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PHARMACEUTICAL AND PERSONAL CARE PRODUCT CARE ANALYSIS

SOLID SAMPLES

PROJECT NAME: URBAN WATERS – ELLIOTT BAY

Contract: 4499
Data Package Identification: DPWG44301

Analysis WG43863, WG43864 & WG44109

23 July 2013

WASHINGTON STATE DEPARTMENT OF ECOLOGY
SOLID SAMPLES

PHARMACEUTICALS AND PERSONAL CARE PRODUCTS ANALYSIS
AXYS METHOD: MLA-075
4499: L19741-1 to -19

Project Name: URBAN WATER – ELLIOTT BAY

25 July 2013

NARRATIVE

This narrative describes the analysis of nineteen solid (marine sediment) samples for the determination of pharmaceutical and personal care products using High Performance Liquid Chromatography coupled with tandem Mass Spectrometry (HPLC- MS/MS).

SAMPLE RECEIPT AND STORAGE

The samples were received on the 7th of June 2013. Details of sample conditions upon receipt are provided on the Sample Receiving forms included with this data package. The samples were stored at -20°C prior to sample preparation, extraction and analysis.

SAMPLE PREPARATION, EXTRACTION AND ANALYSIS

The client samples and QC samples (consisting of a laboratory procedural blank, a laboratory generated reference sample referred to as an 'Ongoing Precision and Recovery' (OPR)) sample and a duplicate sample were analyzed in three analysis batches as WG43863, WG43864 and WG44109. The composition of each analysis batch is shown on the Correlation Table and Batch List forms that accompany the extraction workup sheets included with this data package.

The sample preparation, extraction, instrumental analysis and quantification procedures followed were in accordance with AXYS Method MLA-075: ***Analytical Procedure for the Analysis of Pharmaceutical and Personal Care Products in Solid and Aqueous Samples by LC-MS/MS.*** A method summary (MSU-075) for this method is included with this data package.

An accurately weighed dried sub-sample of each marine sediment sample (between 0.5 and 1 grams) was spiked with surrogate compounds used for target analyte quantification, extracted under acid or alkaline conditions and cleaned up for sample matrix interferences using individual SPE cartridges. The resulting extract was instrumentally analyzed using a Waters 2690 or 2795 HPLC equipped with Micromass Quattro Ultima MS/MS. The instrument and LC conditions used are summarized in the table below.

Target Group	LC Column	Ionization	Acquisition	LC Conditions
List 1	Waters Xtera C18MS (10.0 cm, 2.1 mm i.d., 3.5 µm particle size)	Positive Ion Electrospray	MRM mode, unit resolution	1
List 2	Waters Xtera C18MS (10.0 cm, 2.1 mm i.d., 3.5 µm particle size)	Positive Ion Electrospray	MRM mode, unit resolution	2
List 3	Waters Xtera C18MS (10.0 cm, 2.1 mm i.d., 3.5 µm particle size)	Negative Ion Electrospray	MRM mode, unit resolution	3
List 4	Waters Atlantis HILIC (10.0 cm, 2.1 mm i.d., 3.0 µm particle size)	Positive Ion Electrospray	MRM mode, unit resolution	4
List 5	Waters Xtera C18MS (10.0 cm, 2.1 mm i.d., 3.5 µm particle size)	Positive Ion Electrospray	MRM mode, unit resolution	5

CALCULATION

Target analyte concentrations were determined by isotope dilution or internal standard quantification procedures using MassLynx 4 software. Quantification was conducted by comparing the area of the quantification ion to that of the quantification standard (surrogate) and correcting for response factors.

Linear regression equations with a 1/x weighting fit were determined from a multi-point calibration series prepared alongside the samples. Formulae used to calculate the analyte concentrations are provided in the method summary (MSU-075) included with this data package. Quantification equations for each target analyte are provided in Quantify Compound Summary Report in the Analysis Chromatography section of this data package.

The sample specific detection limit (SDL) was calculated for each target analyte and used as one of the detection qualifiers for the reporting limit (RL). If the software selected an unrepresentative area for the detection limit calculation, the data interpretation chemist or the QA chemist made corrections. If applicable, these corrections were hand noted on the quantification report pages included with the chromatograms.
The reporting limit (RL) was defined as the concentration equivalent to the lowest calibration standard or the SDL, whichever was greater.

REPORTING CONVENTIONS

The AXYS contract number assigned for internal tracking was 4499. The samples were assigned a unique laboratory identifier L19741-X, where X is a numeral. All data reports reference the unique AXYS IDs plus the client sample identifiers.

Any extra work required and performed after the initial instrumental analysis of a sample extract is given an extra "test suffix" code. The single letter code (per extra work performed) is added to the AXYS sample ID as a suffix, and is combined with any other applicable test suffix codes. The extra work codes used to report data in this package include:

(A) = the parent sample for a duplicate pair
R = repeat analysis using a fresh aliquot of sample

The following laboratory qualifier flags were used in this data package:

B = analyte found in the sample and the associated blank
H = result provided as information only; concentration is estimated
MAX = result reported as maximum value due to structural cross interference for compounds
N = authentic recovery is not within method/contract control limits
NQ = data not quantifiable
U = identifies a compound that was not detected
UJ = identifies a compound that was not detected and the detection limit is greater than the lowest calibration equivalent
V = surrogate recovery is not within method/contract control limits
X = results reported separately

The analytical results were reported to three significant figures on a dry mass basis with concentration units of nanograms per gram (ng/g).

QA/QC NOTES

The client samples and QC samples were analyzed in three separate analysis batches (as WG43863, WG43864 and WG44109) with each analysis batch carried intact through the entire analytical process. The sample data were reviewed and evaluated in relation to the batch QC samples.

- Sample analyte concentrations are not blank corrected. The data should be evaluated with consideration of the procedural blank results.

- By virtue of the isotope dilution/internal standard quantification procedures, data are recovery corrected for possible losses during extraction and cleanup.
- Due to the limitation of the software, signal to noise ratio (S/N) was measured as '0' in some cases where even a large peak was present. This has been visually inspected and does not affect the data.
- All linearity, calibration verification, OPR and labeled compound recovery specifications were met with the following exceptions:

Note: Soils/sediments are documented as achieving poorer recoveries than other matrices, however the cause(s) for this is unknown.

List 1 Compounds

WG43863

For the OPR sample (AXYS ID: WG43863-102), the percent recoveries of Oxolinic Acid and Penicillin V were biased high by a lowered instrument response for the surrogate compound 13C3-Trimethoprim used for quantification The results for these compounds were flagged with an 'N' on the report forms. Other data may be similarly affected.

Where the percent recoveries for surrogate compounds fell below 10%, the native analyte was reported in an "information only" capacity and was flagged with an 'H' on the report forms. Where the surrogate percent recovery was observed to be below 1% or did not meet the signal to noise method criteria, the target analytes and the surrogate compound were all deemed to be not quantifiable and were flagged as 'NQ' on the report forms.

The percent recovery of the surrogate compound 13C3-Trimethoprim for the samples 1306020-11, 1306020-15, 1306020-16, 1306020-20, 1306020-30, 1306020-37 and the laboratory procedural blank (AXYS IDs: L19741-7, -8, -9, -12, -14,-18 and WG43863-101) did not meet method criteria and have been flagged with a 'V' on the report forms..

WG44109

For the OPR sample (AXYS ID: WG44109-102), the percent recoveries for several target analytes did not meet method criteria and have been flagged with an 'N' on the report form. Excluding Azithromycin, the same analytes were not detected in any of the field samples. Azithromycin was detected in sample 1306020-07 (AXYS ID: L19741-4); the results may be similarly affected.

Where the percent recoveries for surrogate compounds fell below 10%, the native analyte was reported in an "information only" capacity and was flagged with an 'H' on the report forms. Where the surrogate percent recovery was observed to be below 1% or did not meet the signal to noise method criteria, the target analytes and the surrogate compound were all deemed to be not quantifiable and were flagged as 'NQ' on the report forms.

For some samples, the percent recovery of the surrogate compounds 13C3-Trimethoprim, D5-Fluoxetine and 13C2-Erythromycin-H2O in some samples did not meet method criteria and have been flagged with a 'V' on the report forms.

List 2 Compounds (WG43863)

The target analyte ACTC was detected above the reporting limit for the laboratory procedural blank (AXYS ID: WG43863-101). ACTC was detected in all field samples at a similar concentration with results flagged with a 'B' on the report forms. This should be considered during review and data interpretation.

List 3 Compounds (WG43863)

For the OPR sample (AXYS ID: WG43863-102), the percent recovery of the target analyte Triclosan (132%) was marginally above the upper method criteria limit of (130%) and has been flagged with an 'N' on the report form.

The percent recovery of the surrogate compounds D6-Bisphenol, D6-Gemfibrozil and 13C6-Triclocarban in the laboratory procedural blank, duplicate sample and sample 1306020-36 (AXYS IDs: WG43863-101, -103 and L19741-17 respectively) did not meet method criteria and have been flagged with a 'V' on the report forms. As the isotope dilution method of quantification produces data that are recovery corrected, these variances from method criteria were deemed to not affect the quantification of the target analytes. Percent surrogate recoveries are used as general method performance indicator only.

List 4 Compounds (WG43864)

Clonidine was detected in the laboratory procedural blank (AXYS ID: WG43864-101). The concentrations detected in the client samples should be compared to that of this sample during data review. Where detected, Clonidine was flagged with a 'B' on the report form.

The recovery of multiple surrogates in the several samples did not meet the method criteria; this compound was flagged with a 'V' on the report forms. As the isotope dilution method of quantification produces data that are recovery corrected, these slight variances from the method acceptance criteria were deemed to not affect the quantification of the target analytes. Where the percent recovery for the surrogate compound D3-Cimetidine fell below 10%, the exact associated native analyte was reported in an "information only" capacity and flagged with an 'H' on the report form.

List 5 Compounds (WG43863)

DEET was detected in the laboratory procedural blank (AXYS ID: WG43863-103) at a concentration of 1.54 ng/g. The same analyte was detected in the sample 1306020-19 and duplicate sample (AXYS IDs: L19741-11 and WG43863-103) below or near the same level as the laboratory blank sample. The results were flagged with a 'B' on the report forms. The detection of DEET in the laboratory blank should be considered carefully during data review and interpretation.

For the OPR sample (AXYS ID: WG43863-102), the recovery for Betamethasone was above the upper criteria limit and has been flagged with an 'N' on the report form. The same compound was not detected in any of the field samples.

The recovery of several surrogate compounds in most samples did not meet method criteria and have been flagged with a 'V' on the report forms. As the isotope dilution/internal standard method of quantification produces data that are recovery corrected, the variances from method criteria were deemed to not affect the quantification of the related target analytes. Percent surrogate recoveries are used as general method performance indicator only.

Where the percent recovery of a surrogate compound was below 10%, the exact associated native analyte was reported as "information only" capacity and flagged with an 'H' on the report form. Where the percent recovery for a surrogate compound was below 1% or the instrument response did not meet signal to noise criteria, the associated target analytes were deemed not quantifiable and flagged as 'NQ' on the report forms.

ANALYTICAL DISCUSSION

List 1 Compounds

The results for the initial instrumental analysis of the samples and QC samples (under analysis batch WG43863) did not meet method specifications for some target analytes and surrogate compounds. Accordingly, as remedial action, the entire analysis batch was repeated for this analysis (analysis batch WG44109). With the exception of the target analytes Clinafloxacin, Oxolinic Acid and Penicillin V, the sample and QC sample extracts were instrumentally re-analyzed with overall improvement for data quality; the results were subsequently reported from this data. For Clinafloxacin, Oxolinic Acid and Penicllin V, the initial instrument calibration data did not meet method criteria. As such, the results for these analytes for all client

and QC samples were reported from the original data. Data not reported from analysis batch WG43863 or WG44109 was identified with an 'X' on the report forms. All results reported from the repeat analysis data are indicated with the suffix 'R' added to the AXYS IDs on the report forms.

List 2, 3, 4 and 5 Compounds

No analytical difficulties were encountered.

DATA PACKAGE

This data package has been assigned a unique identifier, DPWG44301, shown on the cover page. Included in this data package following the narrative is the following documentation:

- Method summary
- Method Detection Limits
- Sample 'Cover Page' and 'Correlation Table'
- Sample Receiving Documentation
- RFQQ Request for Qualifications and Quote
- Preparation Logs for Standard Solutions
- Sample Homogenization Records
- Laboratory extraction workup sheets
- Sample data reports (in order of AXYS Sample ID)
- Laboratory QC data reports
- Instrumental QC data reports (organized by analysis date)
- Sample raw data (in order of AXYS Sample ID)
- Laboratory QC raw data
- Instrumental QC raw data (organized by analysis date)
- Unreported raw data

I certify that this data package is in compliance with the terms and conditions of the contract, both technically and for completeness, except for the conditions detailed above. In addition, I certify, that to the best of my knowledge and belief, the data as reported are true and accurate. The following signature, on behalf of AXYS Analytical Services Ltd, authorizes the release of the data contained in this data package.

Signed: Andrew Porat

25-JUL-13
Date Signed

AXYS Analytical Services Ltd.

Summary of AXYS Method MLA-075 Rev 05 Ver 02:

AXYS Method MLA-075: ANALYTICAL PROCEDURES FOR THE ANALYSIS OF PHARMACEUTICAL AND PERSONAL CARE PRODUCTS IN SOLID, AQUEOUS AND TISSUE SAMPLES BY LC-MS/MS

This method is suitable for the determination of a suite of pharmaceutical and personal care compounds in solid and aqueous samples (Lists 1, 2, 3, 4, 5 and 6) and in tissue samples (Lists 1, 3, 4, 5 and 6) samples. The analysis requires extraction at two different pH conditions: basic extraction for analysis of List 4 analytes and acidic extraction for the analysis of List 1, 2, 3, 5 and 6 analytes.

Target Analytes

List 1 (Acid extraction, positive ESI)	
Acetaminophen	Norfloxacin
Ampicillin [1]	Norgestimate
Azithromycin	Ofloxacin
Caffeine	Ormetoprim
Carbadox	Oxacillin [1]
Carbamazepine	Oxolinic acid
Cefotaxime	Penicillin G [1]
Ciprofloxacin [1]	Penicillin V
Clarithromycin	Roxithromycin
Clinafloxacin	Sarafloxacin
Cloxacillin	Sulfachloropyridazine
Dehydronifedipine	Sulfadiazine
Digoxigenin	Sulfadimethoxine
Digoxin	Sulfamerazine
Diltiazem	Sulfamethazine
1,7-Dimethylxanthine	Sulfamethizole
Diphenhydramine	Sulfamethoxazole
Enrofloxacin	Sulfanilamide
Erythromycin	Sulfathiazole
Flumequine	Thiabendazole
Fluoxetine	Trimethoprim
Lincomycin	Tylosin
Lomefloxacin	Virginiamycin M1
Miconazole	

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List 2 (Tetracyclines, positive ESI)	
Anhydrochlortetracycline (ACTC)	4-Epichlortetracycline (ECTC)
Anhydrotetracycline (ATC)	4-Epioxytetracycline (EOTC)
Chlortetracycline (CTC)	4-Epitetracycline (ETC)
Demeclocycline	Isochlortetracycline (ICTC)
Doxycycline	Minocycline
4-Epianhydrochlortetracycline (EACTC)	Oxytetracycline (OTC)
4-Epianhydrotetracycline (EATC)	Tetracycline (TC)
List 3 (Acid extraction, negative ESI)	
Bisphenol A	2-hydroxy-ibuprofen
Furosemide	Ibuprofen
Gemfibrozil	Naproxen
Glipizide	Triclocarban
Glyburide	Triclosan
Hydrochlorothiazide	Warfarin
List 4 (Base extraction, positive ESI)	
Albuterol	Cotinine
Amphetamine	Enalapril
Atenolol	Hydrocodone
Atorvastatin	Metformin
Cimetidine	Oxycodone
Clonidine	Ranitidine
Codeine	Triamterene
List 5 (Acid Extraction, positive ESI)	
Alprazolam	Metoprolol
Amitriptyline	Norfluoxetine
Amlodipine	Norverapamil
Benzoylecgonine	Paroxetine
Benztropine	Prednisolone
Betamethasone	Prednisone
Cocaine	Promethazine
DEET (N,N-diethyl-m-toluamide)	Propoxyphene
Desmethyldiltiazem	Propranolol
Diazepam	Sertraline
Fluocinonide	Simvastatin
Fluticasone propionate	Theophylline

Hydrocortisone	Trenbolone
10-hydroxy-amitriptyline	Trenbolone acetate
Meprobamate	Valsartan
Methylprednisolone	Verapamil
List 6 (Acid Extraction, positive ESI)	
Amsacrine	Iopamidol
Azathioprine	Lomustine
Busulfan	Medroxyprogesterone acetate
Carmustine	Melphalan
Chloramphenicol	Metronidazole
Citalopram	Moxifloxacin [2]
Clotrimazole	Norethindrone
Colchicine	Oxazepam
Cyclophosphamide	Rosuvastatin
Daunorubicin	Tamoxifen
Diatrizoic acid	Teniposide
Doxorubicin	Venlafaxine
Drospirenone	Zidovudine
Etoposide	

[1] Analysis result is classified as 'information value' of estimated concentration.
[2] Moxifloxacin in solid samples is classified as 'information value' of estimated concentration.

EXTRACTION

The analysis requires extraction at two different pH conditions: at pH 10 for analysis of fourteen analytes (List 4); and at pH 2.0 for the analysis of the other analytes (Lists 1, 2, 3, 5 and 6). Prior to extraction and/or clean-up, samples are adjusted to the required pH and spiked with surrogates.

Solid samples are extracted by sonication with aqueous buffered acetonitrile and with pure acetonitrile, concentrated by rotary evaporation, and diluted with ultra pure water to 200 mL. The acidic extract is treated with EDTA. The extracts are filtered, cleaned up by solid phase extraction (SPE), and analyzed by LC/ESI-MS/MS in positive and negative ionization modes requiring a total of five runs to for the complete list of analytes.

All aqueous samples are filtered and the aqueous portion is cleaned up by solid phase extraction before analysis by LC/ESI-MS/MS.

Aqueous samples with no or limited visible particulate (e.g. surface water, ground water, wastewater treatment final effluent, typically with <100 mg/L TSS) normally can be processed with up to 1L samples sizes. The sample is filtered and routinely only the aqueous phase is analyzed. However, upon specific agreement a separate extraction may be performed on the solids phase. The solids extract may in this case either be carried through the analysis

individually as a separate sample that is reported separately, or the aqueous extract and the solids extract may be combined just prior to clean-up and reported as a combined aqueous/solids phase result.

For mixed phase aqueous/solids samples with significant solids and distinct aqueous and solids phases such as wastewater influent or process streams the sample may either be analyzed as an aqueous phase only or as two separate samples, one aqueous and one solid.

COLUMN CHROMATOGRAPHY CLEANUP

Extracts are cleaned up during the SPE extraction.

INSTRUMENTAL ANALYSIS

Analysis of the sample extract is performed on a high performance liquid chromatograph coupled to a triple quadrupole mass spectrometer. The LC/MS/MS is run in MRM (Multiple Reaction Monitoring) mode and quantification is performed by recording the peak areas of the applicable parent ion/daughter ion transitions. Some analytes are analyzed in the ESI positive mode and some are analyzed in the ESI negative mode.

