

Public Health Emergencies with NPS & Tracking and Investigating Outbreaks- *Synthetic Cannabinoid Outbreaks Surveillance*

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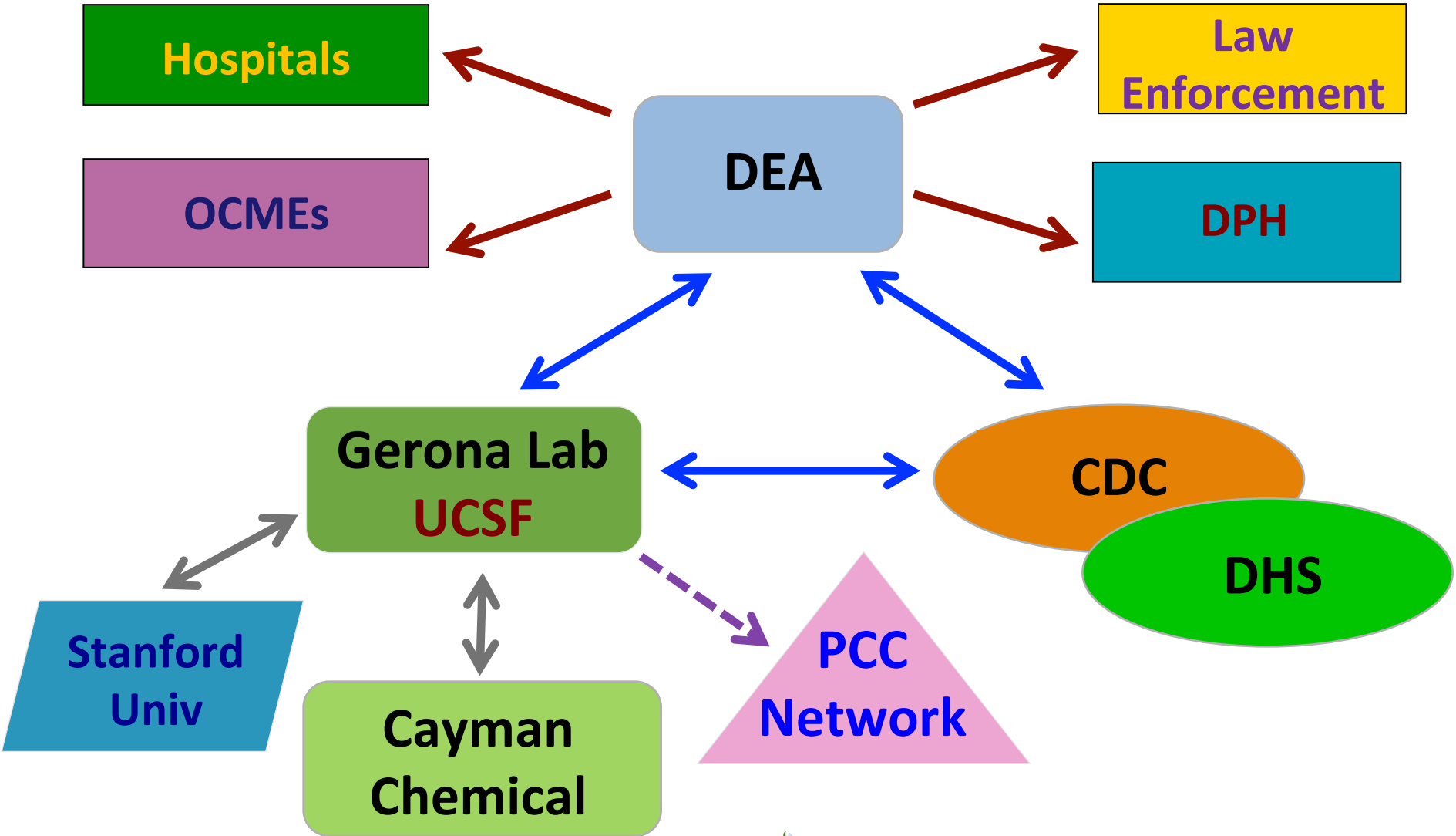
NPS Surveillance in Mass Outbreaks

