FORENSIC TOXICOLOGY LABORATORY
OFFICE OF CHIEF MEDICAL EXAMINER
CITY OF NEW YORK

CARISOPRODOL , MEPROBAMATE and TOPIRAMATE by SOLID PHASE EXTRACTION and GAS CHROMATOGRAPHY/MASS SPECTROMETRY (Selected Ion Monitoring)

PRINCIPLE

Carisoprodol is a carbamate derivative first synthesized in 1959. It is primarily used as a muscle relaxant. Meprobamate is also a carbamate derivative used as a muscle relaxant and the primary metabolite of carisoprodol. Topiramate is a sulfamate-substituted monosaccharide used as an anticonvulsant Carisoprodol, meprobamate and topiramate are quantitated by a selected ion monitoring (SIM) method using methapyrilene as the internal standard.

Carisoprodol, meprobamate and topiramate are extracted from biological specimens by solid phase extraction. Drugs are temporarily bound to a sorbent in the solid phase cartridge as the prepared sample is poured through the column. The column is washed to remove interfering compounds, followed by elution of drugs from the column. The eluate is evaporated, reconstituted and injected in the GCMS. Quantitative analysis is performed by SIM GCMS using a six point calibration curve.

SAFETY

The handling of all biological specimens and reagents is performed within the guidelines which are detailed in the Safety and Health manual.

SPECIMEN PREPARATION

The procedure is routinely applied to the following biological specimens and their aliquots unless otherwise specified:

Blood	0.5 mL of the undiluted specimen
Urine	0.5 mL for qualitative identification
Brain	0.5 mL of a 1:3 homogenate
Gastric Contents	0.5 mL of a 1:10 dilution
Liver	0.5 mL of a 1:5 homogenate
Vitreous Humor	0.5 mL of the undiluted specimen
Bile	0.5 mL of the undiluted specimen

Dilution of Specimens

Specimens are diluted as follows:

Brain 1:3	5.0 g of brain homogenized with 10 mL of distilled water.
Liver 1:5	5.0 g of liver homogenized with 20 mL of distilled water.
Gastric 1:10	2.0 mL of liquid *q.s.* to 20 mL of distilled water, or 2.0 g of a solid specimen homogenized with 18 mL of distilled water.

Note: *Use a homogenate which was prepared within two weeks. Do not use homogenates older than two weeks unless low sample size requires it. Discuss with supervisor and note in case record. The entire submitted amount of gastric contents needs to be homogenized prior to sampling.*

REAGENTS AND MATERIALS

All chemicals should be analytical reagent grade or better.

1. **Deionized water** (distilled can be substituted)
2. **Methanol** (Fisher Scientific - ACS Certified or equivalent)
3. **Certified Negative Blood**. Previously found to have no interfering peaks. Freeze validated negative blood. Discard after 3 months.
4. **Certified Negative Liver**. Previously found to have no interfering peaks. Freeze validated negative liver. Discard after 3 months**.**
5. **Certified Negative Brain**. Previously found to have no interfering peaks. Freeze validated negative brain. Discard after 3 months.
6. 100 mM Sodium Acetate buffer (pH 4.5)

   Dissolve 2.93 g sodium acetate trihydrate in 400 mL DI H_2O; add 1.62 mL glacial acetic acid. Dilute to 500 mL using DI H_2O. Mix. Adjust pH to 4.5 ± 0.1 with sodium acetate or acetic acid.
   Storage: room temperature in glass.
   Stability: 6 month. Inspect daily with use for contamination.
7. **pH 9.0 buffer**

   Dissolve 20 g $KHCO_3$ in 800 mL DI H_2O; add 10 g K_2CO_3. Dilute to 500 mL using DI H_2O. Mix. Adjust pH to 9.0 ± 0.1 with $KHCO_3$ or K_2CO_3.
   Store at room temperature in glass.
   Stability: 6 month. Inspect each day of use contamination.
8. **Eluting solvent**: ethyl acetate:NH_4OH (98:2). Prepare fresh each day of use.
9. Polycrom Clin II Solid Phase Extraction Column, CEREX.
10. System 48 Processor connected to nitrogen source.