Analytes, Ions and Quantification References

List 1 – Acid Extraction, Positive Electrospray Ionization (+)ESI

Target Analyte	Typical Retention Time (min)	Typical RRT	RRT Reference	Parent Ion Mass	Daughter Ion Mass	Quantified against
Sulfanilamide	2.02	0.432	$^{13}C_2$,^{15}N-Acetaminophen	190.0	155.8	$^{13}C_6$-Sulfamethazine
Acetaminophen	4.68	1.000	$^{13}C_2$,^{15}N-Acetaminophen	152.2	110.0	$^{13}C_2$,^{15}N-Acetaminophen
Sulfadiazine	5.32	1.137	$^{13}C_2$,^{15}N-Acetaminophen	251.2	156.1	$^{13}C_6$-Sulfamethazine
1,7-Dimethylxanthine	7.02	0.753	$^{13}C_3$-Caffeine	181.2	124.0	$^{13}C_3$-Caffeine
Sulfathiazole	8.00	0.858	$^{13}C_3$-Caffeine	256.3	156.0	$^{13}C_6$-Sulfamethoxazole
Sulfamerazine	8.78	0.942	$^{13}C_3$-Caffeine	265.0	156.0	$^{13}C_6$-Sulfamethazine
Caffeine	9.32	1.000	$^{13}C_3$-Caffeine	195.0	138.0	$^{13}C_3$-Caffeine
Lincomycin	9.47	0.953	$^{13}C_3$-Trimethoprim	407.2	126.0	$^{13}C_3$-Trimethoprim
Trimethoprim	9.94	1.000	$^{13}C_3$-Trimethoprim	291.2	230.0	$^{13}C_3$-Trimethoprim
Sulfamethizole	10.09	0.983	$^{13}C_6$-Sulfamethazine	271.0	156.0	$^{13}C_6$-Sulfamethoxazole
Cefotaxime	10.09	1.015	$^{13}C_3$-Trimethoprim	456.4	396.1	$^{13}C_3$-Trimethoprim
Sulfamethazine	10.31	1.000	$^{13}C_6$-Sulfamethazine	279.0	156.0	$^{13}C_6$-Sulfamethazine
Ofloxacin	10.53	0.974	$^{13}C_3$,^{15}N-Ciprofloxacin	362.2	318.0	$^{13}C_3$,^{15}N-Ciprofloxacin
Carbadox	10.53	1.005	d_6-Thiabendazole	263.2	231.2	$^{13}C_3$-Trimethoprim
Ormetoprim	10.53	1.059	$^{13}C_3$-Trimethoprim	275.3	259.1	$^{13}C_3$-Trimethoprim
Norfloxacin	10.59	0.980	$^{13}C_3$,^{15}N-Ciprofloxacin	320.0	302.0	$^{13}C_3$,^{15}N-Ciprofloxacin
Thiabendazole	10.59	1.000	d_6-Thiabendazole	202.1	175.1	d_6-Thiabendazole
Ciprofloxacin	10.81	1.000	$^{13}C_3$,^{15}N-Ciprofloxacin	332.2	314.2	$^{13}C_3$,^{15}N-Ciprofloxacin
Sulfachloropyridazine	10.97	1.069	$^{13}C_6$-Sulfamethazine	285.0	156.0	$^{13}C_6$-Sulfamethazine
Lomefloxacin	11.14	1.031	$^{13}C_3$,^{15}N-Ciprofloxacin	352.2	308.1	$^{13}C_3$,^{15}N-Ciprofloxacin
Enrofloxacin	11.22	1.038	$^{13}C_3$,^{15}N-Ciprofloxacin	360.2	316.0	$^{13}C_3$,^{15}N-Ciprofloxacin
Sulfamethoxazole	11.33	1.000	$^{13}C_6$-Sulfamethoxazole	254.0	156.0	$^{13}C_6$-Sulfamethoxazole
Sarafloxacin	11.84	1.095	$^{13}C_3$,^{15}N-Ciprofloxacin	386.1	299.0	$^{13}C_3$,^{15}N-Ciprofloxacin
Clinafloxacin	12.04	1.059	$^{13}C_6$-Sulfamethoxazole	366.3	348.1	$^{13}C_3$,^{15}N-Ciprofloxacin
Digoxigenin	12.68	1.115	$^{13}C_6$-Sulfamethoxazole	391.2	355.2	$^{13}C_3$-Trimethoprim
Oxolinic Acid	13.11	0.819	$^{13}C_3$-Atrazine	262.1	244.0	$^{13}C_3$-Trimethoprim
Sulfadimethoxine	13.33	1.172	$^{13}C_6$-Sulfamethoxazole	311.0	156.0	$^{13}C_6$-Sulfamethoxazole
Azithromycin	13.55	0.846	$^{13}C_3$-Atrazine	749.9	591.6	$^{13}C_3$-Trimethoprim
Penicillin G	14.46	0.903	$^{13}C_3$-Atrazine	367.1	159.9	$^{13}C_3$-Trimethoprim
Diphenhydramine	14.57	0.910	$^{13}C_3$-Atrazine	256.2	167.0	$^{13}C_3$-Trimethoprim
Ampicillin	14.68	0.917	$^{13}C_3$-Atrazine	350.3	160.2	$^{13}C_3$-Trimethoprim

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Flumequine	15.25	0.953	$^{13}C_3$-Atrazine	262.0	173.7	$^{13}C_3$-Trimethoprim
Penicillin V	15.29	0.955	$^{13}C_3$-Atrazine	383.2	159.9	$^{13}C_3$-Trimethoprim
Diltiazem	15.34	0.958	$^{13}C_3$-Atrazine	415.5	178.0	$^{13}C_3$-Trimethoprim
Carbamazepine	15.38	1.007	d_{10}-Carbamazepine	237.4	194.2	d_{10}-Carbamazepine
Erythromycin [1]	15.94	1.000	$^{13}C_2$-Erythromycin	734.4	158	not quantified
Oxacillin	16.30	1.018	$^{13}C_3$-Atrazine	434.1	160.2	$^{13}C_3$-Trimethoprim
Tylosin	16.37	1.022	$^{13}C_3$-Atrazine	916.6	772.5	$^{13}C_6$-Sulfamethazine
Digoxin	16.58	1.036	$^{13}C_3$-Atrazine	798.5	651.3	$^{13}C_3$-Trimethoprim
Dehydronifedipine	16.65	0.981	d_5-Fluoxetine	345.1	284.1	$^{13}C_3$-Trimethoprim
Cloxacillin	16.82	0.991	d_5-Fluoxetine	468.1	160.1	$^{13}C_3$-Trimethoprim
Erythromycin anhydrate [1]	16.90	1.000	$^{13}C_2$-Erythromycin anhydrate	716.4	158	$^{13}C_2$-Erythromycin anhydrate
Fluoxetine	16.97	1.000	d_5-Fluoxetine	310.1	148.0	d_5-Fluoxetine
Virginiamycin M1	17.40	1.025	d_5-Fluoxetine	526.3	508.3	$^{13}C_3$-Trimethoprim
Clarithromycin	17.61	1.038	d_5-Fluoxetine	748.9	158.2	$^{13}C_6$-Sulfamethazine
Roxithromycin	17.83	1.051	d_5-Fluoxetine	837.6	679.0	$^{13}C_6$-Sulfamethazine
Miconazole	20.93	1.233	d_5-Fluoxetine	417.0	161.0	$^{13}C_3$-Trimethoprim
Norgestimate	21.80	1.285	d_5-Fluoxetine	370.5	124.0	$^{13}C_3$-Trimethoprim
Surrogate Standard						
$^{13}C_2$,^{15}N-Acetaminophen	4.68	0.292	$^{13}C_3$-Atrazine	155.2	111.0	$^{13}C_3$-Atrazine
$^{13}C_3$-Caffeine	9.32	0.582	$^{13}C_3$-Atrazine	198.0	140.0	$^{13}C_3$-Atrazine
$^{13}C_3$-Trimethoprim	9.94	0.621	$^{13}C_3$-Atrazine	294.2	233.0	$^{13}C_3$-Atrazine
$^{13}C_6$-Sulfamethazine	10.26	0.641	$^{13}C_3$-Atrazine	285.1	162.1	$^{13}C_3$-Atrazine
d_6-Thiabendazole	10.48	0.655	$^{13}C_3$-Atrazine	208.1	180.1	$^{13}C_3$-Atrazine
$^{13}C_3$,^{15}N-Ciprofloxacin	10.81	0.675	$^{13}C_3$-Atrazine	336.1	318.2	$^{13}C_3$-Atrazine
$^{13}C_6$-Sulfamethoxazole	11.37	0.710	$^{13}C_3$-Atrazine	260.0	162.0	$^{13}C_3$-Atrazine
d_{10}-Carbamazepine	15.28	0.954	$^{13}C_3$-Atrazine	247	204	$^{13}C_3$-Atrazine
$^{13}C_2$-Erythromycin [1]	15.86	0.991	$^{13}C_3$-Atrazine	736.4	160.0	monitor for less than 5%
$^{13}C_2$-Erythromycin anhydrate [1]	16.90	1.056	$^{13}C_3$-Atrazine	718.4	160.0	$^{13}C_3$-Atrazine
d_5-Fluoxetine	16.97	1.060	$^{13}C_3$-Atrazine	315.3	153.0	$^{13}C_3$-Atrazine
Recovery Standard						
$^{13}C_3$-Atrazine	16.01	1.000		219.1	176.9	External Standard

[1] Because of intramolecular dehydration during the analytical procedure erythromycin is quantified as the dehydration product "erythromycin – H_2O". The peak area of the $^{13}C_2$-Erythromycin is monitored and must be less than 5% of the $^{13}C_2$-Erythromycin - H_2O peak area. If it is greater, the Erythromycin - H_2O result is flagged as 'accuracy unknown'.

List 2 – Acid Extraction, Positive Electrospray Ionization (+)ESI

Target Analyte	Typical Retention Time (min)	Typical RRT	RRT Reference	Parent Ion Mass	Daughter Ion Mass	Quantified against
Minocycline	3.45	0.739	d_6-Thiabendazole	458.0	441.0	d_6-Thiabendazole
Epitetracycline (ETC)	5.71	1.223	d_6-Thiabendazole	445.2	410.2	d_6-Thiabendazole
Epioxytetracycline (EOTC)	6.51	1.394	d_6-Thiabendazole	461.2	426.2	d_6-Thiabendazole
Oxytetracycline (OTC)	7.29	1.561	d_6-Thiabendazole	461.2	426.2	d_6-Thiabendazole
Tetracycline (TC)	7.74	1.657	d_6-Thiabendazole	445.2	410.2	d_6-Thiabendazole
Demeclocycline	9.63	0.470	$^{13}C_3$-Atrazine	465.0	430.0	d_6-Thiabendazole
Epichlortetracycline (ECTC)	9.92	0.485	$^{13}C_3$-Atrazine	479.0	444.0	d_6-Thiabendazole
Isochlortetracycline (ICTC) [1]	9.95	0.486	$^{13}C_3$-Atrazine	479.0	462.0	d_6-Thiabendazole
Chlortetracycline (CTC)	11.90	0.581	$^{13}C_3$-Atrazine	479.0	444.0	d_6-Thiabendazole
Doxycycline	14.40	0.703	$^{13}C_3$-Atrazine	445.2	428.2	d_6-Thiabendazole
Epianhydrotetracycline (EATC)	15.08	0.737	$^{13}C_3$-Atrazine	427.2	409.8	d_6-Thiabendazole
Anhydrotetracycline (ATC)	16.45	0.804	$^{13}C_3$-Atrazine	427.2	409.8	d_6-Thiabendazole
Epianhydrochlortetracycline (EACTC)	18.90	0.923	$^{13}C_3$-Atrazine	461.2	444.0	d_6-Thiabendazole
Anhydrochlortetracycline (ACTC)	20.63	1.008	$^{13}C_3$-Atrazine	461.2	444.0	d_6-Thiabendazole
Surrogate Standard						
d_6-Thiabendazole	4.67	0.228	$^{13}C_3$-Atrazine	208.0	180.0	$^{13}C_3$-Atrazine
Recovery Standard						
$^{13}C_3$-Atrazine	20.51	1.000		219.1	176.9	External Standard

[1] The presence of ECTC will create positive interference with ICTC due to use of a common transition ion.

List 3 – Acid Extraction, Negative Electrospray Ionization (-)ESI

Target Analyte	Typical Retention Time (min)	Typical RRT	RRT Reference	Parent Ion Mass	Daughter Ion Mass	Quantified against
Hydrochlorathiazide	2.24	0.440	$^{13}C_6$-2,4,5-T	296.0	268.8	^{13}C-d_3-Naproxen
Hydrochlorathiazide*	2.24	0.440	$^{13}C_6$-2,4,5-T	296.0	204.8	^{13}C-d_3-Naproxen
Furosemide	3.19	0.627	$^{13}C_6$-2,4,5-T	329.0	204.7	^{13}C-d_3-Naproxen
Furosemide*	3.19	0.627	$^{13}C_6$-2,4,5-T	329.0	284.8	^{13}C-d_3-Naproxen
2-hydroxy-ibuprofen	4.10	0.806	$^{13}C_6$-2,4,5-T	221.1	176.8	$^{13}C_3$-Ibuprofen
Glipizide	6.68	1.008	d11-Glipizide	444.2	319.0	d11-Glipizide
Glipizide*	6.68	1.008	d11-Glipizide	444.2	169.8	d11-Glipizide
Naproxen	6.68	1.000	^{13}C-d_3-Naproxen	228.9	168.6	^{13}C-d_3-Naproxen
Bisphenol A	6.77	1.007	d6-Bisphenol A	227.0	211.9	d6-Bisphenol A
Bisphenol A*	6.77	1.007	d6-Bisphenol A	227.0	132.9	d6-Bisphenol A
Warfarin	7.00	1.007	d_5-Warfarin	307.0	161.0	d_5-Warfarin
Glyburide	8.40	1.010	d3-Glyburide	492.1	169.8	d3-Glyburide
Glyburide*	8.40	1.010	d3-Glyburide	492.1	367.0	d3-Glyburide
Ibuprofen	8.48	1.000	$^{13}C_3$-Ibuprofen	205.1	161.1	$^{13}C_3$-Ibuprofen
Gemfibrozil	9.35	1.000	d_6-Gemfibrozil	249.0	121.0	d_6-Gemfibrozil
Triclocarban	9.46	0.997	$^{13}C_6$-Triclocarban	312.9	159.7	$^{13}C_6$-Triclocarban
Triclosan	9.60	1.000	$^{13}C_{12}$-Triclosan	286.8	35.0	$^{13}C_{12}$-Triclosan
Surrogate Standard						
d_{11}-Glipizide	6.63	1.303	$^{13}C_6$-2,4,5-T	455.0	319.0	$^{13}C_6$-2,4,5-T
d_{11}-Glipizide*	6.63	1.303	$^{13}C_6$-2,4,5-T	455.0	169.8	$^{13}C_6$-2,4,5-T
^{13}C-d_3-Naproxen	6.68	1.312	$^{13}C_6$-2,4,5-T	232.9	168.6	$^{13}C_6$-2,4,5-T
d_6-Bisphenol A	6.72	1.320	$^{13}C_6$-2,4,5-T	233.0	214.8	$^{13}C_6$-2,4,5-T
d_6-Bisphenol A*	6.72	1.320	$^{13}C_6$-2,4,5-T	233.0	137.8	$^{13}C_6$-2,4,5-T
d_5-Warfarin	6.95	1.365	$^{13}C_6$-2,4,5-T	312	161.0	$^{13}C_6$-2,4,5-T
d_3-Glyburide	8.32	1.635	$^{13}C_6$-2,4,5-T	495.0	169.9	$^{13}C_6$-2,4,5-T
d_3-Glyburide*	8.32	1.635	$^{13}C_6$-2,4,5-T	495.0	370.1	$^{13}C_6$-2,4,5-T
$^{13}C_3$-Ibuprofen	8.48	1.666	$^{13}C_6$-2,4,5-T	208.2	163.1	$^{13}C_6$-2,4,5-T
d_6-Gemfibrozil	9.35	1.837	$^{13}C_6$-2,4,5-T	255	121	$^{13}C_6$-2,4,5-T
$^{13}C_6$-Triclocarban	9.49	1.864	$^{13}C_6$-2,4,5-T	318.9	159.7	$^{13}C_6$-2,4,5-T
$^{13}C_{12}$-Triclosan	9.60	1.886	$^{13}C_6$-2,4,5-T	298.8	35	$^{13}C_6$-2,4,5-T

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Recovery Standard						
$^{13}C_6$-2,4,5-Trichlorophenoxy-acetic acid ($^{13}C_6$-2,4,5-T)	5.09	1.000		258.8	200.7	External Standard

* Indicates secondary transition for possible diagnostic use.

List 4 – Base Extraction, Positive Electrospray Ionization (+)ESI

Target Analyte	Typical Retention Time (min)	Typical RRT	RRT Reference	Parent Ion Mass	Daughter Ion Mass	Quantified against
Atorvastatin	3.84	0.934	d3-Cotinine	559.3	440.0	d5-Enalapril
Atorvastatin*	3.84	0.934	d3-Cotinine	559.3	466.0	d5-Enalapril
Cotinine	4.11	1.000	d3-Cotinine	177.0	98.0	d3-Cotinine
Cimetidine	4.84	0.994	d3-Cimetidine	253.1	159.0	d3-Cimetidine
Triamterene	5.35	1.099	d3-Cimetidine	254.1	236.9	d4-Clonidine
Triamterene*	5.35	1.099	d3-Cimetidine	254.1	103.7	d4-Clonidine
Enalapril	6.52	1.000	d5-Enalapril	377.2	233.9	d5-Enalapril
Enalapril*	6.52	1.000	d5-Enalapril	377.2	159.8	d5-Enalapril
Oxycodone	6.70	0.953	d6-Oxycodone	316.2	240.9	d6-Oxycodone
Oxycodone*	6.70	0.953	d6-Oxycodone	316.2	298.0	d6-Oxycodone
Clonidine	6.75	0.985	d4-Clonidine	230.0	43.9	d4-Clonidine
Clonidine*	6.75	0.985	d4-Clonidine	230.0	212.5	d4-Clonidine
Amphetamine	8.12	1.000	d5-Amphetamine	136.1	90.8	d5-Amphetamine
Amphetamine*	8.12	1.000	d5-Amphetamine	136.1	118.9	d5-Amphetamine
Albuterol	8.31	0.989	d_3-Albuterol	240.0	148.0	d_3-Albuterol
Codeine	8.56	0.985	d6-Codeine	300.2	214.9	d6-Codeine
Hydrocodone	8.75	0.972	d3-Hydrocodone	300.2	198.8	d3-Hydrocodone
Hydrocodone*	8.75	0.972	d3-Hydrocodone	300.2	170.6	d3-Hydrocodone
Ranitidine	8.81	0.985	d7-Atenolol	315.0	175.9	d_3-Albuterol
Atenolol	8.88	0.993	d7-Atenolol	267.2	144.7	d7-Atenolol
Atenolol*	8.88	0.993	d7-Atenolol	267.2	189.7	d7-Atenolol
Metformin	9.56	1.000	d_6-Metformin	130.1	60.1	d_6-Metformin
Surrogate Standards						
d_3-Cotinine	4.11	0.530	d3-Amitriptyline	180.0	79.9	d3-Amitriptyline
d_3-Cotinine*	4.11	0.530	d3-Amitriptyline	180.0	101.0	d3-Amitriptyline
d_3-Cimetidine	4.87	0.628	d3-Amitriptyline	256.0	161.8	d3-Amitriptyline
d_3-Cimetidine*	4.87	0.628	d3-Amitriptyline	256.0	94.8	d3-Amitriptyline
d_5-Enalapril	6.52	0.841	d3-Amitriptyline	382.0	238.8	d3-Amitriptyline
d_5-Enalapril*	6.52	0.841	d3-Amitriptyline	382.0	164.8	d3-Amitriptyline
d_4-Clonidine	6.85	0.884	d3-Amitriptyline	234.0	47.9	d3-Amitriptyline
d_4-Clonidine*	6.85	0.884	d3-Amitriptyline	234.0	216.7	d3-Amitriptyline

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d_6-Oxycodone	7.03	0.907	d3-Amitriptyline	322.1	262.0	d3-Amitriptyline
d_6-Oxycodone*	7.03	0.907	d3-Amitriptyline	322.1	304.1	d3-Amitriptyline
d_5-Amphetamine	8.12	1.048	d3-Amitriptyline	141.1	92.9	d3-Amitriptyline
d_5-Amphetamine*	8.12	1.048	d3-Amitriptyline	141.1	123.9	d3-Amitriptyline
d_3-Albuterol	8.40	1.084	d3-Amitriptyline	243.0	151.0	d3-Amitriptyline
d_6-Codeine	8.69	1.121	d3-Amitriptyline	306.0	217.9	d3-Amitriptyline
d_6-Codeine*	8.69	1.121	d3-Amitriptyline	306.0	151.8	d3-Amitriptyline
d_7-Atenolol	8.94	1.154	d3-Amitriptyline	274.0	144.7	d3-Amitriptyline
d_7-Atenolol*	8.94	1.154	d3-Amitriptyline	274.0	189.7	d3-Amitriptyline
d_3-Hydrocodone	9.00	1.161	d3-Amitriptyline	303.1	198.9	d3-Amitriptyline
d_3-Hydrocodone*	9.00	1.161	d3-Amitriptyline	303.1	170.8	d3-Amitriptyline
d_6-Metformin	9.56	1.234	d3-Amitriptyline	136.1	60.1	d3-Amitriptyline
Recovery Standards						
d_3-Amitriptyline	7.75	1.000		281.0	232.7	External Standard
d_3-Amitriptyline*	7.75	1.000		281.0	90.7	External Standard
d_9-Albuterol	8.40	1.000		249	148.3	External Standard
d_9-Albuterol*	8.40	1.000		249	167	External Standard

* Indicates secondary transition for possible diagnostic use.

