Toxicology trends and interpretation

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September 26, 2024

Agenda

- NMS Testing Scheme
- ABCs of an NMS Report
- Overview of drug trends in Idaho Casework
- New drugs at the national level
- Q & A

Table 1—Required Minimum Analytical Scope and Sensitivity for Testing of Blood in Suspected Toxicological Cause of Death Determination[1]

Compound	Blood Screen	Blood Confirm
Volatiles (g/dL)		
Acetone Isopropanol	0.01	0.01
Ethanol Methanol	0.02	0.02
Anticonvulsants (ng/mL)		
10-OH-carbazepine Carbamazepine Gabapentin Lamotrigine Levetiracetam Pregabalin Phenytoin Primidone Topiramate	1000	1000
Antidepressants (ng/mL)		
Amitriptyline Bupropion Citalopram Clomipramine Desipramine Doxepin Duloxetine Fluoxetine Imipramine Mirtazapine Nortriptyline O-desmethylvenlafaxine Paroxetine Sertraline Trazodone Venlafaxine	200	200
Antihistamines/Antitussives (ng/mL)		
Chlorpheniramine Diphenhydramine Doxylamine Hydroxyzine Methorphan Promethazine	100	100
Antipsychotics (ng/mL)		
9-hydroxyrisperidone Risperidone	50	50
Chlorpromazine Clozapine Olanzapine Quetiapine	200	200
Barbiturates (ng/mL)		
Butalbital Pentobarbital Phenobarbital Secobarbital	1000	1000

Compound	Blood Screen	Blood Confirm
Benzodiazepines/Sedatives (ng/mL)		
7-aminoclonazepam Alprazolam Clonazepam Lorazepam Zolpidem	15	15
Diazepam Nordiazepam Oxazepam Temazepam	50	50
Cannabinoids (ng/mL)		
THC	N/A	2
THC-COOH	10	10
Carbon Monoxide[2]		
COHb	10%	10%
Dissociatives (ng/mL)		
Ketamine Phencyclidine	20	20
Cocaine (ng/mL)		
Cocaine Cocaethylene	N/A	20
Benzoylecgonine	50	50
Muscle Relaxants (ng/mL)		
Cyclobenzaprine	50	50
Carisoprodol Meprobamate	1000	1000
Opioids (ng/mL)		
Buprenorphine Fentanyl	1	1
6-acetylmorphine	N/A	5
Oxymorphone	5	5
Codeine Hydrocodone Hydromorphone Morphine Oxycodone	10	10
Methadone Tramadol	50	50
Over the Counter Pain Medications (µg/mL)[3]		
Acetaminophen	10	10
Salicylates	50	50
Sympathomimetic Amines (ng/mL)		
Amphetamine Methamphetamine Methylenedioxyamphetamine (MDA) Methylenedioxymethamphetamine (MDMA)	25	25

[1] If a compound does not need to be accounted for in the screen, it is indicated by "N/A";
[2] Suspected carbon monoxide-related cases only;
[3] Required if requested or necessary due to case circumstances.

Table 2—Required Minimum Analytical Scope and Sensitivity for Testing of Blood in Cases with a Known Anatomical Cause of Death

Compound	Blood Screen	Blood Confirmation
Volatiles (g/dL)		
Ethanol	0.02	0.02
Benzodiazepines/Sedatives (ng/mL)		
7-aminoclonazepam Alprazolam Clonazepam Lorazepam	15	15
Diazepam Nordiazepam Oxazepam Temazepam	50	50
Cannabinoids (ng/mL)		
THC-COOH	10	10
Cocaine (ng/mL)		
Benzoylecgonine	50	50
Opioids (ng/mL)		
Fentanyl	1	1
Codeine Hydrocodone Morphine Oxycodone	10	10
Sympathomimetic Amines (ng/mL)		
Amphetamine Methamphetamine	25	25

Standard for the Analytical Scope and Sensitivity of Forensic Toxicological Testing of Blood in Medicolegal Death Investigations

ASB Approved February 2021

ANSI Approved August 2021

Academy Standards Board
410 North 21st Street
Colorado Springs, CO 80904

NMS Testing Scheme

- Postmortem Basic (8051)
  - Alcohol screen/quantitation: ETOH, MEOH, Acetone, IPA
    - GCFID Headspace
  - ELISA screen with confirmations
    - Immunoassay (12 panel)
      - Amp/Methamp/MDMA, Barbs, Benzos, Bupren, Coc, Fent, THC, Ops, Methadone, OC/OM, & PCP
    - GC/MS, LCMSMS

- Postmortem Expanded (8052)
  - Alcohol screen/quantitation: ETOH, MEOH, Acetone, IPA
    - GCFID Headspace
  - ELISA screen with confirmations
    - Barbs, Gabapentin, & THC
  - TOF screen with out-of-scope findings (OSF's)

Screening testing – Basic Panel

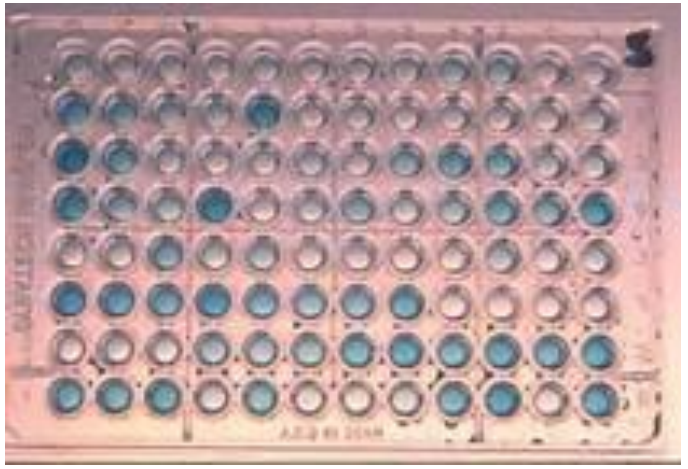
Enzyme Linked Immunosorbent Assay (ELISA)

Targeted to representative compound/class of drugs

Amenable for routine drugs of abuse

- Cannabinoids
- Opiates
- Benzodiazepines
- Methamphetamine
- Phencyclidine
- Cocaine

Qualitative



8051B Reporting Limits

Test 8051B - Postmortem, Basic, Blood (Forensic) - Blood

-Analysis by Enzyme-Linked Immunosorbent Assay (ELISA) for:

Analyte	Rpt. Limit	Analyte	Rpt. Limit
Amphetamines	20 ng/mL	Fentanyl / Acetyl Fentanyl	0.50 ng/mL
Barbiturates	0.040 mcg/mL	Methadone / Metabolite	25 ng/mL
Benzodiazepines	100 ng/mL	Methamphetamine / MDMA	20 ng/mL
Buprenorphine / Metabolite	0.50 ng/mL	Opiates	20 ng/mL
Cannabinoids	10 ng/mL	Oxycodone / Oxymorphone	10 ng/mL
Cocaine / Metabolites	20 ng/mL	Phencyclidine	10 ng/mL

-Analysis by Headspace Gas Chromatography (GC) for:

Analyte	Rpt. Limit	Analyte	Rpt. Limit
Acetone	5.0 mg/dL	Isopropanol	5.0 mg/dL
Ethanol	10 mg/dL	Methanol	10 mg/dL

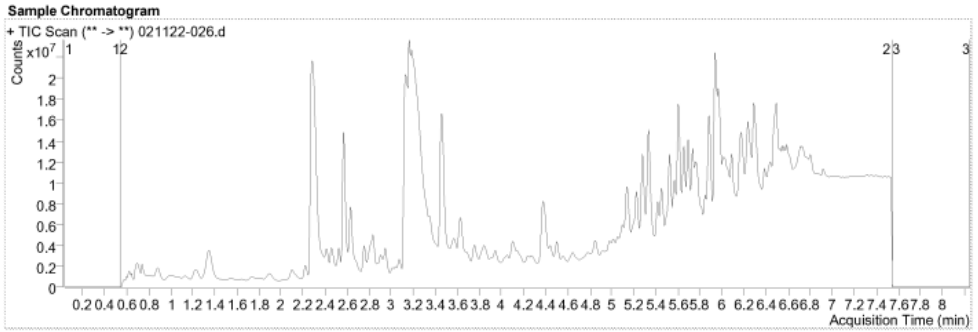
False positives due to decomp:

Amines, Fentanyl, Buprenorphine

Screening testing – Expanded Panel

Time of Flight (TOF) mass spectrometry

Targeted to specific compounds



Internal Standard Results

Compound	RT	RT Diff.	Response	Conc. (%)	Mass Acc. (ppm)
ISTD: D3-Morphine	1.976	0.006	82,980	95.7	-1.48
ISTD: D5-Amphetamine	3.188	0.000	602,971	99.9	3.25
ISTD: D3-BZE	3.857	0.000	27,626	98.1	-5.30
ISTD: D5-Alprazolam	5.963	0.000	1,405,069	97.3	6.73

