Supporting the Responders: Fentanyl Sampling and Decontamination Studies

Lukas Oudejans, Ph.D.
Stuart Willison, Ph.D.

Center for Environmental Solutions and Emergency Response (CESER)
Homeland Security & Materials Management Division

Indiana Alliance of Hazardous Materials Responders
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Outline

- EPA's role in Emergency Response
  - Homeland Security Research Program
- Background on EPA's involvement with synthetic opioids
  - EPA's Fentanyl Fact Sheet
- Detection of Fentanyl: (Environmental) Sampling and Analysis
- Fentanyl Decontamination Research
- Risk Assessment Supporting a Response
- Questions

EPA's Role in Emergency Response

STATUTORY MANDATES

Assist water utilities in protecting their systems and responding to contamination incidents

Respond to environmental contamination incidents

Regulate pollutant discharge into waters

Register antimicrobials

Control hazardous wastes from cradle to grave

PRESIDENTIAL DIRECTIVES

Lead the protection of water infrastructure

Conduct biological and chemical agent cleanup

Develop capable laboratory network and surveillance/monitoring systems

Homeland Security Research Program

Vision

Federal, state, tribal, and local decision makers have timely access to information and the tools they need to ensure community resilience to catastrophes involving environmental contamination that threatens public health and welfare.

Program Objectives

Advance EPA's capabilities and those of our state, tribal, and local partners to respond to and recover from wide-area contamination incidents

Improve the ability of water utilities to prevent, prepare for, respond to and recover from water contamination incidents that threaten public health

RESPONSE MISSION SUPPORT

How do we contain the contaminant?

How do we characterize the contaminated area to inform public health decisions?

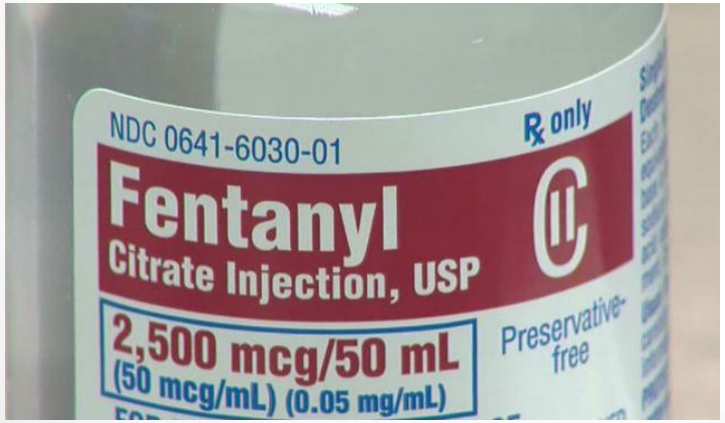
What capabilities do we have to clean-up contaminated areas?

How do we manage waste, both during response and long-term?

USEPA Office of Research and Development

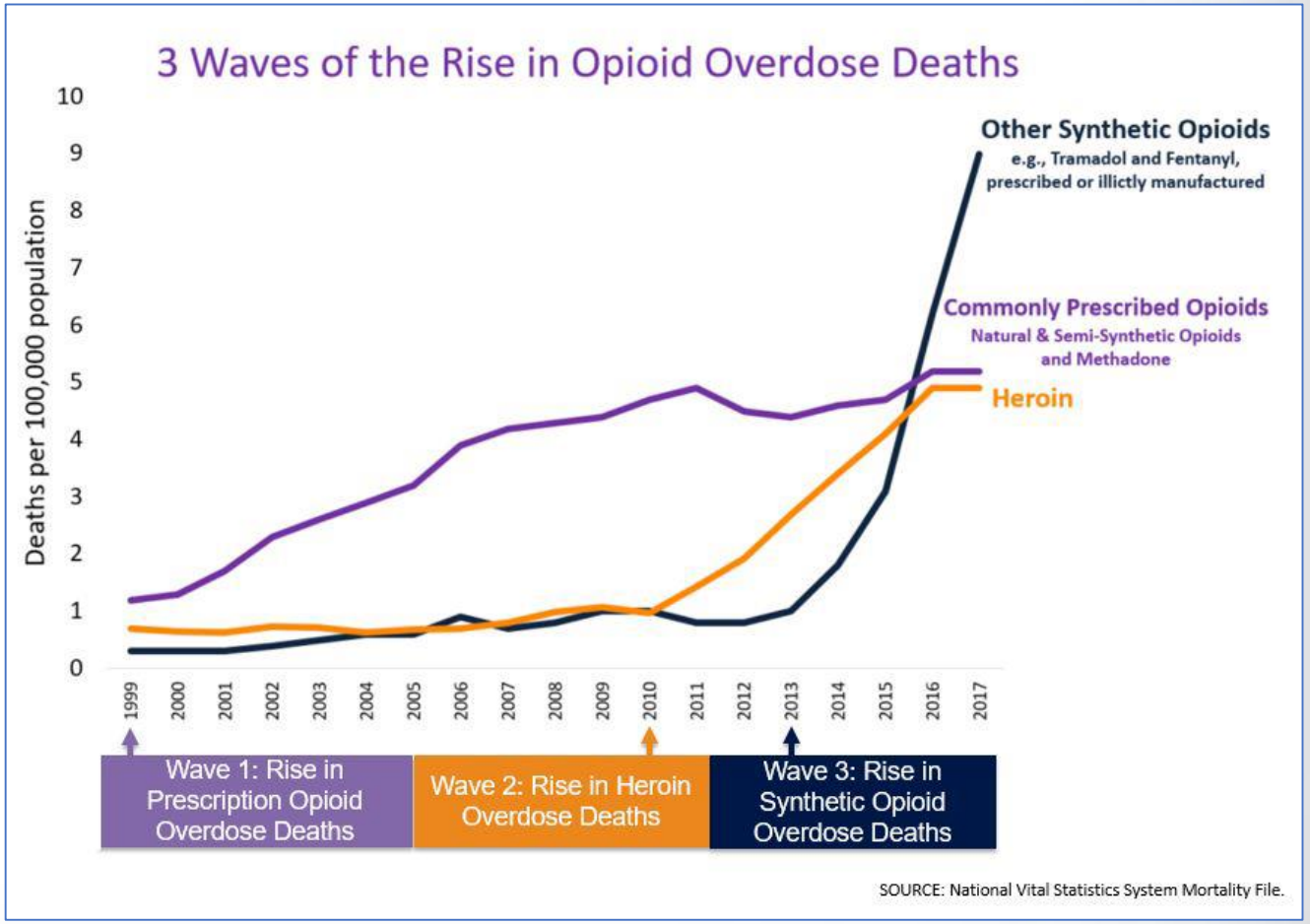
Center for Environmental Solutions and Emergency Response

Case Study:
Fentanyl Contamination
How Can We Sample and Clean it Up?



