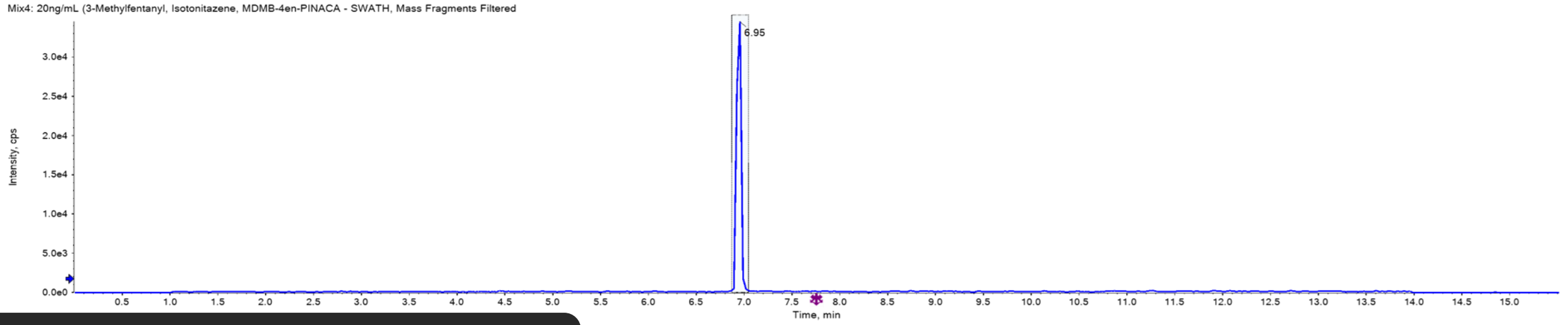
Screening for Neutral Losses and Common Fragments by LC-qToF

Implementation Workshop: ToF/Q-ToF for Identification, Screening, and Confirmation in Forensic Toxicology and Chemistry

Joshua DeBord, PhD – CFSRE / The Fredric Rieders Family Foundation



DISCLOSURES

- I am a paid employee of CFSRE
- I have no conflicts of interest in the material of this presentation
- Speakers have received an honorarium for participating in this webinar
- The webinar is not sponsored by any of the instrument vendors mentioned

NEUTRAL LOSSES AND COMMON FRAGMENTS

- Challenges with screening for NPS
- Introduction to Neutral Losses (NL) and Common Fragments (CF)
  - Nitazenes (and relevant structures)
  - NL/CF Table
- Recommendations for Incorporating NL and CF
  - Basics
  - Specific Targets
- Casework Examples

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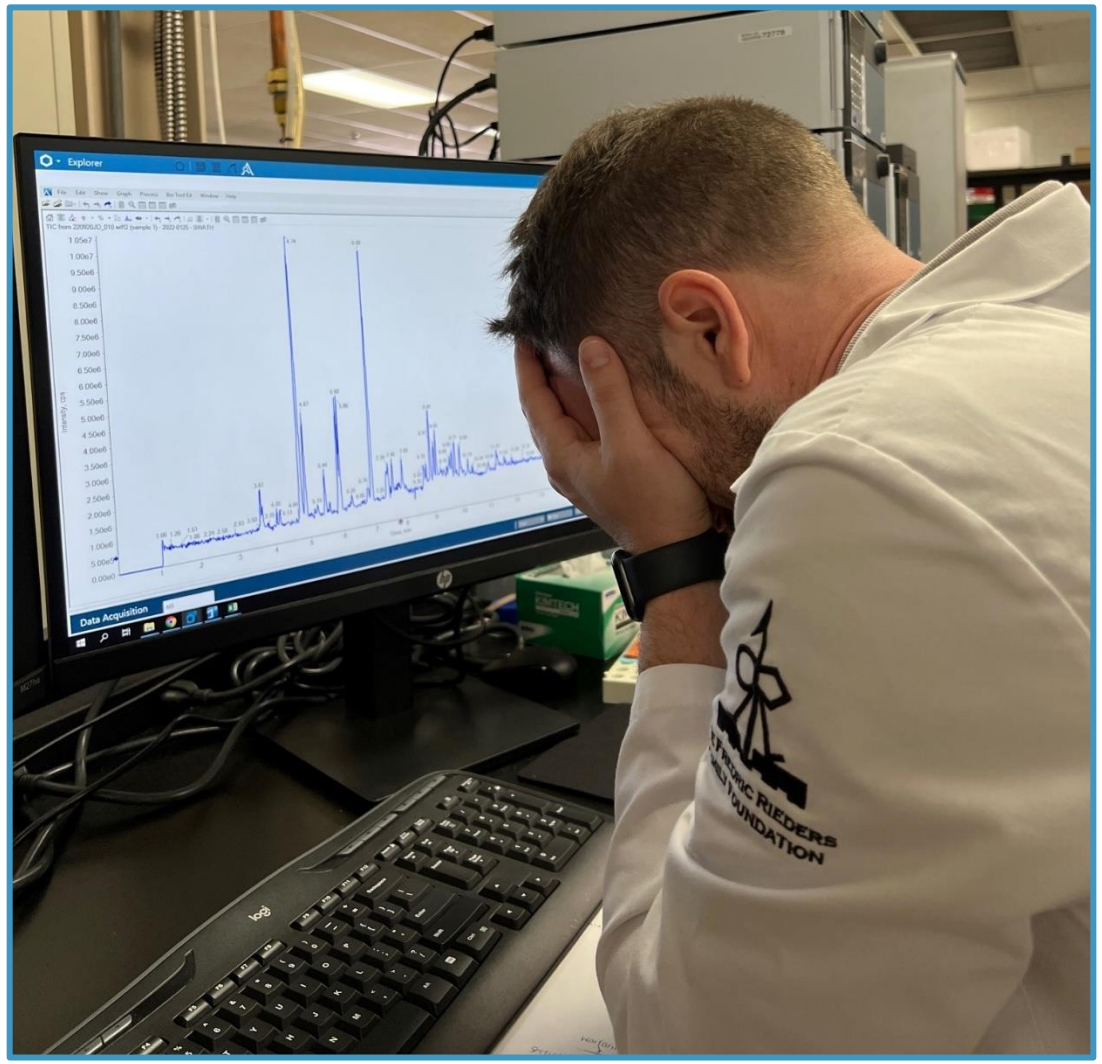
The challenges with NPS

