## I. INTRODUCTION

The LCMSMS can be used to confirm and quantitate most analytes including illicit drugs, prescription drugs, over the counter pharmaceuticals and other drugs.

Samples that require confirmation and/or quantitation by LCMSMS are extracted from a buffered, diluted sample aliquot by adsorption onto a solid phase extraction (SPE) column. Drugs that may be present are then eluted from the SPE column, dried, and reconstituted before injection onto the LCMSMS system.

The detection of each specific analyte is determined by single point calibration cut off for urines. Bloods are quantitated with a multipoint calibration using deuterated internal standard(s) or other internal standard that is appropriate for the analyte.

Matrix-specific (blood and/or urine as needed) positive and negative controls are extracted and analyzed in each analytical batch. The presence of drugs may be confirmed in urine, blood, vitreous fluid or other fluids.

### A. Method Targets

This is a non-targeted quantitation method. The analyte to be quantitated will have been identified by the LCMS screen method, a GCMS method or an immunoassay method.

### B. Safety

This procedure is carried out in a laboratory environment and standard safety procedures should be utilized, including (minimally) safety glasses and lab coat when deemed necessary. Biological specimens subject to the analytical procedure should be handled using universal precautions. Potentially contaminated items and surfaces should be disinfected prior to and after use.

### D. Specimen Requirements

1. 0.5 mL blood, urine or other fluid (in general urine will be confirmation only)

## II. MATERIALS

### A. Equipment

1. General laboratory glassware
2. Vortex, Thermolyne Maxi Mix 1 or equivalent

3. Sonicator, Fisher-Scientific or equivalent (for blood samples)
4. Centrifuge, Beckman TJ-6 or equivalent
5. Trace B Extraction Columns - SPEWARE (Baldwin Park, CA)
6. SPEWARE CEREX System-48 Solid phase extraction manifold
7. SPEWARE CEREX System-48 Sample Concentrator
8. Shimadzu LC/MS/MS System consisting of (or the equivalent of):
    a. Degasser: Shimadzu DGU-20A
    b. Pumps: 2 Shimadzu LC-20AD Prominence
    c. Autosampler: Shimadzu SIL 20AC Prominence
    d. Column Oven: CTO-20A
    e. Pre-Column: SecurityGuard ULTRA Cartridge UHPLC Phenyl for 4.6mmID Columns (Phenomenex) or equivalent.
    f. Column: Kinetex Phenyl Hexyl (Phenomenex)
    g. Detector: Shimadzu LCMS-8030 Mass Spectrometer
    h. Controller: Shimadzu CBM-20A
    i. Data Station: Shimadzu LabSolutions software

**B. Reagents available as stock items:** Sigma or J.T. Baker reagent grade or equivalent unless specified

1. Methanol ($CH_3OH$): Fisher Optimum LCMS Grade or Burdick Jackson pesticide grade
2. Deionized water (DIW): Milli-Q or LCMS grade
3. Drug-free urine or blood (Drug free blood obtained from Hartford Hospital blood bank or equivalent)
4. Formic Acid (HCOOH)
5. Ammonium formate ($NH_4HCO_2$)
6. Glacial acetic acid ($CH_3COOH$)
7. Sodium acetate trihydrate ($NaCH_3COO{\cdot}3H_2O$)
8. Sodium carbonate ($Na_2CO_3$)

9. Sodium bicarbonate ($NaHCO_3$)
10. External control such as UTAK LC-2 Control – UTAK Laboratories (Valencia, CA)

    It is noted that an external control may not be available for all analytes that need quantitation in these cases an in-house control made from a different lot or by a second analyst will be used.

12. β-Glucuronidase (*P. vulgata*; Sigma or equivalent)

**C. Drug Standard Solutions - Standards** will be used based on the analyte to be quantitated or confirmed.

a. Drug Standard Solutions -Cerilliant Corporation (Austin, TX) – or equivalent
b. Deuterated Drug Standard Solution – Cerilliant Corporation (Austin, TX) or equivalent
c. Drug Standard Solutions – Lipomed Inc. (Cambridge, MA) or equivalent

**D. Reagents prepared in the Toxicology Laboratory**

**1. <u>5M Ammonium formate</u>:**

a. Dissolve 3.15 g of ammonium formate in 10 mL volumetric flask.
b. Q.S. to 10 mL with DIW. Stable for one year, stored in the refrigerator.

