Data Challenges in Field Detection of Novel Synthetic Opioids

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Quality Management

- The application of a **quality system** in forensic science supports the validity and reliability of evidence in a court of law
  - The majority of forensic laboratories meet **accreditation** requirements (ISO/IEC 17025) that qualify processes and procedures within a laboratory system

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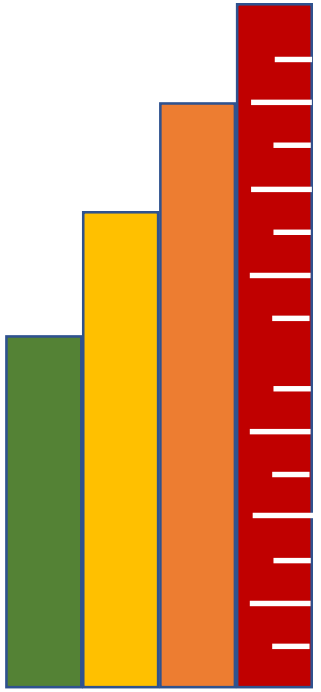
- In the **field**, drug detection technology performance requirements are application-dependent

End-user	Application	Type of Identification
Intelligence agent	Investigative leads Interdiction efforts Surveillance	Preliminary
Law enforcement	Seizure of suspected contraband	Preliminary
First responder Medical personnel	Information on how to handle unknowns Medical treatment	Hazard
Forensic chemist/ technician	Confirmatory field analysis	Confirmatory/SWGDRUG guidelines

Quality Management

A federal survey in 2013 found that about 62% of crime labs do not test drug evidence when the defendant pleads guilty – *NFLIS Survey of Crime Laboratory Drug Chemistry Sections*

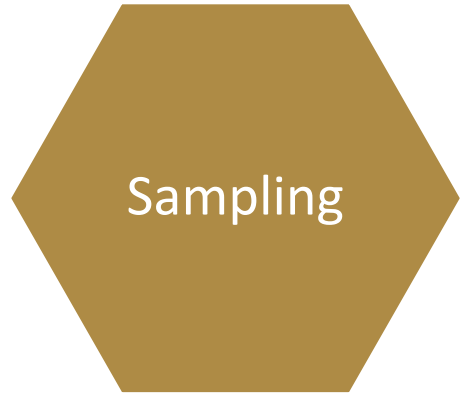


Raising the Bar:

Field technology needs rigorous validation methods and data to demonstrate its validity and reliability


Data Management
Chemical Background
Sampling
Quality Management
Field Verification
Performance Validation
Standard Methods

Sampling and Data Quality



Why standardize sampling methods?

1. Data Quality

- Trace Detectors – Large samples can shift characteristic peaks and produce additional, nonrepresentative peaks
- Color Test – Large samples can saturate color changes
- Raman – Reproducibility
- Signal saturation and instrument down-time

2. Safety

Developed standard method for appropriately sampling bulk materials in the field using a fine needle probe