DIFFICULTIES WITH NPS

- Outside of your scope
- Limited available standards
- Infrequently observed
- Costly to update lab capabilities

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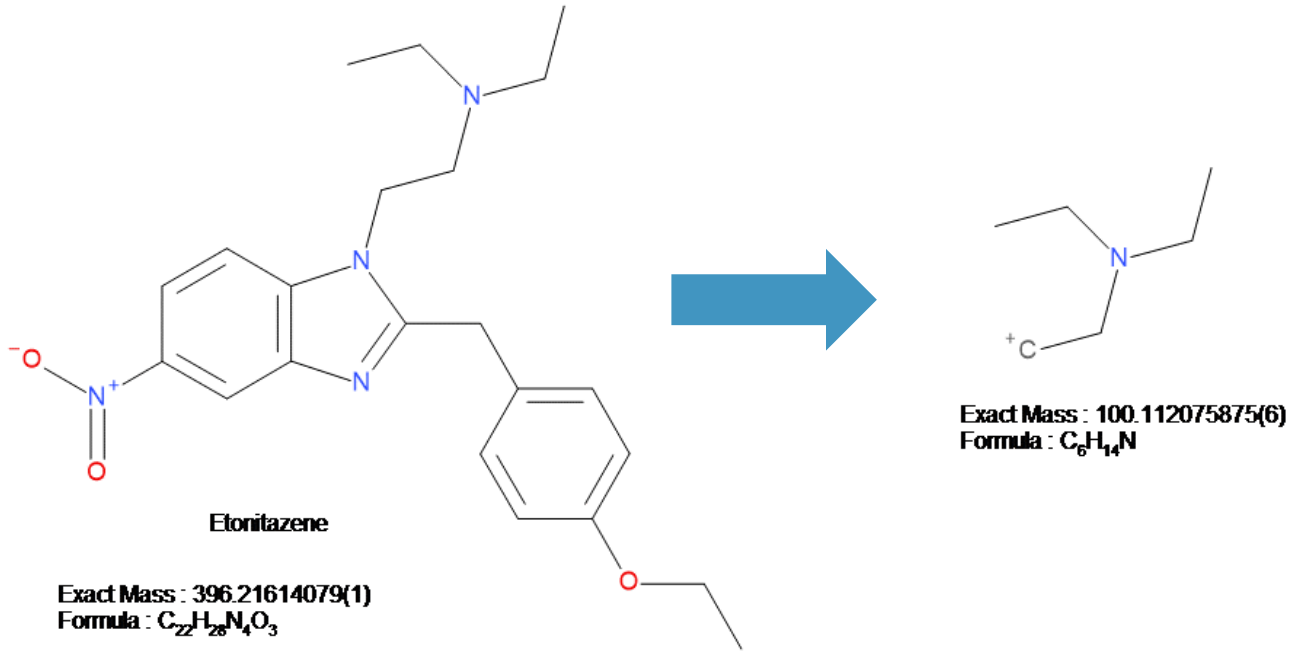
What are Neutral Losses and Common Fragments?

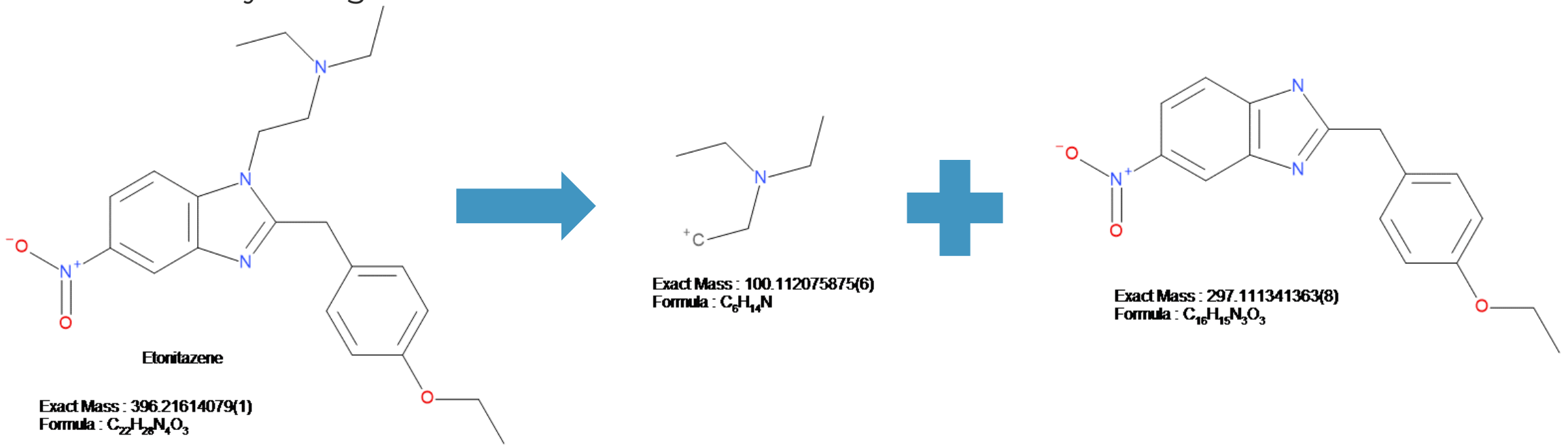
COMMON FRAGMENTS

- Isobaric fragments that are generated from compounds with structural similarity.
- Common among similar NPS (e.g. nitazene analogs, synthetic cannabinoids, fentalogs etc.)



NEUTRAL LOSSES

- $[M+H]^+_{precursor} - [X]^+_{fragment}$
- Most of the time they are easily predictable
- Not necessarily a single structure loss



ONE OF MY FAVORITE TABLES

1	Name	#	Subtype 1	Subtype 2	Subtype 3	Chemical Formu	Precursor (Q1) Mass (D	M+H (Q1) Mass Da	Fragment (Q3) Mass (D	Neutral Losse	Common Fragmen
231	Ethylindole Fentanyl	1836	Opioid	Fentalog	Parent	C24H29N3O	375.23106	376.23896	144.0804	232.16	
232	2',5'-Dimethoxyfentanyl	1874	Opioid	Fentalog	Parent	C24H32N2O3	396.24129	397.24919	165.0906	232.16	
233	N-(DOM) Fentanyl	1917	Opioid	Fentalog	Parent	C26H36N2O3	424.27259	425.28049	193.1229	232.16	
234	N-(2C-E) Fentanyl	1910	Opioid	Fentalog	Parent	C26H36N2O3	424.27259	425.28049	193.1214	232.16	
235	N-(2C-P) Fentanyl	1918	Opioid	Fentalog	Parent	C27H38N2O3	438.28824	439.29614	207.138	232.16	
236	N-(2C-N) Fentanyl	1911	Opioid	Fentalog	Parent	C24H31N3O5	441.22637	442.23427	210.0756	232.16	
237	N-(DOBU) Fentanyl	1919	Opioid	Fentalog	Parent	C29H42N2O3	466.31954	467.32744	235.1695	232.16	
238	N-(2C-B) Fentanyl	1912	Opioid	Fentalog	Parent	C24H31BrN2O3	474.1518	475.1597	242.9962	232.16	
239	BZO-POXIZID	2040	Synthetic Cann	Synthetic Cann	Parent	C20H21N3O2	335.16338	336.17128	77.0377	259.13	77.04
240	ADB-BINAATA	2074	Synthetic Cann	Synthetic Cann	Parent	C19H28N4O2	344.22123	345.22913	86.0956	259.13	86.1
241	AB-BICA	1650	Synthetic Cann	Synthetic Cann	Parent	C21H23N3O2	349.17903	350.18693	91.0543	259.13	
242	AB-FUBICA	1685	Synthetic Cann	Synthetic Cann	Parent	C21H22FN3O2	367.16961	368.17751	109.0439	259.13	109.04
243	CUMYL-THPINACA	1667	Synthetic Cann	Synthetic Cann	Parent	C23H27N3O2	377.21033	378.21823	119.0855	259.13	119.09
244	ATHPINACA	1679	Synthetic Cann	Synthetic Cann	Parent	C24H31N3O2	393.24163	394.24953	135.1167	259.13	135.12
245	N-desethyl Etonitazene	1989	Opioid	Nitazene	Metabolite	C20H24N4O3	368.18484	369.19274	72.0823	297.11	72.08
246	4'-hydroxy Nitazene	1962	Opioid	Nitazene	Metabolite	C20H24N4O3	368.18484	369.19274	72.0785	297.11	72.08
247	N-Pyrrolidino Etonitazene	2001	Opioid	Nitazene	Parent	C22H26N4O3	394.20049	395.20839	98.0956	297.11	
248	Etonitazene	1957	Opioid	Nitazene	Parent	C22H28N4O3	396.21614	397.22404	100.1114	297.11	100.11
249	Pyrrolidino Variant Etonitazene	2100	Opioid	Nitazene	Parent	C23H28N4O3	408.21614	409.22404	112.1111	297.11	
250	N-Piperidinyl Etonitazene	2021	Opioid	Nitazene	Parent	C23H28N4O3	408.21614	409.22404	112.1113	297.11	
251	N-Desethyl Isotonitazene	1952	Opioid	Nitazene	Metabolite	C21H26N4O3	382.20049	383.20839	72.0812	311.13	72.08
252	Metonitazene	1921	Opioid	Nitazene	Parent	C21H26N4O3	382.20049	383.20839	72.0781	311.13	72.08
253	N-Pyrrolidino Isotonitazene	2090	Opioid	Nitazene	Parent	C23H28N4O3	408.21614	409.22404	98.0955	311.13	
254	alpha-Methyl Etonitazene	2095	Opioid	Nitazene	Parent	C23H30N4O3	410.23179	411.23969	100.1119	311.13	100.11
255	Isotonitazene	1903	Opioid	Nitazene	Parent	C23H30N4O3	410.23179	411.23969	100.1128	311.13	100.11
256	Ethylene Etonitazene	2097	Opioid	Nitazene	Parent	C23H30N4O3	410.23179	411.23969	100.111	311.13	100.11
257	Protonitazene	2013	Opioid	Nitazene	Parent	C23H30N4O3	410.23179	411.23969	100.1121	311.13	100.11

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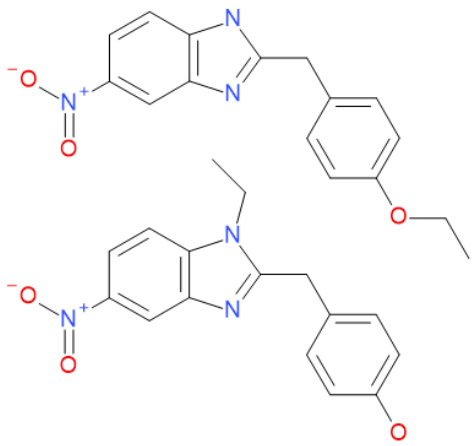
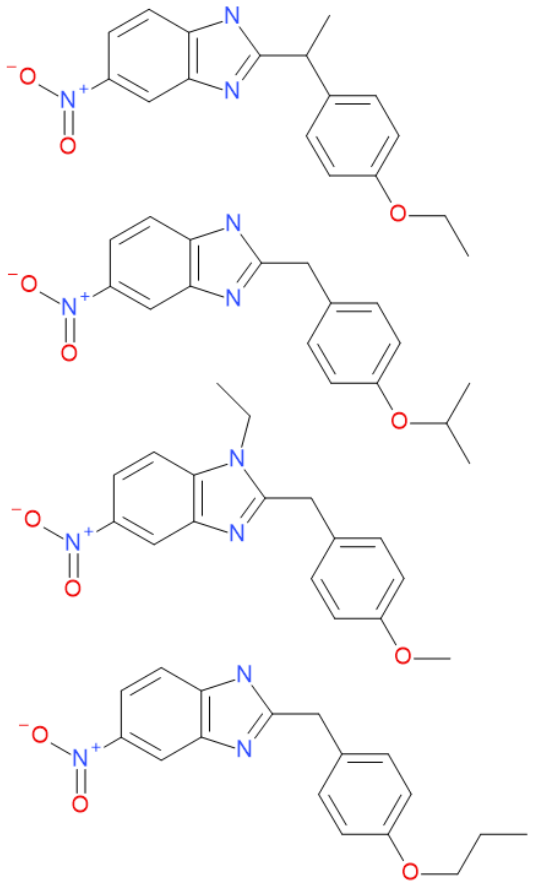
Structures

NITAZENE ANALOGS – NEUTRAL LOSSES

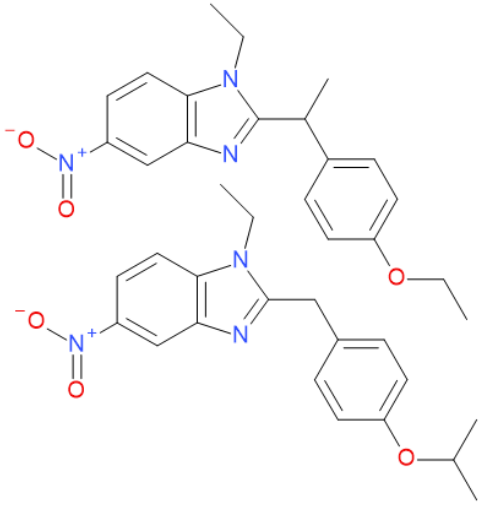
Exact Mass : 297.111341363(8)
Formula : $C_{16}H_{15}N_3O_3$

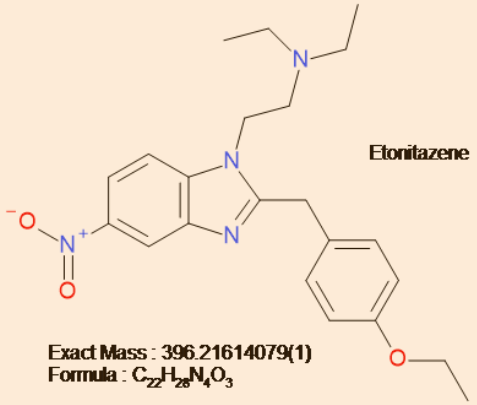


Exact Mass : 311.126991428(9)
Formula : $C_{17}H_{17}N_3O_3$



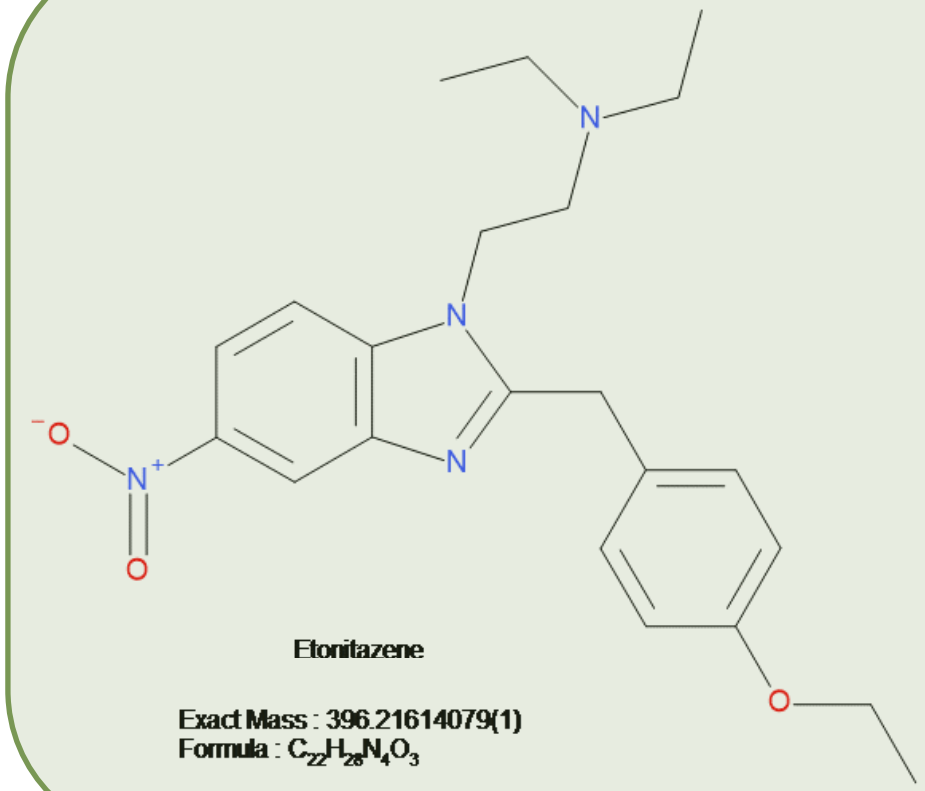
Exact Mass : 339.15829156(1)
Formula : $C_{19}H_{21}N_3O_3$





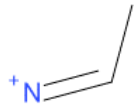
Exact Mass : 396.21614079(1)
Formula : $C_{22}H_{28}N_4O_3$

NITAZENE ANALOGS – COMMON FRAGMENTS

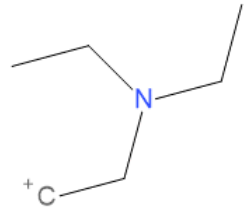


Etonitazene

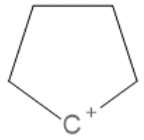
Exact Mass : 396.21614079(1)
Formula : $C_{22}H_{28}N_4O_3$



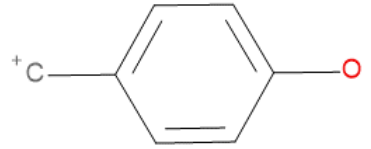
Exact Mass : 44.049475618(3)
Formula : C_2H_6N



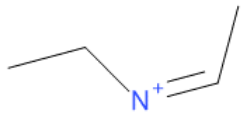
Exact Mass : 100.112075875(6)
Formula : $C_6H_{14}N$



Exact Mass : 69.069876709(4)
Formula : C_5H_9



Exact Mass : 107.049141267(3)
Formula : C_7H_7O



Exact Mass : 72.080775746(4)
Formula : $C_4H_{10}N$

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Implementation

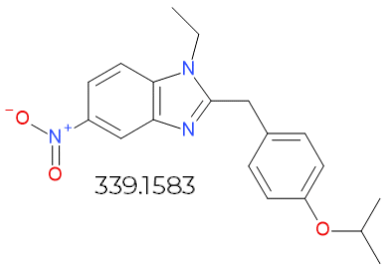
FORENSIC TOXICOLOGY IMPLEMENTATION

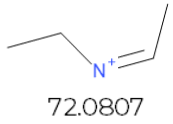
- HR-MS/MS such as qToF big plus
- Modify MS parameters (if necessary)
- Use Recommended Targets
  - Top-tier targets for general use
  - Secondary targets as needed
  - Metabolic targets depending on matrix
- Identify an unknown peak as a potential NPS with filters
- Investigate MS/MS Spectra
- Elucidate structure

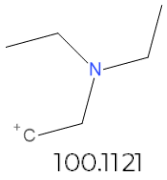
NITAZENE ANALOGS – PRIMARY TARGETS

Fentalog (n=127)					
NL			CF		
m/Z	n	Coverage	m/Z	n	Coverage
116.0473	5	4%	84.0807	5	4%
121.0891	65	51%	105.0699	84	66%
149.0841	28	22%	132.0807	6	5%
232.1576	19	15%	134.0964	38	30%
			140.1070	2	2%
			146.0964	28	22%
			174.1277	6	5%
			188.1434	79	62%
			216.1383	11	9%
			245.1648	3	2%
			246.1489	5	4%
			281.2012	11	9%

Nitazene (n=32)					
NL			CF		
m/Z	n	Coverage	m/Z	n	Coverage
297.1113	6	19%	44.0495	23	72%
311.1270	8	25%	69.0699	2	6%
339.1583	9	28%	72.0807	27	84%
			100.1121	25	78%
			107.0491	14	44%





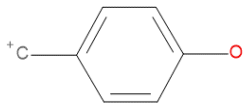


Synthetic Cannabinoids (n=149)					
NL			CF		
m/Z	n	Coverage	m/Z	n	Coverage
45.0209	41	28%	77.0386	6	4%
130.1106	21	14%	86.1000	4	3%
131.0946	19	13%	93.0699	8	5%
135.1048	12	8%	105.0335	6	4%
145.1103	25	17%	107.0855	13	9%
259.1321	6	4%	109.0448	22	15%
			116.0495	20	13%
			119.0855	14	9%
			135.1168	13	9%
			144.0444	28	19%
			145.0396	47	32%
			177.0500	10	7%
			189.0459	4	3%
			212.1070	11	7%
			213.1022	17	11%
			222.9500	4	3%
			241.1335	10	7%
			253.0800	11	7%

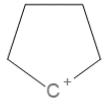
NITAZENE ANALOGS – SECONDARY TARGETS

Fentalog (n=127)					
NL			CF		
m/Z	n	Coverage	m/Z	n	Coverage
116.0473	5	4%	84.0807	5	4%
121.0891	65	51%	105.0699	84	66%
149.0841	28	22%	132.0807	6	5%
232.1576	19	15%	134.0964	38	30%
			140.1070	2	2%
			146.0964	28	22%
			174.1277	6	5%
			188.1434	79	62%
			216.1383	11	9%
			245.1648	3	2%
			246.1489	5	4%
			281.2012	11	9%

Nitazene (n=32)					
NL			CF		
m/Z	n	Coverage	m/Z	n	Coverage
297.1113	6	19%	44.0495	23	72%
311.1270	8	25%	56.0495	2	6%
339.1583	9	28%	69.0699	2	6%
			72.0807	27	84%
			100.1121	25	78%
			107.0491	14	44%

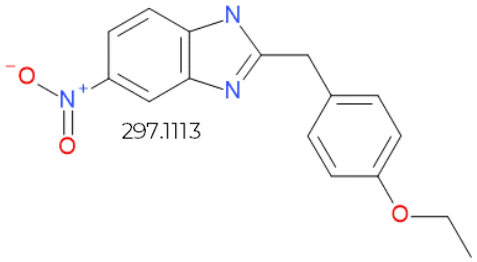


107.0491



69.0699

56.0495



297.1113

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NL			CF		
m/Z	n	Coverage	m/Z	n	Coverage
45.0209	41	28%	77.0386	6	4%
130.1106	21	14%	86.1000	4	3%
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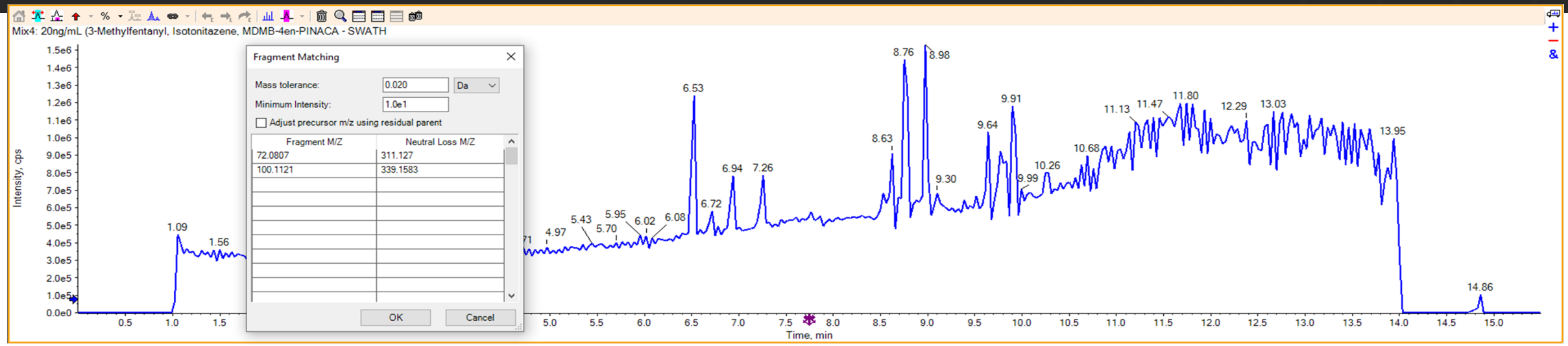
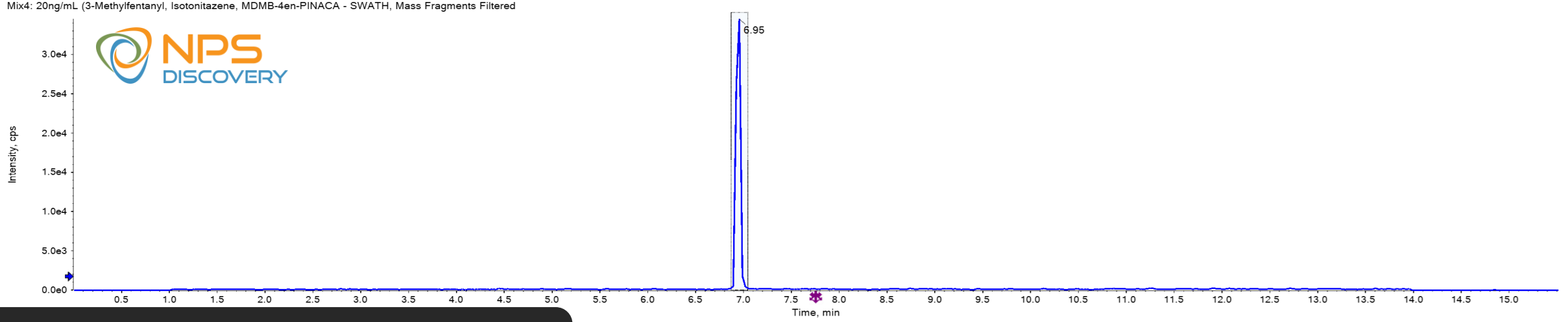
135.1048	12	8%	105.0335	6	4%
145.1103	25	17%	107.0855	13	9%
259.1321	6	4%	109.0448	22	15%
			116.0495	20	13%
			119.0855	14	9%
			135.1168	13	9%
			144.0444	28	19%
			145.0396	47	32%
			177.0500	10	7%
			189.0459	4	3%
			212.1070	11	7%
			213.1022	17	11%
			222.9500	4	3%
			241.1335	10	7%
			253.0800	11	7%

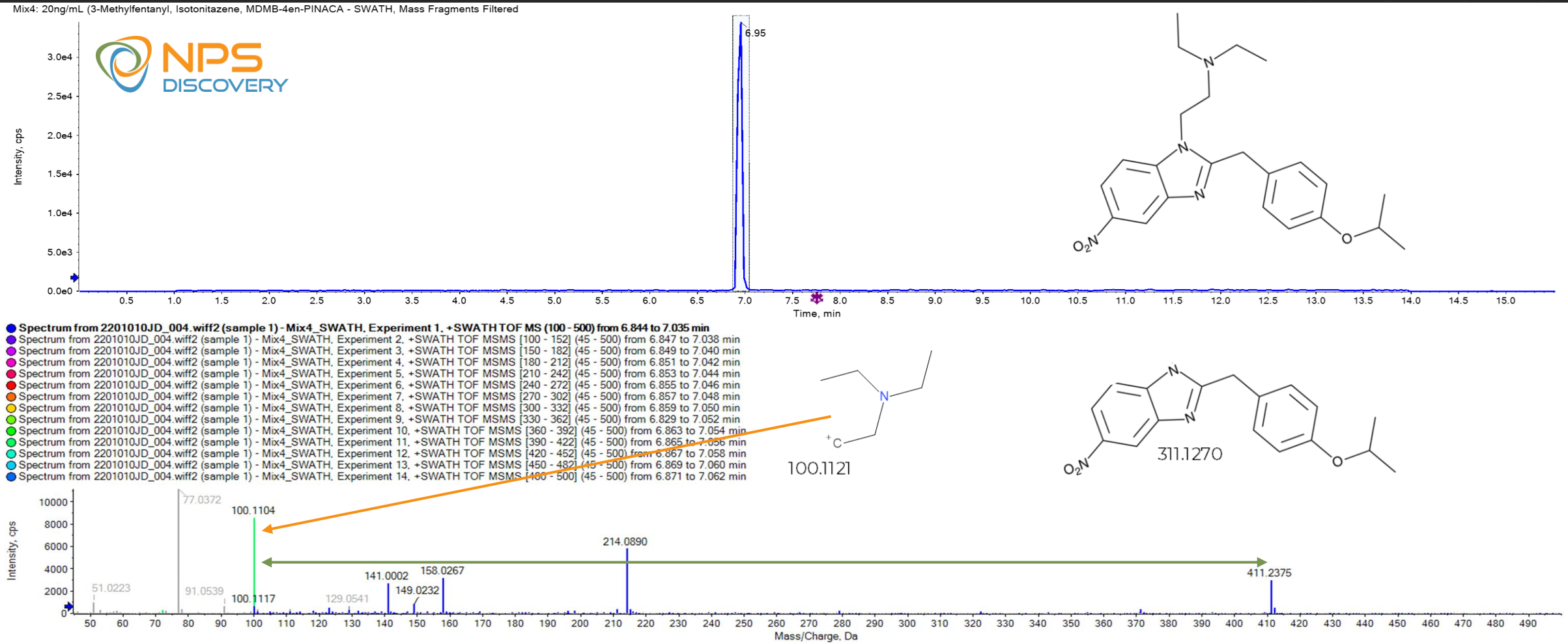
Casework Example

ISOTONITAZENE





ISOTONITAZENE



PROMISES MADE AT SOFT 2022

- All slides (including structure slides) will be on CFSRE / NPS Discovery website
- Incorporate NL and CF filters into CFSRE / NPS Discovery network
- NL and CF toolkit?
  - SCIEX
  - Waters
  - Need to collaborate on others
- Update NL and CF recommendations as the NPS landscape evolves.

Toolkit in Progress!!

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Thank you! Questions?

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