**2. <u>Mobile Phase A ($H_20$ with 5mM ammonium formate and 0.01% formic acid)</u>:**

a. Add 0.5 mL <u>5M Ammonium formate</u> and 0.05 mL formic acid to a 500 mL volumetric flask.
b. Q.S. to 500 mL with high purity water.
c. Transfer solution to a glass bottle reserved for LC/MS use only. Stable for one week.
d. The above instructions make 500 mL of mobile phase; adjust volumes of reagents accordingly if requiring a different final volume.

**3. <u>0.1M Sodium Acetate buffer (pH 4.5):</u>**

a. Combine 5.86 g of sodium acetate trihydrate and 3.24 mL glacial acetic acid in a 1000 mL stoppered graduated cylinder.
b. Q.S. to 1000 mL with deionized water.
c. Store in glass container at room temperature (25$^{o}$C)
d. Stable for one year
e. Inspect for contamination before use. If bacterial contamination is visible, prepare fresh before use.

**4. <u>1.0 M Acetate buffer (pH 5.0)</u>**

a. Dissolve 42.9 g sodium acetate trihydrate in approximately 400 mL DIW
b. Add 10.4 mL glacial acetic acid $C_2H_4O_2$
c. Dilute to 500 mL with DIW
d. Mix. Check pH, adjust pH to 5.0 ± 0.1 with 1.0 M acetic acid if needed.
e. Storage: room temperature in glass or plastic. Stability: 6 months
f. Inspect daily for contamination.

**5. <u>0.1 M Acetate Buffer (pH 5.0)</u>**

a. Dilute 20 mL 1.0 M acetate buffer to 200 mL with DIW

b. Mix. Store at room temperature. Stability: 6 months

**6. <u>β -Glucuronidase, (5,000 F units/mL) in 0.1 M Acetate Buffer (pH 5.0)</u>**

Prepare daily for use, make slight excess for each batch, each 0.5 mL sample requires 1250 F units. Add 250 µL of β -Glucuronidase to each tube.

Example: for 40 total tubes prepare 10 mL
Calculate activity for each lot of β-Glucuronidase as follows:
(Lot specific, value from bottle label)
e.g. 1,439,000 -glucuronidase units/g solid
5,000 Units/mL = 1,439,000
x mg 1000 mg
1. x = 3.47 mg/mL

5,000 Units/mL = 1,439,000
x mg 1000 mg
x = 3.47 mg/mL

**To make 10 mL**

Weigh out 34.7 mg β –Glucuronidase solid. Add to 10 mL of 0.1 M acetate buffer (pH 5.0) Dissolve before use by swirling gently.
Make fresh daily as needed for each batch



7. **<u>0.1M Sodium Carbonate (pH 8.0):</u>**
   a. Add 5.3 g of sodium carbonate to a 500 mL volumetric flask.
   b. Q.S. to 500 mL with deionized water.
   c. Using a validated pH meter, check pH; should be 8.0 ±0.2.
   d. Store in glass container at room temperature (25$^{o}$C)
   e. Stable for one year
   f. Inspect for contamination before use. If bacterial contamination is visible, prepare fresh before use.
8. **0.1M Sodium Bicarbonate (pH 11.0)**:
   a. Add 4.2 g of sodium bicarbonate to a **separate** 500 mL volumetric flask.
   b. Q.S. to 500 mL with deionized water.
   c. Using a validated pH meter, check pH; should be around 11.0 ±0.2.
   d. Store in glass container at room temperature (25$^{o}$C)
   e. Stable for one year
   f. Inspect for contamination before use. If bacterial contamination is visible, prepare fresh before use.

9. **Bicarbonate Buffer pH 9.0: Mixture of 0.1 M Sodium Carbonate and 0.1 M Bicarbonate Solutions**

a. Into a beaker containing the 0.1M Sodium Carbonate solution (lower pH solution)
b. Using a validated pH meter, check pH, adjust with the 0.1M Sodium Bicarbonate solution (higher pH solution) until a pH of 9.0 ± 0.2 is reached.

c. Store in glass container at room temperature (25$^{o}$C)

d. Stable for one year

e. Inspect for contamination before use. If bacterial contamination is visible, prepare fresh before use.