Verkouteren et. al., *Forensic Sci. Int.*, 2011, 206, 190–196

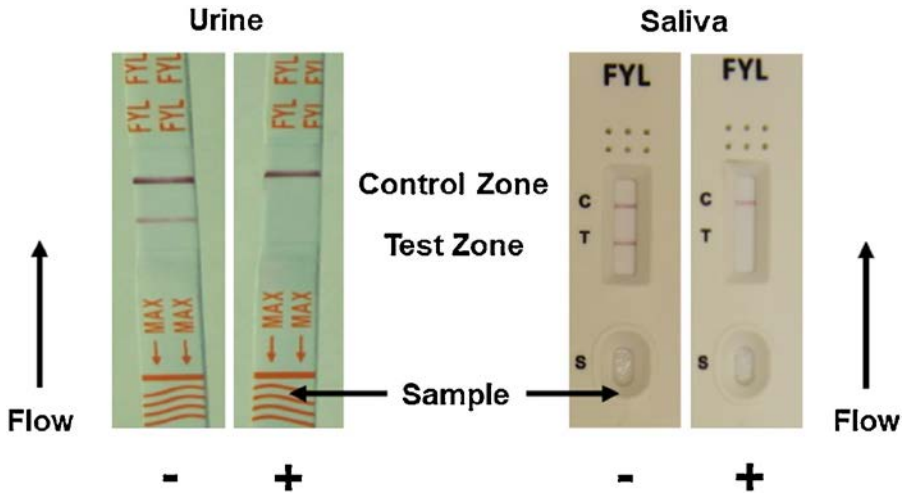
www.proscitech.com

Validation Framework – LFIs

Validation

Angelini et.al., evaluated the effectiveness of commercially-available LFIs designed to detect the synthetic opioid fentanyl in either urine or saliva.

- Determined the **sensitivity** of assays on **10 test compounds – fentanyl analogs** and any **cross reactivity** with known fentanyl analogs (e.g. carfentanil).
- Evaluated urine and saliva samples from rabbits that had been exposed to fentanyl to determine if the LFIs would perform following an **in vivo exposure** situation.
- Evaluated the LFIs with four individual **case samples** known to contain fentanyl.



Angelini et. al., *Forensic Sci. Int.*, 2019, **300**, 75-81

- **Study results:** The LOD for COTS urine- and saliva-based LFIs were 8 and 100 ng/mL, respectively. Positive identification of analytes for in vivo exposure and in real-world cases.

Validation Framework – IMS

Validation

Need: A standard method to compare and validate performance of field technology using common metrics

Sample set:

(1) Detected compounds[a]	(2) Fentanyl detection with additives	(3) Tests for false positives	(4) Sensitivity[b,c]
Fentanyl	1 : 10 Heroin	Hydrocodone	Benzyl fentanyl
Carfentanil	1 : 10 Procaine[b]	Oxycodone	
Furanyl fentanyl (FIBF)	1 : 10 Quinine[b]	Alprazolam	
Butyryl fentanyl (*trans*-3-methyl fentanyl)		Cocaine	
Cyclopropyl fentanyl (*trans*-3-methyl fentanyl)		Heroin	
Acrylfentanyl		THC[d]	
Acetyl fentanyl		Buprenorphine	
U-47700		Quinine	
4-ANPP			

Verkouteren et. al., *Anal.Methods*, 2019, **11**, 6043

- The method proposed provides a basic level of validation for the detection of fentanyl and fentanyl-related substances by IMS
- **Study results:** Baseline measurements for a suite of instruments including reduced mobility values to build a library, resolution measurements, sensitivities (LOD90)

Standard Method – LOD

Web-based tool for manufacturers, vendors, testing labs, and end-users to estimate practical and statistical robust limits of detection

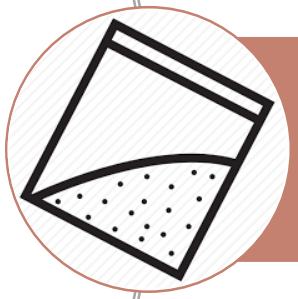
https://www-s.nist.gov/loda/lod_data_input.htm
michael.verkouteren@nist.gov

	The web-tool has a built-in data quality check and will abort for any of the conditions below:
✖	Less than 10 replications in any level
✖	Less than three distinct levels
✖	Absence of a process blank level (mass = 0)
✖	Responses in the highest mass level are not significantly different from those in the process blank level
●	If the data quality is marginal, a message will provide suggestions for improving the quality
✓	If data quality passes, the web-tool will perform the calculation and return the estimate for the LOD and the 90% upper confidence LOD90 limit (a measure of uncertainty).

Validation Limitations

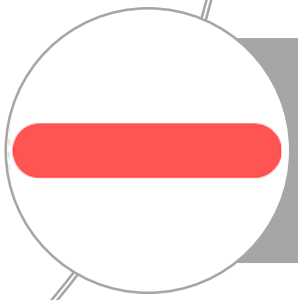
Methods do not address all expected **sources of error** arising from deployed field conditions

ASTM E2520-15 – Add standard dirt during testing



Test known or expected contaminants in specific deployments e.g. contaminants expected on the outside of plastic bags

Sisco et. al., *Forensic Chem.*, 2017, **4**, 108–115



Measure the contribution of environmental background to instrument response by analyzing large numbers of true negative samples on field-deployed instruments

Forbes et al., *Analyst*, 2019, **144**, 6391–6403

Field Performance Verification

- Internal calibrant
  - Temperature, humidity, and pressure
- Positive controls
  - Test materials – quality, stability, and safety
- Negative controls

Chemical Background

Chemical Background

- Detection threshold adjustments based on operational environment (signal to noise)
  - Reduce false positives and false negatives
  - Valuable data for instrument manufacturers

Comparison of background levels to those reported in literature.

	Cocaine	Heroin	Meth
Range of Levels (μg wipe^{-1})	0.01–56.51	0.63–62.25	0.10–22.71
Forensic Lab – Spain (μg 100 cm^{-2}) [15]	3.1–105		
Police Stations (μg wipe^{-1}) [12]	71.43		326.16
Money (μg bill^{-1}) [14]	0.01–922.72	0.02–168.50	0.50–1.00
Public Surfaces (% > 50 ng) [3]	80%		
Cocaine in City Air (pg m^{-3}) [16]	7–304		

Sisco et. al., *Forensic Chem.*, 2019, 16, 100184

Data Management

Goals: 1. Protect the validity and accuracy of data
2. Maintain chain of custody and ensure court admissible results
3. Comply with evidence retention laws

Manufacturers offer data solutions that include:

- Automatically stored results for reporting and evidence submission
- Time-and-date stamps
- Reach-back support: data analysis by staff chemists
- Third party validation of results (upon request)

ASTM Standards for Field Detection of Fentanyl: *In Progress*

- **Committee E54 Homeland Security, work supported by DHS S&T**
- Targeted to First Responders – user community active in development
- Independent of technology but developed based on: GC/MS, IMS, FTIR, Raman, Colorimetric, Immunoassay
  - Includes some evaluation of instrument performance
  - Includes active participation of instrument/device manufacturers
  - Involves large task group of subject matter experts, **led by PNNL** and including NIST

- 3 standards in the works:
  - WK66045, 69940, 69941
- Defines types of samples
  - Bulk and trace
  - Different analogs
  - Different diluents/adulterants
- **Defines testing protocol**
- **Defines acceptable error rates**
- **Provides safety guidance**

Detection Strategies & Challenges

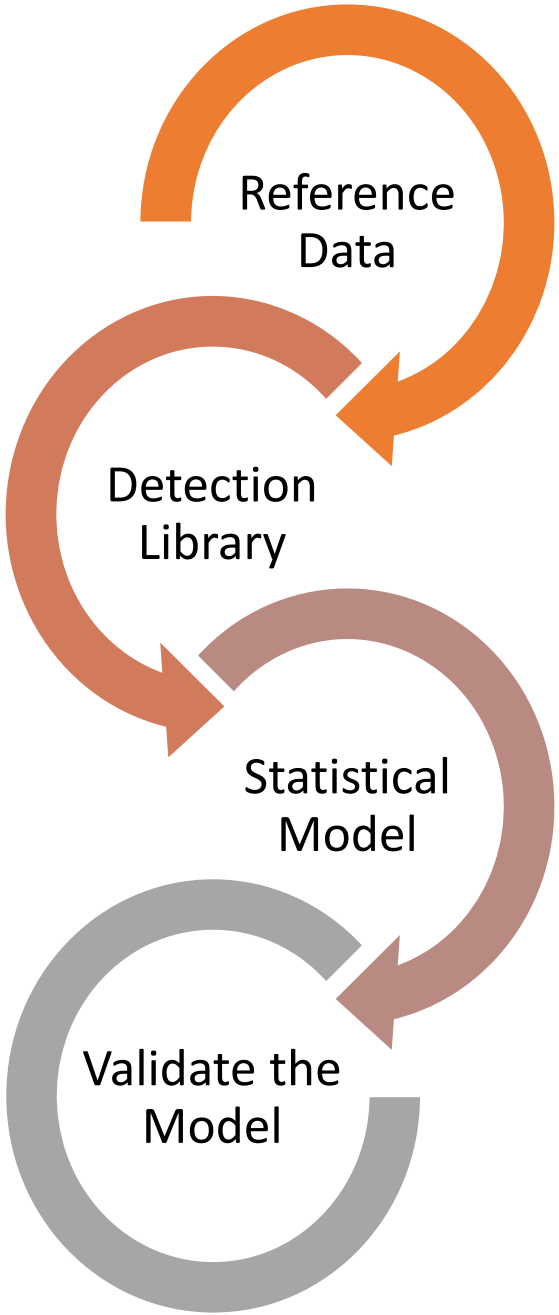
Field Detection Challenges – Opioids

- Data acquired in the field can differ significantly from the data used to create libraries
  - Need enhanced data analytics

- Library compound identification can be the sole basis for reporting results
  - Non-technical operators must interpret complex data that includes mixtures and novel substances

Drug purity	Drug form	Multidrug mixtures	Matrix contributions	Environmental contributions
Pure – safety	Tablets (coatings)	Competitive ionization	Clear vs. opaque packaging	Contaminants
Cutting agents	Liquids	Spectral shifts	Fluorescence	Dirt
Adulterants	Powders	Peak resolution		Heat
Excipients		Cross-reactivity		Humidity
				Pressure

Data Analytics

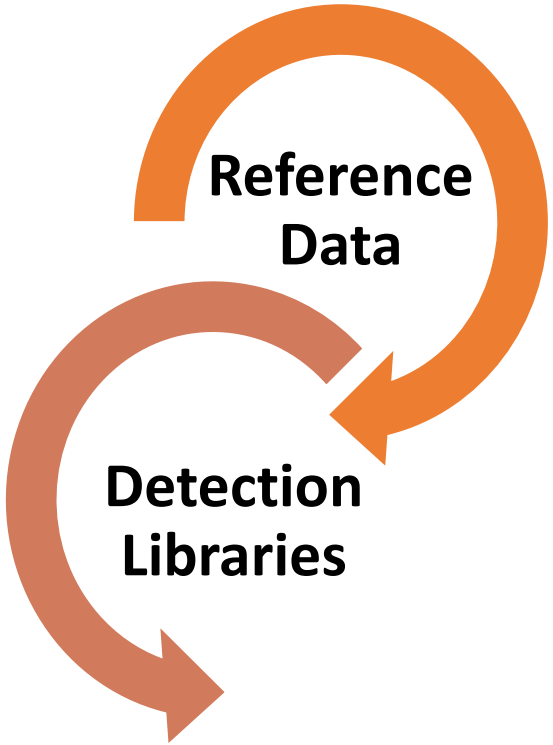


- Traceable standards
- Data curation – standard quality metrics

- Training data set
- “Labeled” data

- Build model based on a statistical approach
- Machine learning
- Predictive analytics

- Improve feature selection
- Complex data
- Data sharing



- **Traceable standards**
- **Data curation** – standard quality metrics

www.cdc.gov

ELSEVIER

Toxicology Letters
Volume 317, 15 December 2019, Pages 53-58

Designing traceable opioid material§ kits to improve laboratory testing during the U.S. opioid overdose crisis

Mike A. Mojica [a], Melissa D. Carter [a] ✉, Samantha L. Isenberg [a], James L. Pirkle [a], Elizabeth I. Hamelin [a], Rebecca L. Shaner [a], Craig Seymour [a], Cody I. Sheppard [a], Grant T. Baldwin [b], Rudolph C. Johnson [a]

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https://doi.org/10.1016/j.toxlet.2019.09.017

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Highlights

- CDC developed the Traceable Opioid Material§ Kits (TOM Kits§) product line.
- TOM Kits§ provide over 150 opioid standards, including over 100 fentanyl analogs.
- This work establishes a model for addressing chemical, public health emergencies.

The kits are free to U.S labs in the public, private, clinical, law enforcement, research, and public health domains with DEA registration (Schedule I)

NPS Data Hub:

A web-based community driven analytical data repository for new psychoactive substances

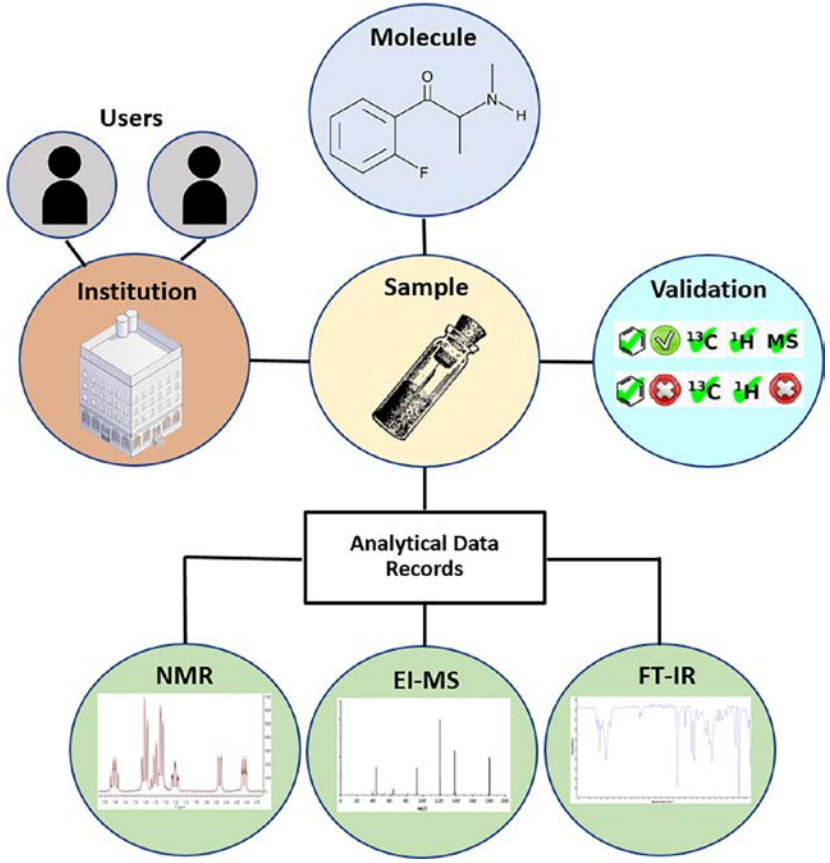
Challenge: Need for reliable data to aid in the identification of novel psychoactive substances (NPS)

Goal: Elicit data from the global forensic community to facilitate identification of unknown substances and eliminate duplication of elucidation efforts.

Reference material

Internal control material

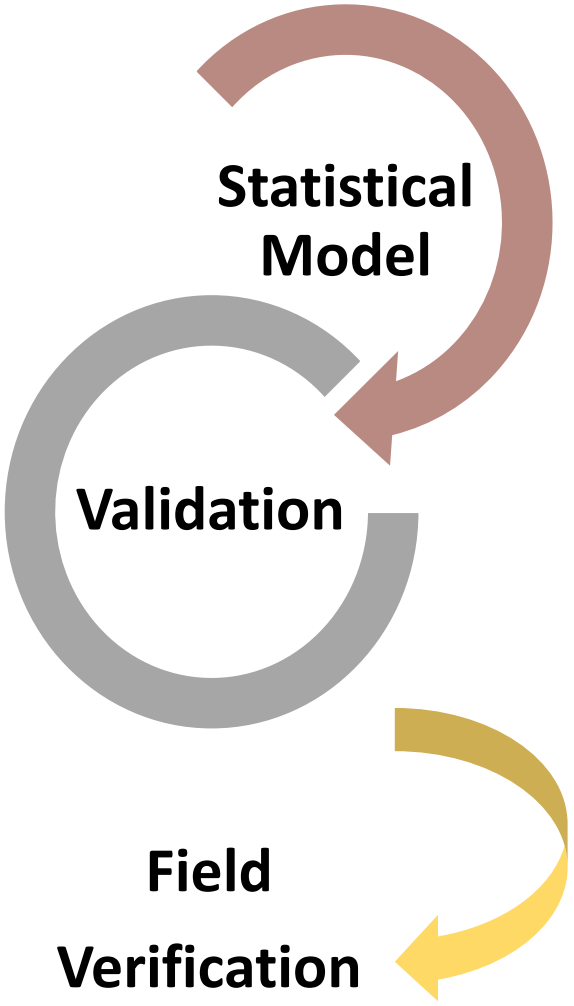
Exhibit/seized material



https://nps-datahub.com

aaron.urbas@nist.gov

Data Analytics



- Build model based on a statistical approach
- Machine learning
- Predictive analytics

- Test with complex data
- Improve feature selection
- Documentation

- In-field quality management protocols
- Test materials and safety

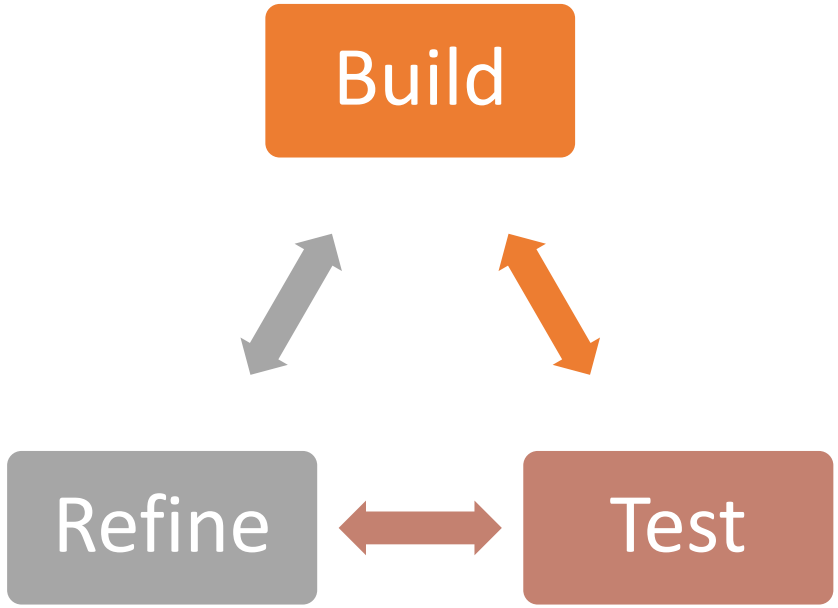
Enhancing Machine Learning

Goal: Build richer test data sets using real-world samples to improve the robustness of statistical models

Challenges: This requires continuous data sharing by a variety of entities – partnerships

- What platform? Standard data format? Who maintains it? Access?
- Sensitive Data
  - Law Enforcement sensitive
  - Public Health sensitive

www.therobotreport.com



Implementing Tools

NIST – Advanced Measurement Laboratory
www.nist.gov

Credit: Image courtesy of Megan Harries
www.nist.gov

Software Accessibility

Education and Training

Open-source software

Freely available software facilitates accessibility, adoption, and scalability

http://github.com/asms3-nist/FentanylClassifier
arun.moorthy@nist.gov

Decision-making algorithms should be:

1. Transparent to the public
2. Provide documentation on the assumptions, limitations, and the feature characteristics supporting the model.