11. Waste Rack, SPE Rack, Collection Tube Rack.
12. Turbovap connected to a nitrogen source.
13. Sonicator
14. Vortex
15. Centrifuge
16. Meprobamate , carisoprodol and topiramate calibrator solutions (100mg/L).

    Carisoprodol working calibrator solution. (100 mg/L)
    Weigh 0.0100 grams of carisoprodol into a 100 mL volumetric flask and qs to 100 mL with methanol. Transfer to properly labeled containers.
    Meprobamate working calibrator solution. (100 mg/L)
    Pipet 1 mL of 1 mg/mL meprobamate reference standard into a 10 mL volumetric flask. QS to 10 mL with methanol. Transfer to properly labeled containers.
    Topiramate working calibrator solution (100 mg/L)
    Pipet 1 mL of 1 mg/mL topiramate reference standard into a 10 mL volumetric flask. QS to 10 mL with methanol. Transfer to properly labeled containers.

    Note: *Include identity, concentration, solvent, lot number, date prepared, and initials of analyst.*

17. **Meprobamate , carisoprodol and topiramate control solutions (100mg/L).**

    Preparation is the same as meprobamate , carisoprodol and topiramate calibrator solutions as listed in step 15, using a different lot of primary standard (if available). If a different primary standard is not available, use a separate aliquot of the primary standard used to make the calibrator.

18. **Methapyriline (MPY) Internal Standard, 50 mg/L.**

    See SOP section “Calibrators and Controls for Basic Drugs by GC and GCMS” for preparation.

19. Gas Chromatography Column:

    Restek RTX-50 (Crossbond 100% methylphenyl polysiloxane). 30M x 0.25 mm ID x 0.25 µm DF, max temperature 320 ^{o}C. Model # 10523

PROCEDURE

1. Aliquot 0.5 mL of validated negative specimen into each tube labeled as calibrator or in-house control or 0.5 mL of sample into a 16 x 125 mm disposable culture tube labeled as to the contents.
2. Add appropriate amounts of standard solutions to negative matrix specimen tubes as follows:

   Six positive calibrators and one blank should be run with each batch of samples. Positive calibrators are prepared in the following concentrations:

I. 0.5 mg/L - add 2.5 µL of 100 mg/L meprobamate, carisoprodol and topiramate calibrator solution

II. 1.0 mg/L - add 5.0 µL of 100 mg/L meprobamate, carisoprodol and topiramate calibrator solution

III. 1.5 mg/L - add 7.5 µL of 100 mg/L meprobamate, carisoprodol and topiramate calibrator solution

IV. 2.0 mg/L - add 10.0 µL of 100 mg/L meprobamate, carisoprodol and topiramate calibrator solution

V. 3.0 mg/L - add 15.0 µL of 100 mg/L meprobamate, carisoprodol and topiramate calibrator solution

VI. 5.0 mg/L - add 25.0 µL of 100 mg/L meprobamate, carisoprodol and topiramate calibrator solution

***Note**: Deionized water is used as the negative matrix for urine and gastric specimens.*

Additionally, two controls for verification of the calibrators are included in the run. Prepare a positive control of 0.5 mg/L by adding 2.5 µL of 100 mg/L topiramate and meprobamate and carisoprodol control solutions to the negative blank material. In addition, prepare a control of 2.5 mg/L by adding 12.5 µL of 100 mg/L topiramate and meprobamate and carisoprodol control solutions to the negative blank material. Prepare both controls in each matrix analyzed in the batch.