Data to be shared during presentation

Central role of lab confirmation in surveillance

Data to be shared during presentation

Synthetic Cannabinoid Outbreaks Surveillance Backbone

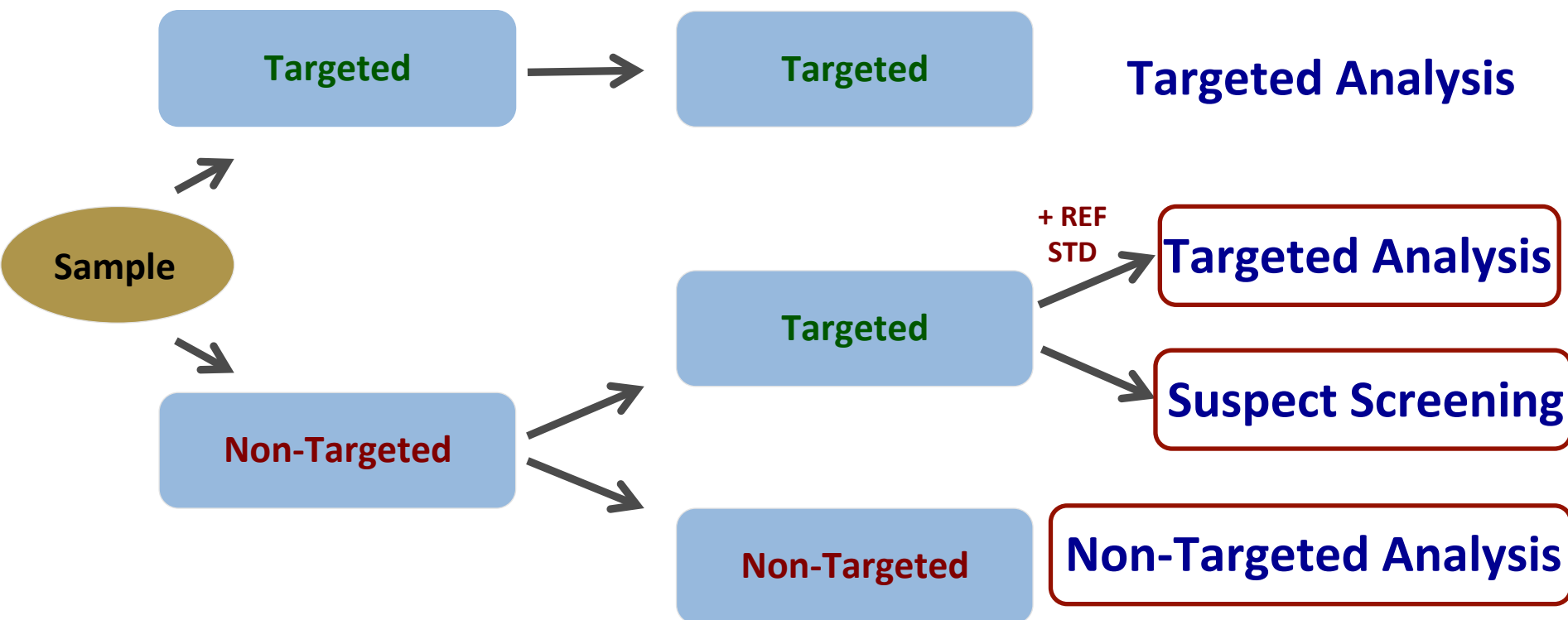


Drug Surveillance facilitated through HRMS

High Resolution Mass Spectrometry

Data Acquisition

Data Analysis



Data Analysis through HRMS

Serum, Plasma, Blood, Urine, CSF
Drug Products/ Paraphernalia

Targeted Analysis

Reference Std Available
Database Available

Accurate Mass, Isotope Cluster,
RT, Spectral Library



LC-QTOF/MS- 265 Synthetic
Cannabinoids/Metabolites
LC-MS/MS- 60 SC Drugs/
Metabolites

LC-QTOF/MS-
Comprehensive Drug
Panel (501 Drugs, 204
Designer Drugs)

Suspect Screening

NO Reference Std Available
Database Available

Accurate Mass, Isotope Cluster,
RT plausibility



LC-QTOF/MS- SCs
800 Parent Drugs /
metabolites
Predicted Metabolites

LC-QTOF/MS-
Stimulants Panel (492)
Hallucinogens Panel (210)
Depressants Panel (205)
Predicted Metabolites