List 5 – Acid Extraction, Positive Electrospray Ionization (+)ESI

Target Analyte	Typical Retention Time (min)	Typical RRT		Parent Ion Mass	Daughter Ion Mass	Quantified against
Theophylline	2.52	1.000	$^{13}C,^{15}N_2$-Theophylline	181.1	123.8	$^{13}C,^{15}N_2$-Theophylline
Theophylline*	2.52	1.000	$^{13}C,^{15}N_2$-Theophylline*	181.1	95.8	$^{13}C,^{15}N_2$-Theophylline*
Benzoylecgonine	5.48	1.028	d8-Benzoylecgonine	290.1	167.8	d8-Benzoylecgonine
Benzoylecgonine*	5.48	1.028	d8-Benzoylecgonine	290.1	104.8	d8-Benzoylecgonine
Metoprolol	8.13	1.009	d7-Metoprolol	268.2	190.7	d7-Metoprolol
Metoprolol*	8.13	1.009	d7-Metoprolol	268.2	115.7	d7-Metoprolol
Cocaine	8.74	1.000	d3-Cocaine	304.1	181.8	d3-Cocaine
Cocaine*	8.74	1.000	d3-Cocaine	304.1	81.9	d3-Cocaine
Meprobamate	11.09	0.785	d7-Propranolol	219.0	157.8	d7-Metoprolol
Meprobamate*	11.09	0.785	d7-Propranolol	219.0	96.9	d7-Metoprolol
10-hydroxy-amitriptyline	11.70	0.829	d7-Propranolol	294.2	215.0	d7-Propranolol
10-hydroxy-amitriptyline*	11.70	0.829	d7-Propranolol	294.2	276.0	d7-Propranolol
Propranolol	14.35	1.016	d7-Propranolol	260.2	115.8	d7-Propranolol
Propranolol*	14.35	1.016	d7-Propranolol	260.2	182.7	d7-Propranolol
Prednisone	16.47	0.953	d4-Hydrocortisone	359.2	341.0	d7-Propranolol
Prednisone*	16.47	0.953	d4-Hydrocortisone	359.2	146.7	d7-Propranolol
Hydrocortisone	17.29	1.000	d4-Hydrocortisone	363.2	120.7	d4-Hydrocortisone
Hydrocortisone*	17.29	1.000	d4-Hydrocortisone	363.2	326.7	d4-Hydrocortisone
Prednisolone	17.29	1.000	d4-Hydrocortisone	361.2	343.0	d7-Propranolol
Prednisolone*	17.29	1.000	d4-Hydrocortisone	361.2	324.7	d7-Propranolol
Promethazine	18.39	1.008	d4-Promethazine	285.1	197.8	d4-Promethazine
Promethazine*	18.39	1.008	d4-Promethazine	285.1	85.7	d4-Promethazine
Desmethyldiltiazem	18.53	1.016	d4-Promethazine	401.2	177.8	d4-Promethazine
Desmethyldiltiazem*	18.53	1.016	d4-Promethazine	401.2	149.5	d4-Promethazine
Paroxetine	20.28	1.007	d6-Paroxetine	330.2	191.8	d6-Paroxetine
Paroxetine*	20.28	1.007	d6-Paroxetine	330.2	69.8	d6-Paroxetine
DEET	20.63	1.014	d7-DEET	192.0	118.6	d7-DEET
DEET	20.63	1.014	d7-DEET	192.0	90.7	d7-DEET
Norverapamil	20.63	1.014	d7-DEET	441.3	164.7	d7-Propranolol
Norverapamil*	20.63	1.014	d7-DEET	441.3	149.7	d7-Propranolol
Verapamil	21.16	0.994	d3-Methylprednisolone	455.3	164.8	d6-Amitriptyline
Verapamil*	21.16	0.994	d3-Methylprednisolone	455.3	149.8	d6-Amitriptyline
Betamethasone	21.29	0.967	d6-Amitriptyline	393.2	355.1	d6-Amitriptyline

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Betamethasone*	21.29	0.967	d6-Amitriptyline	393.2	373.0	d6-Amitriptyline
Methylprednisolone	21.29	1.000	d3-Methylprednisolone	375.2	357.0	d3-Methylprednisolone
Methylprednisolone*	21.29	1.000	d3-Methylprednisolone	375.2	339.0	d3-Methylprednisolone
Propoxyphene	21.56	1.006	d5-Propoxyphene	340.2	57.9	d5-Propoxyphene
Propoxyphene*	21.56	1.006	d5-Propoxyphene	340.2	266.1	d5-Propoxyphene
Amitriptyline	22.02	1.000	d6-Amitriptyline	278.2	232.8	d6-Amitriptyline
Amitriptyline*	22.02	1.000	d6-Amitriptyline	278.2	90.7	d6-Amitriptyline
Trenbolone	22.02	1.000	d6-Amitriptyline	271.2	198.7	d5-Alprazolam
Trenbolone*	22.02	1.000	d6-Amitriptyline	271.2	252.8	d5-Alprazolam
Benztropine	22.55	1.000	d3-Benztropine	308.2	166.7	d3-Benztropine
Benztropine*	22.55	1.000	d3-Benztropine	308.2	151.7	d3-Benztropine
Alprazolam	23.08	1.011	d5-Alprazolam	309.1	280.9	d5-Alprazolam
Alprazolam*	23.08	1.011	d5-Alprazolam	309.1	204.9	d5-Alprazolam
Amlodipine	23.40	0.962	d5-Norfluoxetine	409.1	237.8	d5-Norfluoxetine
Amlodipine*	23.40	0.962	d5-Norfluoxetine	409.1	293.8	d5-Norfluoxetine
Norfluoxetine	24.39	1.002	d5-Norfluoxetine	296.1	133.7	d5-Norfluoxetine
Sertraline	25.87	0.897	d5-Diazepam	306.1	274.8	d7-Propranolol
Sertraline*	25.87	0.897	d5-Diazepam	306.1	158.7	d7-Propranolol
Diazepam	29.14	1.011	d5-Diazepam	285.1	192.8	d5-Diazepam
Diazepam*	29.14	1.011	d5-Diazepam	285.1	153.8	d5-Diazepam
Valsartan	31.92	1.107	d5-Diazepam	436.2	235.0	d5-Propoxyphene
Valsartan*	31.92	1.107	d5-Diazepam	436.2	291.0	d5-Propoxyphene
Fluocinonide	34.90	1.211	d5-Diazepam	495.2	337.0	d5-Alprazolam
Fluocinonide*	34.90	1.211	d5-Diazepam	495.2	475.0	d5-Alprazolam
Trenbolone acetate	37.27	1.293	d5-Diazepam	313.2	253.0	d5-Alprazolam
Trenbolone acetate*	37.27	1.293	d5-Diazepam	313.2	271.0	d5-Alprazolam
Fluticasone propionate	37.74	1.309	d5-Diazepam	501.2	293.0	d7-Metoprolol
Fluticasone propionate*	37.74	1.309	d5-Diazepam	501.2	313.0	d7-Metoprolol
Simvastatin	39.96	1.386	d5-Diazepam	419.3	285.0	d5-Propoxyphene
Simvastatin*	39.96	1.386	d5-Diazepam	419.3	198.9	d5-Propoxyphene
Surrogate Standards						
$^{13}C, ^{15}N_2$-Theophylline	2.52	0.136	$^{13}C_3$-Atrazine	184.0	124.7	$^{13}C_3$-Atrazine
$^{13}C, ^{15}N_2$-Theophylline*	2.52	0.136	$^{13}C_3$-Atrazine	184.0	96.8	$^{13}C_3$-Atrazine
d_8-Benzoylecgonine	5.33	0.288	$^{13}C_3$-Atrazine	298.1	170.9	$^{13}C_3$-Atrazine
d_8-Benzoylecgonine*	5.33	0.288	$^{13}C_3$-Atrazine	298.1	109.8	$^{13}C_3$-Atrazine
d_7-Metoprolol	8.06	0.435	$^{13}C_3$-Atrazine	275.0	190.8	$^{13}C_3$-Atrazine
d_7-Metoprolol*	8.06	0.435	$^{13}C_3$-Atrazine	275.0	122.7	$^{13}C_3$-Atrazine

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d_3-Cocaine	8.74	0.472	$^{13}C_3$-Atrazine	307.1	184.9	$^{13}C_3$-Atrazine
d_3-Cocaine*	8.74	0.472	$^{13}C_3$-Atrazine	307.1	84.8	$^{13}C_3$-Atrazine
d_7-Propranolol	14.12	0.762	$^{13}C_3$-Atrazine	267.0	116.0	$^{13}C_3$-Atrazine
d_7-Propranolol*	14.12	0.762	$^{13}C_3$-Atrazine	267.0	188.7	$^{13}C_3$-Atrazine
d_4-Hydrocortisone	17.29	0.933	$^{13}C_3$-Atrazine	367.0	120.8	$^{13}C_3$-Atrazine
d_4-Hydrocortisone*	17.29	0.933	$^{13}C_3$-Atrazine	367.0	331.0	$^{13}C_3$-Atrazine
d_4-Promethazine	18.24	0.984	$^{13}C_3$-Atrazine	289.0	201.8	$^{13}C_3$-Atrazine
d_4-Promethazine*	18.24	0.984	$^{13}C_3$-Atrazine	289.0	86.0	$^{13}C_3$-Atrazine
d_6-Paroxetine	20.14	1.087	$^{13}C_3$-Atrazine	336.0	197.8	$^{13}C_3$-Atrazine
d_6-Paroxetine*	20.14	1.087	$^{13}C_3$-Atrazine	336.0	75.8	$^{13}C_3$-Atrazine
d_7-DEET	20.35	1.098	$^{13}C_3$-Atrazine	199.1	125.8	$^{13}C_3$-Atrazine
d_7-DEET*	20.35	1.098	$^{13}C_3$-Atrazine	199.1	97.8	$^{13}C_3$-Atrazine
d_3-Methylprednisolone	21.29	1.149	$^{13}C_3$-Atrazine	378.2	360	$^{13}C_3$-Atrazine
d_3-Methylprednisolone*	21.29	1.149	$^{13}C_3$-Atrazine	378.2	342	$^{13}C_3$-Atrazine
d_5-Propoxyphene	21.43	1.157	$^{13}C_3$-Atrazine	345.2	57.9	$^{13}C_3$-Atrazine
d_5-Propoxyphene*	21.43	1.157	$^{13}C_3$-Atrazine	345.2	266.1	$^{13}C_3$-Atrazine
d_6-Amitriptyline	22.02	1.188	$^{13}C_3$-Atrazine	284.0	233.0	$^{13}C_3$-Atrazine
d_6-Amitriptyline*	22.02	1.188	$^{13}C_3$-Atrazine	284.0	90.8	$^{13}C_3$-Atrazine
d_3-Benztropine	22.55	1.217	$^{13}C_3$-Atrazine	311.0	166.7	$^{13}C_3$-Atrazine
d_3-Benztropine*	22.55	1.217	$^{13}C_3$-Atrazine	311.0	151.7	$^{13}C_3$-Atrazine
d_5-Alprazolam	22.82	1.232	$^{13}C_3$-Atrazine	314.1	285.9	$^{13}C_3$-Atrazine
d_5-Alprazolam*	22.82	1.232	$^{13}C_3$-Atrazine	314.1	209.9	$^{13}C_3$-Atrazine
d_5-Norfluoxetine	24.33	1.313	$^{13}C_3$-Atrazine	301.0	138.7	$^{13}C_3$-Atrazine
d_5-Diazepam	28.83	1.556	$^{13}C_3$-Atrazine	290.1	197.9	$^{13}C_3$-Atrazine
d_5-Diazepam*	28.83	1.556	$^{13}C_3$-Atrazine	290.1	153.8	$^{13}C_3$-Atrazine
Recovery Standards						
$^{13}C_3$-Atrazine	18.53	1.000		219.1	176.9	External Standard
$^{13}C_3$-Atrazine *	18.53	1.000		219.1	134.0	External Standard

* Indicates secondary transition for possible diagnostic use.

CALIBRATION

Initial calibration is performed using a series of seven calibration solutions that encompass the working concentration range. Initial calibration solutions contain the suite of labelled surrogate and recovery standards and authentic targets. The concentration of the native analytes in the solutions varies to encompass the working range of the instrument, while the concentrations of the surrogates and recovery standards remain constant. A mid-level solution is analyzed every 12 hours or every 20 samples, whichever occurs first. The List 1, List 3, List 4 and List 5 calibration standards are prepared in 75:25 methanol:0.1% formic acid buffer and the List 2 calibration standards in methanol.

Initial calibration for any native compound requires at least 5 consecutive calibration levels. All 7 calibration solutions in the table below may be analyzed, but in certain cases only 5 or 6 of the levels are used to establish the initial calibration. In the table below the calibration concentrations routinely included are printed in bold type. If the number of routinely included calibration points shown for a compound is less that five, concentrations below and/or above are added as necessary based on analyst judgement to achieve the minimum five consecutive concentration levels. Note that reporting limits are adjusted as necessary to reflect the lowest calibration concentration included in the initial calibration.

Nominal Concentrations of Calibration Solutions

List 1 (Acid extraction, positive ESI)

Compound name	Calibration Standards List 1 (Acid extraction, positive ESI)						
	Level A	Level B	Level C	Level D	Level E	Level F	Level G
Acetaminophen	**3.75**	**12.5**	**37.5**	**187**	**625**	**2500**	**12500**
Ampicillin	*0.375*	*1.25*	*3.75*	*18.7*	*62.5*	*250*	*1250*
Azithromycin	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	*250*	*1250*
Caffeine	**3.75**	**12.5**	**37.5**	**187**	**625**	*2500*	*12500*
Carbadox	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	*250*	*1250*
Carbamazapine	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	**250**	*1250*
Cefotaxime	*1.5*	*5*	*15*	*75*	*250*	*1000*	*5000*
Ciprofloxacin	**1.5**	**5**	**15**	**75**	**250**	*1000*	*5000*
Clarithromycin	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	*250*	*1250*
Clinafloxacin	*1.5*	**5**	**15**	**75**	**250**	*1000*	*5000*
Cloxacillin	*0.75*	**2.5**	**7.5**	**37.5**	**125**	**500**	*2500*
Dehydronifedipine	**0.15**	**0.5**	**1.5**	**7.5**	**25**	**100**	*500*
Digoxigenin	*1.5*	**5**	**15**	**75**	**250**	**1000**	*5000*
Digoxin	**1.5**	**5**	**15**	**75**	**250**	*1000*	*5000*
Diltiazem	**0.075**	**0.25**	**0.75**	**3.75**	**12.5**	**50**	*250*
1,7-Dimethylxanthine	**15**	**50**	**150**	**750**	**2500**	**10000**	*50000*
Diphenhydramine	**0.15**	**0.5**	**1.5**	**7.5**	**25**	**100**	*500*
Enrofloxacin	**0.75**	**2.5**	**7.5**	**37.5**	**125**	*500*	*2500*
Erythromycin	**0.075**	**0.25**	**0.75**	**3.75**	**12.5**	**50**	*250*

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Flumequine	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	*250*	*1250*
Fluoxetine	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	*250*	*1250*
Lincomycin	**0.75**	**2.5**	**7.5**	**37.5**	**125**	*500*	*2500*
Lomefloxacin	**0.75**	**2.5**	**7.5**	**37.5**	**125**	*500*	*2500*
Miconazole	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	*250*	*1250*
Norfloxacin	**3.75**	**12.5**	**37.5**	**187**	**625**	*2500*	*12500*
Norgestimate	**0.75**	**2.5**	**7.5**	**37.5**	**125**	*500*	*2500*
Ofloxacin	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	*250*	*1250*
Ormetoprim	**0.15**	**0.5**	**1.5**	**7.5**	**25**	*100*	*500*
Oxacillin	*0.75*	**2.5**	**7.5**	**37.5**	**125**	*500*	*2500*
Oxolinic acid	*0.15*	**0.5**	**1.5**	**7.5**	**25**	*100*	*500*
Penicillin G	**0.75**	**2.5**	**7.5**	**37.5**	**125**	*500*	*2500*
Penicillin V	*0.75*	**2.5**	**7.5**	**37.5**	**125**	**500**	*2500*
Roxithromycin	**0.075**	**0.25**	**0.75**	**3.75**	**12.5**	*50*	*250*
Sarafloxacin	**3.75**	**12.5**	**37.5**	**187**	**625**	*2500*	*12500*
Sulfachloropyridazine	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	*250*	*1250*
Sulfadiazine	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	**250**	**1250**
Sulfadimethoxine	**0.075**	**0.25**	**0.75**	**3.75**	**12.5**	**50**	*250*
Sulfamerazine	**0.15**	**0.5**	**1.5**	**7.5**	**25**	**100**	*500*
Sulfamethazine	*0.15*	**0.5**	**1.5**	**7.5**	**25**	*100*	*500*
Sulfamethizole	**0.15**	**0.5**	**1.5**	**7.5**	**25**	**100**	*500*
Sulfamethoxazole	*0.15*	**0.5**	**1.5**	**7.5**	**25**	**100**	**500**
Sulfanilamide	**3.75**	**12.5**	**37.5**	**187.5**	**625**	**2500**	*12500*
Sulfathiazole	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	*250*	*1250*
Thiabendazole	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	*250*	*1250*
Trimethoprim	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	**250**	*1250*
Tylosin	**1.5**	**5**	**15**	**75**	**250**	*1000*	*5000*
Virginiamycin M1	**0.75**	**2.5**	**7.5**	**37.5**	**125**	*500*	*2500*
Surrogate Standards							
$^{13}C_2$, ^{15}N-Acetaminophen	50	50	50	50	50	50	50
$^{13}C_3$-Caffeine	75	75	75	75	75	75	75
d_{10}-Carbamazepine	25	25	25	25	25	25	25
$^{13}C_3$, ^{15}N-Ciprofloxacin	100	100	100	100	100	100	100
$^{13}C_2$-Erythromycin	25	25	25	25	25	25	25
d_5-Fluoxetine	25	25	25	25	25	25	25
$^{13}C_6$-Sulfamethazine	25	25	25	25	25	25	25
$^{13}C_6$-Sulfamethoxazole	25	25	25	25	25	25	25
d_6-Thiabendazole	25	25	25	25	25	25	25
$^{13}C_3$-Trimethoprim	25	25	25	25	25	25	25
Recovery Standards							
$^{13}C_3$-Atrazine	50	50	50	50	50	50	50

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List 2 (Tetracyclines)

Compound name	Calibration Standards List 2 (ng/mL) (Tetracyclines)						
	Level A	Level B	Level C	Level D	Level E	Level F	Level G
Anhydrochlortetracycline (ACTC)	*3.75*	*12.5*	**31.25**	**62.5**	**125**	*375*	*1000*
Anhydrotetracycline (ATC)	*3.75*	**12.5**	**31.25**	**62.5**	**125**	*375*	*1000*
Chlortetracycline (CTC)	*1.5*	**5**	**12.5**	**25**	**50**	**150**	*400*
Demeclocycline	**3.75**	**12.5**	**31.2**	**62.5**	**125**	**375**	**1000**
Doxycycline	**1.5**	**5**	**12.5**	**25**	**50**	**150**	**400**
4-Epianhydrochlortetracycline (EACTC)	*15*	**50**	**125**	**250**	**500**	**1500**	*4000*
4-Epianhydrotetracycline (EATC)	**3.75**	**12.5**	**31.2**	**62.5**	**125**	**375**	*1000*
4-Epichlortetracycline (ECTC)	**3.75**	**12.5**	**31.2**	**62.5**	**125**	**375**	**1000**
4-Epioxytetracycline (EOTC)	**1.5**	**5**	**12.5**	**25**	**50**	**150**	*400*
4-Epitetracycline (ETC)	*1.5*	**5**	**12.5**	**25**	**50**	*150*	*400*
Isochlortetracycline (ICTC)	**1.5**	**5**	**12.5**	**25**	**50**	**150**	**400**
Minocycline	*15*	**50**	**125**	**250**	**500**	*1500*	*4000*
Oxytetracycline (OTC)	**1.5**	**5**	**12.5**	**25**	**50**	**150**	*400*
Tetracycline (TC)	**1.5**	**5**	**12.5**	**25**	**50**	**150**	*400*
Surrogate Standards							
d_6-Thiabendazole	25	25	25	25	25	25	25
Recovery Standards							
$^{13}C_3$-Atrazine	50	50	50	50	50	50	50

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List 3 (Acid extraction, negative ESI)

Compound name	Calibration Standards List 3 (ng/mL) (Acid extraction, negative ESI)						
	Level A	Level B	Level C	Level D	Level E	Level F	Level G
Bisphenol A	**125**	**250**	**500**	**1000**	**2000**	**4000**	**8000**
Furosemide	**10**	**33**	**100**	**500**	**1665**	**6660**	*20000*
Gemfibrozil	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	**250**	**750**
Glipizide	**1.5**	**5.0**	**15**	**75**	**250**	**1000**	**3000**
Glyburide	**0.75**	**2.5**	**7.5**	**37.5**	**125**	*500*	*1500*
Hydroclorothiazide	**5.0**	**16.6**	**50**	**150**	*300*	*500*	*625*
2-hydroxy-ibuprofen	**20**	**66**	**200**	**1000**	**3330**	**13330**	*40000*
Ibuprofen	**3.75**	**12.5**	**37.5**	**187**	**625**	**2500**	**7500**
Naproxen	*0.75*	**2.50**	**7.50**	**37.5**	**125**	**500**	**1500**
Triclocarban	**0.75**	**2.5**	**7.5**	**37.5**	**125**	**500**	**1500**
Triclosan	**15**	**50**	**150**	**750**	**2500**	**10000**	**30000**
Warfarin	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	**250**	**750**
Surrogate Standards							
d_6-Bisphenol A	5000	5000	5000	5000	5000	5000	5000
d_6-Gemfibrozil	25	25	25	25	25	25	25
d_{11}-Glipizide	100	100	100	100	100	100	100
d_3-Glyburide	100	100	100	100	100	100	100
$^{13}C_3$-Ibuprofen	100	100	100	100	100	100	100
^{13}C, d_3-Naproxen	75	75	75	75	75	75	75
$^{13}C_6$-Triclocarban	12.5	12.5	12.5	12.5	12.5	12.5	12.5
$^{13}C_{12}$-Triclosan	100	100	100	100	100	100	100
d_5-Warfarin	25	25	25	25	25	25	25
Recovery Standard							
$^{13}C_6$-2,4,5-Trichloropheno-xyacetic Acid($^{13}C_6$-2,4,5-T)	50	50	50	50	50	50	50