3. Add 15 µL of 50 mg/L MPY working internal standard solution to all tubes. The concentration of the internal standard in each sample is 1.5 mg/L.
4. Add 2.5 mL of DI H_2O and 2mL of pH 4.5 Sodium Acetate Buffer. Vortex for 15 seconds. Centrifuge at ≈3000 rpm for 10 minutes.
5. Pour samples into the column and apply positive pressure to achieve a flow rate of 5-10 mL/min.
6. Wash each column with 1mL pH 9.0 Buffer.
7. Wash each column with 1mL DI H_2O.
8. Dry columns for 10 minutes at 25 Psig.
9. Elute each column with 2.0 mL Ethyl Acetate containing 2% NH_4OH. Into a conical 10 mL centrifuge tube.
10. Evaporate samples to dryness at 40° C with nitrogen.
11. Reconstitute the dried extracts with 100 µL of Ethyl Acetate.
12. Label autosampler vials indicating aliquot and toxicology number (ex: 2-YY-xxxx), specimen type, dilution, analyst and date. Immediately seal each vial with an aluminum seal using a crimper to avoid possible contamination from other samples. Samples may also be transferred into screw cap vials and capped immediately. Physically check that the

crimped seal is tight by attempting to rotate the seal. Crimp until tight, using a new seal if necessary. Do not wait until all transfers have been made to seal the vials.

13. Transfer sealed vials to GCMS section for analysis.

INSTRUMENTATION

Agilent 5973 Mass Spectrometer with 5890 GC, Autosampler Agilent 7683, and Agilent Chemstation with current revision of software. The method name for this assay is MSNTOPSIM.M, where N is the instrument number. Each MSD used for Topiramate and Meprobamate and Carisoprodol analysis will have a method with this name in the method directory.

The following ions are monitored for each drug:

Meprobamate	83, 144, 114
Carisoprodol	158, 245, 184
Topiramate	324,189,110
MPY IS	97, 191

TOPLEVEL PARAMETERS

Method Information For: C:\MSDCHEM\1\METHODS\MSNTOPSIM.M

Method Sections to Run:

(X) Save Copy of Method With Data
( ) Pre-Run Cmd/Macro =
(X) Data Acquisition
( ) Data Analysis
( ) Post-Run Cmd/Macro =

METHOD COMMENTS:

HP5973 MSNTOPSIM.M

END OF TOP LEVEL PARAMETERS

INSTRUMENT CONTROL PARAMETERS

Sample Inlet	GC
Injection Source	GC ALS
Mass Spectrometer	Enabled

HP6890 GC METHOD

OVEN

Initial temp	140 °C (On)	Maximum temp	320 °C
Initial time	1.00 min	Equilibration time	0.50 min

Ramps			
#	**Rate**	**Final temp**	**Final time**
1	15.00	295	5.00
2	0.0(Off)		
Post temp	295 °C		
Post time	5.00 min		
Run time	16.33 min		

Front Inlet (Unknown)		*Back Inlet ()*
Mode	Pulsed Splitless	Not used
Initial temp	260 °C (On)	
Pressure	12.77 psi (On)	
Pulse Pressure	30.0 psi	
Pulse Time	0.80 min	
Purge flow	7.5 mL/min	
Purge time	0.00 min	
Total flow	10.3 mL/min	
Gas saver	On	
Saver flow	20.0 mL/min	
Saver time	3.00 min	
Gas type	Helium	

Column 1		*Column 2*
Capillary Column		(not installed)
Model Number	Restek RTX -50	
0.25mm * 15M * 0.25 µm		
Max temperature	320 °C	
Nominal length	30.0 m	
Nominal diameter	250.00 µm	
Nominal film thickness	0.25 µm	
Mode	Constant flow	
Initial flow	1.0 mL/min	
Nominal init pressure	12.77 psi	
Average velocity	38 cm/sec	
Inlet	Front Inlet	
Outlet	MSD	
Outlet pressure	Vacuum	

FRONT DETECTOR (NO DET)	*BACK DETECTOR (NO DET)*

SIGNAL 1	SIGNAL 2
Data rate: 20 Hz	Data rate: 20 Hz
Type: test plot	Type: test plot
Save Data: Off	Save Data: Off
Zero: 0.0 (Off)	Zero: 0.0 (Off)
Range: 0	Range: 0
Fast Peaks: Off	Fast Peaks: Off
Attenuation: 0	Attenuation: 0

