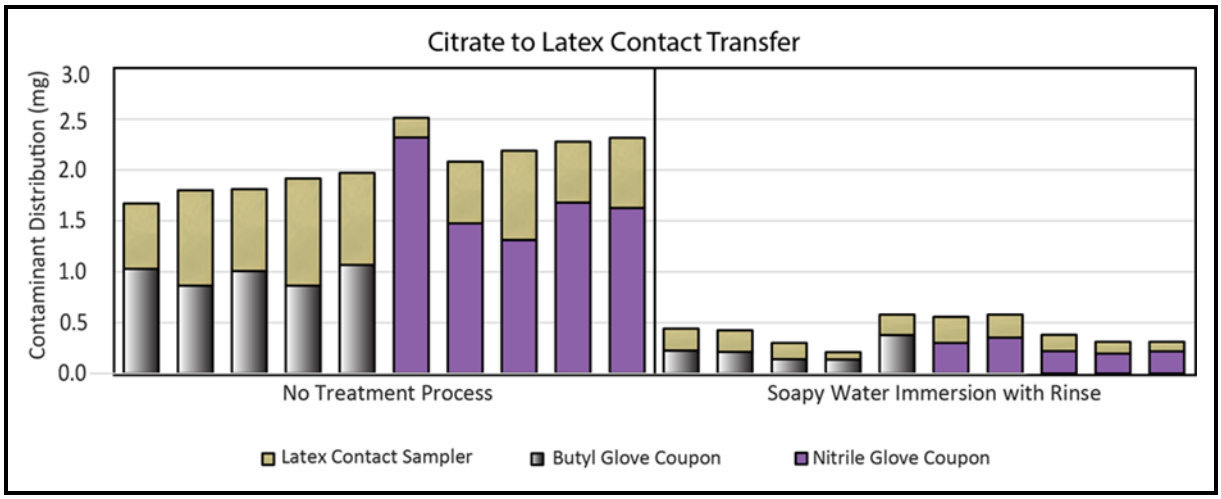

Figure 9. Graphical depiction of the distribution of the contaminant following the contact transfer process. The upper portion (tan) of the graphs represents the contaminant that was transferred to the latex contact samplers.

In contrast with the smooth surfaces of the gloves and latex, the surface of the ACU samplers was rough and permeable, due to the woven nature of the material. For the no treatment condition, where there was more available contaminant for transfer and both the gloves and contact samplers were dry, 70% of the residual citrate was transferred to the surface of the rough ACU material. For the soapy water condition, transfer to the ACU from the wet butyl and nitrile coupons was lower, at 60 and 23%, respectively. The results are provided in Table 7 and illustrated in Figure 10.

Table 7. Citrate Form Transferred to ACU from Glove Materials.

Glove Material	Opioid (mg)			Opioid Transferred (%)	Average Opioid Transfer (%)*
	On Glove	On Latex Sampler	Total Recovered		
No Treatment Controls					
Butyl	0.57	2.16	2.72	79.2	77.4±6.0
	0.71	1.72	2.44	70.7	
	0.54	2.50	3.04	82.2	
Nitrile	0.62	2.19	2.81	77.8	76.6±2.4
	0.66	1.87	2.54	73.9	
	0.59	2.12	2.72	78.1	
Soapy Water Rinse Treatment					
Butyl	0.18	0.24	0.42	56.1	59.5±4.3
	0.11	0.15	0.25	58.0	
	0.14	0.25	0.39	64.4	
Nitrile	0.16	0.07	0.22	29.1	22.6±7.4
	0.19	0.03	0.22	14.6	
	0.07	0.02	0.10	24.0	

*Reported as the mean ± standard deviation
Note: In all cases *n*=3.