Quantitation Results

Compound	RT	RT Diff.	Response	Conc. (%)	Mass Acc. (ppm)
Nicotine	1.360	0.000	1,300,571	94.1	3.19
Hydromorphone	2.340	0.000	9,183	92.0	-2.81
Psilocin	2.552	0.000	149,866	94.9	-1.37
Naloxone	2.764	0.000	13,686	96.6	-0.28
Norpseudoephedrine	2.764	0.000	269,496	85.0	3.30
BZP	2.810	0.000	170,108	92.6	0.54
Methcathinone	2.870	0.000	324,343	98.7	0.75
Oxycodone	2.903	0.003	220,606	97.2	10.34
Methylone	2.969	0.000	296,493	101.9	2.88
Clonidine	2.976	0.000	108,179	101.7	1.38
Theophylline	3.042	0.000	125,556	98.6	1.25
Mescaline	3.128	0.000	38,468	99.0	0.84
MDA	3.234	0.000	221,844	100.2	0.36
O-Desmethyltramadol	3.261	0.000	1,483,311	98.4	5.32
Methamphetamine	3.267	0.000	415,666	97.7	1.07
Monoethylglycinexylidide (MEGX)	3.314	0.000	5,665,536	98.1	6.82
PMA	3.387	0.000	223,075	99.5	-12.49
Olanzapine	3.420	0.000	114,661	95.0	3.09
Tiletamine	3.486	0.000	1,737,813	99.9	5.58
Atropine	3.506	0.000	19,084,247	99.3	11.21
Tetrahydrozoline	3.566	0.000	37,840	97.9	-6.61
Mephedrone	3.619	0.000	462,491	95.9	2.33
Zonisamide	3.678	0.000	240,598	111.9	1.03
Mepivacaine	3.764	0.000	9,866,855	99.4	7.63

Postmortem, Expanded, Blood (Forensic) - NMS Labs

8052: Out of Scope Findings

Data File	100923-060.d	**HBN**	8671586
Sample Type	Sample	**Sample Name**	23391058-001-1C1
Instrument	TOF2	**Position**	P2-A6
Acq Method	TOX-Acquisition.m	**Acquired Time**	10/10/2023 2:16:06 AM

Qualitative Results

Compound	Score	Target RT	RT	RT Diff.	Tgt Mass	Mass	Mass Acc. (ppm)	Response
Propranolol	92.90	5.007	5.058	0.051	259.1572	259.1577	1.78	107,961,237

Additional Information

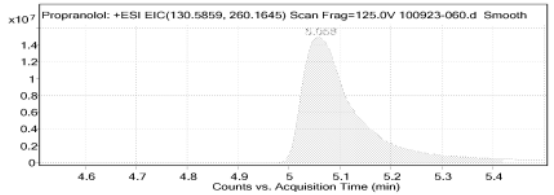
Compound	Notes
Propranolol	Type 2 Action if Positive: Review Supplemental Information: Validated prior to 10/2019.

Compound	Formula	RT Diff.	RT	*m/z*	Mass	Mass Acc. (ppm)	Ions
Propranolol	C16 H21 N O2	0.051	5.058	260.1651	259.1577	1.78	4

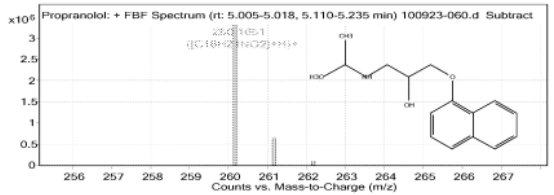
Scoring Table

Overall Score	Score (RT)	Score (MS)	Score (mass)	Score (iso. abund)	Score (iso. spacing)
92.90	83.61	97.32	98.22	94.32	99.14

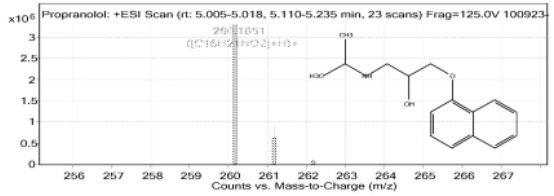
Compound Chromatograms



MS Zoomed Spectrum



MS Zoomed Spectrum

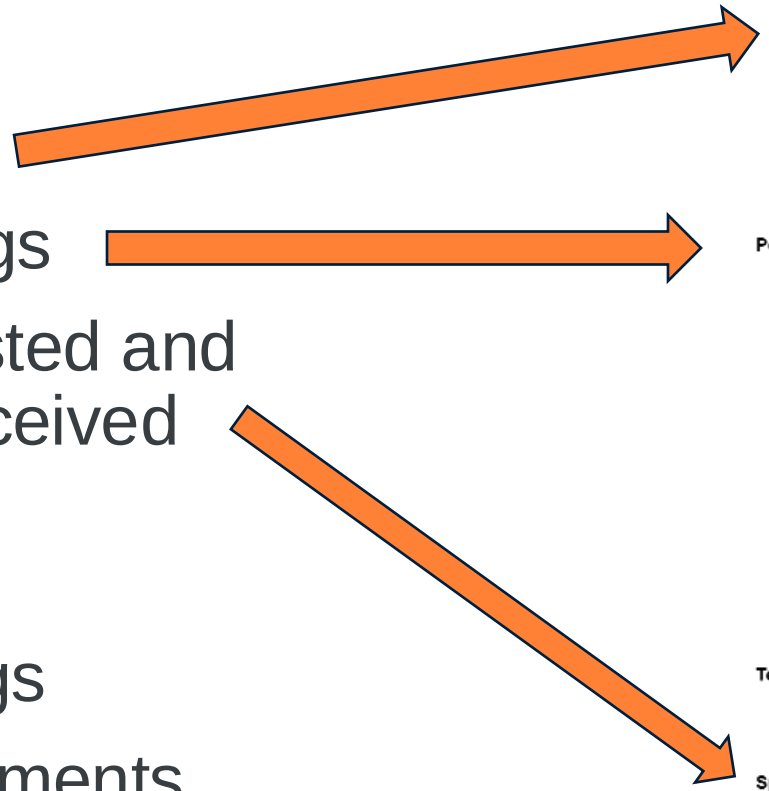


Predicted Isotope Match Table

Isotope	*m/z*	Calc *m/z*	Diff (ppm)	Abund %	Calc Abund %
1	260.1651	260.1645	-2.10	100.0	100.0
2	261.1680	261.1678	-0.79	20.7	18.0
3	262.1704	262.1706	0.42	2.4	1.9
4	263.1658	263.1732	28.33	0.2	0.2

NMS Forensic Report Components

- Page 1
  - –Report Header
  - –Positive Findings
  - –Testing Requested and Specimens Received
- The Rest
  - –Detailed Findings
  - –Reference Comments
  - –Analysis Summary and Reporting Limits



NMS LABS

NMS Labs
200 Welsh Road, Horsham, PA 19044-2208
Phone: (215) 657-4900 Fax: (215) 657-2972
e-mail: nms@nmslabs.com
Robert A. Middleberg, PhD, F-ABFT, DABCC-TC, Laboratory Director

CONFIDENTIAL

Toxicology Report

Report Issued 06/22/2023 09:15

To: **60339**
Tri- County Medical Associates
Attn: Meredith Atkins
200 Welsh Rd.
Horsham, PA 19044-2208

Patient Name	71972-1, 71972-1
Patient ID	71972-1
Chain	NMSCP268543
DOB	Not Given
Sex	Not Given
Workorder	23235932

Page 1 of 2

Positive Findings:

Analyte	Result	Units	Matrix Source
Caffeine	Presump Pos	mcg/mL	001 - Femoral Blood
Cotinine	Presump Pos	ng/mL	001 - Femoral Blood
Naloxone	Presump Pos	ng/mL	001 - Femoral Blood
Benzoylecgonine	770	ng/mL	001 - Femoral Blood
Morphine - Free	8.7	ng/mL	001 - Femoral Blood
Tadalafil	79	ng/mL	001 - Femoral Blood
Amphetamine	9.8	ng/mL	001 - Femoral Blood
Methamphetamine	90	ng/mL	001 - Femoral Blood
Fentanyl	10	ng/mL	001 - Femoral Blood
Norfentanyl	2.1	ng/mL	001 - Femoral Blood
Acetyl Fentanyl	0.21	ng/mL	001 - Femoral Blood
4-ANPP	2.3	ng/mL	001 - Femoral Blood
6-Monoacetylmorphine - Free	16	ng/mL	004 - Urine

See Detailed Findings section for additional information

Testing Requested:

Test	Test Name
8084B	Postmortem, Expanded w/Vitreous Alcohol and 6-MAM Confirmation, Blood (Forensic)

Specimens Received:

ID	Tube/Container	Volume/ Mass	Collection Date/Time	Matrix Source	Labeled As
001	Gray Stopper Glass Tube	9 mL	07/29/2023 10:31	Femoral Blood	2023-1272 C
002	Gray Stopper Glass Tube	8 mL	07/29/2023 10:31	Femoral Blood	2023-1272 D
003	Red Stopper Glass Tube	6 mL	07/29/2023 10:21	Vitreous Fluid	2023-1272 A
004	White Cap Plastic Container	40 mL	07/29/2023 10:29	Urine	2023-1272 B

All sample volumes/weights are approximations.

Specimens received on 08/01/2023.