COLUMN COMP 1	COLUMN COMP 2
(No Detectors Installed)	(No Detectors Installed)

Thermal Aux 2	
Use: MSD Transfer Line Heater	
Description	
Initial temp	280 °C (On)
Initial time	0.00 min
# Rate Final temp Final time	
1 0.0(Off)	

Post Run	
Post Time	5.00 min
Oven Temperature	295 °C
Column 1 Flow	1.2 mL/min

Time Table		
Time	**Specifier**	**Parameter & Setpoint**
7673 Injector		
Front Injector:		
Sample Washes	1	
Sample Pumps	2	
Injection Volume	3.0 microliters	
Syringe Size	10.0 microliters	
PreInj Solvent A Washes	1	
PreInj Solvent B Washes	1	
PostInj Solvent A Washes	3	
PostInj Solvent B Washes	3	
Viscosity Delay	0 seconds	
Plunger Speed	Fast	
PreInjection Dwell	0.00 minutes	
PostInjection Dwell	0.00 minutes	
Back Injector:		
No parameters specified		

MS ACQUISITION PARAMETERS

General Information	
Tune File	Atune.u
Acquistion Mode	SIM
MS Information	
Solvent Delay	5.0 min
EM Absolute	False
EM Offset	200
Resulting EM Voltage	(varies)

[Sim Parameters]

Group 1			
Group ID	1		
Resolution	High		
Plot 1 Ion	97.0		
Ions/Dwell In Group	(Mass, Dwell)	(Mass, Dwell)	(Mass, Dwell)
	(83.0, 300)	(97.0, 50)	(110.0, 50)
	(114.0, 300)	(144.0, 300)	(158.0, 10)
	(184.0, 10)	(189.0, 50)	(191.0 50)
	(245.0, 10)	324.0, 50)	

[MSZones]

MS Quad: 150 °C maximum 200 °C
MS Source: 230 °C maximum 250 °C

END OF MS ACQUISITION PARAMETERS

END OF INSTRUMENT CONTROL PARAMETERS

INSTRUMENT SETUP

A GCMS autotune must be performed at the start of each day samples are injected.

All autosampler syringe wash vials are filled with ethyl acetate.

Prepare a sequence using the following steps.

When Chemstation is opened, the **Openlab ECM Login** screen appears, Enter the instrument name (ms3, ms4, etc.) as appropriate for username and the current password. Verify that Account field says production and Domain field says Built-In. if Chemstation is already running, it may be necessary to log out and relog in. Using the Chemstation software, at the top Method and Run toolbar under **ECM,** select **Logon to ECM**. Follow the instructions above to log on.