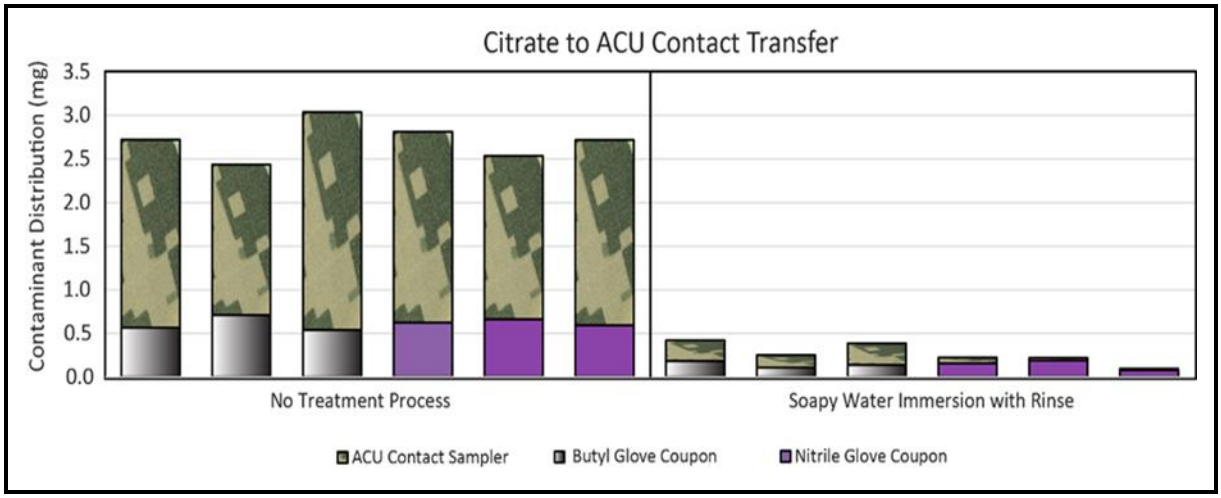

Figure 10. Graphical depiction of the distribution of the contaminant following the contact transfer process. The tan and green patterned upper portion of the graphs represents the contaminant that was transferred to the ACU contact samplers.

3.2.2 Contact Transfer of Free Base Form

Unlike the citrate, the free base on the surfaces of the contaminated glove coupons was essentially unaffected by the soapy water immersion and water rinse. However, due to the difficulty in depositing the free base on the coupons, there was still variability in the amount of contaminant available for transfer across the coupon-sampler pairs. This variability is especially evident in the coupons paired with the ACU contact samplers.

As noted earlier, the free base had to be heated and stirred to reduce its viscosity and make it pliable enough to allow transfer by pipet. With each successive cycle of heating and cooling, the remaining unused portion of the free base became thicker and even more challenging to work with. The ACU studies were conducted later than the latex studies, so there was more variability in the amount of contaminant that was deposited on the gloves.

As with the citrate, the contact transfer comparison was made based on the percent transferred out of the total recovered contaminant. Following the contact period with the latex sampler, the distribution of the free base was consistently divided almost equally between the two types of smooth surfaces. On average, 56% of the free base adhered to the latex while 44% remained on the smooth glove coupons. The results are provided in Table **8** and illustrated in Figure 11.

Table 8. Free Base Form Transferred to Latex from Glove Materials

Glove Material	Opioid (mg)			Opioid Transferred (%)	Average Opioid Transfer (%)*
	On Glove	On Latex Sampler	Total Recovered		
No Treatment Controls					
Butyl	0.96	1.84	2.79	65.8	64.2±1.5
	0.94	1.60	2.54	62.9	
	0.75	1.32	2.07	63.9	
Nitrile	1.06	1.06	2.12	50.2	50.8±2.4
	1.20	1.14	2.34	48.8	
	1.13	1.30	2.44	53.5	
Soapy Water Rinse Treatment					
Butyl	0.75	1.08	1.83	59.1	59.6±2.0
	0.87	1.20	2.07	57.9	
	0.83	1.34	2.18	61.8	
Nitrile	0.96	1.09	2.05	53.3	50.8±2.3
	1.20	1.15	2.35	48.8	
	0.92	0.93	1.85	50.2	

*Reported as the mean ± standard deviation.
Note: In all cases n=3.