**10. Reconstitution Mixture: 20% Methanol in Deionized Water**

a. Into a 100 mL graduated cylinder with a cap, add 80 mL of deionized water.

b. Add 20 mL methanol.

c. Cap and shake. Store at room temperature; stable for 6 months.

d. Before use check for clarity; if cloudy, discard and prepare fresh.

## III. PREPARATION OF STANDARDS:

Whenever possible, calibrator and control solutions will be made from a different lot and/or by separate analysts using different pipettes.

### A. Cerilliant Standard Mix or Single Component Standard:

Note: Equivalent reference standards may be substituted if needed. Whenever possible, prepared calibrators and controls should be made from standards from different manufacturers or different lots.

1. Based on the analyte to be quantitated the analyst will prepare a stock solution at the needed concentration. The Unit Lead should be consulted if the analyst is unsure of the appropriate range for the specific drug.
2. When multiple drugs are to be quantitated a mixed standard stock solution can be made.
3. Methanol or other appropriate solvent will be used as the diluent. The volume of standard to be made will be based on the need of the analysis.
4. Document the dilution preparation as part of the batch documentation and in the appropriate standard preparation notebook.
5. Store sealed in a freezer

6. Stable for 6 months when tightly capped.
7. Final concentrations will be dependent on the analyte to be quantitated.
8. A "Working Calibration Solution" can be made by making further dilutions based on the calibration curve required.
9. General Guidance: the dilutions below may be used as guidance for obtaining required concentrations.

Stock Solution

| **Starting Concentration of CRM*** | **Desired Concentration** | **Amount of Standard** | **Solvent** |
|---|---|---|---|
| **1 mg/mL** | 100 µg/mL | **50 µL** | **450 µL** |
| | 50 µg / mL | **25 µL** | **475 µL** |
| **100 µg /mL** | 50 µg / mL | **250 µL** | **250 µL** |
| | | | |

*Certified Reference Material

Working Solutions

| Starting Concentration of Stock Solution | Desired Concentration | Amount of Standard | QS to (with appropriate Solvent) |
|---|---|---|---|
| 100 µg/mL | 5000 ng/ mL | 250 µL | 5 mL |
| 100 µg/mL | 2000 ng/ mL | 100 µL | 5 mL |
| 100 µg/mL | 1000 ng/ mL | 50 µL | 5 mL |
| 50 µg / mL | 1000 ng/ mL | 100 µL | 5 mL |
| 5000 ng/ mL | 1000 ng / mL | 1000 µL | 5 mL |
| 2000 ng/mL | 400 ng /mL | 1000 µL | 5 mL |
| 2000 ng/mL | 200 ng/mL | 500 µL | 5 mL |
| 1000 ng/mL | 100 ng/mL | 500 µL | 5 mL |

| | | | |
| --- | --- | --- | --- |
| 1000 ng/mL | 200 ng/mL | 1000 µL | 5 mL |

**C. <u>Working Internal Standard Mix</u>**

1. It is preferable to have the internal standard response in a range similar to the mid to lower end of the calibration curve.
2. Starting Guide for preparation, this can be adjusted as needed based on the analyte of interest.
    a. To a 50 mL volumetric flask, add 100 µL of each 1 mg/mL Cerilliant reference deuterated standard or 250 µL of each 100 µg / mL deuterated standard (other concentrations may be used as required).
        i. It is desirous to use a deuterated standard of the analyte to be quantitated; however other appropriate deuterated compounds can be used.
    b. Q.S. to 50 mL with methanol.
    c. Store in freezer (≤ -10°C)
    d. Stable for 6 months when tightly capped.
    e. Final concentrations : 2 µg /mL for standards with a starting concentration of 1 mg/mL and 500 ng/mL for standards with a starting concentration of 100 µg /mL

**IV. PREPARATION OF CONTROLS**

Note: Alternative controls, both commercial and in-house, to those listed below may be employed at the analyst's discretion.

A. **<u>In-House Stock Control (Lipomed)</u>:** In-house controls will be used whenever possible.

Note: Equivalent reference standards may substituted if needed. Prepared calibrators and controls should be made from standards from different manufacturers.

1. Based on the analyte to be quantitated the analyst will prepare a stock solution at the needed concentration. The Unit Lead should be consulted if the analyst is unsure of the appropriate range for the specific drug.