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List 4 (Base extraction, positive ESI)

Compound Name	Calibration Standards List 4 (ng/mL) (Base extraction, positive ESI)						
	Level A	Level B	Level C	Level D	Level E	Level F	Level G
Albuterol	*0.075*	**0.25**	**0.75**	**3.75**	**12.5**	**50**	*250*
Amphetamine	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	**250**	*1250*
Atenolol	**0.15**	**0.50**	**1.50**	**7.50**	**25**	**100**	**500**
Atorvastatin	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	**250**	*1250*
Cimetidine	**0.15**	**0.50**	**1.5**	**7.5**	**25**	**100**	*500*
Clonidine	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	**250**	**1250**
Codeine	**0.75**	**2.5**	**7.5**	**37.5**	**125**	**500**	**2500**
Cotinine	*0.375*	**1.25**	**3.75**	**18.7**	**62.5**	**250**	**1250**
Enalapril	**0.075**	**0.25**	**0.75**	**3.75**	**12.5**	**50**	**250**
Hydrocodone	**0.375**	**1.25**	**3.75**	**18.7**	**62.5**	**250**	*1250*
Metformin	**0.75**	**2.5**	**7.5**	**37.5**	**125**	**500**	**2500**
Oxycodone	**0.15**	**0.50**	**1.50**	**7.50**	**25**	**100**	*500*
Ranitidine	**0.15**	**0.50**	**1.50**	**7.50**	**25**	**100**	*500*
Triamterene	*0.075*	**0.25**	**0.75**	**3.75**	**12.5**	**50**	*250*
Labeled Compounds							
d_3-Albuterol	25	25	25	25	25	25	25
d_5-Amphetamine	5.0	5.0	5.0	5.0	5.0	5.0	5.0
d_7-Atenolol	15	15	15	15	15	15	15
d_3-Cimetidine	7.5	7.5	7.5	7.5	7.5	7.5	7.5
d_4-Clonidine	100	100	100	100	100	100	100
d_6-Codeine	50	50	50	50	50	50	50
d_3-Cotinine	15	15	15	15	15	15	15
d_5-Enalapril	5.0	5.0	5.0	5.0	5.0	5.0	5.0
d_3-Hydrocodone	15	15	15	15	15	15	15
d_6-Metformin	100	100	100	100	100	100	100
d_6-Oxycodone	15	15	15	15	15	15	15
Labeled injection standards							
d_3-Amitriptyline	12.5	12.5	12.5	12.5	12.5	12.5	12.5
d_9-Albuterol	25	25	25	25	25	25	25

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List 5 (Acid extraction, positive ESI)

Compound name	Calibration Standards List 5 (ng/mL) (Acid extraction, positive ESI)						
	Level A	Level B	Level C	Level D	Level E	Level F	Level G
Alprazolam	0.075	0.25	0.75	3.75	12.5	50	150
Amitriptyline	0.075	0.25	0.75	3.75	12.5	50	150
Amlodipine	0.375	1.25	3.75	18.7	62.5	250	750
Benzoylecgonine	0.075	0.25	0.75	3.75	12.5	50	150
Benztropine	0.075	0.25	0.75	3.75	12.5	50	150
Betamethasone	0.375	1.25	3.75	18.7	62.5	250	750
Cocaine	0.0375	0.125	0.375	1.87	6.25	25	75
DEET	0.15	0.5	1.5	7.5	25	100	300
Desmethyldiltiazem	0.0375	0.125	0.375	1.87	6.2	25	75
Diazepam	0.075	0.25	0.75	3.75	12.5	50	150
Fluocinonide	1.50	5.0	15.0	75	250	1000	3000
Fluticasone propionate	0.50	1.67	5.0	25	83.3	333	1000
Hydrocortisone	15.0	50	150	750	2500	10000	30000
10-hydroxy-amitriptyline	0.0375	0.125	0.375	1.87	6.25	25	75
Meprobamate	1.00	3.33	10.0	50	167	667	2000
Methylprednisolone	1.00	3.33	10.0	50	167	667	2000
Metoprolol	0.375	1.25	3.75	18.7	62.5	250	750
Norfluoxetine	0.375	1.25	3.75	18.7	62.5	250	750
Norverapamil	0.0375	0.125	0.375	1.87	6.25	25	75
Paroxetine	1.0	3.33	10.0	50	167	667	2000
Prednisolone	1.5	5.0	15.0	75	250	1000	3000
Prednisone	5.0	16.7	50.0	250	833	3330	10000
Promethazine	0.10	0.33	1.0	5.0	16.7	66.7	200
Propoxyphene	0.075	0.25	0.75	3.75	12.5	50	150
Propranolol	0.50	1.67	5.0	25	83.3	333	1000
Sertraline	0.10	0.33	1.0	5.0	16.6	67	200
Simvastatin	5.0	16.7	50.0	250	833	3330	10000
Theophylline	15	50	150	750	25000	10000	30000
Trenbolone	1.0	3.33	10.0	50	167	667	2000
Trenbolone acetate	0.075	0.25	0.75	3.75	12.5	50	150
Valsartan	1.0	3.33	10.0	50	167	667	2000
Verapamil	0.0375	0.125	0.375	1.87	6.25	25	75
Labeled Compounds							
d_5-Alprazolam	10	10	10	10	10	10	10
d_6-Amitriptyline	10	10	10	10	10	10	10
d_8-Benzoylecgonine	10	10	10	10	10	10	10
d_3-Benztropine	5.0	5.0	5.0	5.0	5.0	5.0	5.0

d_3-Cocaine	10	10	10	10	10	10	10
d_7-DEET	10	10	10	10	10	10	10
d_5-Diazepam	10	10	10	10	10	10	10
d_4-Hydrocortisone	2000	2000	2000	2000	2000	2000	2000
d_3-Methylprednisolone	500	500	500	500	500	500	500
d_7-Metoprolol	100	100	100	100	100	100	100
d_5-Norfluoxetine	50	50	50	50	50	50	50
d_6-Paroxetine	25	25	25	25	25	25	25
d_4-Promethazine	25	25	25	25	25	25	25
d_5-Propoxyphene	15	15	15	15	15	15	15
d_7-Propranolol	100	100	100	100	100	100	100
$^{13}C_1$, $^{15}N_2$-Theophylline	500	500	500	500	500	500	500
Labeled Injection Standards							
$^{13}C_3$-Atrazine	50	50	50	50	50	50	50

ANALYTE IDENTIFICATION

Positive identification of target PPCP compounds, surrogate standard and recovery standards require:

- ≥ 3:1 signal:noise for parent ion to daughter ion transition.
- Guideline (if there is evidence of peak shifting analyst judgement applies): Compound retention time should fall within 0.4 minutes of the predicted retention times from the daily calibration standard. Natives with labelled surrogate standards should elute within 0.1 minutes of the associated labelled surrogates.

QUANTIFICATION

Concentrations of the targets compounds are calculated either by isotope dilution quantification against the surrogate standard or by internal standard quantification against the recovery standard with linear regression calibration, using a 1/X weighting type, excluding origin.

General equation : Y = slope × X + intercept

Where: $Y = \text{Response ratio} = \left(\frac{\text{area Target}}{\text{area SUR}} \times \text{weight SUR spiked (ng)} \right)$

X = weight of target (ng)

SUR = the surrogate standard

The slope and intercept are used to convert raw peak areas in sample chromatograms to final concentrations as follows:

$$\text{Sample Conc.} = \left(\frac{\text{area of Target}}{\text{area SUR}} \times \text{weight SUR spiked (ng)} - \text{intercept}\right) x \left(\frac{1}{\text{slope}}\right) x \left(\frac{1}{\text{samplesize}}\right)$$

The percent recovery of surrogate standards (% SUR) are calculated by internal standard quantification against the recovery standard. Surrogate recoveries are used only as a general QC indicator of overall data quality.

$$\%\ \text{SUR} = 100\ x \left(\frac{\text{area SUR}}{\text{area REC}}\right) x \left(\frac{\text{weight of REC spiked}}{\text{RRF}}\right) x \left(\frac{1}{\text{weight SUR spiked}}\right)$$

Where:

REC = the recovery standard as listed in Tables 13,14,15,16

RRF is the average relative response factor from the Initial Calibration data:

$$\text{RRF} = \left(\frac{\text{area SUR}}{\text{area REC}}\right) x \left(\frac{\text{weight of REC}}{\text{weight of SUR}}\right)$$

REPORTING LIMITS

Sample specific detection limits (SDLs) are calculated by QuanLynx software using 3 times the signal of the noise in the target channel converted to an equivalent sample concentration.

Concentrations and detection limits for the target analytes are reported. The lower reporting limit for each target compound is defined as the concentration equivalent to the lowest calibration standard analyzed or the SDL, whichever is greater. Typical reporting units for all data are ng/g or ng/L. Concentrations for solids are reported on a dry weight basis. Concentrations in aqueous samples are reported on a volume basis. Concentrations for tissues are reported on a wet weight basis.

The following are commonly requested reporting limits:

Method Detection Limit (MDL) - determined as specified by EPA Fed. Reg. 40 CFR Part 136 Appendix B (no iteration option). The 99% confidence level MDL is determined based on analysis of a minimum of 7 replicate matrix spikes fortified at 1-10 times the estimated detection limit. MDL is determined as required based on accreditation, contract and workload requirements.

Lower Method Calibration Limit (LMCL) - determined by prorating the concentration of the lowest calibration limit for sample size and extract volume. The following equation is used. ((lowest level cal conc.) x (extract volume))/sample size. The typical extract volume for PPCP is 4 mL.

For the analysis of PPCP it is AXYS standard to report sample concentrations using the LMCL as the lower reporting limit. In cases where the SDL is higher than the LMCL, the SDL will be used as the lower reporting limit.

The SDL is defined as follows: *Sample Specific Detection Limit or Sample Detection Limit (SDL)* – determined individually for every sample analysis run by converting the area equivalent of 3.0

times (2.5 times for EPA 1600 series methods) the estimated chromatographic noise height to a concentration in the same manner that target peak responses are converted to final concentrations. The SDL accounts for any effect of matrix on the detection system and for recovery achieved through the analytical work-up.

QUALITY ASSURANCE/QUALITY CONTROL

All samples are analyzed in batches with the following composition:

- Batch Size - Each batch consists of up to twenty test samples and additional QC samples.
- Blanks - One procedural blank is analyzed for each batch. The procedural blank is prepared by spiking an aliquot of the surrogate standard solution into a clean matrix. The procedural blank is extracted and analyzed using the same procedures as the test samples in the analysis batch.
- On-going Precision and Recovery (OPR) Samples – On-going Precision and Recovery (OPR) is demonstrated by the analysis of a spiked reference matrix (SPM) analyzed with each batch. The OPR sample is prepared by spiking an aliquot of the authentic spiking solution into an accurately weighed in-house reference matrix (known to contain low background levels of target analytes). The reference sample to be analyzed is assigned to the analyst when the batch is assigned. The matrix is spiked with an aliquot of surrogate standard solution and after an equilibration time of at least 30 minutes is extracted.
- Duplicates - 5% of the test samples within a batch (containing 7 or more test samples) are analyzed in duplicate, or as required by contract, provided sufficient sample is available.
- Surrogate/Authentic/Recovery (SAR) solution is an optional diagnostic test that may be prepared and analyzed with a batch.

The batch composition may vary according to batch or quality control requirements specified by a client. Each batch is carried through the complete analytical process as a unit. For sample data to be reportable the batch QC data must meet the acceptance criteria.

QC Specification Table: Authentic and Surrogate Standard Recoveries in samples

	OPR Recovery and surrogate recovery in sample (% Recovery)		IPR			Blank Level (ng)
			Average Recovery (%)		RSD (%)	
	Low	High	Low	High		
List 1 Compounds (APOS)						
Acetaminophen	70	140	70	140	30	≤15
Ampicillin [2]						
Azithromycin	10	130	10	130	130	≤1.5
Caffeine	25	160	35	150	60	≤15
Carbadox	25	180	35	180	40	≤1.5
Carbamazepine	25	200	35	200	40	≤1.5
Cefotaxime	10	300	10	300	60	≤6
Ciprofloxacin	25	180	35	180	40	≤6
Clarithromycin	50	160	50	160	30	≤1.5
Clinafloxacin	25	300	35	300	70	≤6
Cloxacillin [2]	70	130	70	130	30	≤3
Dehydronifedipine	35	160	40	160	30	≤0.6

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	OPR Recovery and surrogate recovery in sample (% Recovery)		IPR			Blank Level (ng)
			Average Recovery (%)		RSD (%)	
	Low	High	Low	High		
Digoxigenin	50	150	60	140	30	≤6
Digoxin	35	200	40	200	30	≤6
Diltiazem	20	160	25	160	50	≤0.3
1,7-Dimethylxanthine	30	300	40	300	60	≤60
Diphenhydramine	70	130	70	130	30	≤0.6
Enrofloxacin	30	220	40	220	40	≤3
Erythromycin - H_2O	70	130	70	130	30	≤0.3 [3]
Flumequine	40	160	50	160	30	≤1.5
Fluoxetine	60	150	70	140	30	≤1.5
Lincomycin	10	300	10	300	70	≤3
Lomefloxacin, aqueous matrix	50	250	60	250	30	≤3
solid matrix	50	400	60	400	30	≤3
Miconazole	35	130	40	130	30	≤1.5
Norfloxacin	10	250	25	220	40	≤15
Norgestimate	35	130	40	130	30	≤3
Ofloxacin	60	250	70	250	30	≤1.5
Ormetoprim	70	150	70	150	30	≤0.6
Oxacillin [2]	20	130	20	130	40	≤3
Oxolinic Acid	60	150	70	150	30	≤0.6
Penicillin G [2]	10	130	10	130	40	≤3
Penicillin V	40	140	50	140	30	≤3
Roxithromycin	50	140	50	140	30	≤0.3
Sarafloxacin, aqueous matrix	50	200	60	180	30	≤15
solid matrix	50	300	60	300	30	≤15
Sulfachloropyridazine	60	160	70	160	30	≤1.5
Sulfadiazine	70	130	70	130	30	≤1.5
Sulfadimethoxine	35	160	40	160	30	≤0.3
Sulfamerazine	60	140	60	140	30	≤0.6
Sulfamethazine	70	130	70	130	30	≤0.6
Sulfamethizole	30	140	35	140	30	≤0.6
Sulfamethoxazole	70	130	70	130	30	≤0.6
Sulfanilamide	2	160	3	150	150	≤15
Sulfathiazole	30	180	30	160	50	≤1.5
Thiabendazole	60	150	60	150	30	≤1.5
Trimethoprim	50	150	60	150	30	≤1.5
Tylosin	70	130	70	130	30	≤6
Virginiamycin M1	15	300	15	250	90	≤3
Surrogate Standard						
$^{13}C_2$, ^{15}N-Acetaminophen	30	160	40	150	30	
$^{13}C_3$-Caffeine	40	140	50	140	30	
d_{10}-Carbamazepine	40	140	50	140	30	
$^{13}C_3$, ^{15}N-Ciprofloxacin	7	150	9	140	70	
$^{13}C_2$-Erythromycin - H_2O	35	130	35	130	30	
d_5-Fluoxetine	10	160	10	150	70	
$^{13}C_6$-Sulfamethazine	30	160	35	150	40	
$^{13}C_6$-Sulfamethoxazole	30	140	40	130	30	
d_6-Thiabendazole	25	180	30	160	50	

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	OPR Recovery and surrogate recovery in sample (% Recovery)		IPR			Blank Level (ng)
			Average Recovery (%)		RSD (%)	
	Low	High	Low	High		
$^{13}C_3$-Trimethoprim	30	140	40	130	30	
Recovery Standard						
$^{13}C_3$-Atrazine						
List 2 Compounds (TCYS)						
Anhydrochlortetracycline (ACTC)	15	200	20	180	70	≤15
Anhydrotetracycline (ATC)	20	160	20	150	50	≤15
Chlortetracycline (CTC)	30	250	35	250	60	≤6
Demeclocycline	35	180	35	160	50	≤15
Doxycycline	35	180	40	180	40	≤6
Epianhydrochlortetracycline (EACTC)	6	130	7	130	70	≤60
Epianhydrotetracycline (EATC)	15	200	20	200	60	≤15
Epichlortetracycline (ECTC)	25	180	30	160	50	≤15
Epioxytetracycline (EOTC)	25	180	35	160	40	≤6
Epitetracycline (ETC)	35	200	40	180	40	≤6
Isochlortetracycline (ICTC)	25	180	35	160	40	≤6
Minocycline	1	250	2	200	110	≤60
Oxytetracycline (OTC)	20	200	30	200	40	≤6
Tetracycline (TC)	20	200	30	180	40	≤6
Surrogate Standard						
d_6-Thiabendazole	25	140	25	130	50	
Recovery Standard						
$^{13}C_3$-Atrazine						
List 3 Compounds (ANEG)						
Bisphenol A	70	130	70	130	30	≤500
Furosemide	65	130	70	130	30	≤40
Gemfibrozil	60	140	70	130	30	≤1.5
Glipizide	55	170	60	160	30	≤6
Glyburide	50	180	55	170	30	≤3
Hydroxychlorothiazide	45	200	50	180	30	≤20
2-hydroxy-ibuprofen	70	130	70	130	30	≤80
Ibuprofen	70	130	70	130	30	≤15
Naproxen	50	150	60	150	30	≤3
Triclocarban	60	140	70	130	30	≤3
Triclosan	70	130	70	130	30	≤60
Warfarin	70	140	70	140	30	≤1.5
Surrogate Standards						
d_6-Bisphenol A	50	170	60	160	30	
d_6-Gemfibrozil	50	150	55	140	30	
d_{11}-Glipizide	30	180	35	170	50	
d_3-Glyburide	20	160	25	150	40	
$^{13}C_3$-Ibuprofen	50	140	55	140	30	
^{13}C-d_3-Naproxen	30	150	35	140	30	
$^{13}C_6$-Triclocarban	20	160	25	150	50	
$^{13}C_{12}$-Triclosan	20	160	30	150	40	
d_5-Warfarin	35	250	50	250	30	

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	OPR Recovery and surrogate recovery in sample (% Recovery)		IPR			Blank Level (ng)
			Average Recovery (%)		RSD (%)	
	Low	High	Low	High		
Recovery Standard						
$^{13}C_6$-2,4,5-Trichloro-phenoxyacetic acid						
List 4 Compounds (BPOS)						
Albuterol	50	160	50	160	30	≤0.3
Amphetamine	50	160	60	150	30	≤1.5
Atenolol	70	130	70	130	30	≤0.6
Atorvastatin	20	130	25	130	40	≤1.5
Cimetidine	15	130	20	130	50	≤0.6
Clonidine	70	130	70	130	30	≤1.5
Codeine	70	130	70	130	30	≤3
Cotinine	70	130	70	130	30	≤1.5
Enalapril	70	130	70	130	30	≤0.3
Hydrocodone	70	130	70	130	30	≤1.5
Metformin	70	160	70	160	30	≤3
Oxycodone	65	130	70	130	30	≤0.6
Ranitidine	25	140	30	140	50	≤0.6
Triamterene	70	140	70	140	30	≤0.3
Surrogate Standards						
d_3-Albuterol	20	140	30	130	30	
d_5-Amphetamine	20	130	25	130	40	
d_7-Atenolol	50	130	70	130	30	
d_3-Cimetidine	15	130	15	130	50	
d_4-Clonidine	50	130	70	130	30	
d_6-Codeine	50	130	70	130	30	
d_3-Cotinine	50	140	70	135	30	
d_5-Enalapril	50	130	70	130	30	
d_3-Hydrocodone	50	130	70	130	30	
d_6-Metformin	3	130	4	130	130	
d_6-Oxycodone	50	150	60	140	30	
Recovery Standards						
d_3-Amitriptyline						
List 5 Compounds (APOS)						
Alprazolam	70	130	70	130	30	≤0.3
Amitriptyline	70	130	70	130	30	≤0.3
Amlodipine	45	130	50	130	30	≤1.5
Benzoylecgonine	70	130	70	130	30	≤0.3
Benztropine	70	130	70	130	30	≤0.3
Betamethasone	20	240	30	220	40	≤1.5
Cocaine	70	130	70	130	30	≤0.15
DEET	70	130	70	130	30	≤1
Desmethyldiltiazem	3	350	5	320	80	≤0.15
Diazepam	70	130	70	130	30	≤0.3
Fluocinonide	7	230	9	220	70	≤6

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	OPR Recovery and surrogate recovery in sample (% Recovery)		IPR			Blank Level (ng)
			Average Recovery (%)		RSD (%)	
	Low	High	Low	High		
Fluticasone propionate	20	160	25	150	50	≤2
Hydrocortisone	15	220	20	200	80	≤60
10-hydroxy-amitriptyline	70	130	70	130	30	≤0.15
Meprobamate	65	150	70	140	30	≤4
Methylprednisolone	35	240	40	220	50	≤10
Metoprolol	70	130	70	130	30	≤1.5
Norfluoxetine	70	130	70	130	30	≤1.5
Norverapamil	55	130	60	130	30	≤0.15
Paroxetine	70	130	70	130	30	≤4
Prednisolone	35	240	40	220	50	≤6
Prednisone	50	180	60	170	30	≤20
Promethazine	70	130	70	130	30	≤0.4
Propoxyphene	70	130	70	130	30	≤0.3
Propranolol	70	150	70	150	30	≤2
Sertraline	50	130	55	130	30	≤0.4
Simvastatin	1	150	1	140	100	≤20
Theophylline	10	1000	70	900	50	≤60
Trenbolone	70	140	70	135	30	≤4
Trenbolone acetate, aqueous matrix solid matrix	55 55	130 250	60 60	130 250	30 30	≤0.3 ≤0.3
Valsartan	70	130	70	130	30	≤4
Verapamil	70	145	70	140	30	≤0.15
Surrogate Standards						
d_5-Alprazolam	45	130	45	130	30	
d_6-Amitriptyline	10	130	20	130	40	
d_8-Benzoylecgonine	10	170	20	160	40	
d_3-Benztropine	20	140	25	130	40	
d_3-Cocaine	25	140	30	130	50	
d_7-DEET	15	160	20	150	40	
d_5-Diazepam	15	160	25	150	40	
d_4-Hydrocortisone	40	240	45	230	50	
d_3-Methylprednisolone	15	160	20	150	60	
d_7-Metoprolol	25	140	30	140	30	
d_5-Norfluoxetine	20	130	20	130	50	
d_6-Paroxetine	7	150	9	140	60	
d_4-Promethazine	3	140	5	130	80	
d_5-Propoxyphene	30	130	40	130	30	
d_7-Propranolol	25	140	30	130	30	
$^{13}C_1$, $^{15}N_2$-Theophylline	20	200	25	180	60	
Recovery Standards						
$^{13}C_3$-Atrazine						

[1] OPR and IPR limits derived from actual method performance data according to EPA 821B98003, appendix D.
[2] Analysis result is classified as "Information Value" of estimated concentration.
[3] Background level of Erythromycin - H_2O in the associated labeled surrogate may elevate the Erythromycin - H_2O blank value. Sample results may be blank corrected where acceptable by contract.