1. On the Method and Run toolbar, under Sequence, select Load Sequence. Select default.s. Click on Select.
2. In the Method and Run toolbar, under Sequence, select Edit Sequence. At the top of the screen under Data Path, click on Browse. Under Select Data Path, click on the msdchem folder. The click 1 and then click on the Data folder to highlight it. In lower left of dialog box, select Make New Folder. A folder with the name New Folder is created under DATA. Right click on New Folder and Rename or double click to highlight the folder name and change the entry. Rename the file using the format MSNMMDDYYN, where N is instrument number, MM = month, DD = day, YY= year and x = a letter indicating the batch being run, e.g. MS3041111a. Click OK which will take you back to the sample log table.
3. In the Sample column verify the correctness of pre-loaded entries. Starting at the first empty field, enter sample or QC information. For samples this would include aliquot number, laboratory number, specimen source, dilution if any (i.e., 2-11-2432 fem). If the sample has been diluted, enter the appropriate dilution factor in the Multiplier column. For QC samples use an appropriate designator. Enter the next sample in the batch in the next open field down the column.
4. In the Type column, select the corresponding sample type for each vial: Sample, Blank, Calibration or QC.
5. In the Vial column, click in the cell with the number 1, hold down the left mouse button and drag to the last vial number in the sequence (cells will be highlighted). Right click and select Fill Column and Increment. Verify that the vial numbers are correct.
6. In the Method column, verify that the correct method is loaded in the first cell. Then click on the first cell containing the method name, hold down the left mouse and drag to the last vial number in the sequence (cells will be highlighted). Right click and select Fill Column, No Increment. Verify that the method for each vial is correct.
7. In the Data File column, in the cell corresponding to the first vial, enter the data file name in the format MSNMMDDN001, where N = instrument number, MM = month, DD = day, and x = a letter indicating the batch being run, i.e. MS20411a001a. Click on this cell, hold down the left mouse and drag to the last vial number of the sequence (the cells will be highlighted). Right click and select Fill Column and Increment. Verify that the data file information for each vial is correct.
8. In the Comment column, enter any additional information for the vials.
9. In the Multiplier column, enter any sample dilutions.
10. In the Level column, verify that the correct level numbers are entered for calibrators in this batch.
11. Verify No Update is selected for all vials under Update Rf and Update Rt.
12. Review the information typed for the sequence. Correct any information as needed. Verify that the Data Path is C:MSDCHEM\1\Data\current sequence name. Verify that the Method Path is C:MSDCHEM\1\METHODS. Then Click ok.

Note: *Occasionally, it will be desirable to run several subsequences in one batch. Use the instructions below to accomplish this.*

Setting-Up a Subsequence

On the Sample Log Table:

1. Select "**Keyword**" for "Type"
2. Select "**DataPath**" for "Method/Keyword"
3. Under "Comment/KeywordString" type in the *new data path* for your subsequence ie: **C:\MSDCHEM\1\DATA\MSNMMDDYYx** where "N" is the instrument's number and "**x**" is the letter designated to the subsequence (***it must be different than that of the original sequence***).
4. The suffix of the data files must be different from that of the original; ie: MSNMMDD**y**00**1**; ***the subsequence data files must start with 1 again***.
5. After typing in the entire sequence, save sequence accordingly.
6. Go to Sequence → Simulate Sequence → Run Sequence.
7. A dialog box will pop-up: DataPath **C:\MSDCHEM\1\DATA\MSNMMDDYYy** does not exist. Edit Sample Log Table? → Click **No** if the sequence was set up correctly.
8. A 2nd dialog box will pop-up: Create **C:\MSDCHEM\1\DATA\MSNMMDDYYy**? → Click **Yes**.
9. A 3rd dialog box will pop-up: Sequence Verification Done! View it? → Click **Yes** or **No**.

Setting-Up a Subsequence with a Different Method

On the Sample Log Table:

1. After inserting the DataPath keywords and Commands, Insert a Row.
2. Select "**Keyword**" for "Type"
3. Select "**MethodPath**" for "Method/Keyword"
4. Check that the method for each sample is changed to the new method.
5. Follow Steps 5-9 in the "**Setting-Up a Subsequence**" Section (see previous section).

13. On the Method and Run toolbar, under Sequence, select Run Sequence. In the dialog box under Sequence Comment enter the initials of the individual who has entered the sequence in the Operator Field (e.g., MPM). Under Data File Directory verify that the data file path is C:MSDCHEM/1\DATA\batch name.
14. Under Sequence, select Save Sequence As. Under File Name, type in the name of the folder that the batch will be saved to under DATA, MSNMMDDYYx (e.g. MS2041211a) Select Save. The extension ".s" will automatically be added.
15. Under Sequence select Print Sequence. Verify that Brief Format is selected and click on OK. The sequence will be printed. Apply the preprinted labels for documenting verification of process steps to the printed sequence list.
16. Use the printed sequence list to load vials into the appropriate autosampler positions as indicated by the order on the printed sequence list. Check vial information against the sequence list and ensure that the vial is inserted in the correct numeric position in the autosampler as indicated on the sequence list. Document correct positioning by dating and initialing the appropriate line on the sequence list.
17. Under Sequence select Run Sequence. Verify that the Sequence comments and Data Field information are correct (i.e. verify that the proper sequence is loaded. If not, load the proper sequence). Click on Run Sequence.
18. After the batch is finished, unload the vials. Compare the vial information to the sequence list as they are removed, to verify that the correct vial was in the correct position. Date and initial the sequence list when this is completed. Annotate discrepancies if necessary

DATA TRANSFER AND PROCESSING

All processing and review are performed on a processing computer.