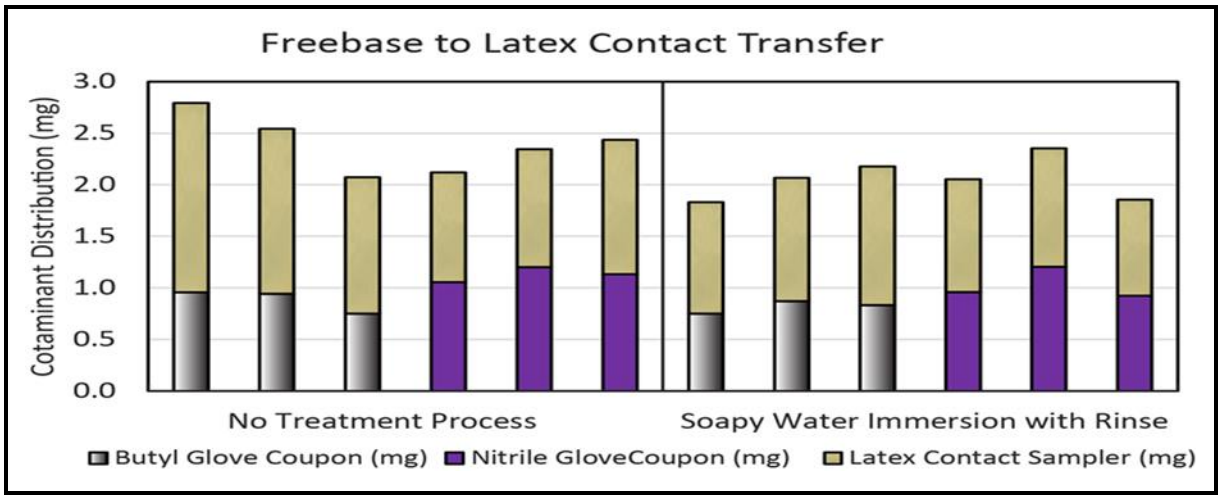

Figure 11. Graphical depiction of the distribution of the free base contaminant following the contact transfer process. The upper portion (tan) of the graphs represents the contaminant that was transferred to the latex contact samplers.

Due to the increased viscosity of the free base, the starting challenge for the studies using the ACU samplers was greater than that for the latex. Similar to the latex study, the free base was consistently divided between the surfaces of the glove coupons and the ACU samplers. There was greater transfer overall however to the rough, dry surfaces of the ACU material. On average, 75% of the free base transferred to the ACU, while 25% adhered to the glove surfaces. The results are provided in Table 9 and illustrated in Figure 12.

Table 9. Free Base Form Transferred to ACU from Glove Materials

Glove Material	Opioid (mg)			Opioid Transferred (%)	Average Opioid Transfer (%)*
	On Glove	On ACU Sampler	Total Recovered		
No Treatment Controls					
Butyl	1.54	3.41	4.95	68.9	67.5±1.7
	1.66	3.15	4.81	65.6	
	1.09	2.30	3.39	67.9	
Nitrile	1.61	3.73	5.34	69.9	72.7±2.8
	1.71	5.30	7.01	75.6	
	1.85	4.88	6.73	72.5	
Soapy Water Rinse Treatment					
Butyl	0.84	3.36	4.19	80.1	79.8±0.9
	1.07	4.44	5.51	80.5	
	1.54	5.72	7.27	78.8	
Nitrile	0.96	3.59	4.55	78.9	79.8±2.5
	2.63	9.28	11.91	77.9	
	1.07	5.08	6.16	82.6	

*Reported as the mean ± standard deviation.
Note: In all cases *n*=3.