Opioid Crisis: Problem Definition

- Declared Nationwide Public Health Emergency (White House October 26, 2017)
- Rise in overdose deaths is largely due to the proliferation of imported or illicitly manufactured fentanyl, a highly potent synthetic opioid, and fentanyl analogs
- 2017: >70,000 drug overdose deaths in USA; >28,000 deaths were associated with synthetic opioids (other than methadone)



Opioid Crisis: Problem Definition

- Fentanyl and fentanyl analogs are a class of synthetic opiates (opioids)
  - Scheduled substances under the Controlled Substance Act
- Most fentanyl powders are imported from China & Mexico
- Fentanyl analogs are ever changing

18 pounds of fentanyl seized in Southern California – enough to make 4 million lethal doses

Fentanyl seizures in O.C. set to double for third year in a row, sheriff says

Fentanyl pills seized by the U.S. Drug Enforcement Administration. (Associated Press)

Los Angeles Times
Oct 18, 2019

CBP Officers Seize Largest Amount of Fentanyl in CBP History

www.cbp.gov, January 31, 2019
Press Event at the Port of Nogales, AZ

Fentanyl Seized at Port of Philadelphia

Enough fentanyl to kill 2 million people seized in NY home, DEA says

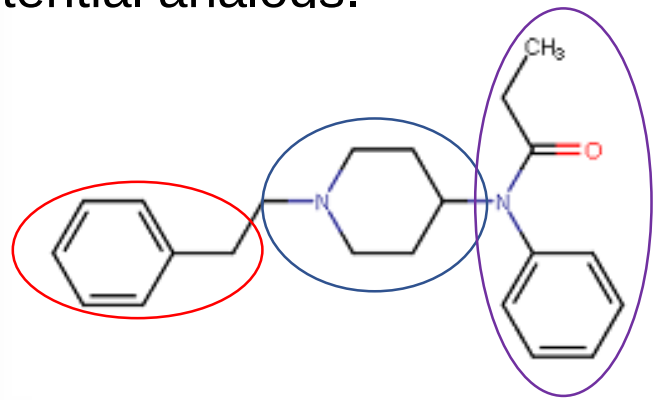
Potential Scenarios

- Law enforcement and Hazmat teams have sought EPA technical support in advising proper PPE and decon approaches at contaminated sites
- Calls about:
  - ✓Mixing houses, pill factories
  - ✓Makeshift laboratories found in apartments, hotels, houses, garages and storage facilities
  - ✓Illegal dumps containing the remnants of laboratories
  - ✓Possible fentanyl release(s) in correctional facilities
- *No EPA responders have responded on site, as of yet*

Lethal doses of heroin (left, 30 mg) and fentanyl (right, 3 mg) By New Hampshire State Police Forensic Lab/Public domain

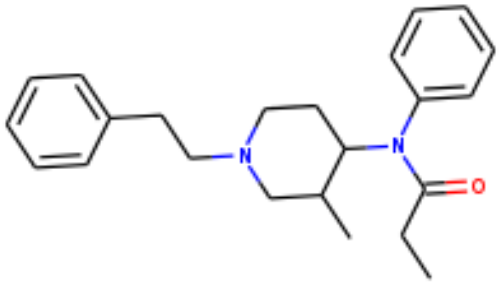
Background on Fentanyl

- Fentanyl analogs typically can be produced by altering the propyl alkyl amide moiety
- Modification is possible at all 3 parts of the molecule resulting in an infinite number of potential analogs.

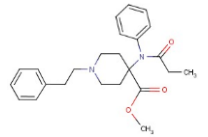


Fentanyl

1. Phenyl alkyl moiety
2. Piperdinyl ring moiety
3. Propyl alkyl amide moiety



3-methyl fentanyl



Carfentanil

Take home message:
Thousands of fentanyl analogs can be made, some of them can be (much) more potent than fentanyl itself

Occupational Exposure Scenarios

Potential exposure (without proper PPE) from

- Inhalation
- Oral (ingestion)
- Dermal
  - Larger amounts only
  - Route to mucous membrane
- Percutaneous
  - Accidental injection

Lethal doses of heroin (left, 30 mg) and fentanyl (right, 3 mg) By New Hampshire State Police Forensic Lab/Public domain

First EPA Effort:

Development of **Fentanyl Fact Sheet** (2017/2018)

- Provide EPA On Scene Coordinators (OSCs) with technical information

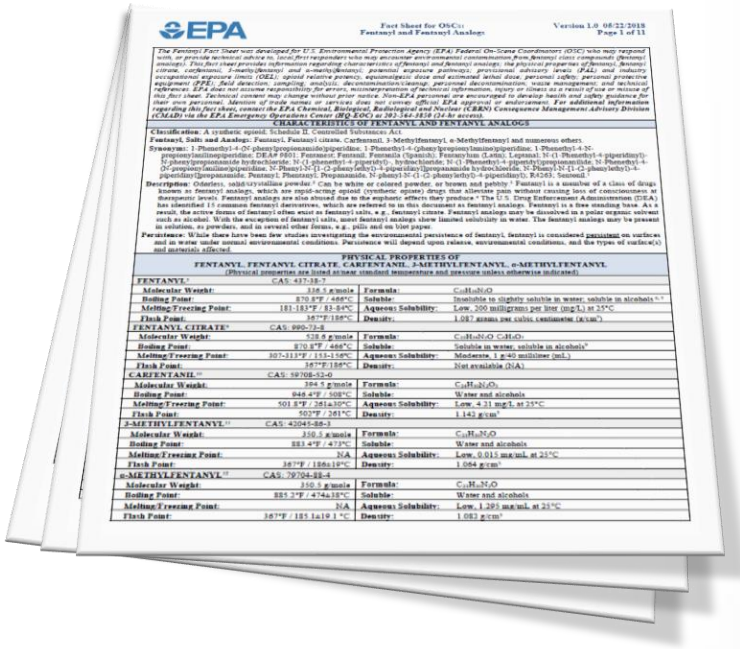
- To get ahead of the curve on possible EPA involvement in the cleanup and remediation

- To provide local, state, tribal, and county Hazmat partners with the most pertinent information needed for a safe response at opioid contaminated sites

First EPA Effort:

Fentanyl Fact Sheet (*May 2018*)

- It is a Fact Sheet, not "guidance" – no statutory/regulatory authority
- https://www.epa.gov/emergency-response/fact-sheet-fentanyl-and-fentanyl-analogs
- Living document
- Update in progress



Identified Research Gaps

- Sampling and Analysis
  - Lack of verified sampling & analytical methods
    - Material specific
- Decontamination/Cleanup
  - No operational relevant information available
    - Material specific
- Toxicology
  - Clinical vs environmental exposure
  - No dermal exposure values
- PPE
  - Inhalation protection always needed
  - Dermal protection may drive PPE selection

Fentanyl
Sampling and Analysis Research

Optimization of Sampling and Analysis

Research:

1. Evaluate analytical methods for environmental samples
   - LC-MS/MS capabilities
2. Evaluation of solvents
   - Elution system
   - Flow rates
   - Wipe wetting solvents
3. Evaluate sampling approaches
   - Surfaces
   - Water