SAVE METHOD TO ECM

1. After the run finishes, the data files will be in the data subdirectory on the local chemstation and also automatically transferred to ECM. From the acquiring computer, make sure the proper method, the one used to acquire the data, is loaded. On the top toolbar under ECM click on Save Method to ECM.
2. Click on GCMS, the correct instrument name folder, the appropriate month and batch to which the method will be saved.

RETRIEVE BATCH FROM ECM

1. At the processing computer, click on Processing Data Analysis. Log on using your OCME network username and password.

2. On Enhanced Data Analysis screen, click on ECM at the top toolbar and select Retrieve entire sequence from ECM.
3. This will open up Openlab ECM screen. Select GCMS, then the appropriate instrument, the month, and, finally the batch to be retrieved. On the status line at the bottom of the screen that the batch is being retrieved. The batch will be downloaded to the following location: C:\msdchem\1\ECM\Retrieve\"batch name"

LOAD METHOD AND BATCH

1. On the left screen under the C drive, open C:\msdchem\1\ecm\retrieve
2. Under retrieve, click on the batch that was retrieved. When all files have been downloaded to the processing computer, verify that the appropriate method is present in the batch.
3. To load the method, right click on the method under the batch being processed and select load. This will bring up "Be sure changes are saved. Load now?" Click yes. If the method is not present, load the method by retrieving the method from ECM.
4. Click on any file in the batch to load it.

PERFORM BATCH CALIBRATION

Under enhanced data analysis:

1. Process the calibrators. Select Tools from the toolbar, DoLIST, and Quant, No Report (QT 1). Press Add, and OK. Select the files for this action to be performed on, in this case, calibrators only. Verify that the selected files are located in the correct subdirectory. Change the path if necessary. Click the → Arrow and Process..
2. Review the integrations of the targeted compounds for each calibrator, checking that the ion peaks are present and integrated correctly (i.e. the baseline is the most scientifically accurate one that can be drawn). Select View from the toolbar, QEDIT. Answer appropriately when prompted to save changes made to quantitation results when moving from file to file. Return to Data Analysis by selecting View from the toolbar, return to Data Analysis.
3. Update the existing calibration table (all levels). Select Calibrate, Update, Quick Levels Update. When prompted to clear responses, select YES. When asked to requant files before update, select NO. Select single data file/level option. Select the appropriate data file to associate with calibration level 1 (0.5 mg/L). Click OK. Repeat for remaining calibration levels (1.0, 1.5, 2.0, 3.0, 5.0 mg/L). Select level 3 when prompted to update retention times.
4. Load the file associated with level 3 (1.5 mg/L), by selecting File, Load Data File. Select Calibrate, Update One Level. Do NOT requant. Select Update One Level, select only

Replace Qualifier Ion Relative Responses, and choose the corresponding existing level ID (#3). Click Do Update.