2. The chart above may be used as guidance in preparing solutions in the needed concentrations.
3. When multiple drugs are to be quantitated a mixed standard stock solution can be made.
4. Methanol or other appropriate solvent will be used as the diluent. The volume of standard to be made will be based on the need of the analysis.
5. Document the dilution preparation as part of the batch documentation.
6. Store sealed in a freezer
7. Stable for 6 months when tightly capped.
8. Final concentrations will be dependent on the analyte to be quantitated.
9. A 'Working Control Solution" can be made through further dilutions made based on the calibration curve required.

B. **External Controls:** External controls may be used but are not required.

1. External controls may be used. These may come from UTAK or equivalent commercially prepared samples.

C. **Negative Controls**

1. Negative control: Drug-free human urine or drug-free human blood.

## V. PROCEDURE

A. Label clean screw cap tubes appropriately with blank, calibrator, control and case number designations.

B. Prepare calibrator and control samples according to tables below based on the appropriate calibration range for the analyte of interest:

1. Blood Calibrators: prepare using 500 µL of Blank blood spiked with the appropriate volume of calibration solution. (See the chart below).

Note: Calibration curves should be created in a range appropriate to the analyte of interest. Consult the Unit Lead for guidance. A minimum of 4 calibrators should be extracted.

2. In-House Blood Controls: prepare using 500 µL of blank blood spiked with the appropriate volume of stock control solution. (See the chart below).

   Note: A minimum of 2 controls will be used one that is below the mid-point of the curve and one that is above the mid-point of the curve. This is to demonstrate condition at the high and low range of the curve.



| **Starting Concentration** | Desired Concentration (ng/mL) | Volume to Add (µL) | Volume of Blank Blood µL |
| --- | --- | --- | --- |
| **100 ng/ mL** | 5 | **25** | **500** |
| | 10 | **50** | **500** |
| | 100 | **500** | **500** |
| **200 ng / mL** | 10 | **25** | **500** |
| | 20 | **50** | **500** |
| | 100 | **250** | **500** |
| | 200 | **500** | **500** |
| **400 ng/mL** | 20 | **25** | **500** |
| | 100 | **125** | **500** |
| | 200 | **250** | **500** |
| **2000 ng / mL** | 200 | **50** | **500** |
| | 500 | **125** | **500** |
| | 1000 | **250** | **500** |

3. In-House Urine Control :

   The in-house stock solution will be used and the Chart above can be used as guidance in the preparation of these levels.

4. Commercial Controls (optional):

| Control Concentration | Pipette Volume To Add: | Blank Matrix Volume to Add: |
| --- | --- | --- |
| **UTAK dilution x4** | 125 µL | 375 µL |
| **UTAK** | 500 µL | 0 µL |

C. **Blood and Urine sample preparations**

1. Add 0.5 mL case specimen, blood or urine, to appropriate labeled tubes.
2. Add 100 µL of deuterated IS to each tube. (A different volume may be required based on the IS used)
    i. **Urine Total conjugated and unconjugated**

        Note: Not all urines require hydrolysis. The analyst may decide which samples to test for total and free analytes based on the needs of the case.

        1. Add 250 µL of β –Glucuronidase in 0.1M acetate buffer, pH 5.0 to hydrolyze urine
        2. Heat for 3 hours at 60°C in water bath. Cool tubes to room temperature.
3. Add 1 mL of 0.10 M sodium acetate buffer (pH 4.5) to each tube.
    i. **Blood sample preparations:** Add 500 µL DI water to each blood tube.

        Note: Adding 500 µL DI water to urine samples is not detrimental.
4. Cap tubes, then vortex each tube for 10 seconds.
    i. **Blood sample preparations:** Sonicate blood samples for 15 minutes.

    Note: Sonicating urine samples is not detrimental.
5. Centrifuge **all** tubes for 8 min at about 5200 rpm.
6. Place the Trace B extraction columns in the SPE column rack in the appropriate order. Position plastic waste tray labeled “Methanol” underneath SPE column rack.
    i. Condition each column sequentially with 1 mL methanol; drain (≈3 psi) to Solvent “Hazardous Waste” stream