Non- Targeted Analysis

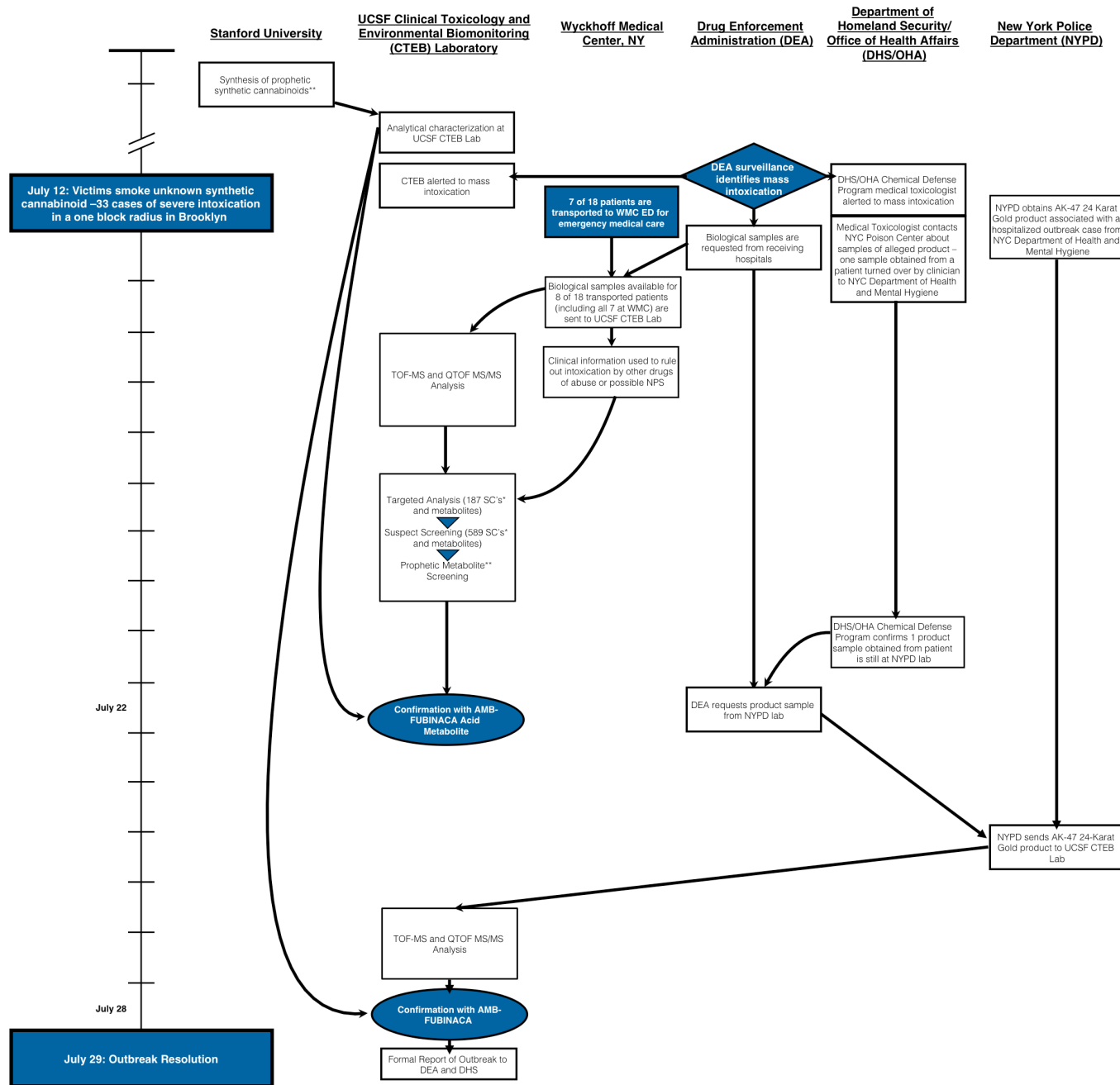
NO Reference Std Available
No Specific Database

Accurate Mass, Isotope Cluster,
RT plausibility



LC-QTOF/MS
MS Formula
MS/MS spectra
search in Open
Source Database and
Spectral Library
In silico
fragmentation

Dynamics of a Mass Outbreak Surveillance



Adams, Trecki, Gerona et al, NEJM, 2017

Prophetic Synthetic Cannabinoids

- NPS are intelligently designed; **future NPS targets can be predicted**
- 179 SCs reported to the EU Early Warning System
- 10 new SCs reported in 2017
- 14 recognizable families of SCs
- **Library of prophetic cannabinoids prepared and characterized for their pharmacology**
- **Library allows rapid confirmation once the compound is detected in biological sample**