5. Review the Compound database. Double click on the internal standard listed on the left to reveal the compounds quantitated with it. Select the calibration tab to reveal compound responses, calibration curves, and r^2. To disable a point on the calibration curve for a compound, delete its response from the table. Click OK or Cancel when review is complete
6. Save Method before proceeding. Select Method from the toolbar, Save method, make sure that the path is correct. Save to OpenLab ECM at this time. On Update Calibration screen, select Update Level. Then click on Responses and Replace and on Retention Times and Replace. Then under Existing level ID, select the cal level to update and click on Do Update.
7. Requantitate the calibrators with the updated calibration curve. Select Tools from the toolbar, DoLIST, Requant, no report (QT 2), Add, and OK. Remove any existing commands. Select files to process. Click the → Arrow and Process. Review with QEDIT. Check the responses, retention times and ion ratios.
8. Regression correlation coefficient (r^2) for each analyte must be equal to or greater than 0.99.
9. Process controls and cases. Select Tools from the toolbar, DoLIST, Quant, No Report (QT 1), Add, and OK. Select appropriate files. Click the → Arrow and Process. Review with QEDIT. The blank must not contain detectable amounts of target analytes or significant interfering peaks.
10. When review is complete, return to Data Analysis. Select report format by choosing Quantitate from the toolbar, Report Options. Check SIM style report and uncheck Internal Standards. Press OK.
11. To print reports, select Tools from the toolbar, DoLIST, Profile Quant w/o Calculations (QT 0,1,'P'), Add, and OK. Select files to print, click the → Arrow and Process.
12. Print the calibration table for the current batch by clicking Calibrate on the command line. Select List, Calibrate Report and click OK. The Calibration report will print to the screen. Review the r^2 values, then right click on the screen report to print it.
13. Save files to ECM. Select ECM from the toolbar, select "Save multiple data files to ECM". Select all files.
14. Save method to ECM. Select ECM from the toolbar, Save Method to ECM. Make sure data path is correct.

BATCH CLEAN UP

1. Select my computer. Find the batch on the C drive at C:\msdchem\1\ecm\retrieve\batch. Right click on the batch to be deleted and select delete. Do not delete a batch that has not been successfully uploaded to ECM.

ACCEPTANCE CRITERIA

1. Review the entire batch , checking that the ion peaks are present and integrated correctly (e.g., that the baseline is the most scientifically accurate one that can be drawn), that the ion ratios are ± 20 % of the average of a calibrator, that the peaks are ± 2 % of the calibrator retention times, and the peaks meet chromatography criteria. The blank must not contain detectable amounts of target analytes or significant interfering peaks. The blood controls must be within ± 20 % of the target value. For tissues, the controls are acceptable up to ± 30 %.

   ***Note**: In some instances ratios will be off in exceptionally low or high concentrations. The analyst must evaluate this and schedule proper dilutions or other methodologies, as needed. See REPORTING section.*

2. Make copies of all controls, the r^2 report and the sequence list, enough to attach a set to each case in the batch.

REPORTING

After the batch has been reviewed and printed, it must be reported, using the following guidelines:

1. Each case printout must have a copy of the sequence and all controls appended.
2. Concentrations greater than or equal to 0.5 mg/L are reported in mg/L. Results are truncated and reported to one decimal point (e.g., 0.575 mg/L is reported as 0.5 mg/L).
3. Concentrations below 0.5 mg/L but meeting all other criteria are reported as “less than 0.5 mg/L”. If the drug is not detected, or the criteria are not met, the drug is reported as “not detected”.
4. Sample concentrations greater than the highest acceptable calibrator must be re-extracted with suitable dilution(s) to bring the concentration below the ULOL.
5. If the positive matrix controls are greater than ± 30 % of target for non-blood matrices, the samples may be reported qualitatively, as “detected”. If quantitative results are needed, the sample must be repeated.

REFERENCES

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Disposition of Toxic Drugs and Chemicals in Man, Randall C. Baselt, Biomedical Publications, Foster City, CA, 8th edition, 2008.

Agilent 6890 GC System Installation Guide.

Agilent 6890 GC System Users Guide.

Agilent 6890 GC System Standard Operating Procedures.

Agilent 5973 & 5973 Network Mass Selective Detector Installation Guide.
Agilent 5973 & 5973 Network Mass Selective Detector Users Guide.
Agilent 5973 & 5973 Network Mass Selective Detector Standard Operating Procedures.
SPEware Corp Cerex Applications Manual.
System 48 Processor Users Guide.
Turbovap Users Guide.