QC Specification Table: Instrumental Acceptance Specifications

QC Parameter	Specification
Instrument Sensitivity	Daily, S:N ≥ 3:1 for all analytes for lowest calibration point.
Initial Calibration (native compounds)	Initial, (1/X) weighted linear regression (followed by regular Cal/Ver procedures and repeated as necessary to maintain Cal/Ver results within established acceptance ranges. Calculated concentrations 70-130%, one point per compound may be 60-140% Internal guideline - correlation coefficient >0.985. Calibration curves with lower correlation coefficient values meeting all above criteria may be accepted based on batch specific QC results and professional judgement. For hydrocortisone, an increased frequency of Initial Calibration variance from method acceptance limits has been observed and is attributed to transient instrumental instability of response correctable by instrumental re-analysis. If the results are deemed to be fit for the intended purpose the hydrocortisone data may be flagged and reported with an explanation of the variance, otherwise instrumental re-analysis to correct the QC variance is required.
OPENING Calibration Verification	Every 20 samples. Determined concentrations within 70-130 % of actual. Allowable exception: A maximum of 1 compound per List or 10% of the compounds on a List, whichever is greater, may fall outside 70-130% provided they are in the range 60-140% of actual.
CLOSING Calibration Verification	Determined concentrations within 70-130 % of actual. Allowable exceptions: 1) Results for the greater of 1 compound or 10% of the compounds on a List may fall outside 60-140% provided the RPD between the CLOSING result and the OPENING result is <40%. 2) Closing calibration verification limits do not apply to Furosemide and Hydrochlorothiazide.
Instrumental Carryover And Instrument Background	Every Initial Calibration, Cal/Ver, or SPM: < 0.3 % carryover and area response of analytes in instrument blank < 800 judged following two previous methanol blank injections.

APPENDIX I: LIMITATIONS TO PERFORMANCE

1. SOIL/SEDIMENT SAMPLES

The following surrogates can show recoveries in soil and sediment samples that do not meet method criteria. The exact reason is not known, as recoveries are in the normal range for other matrices including biosolids samples that undergo identical processing, and for aqueous samples as well. The interaction of dissolved inorganic components of the matrix with the analytes and the material in the Oasis HLB cartridge is the most likely cause for compounds in List 1 and List 5 showing low recovery.

Surrogate	List	Issue
$^{13}C_3$, ^{15}N-Ciprofloxacin	List 1	Low Recovery
^{13}C-d_3-Naproxen	List 3	Low Recovery
$^{13}C_3$-Ibuprofen	List 3	Low Recovery
$^{13}C_6$-Triclocarban	List 3	Low Recovery
d_5-Warfarin	List 3	Low Recovery
d_6-Bisphenol A	List 3	Low Recovery
d_6-Gemfibrozil	List 3	Low Recovery
d_6-Amitryptilline	List 5	Low Recovery
d_3-Benztropine	List 5	Low Recovery
d_3-Cocaine	List 5	Low Recovery
d_5-Norfluoxetine	List 5	Low Recovery
d_6-Paroxetine	List 5	Low Recovery
d_5-Propoxyphene	List 5	Low Recovery
d_7-Propranolol	List 5	Low Recovery

The following analytes show recoveries in the spiked matrix sample (SPM) not meeting existing method specifications. In addition, reporting of analytes in soil/sediment samples can require flagging due to surrogate recovery issues.

Analyte	List	Issue
Cefotaxime	List 1	High Recovery
Enrofloxacin	List 1	High Recovery/Not Reportable
Lomefloxacin	List 1	High Recovery/Not Reportable
Ofloxacin	List 1	High Recovery/Not Reportable
Oxolinic Acid	List 1	High Recovery
Penicillin V	List 1	High Recovery
Sarafloxacin	List 1	High Recovery/Not Reportable
Clinafloxacin	List 1	High Recovery/Not Reportable
Norfloxacin	List 1	High Recovery/Not Reportable
Ciprofloxacin	List 1	Not Reportable
Lincomycin	List 1	Low Recovery
Oxacillin	List 1	Low Recovery
Penicillin G	List 1	Low Recovery
Sulfamethizole	List 1	Low Recovery

2. 1,7-DIMETHYLXANTHINE, THEOPHYLLINE AND THEOBROMINE

1,7-Dimethylxanthine is an analyte in List 1, Theophylline or 1,3-dimethylxanthine is an analyte in List 5 of the same method. These analytes are isomers, and hence co-elute in both List 1 and List 5 instrumental runs, leading to a systematic over-reporting of each compound in the Spiked Matrix (SPM) samples. The recovery criteria for these compounds takes into account the effect of the cross interference on data accuracy. Any positive detection of either analyte is presumed to be a sum of the two analytes. Neither the HPLC, nor the mass spectrometer, can differentiate between the two compounds.

3. ROXITHROMYCIN, CLARITHROMYCIN AND TYLOSIN REQUANTIFICATIO

Roxithromycin, clarithromycin and tylosin are all quantified against ^{13}C-sulfamethazine. This surrogate is chemically different from the analytes, and can sometimes show low recovery in samples even when the three analytes are not affected. If the recovery of ^{13}C-sulfamethazine is less than 10%, upon request, roxithromycin, clarithromycin and tylosin are requantified against the recovery standard ^{13}C-atrazine and flagged as estimated minimum concentrations if detected. The data is evaluated and flagged using procedures outlined in AXYS Document QDO-027 *"Rules for the Application of Non-Quantifiable Flags (NQ) to MLA-075 Results"*.

4. CORRECTION PROCEDURE FOR HYDROCODONE AND CODEINE CROSS INTERFERENCE.

An examination of sample data and investigatory work reveals that there is significant analytical cross-interference between hydrocodone and codeine in the List 4 analysis. This interference arises from the chemical similarity of these compounds. The compounds have the same molecular weight and chemical formula, $C_{18}H_{21}NO_3$, and due to this structural similarity they are not separated on the HPLC column used in this analysis. In addition, full product ion scan data reveals that the quantitation transitions for each of these compounds show mass spectrometric interferences from the presence of the other compound. The extent of this interference is constant across the concentration range of the method, except close to the reporting limit where there is increased uncertainty.

The interference affects all analytical runs including the calibration. Impact on the spiked matrix (SPM/OPR) data is minimal because the effects from the calibration and sample data cancel each other out. Therefore, reported spike recovery data will not change significantly.

Correction

An algebraic correction of the results of hydrocodone and codeine is possible due to the constancy of the cross-interference. Using this algebraic correction enables Axys to report approximate concentrations of hydrocodone and codeine with the interferences taken into account. Use of this correction also enables Axys to detect and correct for false positive occurrence. In addition, the selection of a new quantitation transition for codeine (300.0 → 215.0) has greatly reduced the cross interference of hydrocodone in codeine.

Algebraic Solution

Area Correction

$$H_{199} = \frac{Y - aX}{1 - ab}$$, and

$$C_{215} = \frac{X - bY}{1 - ab}$$

where X, Y = Observed areas of codeine and hydrocodone, respectively
C, H = Corrected areas for codeine and hydrocodone, respectively
a, b = Cross Interference constants, a = 0.564 (codeine in hydrocodone) and b = 0.022 (hydrocodone in codeine).

Correction of Linearity

Because the ratio of codeine:hydrocodone concentration is constant in the linearity calibration solutions, the linearity slope is reduced for each compound by a constant R = 0.737 for hydrocodone and 0.966 for codeine.

Concentration

$$C_{corr} = \frac{C_{uncorr} * A_{corr}}{R * A_{uncorr}},$$

where A_{corr} is H or C
A_{uncorr} is X or Y
R is the linearity correction.

Correction Limits

For hydrocodone, if $\frac{Y - H_{199}}{Y} > 0.5$, the concentration will be reported as ND < Y.

For codeine, if $\frac{X - C_{215}}{X} > 0.5$, the concentration will be reported as ND < X.

Application of the Correction

This correction is carried out in LIMS after data evaluation. The correction is applied to all samples except the calibration runs (calibration correction is already part of the correction), and the calibration verification runs.

Positive or Negative Bias

The sample correction and linearity corrections work in opposite directions. In a scenario where one analyte is present at relatively high levels and the other analyte is not present, or present at low levels, the effect from the linearity correction will dominate. If the relative amounts are comparable, the effect of the sample area correction will dominate.

Uncertainty and Impact on Sample Data

The correction approach takes into account the increased uncertainty due this cross-interference. If the measured area response for a compound is at least two times the correction required, data indicates that the correction can be carried out and the corrected concentration is reported. However, if the correction required is higher than this threshold, the compound is reported as not detected with a detection limit equal to the observed concentration. The effect will be to elevate the detection limit of the lower concentration analyte in the presence of relatively higher concentrations of the alternate analyte.

5. METHYL ESTER INTERFERENCE OF BETA-LACTAM ANTIBIOTICS

Cloxacillin, oxacillin and penicillin G are reported as 'Information Values' of estimated concentration. These compounds are determined by LC-MS/MS using ions from the methanol adduct of the compound ($M+CH_3OH$). There is indication that methyl esters of these compounds can also form in standard solutions over time. Ions from these methyl esters cannot be distinguished from methanol adduct ions formed from the parent compound. The consequence of this reaction could be a slow, but continuous increase of instrument response for these compounds in the calibration solutions. The rate of change in response is different for each compound. This behavior has not yet been observed/documented in client samples. The result of this standard transformation is to confer greater uncertainty on measured concentrations of these three compounds.

6. POTENTIAL AMPHETAMINE INTERFERENCE

The presence of an interfering compound with potential to obscure or cause false positive detection of amphetamine has been observed in some water and solids samples. Use of the secondary transition response, itself prone to interference, is not reliable in overcoming the interference problem. Partial or complete chromatographic resolution of the interfering compound has been observed - i.e. a shift of the native compound peak RT (retention time) relative to that of the d5-amphetamine surrogate is indicative of the interference. Where evidence of this interference is observed amphetamine results are flagged in reports as "estimated maximum possible values".

1. Positive identification of amphetamine requires an RT difference of 0.10 minutes or less between native and labeled amphetamine.
2. Where the RT differences between a candidate peak and labeled amphetamine is greater than +0.10 minutes, the result will be quantified as amphetamine but flagged as an "estimated maximum possible concentration" on reports. The flag must be edited by hand in LIMS; EMPC, K or NDR dependent on client flagging requirements.
3. Where the RT difference between the closest native peak and labeled amphetamine is sufficient to avoid "masking" of any amphetamine response (generally requires an RT difference of 0.25 minutes or greater) amphetamine will be reported as not detected.
4. Where multiple injection data for a sample are available (e.g. a neat and a diluted run), instrument analysts will report amphetamine from the chromatogram producing the most definitive result based on an evaluation of peak shape and peak resolution. The result will

be quantified as amphetamine but flagged as an “estimated maximum possible concentration” on reports. The flag must be edited by hand in LIMS; EMPC, K or NDR dependent on client flagging requirements.

5. Extracts will not be routinely diluted and reinjected for improvement of amphetamine interference alone as there is no evidence that this is systematically effective.

6. For amphetamine with a high peak area response above the SPM, the 1st channel should be confirmed by the 2nd channel. If no peak is present in the 2nd channel, the peak in the 1st channel is possibly not amphetamine and should be removed from the 1st channel.

7. POTENTIAL DEGRADATION OF RANITIDINE IN THE STANDARD SOLUTION

Degradation of ranitidine in the standard solution used to prepare OPR tests has been observed intermittently under the specific conditions of the storage. Where OPR test results indicate the possibility of spiking solution degradation, the ranitidine OPR assigned value is adjusted based on the results of a secondary QC test solution (SAR) prepared from the same ampoule that has been analyzed alongside samples. This problem has been demonstrated to have no impact on sample data accuracy

APPENDIX II: EXTRACTION OF TISSUE SAMPLES

The analysis requires extraction at two different pH conditions: At pH 10 for analysis of fourteen analytes (List 4); and at pH 2.0 for the analysis of the other analytes (Lists 1, 2, 3, and 5).

Two separate tissue sub-samples (one for acidic extraction and the other for basic extraction) are spiked with surrogates, extracted by sonication with pure acetonitrile and then with aqueous buffer (separate extractions at pH 2 and at pH 10, respectively), concentrated by rotary evaporation, decanted, and diluted with ultra pure water to 200 mL. The acidic extract is treated with EDTA. The acidic and basic extracts are then separately cleaned up by solid phase extraction (SPE) and analyzed by LC/ESI-MS/MS in positive and negative ionization modes requiring a total of five runs for the complete list of analytes.

QC Acceptance Limits, Tissues

List 1	OPR Recovery		Sample Surrogate Recovery	
	Low (%)	High (%)	Low (%)	High (%)
Acetaminophen	70	130		
Azithromycin	70	250		
Caffeine	70	130		
Carbadox	10	130		
Carbamazepine	70	150		
Cefotaxime	70	300		
Ciprofloxacin	70	130		
Clarithromycin	70	250		
Clinafloxacin	70	200		
Cloxacillin [2]	70	250		
Dehydronifedipine	70	200		
Diphenhydramine	60	130		
Diltiazem	70	200		
Digoxin	70	250		
Digoxigenin	50	200		
Enrofloxacin	70	130		
Erythromycin-H_2O	70	130		
Flumequine	60	200		
Fluoxetine	70	130		
Lincomycin	70	300		
Lomefloxacin	70	150		
Miconazole	5	130		
Norfloxacin	70	150		
Norgestimate	5	130		
Ofloxacin	70	200		
Ormetoprim	70	130		
Oxacillin [2]	70	200		
Oxolinic acid	70	130		
Penicillin G [2]	20	130		
Penicillin V	70	250		
Roxithromycin	50	200		
Sarafloxacin	50	130		
Sulfachloropyridazine	70	200		

Sulfadiazine	70	300		
Sulfadimethoxine	70	130		
Sulfamerazine	70	200		
Sulfamethazine	70	130		
Sulfamethizole	60	130		
Sulfamethoxazole	70	130		
Sulfanilamide	50	300		
Sulfathiazole	70	130		
Thiabendazole	70	130		
Trimethoprim	70	130		
Tylosin	60	200		
Virginiamycin M1	30	200		
1,7-Dimethylxanthine	70	250		
$^{13}C_2$,^{15}N-acetaminophen	30	150	30	250
$^{13}C_3$-Caffeine	30	150	20	250
d10-Carbamazepine	30	150	30	150
$^{13}C_3$,N^{15}-ciprofloxacin	30	150	30	200
$^{13}C_2$-Erythromycin-H_2O	30	206	5	200
d5-Fluoxetine	30	150	20	150
$^{13}C_6$-Sulfamethazine	30	150	30	150
$^{13}C_6$-Sulfamethoxazole	30	150	10	150
d6-Thiabendazole	30	150	30	150
$^{13}C_3$-Trimethoprim	30	150	30	200

OPR Recovery - List 2
This method has not been validated for List 2 compounds in tissue samples

List 3	**OPR Recovery**		**Sample Surrogate Recovery**	
	Low (%)	**High (%)**	**Low (%)**	**High (%)**
Bisphenol A	60	130		
Furosemide	70	150		
Gemfibrozil	70	130		
Glipizide	70	130		
Glyburide	70	130		
Hydrochlorothiazide	20	130		
2-Hydroxy-Ibuprofen	70	221		
Ibuprofen	70	130		
Naproxen	70	130		
Triclocarban	70	130		
Triclosan	70	146		
Warfarin	70	130		
d6-Bisphenol A	30	150	30	150
d6-Gemfibrozil	20	150	5	150
d11-Glipizide	30	150	30	150
d3-Glyburide	20	150	5	150
$^{13}C_3$-Ibuprofen	30	150	10	150

^{13}C-d3-Naproxen	30	150	30	150
$^{13}C_6$-Triclocarban [1]	NQ	150	NQ	150
$^{13}C_{12}$-Triclosan [1]	5	150	NQ	150
d5-Warfarin	30	150	10	150

List 4	**OPR Recovery**		**Sample Surrogate Recovery**	
	Low (%)	**High (%)**	**Low (%)**	**High (%)**
Albuterol	60	130		
Amphetamine	70	130		
Atenolol	70	130		
Atorvastatin	70	150		
Cimetidine	30	130		
Clonidine	70	130		
Codeine	70	130		
Cotinine	70	130		
Enalapril	70	130		
Hydrocodone	70	130		
Metformin	70	130		
Oxycodone	70	150		
Ranitidine [1]	NQ	150		
Triamterene	70	130		
d3-Albuterol	20	150	5	150
d5-Amphetamine	30	150	5	150
d7-Atenolol	30	150	30	300
d3-Cimetidine [1]	30	150	NQ	500
d4-Clonidine	30	150	30	300
d6-Codeine	10	150	5	150
d3-Cotinine	30	150	30	300
d5-Enalapril	30	150	10	150
d3-Hydrocodone	30	150	20	150
d6-Metformin	10	150	5	200
d6-Oxycodone	30	150	30	150

List 5	**OPR Recovery**		**Sample Surrogate Recovery**	
	Low (%)	**High (%)**	**Low (%)**	**High (%)**
Alprazolam	70	130		
Amitriptyline	70	130		
Amlodipine	70	130		
Benzoylecgonine	70	130		
Benztropine	70	150		
Betamethasone	70	250		
Cocaine	70	130		
DEET	70	150		
Desmethyldiltiazem	70	200		
Diazepam	70	130		
Fluocinonide	70	130		
Fluticasone Propionate	20	130		
Hydrocortisone	70	150		

10-Hydroxy-Amitriptyline	70	130		
Meprobamate	70	130		
Methylprednisolone	50	150		
Metoprolol	70	130		
Norfluoxetine	70	130		
Norverapamil	60	130		
Paroxetine	70	130		
Prednisolone	70	150		
Prednisone	70	150		
Promethazine	70	130		
Propoxyphene	70	130		
Propranolol	70	130		
Sertraline	10	130		
Simvastatin	10	130		
Theophylline	70	273		
Trenbolone	70	130		
Trenbolone acetate	30	130		
Valsartan	20	130		
Verapamil	70	200		
d5-Alprazolam	30	150	30	150
d6-Amitriptyline	30	150	10	150
d8-Benzoylecgonine	30	150	20	150
d3-Benztropine	30	150	10	150
d3-Cocaine	30	150	30	150
d7-DEET	30	150	30	150
d5-Diazepam	30	150	10	150
d3-Methylprednisolone	30	200	30	150
d7-Metoprolol	30	150	30	200
d5-Norfluoxetine	30	150	5	300
d6-Paroxetine	20	150	5	150
d4-Promethazine	30	150	20	150
d5-propoxyphene	30	150	30	200
d7-Propranolol	30	150	30	200
$^{13}C, ^{15}N_2$-Theophylline	30	150	20	150
d4-Hydrocortisone	30	150	30	200

[1] NQ= Not Quantifiable. Low recovery rate may preclude quantification

[2] Analysis result classified as 'Information Value' of estimated concentration.

