Quantitation of the New Synthetic Cathinone N,N-Dimethylpentylone in a Post-Mortem Case Series

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Disclosures

- I have no conflicts of interest to disclose.

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- I am a scientist and employee of FRFF / CFSRE, a 501(c)(3) non-profit research and educational facility.

- This project was supported in part by the National Institute of Justice, Office of Justice Programs, U.S. Department of Justice
  - Award Number 2020-DQ-BX-0007, “Real-Time Sample-Mining and Data-Mining Approaches for the Discovery of Novel Psychoactive Substances (NPS)”
  - The opinions, findings, conclusions and/or recommendations expressed in this publication are those of the author(s) and do not necessarily reflect those of the Department of Justice

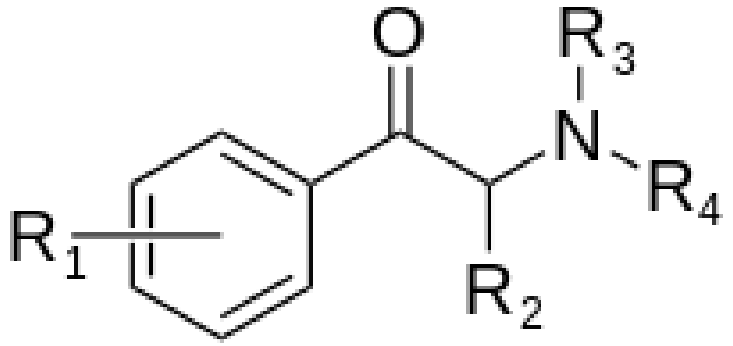
HISTORY: CATHINONES

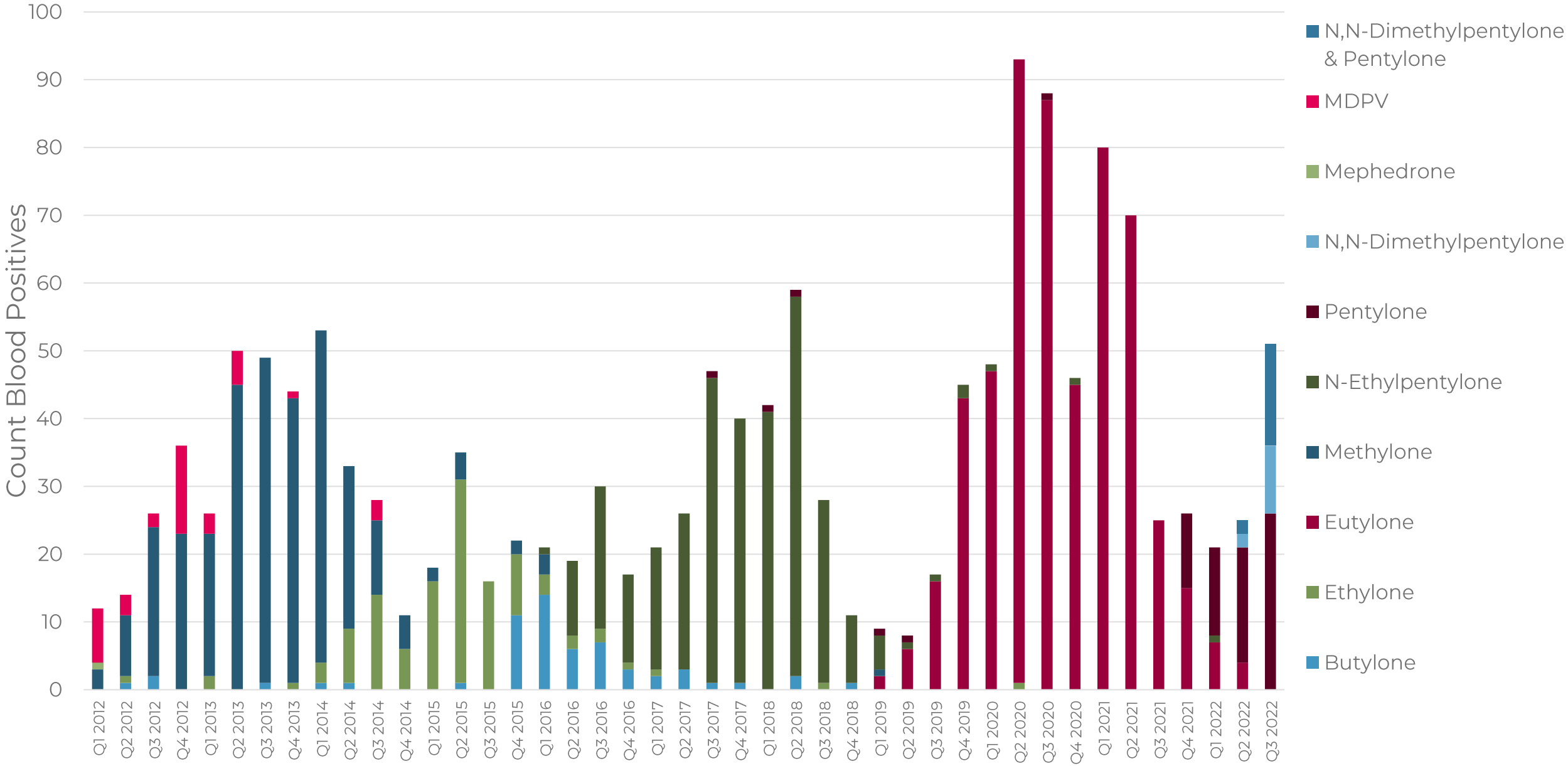
- Khat (*Catha edulis*)

- Effects
  - ↑HR and ↑ BP
  - Motor excitation and euphoria
  - Intimate and sensory-based responses

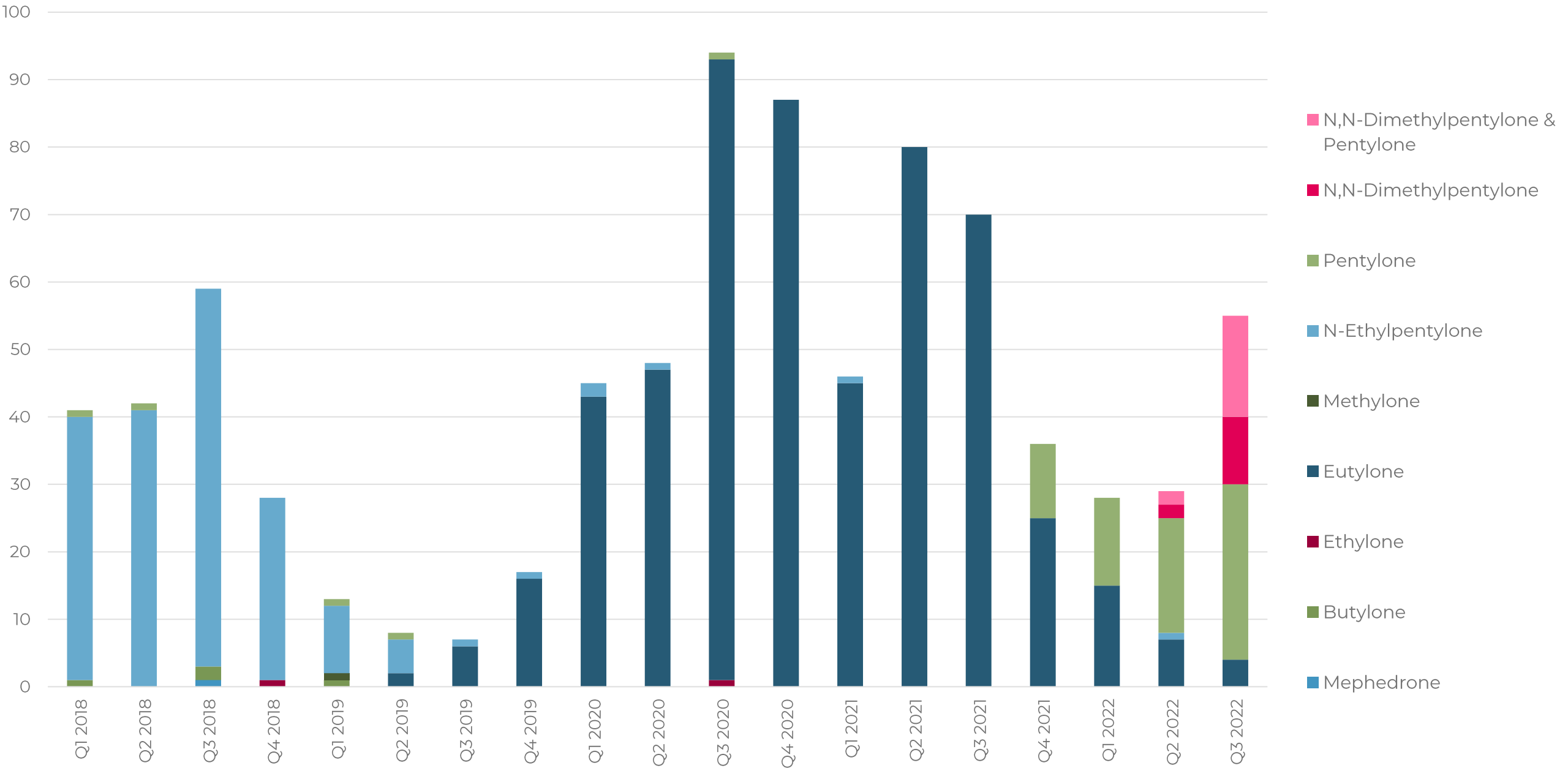
- Sold as “Ecstasy”, “MDMA”, “Molly”

- Substituted Cathinones
  - Methcathinone synthesized in 1929
    - Reports of abuse in 1990s
  - Patent out of Germany 1967
    - Aryl-alpha-Aminoketone Derivatives