7. Remove plastic waste tray labeled “Methanol” and replace with plastic tray labeled “Biohazardous/Buffers”
8. 1 mL DI water; drain (≈ 3 psi) to “Non-Hazardous” regulated waste stream
9. Carefully transfer the sample to the center of the SPE column. Avoid splashing and/or transferring any sediment found at the bottom of the tube.
10. Wash each SPE column sequentially with:
    i. 1 mL bicarbonate buffer (pH 9.0); drain (≈ 3 psi) to non-hazardous regulated waste stream
    ii. 1 mL DI water; drain (≈ 3 psi) to non-hazardous regulated waste stream
11. Dry the columns for 10 minutes using maximum pressure, between 60-80 psi.
12. During this 10 minute window (or earlier), label autosampler LC vials and place in the appropriate position in the SPE collection rack underneath the corresponding SPE column; prepare the elution solvent.
13. The elution solvent ratio is 80: 18: 2 Dichloromethane: IPA: $NH_4OH$. (Adjust volume prepared for the number of samples, minimize excessive hazardous waste, 2mL needed for each tube)
    i. Add the IPA and $NH_4OH$ together first before adding the dichloromethane portion (following this order prevents unsafe buildup of gases).
14. After 10 minutes, replace plastic waste tray with SPE collection rack containing labeled autosampler vials in order corresponding to SPE columns.
15. Elute column with two 1.0mL aliquots of 80:18:2 Dichloromethane:IPA:$NH_4OH$ into the appropriate autosampler vial. Flow at 2-4 mL/min to optimize recovery.
16. Remove top SPE column rack and transfer collection rack from SPE manifold to sample concentrator.
17. Evaporate all vials to dryness at $<40^{o}$ C.
18. Reconstitute each slotted screw cap vial with 520 µL of 20% methanol in DI water.
19. Inject 10 µL of each sample for LC/MS/MS analysis.

## VI. INSTRUMENT PARAMETERS

### A. LC Parameters

1. Shimadzu Prominence LC-20 System

| | |
|---|---|
| **a. Flow** | 0.6 mL/min |
| **b. Autosampler Temperature** | 15°C |
| **c. Injection Volume** | 10 µL |
| **d. Needle Wash** | 500 µL; before and after aspiration |
| **e. Column** | Kinetex 2.6um Phenyl-Hexyl 100A 50 x 4.6 cm |
| | Manufactured by Phenomenex (Torrance, CA) |
| **f. Oven Temperature** | 40°C |
| **g. Gradient** | |

| Time (min) | Mobile Phase B (Methanol) | Mobile Phase A (0.01% Formic Acid in Water) |
|---|---|---|
| **Initial** | 5% | 95% |
| **2.50** | 45% | 55% |
| **4.50** | 45% | 55% |
| **5.50** | 95% | 5% |
| **7.50** | 95% | 5% |
| **7.51** | 5% | 95% |
| **9.00** | STOP | STOP |
| | | |

**B. M/S Acquisition Parameters**: The following conditions can be adjusted if needed based on availability of gases.

| | |
|---|---|
| Interface | DUIS (APCI and ESI) |
| DL Temperature | 250°C |
| Nebulizing Gas | 2 L/min |
| Drying Gas | 15 L/min |

**C. Transition Ions Monitored and Retention Times**:

Transition ions to be monitored and analyte retention times will be dependent of the analyte(s) of interest. A neat standard should be run prior to performing a calibration on an analyte not previously run by the instrument to determine the retention time and transition ions to be monitored. LabSolutions optimization software will be used.

**D. Detection and Identification**: The analyst will review all chromatography, peak integrations, and transition ion ratios used for identifications.

Determination of the presence of target analytes in the sample extract are identified by appearance and ratio of product ions that are characteristic of each drug at the appropriate retention time. In this manner, both retention time (an LC characteristic) and fragmentation pattern and ratio (an MS characteristic) are used as the basis for qualitative identification. For the identification of an analyte to be made, the retention time of the chromatographic peak must be within 0.1 minute of the corresponding analyte in the calibrator sample as well as having ion ratios that are within the following limits. Initially the neat Cerilliant Standard, diluted as appropriate, will be utilized to set the expected ion ratios, however it is recognized that some ion ratios are concentration dependent. As such, ratios may be set on a case by case basis using a standard with a concentration close to the concentration of the analyte of interest in the case.



| Expected (Set) Ion Ratio | Allowance |
| --- | --- |
| > 50% | 20% |
| 20-50% | 25% |
| < 20% | 30% |