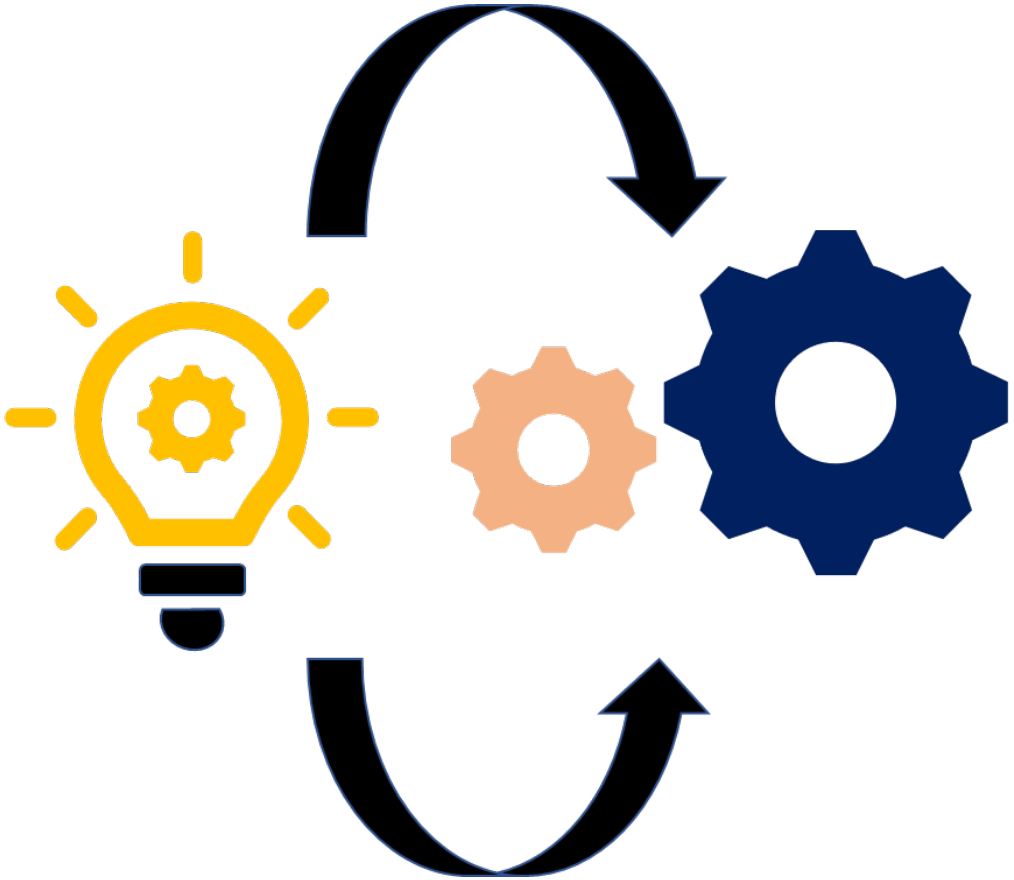
www.elservier.com

Federal Judge Unseals New York Crime Lab's Software for Analyzing DNA Evidence

We asked the judge to make the source code public after scientists and defense attorneys raised concerns that flaws in its design may have resulted in innocent people going to prison.

https://www.propublica.org/

Education and Training



- End-users must have a basic level of understanding of the decision-making tools they utilize including:
  - Statistical assumptions
  - False positive/False negative rates
  - Error rates
  - Limitations of the tool

Conclusions

- Field data can be indirectly used beyond intended scope (presumptive)
  - What should be the quality management criteria for criminal investigative purposes? (e.g. surveillance, probable-cause, etc.)
  - How do we ensure quality systems do not impede adoption of new technologies?
  - How do we manage the trade-offs of field technology with admissibility requirements in a court of law?

- Need: Strengthen the field quality management system to mirror laboratory QM
  - Reference data, standard methods, independent validation, field verification
  - ASTM Standards for Field Detection of Fentanyl: *In Progress*

- Novel synthetic opioids require enhanced detection strategies e.g. machine learning
  - Data sharing, open-source software, education and training

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Thank you!