APPENDIX III: EFFECTS OF ADDING ASCORBIC ACID TO SAMPLES.

Ascorbic acid is added to quench free chlorine in aqueous samples that have been chlorinated. The presence of free chlorine has severe effects on the recovery of analytes and most surrogate compounds. 50 mg/L of ascorbic acid is usually added to samples. The vast majority of analytes and standards are not affected by ascorbic acid addition. It is possible that some analytes may show enhanced recovery. The effects of ascorbic acid on each analyte/standard is shown below.

Analyte	List	Effect	Surrogates	List	Effect
Acetaminophen	List 1	Normal	$^{13}C_2$, ^{15}N-Acetaminophen	List 1	Normal
Azithromycin	List 1	Normal	$^{13}C_3$-Caffeine	List 1	Normal
Caffeine	List 1	Normal	$^{13}C_3$, ^{15}N-Ciprofloxacin	List 1	Normal
Carbadox	List 1	Normal	$^{13}C_2$-Erythromycin-H_2O	List 1	Normal
Carbamazepine	List 1	Normal	d5-Fluoxetine	List 1	Normal
Cefotaxime	List 1	Normal	$^{13}C_6$-Sulfamethazine	List 1	Normal
Ciprofloxacin	List 1	Normal	$^{13}C_6$-Sulfamethoxazole	List 1	Normal
Clarithromycin	List 1	Normal	d6-Thiabendazole	List 1	Normal
Clinafloxacin	List 1	Normal	$^{13}C_3$-Trimethoprim	List 1	Normal
Cloxacillin	List 1	Normal	d6-Thiabendazole	List 2	Normal
Dehydronifedipine	List 1	Normal	d6-Bisphenol	List 3	Normal
Diphenhydramine	List 1	Marginal low bias	d6-Gemfibrozil	List 3	Normal
Diltiazem	List 1	Marginal low bias	d11-Glipizide	List 3	Normal
Digoxin	List 1	Normal	d3-Glyburide	List 3	Normal
Digoxigenin	List 1	Normal	$^{13}C_3$-Ibuprofen	List 3	High bias
Enrofloxacin	List 1	Normal	^{13}C-d3-Naproxen	List 3	Normal
Erythromycin-H_2O	List 1	Normal	$^{13}C_6$-Triclocarban	List 3	Normal
Flumequine	List 1	Normal	$^{13}C_{12}$-Triclosan	List 3	Normal
Fluoxetine	List 1	Normal	d5-Warfarin	List 4	Normal
Lincomycin	List 1	Normal	d3-Albuterol	List 4	Normal
Lomefloxacin	List 1	Normal	d6-Metformin	List 4	Normal
Miconazole	List 1	Normal	d3-Cotinine	List 4	Normal
Norfloxacin	List 1	Normal	d3-Cimetidine	List 4	Normal
Norgestimate	List 1	Normal	d5-Enalapril	List 4	Normal
Ofloxacin	List 1	Normal	d6-Oxycodone	List 4	Normal
Ormetoprim	List 1	Normal	d4-Clonidine	List 4	Normal
Oxacillin	List 1	Normal	d5-Amphetamine	List 4	Normal
Oxolinic Acid	List 1	Normal	d6-Codeine	List 4	Normal
Penicillin G	List 1	Normal	d3-Hydrocodone	List 4	Normal
Penicillin V	List 1	Normal	d7-Atenolol	List 4	Normal
Roxithromycin	List 1	Normal	d5-Alprazolam	List 5	Normal
Sarafloxacin	List 1	Normal	d6-Amitriptyline	List 5	Normal
Sulfachloropyridazine	List 1	Normal	d8-Benzoylecgonine	List 5	Normal
Sulfadiazine	List 1	Normal	d3-Benztropine	List 5	Normal
Sulfadimethoxine	List 1	Normal	d3-Cocaine	List 5	Normal
Sulfamerazine	List 1	Normal	d7-DEET	List 5	Normal
Sulfamethazine	List 1	Normal	d5-Diazepam	List 5	Normal
Sulfamethizole	List 1	Normal	d3-Methylprednisolone	List 5	Normal
Sulfamethoxazole	List 1	Normal	d7-Metoprolol	List 5	Normal
Sulfanilamide	List 1	Normal	d5-Norfluoxetine	List 5	Normal

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Sulfathiazole	List 1	Normal	d6-Paroxetine	List 5	Normal
Thiabendazole	List 1	Normal	d4-Promethazine	List 5	Normal
Trimethoprim	List 1	Normal	d5-propoxyphene	List 5	Normal
Tylosin	List 1	Normal	d7-Propranolol	List 5	Normal
Virginiamycin M1	List 1	Normal	^{13}C, $^{15}N_2$-Theophylline	List 5	Normal
1,7- Dimethylxanthine	List 1	Normal	d4-Hydrocortisone	List 5	Normal
CTC	List 2	Normal			
ECTC	List 2	Normal			
ACTC	List 2	Normal			
EACTC	List 2	Normal			
ICTC	List 2	Normal			
Demeclocycline	List 2	Normal			
Doxycycline	List 2	Normal			
OTC	List 2	Normal			
EOTC	List 2	Normal			
TC	List 2	Normal			
ETC	List 2	Normal			
EATC	List 2	High Bias			
ATC	List 2	Normal			
Minocycline (458>441)	List 2	Normal			
Bisphenol A	List 3	Normal			
Furosemide	List 3	Normal			
Gemfibrozil	List 3	Normal			
Glipizide	List 3	Normal			
Glyburide	List 3	Normal			
Hydrochlorothiazide	List 3	Normal			
2-hydroxy-ibuprofen	List 3	Normal			
Ibuprofen	List 3	Normal			
Naproxen	List 3	Normal			
Triclocarban	List 3	Normal			
Triclosan	List 3	Normal			
Warfarin	List 3	Normal			
Albuterol	List 4	Normal			
Amphetamine	List 4	Normal			
Atenolol	List 4	Normal			
Atorvastatin	List 4	Normal			
Cimetidine	List 4	Normal			
Clonidine	List 4	Normal			
Codeine	List 4	Normal			
Cotinine	List 4	Normal			
Enalapril	List 4	Normal			
Hydrocodone	List 4	Normal			
Metformin	List 4	Normal			
Oxycodone	List 4	Normal			
Ranitidine	List 4	Normal			
Triamterene	List 4	Normal			
Alprazolam	List 5	Normal			
Amitriptyline	List 5	Normal			
Amlodipine	List 5	Normal			
Benzoylecgonine	List 5	Normal			
Benztropine	List 5	Normal			
Betamethasone	List 5	Normal			
Cocaine	List 5	Normal			
DEET	List 5	Normal			
Desmethyldiltiazem	List 5	Normal			

Diazepam	List 5	Normal			
Fluocinonide	List 5	Normal			
Fluticasone Propionate	List 5	Normal			
Hydrocortisone	List 5	Normal			
10-hydroxy-amitriptyline	List 5	Normal			
Meprobamate	List 5	Normal			
Methylprednisolone	List 5	Normal			
Metoprolol	List 5	Normal			
Norfluoxetine	List 5	Normal			
Norverapamil	List 5	Normal			
Paroxetine	List 5	High Bias			
Prednisolone	List 5	Normal			
Prednisone	List 5	Normal			
Promethazine	List 5	Normal			
Propoxyphene	List 5	Normal			
Propranolol	List 5	Normal			
Sertraline	List 5	Normal			
Simvastatin	List 5	Normal			
Theophylline	List 5	Normal			
Trenbolone	List 5	Normal			
Trenbolone acetate	List 5	Normal			
Valsartan	List 5	Normal			
Verapamil	List 5	Normal			

APPENDIX IV: SUMMARY COMPARISON OF USEPA METHOD 1694 AND AXYS METHOD MLA-075.

Area	**EPA 1694**	**MLA-075**
Applicable Matrices	Aqueous, Solids	Aqueous, Solids, ***Tissue***
Analytes Offered	73 compounds, 2 fractions, 4 instrumental runs	***146*** compounds, 2 fractions, ***6*** instrumental runs
Sample Containers	Amber glass	Amber glass or ***HDPE***
Chlorine Quenching (water samples)	80 mg sodium thiosulfate per liter, ascorbic acid allowable alternative	50 mg ascorbic acid per liter
Sample Preservation	pH 5-9 if hold time >48hr or freeze	None
Sample Storage Temperature	< 6ºC or frozen (aqueous, solids)	Aqueous: < 4 ºC; Solids: <-20 ºC
Sample Hold Time (guideline only)	Aqueous, 7 days at < 6ºC, undefined for frozen storage Solids, 7 days at <-10 ºC	Aqueous: 7days for < 4 ºC storage Solids: 7 days for -20 ºC storage
Extract Hold Time	40 days	**40** days
Extraction (separate acid, base fractions)	Aqueous: adjust to pH 2 or pH 10, stabilize with EDTA Solids: adjust to pH 2 or pH 10, stabilize with EDTA, ultrasonic extract into buffered acetonitrile, exchange to water solution	Aqueous: adjust to pH 2 or pH 10, stabilize with EDTA Solids: adjust to pH 2 or pH 10, stabilize with EDTA, ultrasonic extract into buffered acetonitrile, exchange to water solution
Clean-up (separate acid, base fractions)	SPE (HLB), elute in methanol	SPE (HLB), elute in methanol
Instrumental Acquisition	LC-MS/MS, 3 +ESI runs, 1 -ESI run	LC-MS/MS, ***5 +ESI runs***, 1 -ESI run
Calibration Range, ng/mL in standard	Minimum 5 points, range 0.25- 25000 mg/mL	Minimum 5 points, range 0.08- 30000 ng/mL
Calibration Model	Multi-level, constant RRF; alternative models allowable	Multi-level, ***1/x weighted linear regression***
Initial Calibration Limits	RSD of RRF >20% (isotope dilution) or <35% (internal standard)	***Calculated points 70-130% of actual (allowable exception per compound 60-140%)***

Area	EPA 1694	MLA-075
Calibration Verification Limits	70-130%	***Calculated points 70-130% of actual (allowable exception one compound per list or 10% of compounds per list may be 60-140%)***
Quantification Type	Isotope dilution or internal standard	Isotope dilution or internal standard
Quantification References	18 isotopically labeled compounds	***67*** isotopically labeled compounds
Initial Precision and Recovery (IPR) Limits, %	range 6-180 %	performance based, generally ***3- 250 %***
On-Going Precision and Recovery (OPR) Limits, %	range 5-200 %	performance based, generally ***2- 300 %***
Blank Limits, ng per sample	range 1-500 ng	performance based, generally ***0.3 – 80 ng***
Surrogate Recovery Limits, %	range 5- 200 %	performance based, generally ***3- 250 %***
Lower Reporting Limit, ng per sample based on low calibration standard	range 1 – 500 ng	performance based, generally ***0.3 – 500 ng***

APPENDIX V: ANALYSIS OF LIST 6 COMPOUNDS IN AQUEOUS, SOLID AND TISSUE SAMPLES.

The aqueous, solid and tissue sample extraction and cleanup procedures for List 6 compounds are the same as for List 1, 2, 3 and 5 compounds, and List 6 compounds may be analyzed from the same extract.

QC Acceptance Limit Guidelines for List 6 Compounds

	OPR Recovery and surrogate recovery in sample (% Recovery)		IPR			Blank Level (ng)
			Average Recovery (%)		RSD (%)	
	Low	High	Low	High		
List 6 Native Compounds (APOS)						
Amsacrine, aqueous	50	130	60	130	30	≤ 0.8
solid	2	130	3	130	100	
tissue	20	130	20	130	30	
Azathioprine, all matrices	70	130	70	130	30	≤ 8
Busulfan, all matrices	70	130	70	130	30	≤ 24
Carmustine, aqueous	70	130	70	130	30	≤ 80
solid	60	130	60	130	30	
tissue	70	180	70	160	30	
Chloramphenicol, aqueous	70	150	70	150	30	≤ 900
solid	70	150	70	150	30	
tissue	70	250	70	250	30	
Citalopram, aqueous	70	130	70	130	30	≤ 0.4
solid	40	160	50	160	30	
tissue	50	130	60	130	30	
Clotrimazole, all matrices	70	130	70	130	30	≤ 2
Colchicine, aqueous	70	130	70	130	30	≤ 2
solid	70	130	70	130	30	
tissue	70	140	70	140	30	
Cyclophosphamide, aqueous,	70	130	70	130	30	≤ 1.6
solid	70	130	70	130	30	
tissue	70	140	70	130	30	
Daunorubicin, aqueous	60	140	60	130	30	≤ 16
solid	25	260	30	240	70	
tissue	70	130	70	130	30	
Diatrizoic acid, aqueous	70	130	70	130	30	≤ 40
solid	60	140	70	130	30	
tissue	70	130	70	130	30	
Doxorubicin, aqueous	30	180	30	160	45	≤ 24
solid	15	200	15	180	70	
tissue	70	130	70	130	30	
Drospirenone, aqueous	70	130	70	130	30	≤ 8
solid	70	130	70	130	30	
tissue	70	140	70	130	30	
Etoposide, aqueous	70	150	70	140	30	≤ 4
solid	60	140	60	130	30	
tissue	70	130	70	130	30	

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	OPR Recovery and surrogate recovery in sample (% Recovery)		IPR			Blank Level (ng)
			Average Recovery (%)		RSD (%)	
	Low	High	Low	High		
Iopamidol, aqueous	70	140	70	140	30	≤ 80
solid	70	130	70	130	30	
tissue	70	130	70	130	30	
Lomustine, aqueous	40	130	50	130	30	≤ 50
solid	20	140	30	140	40	
tissue	40	130	40	130	30	
Medroxyprogesterone acetate, aqueous	60	130	60	130	30	≤ 4
solid	70	130	70	130	30	
tissue	70	130	70	130	30	
Melphalan, aqueous	50	130	50	130	30	≤ 64
solid	60	130	60	130	30	
tissue	50	130	50	130	30	
Metronidazole, all matrices	70	130	70	130	30	≤ 4
Moxifloxacin, aqueous	70	130	70	130	30	≤ 4
Solid [1]	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
tissue	50	130	50	130	30	≤ 4
Norethindrone, aqueous	60	180	60	170	30	≤ 64
solid	50	140	50	140	30	
tissue	60	200	70	180	30	
Oxazepam, aqueous	70	130	70	130	30	≤ 16
solid	60	130	70	130	30	
tissue	70	130	70	130	30	
Rosuvastatin, all matrices	70	130	70	130	30	≤ 16
Tamoxifen, aqueous	70	130	70	130	30	≤ 0.4
solid	40	180	50	180	30	
tissue	70	130	70	130	30	
Teniposide, aqueous	15	130	15	130	30	≤ 8
solid	15	130	20	130	40	
tissue	40	130	50	130	30	
Venlafaxine, aqueous	70	130	70	130	30	≤ 1.2
solid	70	130	70	130	30	
tissue	25	200	30	180	60	
Zidovudine, all matrices	70	130	70	130	30	≤ 50
Surrogate Standards						
$^{13}C_4$-Azathioprine, aqueous	50	150	50	150	30	
solid	50	150	50	150	30	
tissue	20	150	20	150	40	
d_8-Busulfan, aqueous	50	150	50	150	30	
solid	50	150	50	150	30	
tissue	50	160	50	160	30	
d_6-Citalopram, aqueous	50	150	50	150	30	
solid	2	150	2	150	150	
tissue	50	150	50	150	30	

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	OPR Recovery and surrogate recovery in sample (% Recovery)		IPR			Blank Level (ng)
			Average Recovery (%)		RSD (%)	
	Low	High	Low	High		
d_5-Clotrimazole, aqueous	50	150	50	150	30	
solid	50	150	50	150	30	
tissue	15	150	20	150	40	
d_6-Colchicine, all matrices	50	150	50	150	30	
d_4-Cyclophosphamide, aqueous	50	150	50	150	30	
solid	50	150	50	150	30	
tissue	40	150	40	150	30	
$^{13}C,d_3$-Daunorubicin, aqueous	10	150	10	150	80	
solid	1	150	1	150	250	
tissue	50	150	50	150	30	
d_6-Diatrizoic acid, aqueous	50	150	50	150	30	
solid	2	150	2	150	120	
tissue	15	150	15	150	30	
$^{13}C_3$-Drospirenone, aqueous	50	150	50	150	30	
solid	50	150	50	150	30	
tissue	30	150	40	150	30	
d_3-Etoposide, aqueous	10	150	10	150	80	
solid	50	150	50	150	30	
tissue	50	150	50	150	30	
d_8-Iopamidol, aqueous	15	150	15	150	30	
solid	5	150	7	150	100	
tissue	50	150	50	150	30	
d_6-Medroxyprogesterone acetate, aqueous	50	150	50	150	30	
solid	50	150	50	150	30	
tissue	30	150	30	150	30	
d_8-Melphalan, aqueous	4	150	4	150	60	
solid	10	150	10	150	50	
tissue	2	150	2\3	150	100	
d_4-Metronidazole, aqueous	50	150	50	150	30	
solid	50	150	50	150	30	
tissue	50	180	50	160	30	
$^{13}C,d_3$-Moxifloxacin, aqueous	15	150	15	150	50	
Solid [1]	n.a.	n.a.	n.a.	n.a.	n.a.	
tissue	50	150	50	150	30	
d_6-Norethindrone, aqueous	50	150	50	150	30	
solid	50	180	50	160	30	
tissue	50	150	50	150	30	
d_5-Oxazepam, aqueous	50	150	50	150	30	
solid	50	150	50	150	30	
tissue	40	150	40	150	30	
d_6-Rosuvastatin, aqueous	50	150	50	150	30	
solid	50	150	50	150	30	
tissue	40	150	50	150	30	
d_5-Tamoxifen, aqueous	30	150	40	150	30	
solid	8	150	8	150	80	
tissue	5	150	5	150	60	

	OPR Recovery and surrogate recovery in sample (% Recovery)		IPR			Blank Level (ng)
			Average Recovery (%)		RSD (%)	
	Low	High	Low	High		
d_6-Venlafaxine, aqueous	50	150	50	150	30	
solid	35	150	40	150	30	
tissue	30	150	40	150	30	
d_3-Zidovudine, aqueous	50	150	50	150	30	
solid	50	150	50	150	30	
tissue	50	180	50	180	30	
Recovery Standard						
$^{13}C_3$-Atrazine						

The acceptance limits in the table 21 above are guidelines based on initial estimate: recoveries outside of these limits do not invalidate results

Nominal Concentrations of Native Standard, Surrogate Standard and Recovery Standard Solutions for List 6 Compounds

Compound Name	Nominal concentration of Standard Solution	Typical amount spiked (ng)
Native Standard Solution for List 6 acid extracted analytes	**(µg/mL)**	**ng spiked from 240 µL or 100 µL spike**
Amsacrine	0.24	24
Azathioprine	2.4	240
Busulfan	7.2	720
Carmustine	24	2400
Chloramphenicol	240	24000
Citalopram	0.05	12
Clotrimazole	0.6	60
Colchicine	0.6	60
Cyclophosphamide	0.2	48
Daunorubicin	4.8	480
Diatrizoic acid	5	1200
Doxorubicin	7.2	720
Drospirenone	2.4	240
Etoposide	1.2	120
Iopamidol	10	2400
Lomustine	14.4	1440
Medroxyprogesterone acetate	1.2	120
Melphalan	19.2	1920
Metronidazole	1.2	120
Moxifloxacin	1.2	120
Norethindrone	19.2	1920
Oxazepam	4.8	480

Rosuvastatin	4.8	480
Tamoxifen	0.05	12
Teniposide	2.4	240
Venlafaxine	0.05	12
Zidovudine	14.4	1440
Surrogate Standard Solution for List 6 acid extracted analytes	**(µg/mL)**	**ng spiked from 25 µL spike**
$^{13}C_4$-Azathioprine	9.6	240
d_8-Busulfan	28.8	720
d_6-Citalopram	0.4	10
d_5-Clotrimazole	2.4	60
d_6-Colchicine	2.4	60
d_4-Cyclophosphamide	1.6	40
$^{13}C,d_3$-Daunorubicin	19.2	480
d_6-Diatrizoic Acid	40	1000
$^{13}C_3$-Drospirenone	9.6	240
d_3-Etoposide	4.8	120
d_8-Iopamidol	80	2000
d_6-Medroxyprogesterone acetate	4.8	120
d_8-Melphalan	76.8	1920
d_4-Metronidazole	4.8	120
$^{13}C,d_3$-Moxifloxacin	4.8	120
d_6-Norethindrone	76.8	1920
d_5-Oxazepam	19.2	480
d_6-Rosuvastatin	19.2	480
d_5-Tamoxifen	0.4	10
d_6-Venlafaxine	0.4	10
d_3-Zidovudine	57.6	1440
Recovery Standard Solution for List 6 acid extracted analytes	**(µg/mL)**	**ng spiked from 100 µL spike**
$^{13}C_3$-Atrazine	2.0	200
$^{13}C_6$-2,4,5-Trichlorophenoxyacetic acid	2.0	200