CORE

Indole, Indazole, Benzimidazole, Pyrrole, Naphthyl

LINKER

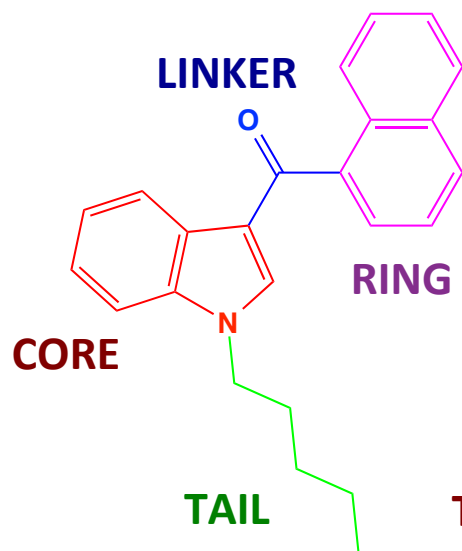
Methanone, Ethanone, Carboxylate, Carboxamide

TAIL

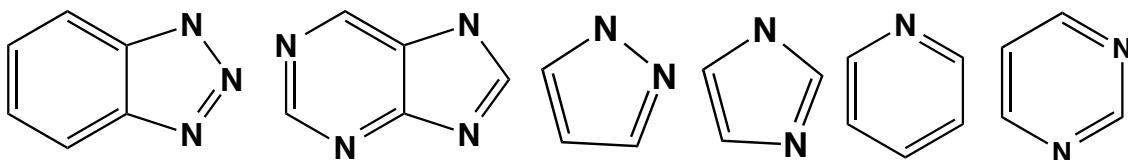
Alkyl, Cycloalkyl, Halobenzyl, Morpholino, Tetrahydropyranyl

PENDANT RING/ CHAIN

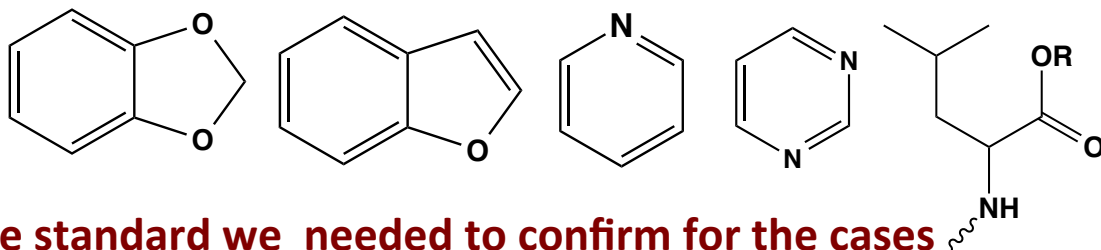
Naphthyl, Phenyl, Cyclopropyl, Adamantyl, Quinidyl, Amino acid derivative



Possible Core Structures



Possible Pendant Rings/Chains



The reference standard we needed to confirm for the cases in July, 2016 was already available in our lab since February, 2016

Utility of Prophetic Cannabinoids in Surveillance

Data to be shared during presentation

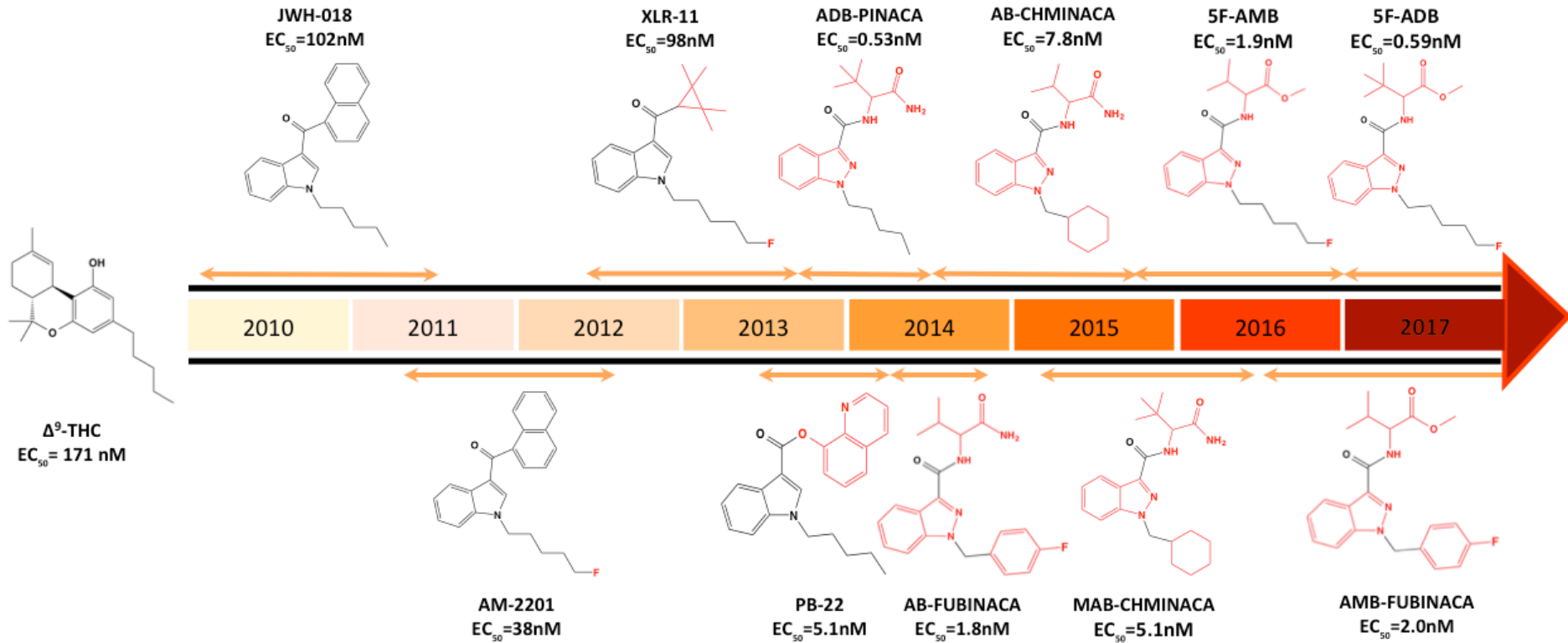
SC Outbreaks Surveillance Study Results

Between 2012- 2017, our surveillance assisted in more than 24 outbreaks and worked on more than 1200 cases

Location	Date	Cases	Compounds Found
Portland, OR/ Casper, WY	Mar-Oct, 2012	10	XLR-11
Brunswick, GA	Aug-Sept, 2013	22	ADB-PINACA
Austin, TX	May, 2014	>20	XLR-11, AB-FUBINACA
Dallas, TX	May, 2014	>100	XLR-11, AB-FUBINACA
Gainesville, FL	May-Jun, 2014	>29	AB-CHMINACA
Manchester, NH	Aug, 2014	>44	AB-PINACA, ADB-PINACA, UR-144
Bryan, TX	Nov, 2014	>41	MAB-CHMINACA
Beaumont, TX	Dec, 2014- Jan, 2015	>62	MAB-CHMINACA, AB-PINACA, ADB-PINACA
Hagerstown, MD	April, 2105	9	MAB-CHMINACA
Jackson, MS	April-May, 2015	313	MAB-CHMINACA
Anchorage, AL	Jul-Sep, 2015	>100	MAB-CHMINACA, AB-CHMINACA, 5F-AMB
Sacramento, CA	Mar, 2016	18	Fentanyl
New York, NY	Jul 12, 2016	33	AMB-FUBINACA
Huntington, WV	Oct, 2016	26	Carfentanil
Denver, CO	Dec, 2016	8	AMB-FUBINACA, ADB-FUBINACA, MDMB-FUBINACA
Gainesville, FL	May, 2017	20	AMB-FUBINACA, ADB-FUBINACA



Molecular Evolution of Synthetic Cannabinoids



Lessons Learned from SC Outbreaks Surveillance

- ❖ Self-reported NPS use is not a reliable data for surveillance
- ❖ Effective NPS analysis requires the ability to perform non-targeted analysis
- ❖ The ability to identify and confirm NPS in surveillance cases benefits a lot from access or ability to synthesize reference standards
- ❖ The turnaround time for changes in NPS chemical composition is faster than method development for targeted drug analysis in the lab
- ❖ Most efficient response to NPS outbreaks requires effective and extensive collaboration between medical toxicologists, ER physicians, public health experts, law enforcement agents, clinical laboratorians, synthetic organic chemists and experts in federal agencies

Surveillance Accomplishments

- ❖ Worked on ~1200 cases (2012-2017)
- ❖ Contributed data to placing at least seven groups of synthetic cannabinoids on temporary schedule- XLR-11/UR-144, ADB-PINACA, AB-FUBINACA, AB-CHMINACA, MAB-CHMINACA, 5F-AMB, AMB-FUBINACA
- ❖ Published 12 papers on synthetic cannabinoids
- ❖ Established collaborations with 15 Poison Centers and 12 OCMEs
- ❖ Established collaborations with various State and Federal Agencies- NIOSH, NTSB, DPH, DEA, DHS
- ❖ Expanded collaborations with industry and various academic institutions

Acknowledgements

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