Data Provided from NMS Labs – Donna Papsun



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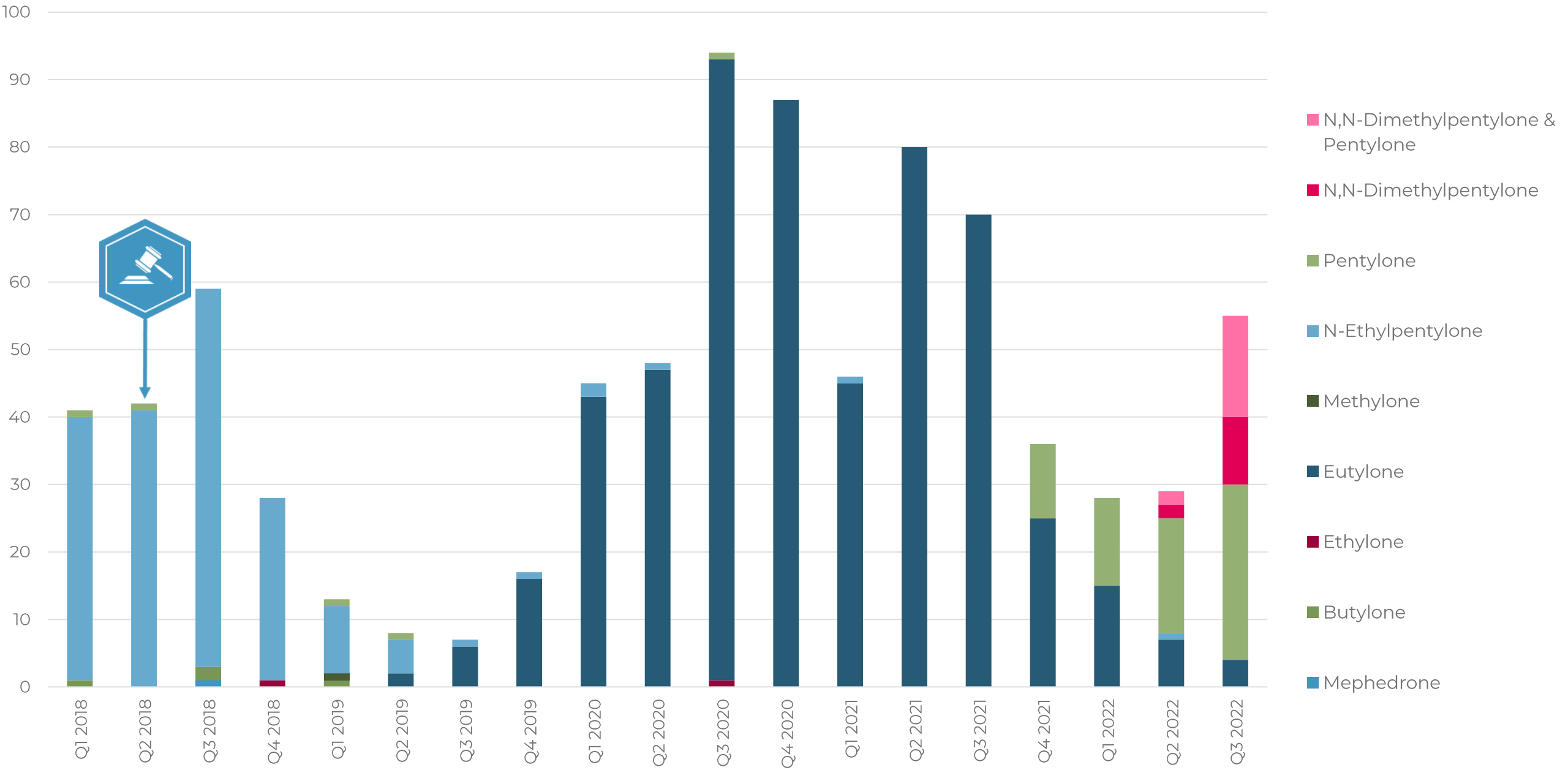

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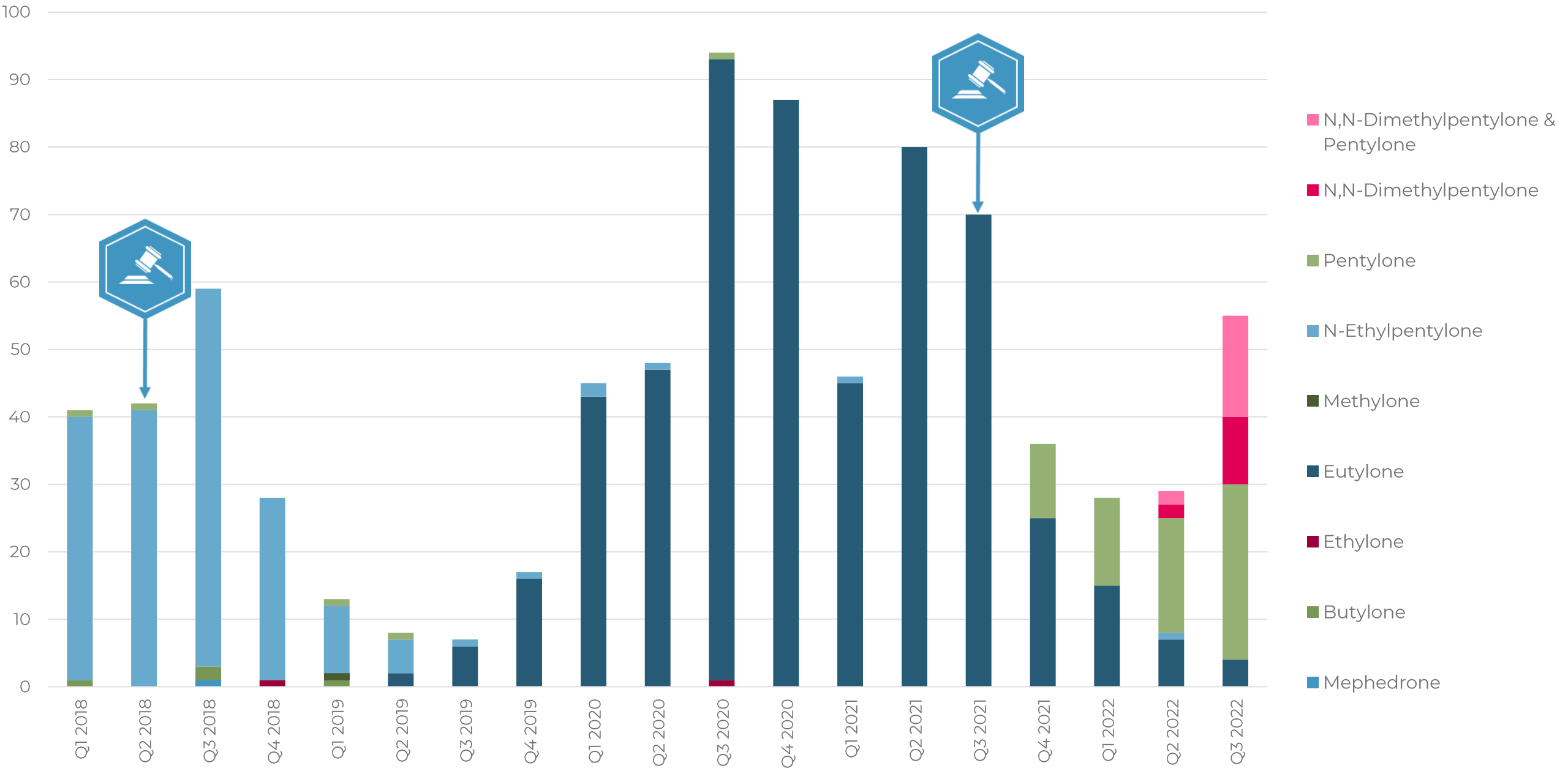
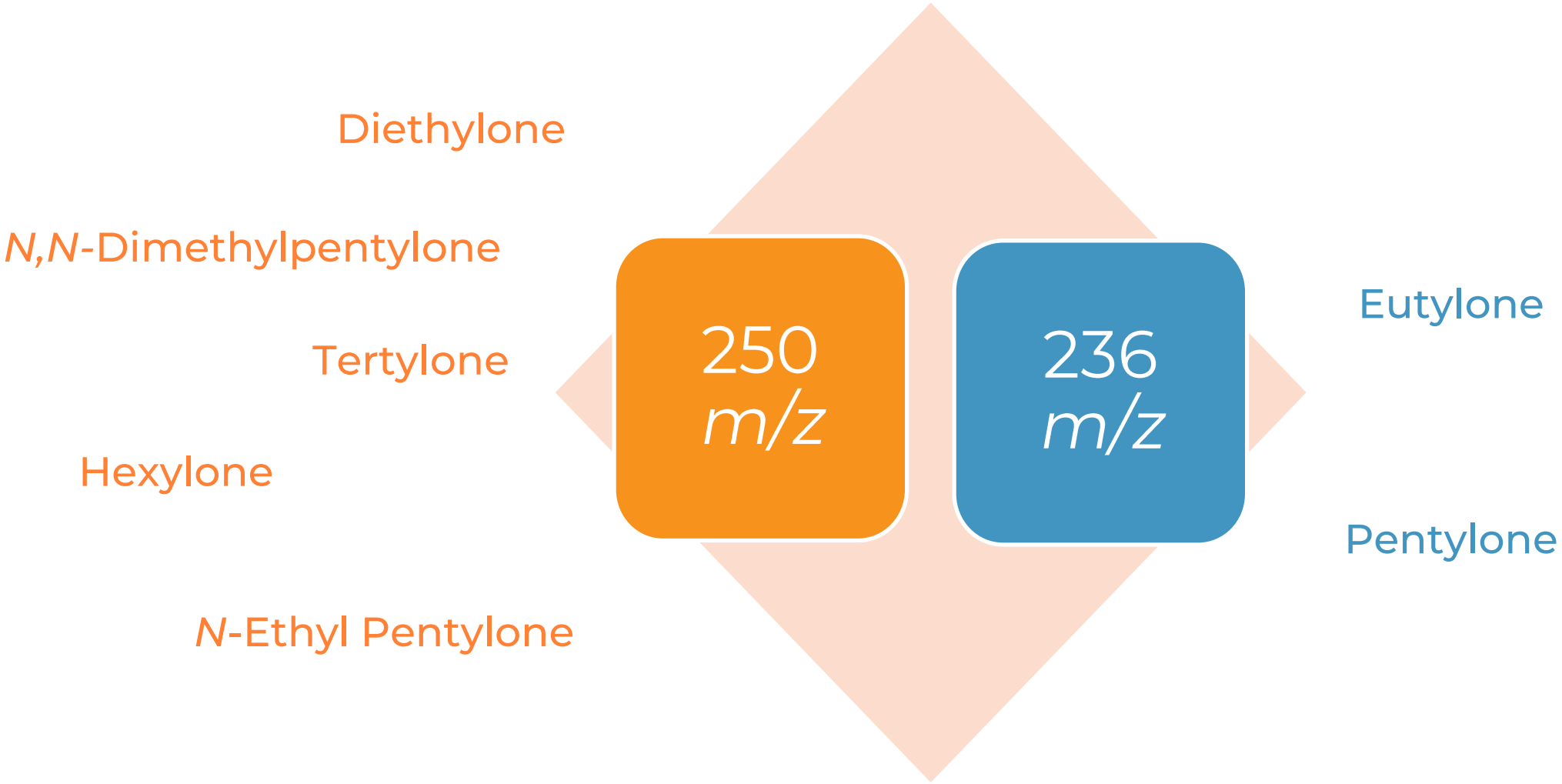