**E. Calibration**: A calibration curve for each drug and metabolite is analyzed with each batch. The calibration correlation coefficient must be ≥ 0.990 when using deuterated internal standards, ≥ 0.98 is acceptable using non deuterated internal standards, or approved by the toxicology Director or Lead. A standard may be removed to attain a correlation coefficient of ≥ 0.990. Following linear regression, reprocessed calibrators generally should be within 20% of their

target value to be included in the final calibration curve used to calculate case samples. Higher percent differences are permitted for calibrators at the limit of quantitation. One calibrator may be dropped from the curve. If the highest calibrator is omitted, samples higher than the next highest calibrator must be diluted or approved by the toxicology Director or Lead to be reported. If the lowest calibrator is omitted, the lower limit of quantitation (LOQ) is the next lowest calibrator value. Calibration for each analysis batch is done independently. The urine control will be quantitated based on the concurrently analyzed standards used to create the blood calibration curve. Calibration is accomplished by the addition of a known amount of analytes in addition to the internal standard into a blank sample of the matrix tested. The response of the system to this calibration defines a run-specific standard curve that is used as the basis for the quantitative calculation in all controls and samples. The system for blood samples is "multi-point calibration, multi-point control."

**F. Quantitation**: Quantitation is accomplished by the comparison of the response ratio of the analyte and the internal standard in a specific sample relative to the response ratios of the calibration curve. The concentration of the analyte in the sample is then extrapolated from the standard curve.

## VII. RESULTS INTERPRETATION

**A. Positive results will be reported only when:**

1. Analyte identification is based on at least two transitions with relative abundances within +/- 20 % of the target, relative to a calibrator.
2. Retention times are within 0.1 min, or +/- 3% relative to a calibrator analyzed in same batch.
3. Qualitative results have at least a 3x signal to noise (S/N) ratio.
4. The integration of the analyte peak has acceptable symmetrical shape and chromatography.
5. All MRMs show peaks at the appropriate retention times.
6. Quality control sample results are acceptable.

## VIII. QUALITY CONTROL

**A. Criteria for Quantitative Results**

1. Statistics will be maintained on all controls.

2. Results must fall within ±20% of the analytes' target concentration.
3. All results are recorded.

**B. Verification of Vial Sequence:** The vial sequence is checked prior to and following injection of samples. These checks will be documented.

**C. Evaluation of Potential Carryover:** Potential Carryover will be determined by a blank sample after the highest calibrator. In addition, a solvent blank will be run after each sample to ensure there is no carryover between samples.

**D. Linearity**: Linearity of the calibration curve is demonstrable in each batch for each analyte as a function of $r^2$ correlation coefficient and quantitative results of control materials.

**E. Sensitivity (LOD, LOQ):** For the purposes of this procedure the limit of quantitation (LOQ) is defined as equal to the lowest concentration of the lowest calibrator. The Limit of Detection (LOD) must have a response of at least 3 times the signal to noise ratio and have acceptable ion ratios.

**F. Specificity:** Specificity is a function of both the resolution of target analyte during the analytical process and the mass spectral fragmentation that analyte molecules undergo during the instrumental analysis.

## IX. QUALITY ASSURANCE

**A. Quality Assurance is provided by the following multi-layer program:**

1. The LC/MS analysis is thoroughly checked by the instrument operator, including vial position on the auto sampler, prior to and following the injection of samples.
2. The LC/MS data is reviewed and signed off by a reviewer distinct from the operator; this review includes an evaluation of qualitative and quantitative (where applicable) results containing:
    a. Control Results
    b. Chromatographic Characteristics
    c. Transcription Errors

1. The reported results are checked against the findings of the run data and during the technical review of case results.
2. The original run is compared to the Final Report during the final technical review, prior to case sign-off.

**X. SOURCES OF ERROR**

It has been established that no known interferences are present in the calibrators/controls. Ion suppression or enhancement and potential interferences from other analytes have not been found for the common drugs and metabolites typically seen in casework.

**XI. References**

A. A Comparison of the Validity of Gas Chromatography-Mass Spectrometry and Liquid Chromatography-Tandem Mass Spectrometry Analysis of Urine Samples for Morphine, Codeine, 6-Acetylmorphine, and Benzoylecgonine; Peter R. Stout, Nichole D. Bynum, John M. Mitchell, Michael R. Baylor and Jeri D. Ropero-Miller; J.Anal Toxicol (2009) 33 (8): 398-408
B. Solid-Phase Extraction Method for Trace B Columns. SPEWARE: Baldwin Park, CA.