NMS LABS

Report Header

NMS Labs
200 Welsh Road, Horsham, PA 19044-2208
Phone: (215) 657-4900 Fax: (215) 657-2972
e-mail: nms@nmslabs.com
Robert A. Middleberg, PhD, F-ABFT, DABCC-TC, Laboratory Director

CONFIDENTIAL

Toxicology Report

Report Issued 06/22/2023 09:15

To: **60339**
Tri- County Medical Associates
Attn: Meredith Atkins
200 Welsh Rd.
Horsham, PA 19044-2208

Patient Name	SMITH, MICHAEL
Patient ID	71972-1
Chain	NMSCP268543
DOB	10/01/1975
Sex	Male
Workorder	23235932

Page 1 of 2

Positive Findings & Testing Requested

Positive Findings:

Analyte	Result	Units	Matrix Source
Ethanol	268	mg/dL	001 - Heart Blood
Blood Alcohol Concentration (BAC)	0.268	g/100 mL	001 - Heart Blood
Caffeine	Presump Pos	mcg/mL	001 - Heart Blood
Naloxone	Presump Pos	ng/mL	001 - Heart Blood
Phenobarbital	3.5	mcg/mL	001 - Heart Blood
Nordiazepam	79	ng/mL	001 - Heart Blood
Amphetamine	11	ng/mL	001 - Heart Blood
Methamphetamine	65	ng/mL	001 - Heart Blood
Fentanyl	7.0	ng/mL	001 - Heart Blood
Norfentanyl	0.63	ng/mL	001 - Heart Blood
4-ANPP	0.97	ng/mL	001 - Heart Blood
Creatinine (Vitreous Fluid)	0.607	mg/dL	003 - Vitreous Fluid
Sodium (Vitreous Fluid)	141	mmol/L	003 - Vitreous Fluid
Potassium (Vitreous Fluid)	16.0	mmol/L	003 - Vitreous Fluid
Chloride (Vitreous Fluid)	117	mmol/L	003 - Vitreous Fluid
Urea Nitrogen (Vitreous Fluid)	7.70	mg/dL	003 - Vitreous Fluid
Ethanol	341	mg/dL	003 - Vitreous Fluid

See Detailed Findings section for additional information

Testing Requested:

Test	Test Name
1919FL	Electrolytes and Glucose Panel (Vitreous), Fluid (Forensic)
8042B	Postmortem, Expanded w/Vitreous Alcohol Confirmation, Blood (Forensic)

Positive Findings & Testing Requested

Positive Findings:

Analyte	Result	Units	Matrix Source
Ethanol	268	mg/dL	001 - Heart Blood
Blood Alcohol Concentration (BAC)	0.268	g/100 mL	001 - Heart Blood
Caffeine	Presump Pos	mcg/mL	001 - Heart Blood
Naloxone	Presump Pos	ng/mL	001 - Heart Blood
Phenobarbital	3.5	mcg/mL	001 - Heart Blood
Nordiazepam	79	ng/mL	001 - Heart Blood
Amphetamine	11	ng/mL	001 - Heart Blood
Methamphetamine	65	ng/mL	001 - Heart Blood
Fentanyl	7.0	ng/mL	001 - Heart Blood
Norfentanyl	0.63	ng/mL	001 - Heart Blood
4-ANPP	0.97	ng/mL	001 - Heart Blood
Creatinine (Vitreous Fluid)	0.607	mg/dL	003 - Vitreous Fluid
Sodium (Vitreous Fluid)	141	mmol/L	003 - Vitreous Fluid
Potassium (Vitreous Fluid)	16.0	mmol/L	003 - Vitreous Fluid
Chloride (Vitreous Fluid)	117	mmol/L	003 - Vitreous Fluid
Urea Nitrogen (Vitreous Fluid)	7.70	mg/dL	003 - Vitreous Fluid
Ethanol	341	mg/dL	003 - Vitreous Fluid

8042 Blood Results

See Detailed Findings section for additional information

Testing Requested:

Test	Test Name
1919FL	Electrolytes and Glucose Panel (Vitreous), Fluid (Forensic)
8042B	Postmortem, Expanded w/Vitreous Alcohol Confirmation, Blood (Forensic)

Positive Findings & Testing Requested

Positive Findings:

Analyte	Result	Units	Matrix Source
Ethanol	268	mg/dL	001 - Heart Blood
Blood Alcohol Concentration (BAC)	0.268	g/100 mL	001 - Heart Blood
Caffeine	Presump Pos	mcg/mL	001 - Heart Blood
Naloxone	Presump Pos	ng/mL	001 - Heart Blood
Phenobarbital	3.5	mcg/mL	001 - Heart Blood
Nordiazepam	79	ng/mL	001 - Heart Blood
Amphetamine	11	ng/mL	001 - Heart Blood
Methamphetamine	65	ng/mL	001 - Heart Blood
Fentanyl	7.0	ng/mL	001 - Heart Blood
Norfentanyl	0.63	ng/mL	001 - Heart Blood
4-ANPP	0.97	ng/mL	001 - Heart Blood
Creatinine (Vitreous Fluid)	0.607	mg/dL	003 - Vitreous Fluid
Sodium (Vitreous Fluid)	141	mmol/L	003 - Vitreous Fluid
Potassium (Vitreous Fluid)	16.0	mmol/L	003 - Vitreous Fluid
Chloride (Vitreous Fluid)	117	mmol/L	003 - Vitreous Fluid
Urea Nitrogen (Vitreous Fluid)	7.70	mg/dL	003 - Vitreous Fluid
Ethanol	341	mg/dL	003 - Vitreous Fluid

See Detailed Findings section for additional information

Directed test
1919 FL Results

Delta-9 THC	0.97	ng/mL	001 - Peripheral Blood
Creatinine (Vitreous Fluid)	1.14	mg/dL	003 - Vitreous Fluid
Sodium (Vitreous Fluid)	141	mmol/L	003 - Vitreous Fluid
Potassium (Vitreous Fluid)	6.65	mmol/L	003 - Vitreous Fluid
Chloride (Vitreous Fluid)	112	mmol/L	003 - Vitreous Fluid
Glucose (Vitreous Fluid)	<10.0	mg/dL	003 - Vitreous Fluid
Urea Nitrogen (Vitreous Fluid)	37.9	mg/dL	003 - Vitreous Fluid

Testing Requested:

Test	Test Name
1919FL	Electrolytes and Glucose Panel (Vitreous), Fluid (Forensic)
8042B	Postmortem, Expanded w/Vitreous Alcohol Confirmation, Blood (Forensic)

Positive Findings & Testing Requested

Positive Findings:

Analyte	Result	Units	Matrix Source
Ethanol	268	mg/dL	001 - Heart Blood
Blood Alcohol Concentration (BAC)	0.268	g/100 mL	001 - Heart Blood
Caffeine	Presump Pos	mcg/mL	001 - Heart Blood
Naloxone	Presump Pos	ng/mL	001 - Heart Blood
Phenobarbital	3.5	mcg/mL	001 - Heart Blood
Nordiazepam	79	ng/mL	001 - Heart Blood
Amphetamine	11	ng/mL	001 - Heart Blood
Methamphetamine	65	ng/mL	001 - Heart Blood
Fentanyl	7.0	ng/mL	001 - Heart Blood
Norfentanyl	0.63	ng/mL	001 - Heart Blood
4-ANPP	0.97	ng/mL	001 - Heart Blood
Creatinine (Vitreous Fluid)	0.607	mg/dL	003 - Vitreous Fluid
Sodium (Vitreous Fluid)	141	mmol/L	003 - Vitreous Fluid
Potassium (Vitreous Fluid)	16.0	mmol/L	003 - Vitreous Fluid
Chloride (Vitreous Fluid)	117	mmol/L	003 - Vitreous Fluid
Urea Nitrogen (Vitreous Fluid)	7.70	mg/dL	003 - Vitreous Fluid
Ethanol	341	mg/dL	003 - Vitreous Fluid

See Detailed Findings section for additional information

Positive B Ethanol
Add Vit Ethanol

Testing Requested:

Test	Test Name
1919FL	Electrolytes and Glucose Panel (Vitreous), Fluid (Forensic)
8042B	Postmortem, Expanded w/Vitreous Alcohol Confirmation, Blood (Forensic)

Specimens Received

Specimens Received:

ID	Tube/Container	Volume/ Mass	Collection Date/Time	Matrix Source	Labeled As
001	Gray Stopper Glass Tube	9 mL	06/22/2023 10:44	Heart Blood	2023-1272 C
002	Gray Stopper Glass Tube	7.75 mL	06/22/2023 10:44	Heart Blood	2023-1272 D
003	Red Stopper Glass Tube	1 mL	06/21/2023 17:30	Vitreous Fluid	2023-1272 A
004	White Cap Plastic Container	40 mL	06/22/2023 10:44	Urine	2023-1272 B

When Does “ None Detected” appear in Positive Findings Box?

Positive Findings:

None Detected

See Detailed Findings section for additional information

Testing Requested:

Test	Test Name
8051B	Postmortem, Basic, Blood (Forensic)

Specimens Received:

ID	Tube/Container	Volume/ Mass	Collection Date/Time	Matrix Source	Labeled As
001	Gray Stopper Glass Tube	11 mL	06/28/2023 09:10	Femoral Blood	23-03282

All sample volumes/weights are approximations.

Specimens received on 07/06/2023.