Data Provided from NMS Labs – Donna Papsun

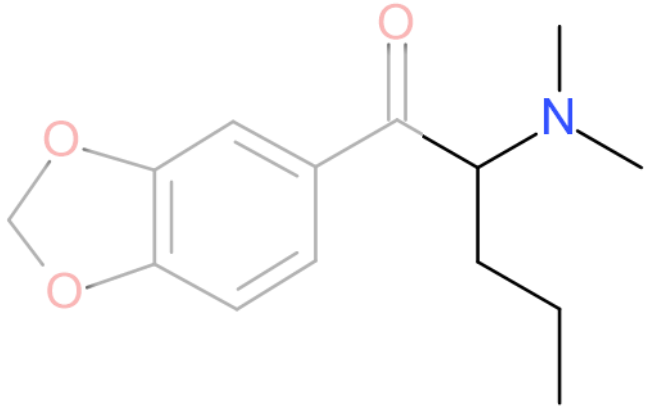
cfsre | NPS DISCOVERY

ANALYTICAL METHOD

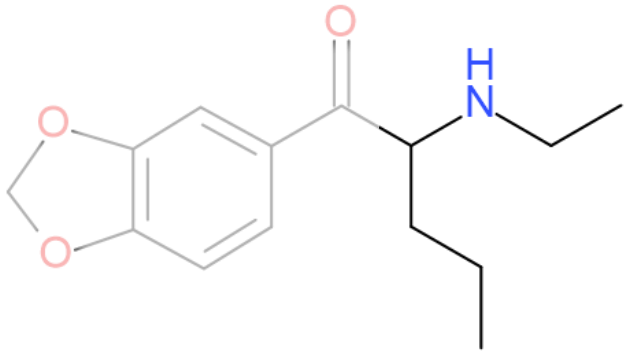
SCOPE OF METHOD



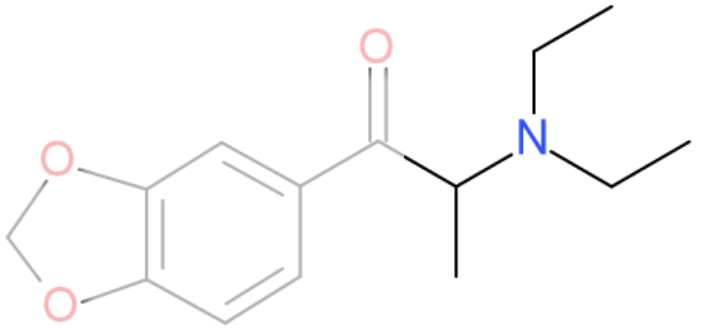
250 m/z compounds



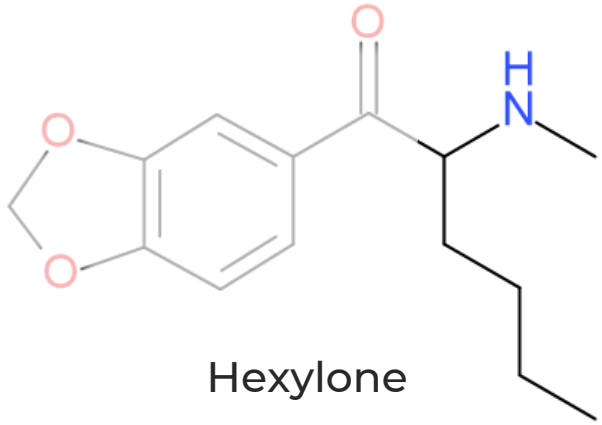
N,*N*-Dimethylpentylone



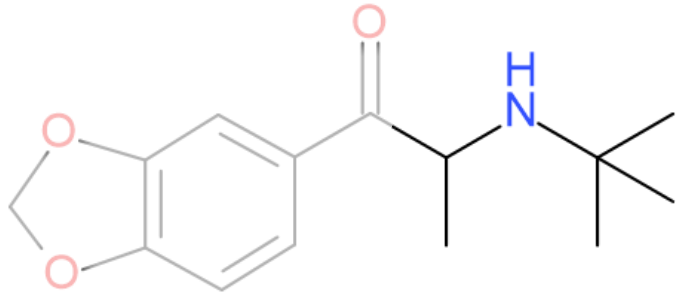
N-Ethyl Pentylone



Diethylone



Hexylone



Tertylone

Instrumentation:

- Waters Acquity I-Class Ultra-Performance Liquid Chromatograph
- Waters Xevo TQ-S Micro Tandem Mass Spectrometer

Mobile Phase Compositions:

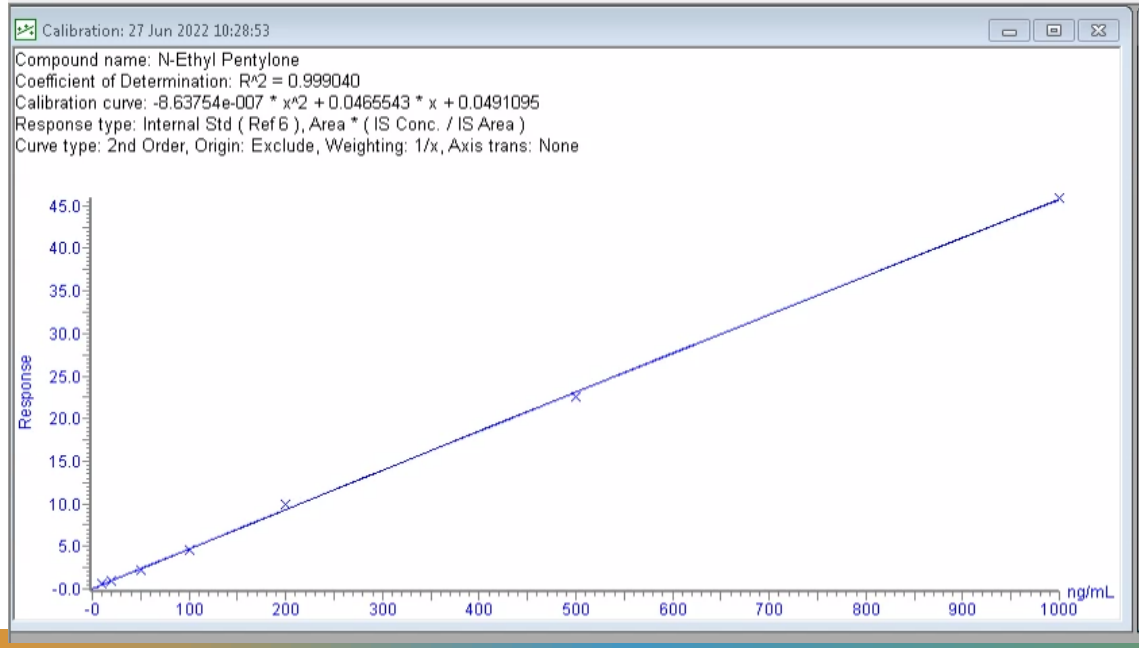
- MPA: 5 mM ammonium formate in water, pH 3
- MPB: 0.1% formic acid in acetonitrile

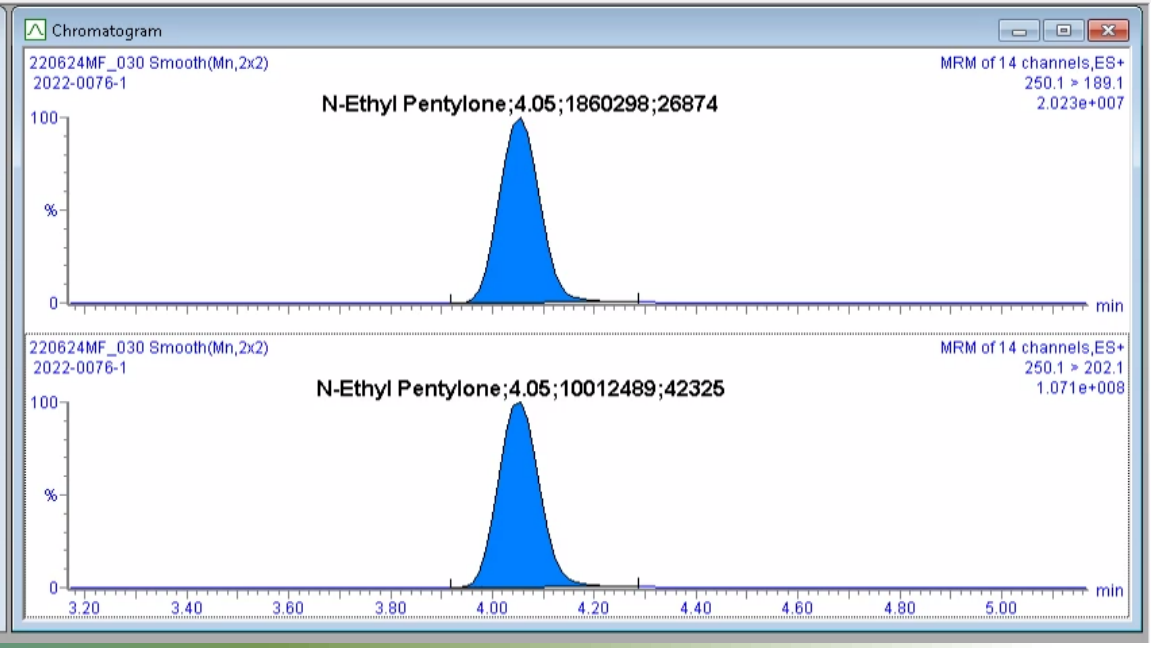
Analytical Column:

- Agilent InfinityLab Poroshell EC-C18 120 (2.7 µm, 3.0 x 100 mm)
- 60°C

Time (min)	Flow (mL/min)	%A	%B
Initial	0.4	90	10
5.5	0.4	65	35
6.0	0.4	5	95
6.1	0.4	90	10
7.0	0.4	90	10

	Vial	#	Name	ID	Type	Std. Conc	ng/mL	%Dev	Area	RT	IS Area	area ratio	S/N	1° Ratio (Actual)	1° Ratio (Pr...	1° Ratio Flag	RRT	2° Ratio (...	2° Ratio (P...	2° Ratio Flag
20	1:C,3	20	220624MF_020	2022-0058	Analyte				1380	4.23	260416	0.005	22	0.555	0.454	NO	1.003			
21	1:C,4	21	220624MF_021	2022-0059	Analyte				797	4.23	299570	0.003	12	0.424	0.454	NO	1.003			
22	1:C,5	22	220624MF_022	2022-0060 Diluted 1:10	Analyte				876	4.22	382283	0.002	12	0.416	0.454	NO	1.000			
23	1:C,6	23	220624MF_023	2022-0067	Analyte				482	4.23	299351	0.002	9	0.206	0.454	YES	1.003			
24	1:C,7	24	220624MF_024	2022-0068	Analyte				854	4.23	359888	0.002	13	0.344	0.454	NO	1.003			
25	1:C,8	25	220624MF_025	2022-0072	Analyte				539	4.22	294022	0.002	7	0.341	0.454	NO	1.000			
26	1:D,1	26	220624MF_026	2022-0073	Analyte				785	4.22	218671	0.004	9	0.341	0.454	NO	1.000			
27	1:D,2	27	220624MF_027	2022-0074	Analyte				1361	4.23	395337	0.003	13	0.397	0.454	NO	1.003			
28	1:D,3	28	220624MF_028	2022-0075	Analyte				401	4.23	322256	0.001	4	0.293	0.454	YES	1.003			
29	1:D,4	29	220624MF_029	2022-0081	Analyte				506	4.23	324567	0.002	9	0.371	0.454	NO	1.003			
30	1:D,5	30	220624MF_030	2022-0076-1	Analyte		124.23		1860298	4.05	319692	5.819	26874	0.186	0.454	YES	0.961			
31	1:D,6	31	220624MF_031	2022-0076-2	Analyte				887	4.22	348658	0.003	12	0.548	0.454	NO	1.000			
32	1:D,7	32	220624MF_032	2022-0076-3	Analyte		96.87		1474676	4.05	324060	4.551	17257	0.178	0.454	YES	0.961			
33	1:D,8	33	220624MF_033	2022-0076-4	Analyte				16184	4.08	416493	0.039	185	0.588	0.454	NO	0.968			
34	1:E,1	34	220624MF_034	2022-0076-5	Analyte				273	4.23	290441	0.001	5	0.140	0.454	YES	1.003			
35	1:E,2	35	220624MF_035	High QC - 800 ng/mL	QC	800.000	786.83	-1.6	8366826	4.22	231481	36.145	73167	0.426	0.454	NO	1.000			
36	1:E,3	36	220624MF_036	Low QC - 40 ng/mL	QC	40.000	38.02	-5.0	548267	4.23	301609	1.818	6165	0.465	0.454	NO	1.003			
37	1:E,4	37	220624MF_037	2022-0076-6	Analyte				1643	4.23	353534	0.005	22	0.453	0.454	NO	1.003			
38	1:E,5	38	220624MF_038	2022-0076-7	Analyte		10.43		194817	4.05	364436	0.535	2254	0.188	0.454	YES	0.961			
39	1:E,6	39	220624MF_039	2022-0076-8	Analyte				961	4.22	324862	0.003	15	0.326	0.454	NO	1.000			
40	1:E,7	40	220624MF_040	2022-0076-9	Analyte				2688	4.23	320069	0.008	30	0.635	0.454	YES	1.003			
41	1:E,8	41	220624MF_041	2022-0076-10	Analyte		39.04		662774	4.07	355330	1.865	11875	0.197	0.454	YES	0.965			
42	1:F,1	42	220624MF_042	2022-0076-11	Analyte				774	4.22	287520	0.003	10	0.357	0.454	NO	1.000			

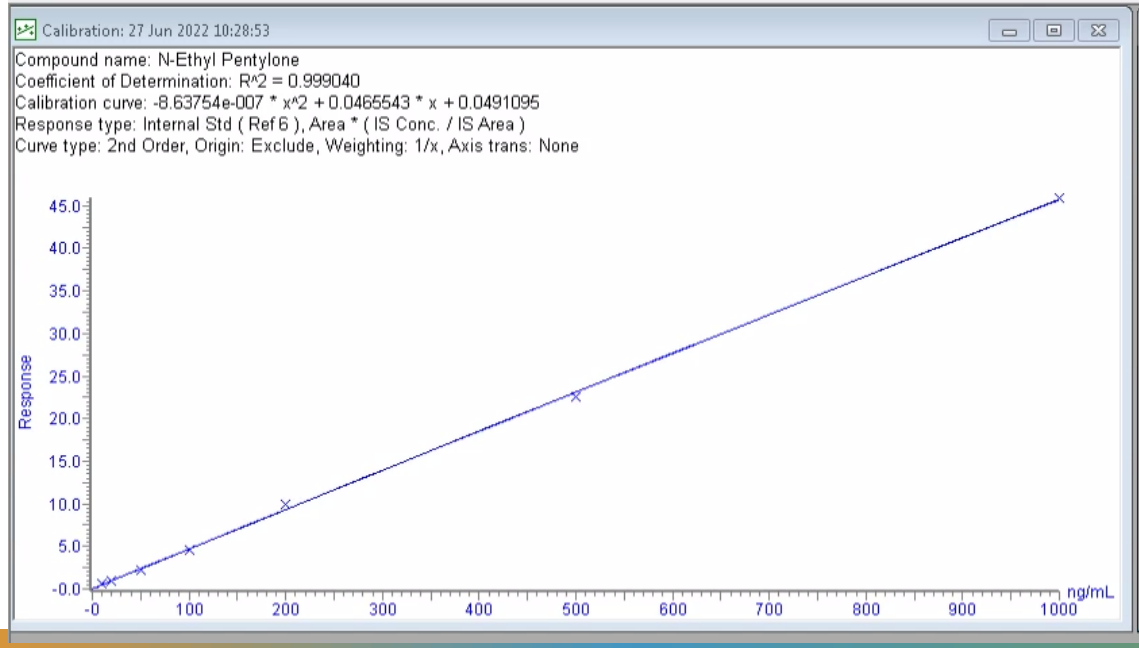


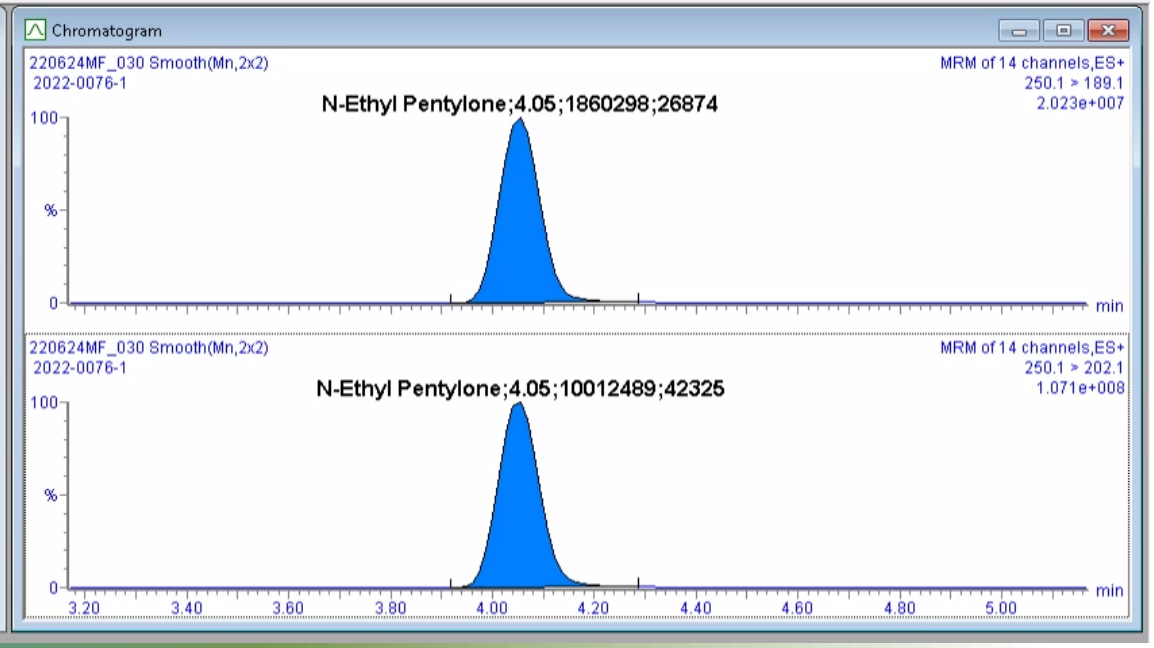


	Vial	#	Name	ID	Type	Std. Conc	ng/mL	%Dev	Area	RT	IS Area	area ratio	S/N	1° Ratio (Actual)	1° Ratio (Pr...	1° Ratio Flag	RRT	2° Ratio (...	2° Ratio (P...	2° Ratio Flag
20	1:C,3	20	220624MF_020	2022-0058	Analyte				1380	4.23	260416	0.005	22	0.555	0.454	NO	1.003			
21	1:C,4	21	220624MF_021	2022-0059	Analyte				797	4.23	299570	0.003	12	0.424	0.454	NO	1.003			
22	1:C,5	22	220624MF_022	2022-0060 Diluted 1:10	Analyte				876	4.22	382283	0.002	12	0.416	0.454	NO	1.000			
23	1:C,6	23	220624MF_023	2022-0067	Analyte				482	4.23	299351	0.002	9	0.206	0.454	YES	1.003			
24	1:C,7	24	220624MF_024	2022-0068	Analyte				854	4.23	359888	0.002	13	0.344	0.454	NO	1.003			
25	1:C,8	25	220624MF_025	2022-0072	Analyte				539	4.22	294022	0.002	7	0.341	0.454	NO	1.000			
26	1:D,1	26	220624MF_026	2022-0073	Analyte				785	4.22	218671	0.004	9	0.341	0.454	NO	1.000			
27	1:D,2	27	220624MF_027	2022-0074	Analyte				1361	4.23	395337	0.003	13	0.397	0.454	NO	1.003			

