HEALTH & ENVIRONMENTAL TESTING LABORATORY
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QUALITATIVE BLOOD DRUG EXTRACTION AND ANALYSIS

Contents

Maine HETL- Forensic Toxicology

QUALITATIVE BLOOD DRUG EXTRACTION AND ANALYSIS

Principle and Scope:

This method describes the procedures for the qualitative detection of drugs in whole blood. A recovery compound is added to the whole blood samples, the compounds of interest and recovery compound are then efficiently partitioned from the blood sample via a liquid/liquid extraction with organic solvent and separated on an HPLC C-18 column. The samples are then analyzed using a tandem mass spectrometer utilizing select ion monitoring (SIM) with the poor responding compounds having an additional simultaneous detection using multiple reaction monitoring (MRM).

It is noted that this method produces semi-quantitative results that are derived from a one-point calibration forced through zero curve, to achieve approximate quantitative results that are only to be used by the analyst as a guide for approximating values. The approximate quantitative values shall never be reported out on any certificates of analysis.

This method shall be run on all drug blood samples prior to confirmation analysis with any exceptions being noted and approved prior to the generation of a result report. This qualitative method shall be primarily used as a screening tool prior to quantitative analysis. For the compounds of interest that are only detected in blood qualitatively this method shall also be utilized for the confirmation of those compounds.

Equipment and Supplies:

Volumetric Flasks various sizes

Volumetric cylinders various sizes

Disposable Glass vials 5-15 mL, silianized/non-silanized

Teflon lined caps

Autosampler vials with silianized/non silianized inserts

Autosampler caps

Vortex mixer

Disposable glass transfer pipettes

Pipettes- various

Evaporator

Specimen Requirements:

- Only whole blood samples shall be analyzed using this method.
- Whole blood samples are collected in tubes provided by HETL or by a qualified medical professional and upon receipt, stored under refrigeration at HETL (<10°C).
- If an elevated concentration of a compound of interest present in the Qualitative B panel, in a subject sample, creates a situation in which all acceptability criteria cannot be met remedial action such as a dilution may be taken.
- If a case sample is found to have insufficient quantity to extract and analyze as a neat sample, then a report shall be issued stating "Sample quantity insufficient for blood drug testing."
- If a blood sample is received by the laboratory with volume not sufficient to perform standard OUI blood drug panel and only a portion of panel can be screened and confirmed for then the following comment shall be included in the COA: "Unable to perform standard OUI blood drug panel due to low sample volume." In addition, prior to starting testing the analyst shall reach out to the investigating officer notifying them that the sample is QNS to perform the standard OUI blood drug panel and discuss course of testing.
- Blood samples that were collected using non-DHHS certified blood collection tubes shall have the following comment included in the COA: "(Color) topped tube used for analysis."

Reagents and Reference Materials:

- Hexane
- Chloroform
- Ethyl acetate
- Methanol - High purity LC-MS quality
- Water - High purity LC-MS quality
- Formic Acid
- Water with 0.1% Formic Acid- High purity LC-MS quality, Fisher brand or equivalent
- Ammonium formate
- 1N HCl
- **Blank Blood Matrix**-approved vendor supplies and checked for quality control prior to purchase. Store at <10°C.

- **Stock Standard Solutions** – Individual solutions of target compounds and internal standards are purchased from traceable, approved vendors such as Cerilliant or Lipomed. All standards shall be stored at conditions recommended by the manufacturer.

Safety Precautions:

The solvents used are considered toxic. Repeated or prolonged exposure can produce targeted organ damage. Proper PPE shall be used when handling solvents.

Blood from unknown case samples shall be handled following Universal Precaution guidelines. Face shield in addition to PPE shall be utilized while pipetting blood.

Reagent Preparation:

All reagent preparations are to be recorded in the LCMS Reagent Preparation Log.

- **QUAL A & B Mobile Phase A**: Water with 0.1% Formic Acid and 5mM Ammonium Formate. Prepare by adding 0.315g Ammonium Formate to 1L of water with 0.1% Formic Acid. This reagent is good for one month from the date of creation or until the earliest expiration date of any components used in the making.

- **QUAL C Mobile Phase A**: Water with 0.1% Formic Acid. This reagent is good for 12 months from the date of opening. This can be purchased as a prepared reagent or prepared in the lab (1 mL formic acid QS to 1 L with LC-MS grade water, good for 1 year from prep date or until the earliest expiration date of any components used in the making.).

- **Mobile Phase B**: Methanol. This reagent is good for 12 months from the date of opening or until the earliest expiration date of any components used in the making.

- **80:20 Hexane: Ethyl Acetate**- To a graduated cylinder or 100 mL volumetric flask, add 80 mL Hexane and QS to 100 mL with ethyl acetate. Different volumes may be prepared as long as proportions are kept the same. This reagent is good for one month or until the earliest expiration date of any components used in the making.

- **50:50 LCMS grade Methanol: LCMS grade Water-**To a graduated cylinder or a 100mL volumetric flask add 50mL of LCMS grade Methanol and QS to 100mL with LCMS grade Water. Different volumes may be prepared as long as the proportions are kept the same. This reagent is good for one month or until the earliest expiration date of any components used in the making.

- **80:20 LCMS grade Water with 0.1% Formic Acid and 5mM Ammonium Formate: Methanol -**To a graduated cylinder or a 100mL volumetric flask add 20mL of LCMS grade Methanol and QS to 100mL with LCMS grade Water with 0.1% Formic Acid and 5mM Ammonium Formate. Different volumes may be prepared as long as the proportions are kept the same. This reagent is good for one month or until the earliest expiration date of any components used in the making.

Qualitative Drug Stock Preparation:
All Screen working stock preparations shall be recorded in the LCMS Reagent Preparation Log.

- **QUAL Mix A Stock:** Add a portion of methanol to a 10 mL volumetric flask add the following stocks or equivalents to the volumetric flask to obtain a final concentration as illustrated in Table 1: Screen Mix A Stock. QS to 10mL with LCMS grade Methanol. This stock is good for 12 months or until the earliest expiration date of any components used in the making.

Table 1: QUAL Mix A Working Stock

Analyte	Concentration	Volume used	Final Concentration
Narcotics Parent Stock	1/10 ug/mL	500uL	50/500 ng/mL
Pain Management Mix	10/100 ul/mL	50uL	50/500 ng/mL
EDDP	100 ug/mL	50uL	500 ng/mL
Benzodiazepine Working Parent Stock	4 ug/mL	500uL	200 ng/mL
Stimulants Working Parent Stock	20 ug/mL	200uL	400 ng/mL
Methanol LCMS Grade		QS to 10 mL	

- **QUAL Mix B Parent 1 & 2 (1000 ng/mL):** To each respective 10mL volumetric flask add a portion of methanol then add stocks or equivalents to the volumetric flask to obtain a final concentration as illustrated in Table 2: Screen Mix B Parent Stocks. QS to 10mL with LCMS grade Methanol. This working stock is good for 12 months or until the earliest expiration date of any components used in the making.

Table 2: QUAL Mix B Parents

Analyte	Concentration	Volume used
QUAL Mix B Parent #1		
Lamotrigine	1 mg/mL	10 uL
Zopiclone	1 mg/mL	10 uL

Carisoprodol	1 mg/mL	10 uL
Propoxyphene	1 mg/mL	10 uL
Meperidine	1 mg/mL	10 uL
Dextromethorphan	1 mg/mL	10 uL
LSD	1 mg/mL	10 uL
Norcodeine	1 mg/mL	10 uL
Diphenhydramine	1 mg/mL	10 uL
Clonidine	1 mg/mL	10 uL
Olanzapine	1 mg/mL	10 uL
Risperidone	1 mg/mL	10 uL
Triazolam	1 mg/mL	10 uL
Chlordiazepoxide	1 mg/mL	10 uL
Buprenorphine	1 mg/mL	10 uL
Norbuprenorphine	100 ug/mL	100 uL
Citalopram	100 ug/mL	100 uL
Methanol LCMS Grade		QS to 10 mL
Analyte	**Concentration**	**Volume used**
QUAL Mix B Parent #2		
Sertraline	1 mg/mL	10 uL
Venlafaxine	1 mg/mL	10 uL
Fluoxetine	1 mg/mL	10 uL
Nortriptyline	1 mg/mL	10 uL
Mirtazapine	1 mg/mL	10 uL
Amitriptyline	1 mg/mL	10 uL
Carbamazepine	1 mg/mL	10 uL
Cyclobenzaprine	1 mg/mL	10 uL
Desipramine	1 mg/mL	10 uL
Doxepin	1 mg/mL	10 uL
Imipramine	1 mg/mL	10 uL
Butalbital	1 mg/mL	10 uL
Phenobarbital	1 mg/mL	10 uL
Secobarbital	1 mg/mL	10 uL
Methanol LCMS Grade		QS to 10 mL

- **QUAL Mix B Stock (100 ng/mL):** Add a portion of methanol to a 10 mL volumetric flask then add 1mL of each Screen Mix B Parent to the volumetric flask. QS to 10mL with LCMS grade Methanol. This working stock is good for 12 months or until the earliest expiration date of any components used in the making.

- **QUAL Mix C Stock (100 ng/mL):** Add a portion of methanol to a 10 mL volumetric flask then add stocks or equivalents to the volumetric flask to obtain a final concentration as illustrated in Table 3: Screen Mix C Working Stock. QS to 10mL with LCMS grade Methanol. This working stock is good for 12 months or until the earliest expiration date of any components used in the making.

Table 3: Screen Mix C Working Stock		
Analyte	**Concentration**	**Volume used**
Δ9-THC	1000 ug/mL	10 uL
OH-Δ9-THC	100 ug/mL	100 uL
COOH-Δ9-THC	100 ug/mL	500 uL
Methanol LCMS Grade		CS to 10 mL

- **QUAL Recovery Compound Reserpine Stock (1000 ng/mL):** Add a portion of methanol to a 10 mL volumetric flask then add 10µL of Reserpine Standard (1000 µg/mL) or equivalents to the volumetric flask to obtain a final concentration of 1000 ng/mL. QS to 10mL with LCMS grade Methanol. This working stock is good for 12 months or until the earliest expiration date of any components used in the making.

Extraction Procedure A & B:

1. Case samples shall be removed from refrigeration storage, allowed to warm to room temperature and placed on a rocker for a minimum of ten minutes.
2. Mixes are prepared as per Table 4: Mix A & B and Control Levels in glass tubes.

Table 4: Mixes A & B and Control Levels			
ID	Blood Volume (µL)	Mix A Working Stock (µL)	Mix B Working Stock (100 ng/mL) (µL)
Mix A	500	100	
Mix B	500		200
QC Negative	500		

3. Transfer 500µL of each case sample into a glass tube.
4. Pulse vortex
5. To each case sample and negative control add 200 µL of Methanol.
6. Add 25µL Reserpine stock (100 ng/mL) to each tube (Note: the same lot of recovery compound shall be used for all samples in an analytical batch.)
7. Pulse vortex
8. In a fume hood add 2 mL Chloroform to each tube and cap.
9. Pulse Vortex 1 minute
10. Centrifuge at high speed for ten minutes
11. In a fume hood remove the supernatant bottom layer and transfer into new labeled glass tubes
12. Dry down at room temp w/ Nitrogen

13. Reconstitute in 200 µL 80:20 mobile phase Water w/0.1% Formic Acid and 5mM Ammonium Formate: Methanol
14. Pulse vortex
15. Transfer to an autosampler vial with insert for analysis

Extraction Procedure C:

1. Case samples shall be removed from refrigeration storage, allowed to warm to room temperature and placed on a rocker for a minimum of ten minutes.
2. Mixes are prepared as per Table 5: Mix C and Control Levels in silanized tubes.

Table 5: Mix C and Negative Control Levels

	Volume Blood (µL)	Mix C Working Stock (µL)
Mix C	500	25
QC Negative	500	

3. Transfer 500µL of each case sample into a glass tube.
4. Pulse vortex
5. Add 25µL Reserpine stock (100 ng/mL) to each tube (Note: the same lot of recovery compound shall be used for all samples in an analytical batch.)
6. Pulse vortex
7. Add 500µL HPLC Grade Water to each tube
8. Pulse vortex
9. Add 100 µL 1N HCl to each tube
10. Pulse vortex
11. In a fume hood add 2.5 mL 80:20 Hexane: Ethyl acetate to each tube and cap.
12. Pulse Vortex 1 minute
13. Centrifuge at high speed for ten minutes
14. In a fume hood remove the supernatant top layer and transfer into new labeled glass tubes
15. Dry down at room temp w/ Nitrogen
16. Reconstitute in 100 µL 50:50 mobile phase Water w/0.1% Formic Acid: Methanol
17. Pulse vortex
18. Transfer to an autosampler vial with silanized insert for analysis

Instrument Maintenance Procedure:

Refer to the HETL LC-MS/MS Instrument Maintenance Procedure a copy of which is located in the immediate area of the instrument.

Instrumentation and Data Acquisition Parameters:

The instrument method parameters will be printed out and placed in a method binder close to the instrument.

- Shimadzu 8030 Tandem Mass Spectrometer and LC system, Agilent 6470A Tandem Mass Spectrometer and LC system (or equivalent)
- LC Guard Cartridge – Phenomenex C18
- LC Column- Phenomenex Kinetex C-18 2.6 um 50 mm, 2.1 ID
- Flow rate 0.6 mL/Min

- Screen A & B Mobile phase A: Water with 0.1% Formic Acid and 5mM Ammonium Formate
- Screen C Mobile Phase A: Water with 0.1% Formic Acid
- Mobile Phase B: Methanol
- Injection volume 20 uL
- LC oven 40ºC

Table 6: Mix A & B LC Pump Gradient

Time	% A: Water with 0.1% Formic Acid and 5mM Ammonium Formate	% B: Methanol
0.01	95	5
0.01	To MS	To MS
9.00	5	95
12.00	To Waste	To Waste
12.00	5	95
12.01	95	5
14.00	Stop	Stop

Table 7: Mix C LC Pump Gradient

Time	% A: Water with 0.1% Formic Acid	% B: Methanol
0.01	50	50
0.10	To MS	To MS
4.50	5	95
5.25	5	95
5.26	50	50
5.80	To Waste	To Waste
8.00	Stop	Stop

Table 8: Instrument Parameters for Target Analytes A

Target Analyte	Precursor Ion (*m/z*)	Product Ion	
Morphine	286	Primary	165
		Secondary	152
Hydromorphone	286	Primary	185
		Secondary	157
Oxymorphone	302	Primary	284
		Secondary	227
Norfentanyl	233	Primary	84

Oxazepam	287	Primary	241
		Secondary	104
Cocaine	304		
Benzoylecgonine	290		
Amphetamine	136		
Methamphetamine	150		
MDA	180		
MDMA	194		
PCP	244	Primary	159
		Secondary	91
Ketamine	238		
Norketamine	224		
Cocaethylene	318		
Methylphenidate	234		
Temazepam	301		
Nordiazepam	271		
Alprazolam	309		
Diazepam	285		
Etizolam	343		
Clonazepam	316		
Zolpidem	308		
7-amino flunitrazepam	284		
Flunitrazepam	314		
Alpha-Hydroxyalprazolam	325		
7-amino clonazepam	286		
lorazepam	321		
3-methylfentanyl	351	Primary	202
		Secondary	105
6-Acetylcodeine	342		
6-acetylmorphine (6-MAM)	328		
Butyrylfentanyl HCL	351	Primary	188
		Secondary	105
Codeine	300		
Dihydrocodeine	302		
EDDP	278		
Fentanyl	337		
Heroin	370		
Hydrocodone	300		

Methadone	310	
Norhydrocodone	286	
Noroxycodone	302	
O-Desmethyltramadol	250	
Oxycodone	316	
Sufentanil	387	238
Tramadol	264	
Trazodone	372	
Meprobamate	219	158
		97
Reserpine	609	

Table 9: Instrument Parameters for Target Analytes B

Target Analyte	Precursor Ion (*m/z*)	Product Ion	
Clonidine	230	Primary	230
		Secondary	213
Norcodeine	286	Primary	286
		Secondary	153
Olanzapine	313	Primary	256
		Secondary	198
Zopiclone	389	Primary	245
		Secondary	217
Lamotrigine	256	Primary	256
		Secondary	211
Mirtazapine	266	Primary	195
		Secondary	72
Meperidine	248	Primary	70
		Secondary	91
LSD	324	Primary	223
		Secondary	208
Phenobarbital	231	Primary	231
		Secondary	42
Risperidone	411	Primary	411
		Secondary	191
Venlafaxine	278	Primary	278
		Secondary	121
Norbuprenorphine	414	Primary	101
		Secondary	83

Diphenhydramine	256	Primary	167
		Secondary	152
Dextromethorphan	272	Primary	215
		Secondary	171
Citalopram	325	Primary	109
		Secondary	262
Butalbital	223	Primary	223
		Secondary	42
Doxepin	280	Primary	107
		Secondary	115
Chlordiazepoxide-	300	Primary	227
		Secondary	165
Buprenorphine	468	Primary	55
		Secondary	396
Carbamazepine	237	Primary	237
		Secondary	194
Imipramine	281	Primary	281
		Secondary	86
Propoxyphene	340	Primary	58
		Secondary	143
Cyclobenzaprine	276	Primary	276
		Secondary	216
Desipramine	267	Primary	72
		Secondary	193
Amitriptyline	278	Primary	91
		Secondary	233
Nortriptyline	264	Primary	233
		Secondary	117
Secobarbital	237	Primary	237
		Secondary	42
Fluoxetine	310	Primary	310
		Secondary	44
Carisoprodol	261	Primary	176
		Secondary	97
Reserpine	609	Primary	609
		Secondary	195
Triazolam	343	Primary	308
		Secondary	238
Sertraline	306	Primary	306
		Secondary	275

Table 10: Instrument Parameters for Target Analytes C

Target Analyte	Precursor Ion (*m/z*)	Product Ion	
Δ9-THC	315	Primary	193
		Secondary	123
OH- Δ9-THC	331	Primary	313
		Secondary	193
COOH-Δ9-THC	345	Primary	299
		Secondary	327
Reserpine	609	Primary	195

Identification & Quantitation

- For all compounds detected by both SIM and MRM: to be deemed positive the MRM must meet all qualitative identification and detection criteria as the SIM alone may not exhibit a robust enough response and/or may be subject to interference, as illustrated in the Qualitative AB Validation Study and the Qualitative AB Addendum Interference Study Plan.
- For identification and detection criteria and guidelines please Refer to: LCMSMS Analysis, Acceptance, & Reporting Criteria Standard Operating Procedure.
- **Limit of Detection (LLOD):** the limits of detection have been determined as illustrated in Table 11: Limits of Detection

Table 11: Limits of Detection for Qualitative Blood Drug

Target Analyte	LLOD (ng/mL)
Morphine	5
Hydromorphone	5
Oxymorphone	5
Olanzapine	10
Norfentanyl	0.5
Oxazepam	4
Cocaine	10
Benzoylecgonine	10
Amphetamine	10
Methamphetamine	10
MDA	10
MDMA	10
PCP	10
Ketamine	10

Norketamine	10
Cocaethylene	10
Methylphenidate	10
Temazepam	4
Nordiazepam	4
Alprazolam	4
Diazepam	4
Etizolam	4
Clonazepam	4
Zolpidem	4
7-amino flunitrazepam	4
Flunitrazepam	4
Alpha-Hydroxyalprazolam	4
7-amino clonazepam	4
Lorazepam	4
3-methylfentanyl	0.5
6-Acetylcodeine	5
6-acetylmorphine (6-MAM)	5
Butyrylfentanyl HCL	0.5
Codeine	5
Dihydrocodeine	5
EDDP	5
Fentanyl	0.5
Heroin	5
Hydrocodone	5
Methadone	5
Norhydrocodone	5
Noroxycodone	5
O-Desmethyltramadol	5
Oxycodone	5
Sufentanil	0.5
Tramadol	5
Trazodone	5
Meprobamate	5
Lamotrigine	10
Dextromethorphan	10
Carisoprodol	10

Propoxyphene	10
Meperidine	10
Butalbital	10
Phenobarbital	10
Secobarbital	10
Clonidine	10
Risperidone	10
Triazolam	10
Citalopram	10
Chlordiazepoxide	10
Sertraline	10
Venlafaxine	10
Fluoxetine	10
Nortriptyline	10
Mirtazapine	10
Amitriptyline	10
Carbamazepine	10
Cyclobenzaprine	10
Desipramine	10
Doxepin	10
Imipramine	10
LSD	10
Zopiclone	10
Buprenorphine	10
Norbuprenorphine	10
Norcodeine	10
Δ9-THC	1
OH-Δ9-THC	1
COOH-Δ9-THC	5

Mix and Quality Control Requirements:

- For Mix and quality control requirements, acceptance criteria, and guidelines please Refer to: LCMSMS Analysis, Acceptance, & Reporting Criteria Standard Operating Procedure.

Documentation:

Each batch (example: QUALAB082819EAF & QUALC082819EAF) folder shall contain:

- Raw/Summary data from the instrument for all mixes and quality controls
- LC-MSMS Batch Review Form
- Qualifier Ion Ratio Report *(when applicable)*
- Instrument Sequence Table

- STARLIMs Batch Sequence
- QUAL Drugs in Blood Bench Sheet Form (AB & C)

Each Sample folder shall contain:

- Laboratory Blood Analysis Request Form
- Receipt/Contract for Examination Form/Chain of Custody
- Blood Kit Inventory Worksheet
- Blood Drug Screen Worksheet
- Raw/Summary data from the instrument including reinjections if applicable
- LC-MSMS Sample Review Form
- Blood Drug Results Worksheet
- Case Review Form

Waste Management:

Residual organic solvent, standards and instrument waste must be disposed in accordance with Federal and Maine law.

Any lab ware exposed to blood shall be disposed of in hazardous waste containers for proper disposal.

References:

Fraser, E. and Ingalls, N., in-house development and validation for detection and quantitation of cannabinoids in blood.

Fraser, E. and Ingalls, N., in-house development and validation for detection and quantitation of narcotics in blood.

Fraser, E. and Ingalls, N., in-house development and validation for detection and quantitation of benzodiazepines in blood.

Fraser, E. and Ingalls, N., in-house development and validation for detection and quantitation of stimulants in blood.

Simultaneous screening for 238 drugs in blood by liquid chromatography-ion spray tandem mass spectrometry with multiple-reaction monitoring. Gergov, Ojanpera, & Vuori. Journal of Chromatography B, 795 41-53 2003.

Cao, Z. Kaleta, E. & Wang, P. Journal of Analytical Toxicology 2015; 39:335-346. Simultaneous Quantitation of 78 Drugs and Metabolites in Urine with a Dilute-And-Shoot LC-MS-MS Assay.

Revision:

REVISED BY	REV#	DATE	Revisions
LN	1	Oct 29, 2019	Table 9: Product Ion and CE added for Venlafaxine, Fluoxetine and Doxepin. Table 11: LLOD changed from 2 to 4 for Temazepam – Lorazepam.
LN	2	Nov 04, 2019	All references to silanized tubes were changed to glass or silanized/non-silanized.
LN	3	Nov 14, 2019	All references to Gabapentin, CBD and CBN were removed. Table 9 was updated to include Ions, CE, and Dwell times for all compounds. Table 11 LLOD for Oxazepam was updated to 4ng/mL.
EAF	4	Dec 23, 2019	Following addendum study added MRM transitions for PCP, & 3-methylfentanyl, butyrylfentanyl. Added dwell times for Sertraline Table 9. In Documentation Batch Folder section: removed "recovery compound report"-unnecessary since it is a duplicate of what is on the Shimadzu reports, added "Qualifer Ion Ratio Report *(when applicable for confirmation).*
EAF	5	Feb 13, 2020	Added information for samples dilutions for Qualitative B compounds. Added Sufentanil MRM per addendum study.
EAF	6	Mar 12, 2020	Updated Qual Mix B Parent table from 5 parents to 2 parents.
EAF	7	June 15, 2020	Updated CE's for Butalbital, Phenobarbital, and Secobarbital per optimization plan.
EAF	8	October 9, 2020	Annual Review: Qual A working stock changed unit of measurement mL to ul (as pipetting is done in uL). Instrument and data parameters: Removed Nebulizing gas flow, DL temperature, Heat block, Drying gas flow, CID gas, all CE, and all Dwell times. All of these parameters are instrument specific and cannot be used for method replications. All of these parameters are still located in the printed instrument data acquisition methods located by the instrument. Documentation: batch folder put "when applicable" after qualifier ion ration report.

EAF	9	December 7, 2020	Added MRM transitions for Meprobamate per Qual A Meprobamate Addendum study.
EAF	10	03/03/2021	Included silianized and non silianized tubes and inserts in materials list. Updated AB extraction procedure to glass tubes. Added Agilent 6470A information/reworded to include Agilent 6470A. Added QNS sample and non-DHHS information to Specimen Requirement section.
EAF	11	03/23/2021	Clerical update to nomenclature: Δ9-THC, OH-Δ9-THC, COOH-Δ9-THC.
EAF	12	03/30/2021	Clerical update to Qualitative C COOH-Δ9-THC primary and secondary ion to match what the method was validated with and the instrument method (the numbers were transposed).
EAF	13	4/12/21	Clerical update to Qualitative C Reserpine MRM transitions to match initial validation study.