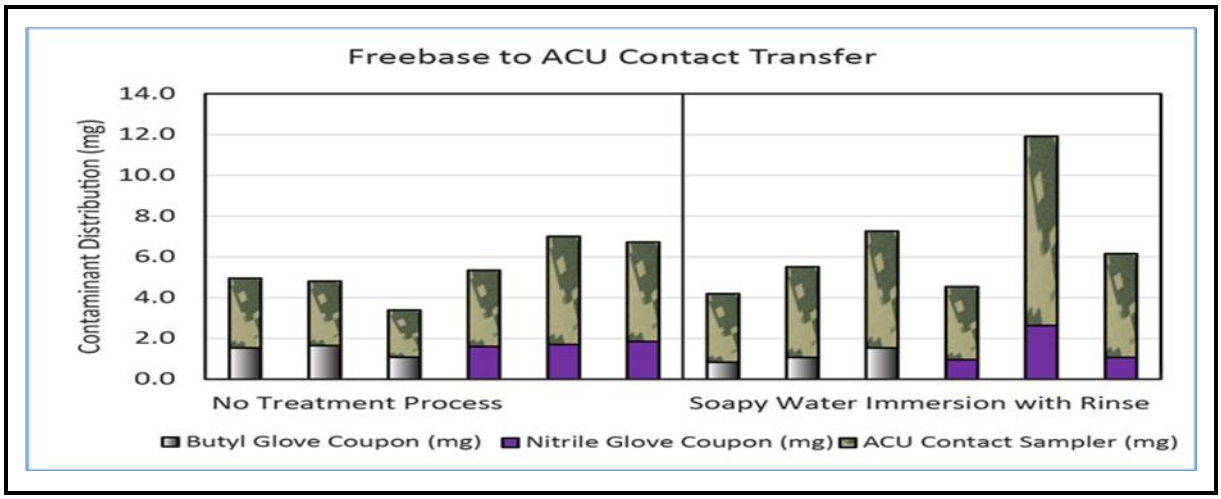

Figure 12. Graphical depiction of the distribution of the free base contaminant following the contact transfer process. The tan and green patterned upper portion of the graphs represents the contaminant that was transferred to the ACU contact samplers.

4. CONCLUSIONS AND RECOMMENDATIONS

The scoping studies presented in this report were designed to probe for answers to questions about the potential hazards associated with certain PBA contaminants, such as opioids. For example, does decontamination by soapy water immersion and water rinsing reduce the potential for contact transfer of an opioid from contaminated protective equipment to other surfaces including skin and clothing? Does the form of the contaminant, such as the free base, salt or a solution thereof, affect the potential for contact transfer? What challenges need to be addressed to provide both experimental and theoretical answers regarding the hazards due to contact transfer? While these questions are asked of a whole class of compounds, carfentanil was chosen as a representative opioid contaminant for use in the study.

The results of this study demonstrate that contaminant form is a key factor in determining the risk associated with contact transfer following decontamination processes. The soapy water immersion and rinse process performed better on the citrate form than the free base form because of the enhanced solubility of the citrate form. Approximately 75% less residual citrate than free base was found on or in the butyl and nitrile substrates evaluated.

These results also demonstrated that, for both the free base and the solvated citrate, residual contaminant remained on the surfaces of the gloves even after the soapy water treatment process. Following contact, an average of between 40 and 80% of the residual contaminant was transferred to the surfaces of the latex and ACU contact samplers. The rough, dry surface of the ACU tended to pick up more of the residual contaminant than the smooth surface of the latex.

The execution of this study revealed the logistical challenges that are faced regarding laboratory infrastructure, experimental throughput, and precision and accuracy when working with solid and non-liquid forms such as the salts and free base. There is an inherently greater risk and higher cost associated with conducting experiments with carfentanil than with traditional agents because of its ultra-potency and non-liquid form.

Personnel safety dictates the necessity of working in a glove box when handling hazardous solids due to the potential for aerosolization. Depending on the size and sophistication of the glove box, sample throughput is reduced when compared to working in a chemical fume hood. Larger amounts of solid agents are generally required to allow for accuracy and consistency in depositing known amounts of contaminant on a surface. These results suggest that evaporative residues of solvated contaminants, such as the citrate in methanol, do not behave physically and chemically the same as the neat materials. For this reason, protocols may need to be established or new equipment purchased to enable the handling of microgram quantities of materials.

The methodology associated with the study of contact transfer of liquid agents and the translation into adverse human health effects is the focus of a current research effort.[6] Future efforts are being planned to leverage the outcomes of that program to provide a path forward to the study of contact transfer involving non-liquid contaminant.

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ACRONYMS AND ABBREVIATIONS

ACU	Army combat uniform
CAD	collisionally activated dissociation
CWA	chemical warfare agent
DCS	dose control sample
DEVCOM CBC	Combat Capabilities Development Command Chemical Biological Center
DTRA	Defense Threat Reduction Agency
ECBC	U.S. Army Edgewood Chemical Biological Center
LC/MS	liquid chromatography/mass spectrometry
MRM	multiple reaction monitoring
PBA	pharmaceutical based agent
PPE	personal protective equipment
PDCATTI	Product Director for Cross-Commodity Advanced Threats & Test Infrastructure
SD2ED	Chemical Contaminant and Decontaminant Test Methodology Source Document: Second Edition
UHPLC	ultra high performance liquid chromatography

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