2022-0075	Analyte				401	4.23	322256	0.001	4	0.293	0.454	YES	1.003
2022-0081	Analyte				506	4.23	324567	0.002	9	0.371	0.454	NO	1.003
2022-0076-1	Analyte		124.23		1860298	4.05	319692	5.819	26874	0.186	0.454	YES	0.961
2022-0076-2	Analyte				887	4.22	348658	0.003	12	0.548	0.454	NO	1.000
2022-0076-3	Analyte		96.87		1474676	4.05	324060	4.551	17257	0.178	0.454	YES	0.961

37	1:E,4	37	220624MF_037	2022-0076-6	Analyte				1643	4.23	353534	0.005	22	0.453	0.454	NO	1.003			
38	1:E,5	38	220624MF_038	2022-0076-7	Analyte		10.43		194817	4.05	364436	0.535	2254	0.188	0.454	YES	0.961			
39	1:E,6	39	220624MF_039	2022-0076-8	Analyte				961	4.22	324862	0.003	15	0.326	0.454	NO	1.000			
40	1:E,7	40	220624MF_040	2022-0076-9	Analyte				2688	4.23	320069	0.008	30	0.635	0.454	YES	1.003			
41	1:E,8	41	220624MF_041	2022-0076-10	Analyte		39.04		662774	4.07	355330	1.865	11875	0.197	0.454	YES	0.965			
42	1:F,1	42	220624MF_042	2022-0076-11	Analyte				774	4.22	287520	0.003	10	0.357	0.454	NO	1.000			





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23	1:C,6	23	220624MF_023	2022-0067	Analyte				482	4.23	299351	0.002	9	0.206	0.454	YES	1.003			
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25	1:C,8	25	220624MF_025	2022-0072	Analyte				539	4.22	294022	0.002	7	0.341	0.454	NO	1.000			
26	1:D,1	26	220624MF_026	2022-0073	Analyte				785	4.22	218671	0.004	9	0.341	0.454	NO	1.000			
27	1:D,2	27	220624MF_027	2022-0074	Analyte				1361	4.23	395337	0.003	13	0.397	0.454	NO	1.003			

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2022-0081	Analyte				506	4.23	324567	0.002	9	0.371	0.454	NO	1.003
2022-0076-1	Analyte		124.23		1860298	4.05	319692	5.819	26874	0.186	0.454	YES	0.961
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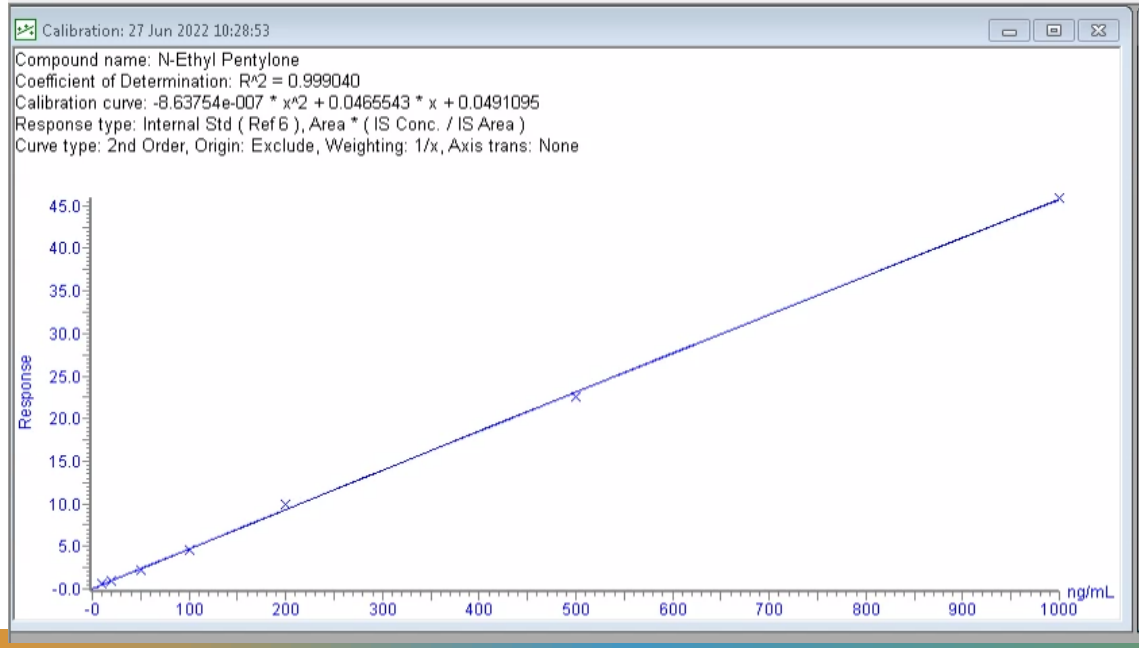
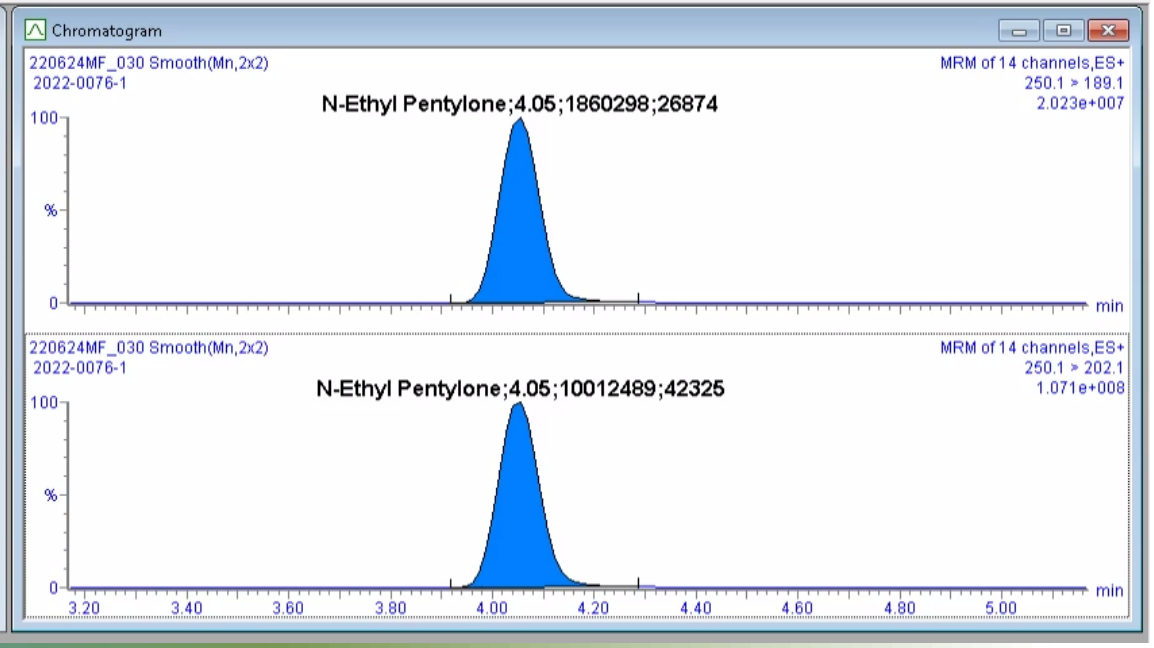
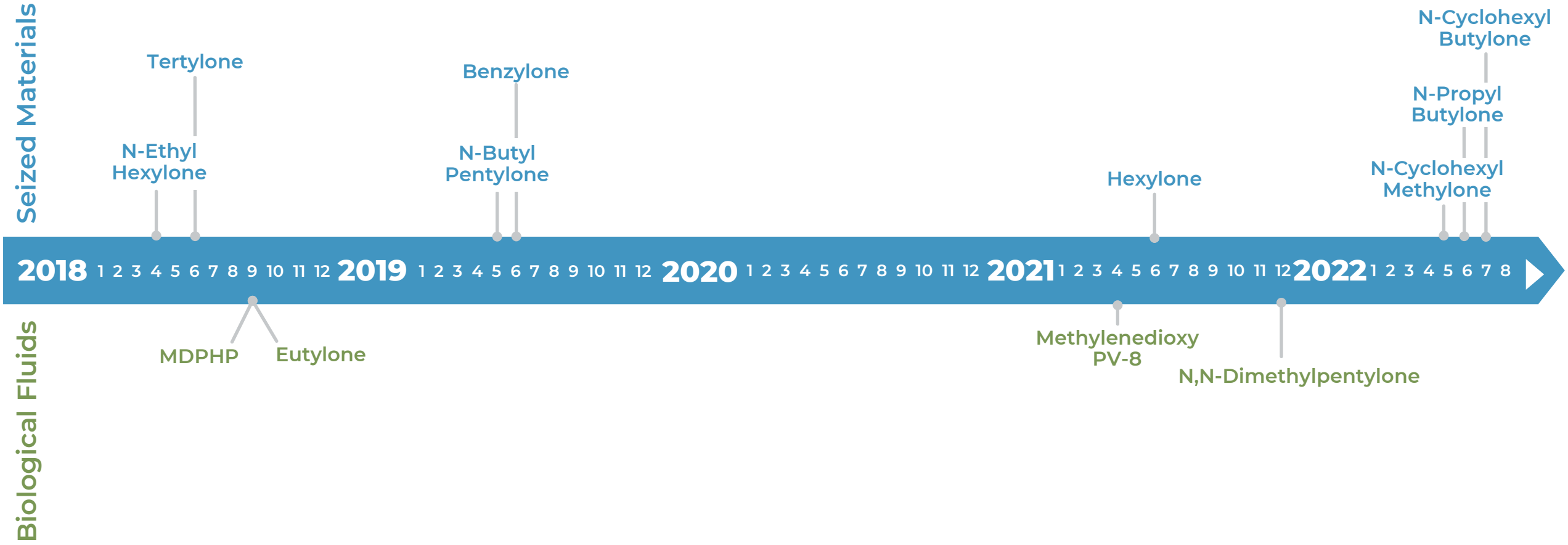
42	1:F,1	42	220624MF_042	2022-0076-11	Analyte				774	4.22	287520	0.003	10	0.357	0.454	NO	1.000			

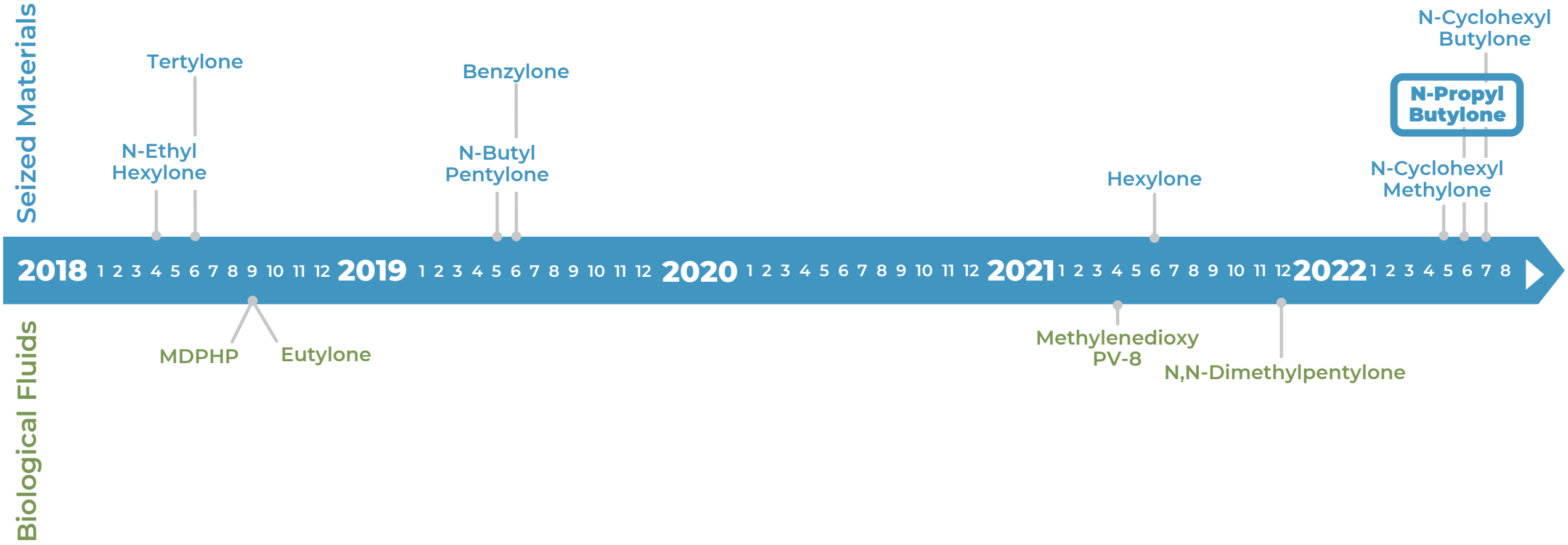


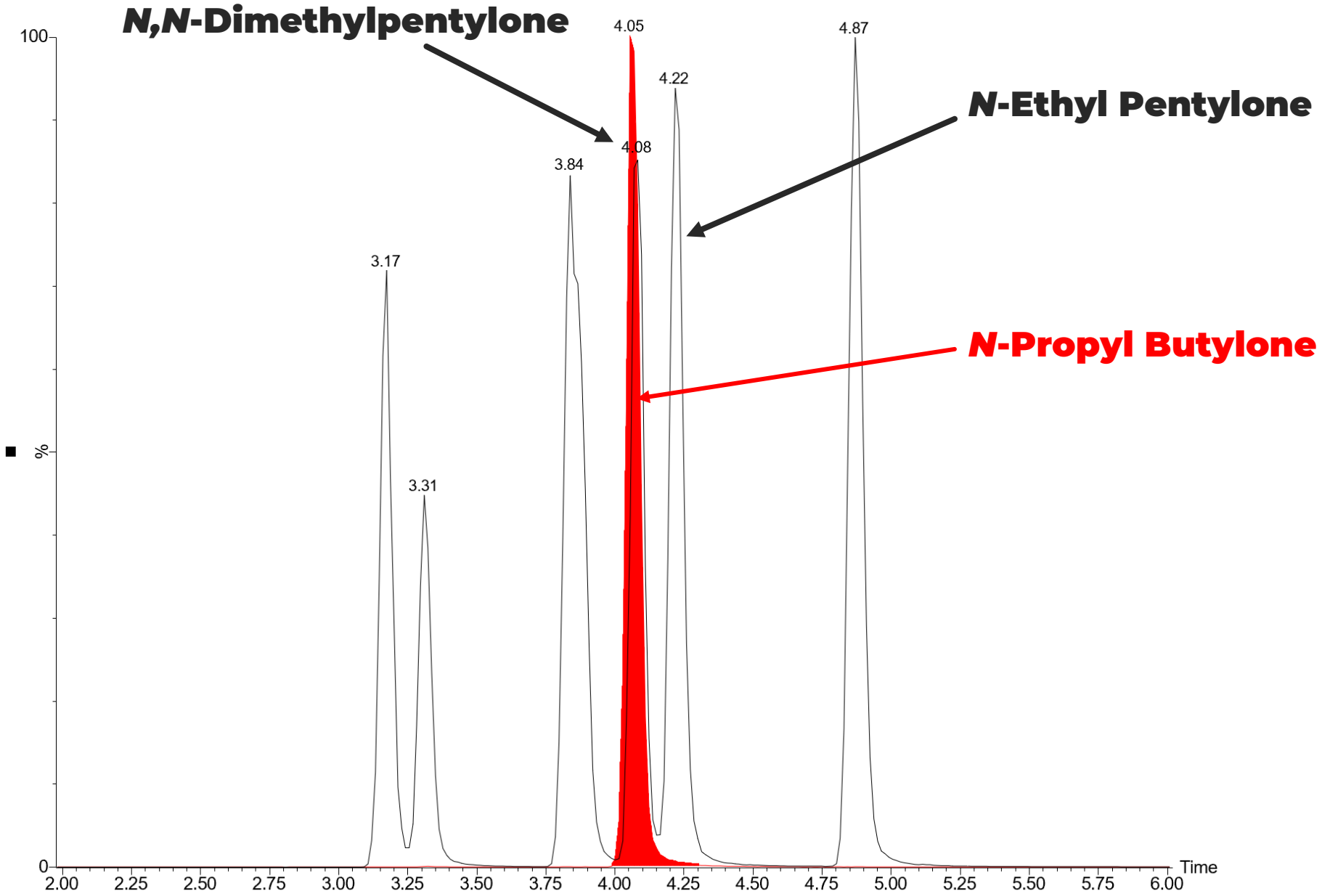


Beta-keto Methylenedioxyamphetamines Monograph Timeline



Beta-keto Methylenedioxyamphetamines Monograph Timeline




N,N-Dimethylpentylone
N-Ethyl Pentylone
N-Propyl Butylone
100
%
0
4.05
4.87
4.22
4.08
3.84
3.17
3.31
Time
2.00
2.25
2.50
2.75
3.00
3.25
3.50
3.75
4.00
4.25
4.50
4.75
5.00
5.25
5.50
5.75
6.00

UPDATED SCOPE

Diethylone

N,*N*-Dimethylpentylone

Tertylone

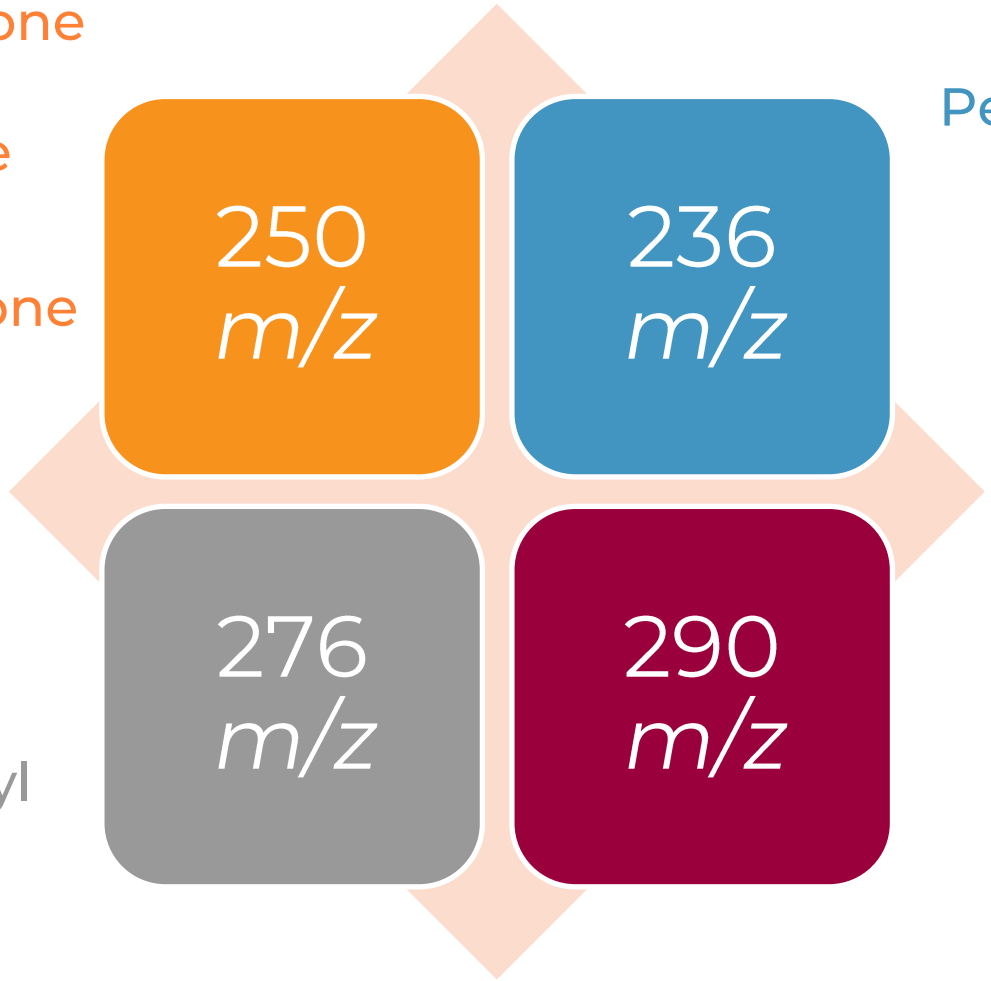
N-Ethyl *N*-Methyl Butylone

Hexylone

N-Propyl Butylone

N-Ethyl Pentylone

N-Isopropyl Butylone



Pentylone

Eutylone

N-Cyclohexyl Methylone

N-Methyl *N*-Cyclohexyl Methylone

N-Cyclohexyl Butylone

Instrumentation:

- Waters Acquity I-Class Ultra-Performance Liquid Chromatograph
- Waters Xevo TQ-S Micro Tandem Mass Spectrometer

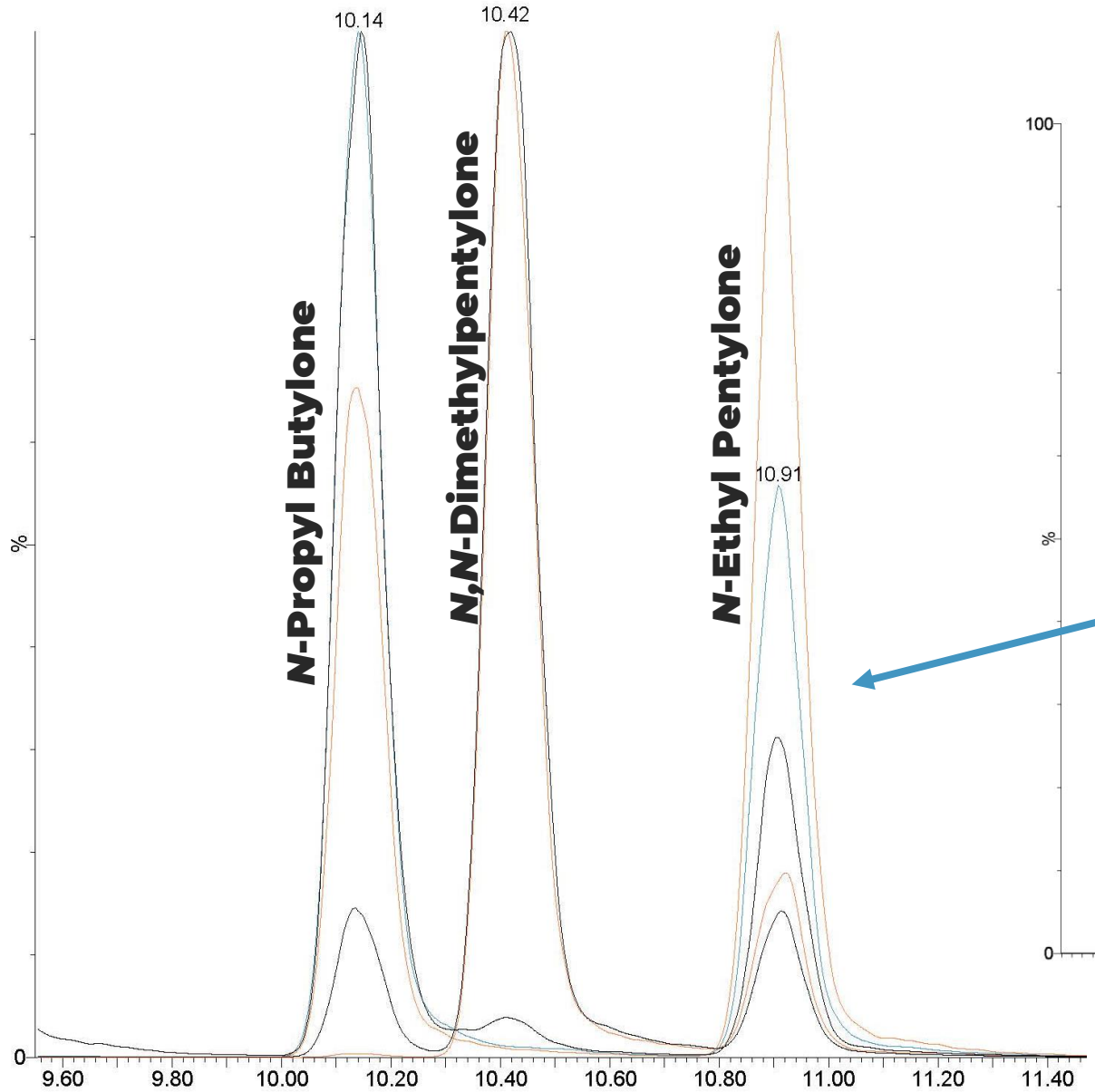
Mobile Phase Compositions:

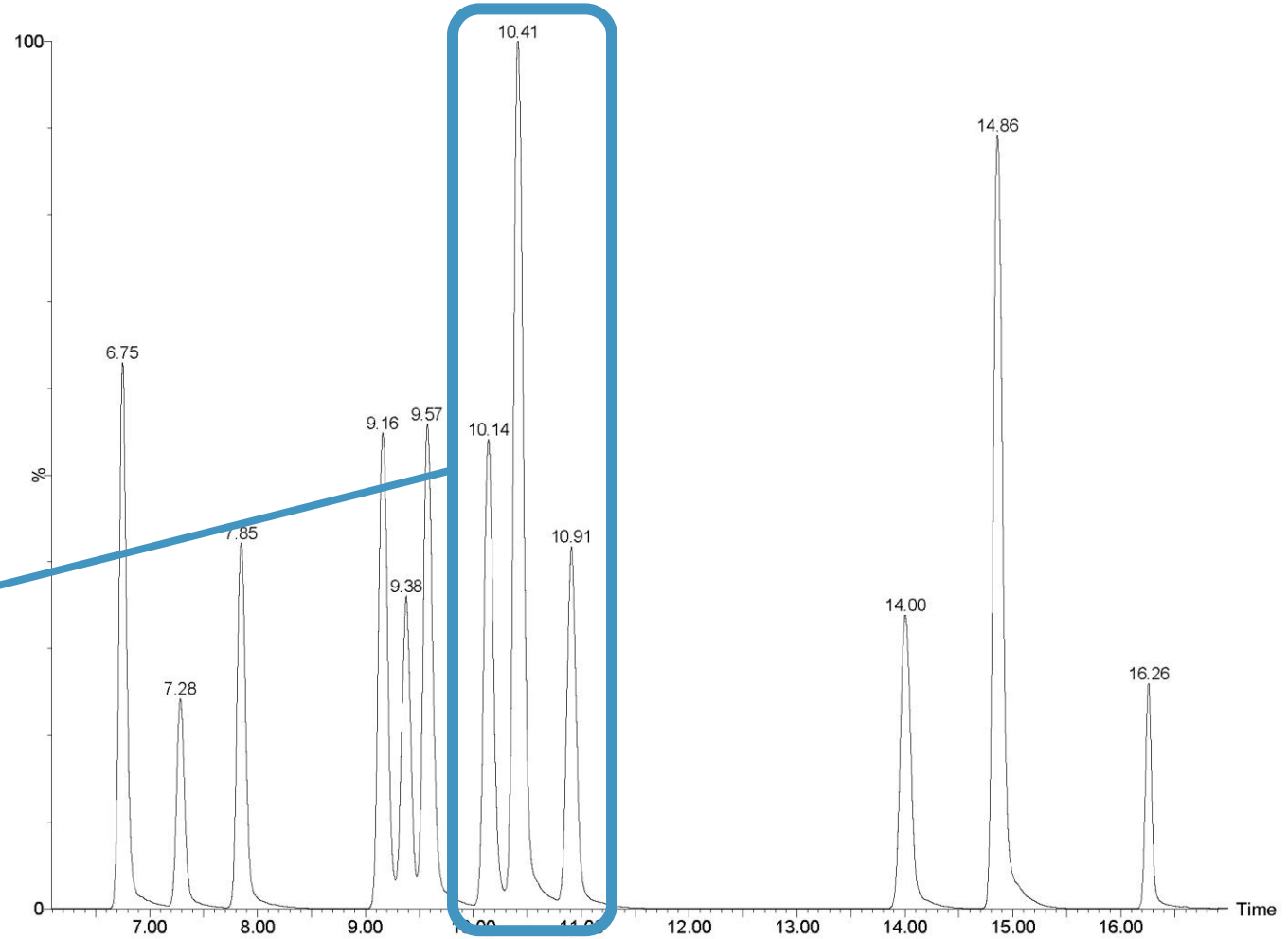
- MPA: 5 mM ammonium formate in water, pH 3
- MPB: 0.1% formic acid in acetonitrile

Analytical Column:

- Agilent InfinityLab Poroshell EC-C18 120 (2.7 µm, 3.0 x **150 mm**)
- 60°C

Time (min)	Flow (mL/min)	%A	%B
Initial	0.4	90	10
0.5	0.4	90	10
12	0.4	80	20
15	0.4	70	30
15.1	0.4	5	95
15.75	0.4	5	95
16	0.4	90	10
17	0.4	90	10


10.14
10.42
N-Propyl Butylone
N,N-Dimethylpentylone
N-Ethyl Pentylone
10.91
%
0
9.60
9.80
10.00
10.20
10.40
10.60
10.80
11.00
11.20
11.40


100
%
0
10.41
14.86
6.75
9.16
9.57
10.14
7.85
10.91
9.38
14.00
7.28
16.26
Time
7.00
8.00
9.00
12.00
13.00
14.00
15.00
16.00

Standard Addition Validation

- Assessment completed according to ASB Standard Documents
  - Calibration range
  - Carryover
  - Recovery, matrix effects, process efficiency
  - Interferences: matrix, internal standard, analyte, commonly encountered drugs
  - Standard addition assessment
  - Dilution Integrity

- "Lones" Assessment Results
  - Calibration range: 10-1000 ng/mL
    - No carryover at 1000 ng/mL
  - Recovery >90%
  - No interferences detected
    - ~300 commonly encountered drugs
  - Standard addition quantitation acceptable for "lones" of interest
    - *N,N*-dimethylpentylone, pentylone, eutylone, *N*-propyl butylone and *N*-cyclohexyl butylone
    - Up-spikes 1, 10, 100 ng/mL

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RESULTS AND CASE HISTORIES

N,N-DIMETHYLPENTYLONE

- 66 postmortem cases
- Demographics (n=46)
  - Age:
    - Average: 37 (±9) years old
    - Range: 16-58 years old
    - Median: 38 years old
  - Male (34), Female (12)
  - States: Florida (31) and New York (29), New Jersey (1)
- Concentrations:
  - Range: 3.3 ng/mL – 4,600 ng/mL
  - Median: 163 ng/mL
  - Average: 351 (±611) ng/mL

2022

July 15, 2022

Contact:

Phone Number: (212) 337-3900

Drug Enforcement Administration

Syracuse Man Pleads Guilty to Distribution of "Molly"

SYRACUSE, NY - Rory R. Williams, aka "Wildman," aka "Wild," aka "Man," aka "Shawn Carter," age 45, of Syracuse, New York, pled guilty yesterday to distributing N-Ethylpentylone, also known as "molly," a Schedule I controlled substance.

The announcement was made by United States Attorney Carla B. Freedman, Matt Scarpino, Special Agent in Charge Frank A. Tarentino III of the New York Division of the Drug Enforcement Administration (DEA), Acting Special Agent in Charge of the Buffalo Field Office of Homeland Security Investigations (HSI), Lieutenant Timothy Pritchard of the Oswego County Drug Task Force, and Chief Joseph Cecile of the Syracuse Police Department.

As part of his guilty plea yesterday, Williams admitted that on November 30, 2021, he distributed approximately 267 grams (approximately 10 ounces) of N-Ethylpentylone, also known as "molly," to a customer outside his residence in Syracuse, New York, in exchange for $2,500. Williams also admitted to distributing controlled substances on other occasions: on March 10, 2022, Williams gave another individual approximately 770 grams of N,N-dimethylpentylone (dipentylone), to deliver to a customer in Oswego, New York, and on December 21, 2020, the defendant distributed approximately 388 grams of eutylone to a customer outside his residence in Syracuse. Both dipentylone and eutylone are also known as "molly." Williams further admitted that on March 10, 2022, he possessed at his residence approximately 7 kilograms of dipentylone, which he intended to distribute to others. Williams also admitted that $203,204 in cash found at his residence was drug proceeds

POSTMORTEM BLOOD CONCENTRATIONS (ng/mL)

	Eutylone	N-ethyl pentylone	N,N-Dimethylpentylone	N-Propyl Butylone
Number of Cases	67	19	66	6
Mean (±SD)	1,020 (±2,242)	385 (±381)	351 (±611)	85 (±88)
Median	110	210	163	50.5
Range	1.2 – 11,000	12-1,200	3.3-4,600	1.7– 220

OTHER TOXICOLOGICAL FINDINGS

Drug	Number of Positives
Pentylone	63
Fentanyl	38
Methamphetamine/Amphetamine	19
Cocaine/Benzoylecgonine	19
Naloxone	16
Eutylone	15
Methadone	6
Diazepam	5
Oxycodone	5
Morphine	4

CASE 1

- 16-year-old male
- Florida
- **History**: The decedent, with another individual, rented a room at a hotel that is known for drug use by the guests. The decedent exited the bathroom and collapsed to the floor. The individual who was with the decedent started CPR and called 911, but the decedent expired on the scene.
- **COD**: Accident
- **Manner of Death**: *N,N*-Dimethylpentylone Toxicity (Other Significant Conditions: Obesity)
- **Other Toxicological Findings**
  - Buproprion (120 ng/mL), Hydroxybuproprion (440 ng/mL)
  - Fluoxetine (950 ng/mL)/Norfluoxetine (670 ng/mL)
  - Hydroxyzine (240 ng/mL)
  - Caffeine
  - Naloxone

***N,N*-Dimethylpentylone** 600 ng/mL
Pentylone 380 ng/mL

CASE 2

- Male (age unknown)
- Florida
- **History**: Individual was found dead in a hotel room by a construction worker. Hypertensive heart disease was discovered during autopsy.
- **Other Toxicological Findings**
  - Fentanyl
  - Para-Fluorofentanyl

***N,N*-Dimethylpentylone** 340 ng/mL
Pentylone Positive (<10 ng/mL)
***N*-Propyl Butylone** 42 ng/mL

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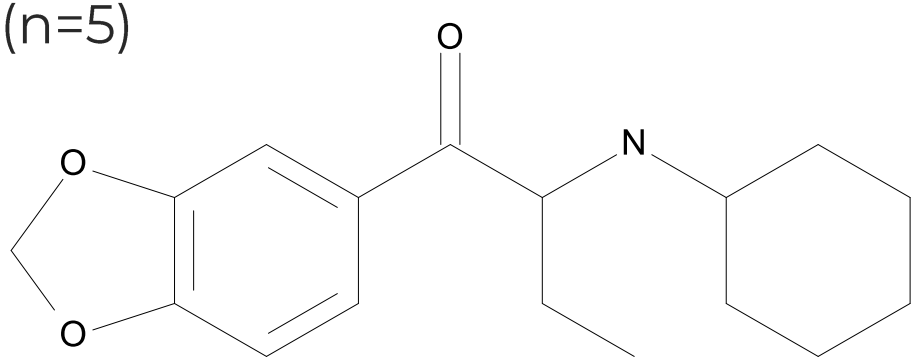
CONCLUSIONS

CONCLUSIONS

- Based on similar trends, *N*,*N*-Dimethylpentylone may dominate the stimulant market for 1-2 years

- New synthetic stimulants may be easily misidentified
  - *N*,*N*-Dimethylpentylone as *N*-ethyl pentylone
  - *N*-propyl butylone as *N*-ethyl pentylone

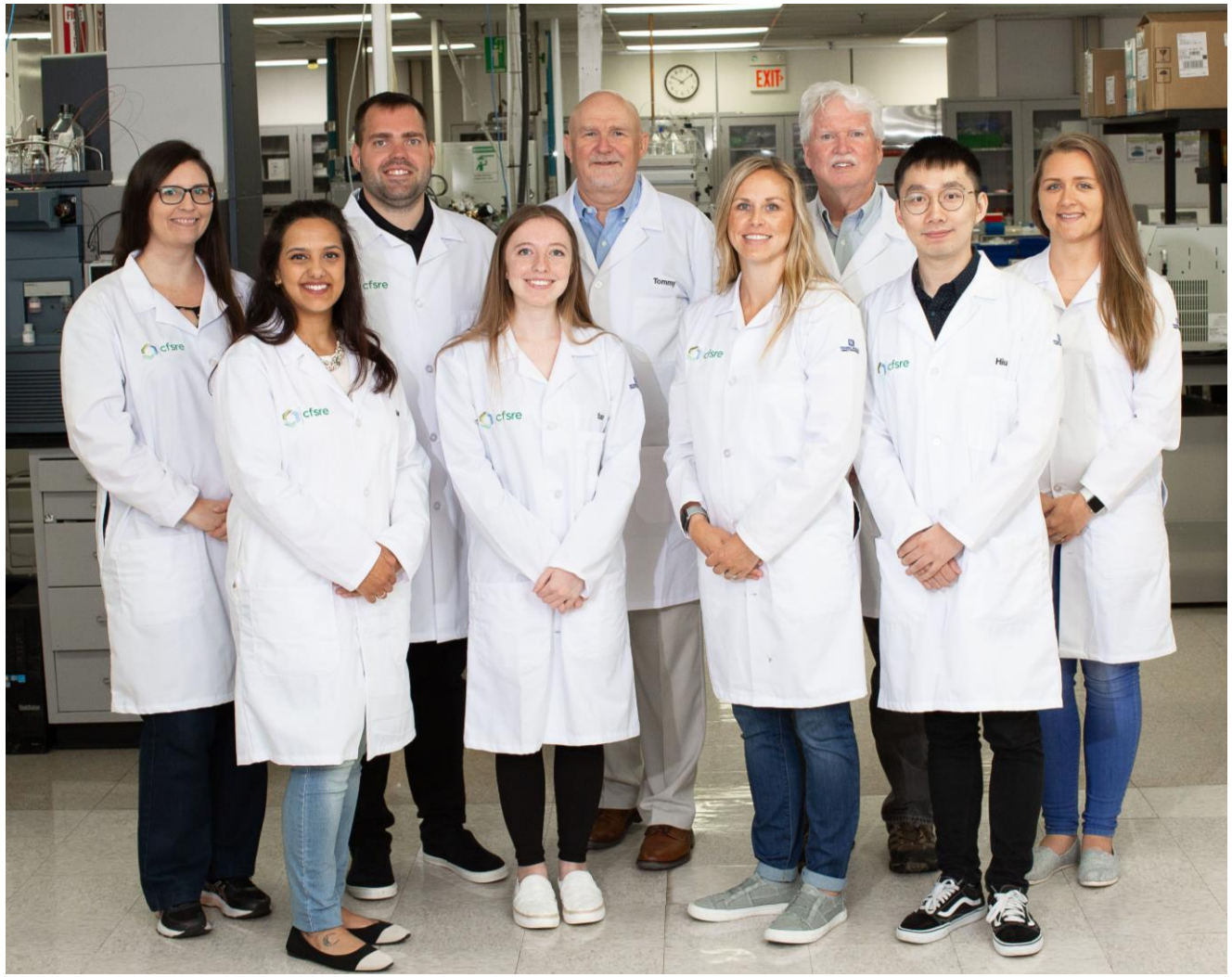
- New Identification of *N*-cyclohexyl butylone (n=5)
  - Range 1.1-96 ng/mL
  - Median 8.1 ng/mL
  - Average 26 (±40) ng/mL



Acknowledgements

- CFSRE Staff
- Medical Examiner's Offices
  - UF Health Pathology Laboratories, Forensic Toxicology Laboratory
  - Morris County Medical Examiner's Office
  - Jefferson County Public Health Service, NY
  - Florida 4th District Chief Medical Examiner
  - Volusia County Medical Examiner Office, FL
- NMS Labs

NMS LABS
When you need to know.™



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Thank you! Questions?

Melissa.Fogarty@cfsre.org