“ None Detected” may disappear if supplemental testing is ordered

Positive Findings:

Analyte	Result	Units	Matrix Source
Atomoxetine	65	ng/mL	001 - Femoral Blood
Lamotrigine	40	mcg/mL	001 - Femoral Blood
Creatinine (Vitreous Fluid)	0.625	mg/dL	002 - Vitreous Fluid
Sodium (Vitreous Fluid)	152	mmol/L	002 - Vitreous Fluid
Potassium (Vitreous Fluid)	13.6	mmol/L	002 - Vitreous Fluid
Chloride (Vitreous Fluid)	130	mmol/L	002 - Vitreous Fluid
Urea Nitrogen (Vitreous Fluid)	14.9	mg/dL	002 - Vitreous Fluid

See Detailed Findings section for additional information

Testing Requested:

Test	Test Name
1002B	Carbon Monoxide Exposure Biouptake Screen, Blood
1919FL	Electrolytes and Glucose Panel (Vitreous), Fluid (Forensic)
8063B	Postmortem, Basic to Expanded Upgrade, Blood (Forensic)
8051B	Postmortem, Basic, Blood (Forensic)

Specimens Received:

ID	Tube/Container	Volume/ Mass	Collection Date/Time	Matrix Source	Labeled As
001	Gray Stopper Glass Tube	11 mL	06/28/2023 09:10	Femoral Blood	23-03282
002	White Cap Plastic Container	2 mL	06/28/2023 09:10	Vitreous Fluid	23-03282

Reporting Limits Can be Affected by Dilutions

Detailed Findings:

Analysis and Comments	Result	Units	Rpt. Limit	Specimen Source	Analysis By
Cotinine	Presump Pos	ng/mL	200	001 - IVC (Inferior Vena Cava) Blood	LC/TOF-MS
This test is an unconfirmed screen. Confirmation by a more definitive technique such as GC/MS is recommended.					
Benzoylecgonine	3300	ng/mL	50	001 - IVC (Inferior Vena Cava) Blood	LC-MS/MS
Cocaine	100	ng/mL	10	001 - IVC (Inferior Vena Cava) Blood	LC-MS/MS
Cocaethylene	19	ng/mL	10	001 - IVC (Inferior Vena Cava) Blood	LC-MS/MS
Delta-9 Carboxy THC	6.0	ng/mL	5.0	001 - IVC (Inferior Vena Cava) Blood	LC-MS/MS
Delta-9 THC	1.0	ng/mL	0.50	001 - IVC (Inferior Vena Cava) Blood	LC-MS/MS
Diphenhydramine	55	ng/mL	50	001 - IVC (Inferior Vena Cava) Blood	LC-MS/MS
Amphetamine	210	ng/mL	5.0	001 - IVC (Inferior Vena Cava) Blood	LC-MS/MS
Methamphetamine	3800	ng/mL	50	001 - IVC (Inferior Vena Cava) Blood	LC-MS/MS

Reference Comments

- Reference comments are the same for every drug in a given matrix regardless of the concentrations reported
- Reference comments include, where possible:
  - Description of the drug (mechanism of action, uses, effects)
  - Clinically therapeutic ranges
  - Metabolism (Half-life, metabolites) and Elimination
  - Fatal concentrations

Reference Comments

Reference Comments:

1. Acetaminophen (Tylenol®) - Subclavian Blood:

Acetaminophen is an over the counter analgesic with antipyretic properties; however, it has no anti-inflammatory actions. It may be found both alone and in combinations with other substances such as codeine, hydrocodone, tramadol, butalbital, and propoxyphene. It appears to be a relatively safe substance when used in analgesic amounts; however, it frequently produces acute hepatic necrosis after overdose.

The usual therapeutic range (following one gram) of acetaminophen is 17-24 mcg/mL of plasma; however, there are considerable individual differences in plasma concentrations. Symptoms of acetaminophen overdose usually are not seen immediately but are reflected in hepatic damage after 1/2 to 6 days with concentrations of 150 mcg/mL at 4 hours or greater than 37.5 mcg/mL at 12 hours after ingestion. A reported range of blood levels in individuals succumbing to acetaminophen overdose ranged from 160-390 mcg/mL. The blood to plasma ratio of acetaminophen is approximately 1.1

2. Cyclobenzaprine (Flexeril®) - Subclavian Blood:

Cyclobenzaprine is a tricyclic compound that acts on the central nervous system to relax skeletal muscle. Its mechanism of action is not well understood; however, it does potentiate norepinephrine, has some anticholinergic effects, and has central nervous system depressant activity. It is generally used as an adjunct to rest and physical therapy in the treatment of painful musculoskeletal conditions.

Commonly, plasma cyclobenzaprine concentrations of 15-30 ng/mL are required for skeletal muscle relaxant effects.

Cyclobenzaprine overdose produces drowsiness, tachycardia, nausea, paresthesia, hypotension, convulsions, cardiac arrhythmias and coma. In two fatal overdose cases, blood concentrations averaged 500 ng/mL, other central nervous system depressants were also contributory in these cases.

Why do NMS reports NOT include this information for postmortem cases?

M. Schulz, A. Schmoldt, H. Andresen-Streichert, S. Iwersen-Bergmann. Revisited: Therapeutic and toxic blood concentrations of more than 1,100 drugs and other xenobiotics. Critical Care 2020

Substance	Blood-plasma concentration (mg/L)			t½ (h)	References
	therapeutic ("normal")	toxic (from)	comatose-fatal (from)		
Captopril	0.05-0.5 (-1)[620]	5-6	60	1-2 (-6)	[42], [47], [84], [159]
Carazolol[23]	-0.015			9	[7]
Carbachol	appr. 0.01 ?		3.6[8, 287]		[3], [160]
Carbamazepine[12]	2-8 (4-12)	10	20	12-60 (7-35)[140]	[12], [56], [161-166], [1231]
Carbaryl		5	6-27		[47], [167]
Carbenoxolone	appr. 5-30			8-20	[66]
Carbidopa	0.02-0.2[316]	0.4[311, 316]		2	[4]
Carbimazole	0.5-3.4[95]			3-6[95]	[8], [13]
Carbinoxamine	appr. 0.02-0.04			appr. 10-15	[168]
Carbocromene (Carbochromene)	0.8-2.4 (-3)			0.2-1.5	[8]
Carbon monoxide	-[200]	17-30%	50-60%		[10], [47], [58], [975-978]
Carbon tetrachloride	-0.07	0.12[8]; 7.1[8, 269]; 11[8]; 10-50	100-200	appr. 24; 42.6[8]	[58], [169-173]
Carboplatin	peak 10-25			2.5-6[106]	[47]
Carbromal(um)[13]	2-10	15-20	40	7-15	[13], [58]
Carfentanil			0.12[8]; 0.145[8]; 0.221[8]; 1.3[8] ng/mL		[979, 980], [1071]

Postmortem Preanalytical Variables - Sample Selection and Integrity Issues

Where is blood from?

Is the “blood” really “blood”?

Autopsy vs. “blind stick”

Is it cardiac blood or “chest” blood?

Or is it pleural fluid, bloody chest fluid?

Is it cavity blood or decomposition fluid?

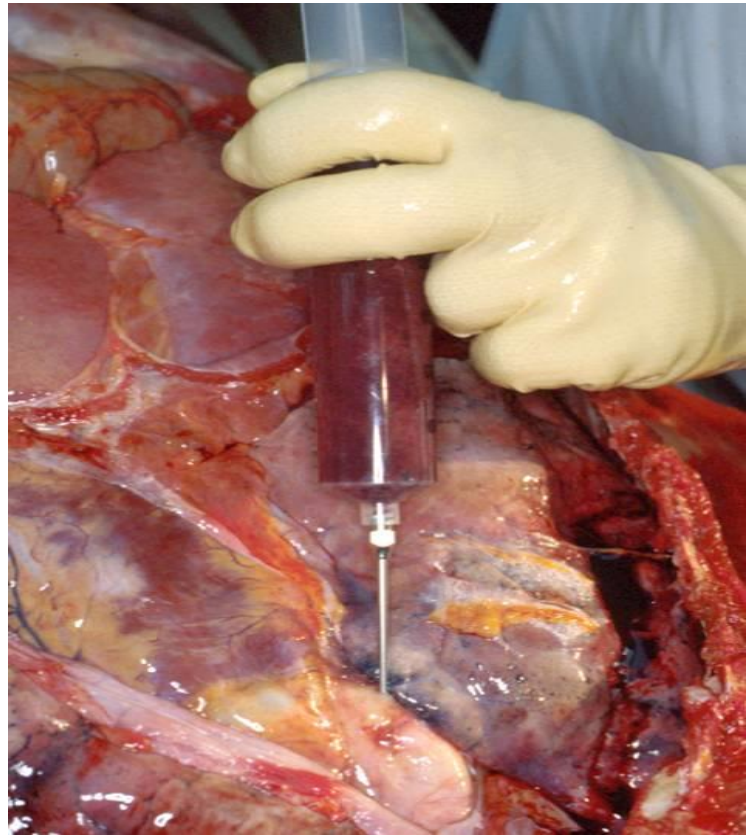
Is femoral blood truly femoral?

Is the blood / tissue contaminated?

Tissue trauma spreads drug to blood

Diffusion or aspiration of gastric fluid?

Ruptured stomach/diaphragm?



Some Examples of PM Interpretation Issues

PM alcohol formation – trauma or decomposition; VH best

Medical artifacts – end of life protocols, drug pumps

Delayed deaths – e.g., APAP, ethylene glycol

Drug instability – e.g., cocaine, 6-AM, olanzapine (preservatives?)

Loss of volatiles – e.g., nitrous oxide, butane

Variable metabolism – genetic polymorphisms, disease

Drug interactions – pharmacokinetic or pharmacodynamic

Tolerance – e.g., opiates / opioids

Postmortem redistribution – release of drug

“Postmortem Redistribution”

Redistribution and diffusion after death

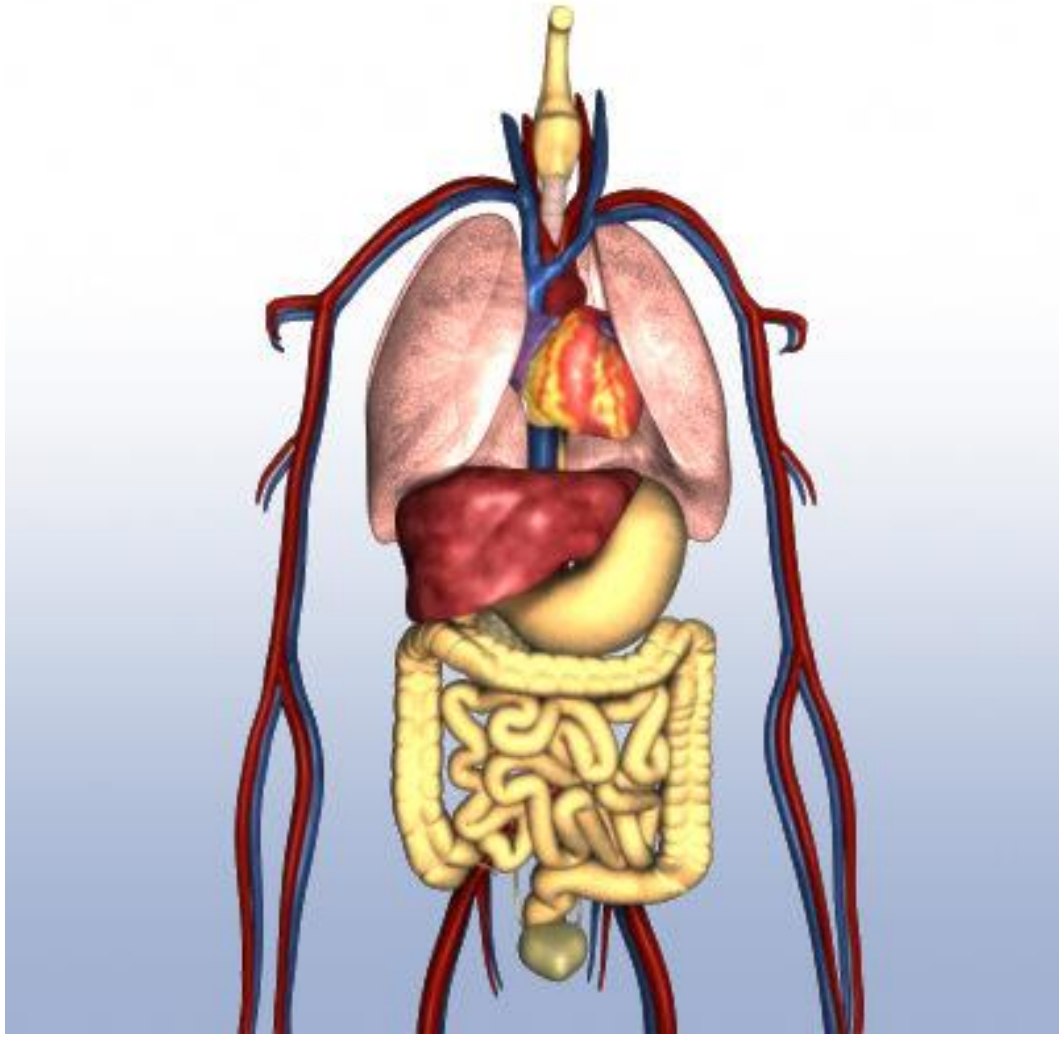
Time and concentration dependent drugs with higher volumes of distribution (V_d)

e.g. basic drugs begin to diffuse from higher to lower areas of concentration

Increases of 2-10-fold or greater in PM blood can occur

Cardiac > subclavian > femoral > popliteal > antemortem

Rapid deaths (lack of distribution)



Why is PMR a Problem?

IF a body's total blood volume is ~4 L and..

IF V_d = 10 L/kg for a particular drug …

Then total apparent volume in a 70 kg person is 700 L

And if a 70 mg drug dose is given….

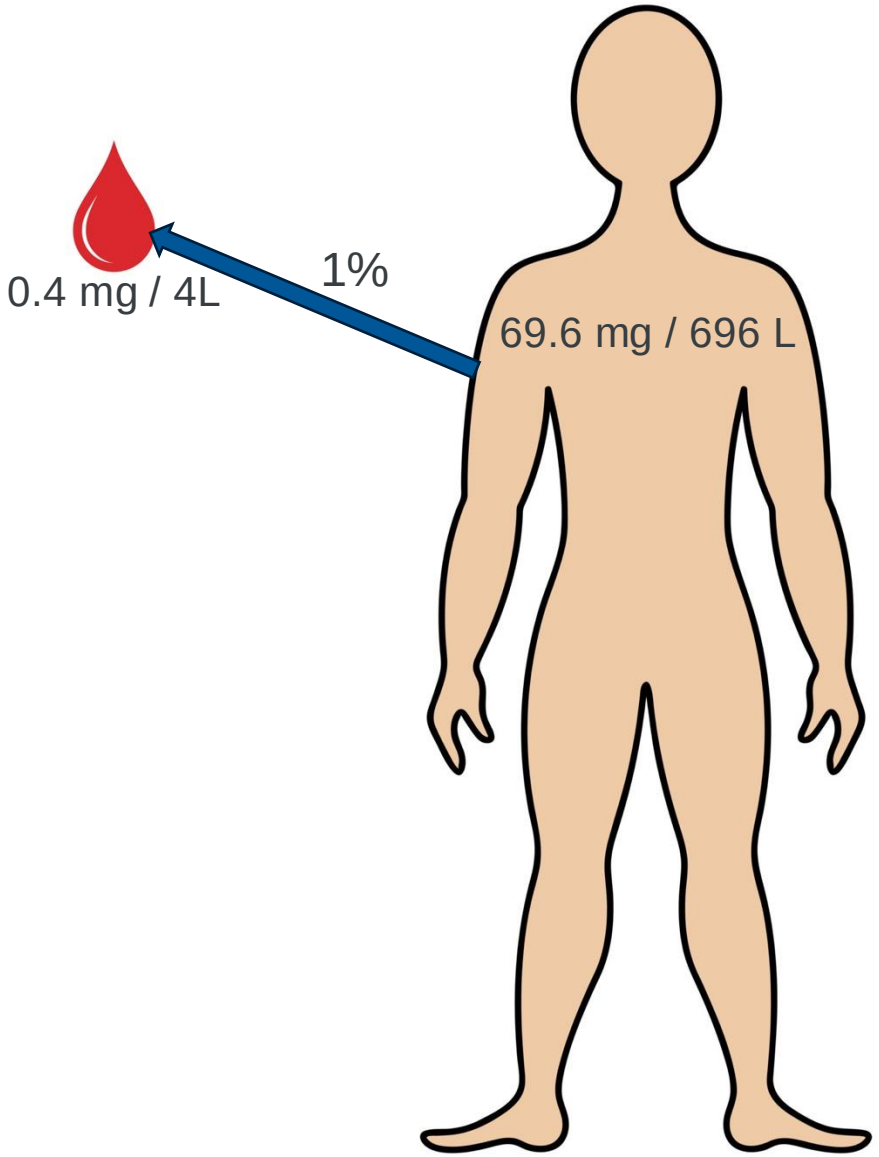
Then 70 mg / 700 L ~ *0.1 mg/L concentration*

Blood = 0.4 mg / 4 L : Body = 69.6 mg / 696 L

IF even a 1% change or shift occurs from the body to blood then drug concentrations may more than double!! Why?

69.6 mg x 1% = 0.7 mg

0.7 mg / 4L = 0.175 mg/L + 0.1 mg/L = 0.275 mg/L



From CAT 2003 Quarterly Meeting; Dr. Graham Jones; Presentation on Interpretation of PM Findings

How are NMS Postmortem Reference Comments best used?

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Article

OXFORD

A model of evaluative opinion to encourage greater transparency and justification of interpretation in postmortem forensic toxicology

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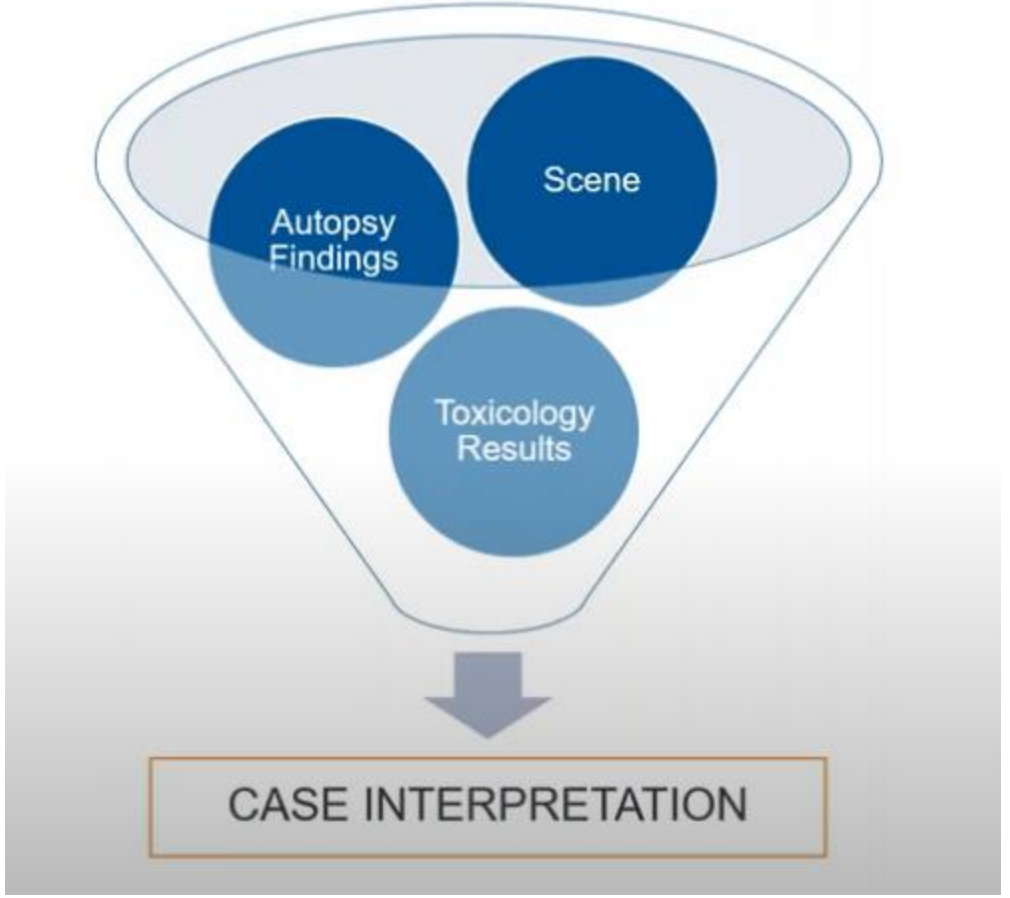
NMS LABS

How are NMS Postmortem Reference Comments best used?

- NMS reference comments, in conjunction a complete death investigation, can be used to assist in determining the level of toxicological significance for reported analytes
- NMS toxicologists are available for additional consultation with the medical examiners / coroners
- Additional learning opportunities
  - NMS Webinar by Dr. Laura Labay
  - Tolerant or Intolerant: Learning from Study Drug Concentrations in the Living and the Dead



Analysis Summary and Reporting Limits

Analysis Summary and Reporting Limits:

All of the following tests were performed for this case. For each test, the compounds listed were included in the scope. The Reporting Limit listed for each compound represents the lowest concentration of the compound that will be reported as being positive. If the compound is listed as None Detected, it is not present above the Reporting Limit. Please refer to the Positive Findings section of the report for those compounds that were identified as being present.

- List of tests performed, and matrix tested
- For each test, the compounds in the scope of testing are listed
- The reporting limit – the lowest concentration that will be reported – is also included
  - If dilutions are performed, the reporting limit will increase

Analysis Summary and Reporting Limits

Directed Analysis

Test 1919FL - Electrolytes and Glucose Panel (Vitreous), Fluid (Forensic) - Vitreous Fluid

-Analysis by Chemistry Analyzer for:

Analyte	Rpt. Limit	Analyte	Rpt. Limit
Chloride (Vitreous Fluid)	50.0 mmol/L	Potassium (Vitreous Fluid)	1.00 mmol/L
Creatinine (Vitreous Fluid)	0.500 mg/dL	Sodium (Vitreous Fluid)	50.0 mmol/L
Glucose (Vitreous Fluid)	10.0 mg/dL	Urea Nitrogen (Vitreous Fluid)	2.00 mg/dL

Test 50012B - Benzodiazepines Confirmation, Blood - Iliac Blood

-Analysis by High Performance Liquid Chromatography/ Tandem Mass Spectrometry (LC-MS/MS) for:

Analyte	Rpt. Limit	Analyte	Rpt. Limit
7-Amino Clonazepam	5.0 ng/mL	Flurazepam	2.0 ng/mL
Alpha-Hydroxyalprazolam	5.0 ng/mL	Hydroxyethylflurazepam	5.0 ng/mL
Alprazolam	5.0 ng/mL	Hydroxytriazolam	5.0 ng/mL
Chlordiazepoxide	20 ng/mL	Lorazepam	5.0 ng/mL
Clobazam	20 ng/mL	Midazolam	5.0 ng/mL
Clonazepam	2.0 ng/mL	Nordiazepam	20 ng/mL
Desalkylflurazepam	5.0 ng/mL	Oxazepam	20 ng/mL
Diazepam	20 ng/mL	Temazepam	20 ng/mL
Estazolam	5.0 ng/mL	Triazolam	2.0 ng/mL

Analysis Summary and Reporting Limits

Test 1919FL - Electrolytes and Glucose Panel (Vitreous), Fluid (Forensic) - Vitreous Fluid

-Analysis by Chemistry Analyzer for:

Analyte	Rpt. Limit	Analyte	Rpt. Limit
Chloride (Vitreous Fluid)	50.0 mmol/L	Potassium (Vitreous Fluid)	1.00 mmol/L
Creatinine (Vitreous Fluid)	0.500 mg/dL	Sodium (Vitreous Fluid)	50.0 mmol/L
Glucose (Vitreous Fluid)	10.0 mg/dL	Urea Nitrogen (Vitreous Fluid)	2.00 mg/dL

Reflexed Analysis

Test 50012B - Benzodiazepines Confirmation, Blood - Iliac Blood

-Analysis by High Performance Liquid Chromatography/ Tandem Mass Spectrometry (LC-MS/MS) for:

Analyte	Rpt. Limit	Analyte	Rpt. Limit
7-Amino Clonazepam	5.0 ng/mL	Flurazepam	2.0 ng/mL
Alpha-Hydroxyalprazolam	5.0 ng/mL	Hydroxyethylflurazepam	5.0 ng/mL
Alprazolam	5.0 ng/mL	Hydroxytriazolam	5.0 ng/mL
Chlordiazepoxide	20 ng/mL	Lorazepam	5.0 ng/mL
Clobazam	20 ng/mL	Midazolam	5.0 ng/mL
Clonazepam	2.0 ng/mL	Nordiazepam	20 ng/mL
Desalkylflurazepam	5.0 ng/mL	Oxazepam	20 ng/mL
Diazepam	20 ng/mL	Temazepam	20 ng/mL
Estazolam	5.0 ng/mL	Triazolam	2.0 ng/mL

Examples of Other Types of Reports – 8084B

Positive Findings:

Analyte	Result	Units	Matrix Source
Caffeine	Presump Pos	mcg/mL	001 - Femoral Blood
Cotinine	Presump Pos	ng/mL	001 - Femoral Blood
Naloxone	Presump Pos	ng/mL	001 - Femoral Blood
Benzoylecgonine	770	ng/mL	001 - Femoral Blood
Morphine - Free	8.7	ng/mL	001 - Femoral Blood
Tadalafil	79	ng/mL	001 - Femoral Blood
Amphetamine	9.8	ng/mL	001 - Femoral Blood
Methamphetamine	90	ng/mL	001 - Femoral Blood
Fentanyl	10	ng/mL	001 - Femoral Blood
Norfentanyl	2.1	ng/mL	001 - Femoral Blood
Acetyl Fentanyl	0.21	ng/mL	001 - Femoral Blood
4-ANPP	2.3	ng/mL	001 - Femoral Blood
6-Monoacetylmorphine - Free	16	ng/mL	004 - Urine

+ Morphine

See Detailed Findings section for additional information

Testing Requested:

Test	Test Name
8084B	Postmortem, Expanded w/Vitreous Alcohol and 6-MAM Confirmation, Blood (Forensic)

Examples of Other Types of Reports – 8084B

Positive Findings:

Analyte	Result	Units	Matrix Source
Caffeine	Presump Pos	mcg/mL	001 - Femoral Blood
Cotinine	Presump Pos	ng/mL	001 - Femoral Blood
Naloxone	Presump Pos	ng/mL	001 - Femoral Blood
Benzoylecgonine	770	ng/mL	001 - Femoral Blood
Morphine - Free	8.7	ng/mL	001 - Femoral Blood
Tadalafil	79	ng/mL	001 - Femoral Blood
Amphetamine	9.8	ng/mL	001 - Femoral Blood
Methamphetamine	90	ng/mL	001 - Femoral Blood
Fentanyl	10	ng/mL	001 - Femoral Blood
Norfentanyl	2.1	ng/mL	001 - Femoral Blood
Acetyl Fentanyl	0.21	ng/mL	001 - Femoral Blood
4-ANPP	2.3	ng/mL	001 - Femoral Blood
6-Monoacetylmorphine - Free	16	ng/mL	004 - Urine

+ Morphine
- 6-MAM

Reflex
6-MAM

See Detailed Findings section for additional information

Testing Requested:

Test	Test Name
8084B	Postmortem, Expanded w/Vitreous Alcohol and 6-MAM Confirmation, Blood (Forensic)

Examples of Other Types of Reports – 8084B (Negative 6-AM)

Positive Findings:

Analyte	Result	Units	Matrix Source
Caffeine	Presump Pos	mcg/mL	001 - Heart Blood
10-Hydroxycarbazepine	21	mcg/mL	001 - Heart Blood
Nortriptyline	1200	ng/mL	001 - Heart Blood
Trazodone	0.21	mcg/mL	001 - Heart Blood
Morphine - Free	160	ng/mL	001 - Heart Blood
Amphetamine	23	ng/mL	001 - Heart Blood
Methamphetamine	240	ng/mL	001 - Heart Blood

See Detailed Findings section for additional information

Testing Requested:

Test	Test Name
8084B	Postmortem, Expanded w/Vitreous Alcohol and 6-MAM Confirmation, Blood (Forensic)

Examples of Other Types of Reports – 8084B (Negative 6-AM)

Test 52316B - Opiates - Free (Unconjugated) Confirmation, Blood (Forensic) - Heart Blood

-Analysis by High Performance Liquid Chromatography/ Tandem Mass Spectrometry (LC-MS/MS) for:

Analyte	Rpt. Limit	Analyte	Rpt. Limit
6-Monoacetylmorphine - Free	1.0 ng/mL	Hydromorphone - Free	1.0 ng/mL
Codeine - Free	5.0 ng/mL	Morphine - Free	5.0 ng/mL
Dihydrocodeine / Hydrocodol - Free	5.0 ng/mL	Oxycodone - Free	5.0 ng/mL
Hydrocodone - Free	5.0 ng/mL	Oxymorphone - Free	1.0 ng/mL

Test 52316U - Heroin Metabolite - Free (Unconjugated) Confirmation, Urine (Forensic) - Urine

-Analysis by High Performance Liquid Chromatography/ Tandem Mass Spectrometry (LC-MS/MS) for:

Analyte	Rpt. Limit	Analyte	Rpt. Limit
6-Monoacetylmorphine - Free	5.0 ng/mL		

Examples of Other Types of Reports – Canceled Test

Positive Findings:

Analyte	Result	Units	Matrix Source
Caffeine	Presump Pos	mcg/mL	001 - Femoral Blood
Clobazam	1000	ng/mL	001 - Femoral Blood
Clonazepam	4.2	ng/mL	001 - Femoral Blood
7-Amino Clonazepam	33	ng/mL	001 - Femoral Blood
Alprazolam	6.1	ng/mL	001 - Femoral Blood
Paroxetine	260	ng/mL	001 - Femoral Blood
Buprenorphine - Free	0.84	ng/mL	001 - Femoral Blood
Norbuprenorphine - Free	1.9	ng/mL	001 - Femoral Blood
Dextrorphan / Levorphanol	7.7	ng/mL	001 - Femoral Blood
Dextro / Levo Methorphan	93	ng/mL	001 - Femoral Blood

See Detailed Findings section for additional information

Testing Requested:

Test	Test Name
8062B	Postmortem, Expanded w/o Alcohol, Blood (Forensic)

Tests Not Performed:

Part or all of the requested testing was unable to be performed. Refer to the **Analysis Summary and Reporting Limits** section for details.

Examples of Other Types of Reports – Canceled Test

Analysis Summary and Reporting Limits:

The following test(s) were performed for this case; the scope of each test includes the analyte(s) listed along with the associated reporting limit(s). The reporting limit is the lowest concentration of the analyte that will be reported as positive. Only results that meet reporting criteria at or above the reporting limit appear in the Positive Findings section of the report.

Test 52198B - Cannabinoids Confirmation, Blood - Femoral Blood

-Analysis by High Performance Liquid Chromatography/ Tandem Mass Spectrometry (LC-MS/MS) for:

Analyte	Rpt. Limit	Analyte	Rpt. Limit
11-Hydroxy Delta-9 THC	N/A	Delta-9 THC	N/A
Delta-9 Carboxy THC	N/A		

Testing Not Performed: Test was canceled due to [Interfering Substance].

Summary

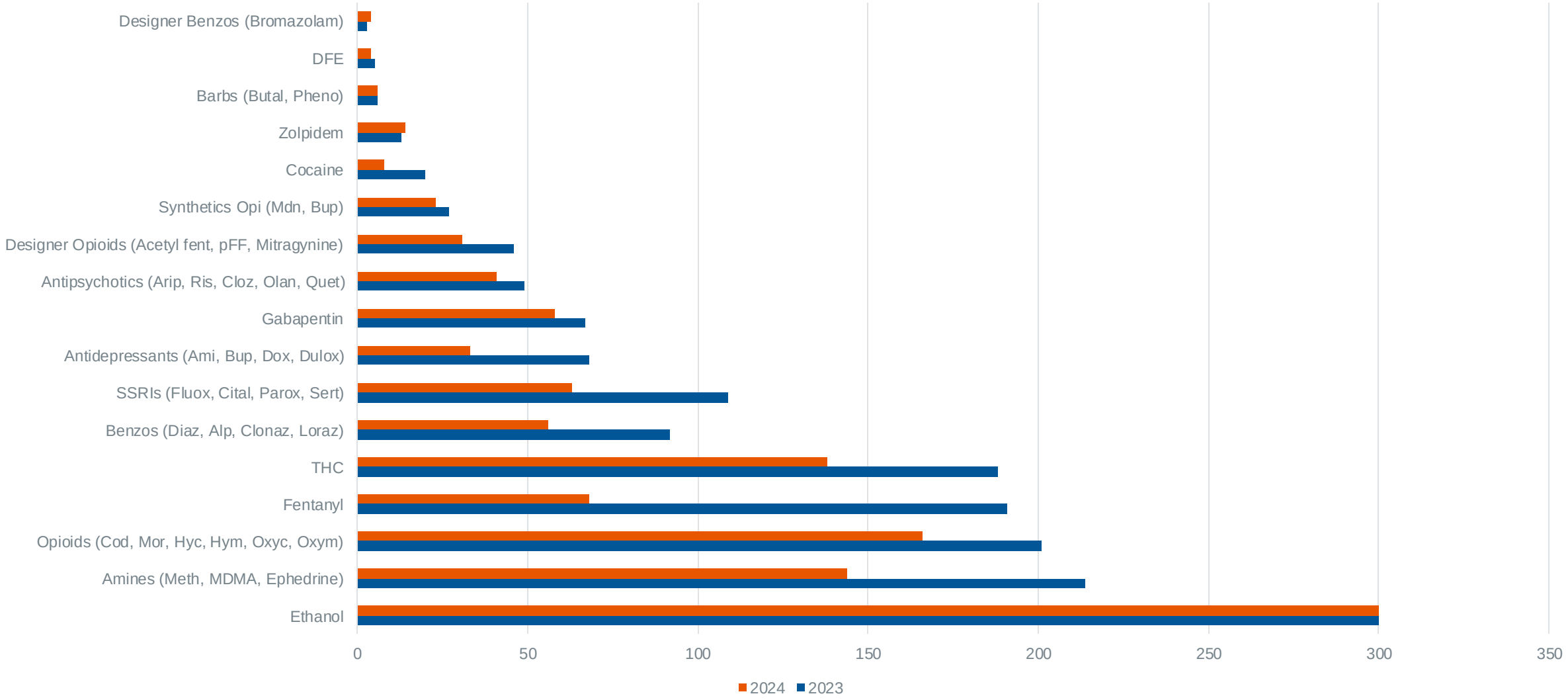
The NMS Forensic Toxicology report provides the client with a comprehensive document that contains many elements needed to a interpret the roles drugs may have had in a death investigation.

However, it is just one component of a three-legged stool that is part of a complete forensic investigation.

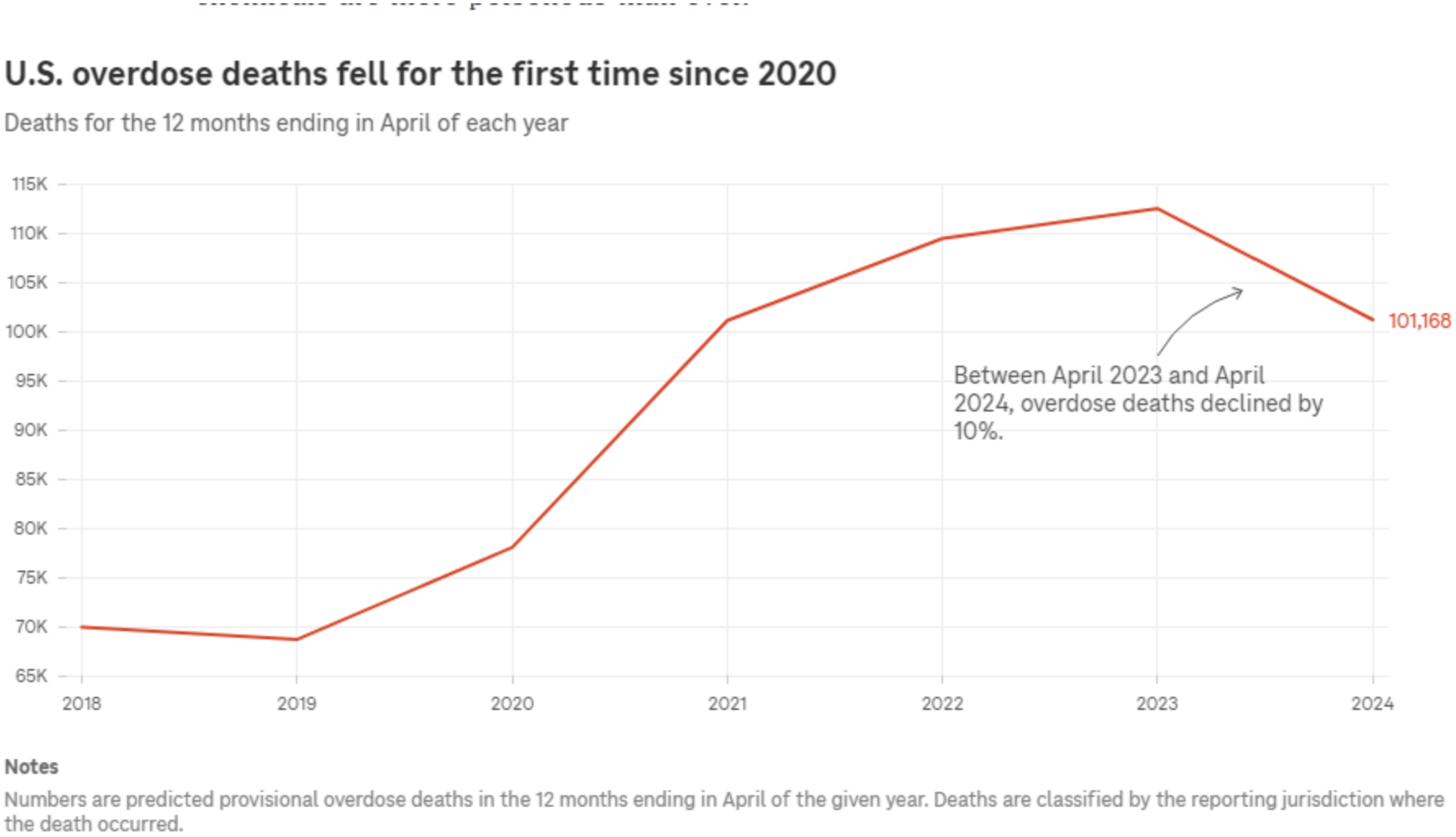
NMS LABS

Questions?

Idaho drug results: 2023-2024



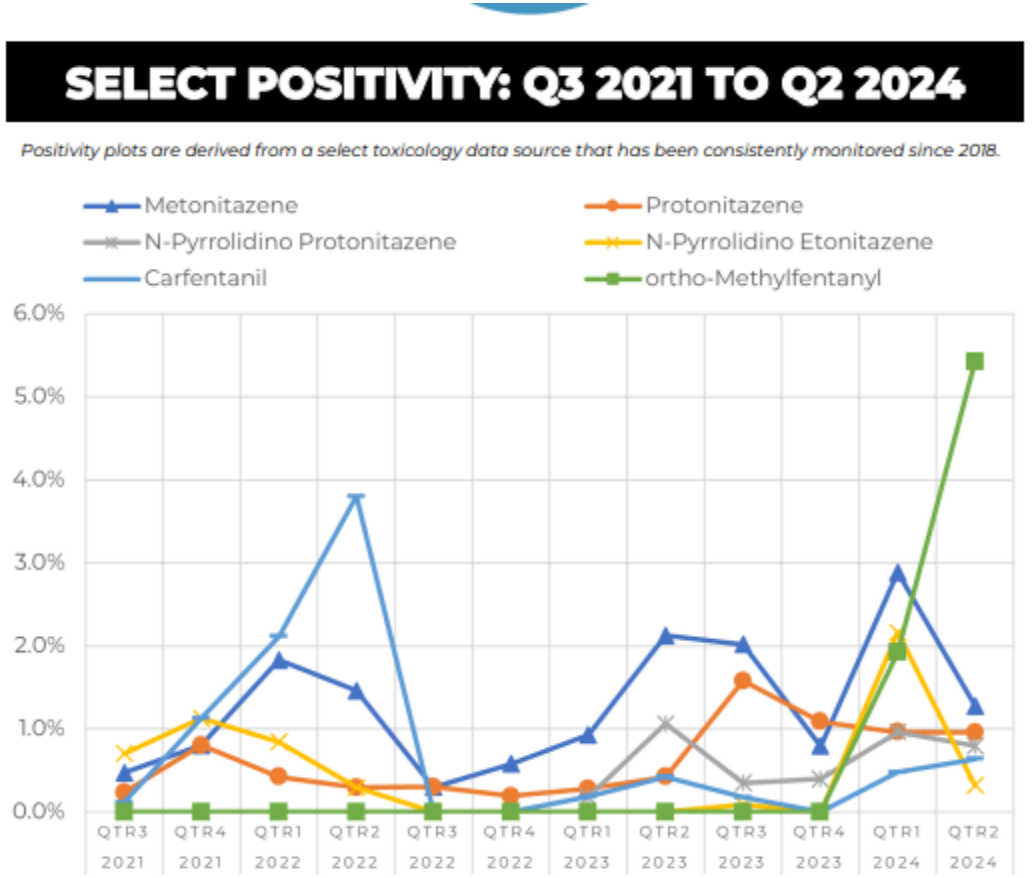
Decrease in drug overdoses



https://www.npr.org/2024/09/18/nx-s1-5107417/overdose-fatal-fentanyl-death-opioid

NPS on the national level

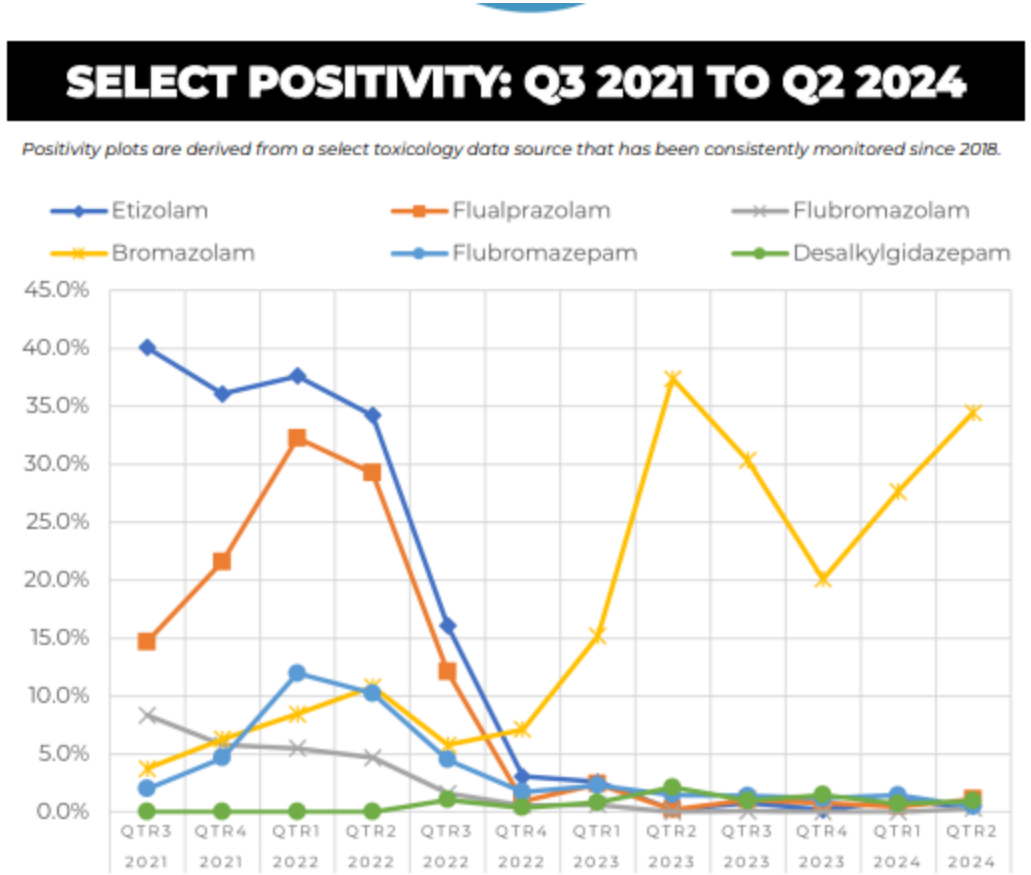
Opioids



https://www.cfsre.org/images/trendreports/2024_Q2_CFSRE_NPS_Discovery_Trend_Reports.pdf

NPS on the national level

Benzodiazepines



https://www.cfsre.org/images/trendreports/2024_Q2_CFSRE_NPS_Discovery_Trend_Reports.pd

Sodium Nitrite

Inorganic Nitrates (NO3-) and Nitrites (NO2-)

Commonly exist as salts (i.e., solidum nitrate)

- Water soluble
- Found
    - Endogenously
    - In water
    - In foods
    - As a food preservative
    - As fertilizers

Suicide by nitrites

Increased popularity since 2018

- **Suicide forums/ online availability**

Causes methemoglobinemia

Characterized by:

- **Chocolate brown blood and/or organs**
- **Cyanotic (gray) discoloration of bodies**
- **Pulmonary or cerebral edema**

Other drug findings: Metoclopramide

- **Recommended in online forums or sold in suicide kits to act as an anti-emetic and prokinetic (accelerate gastric emptying)**

Test Code: 3174B or 3174SP

Ketoacidosis

Ketoacidosis is a potentially life-threatening medical condition where the pH of the blood is reduced due to the build up of β-oxidative ketone bodies

- Commonly the result of complications with:

  Diabetes (Diabetic Ketoacidosis, DKA)

  Alcoholism (Alcoholic Ketoacidosis, AKA)

  Diet (Ketogenic Diet, malnutrition/starvation)

- Ketone bodies are produced when the body cannot efficiently utilize glucose as an energy source

- Symptoms may include nausea, vomiting, abdominal pains, loss of appetite, lethargy, weakness and unconsciousness

Distinguishing between DKA and AKA

	Acetone/IPA	Glucose Vitreous	BHB
DKA	Present	Elevated*	Elevated
AKA	Present	Low/Normal	Elevated
Solvent	Present/Elevated	Low/Normal	Normal

Test Code: 0420B

How can a toxicologist help you

Interpretation of results

Review data for out of scope findings or compounds present below reporting limit

Advise further testing/explain what was in scope

Coordinate CFSRE consultation

Questions?

Brianna.Peterson@nmslabs.com

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