Nominal Concentrations of Calibration Solutions for List 6 Compounds (ng/mL)

Compound name	Calibration Standards List 6 (Acid extraction, positive ESI)						
	Level A	Level B	Level C	Level D	Level E	Level F	Level G
Amsacrine	0.2	0.6	2	6	20	60	200
Azathioprine	2	6	20	60	200	600	2000
Busulfan	6	18	60	180	600	1800	6000
Carmustine	20	60	200	600	2000	6000	20000
Chloramphenicol	220	550	1100	2200	4400	8800	22000
Citalopram	0.1	0.3	1	3	10	30	100
Clotrimazole	0.5	1.5	5	15	50	150	500
Colchicine	0.5	1.5	5	15	50	150	500
Cyclophosphamide	0.4	1.2	4	12	40	120	400

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Daunorubicin	4	12	40	120	400	1200	4000
Diatrizoic acid	10	30	100	300	1000	3000	10000
Doxorubicin	6	18	60	180	600	1800	6000
Drospirenone	2	6	20	60	200	600	2000
Etoposide	1	3	10	30	100	300	1000
Iopamidol	20	60	200	600	2000	6000	20000
Lomustine	12	36	120	360	1200	3600	12000
Medroxyprogesterone acetate	1	3	10	30	100	300	1000
Melphalan	16	48	160	480	1600	4800	16000
Metronidazole	1	3	10	30	100	300	1000
Moxifloxacin	1	3	10	30	100	300	1000
Norethindrone	16	48	160	480	1600	4800	16000
Oxazepam	4	12	40	120	400	1200	4000
Rosuvastatin	4	12	40	120	400	1200	4000
Tamoxifen	0.1	0.3	1	3	10	30	100
Teniposide	2	6	20	60	200	600	2000
Venlafaxine	0.1	0.3	1	3	10	30	100
Zidovudine	12	36	120	360	1200	3600	12000
Surrogate Standards							
$^{13}C_4$-Azathioprine	60	60	60	60	60	60	60
d_8-Busulfan	180	180	180	180	180	180	180
d_6-Citalopram	2.5	2.5	2.5	2.5	2.5	2.5	2.5
d_5-Clotrimazole	15	15	15	15	15	15	15
d_6-Colchicine	15	15	15	15	15	15	15
d_4-Cyclophosphamide	10	10	10	10	10	10	10
$^{13}C,d_3$-Daunorubicin	120	120	120	120	120	120	120
d_6-Diatrizoic Acid	250	250	250	250	250	250	250
$^{13}C_3$-Drospirenone	60	60	60	60	60	60	60
d_3-Etoposide	30	30	30	30	30	30	30
d_8-Iopamidol	500	500	500	500	500	500	500
d_6-Medroxyprogesterone acetate	30	30	30	30	30	30	30
d_8-Melphalan	480	480	480	480	480	480	480
d_4-Metronidazole	30	30	30	30	30	30	30
$^{13}C,d_3$-Moxifloxacin	30	30	30	30	30	30	30
d_6-Norethindrone	480	480	480	480	480	480	480
d_5-Oxazepam	120	120	120	120	120	120	120
d_6-Rosuvastatin	120	120	120	120	120	120	120
d_5-Tamoxifen	2.5	2.5	2.5	2.5	2.5	2.5	2.5
d_6-Venlafaxine	2.5	2.5	2.5	2.5	2.5	2.5	2.5
d_3-Zidovudine	360	360	360	360	360	360	360
Recovery Standards							
$^{13}C_3$-Atrazine	50	50	50	50	50	50	50

List 6 – Acid Extraction, Positive Electrospray Ionization (+)ESI: Analytes, Ions and Quantification References

(The acquisition ion masses in this table reflect the instrument settings. The actual MS/MS resolution is normally 1 amu.)

Target Analyte	Typical Retention Time (min)	Typical RRT	RRT Reference	Parent Ion Mass	Daughter Ion Mass	Quantified against
Iopamidol	2.4	1.000	d_8-Iopamidol	795.0	777.9 (558.8) *	d_8-Iopamidol
Diatrizoic acid	4.3	1.000	d_6-Diatrizoic acid	631.9	360.9 (614.6) *	d_6-Diatrizoic acid
Metronidazole	6.5	1.032	d_4-Metronidazole	171.9	128 (82.1) *	d_4-Metronidazole
Carmustine	10.2	0.895	$^{13}C_4$-Azathioprine	185 ** (187) *	80 (82) *	$^{13}C_4$-Azathioprine
Azathioprine	11.3	0.991	$^{13}C_4$-Azathioprine	277.9	142.0 (232.0) *	$^{13}C_4$-Azathioprine
Busulfan	11.8	1.017	d_8-Busulfan	264	151 (247) *	d_8-Busulfan
Zidovudine	12.0	1.000	d_3-Zidovudine	268.0	127.0 (110.0) *	d_3-Zidovudine
Moxifloxacin	14.5	1.000	$^{13}C,d_3$-Moxifloxacin	402.1	384.2 (358.2) *	$^{13}C,d_3$-Moxifloxacin
Chloramphenicol	14.7	0.980	d_4-Cyclophosphamide	340	275 (323) *	d_4-Cyclophosphamide
Cyclophosphamide	15.1	1.007	d_4-Cyclophosphamide	260.9	140.0 (233.0) *	d_4-Cyclophosphamide
Venlafaxine	15.1	1.000	d_6-Venlafaxine	278.3	58.4 (260.2) *	d_6-Venlafaxine
Amsacrine	15.1	1.000	d_6-Venlafaxine	394.0	315.1 (179.1) *	d_6-Venlafaxine
Melphalan	15.6	1.006	d_8-Melphalan	305	288 (246) *	d_8-Melphalan
Colchicine	16.0	1.000	d_6-Colchicine	400.1	358.1 (341.1) *	d_6-Colchicine
Lomustine	16.1	1.066	d_6-Venlafaxine	205 **	123 (80.1) *	d_6-Venlafaxine
Etoposide	16.2	1.000	d_3-Etoposide	606.2	229.2 (589.2) *	d_3-Etoposide
Citalopram	16.2	1.000	d_6-Citalopram	325.1	109.1 (262.1) *	d_6-Citalopram
Doxorubicin	16.4	0.932	$^{13}C,d_3$-Daunorubicin	544.0	397.0 (361.0) *	$^{13}C,d_3$-Daunorubicin

Daunorubicin	17.7	1.006	$^{13}C,d_3$-Daunorubicin	528.1	321.1 (363.1) *	$^{13}C,d_3$-Daunorubicin
Oxazepam	17.8	1.006	d_5-Oxazepam	287.0	241.0 (269.0) *	d_5-Oxazepam
Teniposide	18.2	1.123	d_3-Etoposide	674.1	229.1 (383.2) *	d_3-Etoposide
Rosuvastatin	18.5	1.000	d_6-Rosuvastatin	482.1	258.1 (300.1) *	d_6-Rosuvastatin
Norethindrone	19.2	1.005	d_6-Norethindrone	299.0	109.1 (91.1) *	d_6-Norethindrone
Drospirenone	19.9	1.000	$^{13}C_3$-Drospirenone	367.2	97.1 (349.2) *	$^{13}C_3$-Drospirenone
Clotrimazole	20.1	1.000	d_5-Clotrimazole	277	165 (199) *	d_5-Clotrimazole
Tamoxifen	20.9	1.000	d_5-Tamoxifen	372.3	72.3 (129.2) *	d_5-Tamoxifen
Medroxyprogesterone acetate	21.6	1.000	d_6-Medroxyprogesterone acetate	387.2	327.2 (123.1) *	d_6-Medroxyprogesterone acetate
Surrogate Standard						
d_8-Iopamidol	2.4	0.136	$^{13}C_3$-Atrazine	803.0	785.9 (562.9) *	$^{13}C_3$-Atrazine
d_6-Diatrizoic acid	4.3	0.244	$^{13}C_3$-Atrazine	637.9	367.0 (620.6) *	$^{13}C_3$-Atrazine
d_4-Metronidazole	6.3	0.358	$^{13}C_3$-Atrazine	176.0	128 (82.1) *	$^{13}C_3$-Atrazine
$^{13}C_4$-Azathioprine	11.4	0.648	$^{13}C_3$-Atrazine	281.9	146.0 (236.0) *	$^{13}C_3$-Atrazine
d_8-Busulfan	11.6	0.659	$^{13}C_3$-Atrazine	272	159.1 (255) *	$^{13}C_3$-Atrazine
d_3-Zidovudine	12.0	0.682	$^{13}C_3$-Atrazine	271.0	130.1 (113.0) *	$^{13}C_3$-Atrazine
$^{13}C,d_3$-Moxifloxacin	14.5	0.824	$^{13}C_3$-Atrazine	406.1	388.2 (362.2) *	$^{13}C_3$-Atrazine
d_4-Cyclophosphamide	15.0	0.852	$^{13}C_3$-Atrazine	265.2	140.0 (234.9) *	$^{13}C_3$-Atrazine
d_6-Venlafaxine	15.1	0.858	$^{13}C_3$-Atrazine	284.4	64.4 (266.3) *	$^{13}C_3$-Atrazine
d_8-Melphalan	15.5	0.881	$^{13}C_3$-Atrazine	313	296 (254.1) *	$^{13}C_3$-Atrazine
d_6-Colchicine	16.0	0.909	$^{13}C_3$-Atrazine	406.0	362.1 (344.1) *	$^{13}C_3$-Atrazine

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d_6-Citalopram	16.2	0.920	$^{13}C_3$-Atrazine	331.2	109.1 (262.2) *	$^{13}C_3$-Atrazine
d_3-Etoposide	16.2	0.920	$^{13}C_3$-Atrazine	609.2	229.1 (592.2) *	$^{13}C_3$-Atrazine
$^{13}C,d_3$-Daunorubicin	17.6	1.000	$^{13}C_3$-Atrazine	532.1	325.1 (367.1) *	$^{13}C_3$-Atrazine
d_5-Oxazepam	17.7	1.006	$^{13}C_3$-Atrazine	292.0	246.1 (274.1) *	$^{13}C_3$-Atrazine
d_6-Rosuvastatin	18.5	1.051	$^{13}C_3$-Atrazine	488.1	264.2 (306.2) *	$^{13}C_3$-Atrazine
d_6-Norethindrone	19.1	1.085	$^{13}C_3$-Atrazine	305.1	237.2 (114.9, 91.1) *	$^{13}C_3$-Atrazine
$^{13}C_3$-Drospirenone	19.9	1.131	$^{13}C_3$-Atrazine	370.1	97.1 (352.2) *	$^{13}C_3$-Atrazine
d_5-Clotrimazole	20.1	1.142	$^{13}C_3$-Atrazine	282	170 (199) *	$^{13}C_3$-Atrazine
d_5-Tamoxifen	20.9	1.188	$^{13}C_3$-Atrazine	377.4	72.3	$^{13}C_3$-Atrazine
d_6-Medroxyprogesterone acetate	21.6	1.227	$^{13}C_3$-Atrazine	393.1	330.2 (126.1) *	$^{13}C_3$-Atrazine
Recovery Standard						
$^{13}C_3$-Atrazine	17.6			219.1	176.9 (134.0) *	External Standard

* = Confirmation ions in instances of interference

** = Parent ion monitored from the breakdown product

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MLA-075 Rev 02, List 1 analytes (Acidic extraction, positive ESI)
Method Detection Limit for PPCP in Solids Samples
March 2010

MDL Results

Axys Method:	MLA-075 Rev 02, List 1 analytes
Analysis Type:	PPCP (Pharmaceuticals and Personal Care Products), List 1 analytes
Instrument Type:	LC-MS/MS
Matrix Spiked:	SOLIDS
Axys Workgroup:	WG32245
Column Type:	C18
MDL Protocol:	Federal Register 40 CFR Part 136, Appendix B, rev. 1.11, no iteration

MDL 1 Data Filename:	QA0J_064 S: 17	**Sample ID:**	WG32245-107	**Instr. Analysis Date:**	6-Apr-2010
MDL 2 Data Filename:	QA0J_064 S: 18	**Sample ID:**	WG32245-108	**Instr. Analysis Date:**	6-Apr-2010
MDL 3 Data Filename:	QA0J_064 S: 19	**Sample ID:**	WG32245-109	**Instr. Analysis Date:**	6-Apr-2010
MDL 4 Data Filename:	QA0J_064 S: 20	**Sample ID:**	WG32245-110	**Instr. Analysis Date:**	6-Apr-2010
MDL 5 Data Filename:	QA0J_064 S: 21	**Sample ID:**	WG32245-111	**Instr. Analysis Date:**	7-Apr-2010
MDL 6 Data Filename:	QA0J_064 S: 22	**Sample ID:**	WG32245-112	**Instr. Analysis Date:**	7-Apr-2010
MDL 7 Data Filename:	QA0J_064 S: 23	**Sample ID:**	WG32245-113	**Instr. Analysis Date:**	7-Apr-2010
MDL 8 Data Filename:	QA0J_064 S: 24	**Sample ID:**	WG32245-114	**Instr. Analysis Date:**	7-Apr-2010

ALL CONCENTRATIONS REPORTED ON THIS FORM ARE CONCENTRATIONS IN SAMPLES
Based on 1 g of solids

Native Analyte	Method Detection Limit, ng/g	Spiking Level ng/g	Number of Observations	Mean ng/g	Standard Devation	Student's t-Value	
ACETAMINOPHEN	3.3	50	8	46.4	1.1	2.998	
AZITHROMYCIN	1.2	5	8	4.38	0.42	2.998	
CAFFEINE	11	50	8	50.2	3.73	2.998	
CARBADOX	1.4	5	8	3.83	0.46	2.998	
CARBAMAZEPINE	0.59	5	8	5.75	0.20	2.998	see below
CEFOTAXIME	7.8	20	8	19.9	2.59	2.998	
CIPROFLOXACIN	3.7	20	8	25.8	1.2	2.998	
CLARITHROMYCIN	1.1	5	8	4.31	0.37	2.998	
CLINAFLOXACIN	6.3	20	8	43.1	2.1	2.998	
CLOXACILLIN	1.8	10	8	10.5	0.59	2.998	
DEHYDRONIFEDIPINE	0.41	2	8	2.22	0.14	2.998	
DIPHENHYDRAMINE	0.27	2	8	1.94	0.09	2.998	
DILTIAZEM	0.15	1	8	0.963	0.05	2.998	
DIGOXIN	16	20	8	27.7	5.49	2.998	
DIGOXIGENIN	7.5	20	8	24.5	2.51	2.998	
ENROFLOXACIN	2.9	10	8	15.4	0.96	2.998	
ERYTHROMYCIN-H2O	0.26	1	8	1.07	0.09	2.998	see below
FLUMEQUINE	1.1	5	8	5.36	0.38	2.998	
FLUOXETINE	0.78	5	8	5.24	0.26	2.998	
LINCOMYCIN	2.8	10	8	8.37	0.92	2.998	
LOMEFLOXACIN	5.9	10	8	20.7	1.97	2.998	
MICONAZOLE	0.38	5	8	3.86	0.13	2.998	
NORFLOXACIN	7.6	50	8	57.1	2.52	2.998	
NORGESTIMATE	1.7	10	8	8.70	0.57	2.998	
OFLOXACIN	1.9	5	8	8.98	0.63	2.998	
ORMETOPRIM	0.22	2	8	1.86	0.1	2.998	
OXACILLIN	1.4	10	8	9.77	0.48	2.998	
OXOLINIC ACID	0.46	2	8	2.25	0.15	2.998	
PENICILLIN G	0.56	10	8	1.43	0.19	2.998	
PENICILLIN V	1.9	10	8	10.6	0.62	2.998	
ROXITHROMYCIN	0.21	1	8	0.788	0.07	2.998	
SARAFLOXACIN	21	50	8	92.3	6.98	2.998	
SULFACHLOROPYRIDAZINE	1.6	5	8	4.81	0.5	2.998	
SULFADIAZINE	1.3	5	8	4.87	0.44	2.998	
SULFADIMETHOXINE	0.29	1	8	1.01	0.10	2.998	
SULFAMERAZINE	0.75	2	8	1.40	0.25	2.998	
SULFAMETHAZINE	1.5	2	8	2.14	0.52	2.998	
SULFAMETHIZOLE	0.43	2	8	1.79	0.14	2.998	

SULFAMETHOXAZOLE	0.75	2	8	1.95	0.25	2.998
SULFANILAMIDE	14.5	50	8	39.9	4.83	2.998
SULFATHIAZOLE	0.94	5	8	4.34	0.31	2.998
THIABENDAZOLE	1.0	5	8	4.64	0.35	2.998
TRIMETHOPRIM	0.85	5	8	5.02	0.28	2.998
TYLOSIN	4.8	20	8	18.9	1.59	2.998
VIRGINIAMYCIN	1.3	10	8	11.4	0.44	2.998
1,7 DIMETHYLXANTHINE	37	200	8	341	12.31	2.998

Axys Method: MLA-075 Rev 04 Ver 02, List 1 analytes
Analysis Type: PPCP (Pharmaceuticals and Personal Care Products), List 1 analytes
Instrument Type: LC-MS/MS
Matrix Spiked: SOLIDS
Axys Workgroup: WG39040
Column Type: C18
MDL Protocol: Federal Register 40 CFR Part 136, Appendix B, rev. 1.11, no iteration

MDL 1 Data Filename:	QA2J_015 S: 31	**Sample ID:**	WG39040-107	**Instr. Analysis Date:**	12-Feb-2012
MDL 2 Data Filename:	QA2J_015 S: 32	**Sample ID:**	WG39040-108	**Instr. Analysis Date:**	12-Feb-2012
MDL 3 Data Filename:	QA2J_015 S: 33	**Sample ID:**	WG39040-109	**Instr. Analysis Date:**	12-Feb-2012
MDL 4 Data Filename:	QA2J_015 S: 34	**Sample ID:**	WG39040-110	**Instr. Analysis Date:**	12-Feb-2012
MDL 5 Data Filename:	QA2J_015 S: 35	**Sample ID:**	WG39040-111	**Instr. Analysis Date:**	12-Feb-2012
MDL 6 Data Filename:	QA2J_015 S: 36	**Sample ID:**	WG39040-112	**Instr. Analysis Date:**	12-Feb-2012
MDL 7 Data Filename:	QA2J_015 S: 37	**Sample ID:**	WG39040-113	**Instr. Analysis Date:**	12-Feb-2012
MDL 8 Data Filename:	QA2J_015 S: 38	**Sample ID:**	WG39040-114	**Instr. Analysis Date:**	12-Feb-2012

ALL CONCENTRATIONS REPORTED ON THIS FORM ARE CONCENTRATIONS IN SAMPLES
Based on 1 g of solids

Native Analyte	Method Detection Limit, ng/g	Spiking Level ng/g	Number of Observations	Mean ng/g	Standard Devation	Student's t-Value
CARBAMAZEPINE	0.29	5	8	4.86	0.10	2.998
ERYTHROMYCIN-H2O	0.81	1	8	3.37	0.27	2.998

= Meets all 40 CFR MDL protocol requirements
= MDL lower than $^{1}/_{10}$ of the spiking level

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MLA-075 Rev 02, List 2 analytes (Tetracyclines, Acidic extraction, positive ESI)
Method Detection Limit for PPCP in Solids Samples
March 2010

MDL Results

Axys Method: MLA-075 Rev 02, List 2 analytes
Analysis Type: PPCP (Pharmaceuticals and Personal Care Products), List 2 analytes
Instrument Type: LC-MS/MS
Matrix Spiked: SOLIDS
Axys Workgroup: WG32245
Column Type: C18
MDL Protocol: Federal Register 40 CFR Part 136, Appendix B, rev. 1.11, no iteration

MDL 1 Data Filename:	QB0K_082 S: 28	**Sample ID:**	WG32245-107 I2	**Instr. Analysis Date:**	20/04/2010
MDL 2 Data Filename:	QB0K_082 S: 29	**Sample ID:**	WG32245-108 I2	**Instr. Analysis Date:**	20/04/2010
MDL 3 Data Filename:	QB0K_082 S: 30	**Sample ID:**	WG32245-109 I2	**Instr. Analysis Date:**	20/04/2010
MDL 4 Data Filename:	QB0K_082 S: 31	**Sample ID:**	WG32245-110 I2	**Instr. Analysis Date:**	20/04/2010
MDL 5 Data Filename:	QB0K_082 S: 32	**Sample ID:**	WG32245-111 I2	**Instr. Analysis Date:**	20/04/2010
MDL 6 Data Filename:	QB0K_082 S: 33	**Sample ID:**	WG32245-112 I2	**Instr. Analysis Date:**	20/04/2010
MDL 7 Data Filename:	QB0K_082 S: 34	**Sample ID:**	WG32245-113 I2	**Instr. Analysis Date:**	20/04/2010
MDL 8 Data Filename:	QB0K_082 S: 35	**Sample ID:**	WG32245-114 I2	**Instr. Analysis Date:**	20/04/2010