Fentanyl Compounds:

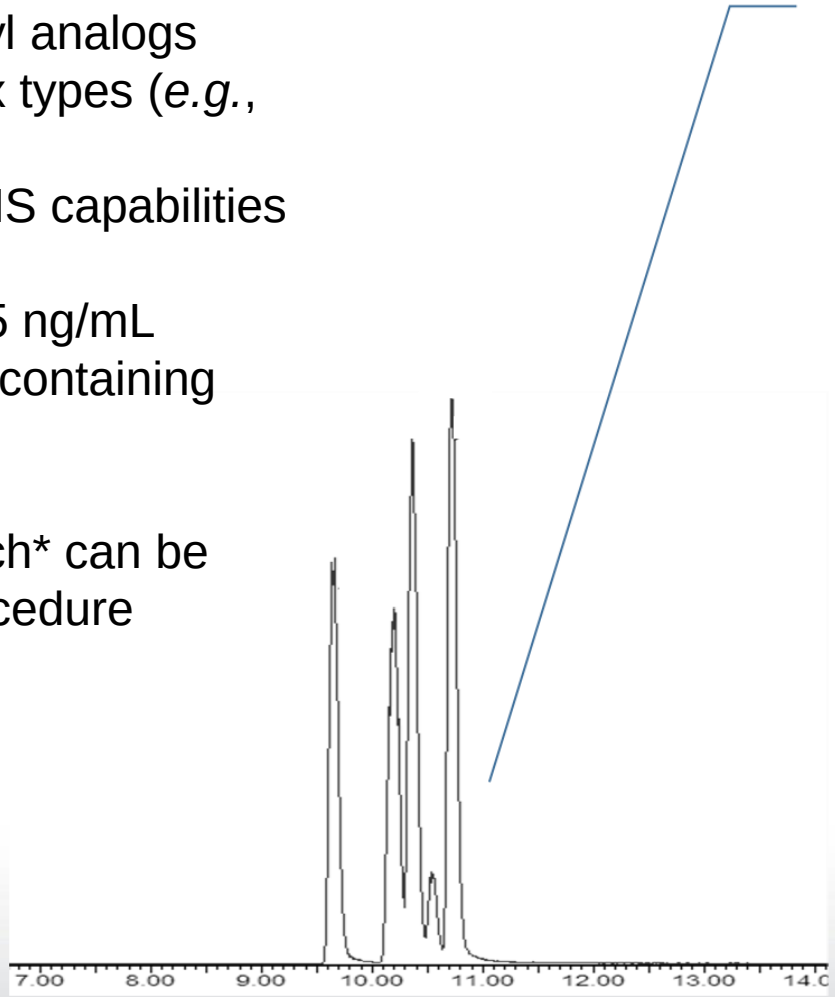
- Carfentanil
- Furanyl Fentanyl
- 3-methyl Fentanyl
- Fentanyl
- Acryl Fentanyl
- Acetyl Fentanyl

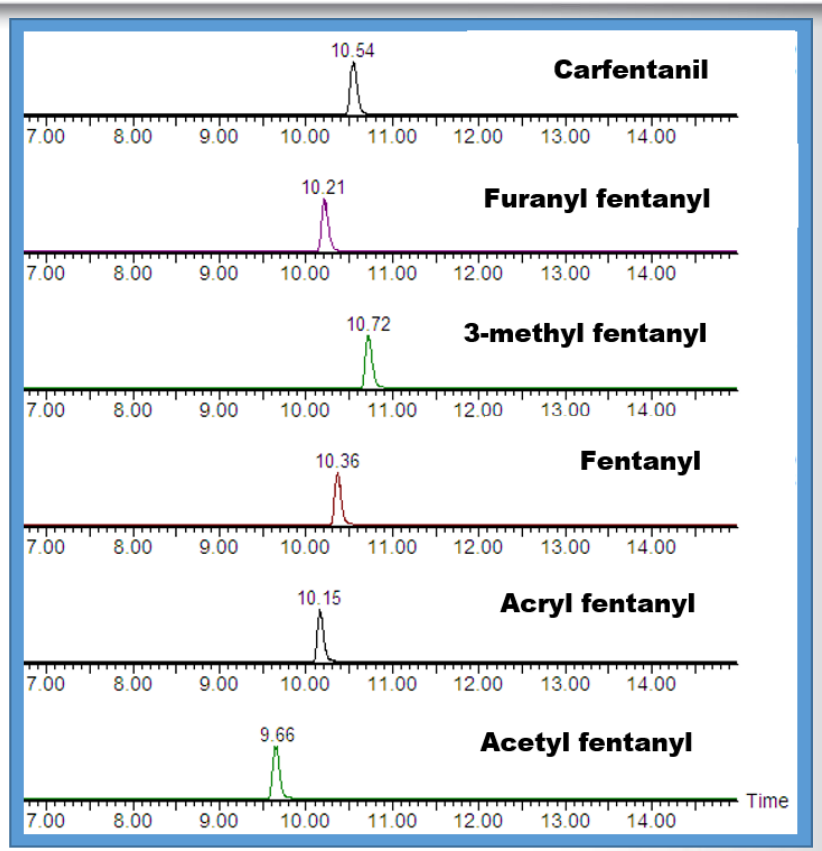
- Isotopically-labeled (IS)
  - Cafentanil-D_5
  - Fentanyl-D_5
  - Acetyl Fentanyl-$^{13}C_6$

Research Supporting Fentanyl Site Cleanup

Method Development & Optimization

- Investigation of fentanyl and fentanyl analogs of interest with environmental matrix types (*e.g.*, water, surfaces)
    - LC-MS/MS and UPLC-MS/MS capabilities
- Sensitive and robust capability (0.05 ng/mL range) with methanol/water eluents containing an acidic modifier
- Previous pesticide sampling research* can be used to optimize wipe sampling procedure





*S.A. Willison et al., *Science of the Total Environment*, 655 (2019) 539.

Preliminary Wipe Method Development and Evaluation

- Metal surface spiked with fentanyl analogs
  - 0.2 ng/cm^2 surface concentration[†]
- Two wipes for each 100 cm^2 coupon
  - Horizontal Z-pattern, then around perimeter
  - Vertical Z-pattern, then around perimeter
- Wetting solvent may affect recovery results
  - MeOH > IPA > 90:10 H_2O/ACN

Wipe Wetting Solvent	90:10 H_2O/ACN		IPA		MeOH	
Analyte	Avg* % Rec.	% RSD	Avg* % Rec.	% RSD	Avg* % Rec.	% RSD
Carfentanil	50	15	55	18	70	18
Furanyl fentanyl	33	18	42	22	59	10
3-methyl fentanyl	43	16	44	20	61	11
Fentanyl	62	24	53	19	81	12
Acryl fentanyl	45	15	40	16	61	7
Acetyl fentanyl	77	18	48	20	71	5

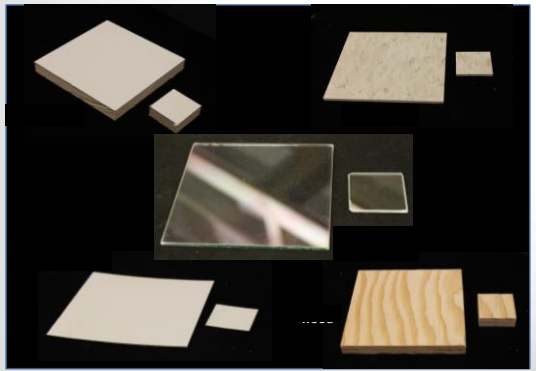
*Average of 8 samples

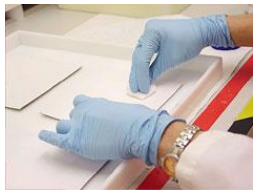
Values above 70%

[†] E. Sisco, M. Najarro, A Burns, *Forensic Chemistry*, 11 (2018) 47.

Preliminary Surface Evaluation

- Surface spiked with fentanyl analogs
  - 0.2 ng/cm^2 surface concentration
- Two wipes for each 100 cm^2 coupon
  - Horizontal Z-pattern, then around perimeter
  - Vertical Z-pattern, then around perimeter
- Placed in VOA vial, added IS, 10 mL of extraction solvent, sonicated for 10 minutes, filtered, and analyzed





Surface	Metal		Laminate	
Analyte	Avg* % Rec.	% RSD	Avg* % Rec.	% RSD
Carfentanil	116	17	81	16
Furanyl fentanyl	64	10	73	5
3-methyl fentanyl	72	8	79	4
Fentanyl	120	9	93	7
Acryl fentanyl	64	12	71	6
Acetyl fentanyl	117	10	99	8

*Average of 8 samples
Values above 70%

Conclusions and Future Studies

- **Flow rates and elution solvents of LC/MS/MS system may affect sensitivity**

- **Wipe wetting solvents may affect recovery results.**
  - Methanol is the solvent of choice at this moment

On-going & future research efforts include:

- **Surface contamination evaluations to inform wipe sampling and analytical methods**
  - Alternative wipe materials (e.g., pre-packaged, pre-wetted wipes) and their effects on recovery results
  - Alternative surfaces of interest (e.g., household surfaces)
  - Alternative matrix types (e.g., water contamination)

Fentanyl Decontamination Research

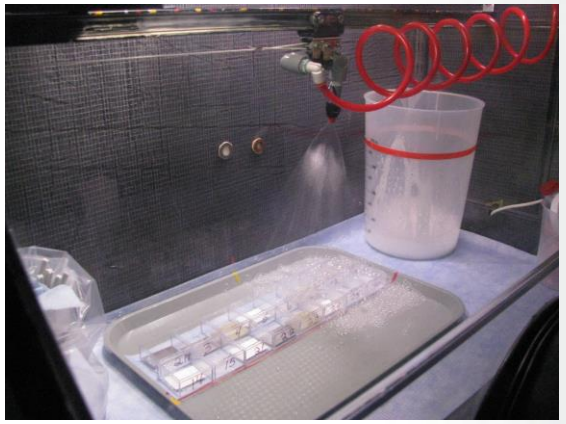
Decontamination / Cleanup

State of the Science:

- Scientific data for fentanyl/opioid environmental cleanup are lacking
- Scientific data were limited to basic reaction chemistries
- Cleanup responses appear to rely mainly on the physical removal of fentanyl (instead of degradation of fentanyl)
  - This creates fentanyl/opioid containing waste
- Cleanup following meth cleanup recommendations *may* be adequate (*Indianapolis fentanyl house case*)
- Misinterpretation of cleanup information when using a specific detergent

EPA/ORD Surface Decon Research

- Decontamination of building materials contaminated with fentanyl-HCl powder (1 mg)
- Bench-scale, yet realistic scenario, study
  - Various decontaminants / active ingredients
  - Representative decon solution amounts applied
  - Relevant nonporous building materials
  - Impact of benign additives on efficacy



Spray application setup – EPA/Battelle 2018/2019

Dahlgren Decon
peracetic acid

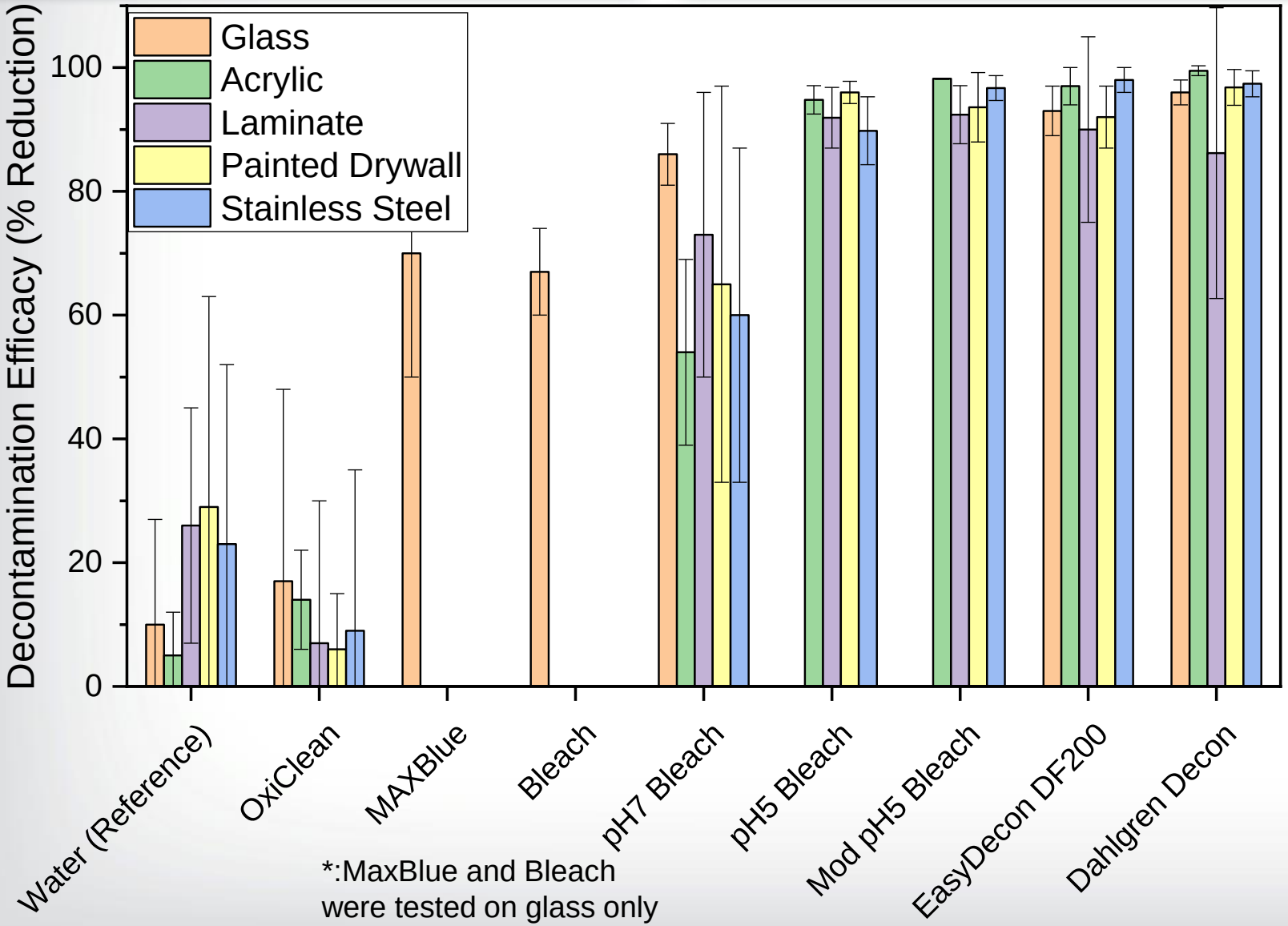
EasyDecon DF200
hydrogen peroxide

OxiClean
percarbonate

Bleach
hypochlorite

MaxBlue
*trichlor**

Preliminary Decon Efficacy Results (1 hr Contact Time)



*:MaxBlue and Bleach were tested on glass only

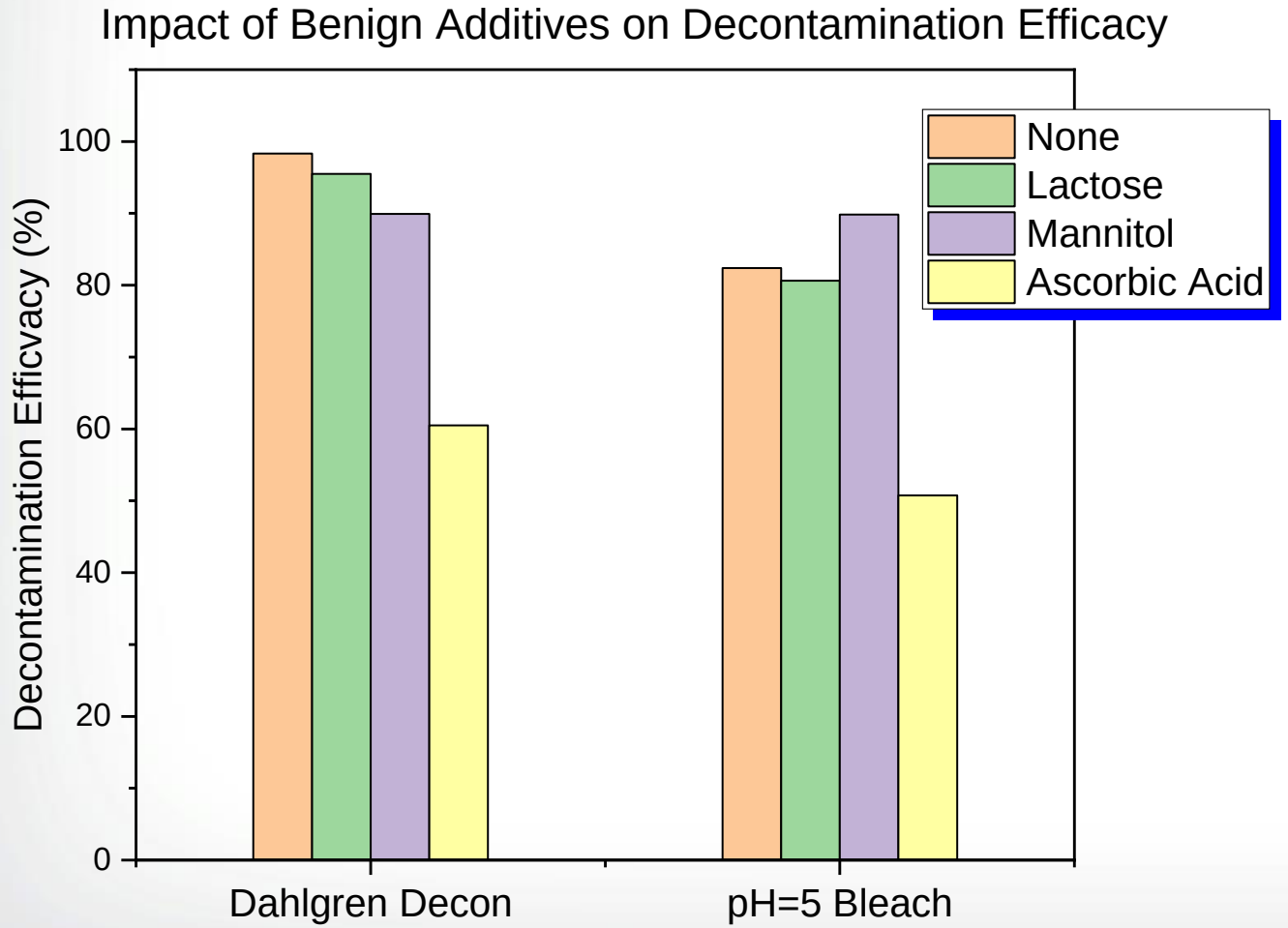
- Water and OxiClean show no degradation capabilities
- Minimal material dependence in decontamination efficacy for these relatively nonporous materials
- Highest efficacies observed for Dahlgren Decon, EasyDecon DF200, and pH5 bleach
- All decontamination products prepared as per manufacturer or label descriptions except for bleach

So where is my favorite Decon Product?

	EasyDECON® DF200	Meth Remover®
Manufacturer	EFT/Intelagard	Apple Environmental
Active ingredient	Hydrogen Peroxide (HP)	Hydrogen Peroxide (HP)
Other ingredients	Surfactant (proprietary), diacetin, water	Disodium carbonate 1-5%, ethanol 1-5%, water
Concentrations in parts	7.9% HP in Part 2 by wt. [SDS]	<8% HP in Part 2 [SDS]
Active ingredient concentration in mixed/final product	4.3% HP (measured)	~ 4% HP (estimate)
pH final product	9.4 (measured)	?

By first approximation, these two products may provide same ability to degrade fentanyl

Caution about presence of benign additives

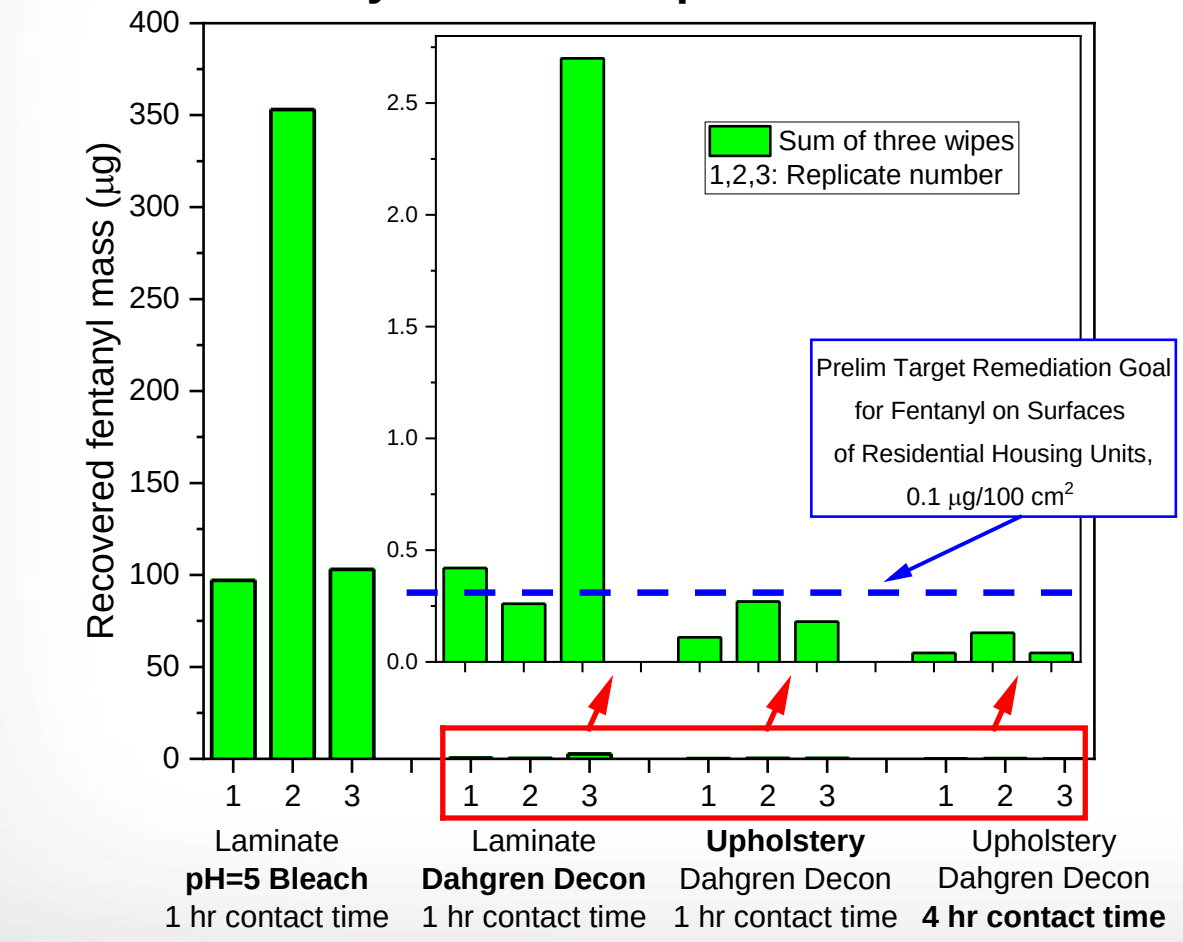


*: 5% fentanyl in additive tested

Fentanyl may be found as a mixture with benign additives.

- ❑ Efficacy can be lower in presence of benign additives that may create a material demand for the decontamination solution
- ❑ Second application of the same decontaminant may overcome some of the losses in active ingredient (not verified)

How Clean is Clean?
Medium size Coupon Decon Tests



- Residual fentanyl may be below preliminary remediation target for fentanyl (adjusted for sampled surface size)
- This is based on bench-scale research
  - Ideal conditions
  - No additives present
- Occasionally observed “clumps” of fentanyl (aggregated in decon solution) may result in higher recoveries [test #3, laminate]

Decontamination Conclusions

- **Decon solutions for fentanyl-contaminated materials are available**
  - Fentanyl may clump together
  - Additives may impact expected decontamination efficacy
- **Cleanup approaches still need to be assessed**
- **More decontamination research is required to assess:**
  - Formation of (stable) and toxic by-products during decon
  - Impact of other chemicals on efficacy
  - How to decon porous materials
  - PPE decontamination options
  - Decon of other fentanyl analogs
- **Upcoming Research:**
  - Scale up to address decontamination application approaches
  - Volumetric decontamination of materials

Acknowledgments / Points of Contact

EPA, Fentanyl Fact Sheet:

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EPA, Fentanyl Research Partners:

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Michigan DHHS, Massachusetts DEQ

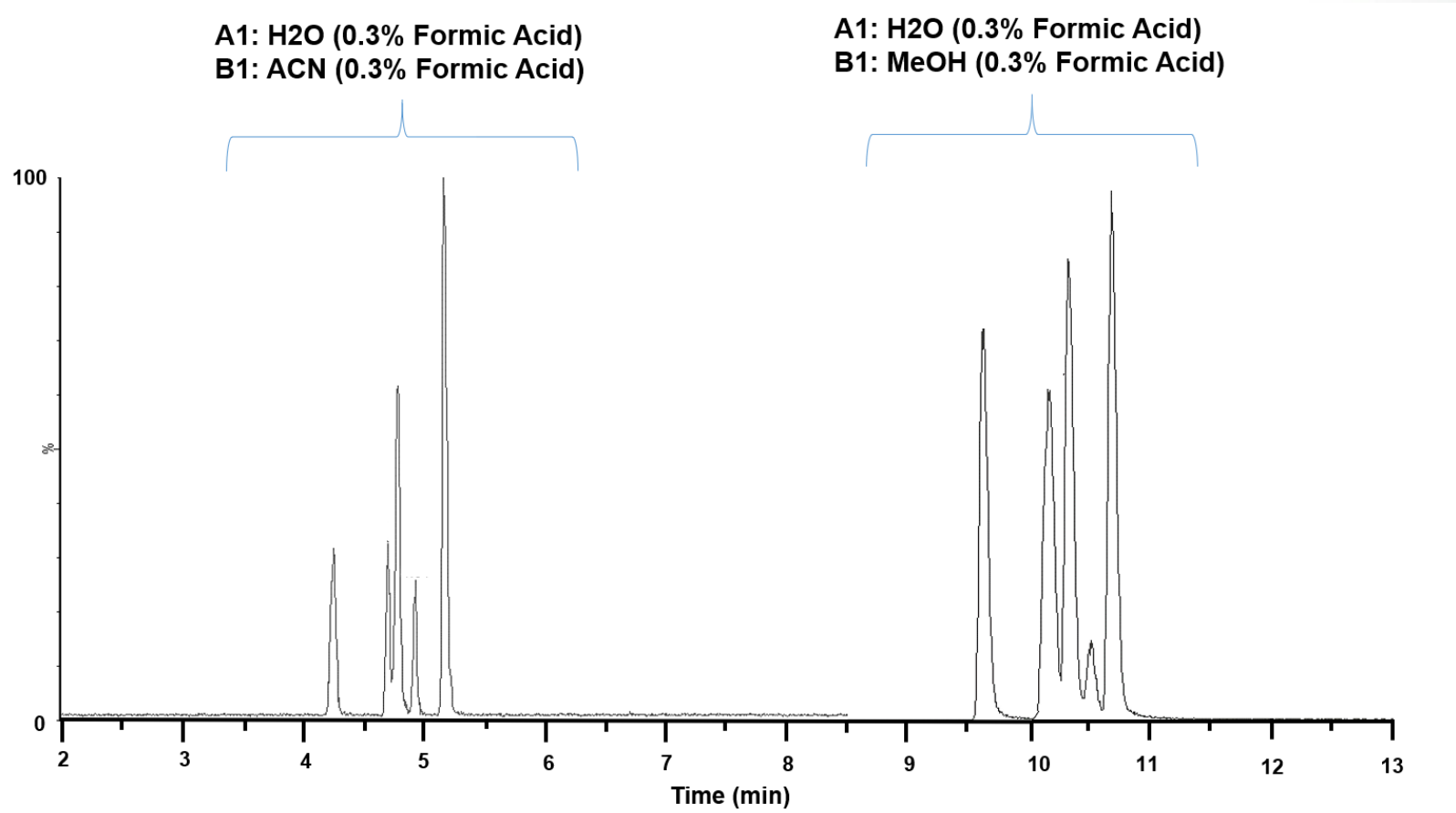
EPA, ORD/CESER/HSMMD

Stuart Willison, Matthew Magnuson, and Lukas Oudejans

Backup Slides

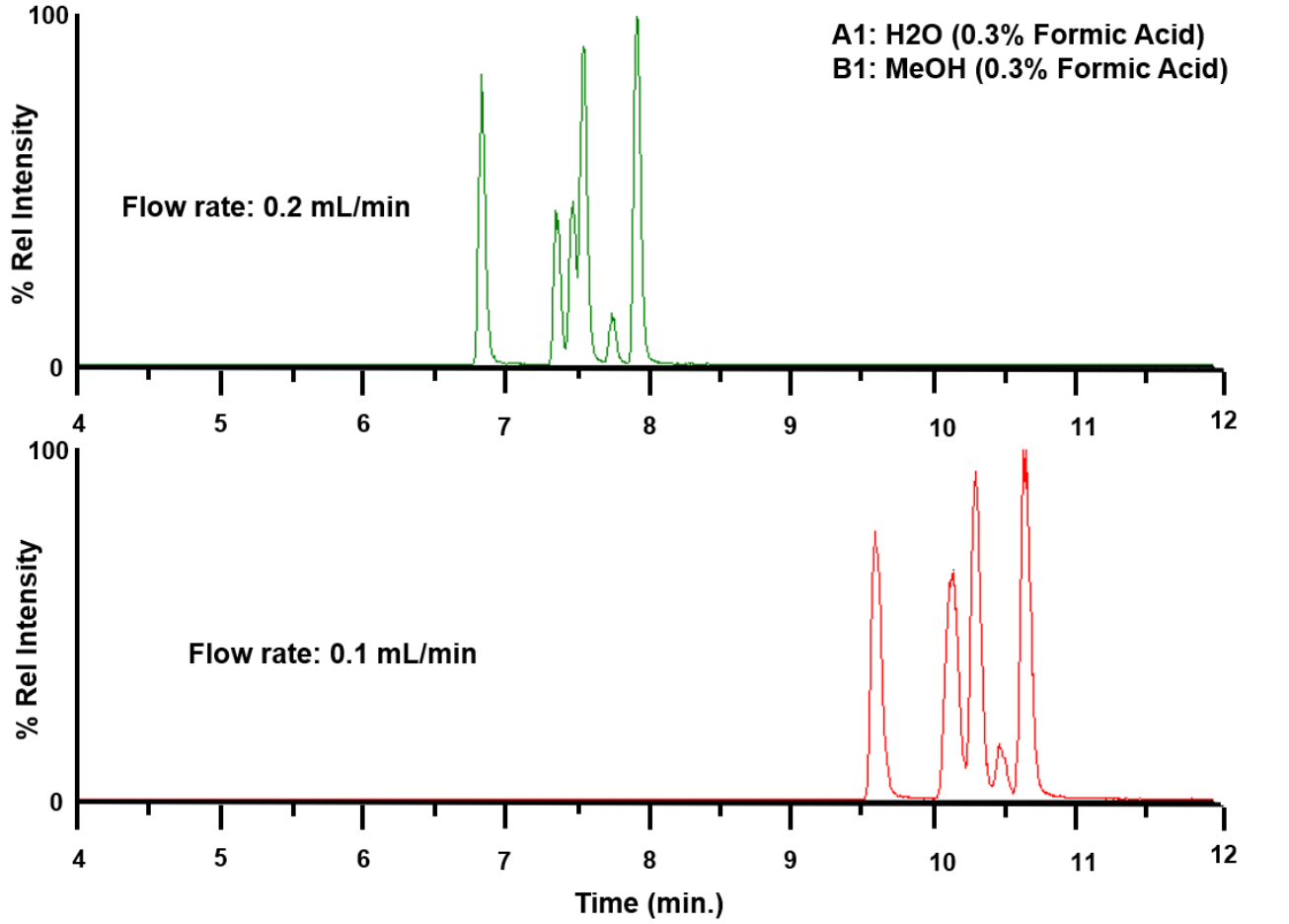
Research Supporting Fentanyl Site Cleanup

- Elution System
  - ACN allows for faster elution times, but not as sensitive
  - Increasing acidic modifier increases signal intensities
  - Additional modifiers had minimal effects



Research Supporting Fentanyl Site Cleanup

- Elution System
  - Flow rate can improve run times, but system pressures are increased and sensitivity affected
  - Analytical run times < 15 minutes
  - Sensitivity achieved at 50 pg/mL
  - Literature* precedent for lower flow rates



*D. R. Baker, B. Kasprzyk-Hodern, *J Chromatogr. A*, 1218 (2011) 1620.; J. P. Murphy, J. Johnson, P. D. Rainville, *Waters White Paper*, 2014.

Fentanyl
Risk Assessment in Supporting a Response

Supporting Research: Risk Assessment Supporting Response

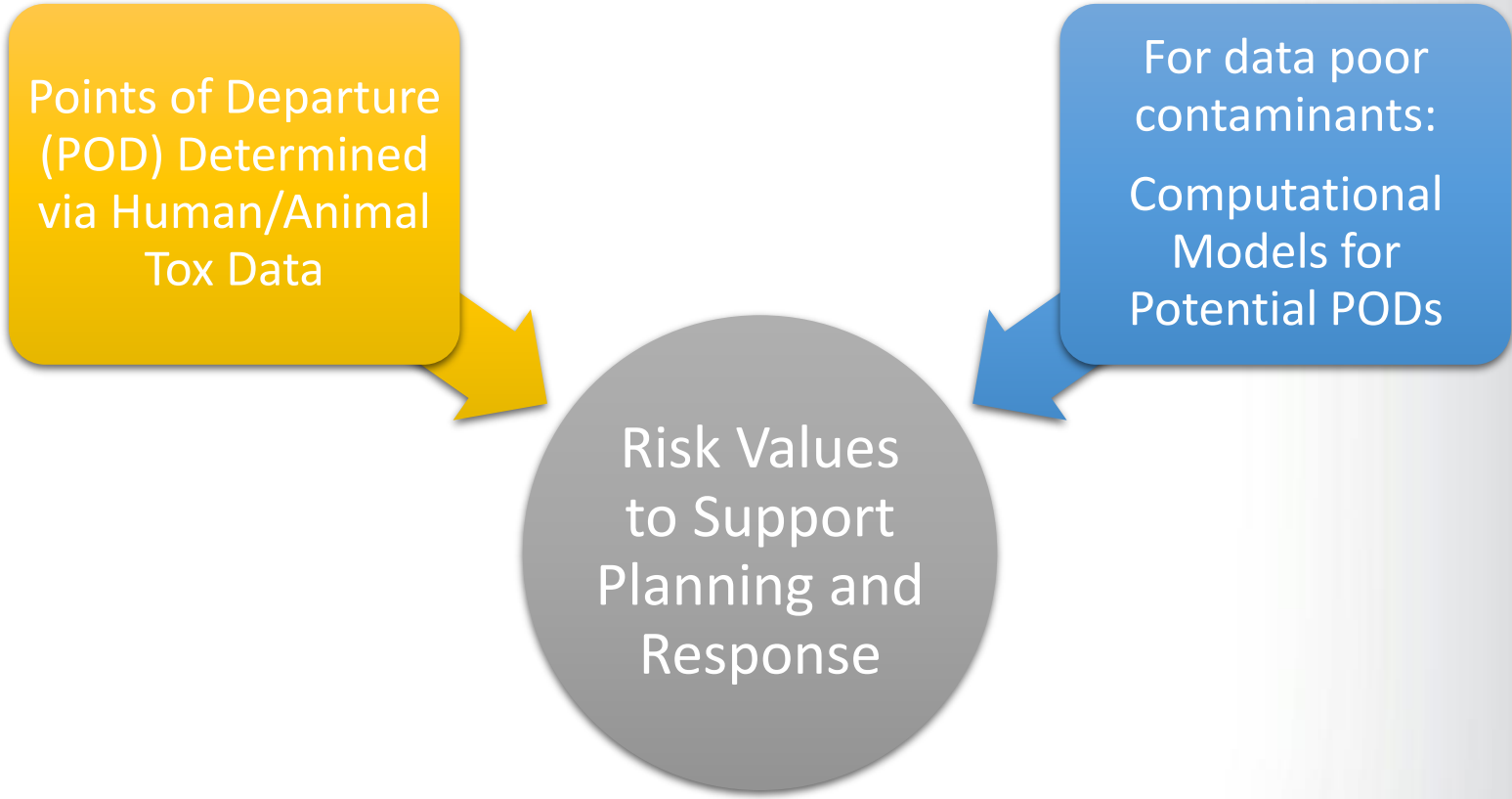
After the release of a chemical threat, absolute health protection cannot be guaranteed

Risk assessors ask:

- What health effects might occur?
- What doses cause them?
- How long must exposure persist to cause these effects?

Risk values need to incorporate the types of health effects expected from acute/short-duration exposures that exceed background levels and health-protective risk values

EPA responders require reliable values (SOP and peer review/quality assurance)

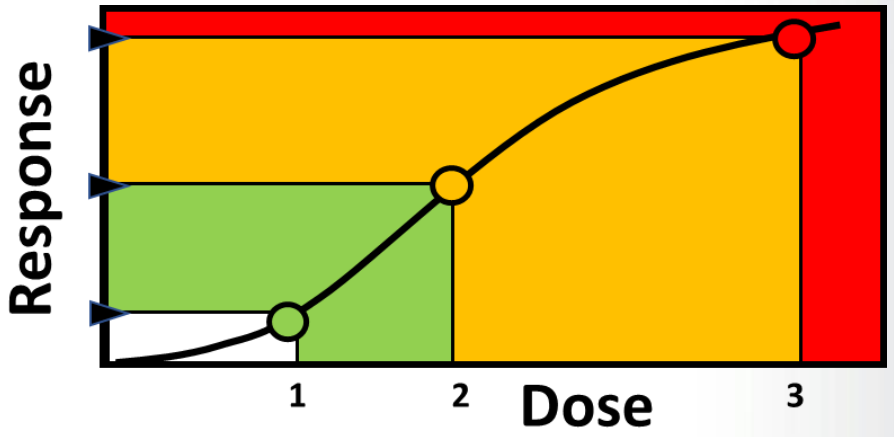


Building capability to develop pre-incident or just in time

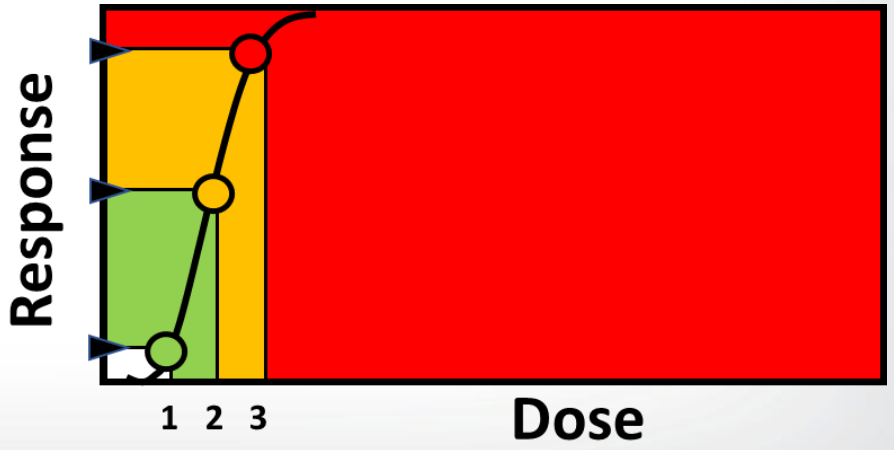
Toxicity: Dose and Response

The Dose makes the Poison.*

- Many chemicals have a shallow dose-response curve: Noticing mild effects can warn of more severe effects.



- Fentanyl has a steep dose-response curve: Severe effects can occur at doses only slightly higher than those producing mild effects.



** Paracelsus, 1538*

Risk, Exposure, and Detection

Minute amounts of fentanyl contamination
- Are difficult to detect
- Cause tiny, but lethal exposures / doses

Surface contamination complicates
- Decontamination methods
- Understanding multi-route exposures

Fentanyl exposures occur
- Via the oral, dermal and inhalation routes
- Via ocular contact, too!

Without adequate risk values and exposure models, we cannot confirm that we can detect or decontaminate to levels of fentanyl contamination that are without risk.

Taken from the Sun UK
(Canadian Public Health Poster)