ALL CONCENTRATIONS REPORTED ON THIS FORM ARE CONCENTRATIONS IN SAMPLES
Based on 1 g of solids

Native Analyte	Method Detection Limit, ng/g	Spiking Level ng/g	Number of Observations	Mean ng/g	Standard Devation ng/g	Student's t-Value	Mean % recovery
Anhydrochlortetracycline (ACTC)	11	50.0	8	34.6	3.6	2.998	69
Anhydrotetracycline (ATC)	14	50.0	8	29.3	4.6	2.998	59
Chlortetracycline (CTC)	12	20.0	8	31.9	3.9	2.998	159
Demeclocycline	9.7	50.0	8	38.1	3.2	2.998	76
Doxycycline	5.7	20.0	8	19.6	1.9	2.998	98
4-Epianhydrochlortetracycline (EACTC)	23	200	8	62.8	7.5	2.998	31
4-Epianhydrotetracycline (EATC)	15	50.0	8	27.4	4.9	2.998	55
4-Epichlortetracycline (ECTC)	24	50.0	8	50.8	8.0	2.998	102
4-Epioxytetracycline (EOTC)	6.5	20.0	8	20.2	2.2	2.998	101
4-Epitetracycline (ETC)	9.5	20.0	8	26.8	3.2	2.998	134
Isochlortetracycline (ICTC)	3.8	20.0	8	14.9	1.3	2.998	74
Minocycline	14	200	7	57.1	4.4	3.143	29
Oxytetracycline (OTC)	7.5	20.0	8	22.8	2.5	2.998	114
Tetracycline (TC)	7.0	20.0	8	22.4	2.3	2.998	112

= Meets all 40 CFR MDL protocol requirements
= MDL outside 0.1 to 1.0 times the spiking level

AXYS Analytical Services Ltd

MLA-075 Rev 02, List 3 analytes (Acidic extraction, negative ESI)
Method Detection Limit for PPCP in Solids Samples
March 2010

MDL Results

Axys Method: MLA-075 Rev 02, List 3 analytes
Analysis Type: PPCP (Pharmaceuticals and Personal Care Products), List 3 analytes
Instrument Type: LC-MS/MS
Matrix Spiked: SOLIDS
Axys Workgroup: WG32245
Column Type: C18
MDL Protocol: Federal Register 40 CFR Part 136, Appendix B, rev. 1.11, no iteration

MDL 1 Data Filename:	QF0K_072 S: 28	**Sample ID:**	WG32245-107	**Instr. Analysis Date:**	1-Apr-2010
MDL 2 Data Filename:	QF0K_072 S: 29	**Sample ID:**	WG32245-108	**Instr. Analysis Date:**	1-Apr-2010
MDL 3 Data Filename:	QF0K_072 S: 30	**Sample ID:**	WG32245-109	**Instr. Analysis Date:**	1-Apr-2010
MDL 4 Data Filename:	QF0K_072 S: 31	**Sample ID:**	WG32245-110	**Instr. Analysis Date:**	1-Apr-2010
MDL 5 Data Filename:	QF0K_072 S: 32	**Sample ID:**	WG32245-111	**Instr. Analysis Date:**	1-Apr-2010
MDL 6 Data Filename:	QF0K_072 S: 33	**Sample ID:**	WG32245-112	**Instr. Analysis Date:**	1-Apr-2010
MDL 7 Data Filename:	QF0K_072 S: 34	**Sample ID:**	WG32245-113	**Instr. Analysis Date:**	1-Apr-2010
MDL 8 Data Filename:	QF0K_072 S: 35	**Sample ID:**	WG32245-114	**Instr. Analysis Date:**	1-Apr-2010

ALL CONCENTRATIONS REPORTED ON THIS FORM ARE CONCENTRATIONS IN SAMPLES
Based on 1 g of solids

Native Analyte	Method Detection Limit, ng/g	Spiking Level ng/g	Number of Observations	Mean ng/g	Standard Devation	Student's t-Value	Mean % recovery
Bisphenol A-1	255	1017	8	1055	85	2.998	104
Furosemide-1	52	133	8	131	17.4	2.998	99
Gemfibrozil	1.6	5.00	8	5.64	0.54	2.998	113
Glipizide-1	6.6	20.0	8	22.4	2.21	2.998	112
Glyburide-1	7.8	10.0	8	11.1	2.60	2.998	111
Hydrochlorothiazide-1	11	66.7	8	23.7	3.60	2.998	36
2-hydroxy-ibuprofen	100	267	8	343	33.5	2.998	129
Ibuprofen	20	50.0	8	60.8	6.54	2.998	122
Naproxen	12	10.0	8	12.9	3.90	2.998	129
Triclocarban	2.0	10.0	8	11.2	0.68	2.998	112
Triclosan	126	206	8	234	41.9	2.998	114
Warfarin	1.9	5.00	8	5.73	0.65	2.998	115

= Meets all 40 CFR MDL protocol requirements
= MDL outside 0.1 to 1.0 times the spiking level

AXYS Analytical Services Ltd

MLA-075 Rev 02, List 4 analytes (Basic extraction, positive ESI)
Method Detection Limit for PPCP in Solids Samples
March 2010

MDL Results

Axys Method: MLA-075 Rev 02, List 4 analytes
Analysis Type: PPCP (Pharmaceuticals and Personal Care Products), List 4 analytes
Instrument Type: LC-MS/MS
Matrix Spiked: SOLIDS
Axys Workgroup: WG32246
Column Type: HILIC
MDL Protocol: Federal Register 40 CFR Part 136, Appendix B, rev. 1.11, no iteration

MDL 1 Data Filename:	QG0K_074 S: 25	**Sample ID:**	WG32246-107 I	**Instr. Analysis Date:**	8-Apr-2010
MDL 2 Data Filename:	QG0K_074 S: 26	**Sample ID:**	WG32246-108 I	**Instr. Analysis Date:**	8-Apr-2010
MDL 3 Data Filename:	QG0K_074 S: 27	**Sample ID:**	WG32246-109 I	**Instr. Analysis Date:**	8-Apr-2010
MDL 4 Data Filename:	QG0K_074 S: 28	**Sample ID:**	WG32246-110 I	**Instr. Analysis Date:**	8-Apr-2010
MDL 5 Data Filename:	QG0K_074 S: 29	**Sample ID:**	WG32246-111 I	**Instr. Analysis Date:**	8-Apr-2010
MDL 6 Data Filename:	QG0K_074 S: 30	**Sample ID:**	WG32246-112 I	**Instr. Analysis Date:**	8-Apr-2010
MDL 7 Data Filename:	QG0K_074 S: 31	**Sample ID:**	WG32246-113 I	**Instr. Analysis Date:**	8-Apr-2010
MDL 8 Data Filename:	QG0K_074 S: 32	**Sample ID:**	WG32246-114 I	**Instr. Analysis Date:**	8-Apr-2010

ALL CONCENTRATIONS REPORTED ON THIS FORM ARE CONCENTRATIONS IN SAMPLES
Based on 1 g of solids

Native Analyte	Method Detection Limit, ng/g	Spiking Level ng/g	Number of Observations	Mean ng/g	Standard Devation	Student's t-Value	Mean % recovery
ALBUTEROL	0.81	1.00	8	1.10	0.269	2.998	110
AMPHETAMINE	6.11	5.00	8	6.41	2.039	2.998	128
ATENOLOL	0.84	2.00	8	1.90	0.280	2.998	95
ATORVASTATIN	0.71	5.00	8	3.70	0.237	2.998	74
CIMETIDINE	0.42	2.00	8	1.78	0.139	2.998	89
CLONIDINE	1.31	5.00	8	3.94	0.435	2.998	79
CODEINE	4.21	10.0	8	10.2	1.405	2.998	102
COTININE	0.46	5.00	8	3.96	0.152	2.998	79
ENALAPRIL	0.34	1.00	8	0.98	0.114	2.998	98
HYDROCODONE	2.23	5.00	8	6.37	0.744	2.998	127
METFORMIN	10.8	10	8	11.45	3.598	2.998	115
OXYCODONE	0.60	2.00	8	1.45	0.202	2.998	72
RANITIDINE	0.87	2.00	8	1.58	0.291	2.998	79
TRIAMTERENE	0.25	1.00	8	0.94	0.083	2.998	94

= Meets all 40 CFR MDL protocol requirements
= MDL outside 0.1 to 1.0 times the spiking level

AXYS Analytical Services Ltd

MLA-075 Rev 02, List 5 analytes (Acidic extraction, positive ESI)
Method Detection Limit for PPCP in Solids Samples
March 2010

MDL Results

Axys Method: MLA-075 Rev 02, List 5 analytes
Analysis Type: PPCP (Pharmaceuticals and Personal Care Products), List 5 analytes
Instrument Type: LC-MS/MS
Matrix Spiked: SOLIDS
Axys Workgroup: WG32245
Column Type: C18
MDL Protocol: Federal Register 40 CFR Part 136, Appendix B, rev. 1.11, no iteration

MDL 1 Data Filename:	QE0J_071 S: 18	**Sample ID:**	WG32245-107 I	**Instr. Analysis Date:**	17-Apr-2010
MDL 2 Data Filename:	QE0J_071 S: 19	**Sample ID:**	WG32245-108 I	**Instr. Analysis Date:**	17-Apr-2010
MDL 3 Data Filename:	QE0J_071 S: 20	**Sample ID:**	WG32245-109 I	**Instr. Analysis Date:**	17-Apr-2010
MDL 4 Data Filename:	QE0J_071 S: 21	**Sample ID:**	WG32245-110 I	**Instr. Analysis Date:**	17-Apr-2010
MDL 5 Data Filename:	QE0J_071 S: 22	**Sample ID:**	WG32245-111 I	**Instr. Analysis Date:**	17-Apr-2010
MDL 6 Data Filename:	QE0J_071 S: 23	**Sample ID:**	WG32245-112 I	**Instr. Analysis Date:**	17-Apr-2010
MDL 7 Data Filename:	QE0J_071 S: 24	**Sample ID:**	WG32245-113 I	**Instr. Analysis Date:**	17-Apr-2010
MDL 8 Data Filename:	QE0J_071 S: 25	**Sample ID:**	WG32245-114 I	**Instr. Analysis Date:**	17-Apr-2010

ALL CONCENTRATIONS REPORTED ON THIS FORM ARE CONCENTRATIONS IN SAMPLES
Based on 1 g of solids

Native Analyte	Method Detection Limit, ng/g	Spiking Level ng/g	Number of Observations	Mean ng/g	Standard Devation ng/g	Student's t-Value	
Alprazolam-1	0.35	1.00	8	0.91	0.12	2.998	
Amitriptyline-1	0.29	1.00	8	1.15	0.10	2.998	
Amlodipine-1	2.1	5.00	8	5.09	0.70	2.998	
Benzoylecgonine-1	0.16	1.00	8	0.98	0.06	2.998	
Benztropine-1	0.27	1.00	8	1.15	0.09	2.998	see below
Betamethasone-1	11	5.00	8	5.79	3.67	2.998	
Cocaine-1	0.07	0.50	8	0.55	0.02	2.998	
DEET-1	0.32	0.50	8	0.69	0.11	2.998	
Desmethyldiltiazem-1	0.16	0.50	8	0.76	0.05	2.998	
Diazepam-1	0.38	1.00	8	0.96	0.13	2.998	
Fluocinonide-1	3.7	20.0	8	18.9	1.25	2.998	
Fluticasone Propionate-1	5.3	6.67	8	4.07	1.77	2.998	
Hydrocortisone-1	134	200	8	201	45	2.998	
10-hydroxy-amitriptyline-1	0.18	0.50	8	0.49	0.06	2.998	
Meprobamate-1	4.8	13.3	8	15.40	1.61	2.998	
Methylprednisolone-1	10	13.3	8	20.0	3.44	2.998	see below
Metoprolol-1	2.3	5.00	8	5.39	0.76	2.998	
Norfluoxetine	1.0	5.00	8	5.29	0.34	2.998	
Norverapamil-1	0.15	0.50	8	0.51	0.05	2.998	
Paroxetine-1	3.6	13.3	8	14.4	1.19	2.998	
Prednisolone-1	6.4	20.0	8	20.1	2.12	2.998	
Prednisone-1	33	66.7	8	61.9	11.2	2.998	
Promethazine-1	0.30	1.33	8	1.24	0.10	2.998	
Propoxyphene-1	0.60	1.00	8	1.04	0.20	2.998	
Propranolol-1	1.3	6.67	8	7.29	0.42	2.998	
Sertraline-1	0.23	1.33	8	1.14	0.08	2.998	
Simvastatin-1	24	66.7	8	57.4	7.90	2.998	
Theophylline-1	287	200	8	513	96	2.998	
Trenbolone-1	5.4	13.33	8	15.8	1.81	2.998	
Trenbolone acetate-1	1.5	1.00	8	1.05	0.49	2.998	
Valsartan-1	4.6	13.33	8	13.6	1.53	2.998	
Verapamil-1	0.16	0.50	8	0.45	0.05	2.998	

Axys Method: MLA-075 Rev 04 Ver 01, List 5 analytes
Analysis Type: PPCP (Pharmaceuticals and Personal Care Products), List 5 analytes
Instrument Type: LC-MS/MS
Matrix Spiked: SOLIDS

Axys Workgroup: WG39040
Column Type: C18
MDL Protocol: Federal Register 40 CFR Part 136, Appendix B, rev. 1.11, no iteration

MDL 1 Data Filename:	QE2Q_037 S: 18	**Sample ID:**	WG39040-107	**Instr. Analysis Date:**	12-Feb-2012
MDL 2 Data Filename:	QE2Q_037 S: 19	**Sample ID:**	WG39040-108	**Instr. Analysis Date:**	12-Feb-2012
MDL 3 Data Filename:	QE2Q_037 S: 20	**Sample ID:**	WG39040-109	**Instr. Analysis Date:**	12-Feb-2012
MDL 4 Data Filename:	QE2Q_037 S: 21	**Sample ID:**	WG39040-110	**Instr. Analysis Date:**	12-Feb-2012
MDL 5 Data Filename:	QE2Q_037 S: 22	**Sample ID:**	WG39040-111	**Instr. Analysis Date:**	12-Feb-2012
MDL 6 Data Filename:	QE2Q_037 S: 23	**Sample ID:**	WG39040-112	**Instr. Analysis Date:**	12-Feb-2012
MDL 7 Data Filename:	QE2Q_037 S: 24	**Sample ID:**	WG39040-113	**Instr. Analysis Date:**	12-Feb-2012
MDL 8 Data Filename:	QE2Q_037 S: 25	**Sample ID:**	WG39040-114	**Instr. Analysis Date:**	12-Feb-2012

ALL CONCENTRATIONS REPORTED ON THIS FORM ARE CONCENTRATIONS IN SAMPLES
Based on 1 g of solids

Native Analyte	Method Detection Limit, ng/g	Spiking Level ng/g	Number of Observations	Mean ng/g	Standard Devation ng/g	Student's t-Value
Benztropine-1	0.19	1.00	8	1.82	0.06	2.998
Methylprednisolone-1	4.0	13.33	8	13.6	1.35	2.998

= Meets all 40 CFR MDL protocol requirements
= MDL lower than $^{1}/_{10}$ of the spiking level
= MDL higher than the spiking level

Washington State Department of Ecology

CORRELATION TABLE

PHARMACEUTICAL AND PERSONAL CARE PRODUCT CARE ANALYSIS

Lab Name: AXYS Analytical Services Ltd.	**Project Manager: Georgina Brooks**
Project: N/A	**Contract No: 4499**
Project Name:Urban Waters - Elliott Bay	**AXYS Method: MLA-075**
Data Package Identification: DPWG44301	**Program: Solid Samples**
Client Sample No.	**Lab Sample ID**
LAB BLANK	WG43863-101
OPR	WG43863-102
LAB BLANK	WG43864-101
OPR	WG43864-102
LAB BLANK	WG44109-101
OPR	WG44109-102
1306020-01	L19741-1
1306020-02	L19741-2
1306020-03	L19741-3
1306020-07	L19741-4
1306020-08	L19741-5 WG43863-103 DUPLICATE
1306020-08	L19741-5 WG43864-103 DUPLICATE
1306020-09	L19741-6
1306020-11	L19741-7
1306020-15	L19741-8
1306020-16	L19741-9
1306020-17	L19741-10 WG44109-103 DUPLICATE
1306020-19	L19741-11
1306020-20	L19741-12
1306020-21	L19741-13
1306020-30	L19741-14
1306020-34	L19741-15
1306020-35	L19741-16
1306020-36	L19741-17
1306020-37	L19741-18
1306020-28	L19741-19

4499

Chain of Custody
EAP, MMU, Marine Sediment Monitoring Team

1306020-28-19

6/5/2013 urbanw. 2013 JUN 197 MED

Date	Project	Year	Month	Station	ParameterText	MEL Sample ID
6/5/2013	Urban Waters	2013	Jun	114	PPCP & PFC	1306020-01 49741-1
6/4/2013	Urban Waters	2013	Jun	115	PPCP & PFC	1306020-02 -2
6/3/2013	Urban Waters	2013	Jun	172	PPCP & PFC	1306020-03 -3
6/4/2013	Urban Waters	2013	Jun	176	PPCP & PFC	1306020-07 -4
6/4/2013	Urban Waters	2013	Jun	177	PPCP & PFC	1306020-08 -5
6/4/2013	Urban Waters	2013	Jun	178	PPCP & PFC	1306020-09 -6
~~6/4/2013~~	~~Urban Waters~~	~~2013~~	~~Jun~~	~~178~~	~~PPCP & PFC~~	~~1306020-09~~ ~~-6~~ MED
6/4/2013	Urban Waters	2013	Jun	180	PPCP & PFC	1306020-11 -7
6/5/2013	Urban Waters	2013	Jun	184	PPCP & PFC	1306020-15 -8
6/4/2013	Urban Waters	2013	Jun	185	PPCP & PFC	1306020-16 -9
6/5/2013	Urban Waters	2013	Jun	186	PPCP & PFC	1306020-17 -10
6/5/2013	Urban Waters	2013	Jun	188	PPCP & PFC	1306020-19 -11
6/3/2013	Urban Waters	2013	Jun	189	PPCP & PFC	1306020-20 -12
6/3/2013	Urban Waters	2013	Jun	190	PPCP & PFC	1306020-21 -13
6/3/2013	Urban Waters	2013	Jun	199	PPCP & PFC	1306020-30 -14
6/5/2013	Urban Waters	2013	Jun	203	PPCP & PFC	1306020-34 -15
6/5/2013	Urban Waters	2013	Jun	204	PPCP & PFC	1306020-35 -16
6/5/2013	Urban Waters	2013	Jun	205	PPCP & PFC	1306020-36 -17
6/5/2013	Urban Waters	2013	Jun	U1	PPCP & PFC	1306020-37 -18

Relinquished By	Date/Time	Received By	Date/Time	Comments
Margaret Dutch	6/5/2013	OC freezer	6/5/2013	
OC freezer	6/6/2013	Margaret Dutch	6/6/2013	
Margaret Dutch	6/6/2013	[illegible]	6/6/2013	
[illegible]	6/7/2013	M. Wilman	07-JUN-13	11:15

Print Date 6/5/2013

AXYS Analytical Services Ltd
SAMPLE RECEIVING RECORD

Waybill : Yes /No
Waybill #: HAND DELIVERED 07 JUN 13
Date Shipped: 06-JUN-13
Date /Time Received: 07-JUN-13 11:15

AXYS Client & Contract # **4499-Washington State Dept of Ecology**

Project Number:
Receipt No: WB14889
Login Number:

Received By: MGIERDEN
Log in by: mgierden
Signature:
Axys Sample ID's: L19741-1 to 19

Matrix Type: 19 Marine seds

Condition of Shipping Container: Intact

Temperature upon Receipt: -3.6 Celcius ice packs frozen, no temp blank present
Thermometer ID: 3290
Corrected Temperature: -3.6 Celcius

Custody Seals: Shipping Containers Yes /No Intact Yes /No Seal Numbers Yes /No
Samples Yes /No Intact Yes /No Seal Numbers Yes /No

Chain of Custody or Documents:	Yes /No	Tracking Report /Packing List:	Yes /No
Sample ID's	Yes /No	Sample Tag Numbers	Yes /No
Collection Location	Yes /No	Sample Type	Yes /No
Date & Time Collection	Yes /No	Preservative Added	Yes /No
Collector's Name	Yes /No	Preservation Requested	Yes /No

Sample Tags	Yes /No		
Sample Labels	Yes /No		
Sample Labels Cross Referenced to COC	Yes /No	Information Agrees	Yes /No
Sample Tags Cross Referenced to Sample Labels	Yes /No	Information Agrees	Yes /No
Sample Tags Cross Referenced to COC	Yes /No	Information Agrees	Yes /No

Comments:

L19741-19 this sample was hand written on to the COC. g Brooks 10-June-2013. by the client.

Action Taken: