



16.1.9.3 BIOANALYTICAL REPORTS

Determination of Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Samples by LC-MS/MS (Study AA99071-10)



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Determination of Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA) Samples from "A Randomized, Controlled, Open-label, 3-Arm Parallel Group, Single-Center Study to Demonstrate Reductions in Exposure to Selected Smoke Constituents in Smoking, Healthy Subjects Switching to the Tobacco Heating System 2.2 (THS 2.2) or Smoking Abstinence, Compared to Continuing to Use Conventional Cigarettes, for 5 Days in Confinement" by LC-MS/MS

Study: AA99071-10

Bioanalytical Final Report

Philip Morris Products S.A.
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2000 Neuchâtel, Switzerland

Protocol ZRHR-REXC-03-EU

Report Date: 12-Mar-2015

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Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

STUDY LOCATION

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Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

APPROVAL SIGNATURES**TEST SITE****Celerion:**

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Kirk Newland, B.S.
Technical Director, Tobacco Sciences

12-Mar-2015

Date

Management

Rafiqul Islam, M.S.
Senior Director, Bioanalytical Services

12-Mar-2015

Date



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

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16.03.2015

Date



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STATEMENT OF COMPLIANCE

The bioanalytical phase of the study was performed according to applicable GLP requirements and in compliance with Standard Operating Procedures (SOPs) in effect in the bioanalytical laboratory of Celerion, Lincoln, Nebraska. The SOPs are written based on the principles and requirements described in United States Food and Drug Administration Title 21 Code of Federal Regulations (CFR) Part 58, the Guidance for Industry – Bioanalytical Method Validation (CDER, May 2001), and Guideline on Bioanalytical Method Validation (European Medicines Agency [EMA/CHMP/EWP/192217/2009], Effective February 2012).

This production study was conducted in accordance with the guidelines documented in the bioanalytical study plan. To ensure the integrity of the reported data, the bioanalytical laboratory verified all results. The Quality Assurance unit of Celerion, Lincoln, Nebraska, audited the study. A Quality Assurance statement was then issued and is included within this document.

The data summaries, results, and conclusions in this bioanalytical report have been reviewed and were found to be consistent and scientifically rational. All deviations from the protocol and/or significant deviations from SOPs documented in this report have been reviewed and are scientifically valid.

I accept responsibility for the scientific integrity of the data included within this bioanalytical report.

Kirk Newland, B.S.
Technical Director, Tobacco Sciences

12-Mar-2015

Date




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QUALITY ASSURANCE STATEMENT

Phase Audited	Audit Date(s)	Date Reported to Study Director/ Bioanalytical Principal Investigator	Date Audit Report Signed by Management
Bioanalytical Study Plan	18-Jun-2013	18-Jun-2013	24-Jul-2013
Critical Phase Inspection	21, 22-Oct-2013	23-Oct-2013	22-Oct-2013
Database	11, 12-Nov-2013	12-Nov-2013	15-Nov-2013
Bioanalytical Report (Final Draft)	18-Apr-2014	23-Apr-2014	23-Apr-2014
Bioanalytical Report (Final)	11-Mar-2015	11-Mar-2015	11-Mar-2015

Celerion Quality Assurance audited various phases of this study as shown above. This statement confirms that the methods, procedures, and results as presented in this report accurately reflect the raw data of the study.


Amy Sherwood, A.A.S.
Quality Assurance Auditor

12mar2015
Date



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1. INTRODUCTION

The purpose of this bioanalytical study (hereafter referred to as study) was to determine the concentration of cotinine and *trans*-3'-hydroxycotinine in human plasma (K₂EDTA) samples by a validated LC-MS/MS method. The study samples were collected in the clinical study ZRHR-REXC-03-EU, entitled, "A Randomized, Controlled, Open-label, 3-Arm Parallel Group, Single-Center Study to Demonstrate Reductions in Exposure to Selected Smoke Constituents in Smoking, Healthy Subjects Switching to the Tobacco Heating System 2.2 (THS 2.2) or Smoking Abstinence, Compared to Continuing to Use Conventional Cigarettes, for 5 Days in Confinement" [3]. Sample analysis was conducted between 16-Sep-2013 and 01-Nov-2013.

This report provides the results and supporting documentation from the analysis of study samples and includes an evaluation of assay performance.

2. EXPERIMENTAL

2.1. Test Item

The test items are defined in the clinical study protocol [3].

2.2. Reference Items and Internal Standards

	Analyte	Internal Standard (IS)
ID	Cotinine	d ₃ -Cotinine
Source	(b) (4)	(b) (4)
Lot No.	FN061710-01	FN102110-02
Purity / Concentration	99.8% (1047 µg/mL)	99.7% (100.0 µg/mL)
Celerion Assigned Correction Factor	1.0000	1.0000
Expiry Date	30-Jun-2015	31-Oct-2015
Storage Conditions	Freezer (-20 C), protected from light	Freezer (-20 C), protected from light

	Analyte	Internal Standard (IS)
ID	<i>trans</i> -3'-Hydroxycotinine	d ₃ - <i>trans</i> -3'-Hydroxycotinine
Source	(b) (4)	(b) (4)
Lot No.	C8-127-040	C8-127-047
Potency	99.7%	99.9%
Celerion Assigned Correction Factor	0.9969	0.9990
Expiry Date	02-Apr-2014	11-Apr-2014
Storage Conditions	Freezer (-20 C), protected from light	Freezer (-20 C), protected from light

The certificate(s) of analysis for the reference items and internal standards are presented in [Attachment 6](#).



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Reference items and internal standards are retained under the conditions that are specified until they become expired. They will then be removed from the active library or stored for an additional period for the testing of long-term stability.

2.3. Biological Matrix

Human plasma, with K₂EDTA as anticoagulant, was collected in-house at Celerion in Lincoln, Nebraska. Human plasma stored at -20°C may be stored for a period less than 24 months prior to use. Human plasma (K₂EDTA), free of significant interference, was used to prepare quality control (QC) samples. Deionized water was used to prepare calibration standard samples and used as control matrix.

2.4. Test System

2.4.1. Procedure and Instruments

Procedure and Instrumentation	
Extraction Method	Solid-phase extraction
Chromatography system	Perkin Elmer Series 200 Micropump HPLC [^]
MS/MS system	AB SCIEX API 5000 TM and QTRAP [®] 5500 [^]
Regression Type	Weighted linear regression curve (1/concentration ²)
Quantitation Method	Peak Area Ratio
Assay Volume	0.300 mL

[^] = Qualified systems

2.4.2. Computer Application Software

Software	
LC-MS/MS software	Applied Biosystems Analyst [®] 1.5.1 [^]
LIMS	Thermo Electron Corporation Watson TM 7.3 Bioanalytical LIMS 7.3 [^]
LIMS application	Inspector Version 1.1.1 [^]
Laboratory Documentation System	Labnotes TM Web Client 1.21 [^]
Office applications	Microsoft [®] Office 2007 Package

[^] = Validated systems

2.5. Calibration Standards, Quality Control Samples and Dilution Quality Control Samples

Non-zero calibration standards were prepared fresh daily at the concentration levels of 1.00, 2.00, 4.00, 10.0, 25.0, 50.0, 75.0, 90.0, and 100 ng/mL of cotinine and *trans*-3'-hydroxycotinine from calibration standard spiking solutions which were prepared on 09-Sep-2013 and stored at -20°C for a period less than 323 days prior to use. The calibration standard spiking solutions were prepared at 5x concentrations. To achieve the required standard concentration, 0.0600 mL of standard spiking solution is added to 0.300 mL of ultrapure water.



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Quality control (QC) samples at the concentration levels of 3.00, 50.0, and 75.0 ng/mL and dilution quality control (DQC) samples at the concentration level of 200 ng/mL of cotinine and *trans*-3'-hydroxycotinine were prepared in bulk on 03-Sep-2013, aliquoted and stored at -20°C. Quality control samples aliquoted into clear polypropylene tubes were stored with the clinical samples after receipt at the bioanalytical laboratory. Quality control samples were analyzed within the established validation stability period of 185 days.

Standard calibrators and quality control samples were prepared from separate stock solutions.

2.6. Study Samples

2.6.1. Sample Source and Date of Receipt

Study samples were collected between 12-Jul-2013 and 19-Sep-2013 and were received frozen on dry ice between 22-Jul-2013 and 31-Oct-2013 from Covance Central Laboratory Services, Meyrin, Switzerland.

2.6.2. Sample Identification

Study samples were identified based on the subject screening number and time point documented on the sample label.

2.6.3. Sample Storage and Stability

Study samples were stored from sample collection in clear polypropylene tubes to the end of sample analysis at a nominal temperature of -20°C for a duration not exceeding 113 days.

Study samples were analyzed without exceeding long-term, short-term, freeze-thaw, or post-preparative stability. The following evaluations have been conducted:

Stability Summary [5]	
Long-term Stability	739 days in polypropylene tubes at -20 C
Short-term Stability	27 hours in polypropylene tubes at ambient temperature under white light
Freeze-thaw Stability	6 cycles in polypropylene tubes at -20 C under white light 7 cycles in polypropylene tubes at -20°C under UV-shielded light
Post-preparative Stability	135 hours in a polypropylene 96 well plate at 5 C
Processed Sample Integrity	93 hours in a polypropylene 96 well plate at 5 C
Sample Shipping Stability	10 days in polypropylene tubes at -80 C



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2.6.4. Sample Summary

The Sponsor's protocol specifies 160 subjects, with 2 sampling times [3]. In study AA99071, a single subject discontinued from the clinical phase after randomization. The samples from this subject were analyzed and the results reported. Additional information regarding the subject discontinuance is provided in [Section 8.2](#).

	No. of Samples
Specified in protocol/received	320/328
Analysis not required (subject discontinued from enrollment)	8
Duplicates received	328
Total number of study samples analyzed	320

Following analysis, the study samples were kept frozen at -20°C. After submission of the final bioanalytical report the study samples will be further stored under the same conditions for up to 1 month on-site. Then, upon agreement with the Sponsor, the study samples will be destroyed after the completion of the clinical study report and Sponsor notification.

3. SAMPLE ANALYSIS

3.1. Analytical Method

The determination of cotinine and *trans*-3'-hydroxycotinine in human plasma (K₂EDTA) was carried out over a calibration range of 1.00 ng/mL to 100 ng/mL. The analytical procedure was performed at Celerion, Lincoln, Nebraska and is documented in the Method Validation Report for Celerion Study AA33664-01 [5]. The analytical method is documented in BAM SOP AA33664-01 [6]. See [Attachment 7](#).

An aliquot of human plasma (EDTA) containing each analyte and internal standard was extracted using a solid phase extraction procedure. The extracted samples were analyzed by an HPLC equipped with an AB SCIEX API 5000™ or QTRAP® 5500 mass spectrometer. Positive ions were monitored in the multiple reaction monitoring (MRM) mode. Quantitation was determined using a weighted linear regression analysis ($1/x^2$) of peak area ratios of each analyte and internal standard.

Though listed as a standard, the control blank sample with internal standard (Standard A) was not used to plot the calibration curve.



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3.2. Acceptance Criteria

3.2.1. Analytical Run Acceptance Criteria

An analytical run is acceptable if all of the following criteria are met:

- at least 75% of the non-zero calibration standards were within $\pm 15.0\%$ ($\pm 20.0\%$ for the lower limit of quantification (LLOQ) calibration standard) of their nominal concentration,
- at least two-thirds of the QC samples and at least 50% at each concentration level were within $\pm 15.0\%$ of their nominal concentration,
- at least 50% of the standard zero samples are free of interference at the retention time of the analyte(s) of interest,
- at least 50% of the blank samples are free of interference both at the retention time of the analyte(s) of interest and at the retention time of the IS,
- at least two-thirds of all blank and standard zero samples fulfilled the above described interference criteria.

Interference at the retention time of the analyte of interest is defined as a response greater than 20% of the mean analyte response of the LLOQ calibration standard(s).

Interference at the retention time of the IS is defined as a response greater than 5% of the mean IS response of the LLOQ calibration standard(s).

Individual data of QC samples (including DQCs) that were out of their acceptance criteria are flagged appropriately in the study file and in the bioanalytical report. QCs will be excluded from statistics only for analytical reasons (see [Attachment 5](#)).

3.2.2. Acceptance Criteria for System Suitability Testing

The system suitability testing performed with each analytical run is designed to assess the sensitivity, reproducibility of response (absence of response drift based on interpolated concentrations), and carry-over.

- Sensitivity assessed at the start and end of each analytical run is performed by evaluating the signal-to-noise ratio (SNR) of extracted system suitability samples spiked at the lower limit of quantitation. The SNR must be greater than 5:1 unless otherwise specified in the method.
- System stability (reproducibility of response) is performed by replicate injections at the start (5) and the end (2) of the analytical run with pooled high concentration system suitability samples. The percent coefficient of variation (% CV) of the calculated concentration must be less than or equal to 6%. The mean of the calculated concentration of the last 2 replicates or middle replicates (if applicable) of high concentration system suitability samples must be within 15% difference of the mean of the calculated concentration of the first 5 high concentration system suitability samples.



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- The carryover percentage is assessed at the beginning and end of each analytical run. This test is performed by injecting a blank (reconstitution solution) sample immediately after a high concentration system suitability sample. The area counts of the analyte in the blank injection are divided by the analyte area counts in the high concentration system suitability sample and the result is multiplied by 100.

$$\% \text{ carryover} = \left(\frac{\text{area (blank sample)}}{\text{area (high sys suit)}} \right) * 100$$

Analyte	Carryover criteria (needs to be less than)
Cotinine	0.1%
<i>trans</i> -3'-Hydroxycotinine	0.1%

3.2.3. Acceptance Criteria for Sample Dilution

The accuracy of study sample dilution is verified by the DQC samples. At least 50% of the DQC samples must be within $\pm 15.0\%$ of their nominal concentration for the respective dilution factor to be accepted.

3.2.4. Acceptance Criteria for ISR

The % difference was calculated for each pair of original and repeat analyses as follows:

$$\% \text{ difference} = 100 * \frac{|\text{repeat value} - \text{original value}|}{(\text{repeat value} + \text{original value}) / 2}$$

If the % difference was less than or equal to 20%, a pair of results was considered a passing match. Any pair with a % difference of more than 67% (indicating that the repeat value is either less than half or more than twice the original concentration) was considered an event and was investigated. The analytical method will be considered reproducible if at least 67% of the result pairs match. If less than 67% of the pairs match, an event investigation was initiated.

4. RESULTS

Due to rounding procedures, recalculations using the results presented in this report may differ slightly from the reported statistics.

A summary of analytical runs performed is presented in [Table 1](#).

4.1. Quality Control and Dilution Quality Control Sample Performance

Between-analytical run precision and accuracy results for QC samples prepared 3.00, 50.0, and 75.0 ng/mL for cotinine and *trans*-3'-hydroxycotinine are summarized in [Table 2](#) and [Table 3](#), respectively. The accuracy of sample dilution was verified by the performance of dilution QC samples. Results for dilution QC samples are summarized in [Table 2](#) and [Table 3](#) for cotinine and *trans*-3'-hydroxycotinine, respectively.



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4.2. Calibration Standard Performance

Back-calculated calibration curve standard concentrations are provided in [Table 4](#) and [Table 5](#) for cotinine and *trans*-3'-hydroxycotinine, respectively.

4.3. Standard Curve Parameters

Standard curve parameters from 11 and 10 successful analytical runs are provided in [Table 6](#) and [Table 7](#) for cotinine and *trans*-3'-hydroxycotinine, respectively. A representative calibration curve is illustrated in [Figure 1](#) and [Figure 2](#) for cotinine and *trans*-3'-hydroxycotinine, respectively.

4.4. Study Sample Concentrations

Study sample concentrations are provided in [Table 8](#) and [Table 9](#) for cotinine and *trans*-3'-hydroxycotinine, respectively. The column "Split" refers to the "for analysis" or "back-up" sample collected.

Study samples, if any, with no significant peak at the mass transition and retention time of cotinine and *trans*-3'-hydroxycotinine, respectively, or with peak area ratios below that of the LLOQ standard, are reported as being below the limit of quantitation (BLQ).

4.5. Reassays

4.5.1. Reassays for Analytical Reasons

Study samples needing re-analysis according to [section 3.2.1](#) for cotinine and *trans*-3'-hydroxycotinine are identified in [Table 10](#) and [Table 11](#), respectively.

4.5.2. Reassays for Non-analytical Reasons (Value Requiring Confirmation, VRC)

There were no study samples that were reassayed due to non-analytical reasons.

4.5.3. Sponsor Selected Reassays

There were no Sponsor selected reassays.

4.5.4. Incurred Sample Reproducibility

The method for the determination of cotinine and *trans*-3'-hydroxycotinine was considered reproducible, 100% out of 35 repeat analyses for cotinine and 100% out of 35 repeat analyses for *trans*-3'-hydroxycotinine met acceptance criteria as defined in [section 3.2.4](#). Results are presented in [Table 12](#) and [Table 13](#).

5. CHROMATOGRAMS

Representative chromatograms are provided in [Attachment 8](#).



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6. DEVIATIONS

6.1. DEV-LNK-13-0559 from LNK SOP.0012, Section 4, was initiated as to Shipments 7 and 8 were not counted within 3 working days of sample receipt. There is no impact as the samples were checked to ensure that they were received frozen and in good order upon arrival. Samples were counted and checked in prior to being scheduled for analysis.

7. EVENTS

There were no unexpected observations or results during the conduct of the study regarded as events which required investigation.

8. ANALYTICAL NOTES

8.1. When a sample was reassayed for only one compound and the reassay result for the other compound was not needed, the unneeded reassay result was deactivated as "Not Used" and was not reported.

8.2. During the course of analysis of study AA99077 (ZRHR-REXC-04-JP), it was determined that incomplete documentation of subject consent for further analysis of bioanalytical samples after subject discontinuation existed. A review of the possible impacted studies included ZRHR-REXC-03-EU (AA99071). One subject, 0083, discontinued from the clinical phase post-randomization. Consent for analysis was later confirmed by the Principal Investigator. The results from subject 0083 were included with the final deliverables for this study.

9. ARCHIVES

At a minimum the following records will be retained:

- Study Plan Bioanalysis (and all amendments, if applicable)
- Raw data
- Study related correspondence
- Bioanalytical report (and all amendments, if applicable)

These documents will be kept in the archives of Celerion for at least ten (10) years, taken from the date of Bioanalytical Principal Investigator's signature on the final bioanalytical report. After this time the Sponsor will be contacted to decide if the records should be retained for a further defined time at Celerion, returned to the Sponsor, or disposed of. Study data and documentation are archived at the Celerion Lincoln facility for 90 days, after which the records may be transferred to:

Iron Mountain
1601 Leavenworth
Omaha, Nebraska 68102



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10. CONCLUSION

In this bioanalytical study the concentration was determined in a total of 320 samples for cotinine and 320 samples for *trans*-3'-hydroxycotinine in human plasma (K₂EDTA) samples collected in the Philip Morris International Research and Development clinical study ZRHR-REXC-03-EU using a validated LC-MS/MS method.

The overall performance of the LC-MS/MS method met acceptance criteria and the results obtained were of the required integrity and quality. These data can be used for further interpretation.

11. REFERENCES

- [1] Guidance for Industry – Bioanalytical Method Validation: US Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER), Center for Veterinary Medicine (CVM) May 2001
- [2] OECD Principles on Good Laboratory Practice (as revised in 1997), ENV/MC/CHEM(98)17, OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, No. 1, OECD Publishing, Paris, France (2003).
- [3] Protocol ZRHR-REXC-03-EU: "A Randomized, Controlled, Open-label, 3-Arm Parallel Group, Single-Center Study to Demonstrate Reductions in Exposure to Selected Smoke Constituents in Smoking, Healthy Subjects Switching to the Tobacco Heating System 2.2 (THS 2.2) or Smoking Abstinence, Compared to Continuing to Use Conventional Cigarettes, for 5 Days in Confinement"
- [4] Study Plan Bioanalysis: Determination of Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA) Samples from "A Randomized, Controlled, Open-label, 3-Arm Parallel Group, Single-Center Study to Demonstrate Reductions in Exposure to Selected Smoke Constituents in Smoking, Healthy Subjects Switching to the Tobacco Heating System 2.2 (THS 2.2) or Smoking Abstinence, Compared to Continuing to Use Conventional Cigarettes, for 5 Days in Confinement" by LC-MS/MS, Celerion Study AA99071-10
- [5] Validation of an LC-MS/MS Method for the Determination of Nicotine, Cotinine, and *trans*-3'-Hydroxycotinine in Human Plasma (EDTA), Celerion Study AA33664-01
- [6] Bioanalytical Method SOP for the Determination of Nicotine, Cotinine, and *trans*-3'-Hydroxycotinine in Human Plasma (EDTA), Celerion Study AA33664-01



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RESULT TABLES

Table 1 Summary of Analytical Runs Performed

Analyte Name	Run ID	Regression Status	Extraction Date	Assay Date	Description	Comment
Cotinine	1	Accepted	16-Sep-2013	16-Sep-2013	SEE WORKLIST FOR SUB AND TIMEPOINT	OK
Cotinine	2	Accepted	16-Sep-2013	17-Sep-2013	SEE WORKLIST FOR SUB AND TIMEPOINTS	OK
Cotinine	3	Accepted	15-Oct-2013	15-Oct-2013	SEE WORKLIST FOR SUB AND TIMEPOINTS	OK
Cotinine	4	Accepted	15-Oct-2013	16-Oct-2013	REASSAYS	OK
Cotinine	5	Accepted	15-Oct-2013	16-Oct-2013	REASSAYS	OK
Cotinine	6	Accepted	21-Oct-2013	21-Oct-2013	SUBJECTS 0210-0283 PERIOD 1	OK
Cotinine	7	Accepted	21-Oct-2013	22-Oct-2013	SUBJECTS 0285-0328 PERIOD 1+ REASSAYS	OK
Cotinine	8	Accepted	21-Oct-2013	22-Oct-2013	REASSAYS + SUBJECT 0193-0206 PD 1	OK
Cotinine	9	Accepted	23-Oct-2013	23-Oct-2013	REASSAYS	OK
Cotinine	10	Accepted	25-Oct-2013	25-Oct-2013	ISRs	OK
Cotinine	11	Accepted	29-Oct-2013	29-Oct-2013	SUB 34 and 35 DAY 6 0HR	OK
Cotinine	12	Accepted	01-Nov-2013	01-Nov-2013	REASSAYS (Cotinine Only)	OK
Trans-3-Hydroxycotinine	1	Accepted	16-Sep-2013	16-Sep-2013	SEE WORKLIST FOR SUB AND TIMEPOINT	OK
Trans-3-Hydroxycotinine	2	Accepted	16-Sep-2013	17-Sep-2013	SEE WORKLIST FOR SUB AND TIMEPOINTS	OK
Trans-3-Hydroxycotinine	3	Accepted	15-Oct-2013	15-Oct-2013	SEE WORKLIST FOR SUB AND TIMEPOINTS	OK
Trans-3-Hydroxycotinine	4	Accepted	15-Oct-2013	16-Oct-2013	REASSAYS	OK
Trans-3-Hydroxycotinine	5	Accepted	15-Oct-2013	16-Oct-2013	REASSAYS	OK
Trans-3-Hydroxycotinine	6	Accepted	21-Oct-2013	21-Oct-2013	SUBJECTS 0210-0283 PERIOD 1	OK
Trans-3-Hydroxycotinine	7	Accepted	21-Oct-2013	22-Oct-2013	SUBJECTS 0285-0328 PERIOD 1+ REASSAYS	OK
Trans-3-Hydroxycotinine	8	Accepted	21-Oct-2013	22-Oct-2013	REASSAYS + SUBJECT 0193-0206 PD 1	OK
Trans-3-Hydroxycotinine	9	Accepted	23-Oct-2013	23-Oct-2013	REASSAYS	OK
Trans-3-Hydroxycotinine	10	Accepted	25-Oct-2013	25-Oct-2013	ISRs	OK
Trans-3-Hydroxycotinine	11	Accepted	29-Oct-2013	29-Oct-2013	SUB 34 and 35 DAY 6 0HR	OK

"Regression Status" reflects the status of the run with respect to run acceptance criteria



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Table 2 Quality Control and Dilution Quality Control Sample Data (Between-Analytical Run Precision and Accuracy) for Cotinine

Assay Date	Run ID	QC A 3.00 ng/mL	QC G 50.0 ng/mL	QC C 75.0 ng/mL	QC D DF10 200 ng/mL	QC D DF5 200 ng/mL
16-Sep-2013	1	3.22	49.1	69.5		
		3.13	50.1	74.3		
17-Sep-2013	2	3.18	49.3	71.2		
		2.88	47.3	70.9		
15-Oct-2013	3	3.12	45.9	73.0		
		3.33	51.0	70.2		
16-Oct-2013	4	3.16	49.3	71.4	209	
		3.32	52.7	73.7	208	
					191	
16-Oct-2013	5	3.20	49.6	70.9	189	
		3.28	52.2	74.4	207	
					212	
21-Oct-2013	6	3.20	52.4	74.6		195
		3.08	50.2	72.7		206
						205
22-Oct-2013	7	3.18	50.0	71.5	195	194
		3.33	53.9	75.8	209	204
					207	202
22-Oct-2013	8	3.04	51.2	72.8	196	192
		3.16	52.6	73.8	203	187
					204	204
23-Oct-2013	9	3.26	48.8	71.9	193	195
		3.26	53.4	75.6	214	201
					208	211
29-Oct-2013	11	3.27	50.6	72.3		
		3.37	50.5	71.0		
01-Nov-2013	12	3.20	52.0	69.6		172
		3.32	49.8	72.6		205
						207
Mean		3.20	50.5	72.4	203	199
S.D.		0.113	1.95	1.82	8.06	9.89
%CV		3.5	3.9	2.5	4.0	5.0
%Theoretical		106.7	101.0	96.5	101.5	99.5
%Bias		6.7	1.0	-3.5	1.5	-0.5
n		22	22	22	15	15



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Table 3 Quality Control and Dilution Quality Control Sample Data (Between-Analytical Run Precision and Accuracy) for *trans*-3'-Hydroxycotinine

Assay Date	Run ID	QC A 3.00 ng/mL	QC G 50.0 ng/mL	QC C 75.0 ng/mL	QC D DF10 200 ng/mL	QC D DF5 200 ng/mL
16-Sep-2013	1	3.13	45.7	68.4		
		3.04	48.6	71.9		
17-Sep-2013	2	2.97	46.7	68.2		
		2.97	46.2	70.1		
15-Oct-2013	3	2.99	44.0	71.8		
		3.14	48.4	69.2		
16-Oct-2013	4	2.98	47.6	70.6	199	
		3.01	49.2	72.4	205	
					189	
16-Oct-2013	5	3.03	50.1	71.1	188	
		3.09	49.3	73.3	206	
					205	
21-Oct-2013	6	3.06	49.2	74.2		194
		3.08	48.0	71.4		205
						206
22-Oct-2013	7	2.95	45.9	68.2	193	189
		3.03	48.1	72.4	204	201
					204	190
22-Oct-2013	8	3.07	50.7	70.0	195	190
		3.07	50.1	73.9	203	189
					202	202
23-Oct-2013	9	3.14	47.2	69.8	191	188
		3.05	51.6	74.4	208	201
					203	205
29-Oct-2013	11	3.01	48.6	73.6		
		3.24	49.2	72.4		
Mean		3.05	48.2	71.4	200	197
S.D.		0.0716	1.87	2.00	6.67	7.27
%CV		2.3	3.9	2.8	3.3	3.7
%Theoretical		101.7	96.4	95.2	100.0	98.5
%Bias		1.7	-3.6	-4.8	0.0	-1.5
n		20	20	20	15	12



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Table 4 Back-calculated Calibration Standard Concentrations for Cotinine

Assay Date	Run ID	STD B 1.00 ng/mL	STD C 2.00 ng/mL	STD D 4.00 ng/mL	STD E 10.0 ng/mL	STD F 25.0 ng/mL	STD G 50.0 ng/mL	STD H 75.0 ng/mL	STD I 90.0 ng/mL	STD J 100 ng/mL
16-Sep-2013	1	0.977	2.05	4.19	9.67	25.7	51.8	72.6	92.9	91.9
17-Sep-2013	2	0.985	2.05	4.08	9.77	25.4	51.6	72.9	94.1	93.2
15-Oct-2013	3	1.01	1.94	4.12	9.74	25.6	52.9	73.4	94.4	90.8
16-Oct-2013	4	1.01	1.94	4.15	9.83	26.2	52.2	70.9	92.4	94.0
16-Oct-2013	5	0.996	1.98	4.14	9.79	25.7	51.4	73.9	93.6	91.4
21-Oct-2013	6	0.978	2.03	4.22	10.0	25.3	52.1	72.3	90.6	92.4
22-Oct-2013	7	0.989	2.03	4.08	9.57	26.2	52.3	71.9	92.3	93.7
22-Oct-2013	8	0.985	2.02	4.15	10.1	25.4	52.1	72.1	91.9	92.1
23-Oct-2013	9	1.01	1.91	4.17	9.65	25.3	51.8	73.9	93.8	94.8
29-Oct-2013	11	0.992	2.00	4.16	9.60	25.6	52.9	73.3	94.5	89.8
01-Nov-2013	12	0.986	2.04	4.10	9.67	25.4	51.7	70.4	95.4	95.1
Mean		0.993	2.00	4.14	9.76	25.6	52.1	72.5	93.3	92.7
S.D.		0.0124	0.0495	0.0442	0.164	0.322	0.490	1.14	1.39	1.67
%CV		1.2	2.5	1.1	1.7	1.3	0.9	1.6	1.5	1.8
%Bias		-0.7	0.0	3.5	-2.4	2.4	4.2	-3.3	3.7	-7.3
n		11	11	11	11	11	11	11	11	11



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Table 5 Back-calculated Calibration Standard Concentrations for *trans*-3'-Hydroxycotinine

Assay Date	Run ID	STD B 1.00 ng/mL	STD C 2.00 ng/mL	STD D 4.00 ng/mL	STD E 10.0 ng/mL	STD F 25.0 ng/mL	STD G 50.0 ng/mL	STD H 75.0 ng/mL	STD I 90.0 ng/mL	STD J 100 ng/mL
16-Sep-2013	1	0.982	2.08	3.96	9.83	26.1	53.9	77.9	77.7	98.0
17-Sep-2013	2	0.975	2.06	4.14	9.84	25.7	54.3	77.9	76.8	96.6
15-Oct-2013	3	0.991	2.00	4.13	10.1	25.7	52.7	77.0	76.7	101
16-Oct-2013	4	0.988	2.04	4.06	9.73	26.0	53.8	78.1	76.6	99.7
16-Oct-2013	5	0.970	2.09	4.07	10.1	26.0	52.9	75.6	76.9	99.4
21-Oct-2013	6	0.987	2.05	3.99	9.99	25.9	53.6	78.4	77.4	97.7
22-Oct-2013	7	0.993	2.05	3.95	9.68	25.7	51.9	74.9	*73.4	96.5
22-Oct-2013	8	1.01	1.94	4.15	9.55	26.4	53.1	77.1	77.7	102
23-Oct-2013	9	1.00	1.96	4.18	9.49	25.7	52.7	79.0	79.4	101
29-Oct-2013	11	0.988	2.01	4.16	9.83	26.1	52.8	78.4	77.5	97.9
Mean		0.988	2.03	4.08	9.81	25.9	53.2	77.4	77.4	99.0
S.D.		0.0115	0.0496	0.0865	0.210	0.236	0.720	1.30	0.861	1.93
%CV		1.2	2.4	2.1	2.1	0.9	1.4	1.7	1.1	1.9
%Bias		-1.2	1.5	2.0	-1.9	3.6	6.4	3.2	-14.0	-1.0
n		10	10	10	10	10	10	10	9	10

Reason Deactivated

* Rejected



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Table 6 Standard Curve Parameters for Cotinine

Assay Date	Run ID	Slope	Intercept	R-Squared
16-Sep-2013	1	0.0583913781	0.00138872783	0.9975
17-Sep-2013	2	0.0589312810	-0.000160912613	0.9983
15-Oct-2013	3	0.0599536661	-0.00194305385	0.9971
16-Oct-2013	4	0.0596812078	0.00122253894	0.9977
16-Oct-2013	5	0.0602541639	-0.00136534273	0.9979
21-Oct-2013	6	0.0589736681	-0.00230569334	0.9979
22-Oct-2013	7	0.0584390981	-0.00226396388	0.9978
22-Oct-2013	8	0.0590897471	0.00237406832	0.9980
23-Oct-2013	9	0.0585013271	0.000321468051	0.9982
29-Oct-2013	11	0.0596022692	-0.00634457048	0.9967
01-Nov-2013	12	0.0613901940	-0.00744375488	0.9978
Mean		0.0593825455	-0.00150186260	0.9977
S.D.		0.000914310150	0.00310034727	0.0005
%CV		1.5	-206.4	0.1
n		11	11	11



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₃EDTA)
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Table 7 Standard Curve Parameters for *trans*-3'-Hydroxycotinine

Assay Date	Run ID	Slope	Intercept	R-Squared
16-Sep-2013	1	0.0448526430	-0.00180682717	0.9950
17-Sep-2013	2	0.0449174631	-0.00329740055	0.9943
15-Oct-2013	3	0.0447040520	-0.000835294773	0.9956
16-Oct-2013	4	0.0448523389	-0.00128339261	0.9947
16-Oct-2013	5	0.0446449100	-0.00195719024	0.9951
21-Oct-2013	6	0.0442997462	-0.00230831713	0.9952
22-Oct-2013	7	0.0458720232	-0.00329418739	0.9990
22-Oct-2013	8	0.0447287669	-0.00188400922	0.9949
23-Oct-2013	9	0.0443218493	0.000239300522	0.9958
29-Oct-2013	11	0.0439970153	-0.00303555468	0.9953
Mean		0.0447190808	-0.00194628732	0.9955
S.D.		0.000501670792	0.00112713428	0.0013
%CV		1.1	-57.9	0.1
n		10	10	10



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Table 8 Study Sample Concentrations for Cotinine

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
0511154000001	4	0010	0	0	175	1	OK		Cotinine
0511154000002	1	0010	6	0	2.24	1	OK		Cotinine
0511154000003	4	0011	0	0	165	1	OK		Cotinine
0511154000004	4	0011	6	0	194	1	OK		Cotinine
0511154000005	4	0014	0	0	142	1	OK		Cotinine
0511154000006	4	0014	6	0	242	1	OK		Cotinine
0511154000007	4	0015	0	0	180	1	OK		Cotinine
0511154000008	1	0015	6	0	BLQ<(1.00)	1	OK		Cotinine
0511154000009	4	0016	0	0	192	1	OK		Cotinine
0511154000010	5	0016	6	0	389	1	OK		Cotinine
0511154000011	5	0017	0	0	196	1	OK		Cotinine
0511154000012	1	0017	6	0	1.35	1	OK		Cotinine
0511154000013	5	0020	0	0	212	1	OK		Cotinine
0511154000014	5	0020	6	0	186	1	OK		Cotinine
0511154000015	5	0022	0	0	442	1	OK		Cotinine
0511154000016	5	0022	6	0	552	1	OK		Cotinine
0511154000017	5	0023	0	0	201	1	OK		Cotinine
0511154000018	5	0023	6	0	203	1	OK		Cotinine
0511154000019	5	0025	0	0	157	1	OK		Cotinine
0511154000020	5	0025	6	0	218	1	OK		Cotinine
0511154000021	5	0028	0	0	196	1	OK		Cotinine
0511154000022	1	0028	6	0	1.23	1	OK		Cotinine
0511154000023	5	0029	0	0	210	1	OK		Cotinine
0511154000024	5	0029	6	0	201	1	OK		Cotinine
0511154000025	5	0031	0	0	249	1	OK		Cotinine



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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000026	5	0031	6	0	311	1	OK		Cotinine
05111540000027	5	0035	0	0	134	1	OK		Cotinine
05111540000028	12	0035	6	0	177	1	OK		Cotinine
05111540000029	5	0038	0	0	348	1	OK		Cotinine
05111540000030	5	0038	6	0	365	1	OK		Cotinine
05111540000031	5	0039	0	0	156	1	OK		Cotinine
05111540000032	5	0039	6	0	149	1	OK		Cotinine
05111540000033	5	0044	0	0	147	1	OK		Cotinine
05111540000034	5	0044	6	0	112	1	OK		Cotinine
05111540000035	5	0049	0	0	262	1	OK		Cotinine
05111540000036	1	0049	6	0	1 15	1	OK		Cotinine
05111540000037	5	0052	0	0	217	1	OK		Cotinine
05111540000038	1	0052	6	0	2 80	1	OK		Cotinine
05111540000039	5	0053	0	0	218	1	OK		Cotinine
05111540000040	5	0053	6	0	256	1	OK		Cotinine
05111540000041	5	0057	0	0	334	1	OK		Cotinine
05111540000042	5	0057	6	0	260	1	OK		Cotinine
05111540000043	5	0060	0	0	274	1	OK		Cotinine
05111540000044	5	0060	6	0	357	1	OK		Cotinine
05111540000045	5	0062	0	0	192	1	OK		Cotinine
05111540000046	1	0062	6	0	1 19	1	OK		Cotinine
05111540000095	5	0030	0	0	101	1	OK		Cotinine
05111540000096	5	0030	6	0	148	1	OK		Cotinine
05111540000099	5	0034	0	0	221	1	OK		Cotinine
05111540000100	12	0034	6	0	168	1	OK		Cotinine
05111540000103	5	0055	0	0	194	1	OK		Cotinine
05111540000104	5	0055	6	0	193	1	OK		Cotinine
05111540000107	4	0064	0	0	103	1	OK		Cotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000108	2	0064	6	0	91.9	1	OK		Cotinine
05111540000111	4	0008	0	0	312	1	OK		Cotinine
05111540000112	4	0008	6	0	349	1	OK		Cotinine
05111540000115	4	0001	0	0	162	1	OK		Cotinine
05111540000116	4	0001	6	0	317	1	OK		Cotinine
05111540000119	4	0004	0	0	182	1	OK		Cotinine
05111540000120	4	0004	6	0	278	1	OK		Cotinine
05111540000123	4	0013	0	0	280	1	OK		Cotinine
05111540000124	1	0013	6	0	2.30	1	OK		Cotinine
05111540000127	5	0021	0	0	304	1	OK		Cotinine
05111540000128	5	0021	6	0	318	1	OK		Cotinine
05111540000131	5	0037	0	0	200	1	OK		Cotinine
05111540000132	5	0037	6	0	236	1	OK		Cotinine
05111540000135	5	0042	0	0	243	1	OK		Cotinine
05111540000136	5	0042	6	0	228	1	OK		Cotinine
05111540000139	5	0051	0	0	176	1	OK		Cotinine
05111540000140	1	0051	6	0	1.35	1	OK		Cotinine
05111540000143	4	0063	0	0	220	1	OK		Cotinine
05111540000144	2	0063	6	0	1.28	1	OK		Cotinine
05111540000147	4	0066	0	0	136	1	OK		Cotinine
05111540000148	4	0066	6	0	237	1	OK		Cotinine
05111540000151	2	0067	0	0	90.8	1	OK		Cotinine
05111540000152	2	0067	6	0	88.5	1	OK		Cotinine
05111540000155	4	0069	0	0	239	1	OK		Cotinine
05111540000156	4	0069	6	0	238	1	OK		Cotinine
05111540000159	4	0071	0	0	335	1	OK		Cotinine
05111540000160	2	0071	6	0	2.20	1	OK		Cotinine
05111540000163	4	0072	0	0	216	1	OK		Cotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000164	4	0072	6	0	329	1	OK		Cotinine
05111540000167	4	0074	0	0	228	1	OK		Cotinine
05111540000168	4	0074	6	0	226	1	OK		Cotinine
05111540000171	4	0076	0	0	206	1	OK		Cotinine
05111540000172	2	0076	6	0	3 40	1	OK		Cotinine
05111540000175	4	0080	0	0	185	1	OK		Cotinine
05111540000176	4	0080	6	0	267	1	OK		Cotinine
05111540000179	4	0083	0	0	239	1	OK		Cotinine
05111540000180	4	0083	6	0	339	1	OK		Cotinine
05111540000183	2	0085	0	0	61 4	1	OK		Cotinine
05111540000187	4	0086	0	0	244	1	OK		Cotinine
05111540000188	2	0086	6	0	3 52	1	OK		Cotinine
05111540000191	4	0087	0	0	300	1	OK		Cotinine
05111540000192	4	0087	6	0	338	1	OK		Cotinine
05111540000195	4	0088	0	0	156	1	OK		Cotinine
05111540000196	4	0088	6	0	163	1	OK		Cotinine
05111540000199	4	0090	0	0	131	1	OK		Cotinine
05111540000200	2	0090	6	0	88 3	1	OK		Cotinine
05111540000203	4	0093	0	0	254	1	OK		Cotinine
05111540000204	4	0093	6	0	277	1	OK		Cotinine
05111540000207	2	0104	0	0	85 4	1	OK		Cotinine
05111540000208	2	0104	6	0	BLQ<(1 00)	1	OK		Cotinine
05111540000211	4	0105	0	0	593	1	OK		Cotinine
05111540000212	4	0105	6	0	608	1	OK		Cotinine
05111540000215	4	0106	0	0	236	1	OK		Cotinine
05111540000216	4	0106	6	0	183	1	OK		Cotinine
05111540000219	4	0107	0	0	223	1	OK		Cotinine
05111540000220	4	0107	6	0	258	1	OK		Cotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000223	4	0110	0	0	296	1	OK		Cotinine
05111540000224	4	0110	6	0	336	1	OK		Cotinine
05111540000227	4	0112	0	0	212	1	OK		Cotinine
05111540000228	4	0112	6	0	252	1	OK		Cotinine
05111540000231	4	0114	0	0	134	1	OK		Cotinine
05111540000232	2	0114	6	0	1 87	1	OK		Cotinine
05111540000235	4	0118	0	0	355	1	OK		Cotinine
05111540000236	4	0118	6	0	392	1	OK		Cotinine
05111540000239	4	0121	0	0	110	1	OK		Cotinine
05111540000240	4	0121	6	0	118	1	OK		Cotinine
05111540000243	4	0122	0	0	231	1	OK		Cotinine
05111540000244	4	0122	6	0	287	1	OK		Cotinine
05111540000247	4	0123	0	0	147	1	OK		Cotinine
05111540000248	2	0123	6	0	2 15	1	OK		Cotinine
05111540000251	4	0117	0	0	106	1	OK		Cotinine
05111540000252	4	0117	6	0	198	1	OK		Cotinine
05111540000255	2	0126	0	0	82 5	1	OK		Cotinine
05111540000256	2	0126	6	0	96 7	1	OK		Cotinine
05111540000259	4	0127	0	0	214	1	OK		Cotinine
05111540000260	2	0127	6	0	4 94	1	OK		Cotinine
05111540000263	4	0128	0	0	187	1	OK		Cotinine
05111540000264	2	0128	6	0	2 19	1	OK		Cotinine
05111540000267	4	0129	0	0	318	1	OK		Cotinine
05111540000268	4	0129	6	0	248	1	OK		Cotinine
05111540000271	7	0130	0	0	245	1	OK		Cotinine
05111540000272	7	0130	6	0	310	1	OK		Cotinine
05111540000275	7	0133	0	0	276	1	OK		Cotinine
05111540000276	3	0133	6	0	1 87	1	OK		Cotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000279	3	0134	0	0	97.5	1	OK		Cotinine
05111540000280	7	0134	6	0	229	1	OK		Cotinine
05111540000283	7	0136	0	0	304	1	OK		Cotinine
05111540000284	7	0136	6	0	240	1	OK		Cotinine
05111540000287	7	0137	0	0	118	1	OK		Cotinine
05111540000288	3	0137	6	0	BLQ<(1.00)	1	OK		Cotinine
05111540000291	7	0139	0	0	211	1	OK		Cotinine
05111540000292	7	0139	6	0	166	1	OK		Cotinine
05111540000295	7	0140	0	0	171	1	OK		Cotinine
05111540000296	7	0140	6	0	186	1	OK		Cotinine
05111540000299	3	0145	0	0	63.6	1	OK		Cotinine
05111540000300	3	0145	6	0	BLQ<(1.00)	1	OK		Cotinine
05111540000303	3	0147	0	0	97.0	1	OK		Cotinine
05111540000304	7	0147	6	0	162	1	OK		Cotinine
05111540000307	7	0148	0	0	364	1	OK		Cotinine
05111540000308	7	0148	6	0	340	1	OK		Cotinine
05111540000311	7	0149	0	0	108	1	OK		Cotinine
05111540000312	7	0149	6	0	187	1	OK		Cotinine
05111540000315	7	0150	0	0	300	1	OK		Cotinine
05111540000316	3	0150	6	0	7.04	1	OK		Cotinine
05111540000319	3	0152	0	0	73.9	1	OK		Cotinine
05111540000320	8	0152	6	0	149	1	OK		Cotinine
05111540000323	8	0153	0	0	188	1	OK		Cotinine
05111540000324	8	0153	6	0	196	1	OK		Cotinine
05111540000327	3	0155	0	0	62.0	1	OK		Cotinine
05111540000328	3	0155	6	0	67.0	1	OK		Cotinine
05111540000331	8	0156	0	0	305	1	OK		Cotinine
05111540000332	8	0156	6	0	413	1	OK		Cotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000335	8	0160	0	0	272	1	OK		Cotinine
05111540000336	8	0160	6	0	269	1	OK		Cotinine
05111540000339	8	0162	0	0	113	1	OK		Cotinine
05111540000340	8	0162	6	0	311	1	OK		Cotinine
05111540000343	8	0167	0	0	159	1	OK		Cotinine
05111540000344	8	0167	6	0	329	1	OK		Cotinine
05111540000347	8	0169	0	0	121	1	OK		Cotinine
05111540000348	3	0169	6	0	BLQ<(1.00)	1	OK		Cotinine
05111540000351	3	0170	0	0	87.7	1	OK		Cotinine
05111540000352	8	0170	6	0	110	1	OK		Cotinine
05111540000355	8	0177	0	0	292	1	OK		Cotinine
05111540000356	8	0177	6	0	329	1	OK		Cotinine
05111540000359	8	0181	0	0	317	1	OK		Cotinine
05111540000360	8	0181	6	0	492	1	OK		Cotinine
05111540000363	8	0183	0	0	121	1	OK		Cotinine
05111540000364	3	0183	6	0	75.8	1	OK		Cotinine
05111540000367	8	0185	0	0	172	1	OK		Cotinine
05111540000368	3	0185	6	0	1.03	1	OK		Cotinine
05111540000371	8	0187	0	0	224	1	OK		Cotinine
05111540000372	8	0187	6	0	215	1	OK		Cotinine
05111540000375	8	0189	0	0	162	1	OK		Cotinine
05111540000376	8	0189	6	0	193	1	OK		Cotinine
05111540000379	8	0190	0	0	204	1	OK		Cotinine
05111540000380	8	0190	6	0	312	1	OK		Cotinine
05111540000383	8	0191	0	0	174	1	OK		Cotinine
05111540000384	8	0191	6	0	147	1	OK		Cotinine
05111540000387	8	0192	0	0	302	1	OK		Cotinine
05111540000388	8	0192	6	0	417	1	OK		Cotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000391	6	0264	0	0	138	1	OK		Cotinine
05111540000392	6	0264	6	0	44.1	1	OK		Cotinine
05111540000395	6	0265	0	0	195	1	OK		Cotinine
05111540000396	9	0265	6	0	1.86	1	OK		Cotinine
05111540000399	8	0193	0	0	198	1	OK		Cotinine
05111540000400	8	0193	6	0	264	1	OK		Cotinine
05111540000403	8	0195	0	0	71.9	1	OK		Cotinine
05111540000404	8	0195	6	0	119	1	OK		Cotinine
05111540000407	8	0196	0	0	57.8	1	OK		Cotinine
05111540000408	8	0196	6	0	125	1	OK		Cotinine
05111540000411	8	0197	0	0	143	1	OK		Cotinine
05111540000412	9	0197	6	0	1.57	1	OK		Cotinine
05111540000415	8	0198	0	0	167	1	OK		Cotinine
05111540000416	8	0198	6	0	299	1	OK		Cotinine
05111540000419	8	0200	0	0	132	1	OK		Cotinine
05111540000420	8	0200	6	0	153	1	OK		Cotinine
05111540000423	8	0202	0	0	291	1	OK		Cotinine
05111540000424	8	0202	6	0	390	1	OK		Cotinine
05111540000427	8	0203	0	0	157	1	OK		Cotinine
05111540000428	9	0203	6	0	1.04	1	OK		Cotinine
05111540000431	8	0204	0	0	120	1	OK		Cotinine
05111540000432	8	0204	6	0	142	1	OK		Cotinine
05111540000435	8	0206	0	0	243	1	OK		Cotinine
05111540000436	8	0206	6	0	322	1	OK		Cotinine
05111540000439	6	0210	0	0	373	1	OK		Cotinine
05111540000440	6	0210	6	0	287	1	OK		Cotinine
05111540000441		0211	0	0		2	Other	Analysis not required	Cotinine
05111540000443		0211	0	0		1	Other	Analysis not required	Cotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000447	6	0216	0	0	247	1	OK		Cotinine
05111540000448	6	0216	6	0	244	1	OK		Cotinine
05111540000451	6	0218	0	0	143	1	OK		Cotinine
05111540000452	9	0218	6	0	1 08	1	OK		Cotinine
05111540000455	6	0220	0	0	147	1	OK		Cotinine
05111540000456	6	0220	6	0	59.2	1	OK		Cotinine
05111540000459	6	0224	0	0	207	1	OK		Cotinine
05111540000460	6	0224	6	0	201	1	OK		Cotinine
05111540000463	6	0228	0	0	310	1	OK		Cotinine
05111540000464	6	0228	6	0	380	1	OK		Cotinine
05111540000467	6	0229	0	0	56.9	1	OK		Cotinine
05111540000468	6	0229	6	0	87.0	1	OK		Cotinine
05111540000471	6	0230	0	0	163	1	OK		Cotinine
05111540000472	6	0230	6	0	144	1	OK		Cotinine
05111540000475	6	0232	0	0	146	1	OK		Cotinine
05111540000476	6	0232	6	0	265	1	OK		Cotinine
05111540000479	6	0234	0	0	190	1	OK		Cotinine
05111540000480	6	0234	6	0	255	1	OK		Cotinine
05111540000483	6	0240	0	0	256	1	OK		Cotinine
05111540000484	9	0240	6	0	1.55	1	OK		Cotinine
05111540000487	6	0241	0	0	219	1	OK		Cotinine
05111540000488	6	0241	6	0	264	1	OK		Cotinine
05111540000489		0242	0	0		2	Other	Analysis not required	Cotinine
05111540000491		0242	0	0		1	Other	Analysis not required	Cotinine
05111540000495	6	0244	0	0	155	1	OK		Cotinine
05111540000496	6	0244	6	0	254	1	OK		Cotinine
05111540000497		0245	0	0		2	Other	Analysis not required	Cotinine
05111540000499		0245	0	0		1	Other	Analysis not required	Cotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000501		0247	0	0		2	Other	Analysis not required	Cotinine
05111540000503		0247	0	0		1	Other	Analysis not required	Cotinine
05111540000507	6	0249	0	0	263	1	OK		Cotinine
05111540000508	9	0249	6	0	1 79	1	OK		Cotinine
05111540000511	6	0251	0	0	223	1	OK		Cotinine
05111540000512	9	0251	6	0	BLQ<(1 00)	1	OK		Cotinine
05111540000515	6	0252	0	0	176	1	OK		Cotinine
05111540000516	9	0252	6	0	BLQ<(1 00)	1	OK		Cotinine
05111540000519	6	0255	0	0	189	1	OK		Cotinine
05111540000520	6	0255	6	0	300	1	OK		Cotinine
05111540000523	6	0256	0	0	276	1	OK		Cotinine
05111540000524	6	0256	6	0	492	1	OK		Cotinine
05111540000527	6	0262	0	0	160	1	OK		Cotinine
05111540000528	6	0262	6	0	166	1	OK		Cotinine
05111540000531	6	0266	0	0	267	1	OK		Cotinine
05111540000532	9	0266	6	0	1 07	1	OK		Cotinine
05111540000533		0269	0	0		2	Other	Analysis not required	Cotinine
05111540000535		0269	0	0		1	Other	Analysis not required	Cotinine
05111540000539	6	0272	0	0	263	1	OK		Cotinine
05111540000540	9	0272	6	0	530	1	OK		Cotinine
05111540000543	6	0273	0	0	215	1	OK		Cotinine
05111540000544	9	0273	6	0	2 04	1	OK		Cotinine
05111540000547	6	0276	0	0	54 3	1	OK		Cotinine
05111540000548	6	0276	6	0	158	1	OK		Cotinine
05111540000551	6	0277	0	0	191	1	OK		Cotinine
05111540000552	6	0277	6	0	402	1	OK		Cotinine
05111540000555	6	0278	0	0	239	1	OK		Cotinine
05111540000556	6	0278	6	0	221	1	OK		Cotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000559	6	0279	0	0	239	1	OK		Cotinine
05111540000560	6	0279	6	0	207	1	OK		Cotinine
05111540000563	6	0281	0	0	226	1	OK		Cotinine
05111540000564	6	0281	6	0	325	1	OK		Cotinine
05111540000567	6	0282	0	0	317	1	OK		Cotinine
05111540000568	6	0282	6	0	257	1	OK		Cotinine
05111540000571	6	0283	0	0	202	1	OK		Cotinine
05111540000572	6	0283	6	0	227	1	OK		Cotinine
05111540000575	7	0285	0	0	276	1	OK		Cotinine
05111540000576	7	0285	6	0	306	1	OK		Cotinine
05111540000579	7	0287	0	0	231	1	OK		Cotinine
05111540000580	7	0287	6	0	401	1	OK		Cotinine
05111540000581		0288	0	0		2	Other	Analysis not required	Cotinine
05111540000583		0288	0	0		1	Other	Analysis not required	Cotinine
05111540000587	7	0289	0	0	181	1	OK		Cotinine
05111540000588	9	0289	6	0	1 72	1	OK		Cotinine
05111540000591	7	0291	0	0	233	1	OK		Cotinine
05111540000592	9	0291	6	0	553	1	OK		Cotinine
05111540000595	7	0292	0	0	254	1	OK		Cotinine
05111540000596	7	0292	6	0	5 76	1	OK		Cotinine
05111540000599	7	0296	0	0	149	1	OK		Cotinine
05111540000600	7	0296	6	0	239	1	OK		Cotinine
05111540000603	7	0298	0	0	192	1	OK		Cotinine
05111540000604	7	0298	6	0	323	1	OK		Cotinine
05111540000607	7	0299	0	0	187	1	OK		Cotinine
05111540000611	7	0300	0	0	42 0	1	OK		Cotinine
05111540000612	7	0300	6	0	20 2	1	OK		Cotinine
05111540000615	7	0301	0	0	167	1	OK		Cotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000616	7	0301	6	0	265	1	OK		Cotinine
05111540000619	7	0306	0	0	287	1	OK		Cotinine
05111540000620	7	0306	6	0	9 85	1	OK		Cotinine
05111540000623	7	0307	0	0	190	1	OK		Cotinine
05111540000624	7	0307	6	0	330	1	OK		Cotinine
05111540000627	7	0308	0	0	307	1	OK		Cotinine
05111540000628	9	0308	6	0	388	1	OK		Cotinine
05111540000629		0309	0	0		2	Other	Analysis not required	Cotinine
05111540000631		0309	0	0		1	Other	Analysis not required	Cotinine
05111540000633		0312	0	0		2	Other	Analysis not required	Cotinine
05111540000635		0312	0	0		1	Other	Analysis not required	Cotinine
05111540000639	7	0313	0	0	174	1	OK		Cotinine
05111540000640	7	0313	6	0	307	1	OK		Cotinine
05111540000643	7	0315	0	0	152	1	OK		Cotinine
05111540000644	7	0315	6	0	241	1	OK		Cotinine
05111540000647	7	0316	0	0	37 6	1	OK		Cotinine
05111540000648	7	0316	6	0	69 6	1	OK		Cotinine
05111540000651	7	0317	0	0	183	1	OK		Cotinine
05111540000652	9	0317	6	0	1 34	1	OK		Cotinine
05111540000655	7	0318	0	0	219	1	OK		Cotinine
05111540000656	7	0318	6	0	417	1	OK		Cotinine
05111540000659	7	0320	0	0	334	1	OK		Cotinine
05111540000660	9	0320	6	0	445	1	OK		Cotinine
05111540000663	7	0321	0	0	236	1	OK		Cotinine
05111540000664	7	0321	6	0	400	1	OK		Cotinine
05111540000667	7	0322	0	0	99 5	1	OK		Cotinine
05111540000668	7	0322	6	0	119	1	OK		Cotinine
05111540000671	7	0325	0	0	356	1	OK		Cotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000672	7	0325	6	0	7.37	1	OK		Cotinine
05111540000675	7	0328	0	0	157	1	OK		Cotinine
05111540000676	7	0328	6	0	157	1	OK		Cotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Table 9 Study Sample Concentrations for *trans*-3'-Hydroxycotinine

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
0511154000001	4	0010	0	0	101	1	OK		Trans-3-Hydroxycotinine
0511154000002	1	0010	6	0	1 71	1	OK		Trans-3-Hydroxycotinine
0511154000003	1	0011	0	0	86 0	1	OK		Trans-3-Hydroxycotinine
0511154000004	1	0011	6	0	48 5	1	OK		Trans-3-Hydroxycotinine
0511154000005	1	0014	0	0	91 7	1	OK		Trans-3-Hydroxycotinine
0511154000006	1	0014	6	0	51 6	1	OK		Trans-3-Hydroxycotinine
0511154000007	1	0015	0	0	98 0	1	OK		Trans-3-Hydroxycotinine
0511154000008	1	0015	6	0	1 24	1	OK		Trans-3-Hydroxycotinine
0511154000009	1	0016	0	0	90 1	1	OK		Trans-3-Hydroxycotinine
0511154000010	5	0016	6	0	142	1	OK		Trans-3-Hydroxycotinine
0511154000011	1	0017	0	0	52 0	1	OK		Trans-3-Hydroxycotinine
0511154000012	1	0017	6	0	1 78	1	OK		Trans-3-Hydroxycotinine
0511154000013	5	0020	0	0	115	1	OK		Trans-3-Hydroxycotinine
0511154000014	1	0020	6	0	97 9	1	OK		Trans-3-Hydroxycotinine
0511154000015	5	0022	0	0	352	1	OK		Trans-3-Hydroxycotinine
0511154000016	5	0022	6	0	238	1	OK		Trans-3-Hydroxycotinine
0511154000017	5	0023	0	0	150	1	OK		Trans-3-Hydroxycotinine
0511154000018	1	0023	6	0	89 2	1	OK		Trans-3-Hydroxycotinine
0511154000019	5	0025	0	0	126	1	OK		Trans-3-Hydroxycotinine
0511154000020	5	0025	6	0	98 9	1	OK		Trans-3-Hydroxycotinine
0511154000021	5	0028	0	0	132	1	OK		Trans-3-Hydroxycotinine
0511154000022	1	0028	6	0	2 45	1	OK		Trans-3-Hydroxycotinine
0511154000023	5	0029	0	0	155	1	OK		Trans-3-Hydroxycotinine
0511154000024	1	0029	6	0	71 3	1	OK		Trans-3-Hydroxycotinine
0511154000025	5	0031	0	0	157	1	OK		Trans-3-Hydroxycotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000026	5	0031	6	0	100	1	OK		Trans-3-Hydroxycotinine
05111540000027	1	0035	0	0	86.2	1	OK		Trans-3-Hydroxycotinine
05111540000028	11	0035	6	0	62.4	1	OK		Trans-3-Hydroxycotinine
05111540000029	5	0038	0	0	223	1	OK		Trans-3-Hydroxycotinine
05111540000030	5	0038	6	0	117	1	OK		Trans-3-Hydroxycotinine
05111540000031	1	0039	0	0	83.3	1	OK		Trans-3-Hydroxycotinine
05111540000032	1	0039	6	0	56.5	1	OK		Trans-3-Hydroxycotinine
05111540000033	1	0044	0	0	35.7	1	OK		Trans-3-Hydroxycotinine
05111540000034	1	0044	6	0	26.0	1	OK		Trans-3-Hydroxycotinine
05111540000035	5	0049	0	0	106	1	OK		Trans-3-Hydroxycotinine
05111540000036	1	0049	6	0	1.50	1	OK		Trans-3-Hydroxycotinine
05111540000037	1	0052	0	0	91.5	1	OK		Trans-3-Hydroxycotinine
05111540000038	1	0052	6	0	4.12	1	OK		Trans-3-Hydroxycotinine
05111540000039	5	0053	0	0	121	1	OK		Trans-3-Hydroxycotinine
05111540000040	1	0053	6	0	90.7	1	OK		Trans-3-Hydroxycotinine
05111540000041	1	0057	0	0	51.0	1	OK		Trans-3-Hydroxycotinine
05111540000042	1	0057	6	0	31.6	1	OK		Trans-3-Hydroxycotinine
05111540000043	1	0060	0	0	42.6	1	OK		Trans-3-Hydroxycotinine
05111540000044	1	0060	6	0	36.0	1	OK		Trans-3-Hydroxycotinine
05111540000045	1	0062	0	0	65.0	1	OK		Trans-3-Hydroxycotinine
05111540000046	1	0062	6	0	1.65	1	OK		Trans-3-Hydroxycotinine
05111540000095	1	0030	0	0	34.3	1	OK		Trans-3-Hydroxycotinine
05111540000096	1	0030	6	0	34.0	1	OK		Trans-3-Hydroxycotinine
05111540000099	1	0034	0	0	88.0	1	OK		Trans-3-Hydroxycotinine
05111540000100	11	0034	6	0	57.5	1	OK		Trans-3-Hydroxycotinine
05111540000103	1	0055	0	0	96.7	1	OK		Trans-3-Hydroxycotinine
05111540000104	5	0055	6	0	109	1	OK		Trans-3-Hydroxycotinine
05111540000107	2	0064	0	0	45.3	1	OK		Trans-3-Hydroxycotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000108	2	0064	6	0	20.7	1	OK		Trans-3-Hydroxycotinine
05111540000111	4	0008	0	0	167	1	OK		Trans-3-Hydroxycotinine
05111540000112	1	0008	6	0	97.4	1	OK		Trans-3-Hydroxycotinine
05111540000115	1	0001	0	0	61.6	1	OK		Trans-3-Hydroxycotinine
05111540000116	1	0001	6	0	70.3	1	OK		Trans-3-Hydroxycotinine
05111540000119	1	0004	0	0	69.9	1	OK		Trans-3-Hydroxycotinine
05111540000120	1	0004	6	0	97.6	1	OK		Trans-3-Hydroxycotinine
05111540000123	4	0013	0	0	105	1	OK		Trans-3-Hydroxycotinine
05111540000124	1	0013	6	0	4.80	1	OK		Trans-3-Hydroxycotinine
05111540000127	1	0021	0	0	73.4	1	OK		Trans-3-Hydroxycotinine
05111540000128	1	0021	6	0	56.4	1	OK		Trans-3-Hydroxycotinine
05111540000131	1	0037	0	0	67.4	1	OK		Trans-3-Hydroxycotinine
05111540000132	1	0037	6	0	62.4	1	OK		Trans-3-Hydroxycotinine
05111540000135	1	0042	0	0	83.4	1	OK		Trans-3-Hydroxycotinine
05111540000136	1	0042	6	0	46.6	1	OK		Trans-3-Hydroxycotinine
05111540000139	1	0051	0	0	66.9	1	OK		Trans-3-Hydroxycotinine
05111540000140	1	0051	6	0	2.32	1	OK		Trans-3-Hydroxycotinine
05111540000143	4	0063	0	0	112	1	OK		Trans-3-Hydroxycotinine
05111540000144	2	0063	6	0	2.21	1	OK		Trans-3-Hydroxycotinine
05111540000147	2	0066	0	0	71.5	1	OK		Trans-3-Hydroxycotinine
05111540000148	2	0066	6	0	61.0	1	OK		Trans-3-Hydroxycotinine
05111540000151	2	0067	0	0	50.7	1	OK		Trans-3-Hydroxycotinine
05111540000152	2	0067	6	0	28.8	1	OK		Trans-3-Hydroxycotinine
05111540000155	2	0069	0	0	39.3	1	OK		Trans-3-Hydroxycotinine
05111540000156	2	0069	6	0	30.7	1	OK		Trans-3-Hydroxycotinine
05111540000159	4	0071	0	0	114	1	OK		Trans-3-Hydroxycotinine
05111540000160	2	0071	6	0	2.05	1	OK		Trans-3-Hydroxycotinine
05111540000163	4	0072	0	0	150	1	OK		Trans-3-Hydroxycotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000164	4	0072	6	0	137	1	OK		Trans-3-Hydroxycotinine
05111540000167	2	0074	0	0	71.6	1	OK		Trans-3-Hydroxycotinine
05111540000168	2	0074	6	0	43.2	1	OK		Trans-3-Hydroxycotinine
05111540000171	2	0076	0	0	53.5	1	OK		Trans-3-Hydroxycotinine
05111540000172	2	0076	6	0	2.38	1	OK		Trans-3-Hydroxycotinine
05111540000175	4	0080	0	0	140	1	OK		Trans-3-Hydroxycotinine
05111540000176	2	0080	6	0	77.1	1	OK		Trans-3-Hydroxycotinine
05111540000179	4	0083	0	0	135	1	OK		Trans-3-Hydroxycotinine
05111540000180	4	0083	6	0	120	1	OK		Trans-3-Hydroxycotinine
05111540000183	2	0085	0	0	23.1	1	OK		Trans-3-Hydroxycotinine
05111540000187	2	0086	0	0	72.2	1	OK		Trans-3-Hydroxycotinine
05111540000188	2	0086	6	0	1.91	1	OK		Trans-3-Hydroxycotinine
05111540000191	4	0087	0	0	145	1	OK		Trans-3-Hydroxycotinine
05111540000192	4	0087	6	0	150	1	OK		Trans-3-Hydroxycotinine
05111540000195	2	0088	0	0	81.2	1	OK		Trans-3-Hydroxycotinine
05111540000196	2	0088	6	0	55.6	1	OK		Trans-3-Hydroxycotinine
05111540000199	2	0090	0	0	9.54	1	OK		Trans-3-Hydroxycotinine
05111540000200	2	0090	6	0	7.57	1	OK		Trans-3-Hydroxycotinine
05111540000203	2	0093	0	0	98.3	1	OK		Trans-3-Hydroxycotinine
05111540000204	2	0093	6	0	67.0	1	OK		Trans-3-Hydroxycotinine
05111540000207	2	0104	0	0	73.8	1	OK		Trans-3-Hydroxycotinine
05111540000208	2	0104	6	0	BLQ<(1.00)	1	OK		Trans-3-Hydroxycotinine
05111540000211	4	0105	0	0	251	1	OK		Trans-3-Hydroxycotinine
05111540000212	4	0105	6	0	164	1	OK		Trans-3-Hydroxycotinine
05111540000215	2	0106	0	0	52.5	1	OK		Trans-3-Hydroxycotinine
05111540000216	2	0106	6	0	30.6	1	OK		Trans-3-Hydroxycotinine
05111540000219	2	0107	0	0	64.5	1	OK		Trans-3-Hydroxycotinine
05111540000220	2	0107	6	0	83.5	1	OK		Trans-3-Hydroxycotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000223	4	0110	0	0	152	1	OK		Trans-3-Hydroxycotinine
05111540000224	4	0110	6	0	101	1	OK		Trans-3-Hydroxycotinine
05111540000227	2	0112	0	0	84.0	1	OK		Trans-3-Hydroxycotinine
05111540000228	2	0112	6	0	58.1	1	OK		Trans-3-Hydroxycotinine
05111540000231	2	0114	0	0	45.7	1	OK		Trans-3-Hydroxycotinine
05111540000232	2	0114	6	0	BLQ<(1.00)	1	OK		Trans-3-Hydroxycotinine
05111540000235	4	0118	0	0	152	1	OK		Trans-3-Hydroxycotinine
05111540000236	2	0118	6	0	82.5	1	OK		Trans-3-Hydroxycotinine
05111540000239	2	0121	0	0	63.2	1	OK		Trans-3-Hydroxycotinine
05111540000240	2	0121	6	0	43.5	1	OK		Trans-3-Hydroxycotinine
05111540000243	2	0122	0	0	53.9	1	OK		Trans-3-Hydroxycotinine
05111540000244	2	0122	6	0	48.4	1	OK		Trans-3-Hydroxycotinine
05111540000247	2	0123	0	0	67.9	1	OK		Trans-3-Hydroxycotinine
05111540000248	2	0123	6	0	1.80	1	OK		Trans-3-Hydroxycotinine
05111540000251	2	0117	0	0	43.0	1	OK		Trans-3-Hydroxycotinine
05111540000252	2	0117	6	0	42.3	1	OK		Trans-3-Hydroxycotinine
05111540000255	2	0126	0	0	21.6	1	OK		Trans-3-Hydroxycotinine
05111540000256	2	0126	6	0	21.1	1	OK		Trans-3-Hydroxycotinine
05111540000259	2	0127	0	0	96.8	1	OK		Trans-3-Hydroxycotinine
05111540000260	2	0127	6	0	4.06	1	OK		Trans-3-Hydroxycotinine
05111540000263	2	0128	0	0	54.0	1	OK		Trans-3-Hydroxycotinine
05111540000264	2	0128	6	0	1.18	1	OK		Trans-3-Hydroxycotinine
05111540000267	2	0129	0	0	80.6	1	OK		Trans-3-Hydroxycotinine
05111540000268	2	0129	6	0	46.0	1	OK		Trans-3-Hydroxycotinine
05111540000271	3	0130	0	0	43.3	1	OK		Trans-3-Hydroxycotinine
05111540000272	3	0130	6	0	46.1	1	OK		Trans-3-Hydroxycotinine
05111540000275	7	0133	0	0	161	1	OK		Trans-3-Hydroxycotinine
05111540000276	3	0133	6	0	2.57	1	OK		Trans-3-Hydroxycotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000279	3	0134	0	0	62.2	1	OK		Trans-3-Hydroxycotinine
05111540000280	7	0134	6	0	101	1	OK		Trans-3-Hydroxycotinine
05111540000283	7	0136	0	0	128	1	OK		Trans-3-Hydroxycotinine
05111540000284	3	0136	6	0	74.9	1	OK		Trans-3-Hydroxycotinine
05111540000287	3	0137	0	0	81.5	1	OK		Trans-3-Hydroxycotinine
05111540000288	3	0137	6	0	1.64	1	OK		Trans-3-Hydroxycotinine
05111540000291	3	0139	0	0	59.8	1	OK		Trans-3-Hydroxycotinine
05111540000292	3	0139	6	0	28.4	1	OK		Trans-3-Hydroxycotinine
05111540000295	3	0140	0	0	76.1	1	OK		Trans-3-Hydroxycotinine
05111540000296	3	0140	6	0	59.8	1	OK		Trans-3-Hydroxycotinine
05111540000299	3	0145	0	0	53.5	1	OK		Trans-3-Hydroxycotinine
05111540000300	3	0145	6	0	BLQ<(1.00)	1	OK		Trans-3-Hydroxycotinine
05111540000303	3	0147	0	0	76.3	1	OK		Trans-3-Hydroxycotinine
05111540000304	3	0147	6	0	71.3	1	OK		Trans-3-Hydroxycotinine
05111540000307	3	0148	0	0	99.6	1	OK		Trans-3-Hydroxycotinine
05111540000308	3	0148	6	0	73.2	1	OK		Trans-3-Hydroxycotinine
05111540000311	3	0149	0	0	82.6	1	OK		Trans-3-Hydroxycotinine
05111540000312	3	0149	6	0	96.3	1	OK		Trans-3-Hydroxycotinine
05111540000315	3	0150	0	0	61.1	1	OK		Trans-3-Hydroxycotinine
05111540000316	3	0150	6	0	2.24	1	OK		Trans-3-Hydroxycotinine
05111540000319	3	0152	0	0	43.0	1	OK		Trans-3-Hydroxycotinine
05111540000320	3	0152	6	0	54.0	1	OK		Trans-3-Hydroxycotinine
05111540000323	8	0153	0	0	128	1	OK		Trans-3-Hydroxycotinine
05111540000324	8	0153	6	0	106	1	OK		Trans-3-Hydroxycotinine
05111540000327	3	0155	0	0	27.0	1	OK		Trans-3-Hydroxycotinine
05111540000328	3	0155	6	0	23.5	1	OK		Trans-3-Hydroxycotinine
05111540000331	8	0156	0	0	176	1	OK		Trans-3-Hydroxycotinine
05111540000332	8	0156	6	0	148	1	OK		Trans-3-Hydroxycotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000335	8	0160	0	0	101	1	OK		Trans-3-Hydroxycotinine
05111540000336	3	0160	6	0	79.6	1	OK		Trans-3-Hydroxycotinine
05111540000339	3	0162	0	0	71.7	1	OK		Trans-3-Hydroxycotinine
05111540000340	8	0162	6	0	104	1	OK		Trans-3-Hydroxycotinine
05111540000343	8	0167	0	0	97.5	1	OK		Trans-3-Hydroxycotinine
05111540000344	8	0167	6	0	107	1	OK		Trans-3-Hydroxycotinine
05111540000347	3	0169	0	0	55.9	1	OK		Trans-3-Hydroxycotinine
05111540000348	3	0169	6	0	BLQ<(1.00)	1	OK		Trans-3-Hydroxycotinine
05111540000351	3	0170	0	0	35.2	1	OK		Trans-3-Hydroxycotinine
05111540000352	3	0170	6	0	33.1	1	OK		Trans-3-Hydroxycotinine
05111540000355	8	0177	0	0	163	1	OK		Trans-3-Hydroxycotinine
05111540000356	8	0177	6	0	123	1	OK		Trans-3-Hydroxycotinine
05111540000359	8	0181	0	0	140	1	OK		Trans-3-Hydroxycotinine
05111540000360	8	0181	6	0	159	1	OK		Trans-3-Hydroxycotinine
05111540000363	3	0183	0	0	68.7	1	OK		Trans-3-Hydroxycotinine
05111540000364	3	0183	6	0	25.5	1	OK		Trans-3-Hydroxycotinine
05111540000367	8	0185	0	0	111	1	OK		Trans-3-Hydroxycotinine
05111540000368	3	0185	6	0	1.87	1	OK		Trans-3-Hydroxycotinine
05111540000371	3	0187	0	0	88.0	1	OK		Trans-3-Hydroxycotinine
05111540000372	3	0187	6	0	48.9	1	OK		Trans-3-Hydroxycotinine
05111540000375	8	0189	0	0	102	1	OK		Trans-3-Hydroxycotinine
05111540000376	3	0189	6	0	70.4	1	OK		Trans-3-Hydroxycotinine
05111540000379	8	0190	0	0	100	1	OK		Trans-3-Hydroxycotinine
05111540000380	3	0190	6	0	92.7	1	OK		Trans-3-Hydroxycotinine
05111540000383	3	0191	0	0	56.4	1	OK		Trans-3-Hydroxycotinine
05111540000384	3	0191	6	0	60.9	1	OK		Trans-3-Hydroxycotinine
05111540000387	8	0192	0	0	151	1	OK		Trans-3-Hydroxycotinine
05111540000388	8	0192	6	0	132	1	OK		Trans-3-Hydroxycotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000391	6	0264	0	0	48.5	1	OK		Trans-3-Hydroxycotinine
05111540000392	6	0264	6	0	12.6	1	OK		Trans-3-Hydroxycotinine
05111540000395	6	0265	0	0	91.2	1	OK		Trans-3-Hydroxycotinine
05111540000396	9	0265	6	0	1.66	1	OK		Trans-3-Hydroxycotinine
05111540000399	8	0193	0	0	69.1	1	OK		Trans-3-Hydroxycotinine
05111540000400	8	0193	6	0	62.2	1	OK		Trans-3-Hydroxycotinine
05111540000403	8	0195	0	0	53.9	1	OK		Trans-3-Hydroxycotinine
05111540000404	8	0195	6	0	56.9	1	OK		Trans-3-Hydroxycotinine
05111540000407	8	0196	0	0	35.2	1	OK		Trans-3-Hydroxycotinine
05111540000408	8	0196	6	0	43.2	1	OK		Trans-3-Hydroxycotinine
05111540000411	8	0197	0	0	32.3	1	OK		Trans-3-Hydroxycotinine
05111540000412	9	0197	6	0	1.11	1	OK		Trans-3-Hydroxycotinine
05111540000415	8	0198	0	0	94.9	1	OK		Trans-3-Hydroxycotinine
05111540000416	8	0198	6	0	102	1	OK		Trans-3-Hydroxycotinine
05111540000419	8	0200	0	0	61.8	1	OK		Trans-3-Hydroxycotinine
05111540000420	8	0200	6	0	32.1	1	OK		Trans-3-Hydroxycotinine
05111540000423	8	0202	0	0	139	1	OK		Trans-3-Hydroxycotinine
05111540000424	8	0202	6	0	143	1	OK		Trans-3-Hydroxycotinine
05111540000427	8	0203	0	0	57.0	1	OK		Trans-3-Hydroxycotinine
05111540000428	9	0203	6	0	1.30	1	OK		Trans-3-Hydroxycotinine
05111540000431	8	0204	0	0	35.5	1	OK		Trans-3-Hydroxycotinine
05111540000432	8	0204	6	0	20.9	1	OK		Trans-3-Hydroxycotinine
05111540000435	8	0206	0	0	101	1	OK		Trans-3-Hydroxycotinine
05111540000436	8	0206	6	0	82.9	1	OK		Trans-3-Hydroxycotinine
05111540000439	6	0210	0	0	202	1	OK		Trans-3-Hydroxycotinine
05111540000440	6	0210	6	0	69.2	1	OK		Trans-3-Hydroxycotinine
05111540000441		0211	0	0		2	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000443		0211	0	0		1	Other	Analysis not required	Trans-3-Hydroxycotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000447	6	0216	0	0	150	1	OK		Trans-3-Hydroxycotinine
05111540000448	6	0216	6	0	95.8	1	OK		Trans-3-Hydroxycotinine
05111540000451	6	0218	0	0	98.8	1	OK		Trans-3-Hydroxycotinine
05111540000452	9	0218	6	0	1.50	1	OK		Trans-3-Hydroxycotinine
05111540000455	6	0220	0	0	74.8	1	OK		Trans-3-Hydroxycotinine
05111540000456	6	0220	6	0	19.1	1	OK		Trans-3-Hydroxycotinine
05111540000459	6	0224	0	0	68.2	1	OK		Trans-3-Hydroxycotinine
05111540000460	6	0224	6	0	50.1	1	OK		Trans-3-Hydroxycotinine
05111540000463	6	0228	0	0	98.7	1	OK		Trans-3-Hydroxycotinine
05111540000464	6	0228	6	0	88.5	1	OK		Trans-3-Hydroxycotinine
05111540000467	6	0229	0	0	39.7	1	OK		Trans-3-Hydroxycotinine
05111540000468	6	0229	6	0	36.3	1	OK		Trans-3-Hydroxycotinine
05111540000471	6	0230	0	0	41.7	1	OK		Trans-3-Hydroxycotinine
05111540000472	6	0230	6	0	23.9	1	OK		Trans-3-Hydroxycotinine
05111540000475	6	0232	0	0	63.8	1	OK		Trans-3-Hydroxycotinine
05111540000476	6	0232	6	0	72.5	1	OK		Trans-3-Hydroxycotinine
05111540000479	6	0234	0	0	63.7	1	OK		Trans-3-Hydroxycotinine
05111540000480	6	0234	6	0	54.5	1	OK		Trans-3-Hydroxycotinine
05111540000483	6	0240	0	0	106	1	OK		Trans-3-Hydroxycotinine
05111540000484	9	0240	6	0	1.86	1	OK		Trans-3-Hydroxycotinine
05111540000487	6	0241	0	0	95.2	1	OK		Trans-3-Hydroxycotinine
05111540000488	6	0241	6	0	88.5	1	OK		Trans-3-Hydroxycotinine
05111540000489		0242	0	0		2	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000491		0242	0	0		1	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000495	6	0244	0	0	96.3	1	OK		Trans-3-Hydroxycotinine
05111540000496	6	0244	6	0	78.6	1	OK		Trans-3-Hydroxycotinine
05111540000497		0245	0	0		2	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000499		0245	0	0		1	Other	Analysis not required	Trans-3-Hydroxycotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000501		0247	0	0		2	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000503		0247	0	0		1	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000507	6	0249	0	0	142	1	OK		Trans-3-Hydroxycotinine
05111540000508	9	0249	6	0	1 94	1	OK		Trans-3-Hydroxycotinine
05111540000511	6	0251	0	0	93 2	1	OK		Trans-3-Hydroxycotinine
05111540000512	9	0251	6	0	BLQ<(1 00)	1	OK		Trans-3-Hydroxycotinine
05111540000515	6	0252	0	0	119	1	OK		Trans-3-Hydroxycotinine
05111540000516	9	0252	6	0	1 59	1	OK		Trans-3-Hydroxycotinine
05111540000519	6	0255	0	0	115	1	OK		Trans-3-Hydroxycotinine
05111540000520	6	0255	6	0	80 1	1	OK		Trans-3-Hydroxycotinine
05111540000523	6	0256	0	0	122	1	OK		Trans-3-Hydroxycotinine
05111540000524	6	0256	6	0	135	1	OK		Trans-3-Hydroxycotinine
05111540000527	6	0262	0	0	101	1	OK		Trans-3-Hydroxycotinine
05111540000528	6	0262	6	0	71 0	1	OK		Trans-3-Hydroxycotinine
05111540000531	6	0266	0	0	99 8	1	OK		Trans-3-Hydroxycotinine
05111540000532	9	0266	6	0	BLQ<(1 00)	1	OK		Trans-3-Hydroxycotinine
05111540000533		0269	0	0		2	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000535		0269	0	0		1	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000539	6	0272	0	0	165	1	OK		Trans-3-Hydroxycotinine
05111540000540	6	0272	6	0	144	1	OK		Trans-3-Hydroxycotinine
05111540000543	6	0273	0	0	101	1	OK		Trans-3-Hydroxycotinine
05111540000544	9	0273	6	0	1 85	1	OK		Trans-3-Hydroxycotinine
05111540000547	6	0276	0	0	37 9	1	OK		Trans-3-Hydroxycotinine
05111540000548	6	0276	6	0	57 4	1	OK		Trans-3-Hydroxycotinine
05111540000551	6	0277	0	0	92 8	1	OK		Trans-3-Hydroxycotinine
05111540000552	6	0277	6	0	151	1	OK		Trans-3-Hydroxycotinine
05111540000555	6	0278	0	0	101	1	OK		Trans-3-Hydroxycotinine
05111540000556	6	0278	6	0	65 8	1	OK		Trans-3-Hydroxycotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000559	6	0279	0	0	62.6	1	OK		Trans-3-Hydroxycotinine
05111540000560	6	0279	6	0	43.1	1	OK		Trans-3-Hydroxycotinine
05111540000563	6	0281	0	0	59.2	1	OK		Trans-3-Hydroxycotinine
05111540000564	6	0281	6	0	60.7	1	OK		Trans-3-Hydroxycotinine
05111540000567	6	0282	0	0	78.5	1	OK		Trans-3-Hydroxycotinine
05111540000568	6	0282	6	0	58.0	1	OK		Trans-3-Hydroxycotinine
05111540000571	6	0283	0	0	133	1	OK		Trans-3-Hydroxycotinine
05111540000572	6	0283	6	0	88.2	1	OK		Trans-3-Hydroxycotinine
05111540000575	7	0285	0	0	113	1	OK		Trans-3-Hydroxycotinine
05111540000576	7	0285	6	0	70.2	1	OK		Trans-3-Hydroxycotinine
05111540000579	7	0287	0	0	86.9	1	OK		Trans-3-Hydroxycotinine
05111540000580	7	0287	6	0	83.8	1	OK		Trans-3-Hydroxycotinine
05111540000581		0288	0	0		2	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000583		0288	0	0		1	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000587	7	0289	0	0	52.7	1	OK		Trans-3-Hydroxycotinine
05111540000588	9	0289	6	0	1.16	1	OK		Trans-3-Hydroxycotinine
05111540000591	7	0291	0	0	124	1	OK		Trans-3-Hydroxycotinine
05111540000592	7	0291	6	0	187	1	OK		Trans-3-Hydroxycotinine
05111540000595	7	0292	0	0	40.6	1	OK		Trans-3-Hydroxycotinine
05111540000596	9	0292	6	0	1.77	1	OK		Trans-3-Hydroxycotinine
05111540000599	7	0296	0	0	44.0	1	OK		Trans-3-Hydroxycotinine
05111540000600	7	0296	6	0	54.2	1	OK		Trans-3-Hydroxycotinine
05111540000603	7	0298	0	0	140	1	OK		Trans-3-Hydroxycotinine
05111540000604	7	0298	6	0	113	1	OK		Trans-3-Hydroxycotinine
05111540000607	7	0299	0	0	50.1	1	OK		Trans-3-Hydroxycotinine
05111540000611	7	0300	0	0	16.9	1	OK		Trans-3-Hydroxycotinine
05111540000612	7	0300	6	0	6.11	1	OK		Trans-3-Hydroxycotinine
05111540000615	7	0301	0	0	94.8	1	OK		Trans-3-Hydroxycotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000616	7	0301	6	0	85.6	1	OK		Trans-3-Hydroxycotinine
05111540000619	7	0306	0	0	62.2	1	OK		Trans-3-Hydroxycotinine
05111540000620	9	0306	6	0	2.64	1	OK		Trans-3-Hydroxycotinine
05111540000623	7	0307	0	0	73.8	1	OK		Trans-3-Hydroxycotinine
05111540000624	7	0307	6	0	74.5	1	OK		Trans-3-Hydroxycotinine
05111540000627	7	0308	0	0	58.2	1	OK		Trans-3-Hydroxycotinine
05111540000628	9	0308	6	0	63.7	1	OK		Trans-3-Hydroxycotinine
05111540000629		0309	0	0		2	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000631		0309	0	0		1	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000633		0312	0	0		2	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000635		0312	0	0		1	Other	Analysis not required	Trans-3-Hydroxycotinine
05111540000639	7	0313	0	0	50.0	1	OK		Trans-3-Hydroxycotinine
05111540000640	7	0313	6	0	58.6	1	OK		Trans-3-Hydroxycotinine
05111540000643	7	0315	0	0	92.3	1	OK		Trans-3-Hydroxycotinine
05111540000644	7	0315	6	0	70.0	1	OK		Trans-3-Hydroxycotinine
05111540000647	7	0316	0	0	20.6	1	OK		Trans-3-Hydroxycotinine
05111540000648	7	0316	6	0	24.9	1	OK		Trans-3-Hydroxycotinine
05111540000651	7	0317	0	0	100	1	OK		Trans-3-Hydroxycotinine
05111540000652	9	0317	6	0	1.94	1	OK		Trans-3-Hydroxycotinine
05111540000655	7	0318	0	0	161	1	OK		Trans-3-Hydroxycotinine
05111540000656	7	0318	6	0	162	1	OK		Trans-3-Hydroxycotinine
05111540000659	7	0320	0	0	144	1	OK		Trans-3-Hydroxycotinine
05111540000660	9	0320	6	0	144	1	OK		Trans-3-Hydroxycotinine
05111540000663	7	0321	0	0	51.1	1	OK		Trans-3-Hydroxycotinine
05111540000664	7	0321	6	0	63.4	1	OK		Trans-3-Hydroxycotinine
05111540000667	7	0322	0	0	35.5	1	OK		Trans-3-Hydroxycotinine
05111540000668	7	0322	6	0	30.9	1	OK		Trans-3-Hydroxycotinine
05111540000671	7	0325	0	0	113	1	OK		Trans-3-Hydroxycotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111540000672	9	0325	6	0	3.77	1	OK		Trans-3-Hydroxycotinine
05111540000675	7	0328	0	0	27.4	1	OK		Trans-3-Hydroxycotinine
05111540000676	7	0328	6	0	38.1	1	OK		Trans-3-Hydroxycotinine



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

Table 10 Summary of Reassay for Analytical Reasons for Cotinine

Run ID	Reason	Sample Name
1	AAR	AA99071-10 05111540000115 0001 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000116 0001 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000119 0004 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000120 0004 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000111 0008 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000112 0008 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000001 0010 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000003 0011 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000004 0011 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000123 0013 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000005 0014 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000006 0014 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000007 0015 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000009 0016 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000010 0016 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000011 0017 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000013 0020 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000014 0020 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000127 0021 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000128 0021 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000015 0022 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000016 0022 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000017 0023 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000018 0023 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000019 0025 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000020 0025 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000021 0028 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000023 0029 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000024 0029 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000095 0030 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000096 0030 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000025 0031 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000026 0031 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000099 0034 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000027 0035 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000131 0037 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000132 0037 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000029 0038 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000030 0038 N/A P1 Day 6 0h PL-1



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

Run ID	Reason	Sample Name
1	AAR	AA99071-10 05111540000031 0039 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000032 0039 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000135 0042 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000136 0042 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000033 0044 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000034 0044 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000035 0049 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000139 0051 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000037 0052 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000039 0053 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000040 0053 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000103 0055 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000104 0055 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000041 0057 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000042 0057 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000043 0060 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000044 0060 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000045 0062 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000143 0063 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000107 0064 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000147 0066 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000148 0066 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000155 0069 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000156 0069 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000159 0071 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000163 0072 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000164 0072 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000167 0074 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000168 0074 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000171 0076 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000175 0080 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000176 0080 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000179 0083 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000180 0083 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000187 0086 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000191 0087 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000192 0087 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000195 0088 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000196 0088 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000199 0090 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000203 0093 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000204 0093 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000211 0105 N/A P1 Day 0 0h PL-1



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

Run ID	Reason	Sample Name
2	AAR	AA99071-10 05111540000212 0105 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000215 0106 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000216 0106 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000219 0107 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000220 0107 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000223 0110 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000224 0110 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000227 0112 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000228 0112 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000231 0114 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000251 0117 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000252 0117 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000235 0118 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000236 0118 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000239 0121 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000240 0121 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000243 0122 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000244 0122 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000247 0123 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000259 0127 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000263 0128 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000267 0129 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000268 0129 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000271 0130 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000272 0130 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000275 0133 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000280 0134 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000283 0136 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000284 0136 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000287 0137 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000291 0139 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000292 0139 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000295 0140 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000296 0140 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000304 0147 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000307 0148 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000308 0148 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000311 0149 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000312 0149 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000315 0150 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000320 0152 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000323 0153 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000324 0153 N/A P1 Day 6 0h PL-1



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10

Run ID	Reason	Sample Name
3	AAR	AA99071-10 05111540000331 0156 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000332 0156 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000335 0160 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000336 0160 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000339 0162 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000340 0162 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000343 0167 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000344 0167 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000347 0169 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000352 0170 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000355 0177 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000356 0177 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000359 0181 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000360 0181 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000363 0183 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000367 0185 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000371 0187 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000372 0187 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000375 0189 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000376 0189 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000379 0190 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000380 0190 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000383 0191 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000384 0191 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000387 0192 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000388 0192 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000452 0218 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000484 0240 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000508 0249 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000512 0251 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000516 0252 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000396 0265 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000532 0266 N/A P1 Day 6 0h PL-1
6	AAR	AA99071-10 05111540000540 0272 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000544 0273 N/A P1 Day 6 0h PL-1
7	DCU	AA99071-10 05111540000588 0289 N/A P1 Day 6 0h PL-1
7	AAR	AA99071-10 05111540000592 0291 N/A P1 Day 6 0h PL-1
7	DCU	AA99071-10 05111540000652 0317 N/A P1 Day 6 0h PL-1
8	DCU	AA99071-10 05111540000412 0197 N/A P1 Day 6 0h PL-1
8	DCU	AA99071-10 05111540000428 0203 N/A P1 Day 6 0h PL-1
11	AAR	AA99071-10 05111540000100 0034 N/A P1 Day 6 0h PL-1
11	AAR	AA99071-10 05111540000028 0035 N/A P1 Day 6 0h PL-1



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Table 11 Summary of Reassay for Analytical Reasons for *trans*-3'-Hydroxycotinine

Run ID	Reason	Sample Name
1	AAR	AA99071-10 05111540000111 0008 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000001 0010 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000123 0013 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000010 0016 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000013 0020 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000015 0022 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000016 0022 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000017 0023 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000019 0025 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000020 0025 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000021 0028 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000023 0029 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000025 0031 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000026 0031 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000029 0038 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000030 0038 N/A P1 Day 6 0h PL-1
1	AAR	AA99071-10 05111540000035 0049 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000039 0053 N/A P1 Day 0 0h PL-1
1	AAR	AA99071-10 05111540000104 0055 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000143 0063 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000159 0071 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000163 0072 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000164 0072 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000175 0080 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000179 0083 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000180 0083 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000191 0087 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000192 0087 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000211 0105 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000212 0105 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000223 0110 N/A P1 Day 0 0h PL-1
2	AAR	AA99071-10 05111540000224 0110 N/A P1 Day 6 0h PL-1
2	AAR	AA99071-10 05111540000235 0118 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000275 0133 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000280 0134 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000283 0136 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000323 0153 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000324 0153 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000331 0156 N/A P1 Day 0 0h PL-1



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Run ID	Reason	Sample Name
3	AAR	AA99071-10 05111540000332 0156 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000335 0160 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000340 0162 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000343 0167 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000344 0167 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000355 0177 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000356 0177 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000359 0181 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000360 0181 N/A P1 Day 6 0h PL-1
3	AAR	AA99071-10 05111540000367 0185 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000375 0189 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000379 0190 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000387 0192 N/A P1 Day 0 0h PL-1
3	AAR	AA99071-10 05111540000388 0192 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000452 0218 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000484 0240 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000508 0249 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000512 0251 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000516 0252 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000396 0265 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000532 0266 N/A P1 Day 6 0h PL-1
6	DCU	AA99071-10 05111540000544 0273 N/A P1 Day 6 0h PL-1
7	DCU	AA99071-10 05111540000588 0289 N/A P1 Day 6 0h PL-1
7	DCU	AA99071-10 05111540000596 0292 N/A P1 Day 6 0h PL-1
7	DCU	AA99071-10 05111540000620 0306 N/A P1 Day 6 0h PL-1
7	DCU	AA99071-10 05111540000652 0317 N/A P1 Day 6 0h PL-1
7	DCU	AA99071-10 05111540000672 0325 N/A P1 Day 6 0h PL-1
8	DCU	AA99071-10 05111540000412 0197 N/A P1 Day 6 0h PL-1
8	DCU	AA99071-10 05111540000428 0203 N/A P1 Day 6 0h PL-1



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Table 12 Incurred Sample Reproducibility Assessment for Cotinine

Subject	Period	Time Point	Analyte	Units	Original Value	Reassay Value	Mean Value	% Difference	Reproducible?	Event?	% of Passing ISR Samples
0016	1	Day 6 0h	Cotinine	ng/mL	389	394	392	1.28	Pass	No	100.0
0022	1	Day 6 0h	Cotinine	ng/mL	552	562	557	1.80	Pass	No	
0029	1	Day 0 0h	Cotinine	ng/mL	210	214	212	1.89	Pass	No	
0038	1	Day 0 0h	Cotinine	ng/mL	348	355	352	1.99	Pass	No	
0049	1	Day 0 0h	Cotinine	ng/mL	262	271	267	3.37	Pass	No	
0052	1	Day 6 0h	Cotinine	ng/mL	2.80	2.62	2.71	6.64	Pass	No	
0008	1	Day 0 0h	Cotinine	ng/mL	312	314	313	0.64	Pass	No	
0013	1	Day 6 0h	Cotinine	ng/mL	2.30	2.36	2.33	2.58	Pass	No	
0067	1	Day 0 0h	Cotinine	ng/mL	90.8	94.1	92.5	3.57	Pass	No	
0071	1	Day 6 0h	Cotinine	ng/mL	2.20	2.18	2.19	0.91	Pass	No	
0076	1	Day 6 0h	Cotinine	ng/mL	3.40	3.48	3.44	2.33	Pass	No	
0083	1	Day 6 0h	Cotinine	ng/mL	339	337	338	0.59	Pass	No	
0104	1	Day 0 0h	Cotinine	ng/mL	85.4	89.9	87.7	5.13	Pass	No	
0105	1	Day 0 0h	Cotinine	ng/mL	593	580	587	2.21	Pass	No	
0126	1	Day 6 0h	Cotinine	ng/mL	96.7	99.4	98.1	2.75	Pass	No	
0127	1	Day 6 0h	Cotinine	ng/mL	4.94	5.12	5.03	3.58	Pass	No	
0145	1	Day 0 0h	Cotinine	ng/mL	63.6	62.8	63.2	1.27	Pass	No	
0150	1	Day 6 0h	Cotinine	ng/mL	7.04	6.97	7.01	1.00	Pass	No	
0155	1	Day 6 0h	Cotinine	ng/mL	67.0	66.2	66.6	1.20	Pass	No	
0156	1	Day 6 0h	Cotinine	ng/mL	413	398	406	3.69	Pass	No	
0181	1	Day 6 0h	Cotinine	ng/mL	492	498	495	1.21	Pass	No	
0183	1	Day 6 0h	Cotinine	ng/mL	75.8	74.8	75.3	1.33	Pass	No	
0264	1	Day 6 0h	Cotinine	ng/mL	44.1	42.9	43.5	2.76	Pass	No	
0196	1	Day 0 0h	Cotinine	ng/mL	57.8	61.1	59.5	5.55	Pass	No	



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Subject	Period	Time Point	Analyte	Units	Original Value	Reassay Value	Mean Value	% Difference	Reproducible?	Event?	% of Passing ISR Samples
0202	1	Day 6 0h	Cotinine	ng/mL	390	387	389	0.77	Pass	No	
0210	1	Day 0 0h	Cotinine	ng/mL	373	368	371	1.35	Pass	No	
0256	1	Day 6 0h	Cotinine	ng/mL	492	482	487	2.05	Pass	No	
0281	1	Day 6 0h	Cotinine	ng/mL	325	324	325	0.31	Pass	No	
0287	1	Day 6 0h	Cotinine	ng/mL	401	393	397	2.02	Pass	No	
0292	1	Day 6 0h	Cotinine	ng/mL	5.76	5.94	5.85	3.08	Pass	No	
0300	1	Day 6 0h	Cotinine	ng/mL	20.2	20.3	20.3	0.49	Pass	No	
0308	1	Day 6 0h	Cotinine	ng/mL	388	389	389	0.26	Pass	No	
0318	1	Day 6 0h	Cotinine	ng/mL	417	407	412	2.43	Pass	No	
0320	1	Day 6 0h	Cotinine	ng/mL	445	433	439	2.73	Pass	No	
0325	1	Day 6 0h	Cotinine	ng/mL	7.37	7.40	7.39	0.41	Pass	No	



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Table 13 Incurred Sample Reproducibility Assessment for *trans*-3'-Hydroxycotinine

Subject	Period	Time Point	Analyte	Units	Original Value	Reassay Value	Mean Value	% Difference	Reproducible?	Event?	% of Passing ISR Samples
0016	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	142	138	140	2.86	Pass	No	100.0
0022	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	238	228	233	4.29	Pass	No	
0029	1	Day 0 0h	Trans-3-Hydroxycotinine	ng/mL	155	157	156	1.28	Pass	No	
0038	1	Day 0 0h	Trans-3-Hydroxycotinine	ng/mL	223	221	222	0.90	Pass	No	
0049	1	Day 0 0h	Trans-3-Hydroxycotinine	ng/mL	106	107	107	0.93	Pass	No	
0052	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	4.12	3.46	3.79	17.41	Pass	No	
0008	1	Day 0 0h	Trans-3-Hydroxycotinine	ng/mL	167	160	164	4.27	Pass	No	
0013	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	4.80	4.49	4.65	6.67	Pass	No	
0067	1	Day 0 0h	Trans-3-Hydroxycotinine	ng/mL	50.7	49.7	50.2	1.99	Pass	No	
0071	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	2.05	2.02	2.04	1.47	Pass	No	
0076	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	2.38	2.21	2.30	7.39	Pass	No	
0083	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	120	114	117	5.13	Pass	No	
0104	1	Day 0 0h	Trans-3-Hydroxycotinine	ng/mL	73.8	78.1	76.0	5.66	Pass	No	
0105	1	Day 0 0h	Trans-3-Hydroxycotinine	ng/mL	251	238	245	5.31	Pass	No	
0126	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	21.1	20.7	20.9	1.91	Pass	No	
0127	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	4.06	4.25	4.16	4.57	Pass	No	
0145	1	Day 0 0h	Trans-3-Hydroxycotinine	ng/mL	53.5	54.5	54.0	1.85	Pass	No	
0150	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	2.24	2.16	2.20	3.64	Pass	No	
0155	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	23.5	22.9	23.2	2.59	Pass	No	
0156	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	148	146	147	1.36	Pass	No	
0181	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	159	157	158	1.27	Pass	No	
0183	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	25.5	25.3	25.4	0.79	Pass	No	
0264	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	12.6	12.2	12.4	3.23	Pass	No	
0196	1	Day 0 0h	Trans-3-Hydroxycotinine	ng/mL	35.2	36.6	35.9	3.90	Pass	No	



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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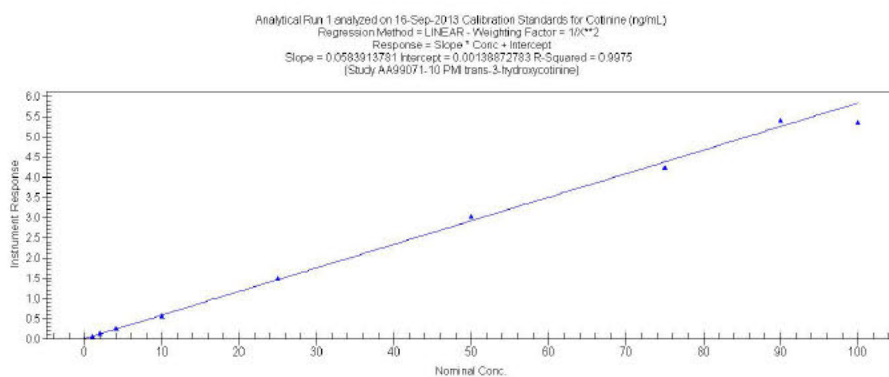
Subject	Period	Time Point	Analyte	Units	Original Value	Reassay Value	Mean Value	% Difference	Reproducible?	Event?	% of Passing ISR Samples
0202	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	143	136	140	5.00	Pass	No	
0210	1	Day 0 0h	Trans-3-Hydroxycotinine	ng/mL	202	200	201	1.00	Pass	No	
0256	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	135	133	134	1.49	Pass	No	
0281	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	60.7	60.6	60.7	0.16	Pass	No	
0287	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	83.8	85.6	84.7	2.13	Pass	No	
0292	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	1.77	1.71	1.74	3.45	Pass	No	
0300	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	6.11	5.22	5.67	15.70	Pass	No	
0308	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	63.7	60.5	62.1	5.15	Pass	No	
0318	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	162	164	163	1.23	Pass	No	
0320	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	144	144	144	0.00	Pass	No	
0325	1	Day 6 0h	Trans-3-Hydroxycotinine	ng/mL	3.77	3.58	3.68	5.16	Pass	No	



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₃EDTA)
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FIGURES

Figure 1 Calibration Curve for Cotinine in Control Matrix, Watson Run ID 1¹

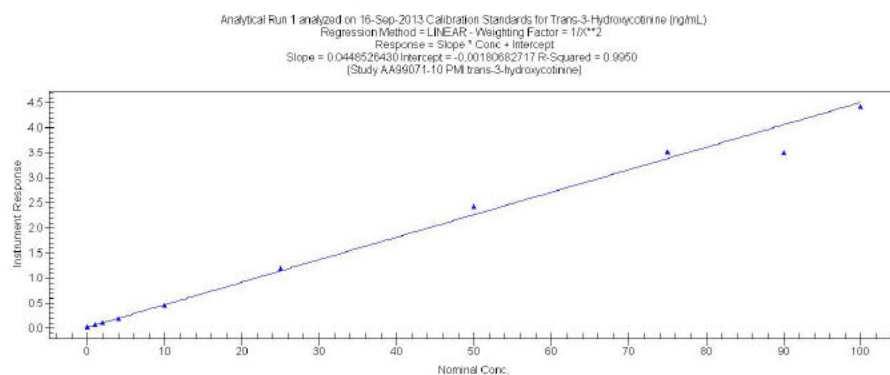


¹ Note: Though included on the figure above, the Standard 0 (blank sample extracted with internal standard) was not used as a standard to calculate the calibration curve parameters.



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Figure 2 Calibration Curve for *trans*-3'-Hydroxycotinine in Control Matrix, Watson Run ID 1²



² Note: Though included on the figure above, the Standard 0 (blank sample extracted with internal standard) was not used as a standard to calculate the calibration curve parameters.



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ATTACHMENTS

Attachment 1 General List of Abbreviations used at Celerion

Abbreviations are used in this document as applicable.

Abbreviation	Description
°C	Degree Celsius (centigrade)
µg	Microgram
AAR	Above the acceptable range
AB	Applied Biosystems
API	Atmospheric pressure ionization
ASCII	American standard code for information interchange
BAM	Bioanalytical method
BLK	Blank
BLQ	Below limit of quantification
CC	Conventional Cigarette
CDER	Center for Drug Evaluation and Research
CFR	Code of Federal Regulations
CRO	Contract research organisation
CV	Coefficient of variation
Da	Dalton
DCU	Diluted concentration unreliable
DFNR	Dilution factor not reliable
DQC	Dilution quality control sample
ELISA	Enzyme-linked immunosorbent assay
EDTA	Ethylenediaminetetraacetic acid
EQB	Exceeding quadratic bounds
EXT	Extraction
fg	Femtogram
g	Gram
GLP	Good laboratory practices
h	Hour
HDPE	High density polyethylene
HPLC	High performance liquid chromatography



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₃EDTA)
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Abbreviation	Description
HSR	High standard removed
ID	Identifier
INC	Incongruous
INS	Instrumentation
IS	Internal standard
ISA	Insufficient volume for full analysis
ISP	Incomplete sample processing
ISR	Incurred sample reproducibility
ISV	Insufficient volume
IVR	Insufficient volume to reassay
L	Litre, liter
LLOQ	Lower limit of quantitation
LNK	Celerion, Lincoln site
M	Molar
mg	Milligram
mL	Millilitre, milliliter
mol	Mole
MS	Mass spectrometry
MW	Molecular weight
n	Number of data points
N/AP	Not applicable
N/AV	Not available
NFV	Not full volume
ng	Nanogram
No	Number
NU	Not used
OECD	Organization for Economic Cooperation and Development
PD	Period
pg	Picogram
QC	Quality control
QCs	Quality control samples
R E	Relative error
REF	Reference



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₃EDTA)
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Abbreviation	Description
RI	Reinjection
RIA	Rarioimmunoassay
RT	Room temperature
RR	Reanalysis
RVL	Remaining volume low
S A	Smoking Abstinence
S D	Standard deviation
SOP	Standard operating procedure
SPE	Solid-phase extraction
SST	System suitability test
STD	Standard
Sub	Subject
SVD	Sample volume depleted
TBD	To be determined
Temp	Temperature
THS	Tobacco Heating System
UCR	Unacceptable chromatography
UISR	Unacceptable internal standard response
ULOQ	Upper limit of quantitation
U S FDA	United States Food and Drug Administration
USP	US pharmacopeia
\bar{x}	Mean



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₃EDTA)
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Attachment 2 Temperature Definitions at Celerion

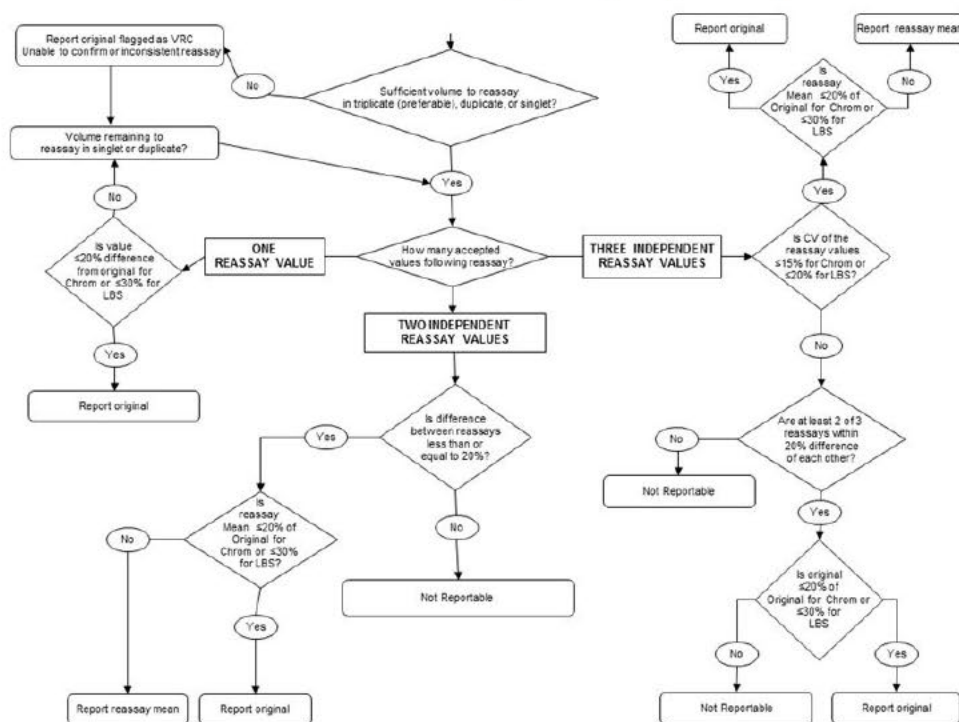
Values for temperatures are nominal temperatures representing the following temperature ranges:

Nominal temperature	Temperature Range
-80 C	-65 C to -90 C
-20 C	-10 C to -30 C
5 C	2 C to 8 C
Room temperature	15 C to 25 C
24 C	22 C to 26 C



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
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Attachment 3 Procedure for VRC and SSR Reassays and Reporting of Reassay Results



To compare reassays:

$$\frac{|\text{Re assay Value 1} - \text{Re assay Value 2}|}{\text{Mean of Re assay Value 1 and 2}} * 100\%$$

To compare to original:

$$\frac{|\text{Mean of Re assays} - \text{Original Value}|}{\text{Original Value}} * 100\%$$

An LC-MS/MS value as outlined in the decision tree is obtained from a single determination

If BLQ is obtained for a value, the nominal concentration of the LLOQ is used when comparing reassays in this decision tree.



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₃EDTA)
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Attachment 4 General List of Calculation Formulae

Mean:
$$x_{\text{Mean}} = \frac{1}{n} \sum_{i=1}^n x_i$$

Standard Deviation (SD):
$$SD = \sqrt{\frac{1}{n-1} \sum_{i=1}^n (x_i - x_{\text{Mean}})^2}$$

Precision (RSD, CV):
$$CV \% = \left(\frac{SD}{x_{\text{Mean}}} \right) * 100$$

Accuracy (% Theoretical):
$$\text{Accuracy \%} = \left(\frac{x}{x_{\text{Nominal}}} \right) * 100$$

$$\text{Accuracy of Mean \%} = \left(\frac{x_{\text{Mean}}}{x_{\text{Nominal}}} \right) * 100$$

Inaccuracy (% Bias, % RE):
$$\text{Bias \%} = \left(\frac{(x - x_{\text{Nominal}})}{x_{\text{Nominal}}} \right) * 100$$

$$\text{Bias of Mean \%} = \left(\frac{(x_{\text{Mean}} - x_{\text{Nominal}})}{x_{\text{Nominal}}} \right) * 100$$

x = value (e.g. analyte concentration, OD value, cpm value, peak signal)

n = number of values

$$\text{Potency} = \frac{100 - \left(\frac{\% \text{ Salts}}{\text{Determined By Assay}} + \frac{\% \text{ Water}}{\text{Content}} + \frac{\% \text{ Residual}}{\text{Solvent}} + \frac{\% \text{ Other}}{\text{Impurity}} \right)}{100} * \frac{\% \text{ Chromatographic Purity}}{100} * \frac{\% \text{ Chiral Purity}}{100} * \frac{\% \text{ Isotopic Purity}}{100} * \frac{\% \text{ Other Purity}}{100} * \frac{\text{MW Free Base}}{\text{MW Salt}}$$

$$\% \text{ Difference} = \left[\frac{\left| \frac{(\text{Re assay} - \text{Original})}{2} \right|}{\left(\frac{(\text{Re assay} + \text{Original})}{2} \right)} \right] * 100$$



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Attachment 5 Reassay Descriptions

Analytical Reason (Code)	Description
Above the Accepted Range (AAR)	Identifies a study sample whose calculated concentration is greater than the upper limit of quantitation (ULOQ). This study sample will be diluted before being reassayed.
Diluted Concentration Unreliable (DCU)	Identifies a study sample that has been diluted and determined to have a concentration below LLOQ (BLQ, below limit of quantification) before correction for the final dilution factor.
Dilution Factor Not Reliable (DFNR)	Identifies a study sample that has been diluted, and determined to have a measurable concentration, however >50% of the dilution QC samples (having the same dilution factor) did not meet their acceptance criteria. Identifies a dilution QC sample that does not fulfil the acceptance criterion and is excluded from the DQC statistics.
Highest / Lowest Standard Removed (HSR / LSR)	If the working range of the method is truncated as a result of - the ULOQ calibration standard being rejected or unavailable (e.g. incomplete sample processing or incomplete instrument analysis, unacceptable chromatography), all study samples with concentrations greater than the highest acceptable standard are identified as 'highest standard removed' (HSR). - the calibration standard at the LLOQ being rejected or unavailable (e.g. incomplete sample processing or incomplete instrument analysis, unacceptable chromatography), all study samples with concentrations below the lowest acceptable standard are identified as 'lowest standard removed' (LSR).
Incomplete Sample Processing (ISP)	Identifies a study sample, calibration standard, or QC sample for which data could not be obtained due to processing problems that occurred during the extraction or assay documented by the analyst prior to instrumental analysis.
Insufficient Volume for Reassay (IVR)	Identified a study sample that has insufficient sample volume for reanalysis (including all received splits)
Incomplete Instrument Analysis (IIA)	Identifies a study sample, calibration standard, or QC sample for which data could not be obtained due to processing problems that occurred during HPLC injection or instrumental analysis and were documented by the analyst.
Unacceptable Chromatography (UCR)	Identifies a study sample, calibration standard, or QC sample judged to demonstrate unacceptable chromatography according to the applicable Celerion procedures (e.g. split peak, poor peak symmetry, unseparated interference).



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₃EDTA)
Celerion Study AA99071-10

Attachment 6 Certificates of Analysis



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₃EDTA)
Celerion Study AA99071-10

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Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₃EDTA)
Celerion Study AA99071-10

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Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₃EDTA)
Celerion Study AA99071-10

Attachment 7 Bioanalytical Method Summary



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10



BIOANALYTICAL METHOD SUMMARY (BMS)

Doc No: FORL_QM000496 – CR204A2

Version N°: 2.0

Page 1 of 2

Biomarker: Cotinine		Matrix: Plasma	
MVR/SOP no. & date: AA33664-01 / 20-Oct-2014		CRO/Laboratory: Celerion-Lincoln	
LLOQ: 1.00 ng/mL		ULOQ: 100 ng/mL	
Validation	<input checked="" type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Cross Comments (required for Partial/Cross):		
Assay:	<input checked="" type="checkbox"/> Chromatographic <input type="checkbox"/> Ligand binding <input type="checkbox"/> Enzymatic <input type="checkbox"/> Other describe:		
	<input type="checkbox"/> LC/MS <input checked="" type="checkbox"/> LC/MS/MS <input type="checkbox"/> GC/MS <input type="checkbox"/> GC/MS/MS		
	<input type="checkbox"/> ELISA		
Equipment and short description of extraction and analysis: An aliquot of human plasma containing the analyte and internal standard was extracted using a solid-phase extraction procedure. The extracted samples were analyzed by a HPLC equipped with an AB SCIEX API 5000™ or QTRAP® 5500 mass spectrometer. Positive ions were monitored in the multiple reaction monitoring (MRM) mode. Quantitation was determined using a weighted linear regression analysis (1/concentration ²) of peak area ratios of each analyte and internal standard.			
Selectivity/Sensitivity/Matrix effect:		No significant matrix effect was observed in 6 of the 6 human plasma (EDTA) lots that were spiked near the concentration of the LLOQ and in any of the 6 human plasma (EDTA) lots that were spiked near the concentration of the high QC sample	
Accuracy:		Intra-batch: -7.2 to 3.3% R.E. Inter-batch: -4.3 to 2.1% R.E.	
Precision:		Intra-batch: 1.1 to 4.3% C.V. Inter-batch: 2.1 to 4.2% C.V.	
Recovery:		91% at 2.00 ng/mL in human plasma 90% at 10.0 ng/mL in human plasma 90% at 75.0 ng/mL in human plasma	
Freeze and thaw stability:		6 freeze/cycles in polypropylene tubes at -20°C under white light 7 freeze/cycles in polypropylene tubes at -20°C under UV-shielded light	
Short-term temperature stability:		27 hours in polypropylene tubes at ambient temperature under white light	
Long-term stability:		739 days in polypropylene tubes at -20°C	
Stock solution stability:		39 days at 200 µg/mL in water in a polypropylene container at -20°C	
Post-preparative stability:		135 hours in a polypropylene 96 well plate at 5°C	
Accreditation/ GLP compliance/ QA statements:		GLP Compliance as Assay Validation conforms to Celerion Standard Operating Procedures which were written in compliance with FDA: Guidance to Industry "Bioanalytical Method Validation"	



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₃EDTA)
Celerion Study AA99071-10



BIOANALYTICAL METHOD SUMMARY (BMS)

Doc No: FOR_QM00496 – CR204A2

Version N°: 2.0

Page 2 of 2

BMS completed by:		
Name:	Date:	Signature:
Erica Nachi	03-Mar-2015	



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10



PMI RESEARCH & DEVELOPMENT

BIOANALYTICAL METHOD SUMMARY (BMS)

Doc No: FDR_OM000496 - CR204A2

Version N°: 2.0

Page 1 of 2

Biomarker: <i>trans</i> -3'-hydroxycotinine		Matrix: Plasma
MVR/SOP no. & date: AA33664-01 / 20-Oct-2014		CRO/Laboratory: Celerion-Lincoln
LLOQ: 1.00 ng/mL		ULOQ: 100 ng/mL
Validation	<input checked="" type="checkbox"/> Full <input type="checkbox"/> Partial <input type="checkbox"/> Cross Comments (required for Partial/Cross):	
Assay:	<input checked="" type="checkbox"/> Chromatographic <input type="checkbox"/> Ligand binding <input type="checkbox"/> Enzymatic <input type="checkbox"/> Other describe: <input type="checkbox"/> LC/MS <input checked="" type="checkbox"/> LC/MS/MS <input type="checkbox"/> GC/MS <input type="checkbox"/> GC/MS/MS <input type="checkbox"/> ELISA	
Equipment and short description of extraction and analysis: An aliquot of human plasma containing the analyte and internal standard was extracted using a solid-phase extraction procedure. The extracted samples were analyzed by a HPLC equipped with an AB SCIEX API 5000™ or QTRAP® 5500 mass spectrometer. Positive ions were monitored in the multiple reaction monitoring (MRM) mode. Quantitation was determined using a weighted linear regression analysis (1/concentration ²) of peak area ratios of each analyte and internal standard.		
Selectivity/Sensitivity/Matrix effect:	No significant matrix effect was observed in 4 of the 6 human plasma (EDTA) lots that were spiked near the concentration of the LLOQ and in any of the 6 human plasma (EDTA) lots that were spiked near the concentration of the high QC sample	
Accuracy:	Intra-batch: -6.6 to 4.0% R.E. Inter-batch: -4.2 to 1.3% R.E.	
Precision:	Intra-batch: 1.7 to 4.7% C.V. Inter-batch: 2.3 to 3.7% C.V.	
Recovery:	75% at 2.00 ng/mL in human plasma 77% at 10.0 ng/mL in human plasma 76% at 75.0 ng/mL in human plasma	
Freeze and thaw stability:	6 freeze/cycles in polypropylene tubes at -20°C under white light 7 freeze/cycles in polypropylene tubes at -20°C under UV-shielded light	
Short-term temperature stability:	27 hours in polypropylene tubes at ambient temperature under white light	
Long-term stability:	739 days in polypropylene tubes at -20°C	
Stock solution stability:	572 days at 1000 µg/mL in water in a polypropylene container at -20°C	
Post-preparative stability:	135 hours in a polypropylene 96 well plate at 5°C	
Accreditation/ GLP compliance/ QA statements:	GLP Compliance as Assay Validation conforms to Celerion Standard Operating Procedures which were written in compliance with FDA: Guidance to Industry "Bioanalytical Method Validation"	



Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₃EDTA)
Celerion Study AA99071-10



BIOANALYTICAL METHOD SUMMARY (BMS)

Doc No: FOR_QM000496 – CR204A2

Version N°: 2.0

Page 2 of 2

BMS completed by:		
Name:	Date:	Signature:
Erica Nachi	03 mar-2015	Erica J Nachi



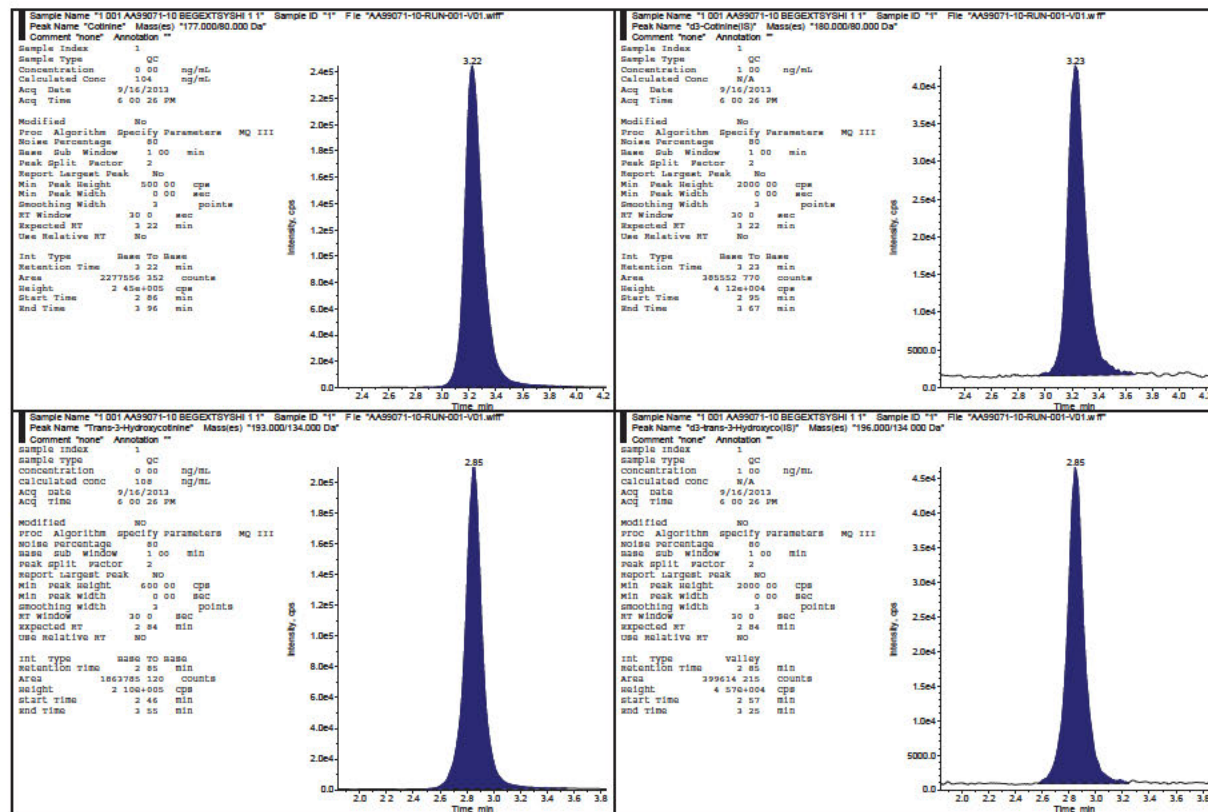
Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₃EDTA)
Celerion Study AA99071-10

Attachment 8 Chromatograms

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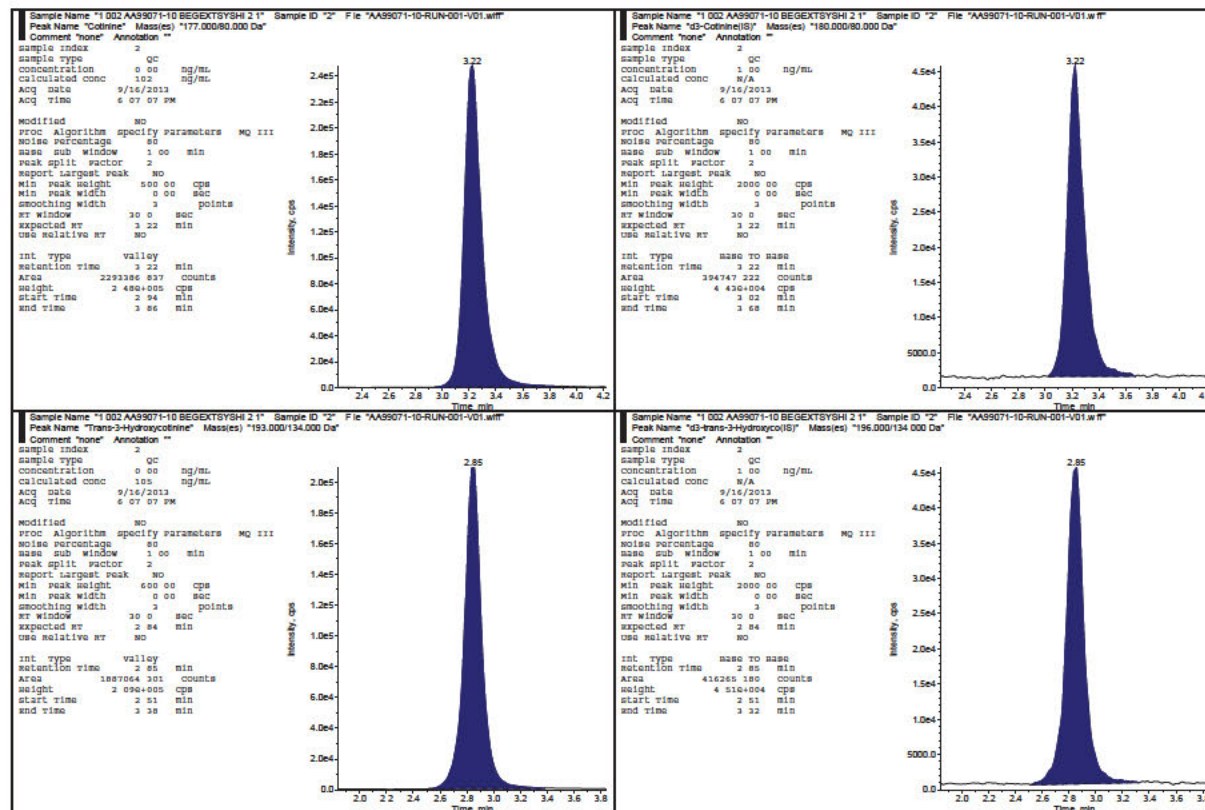


Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10



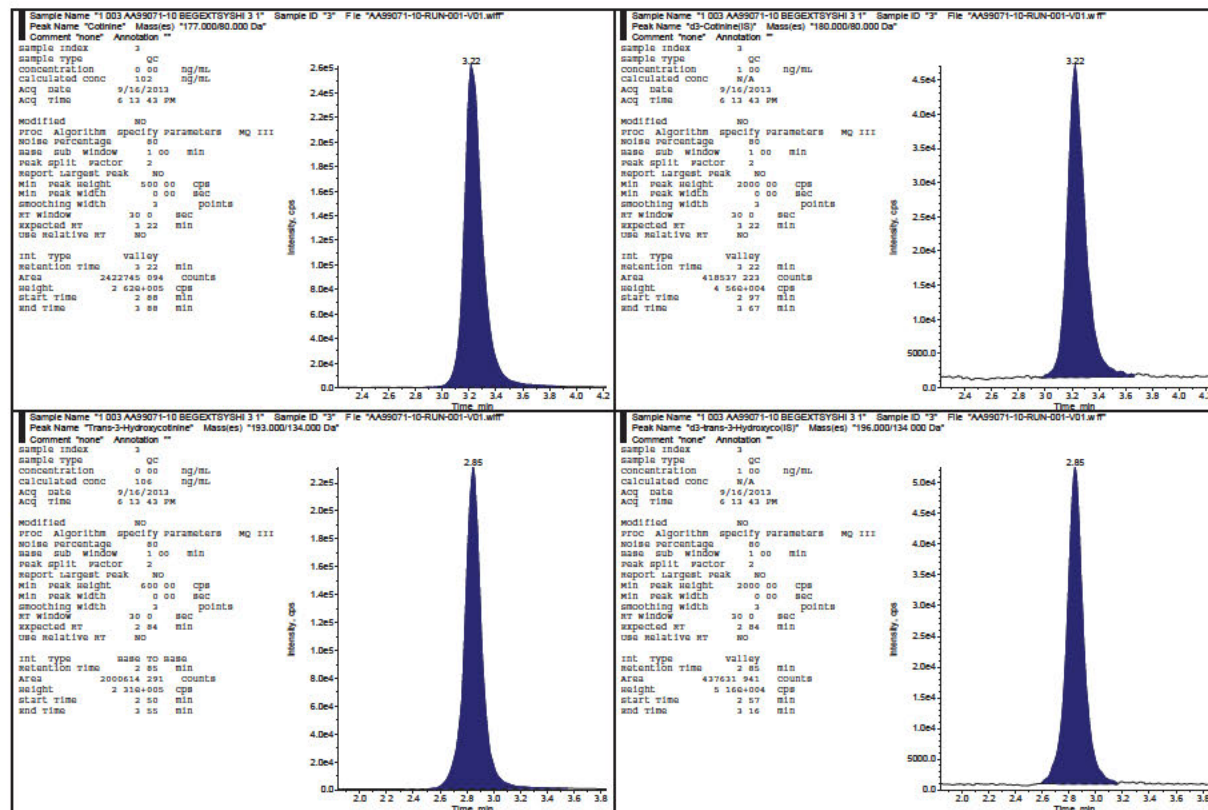


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Celerion Study AA99071-10



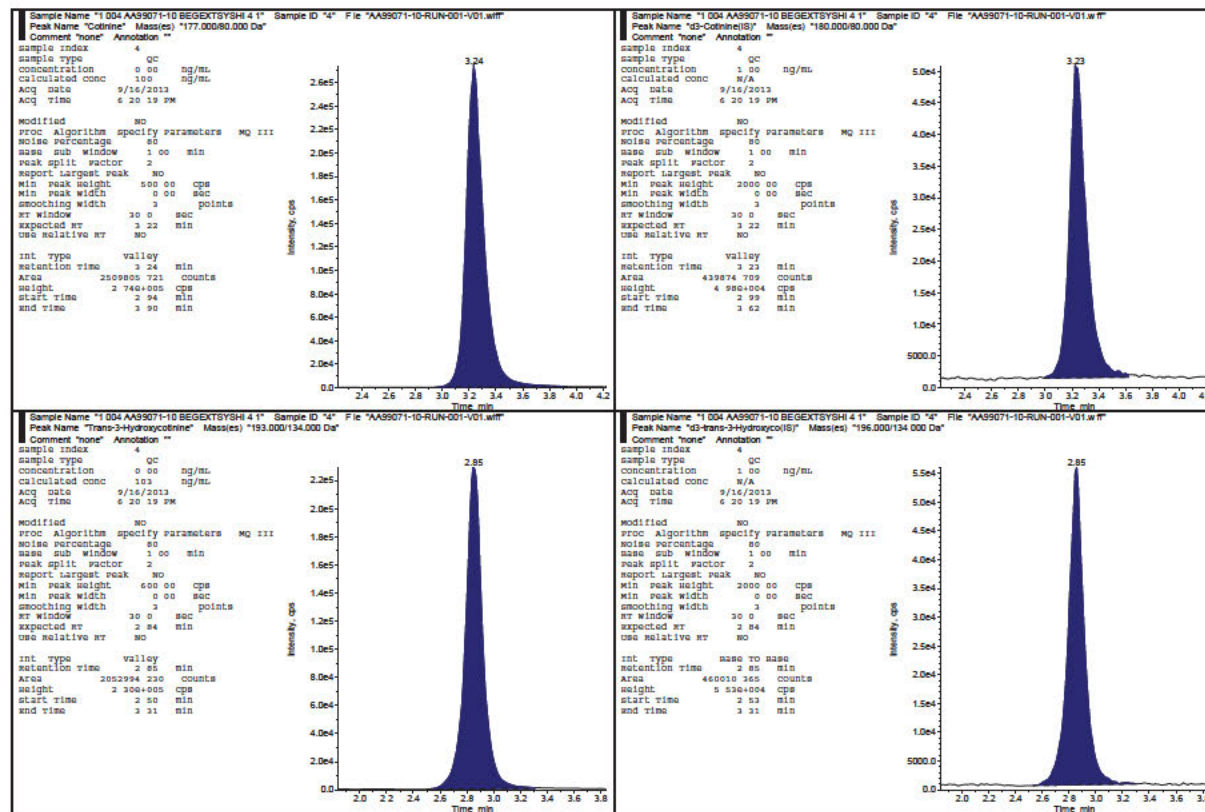


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Celerion Study AA99071-10



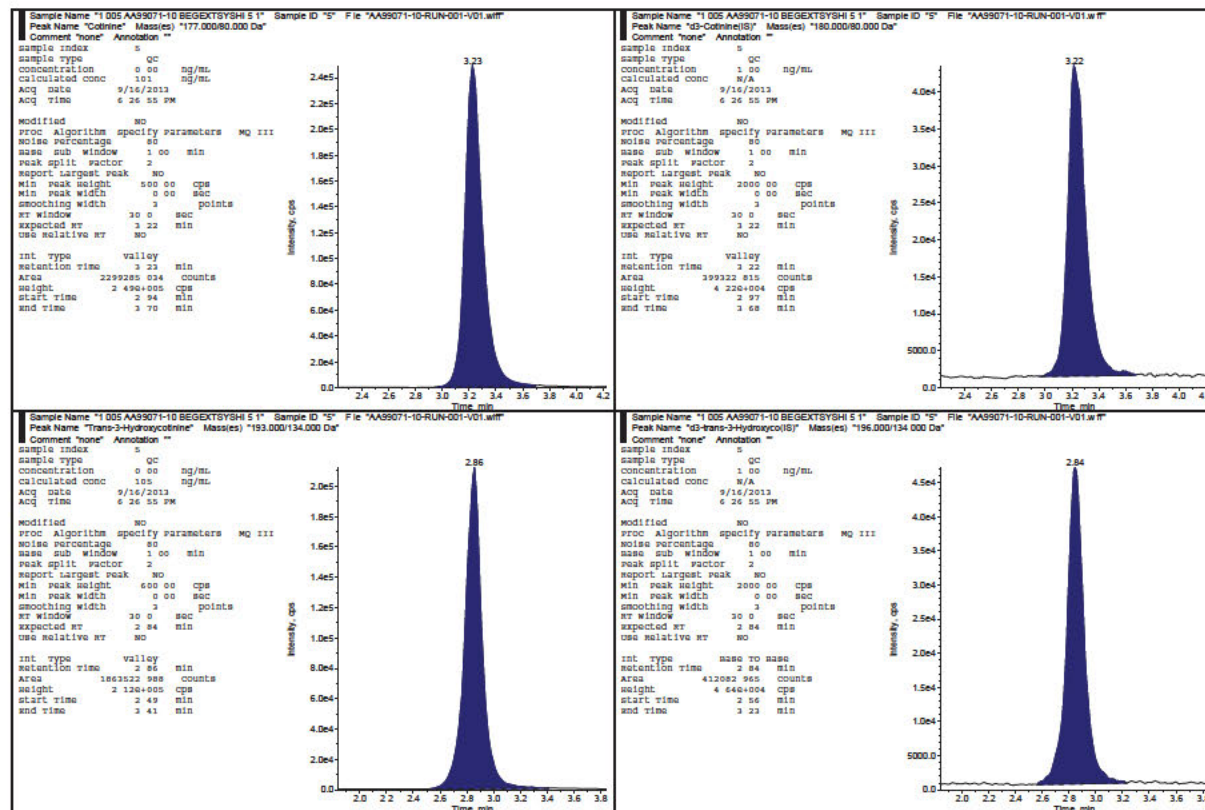


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Celerion Study AA99071-10



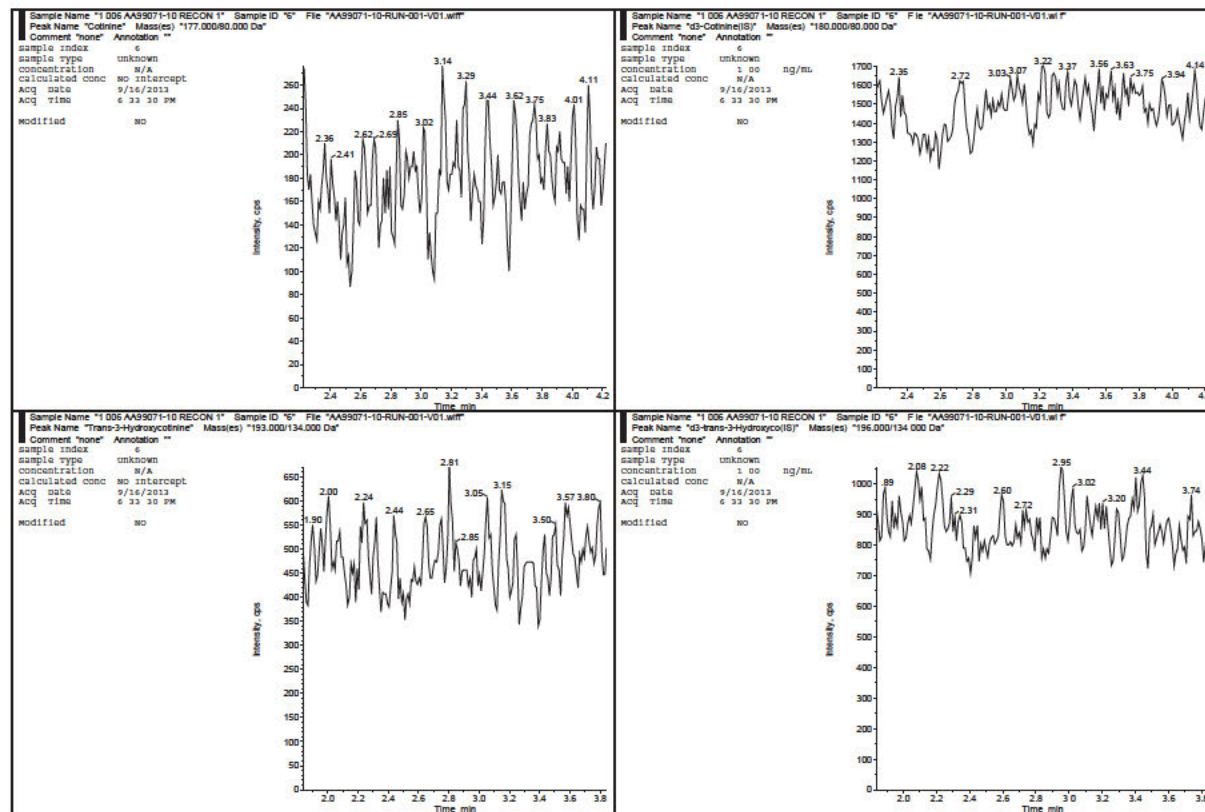


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Celerion Study AA99071-10



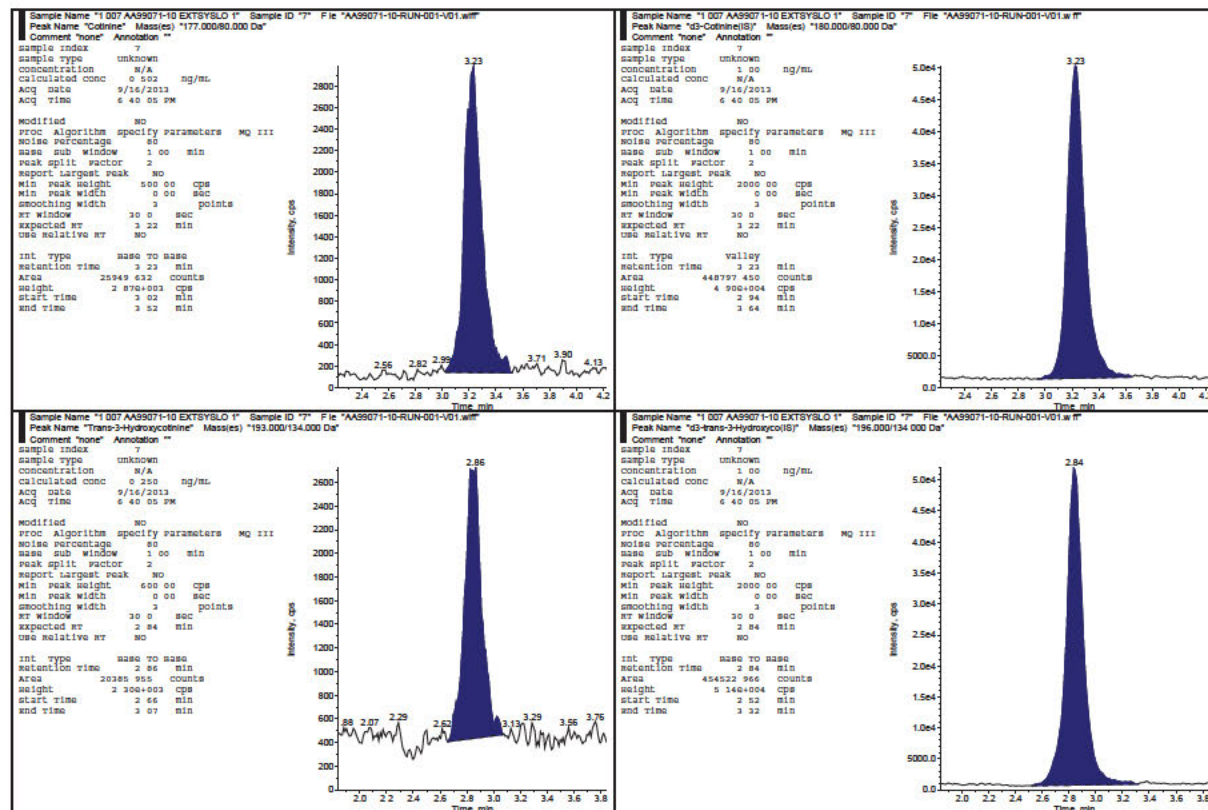


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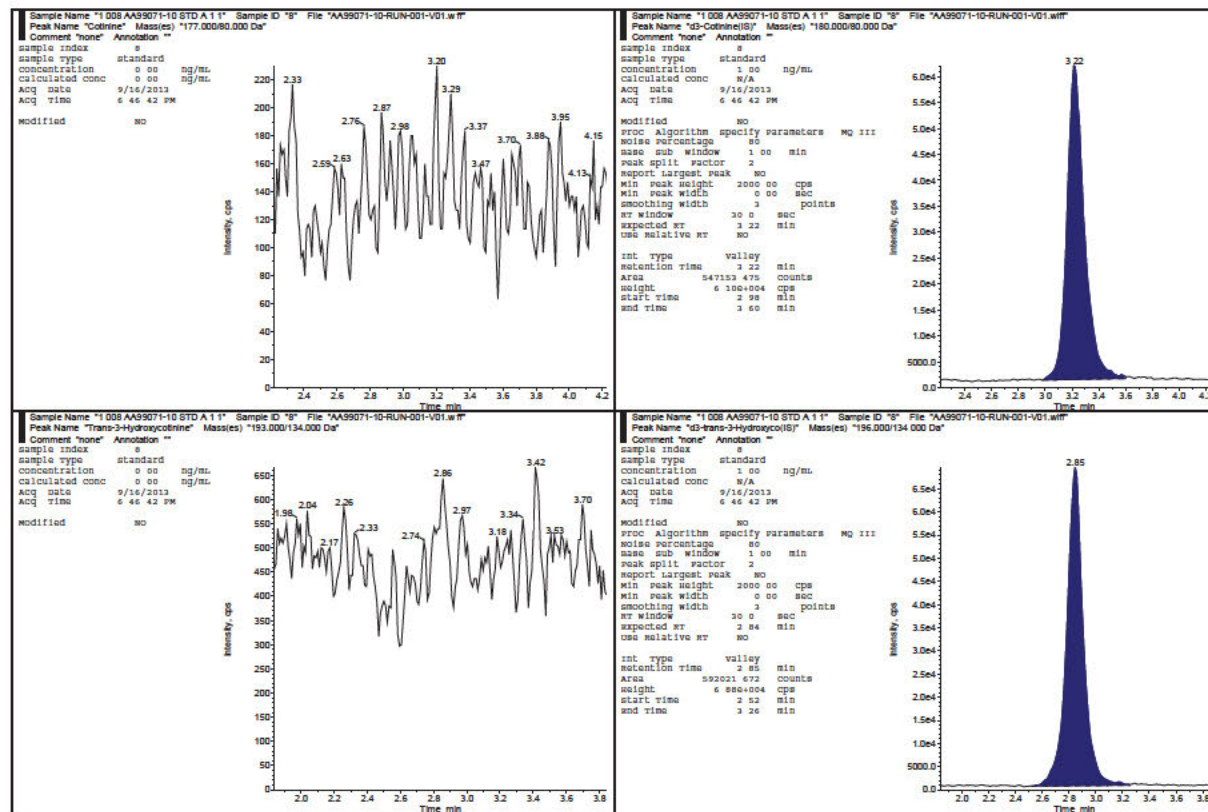


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Celerion Study AA99071-10



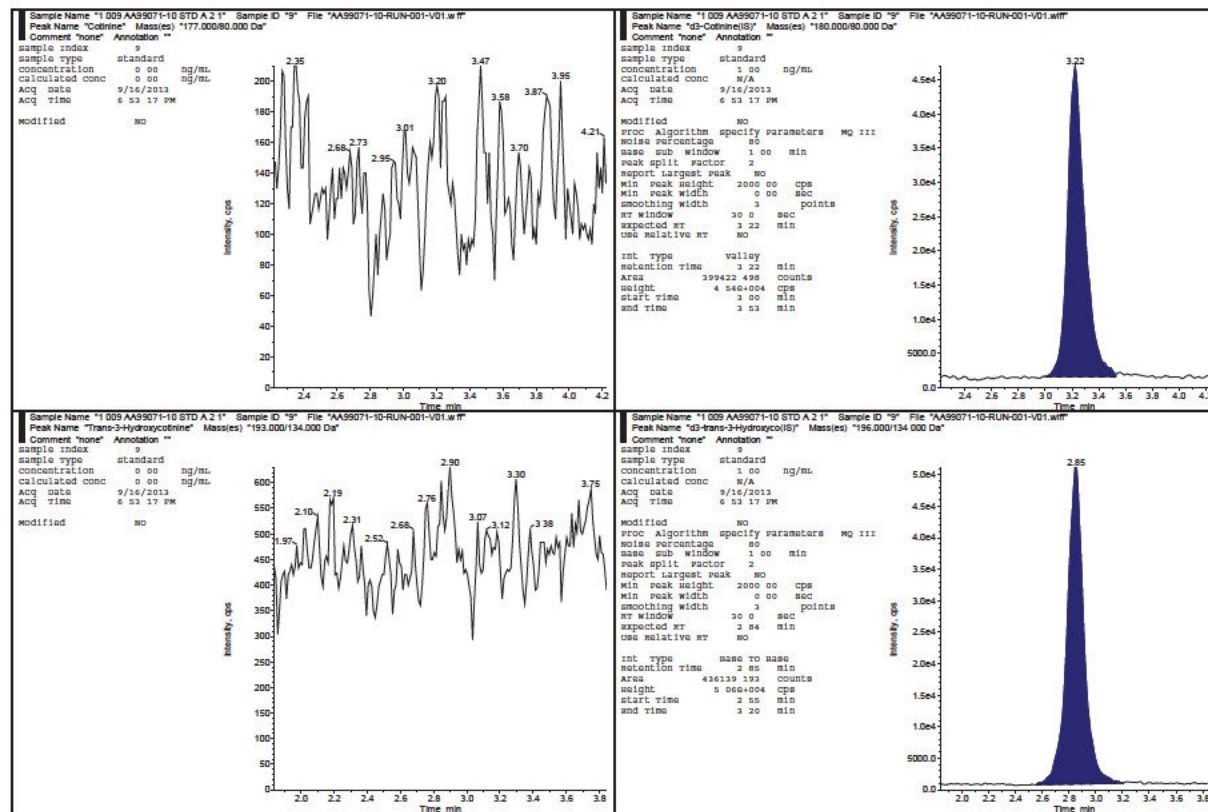


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Celerion Study AA99071-10



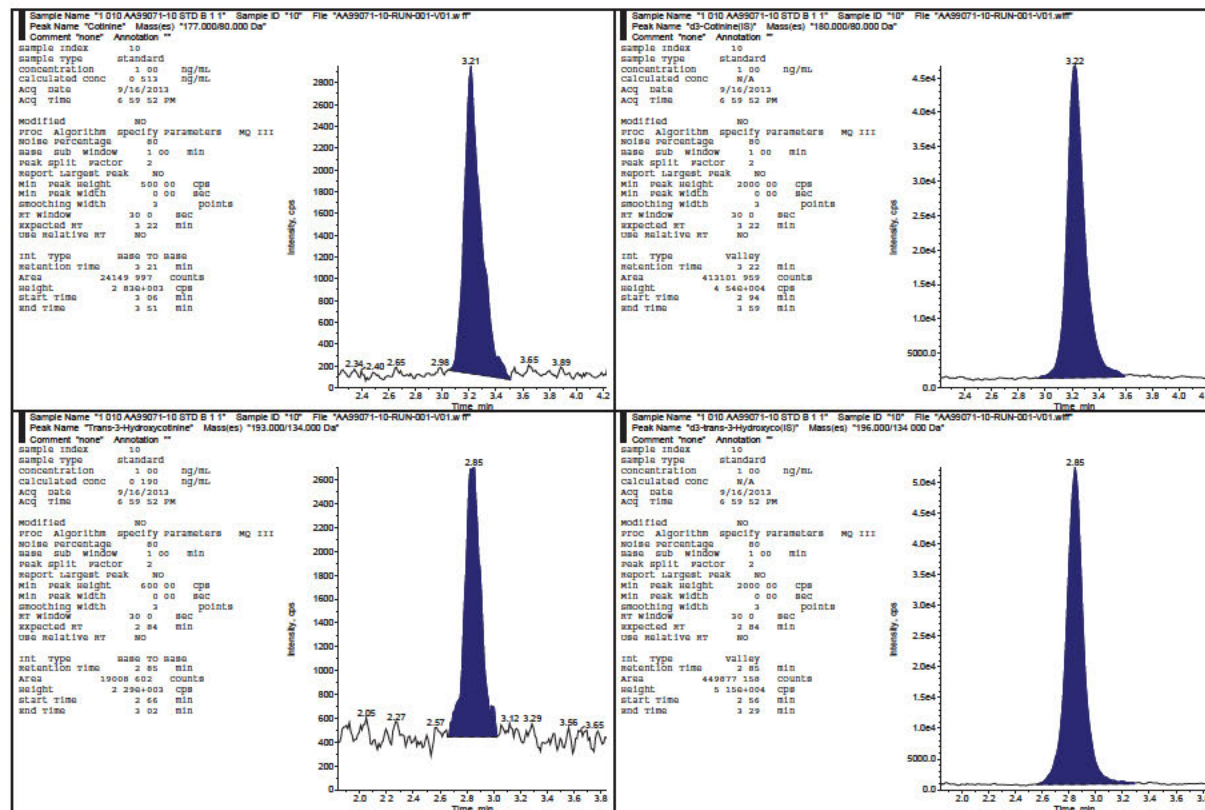


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Celerion Study AA99071-10



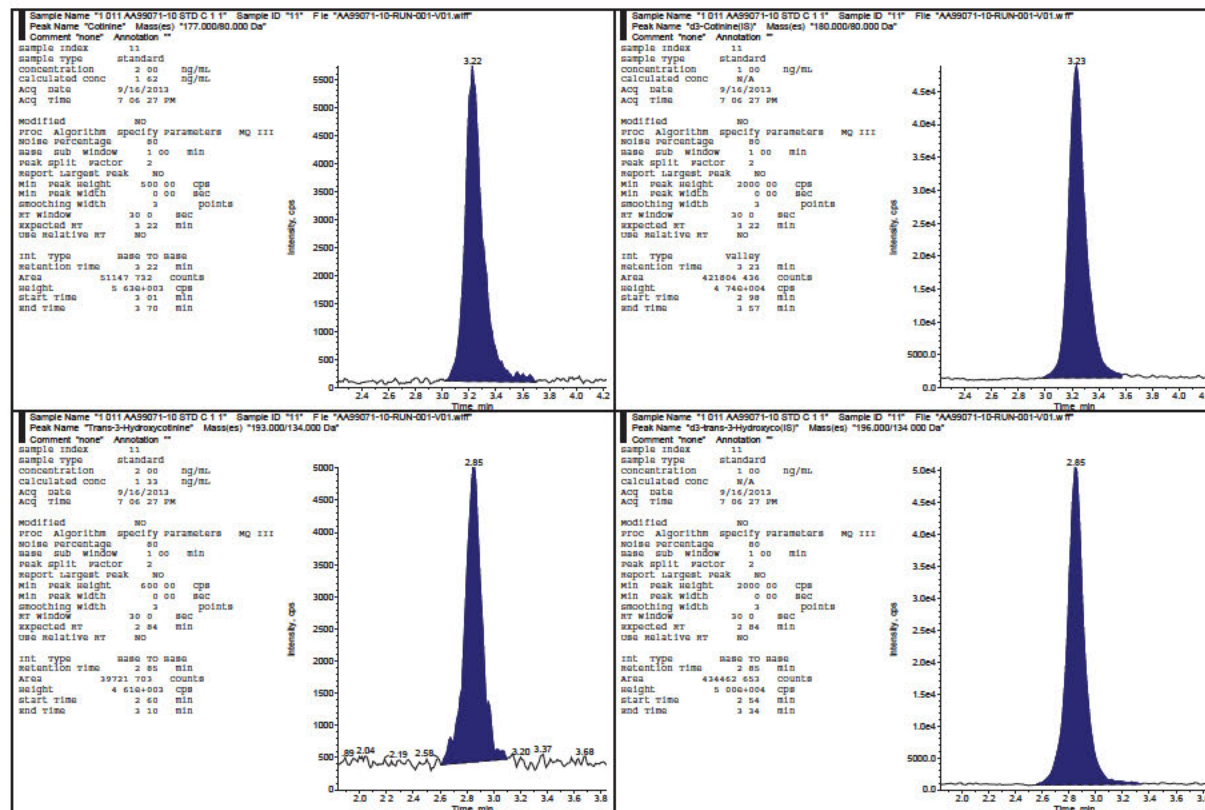


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Celerion Study AA99071-10



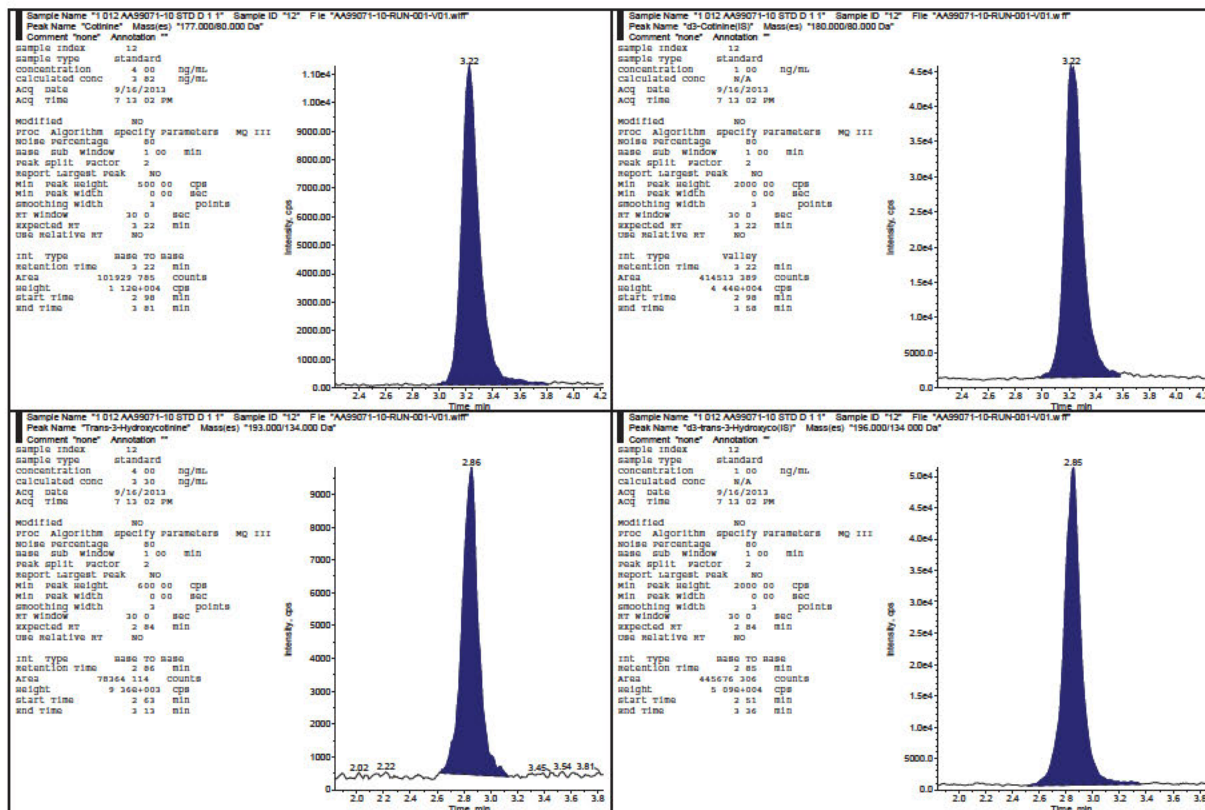


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Celerion Study AA99071-10



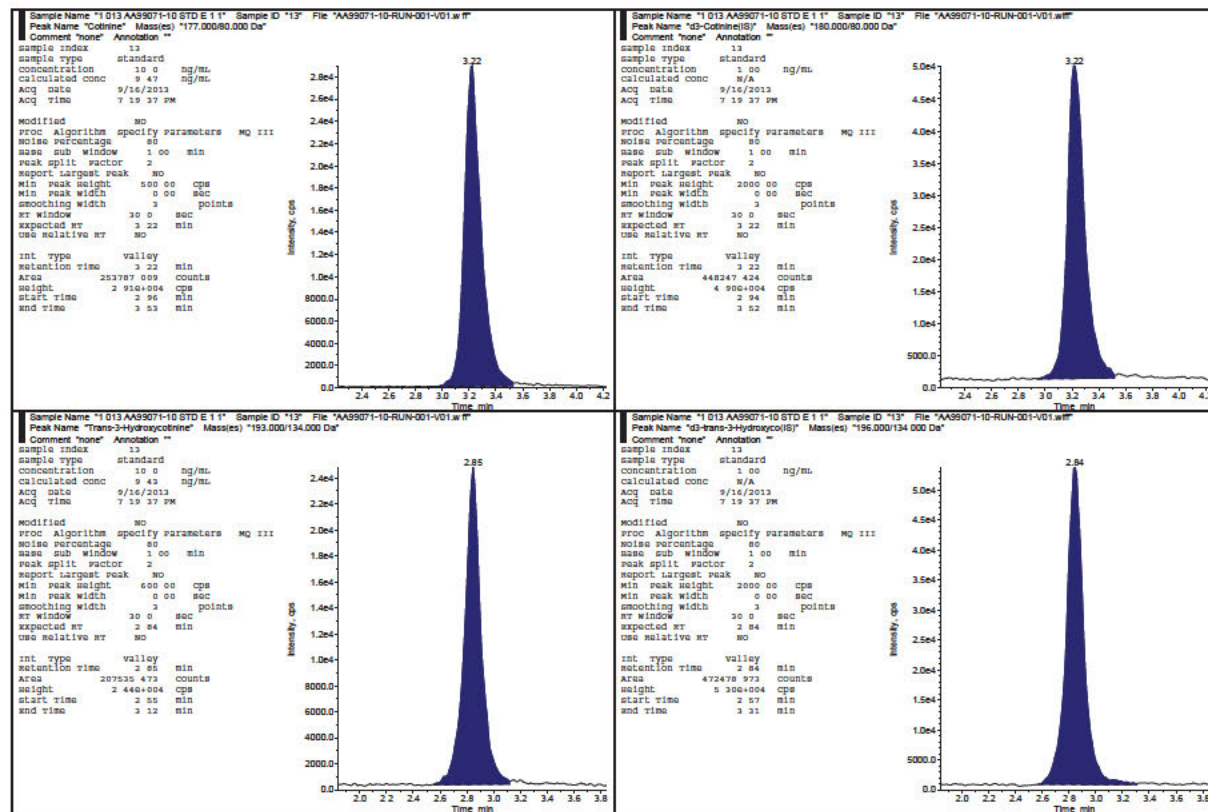


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Celerion Study AA99071-10



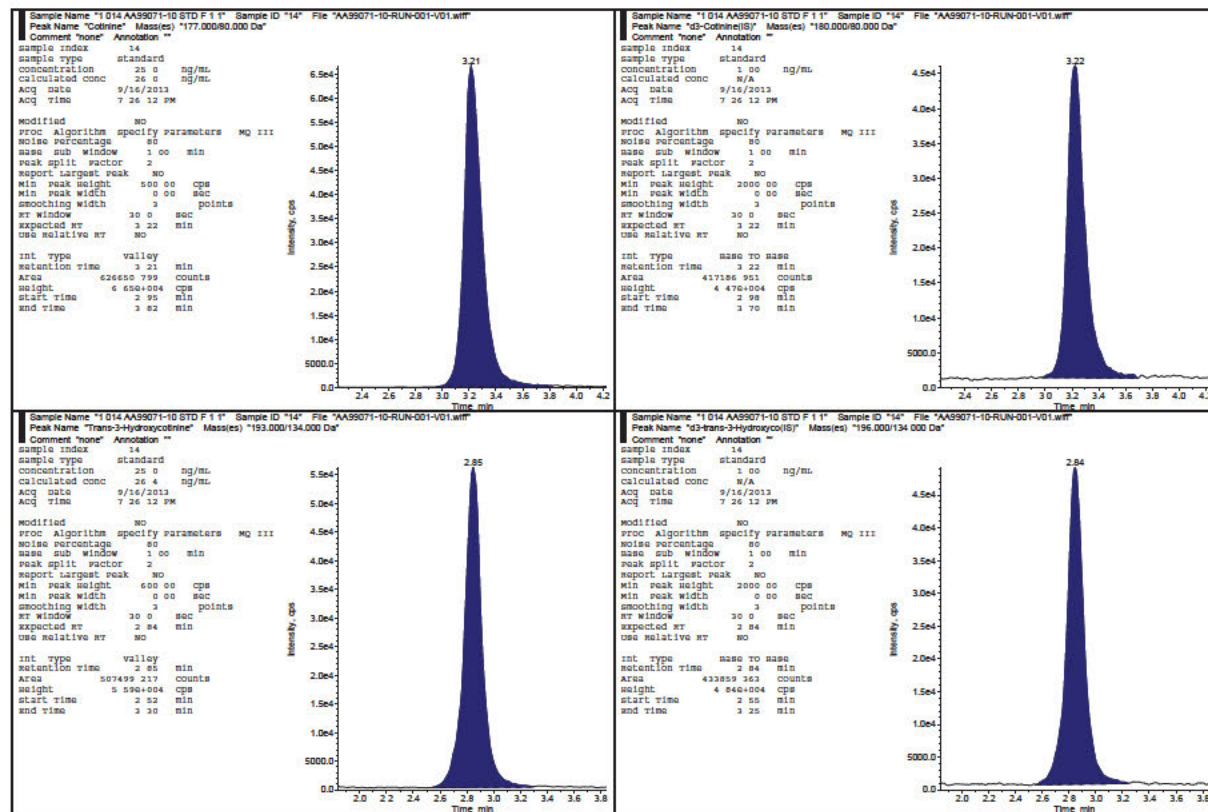


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Celerion Study AA99071-10



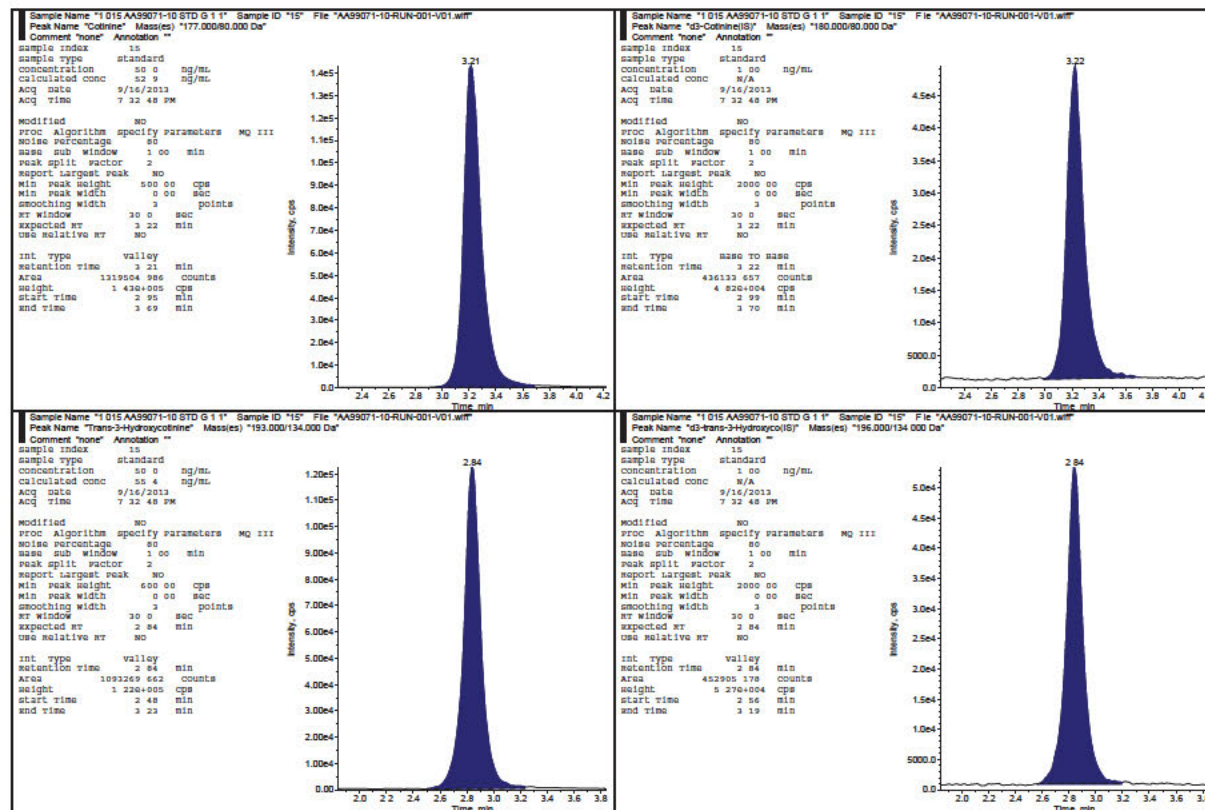


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Celerion Study AA99071-10



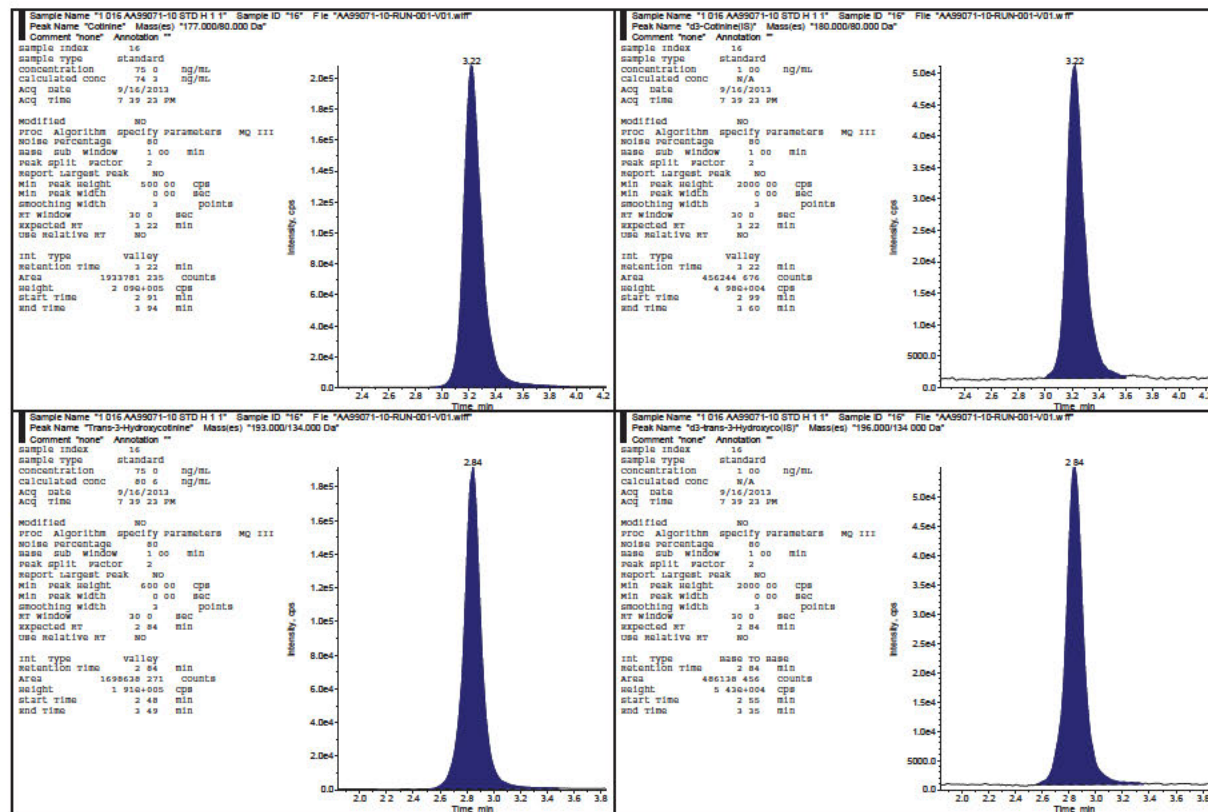


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Celerion Study AA99071-10



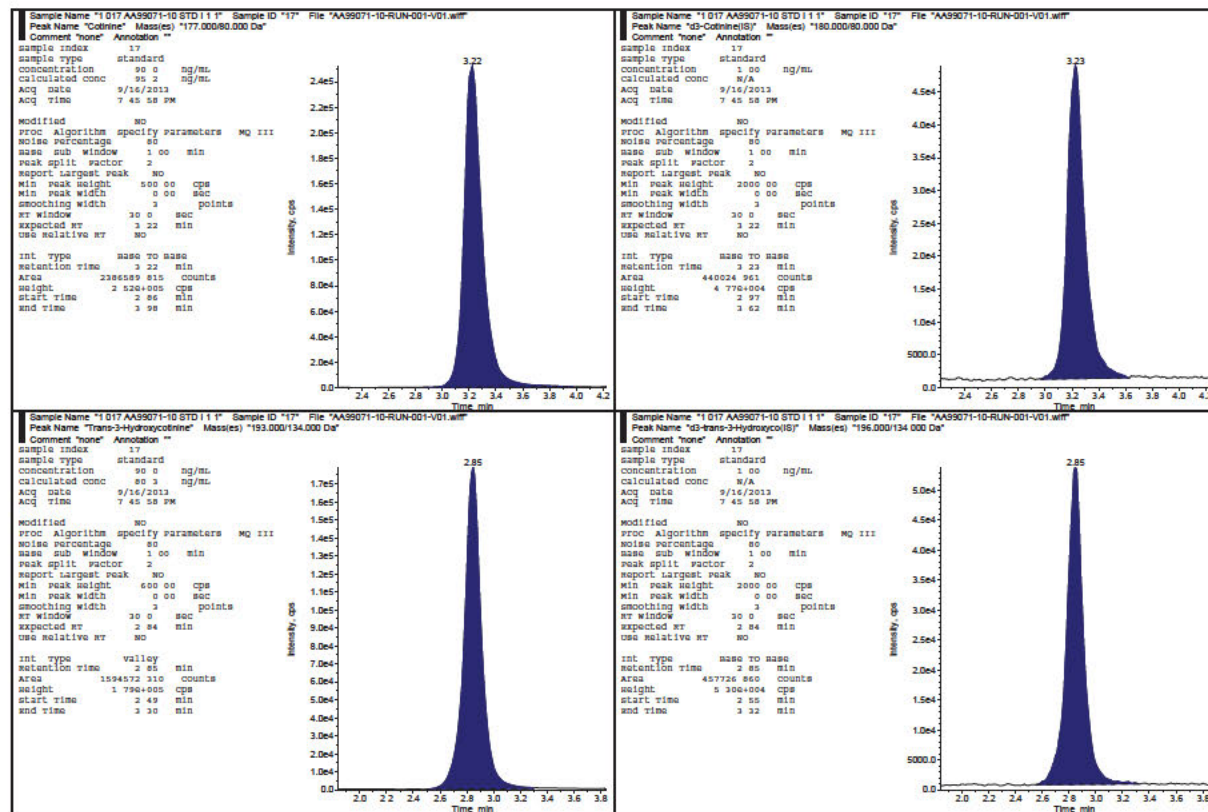


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Celerion Study AA99071-10



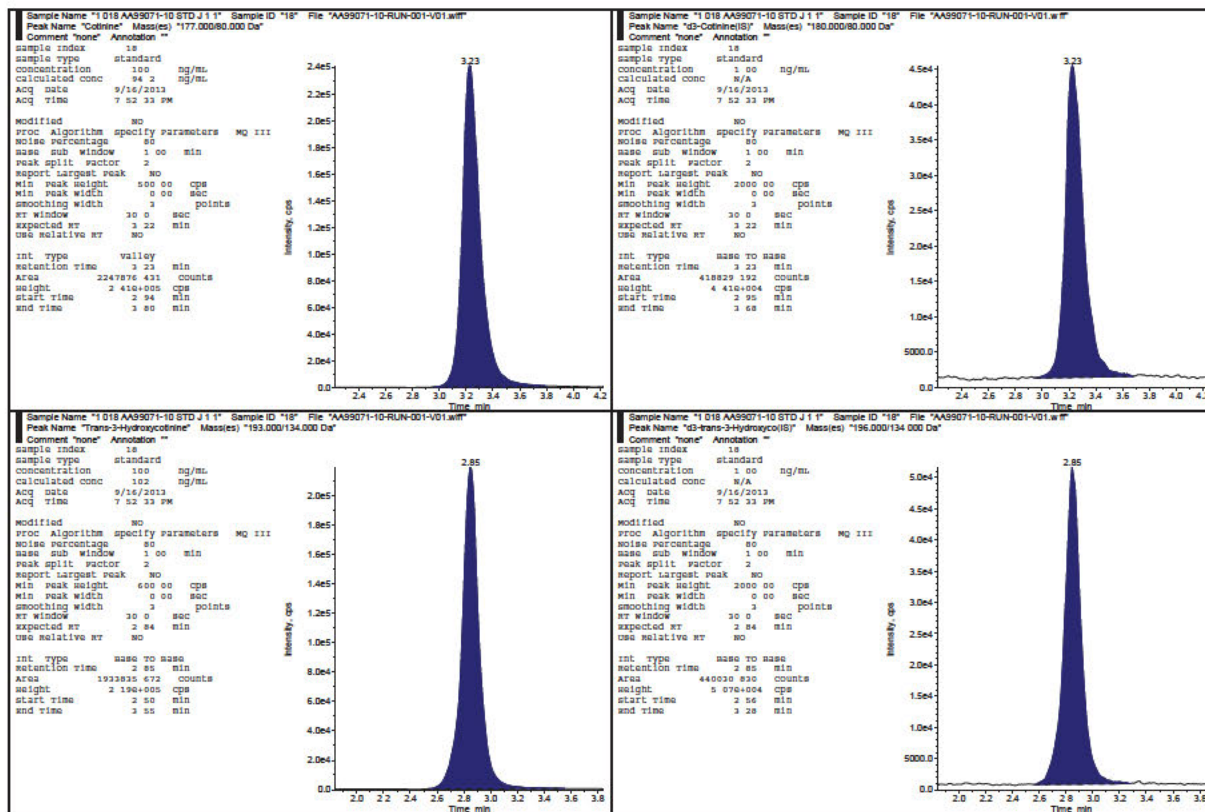


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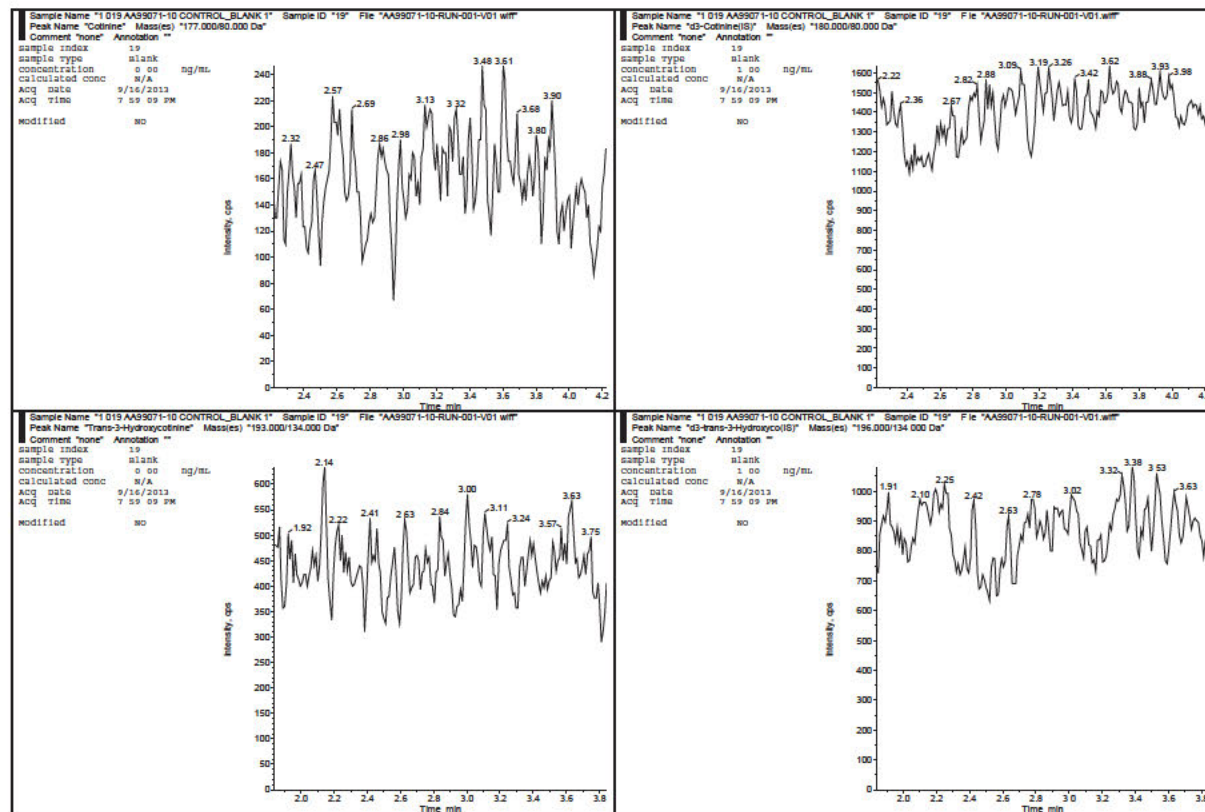


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Celerion Study AA99071-10



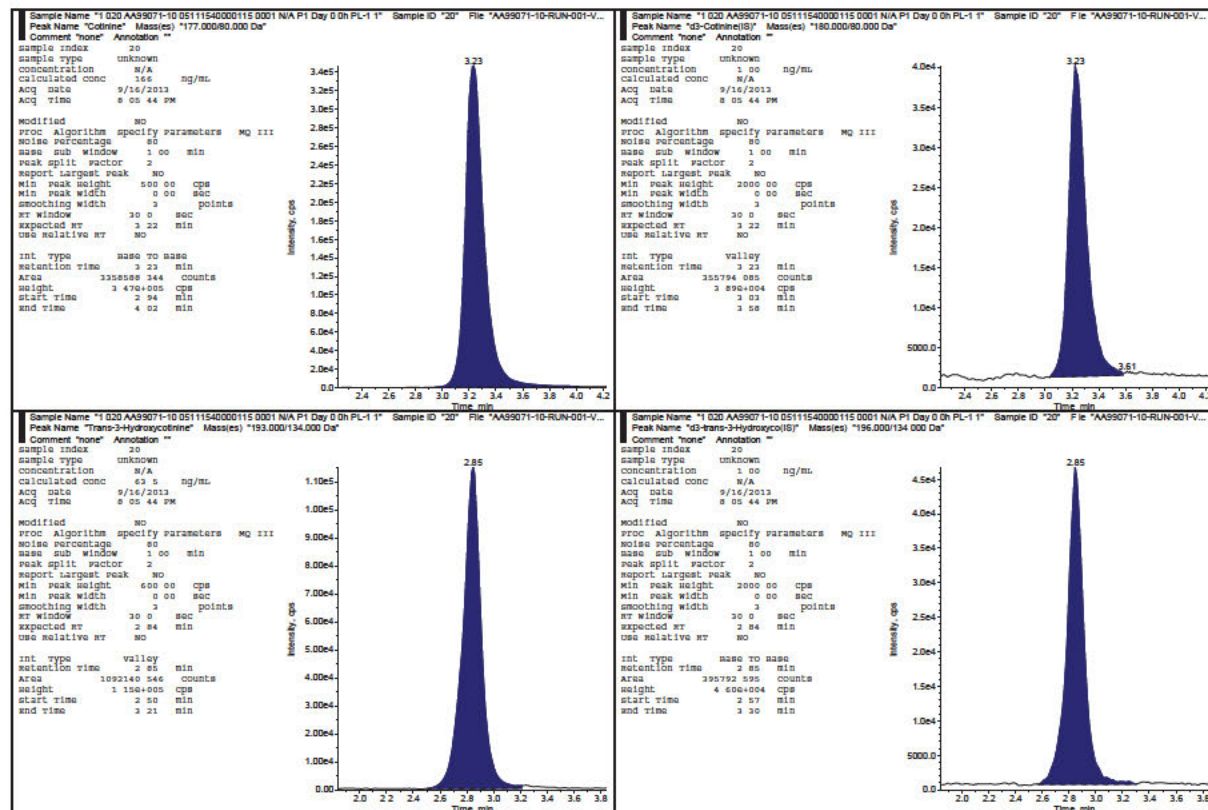


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Celerion Study AA99071-10



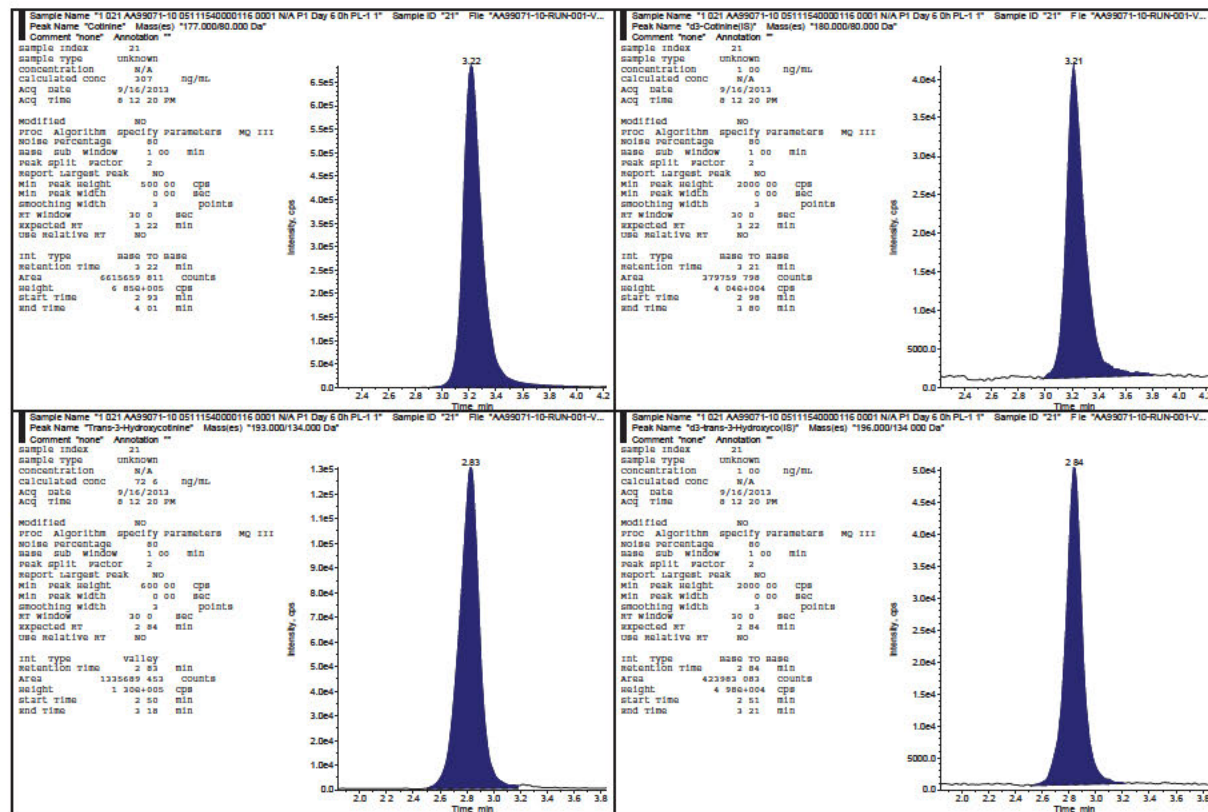


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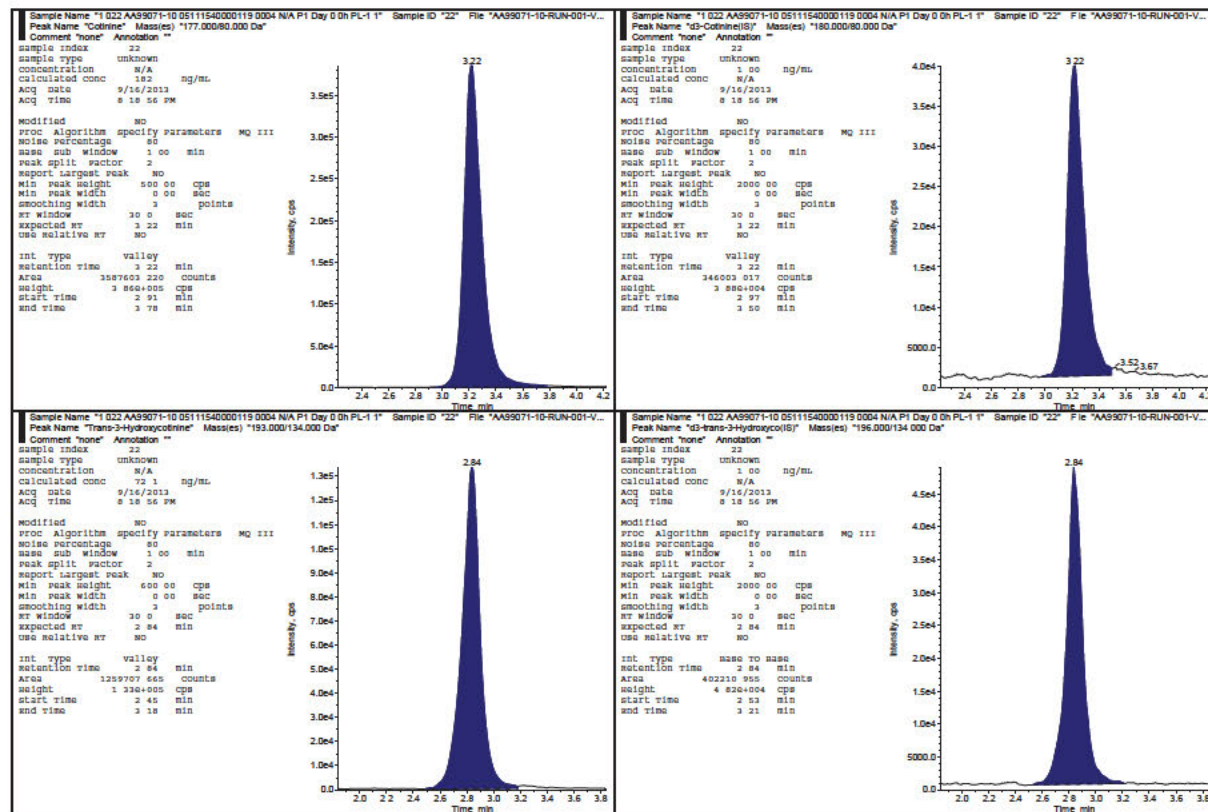


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Celerion Study AA99071-10



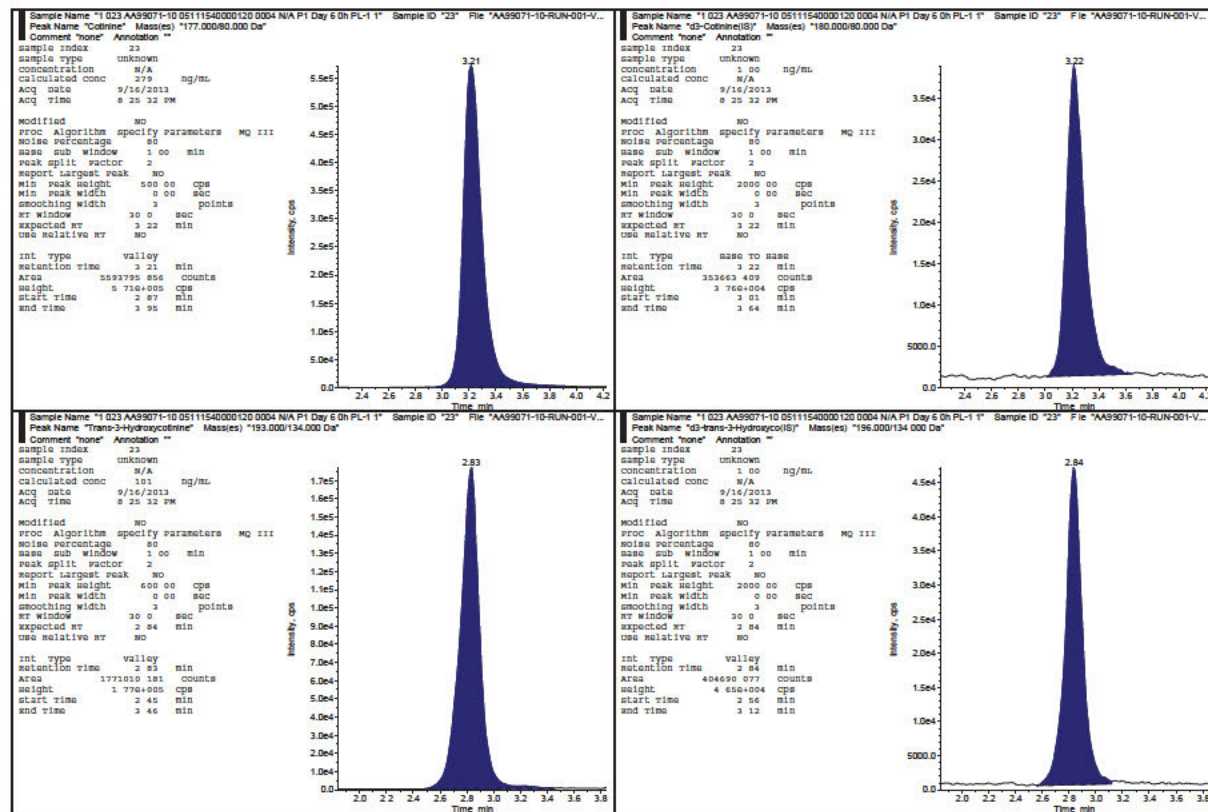


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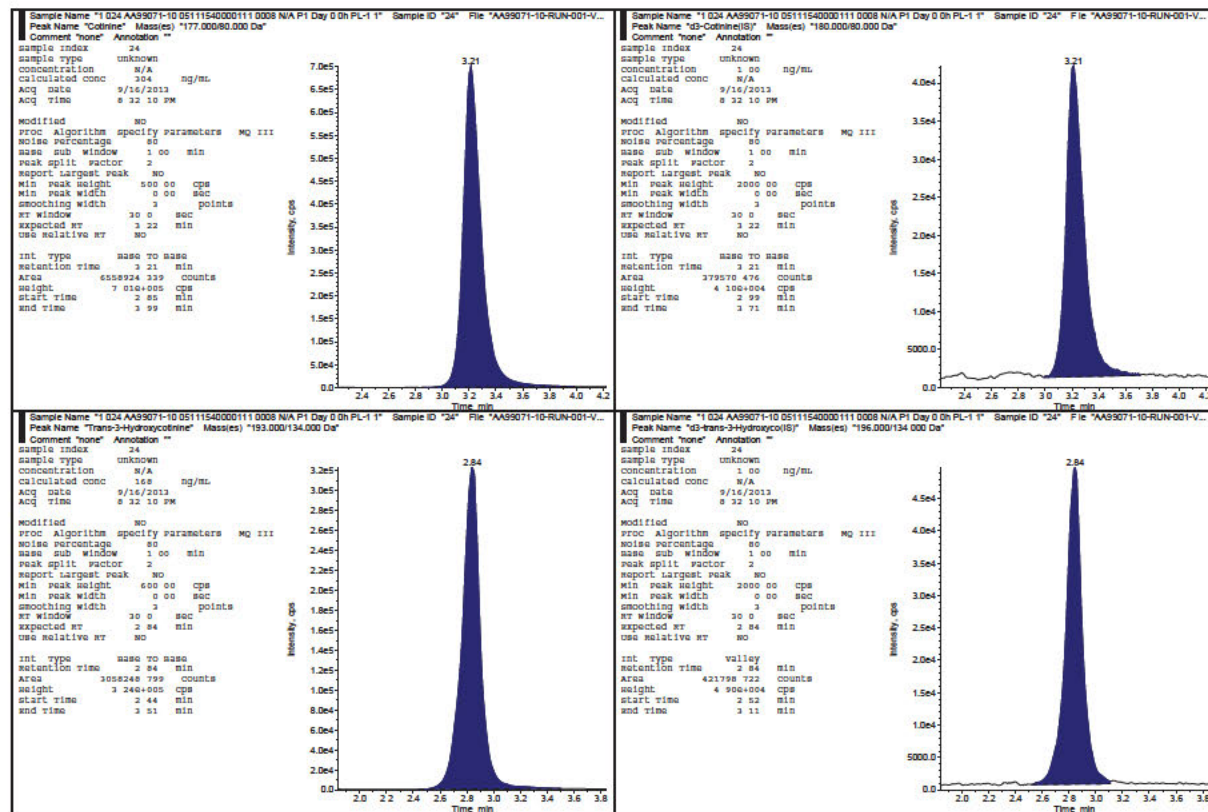


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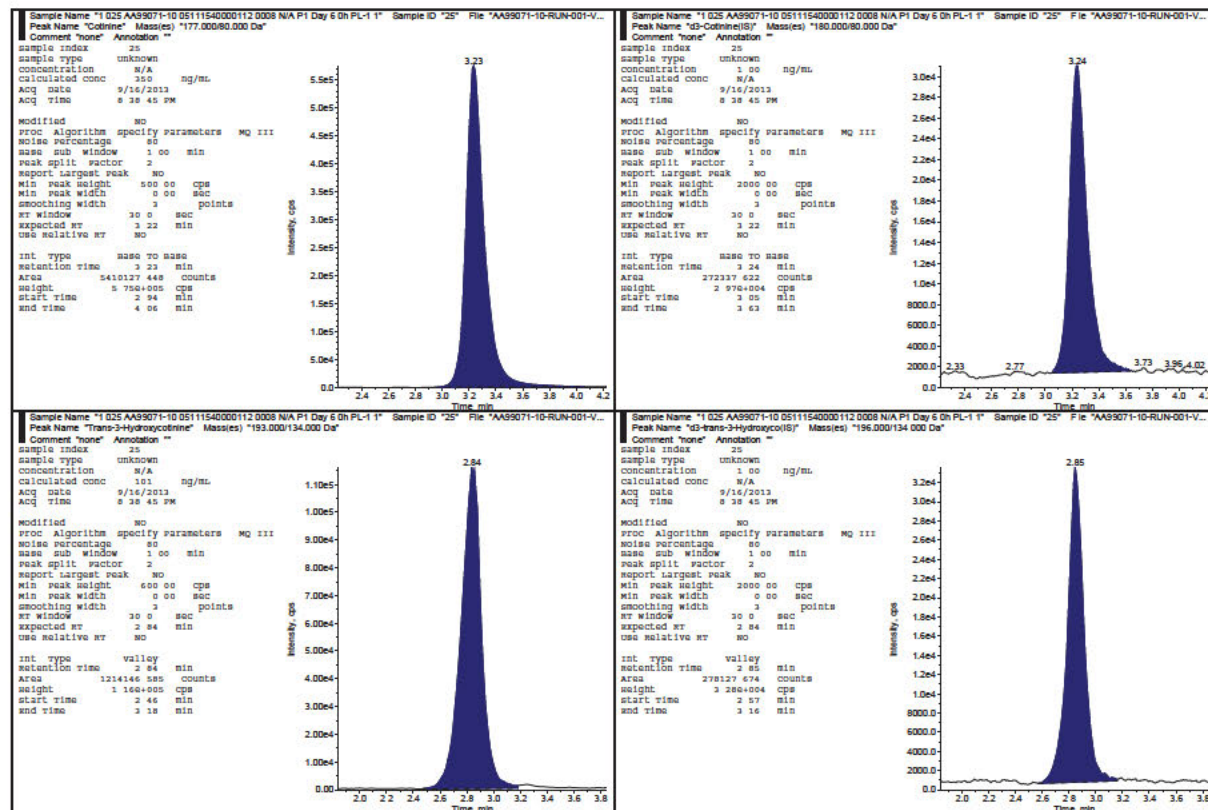


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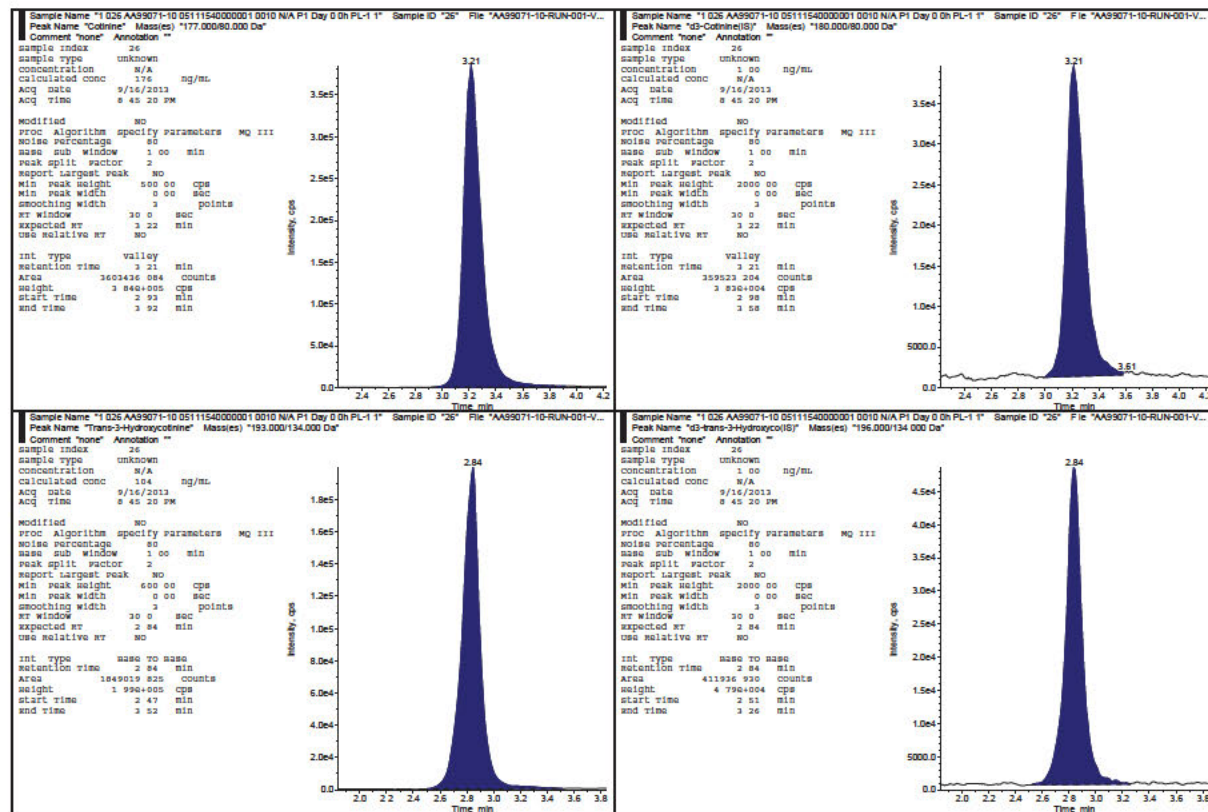


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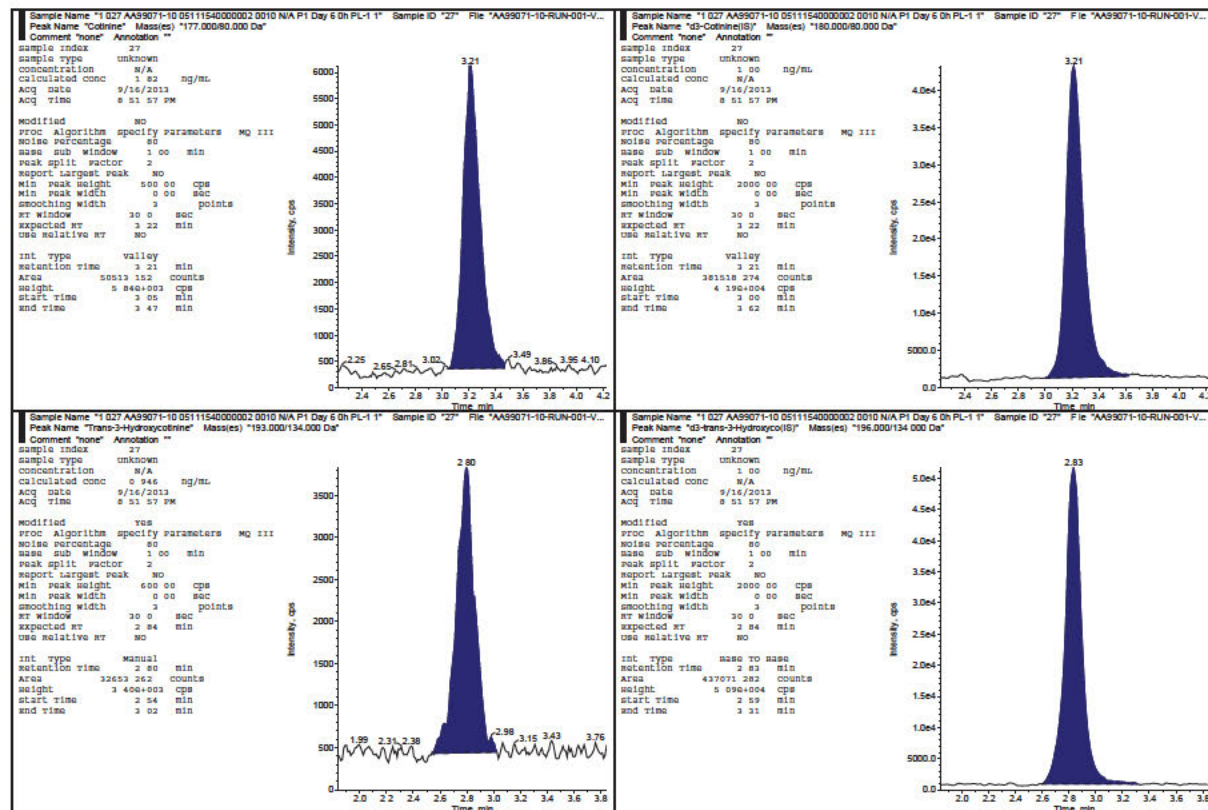


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Celerion Study AA99071-10



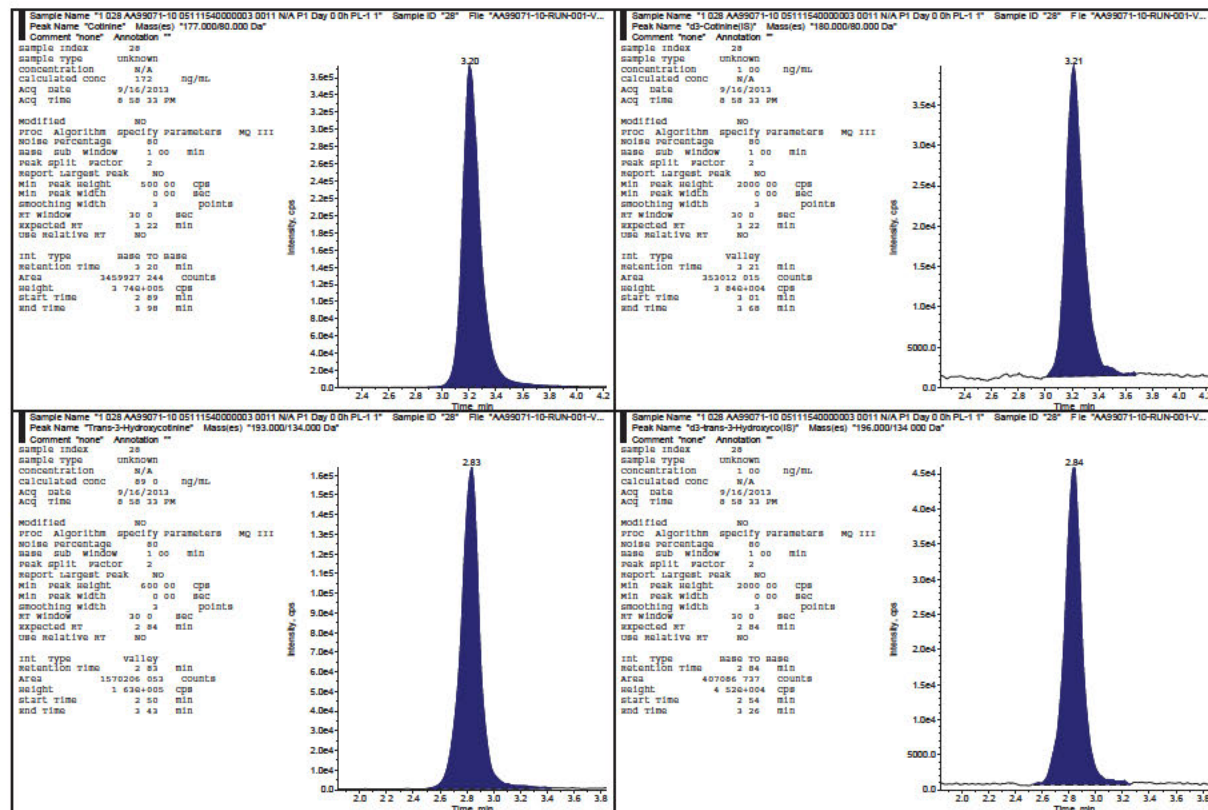


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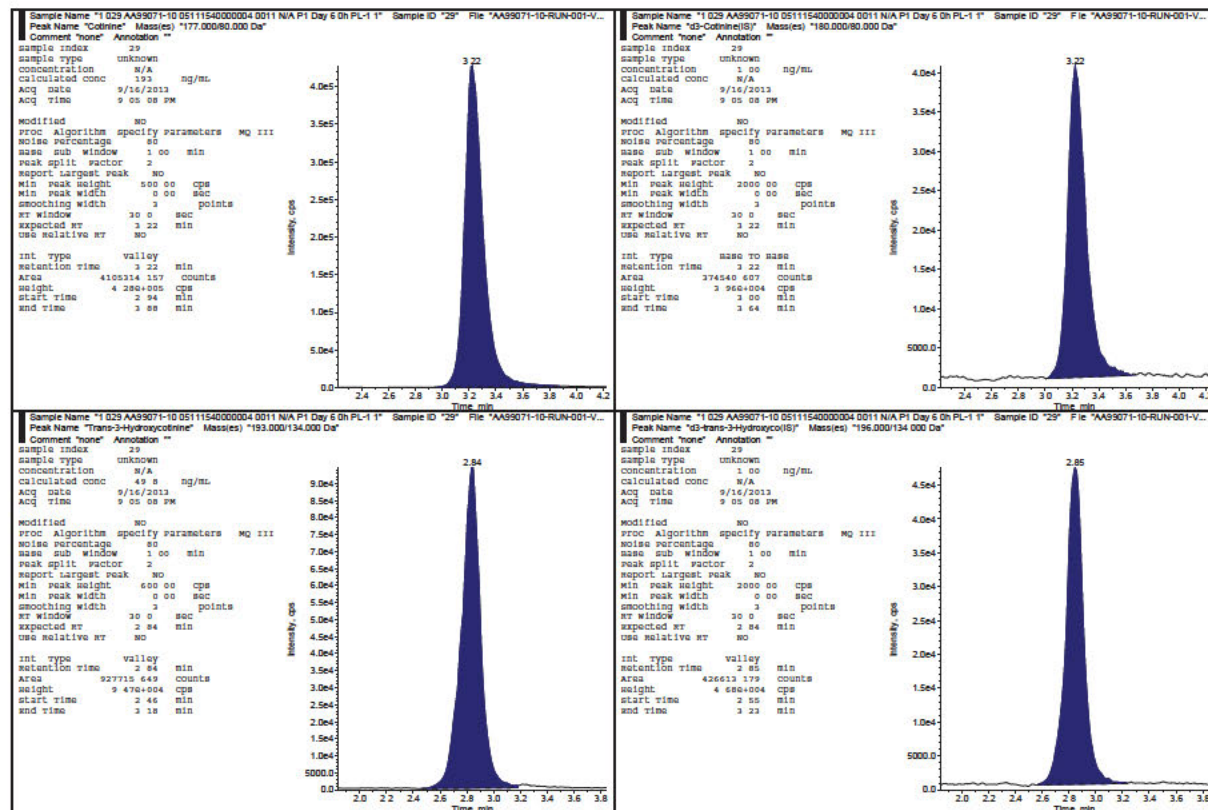


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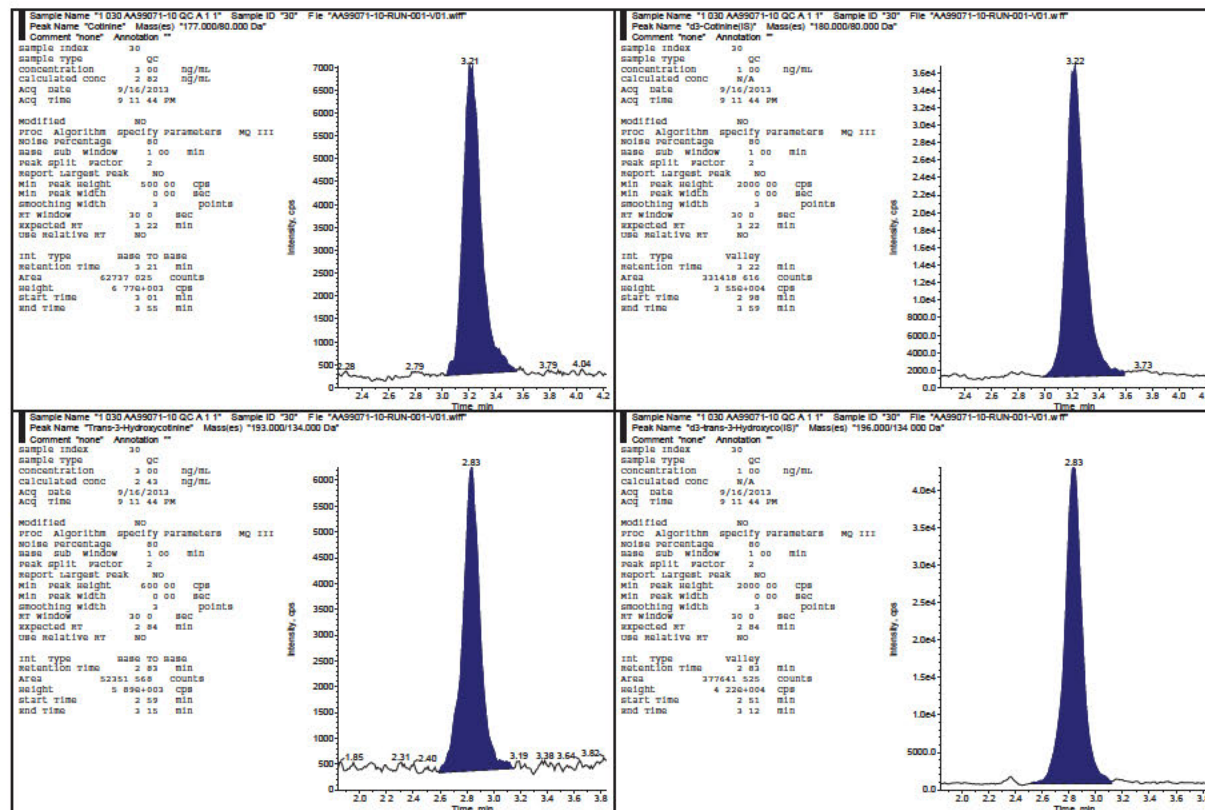


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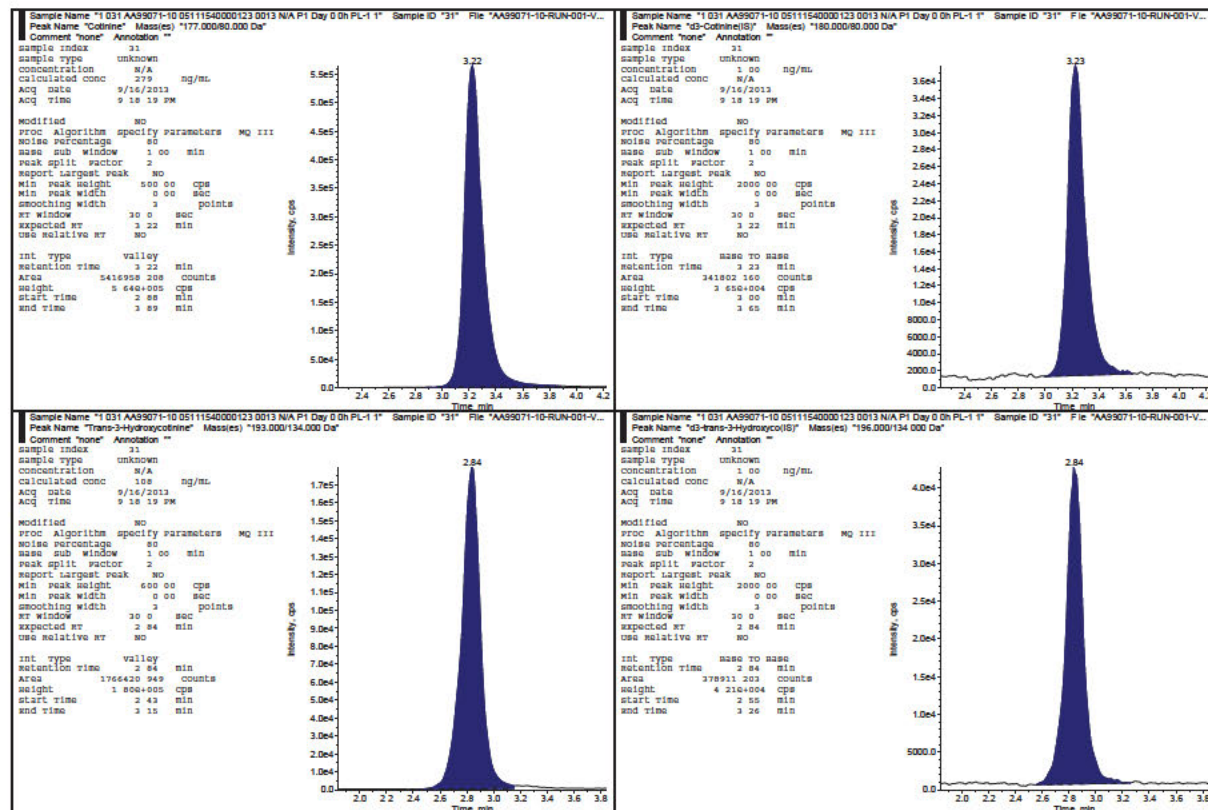


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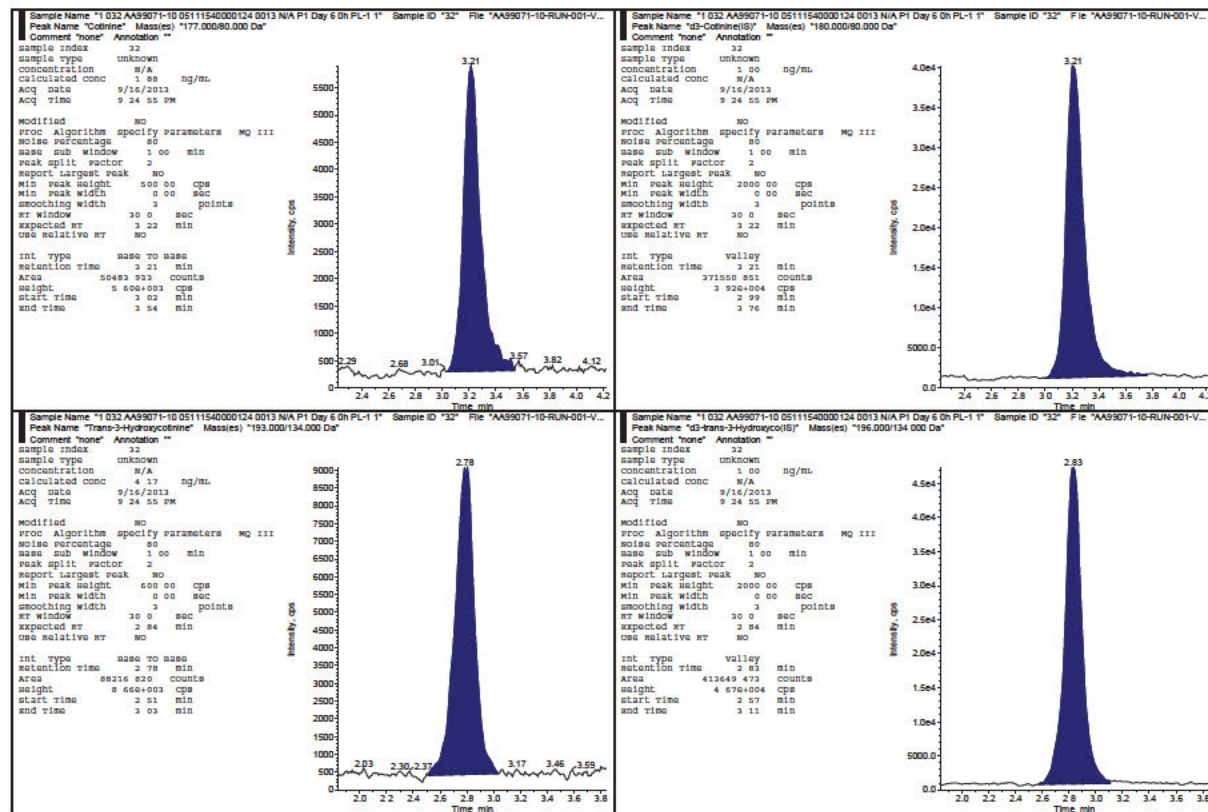


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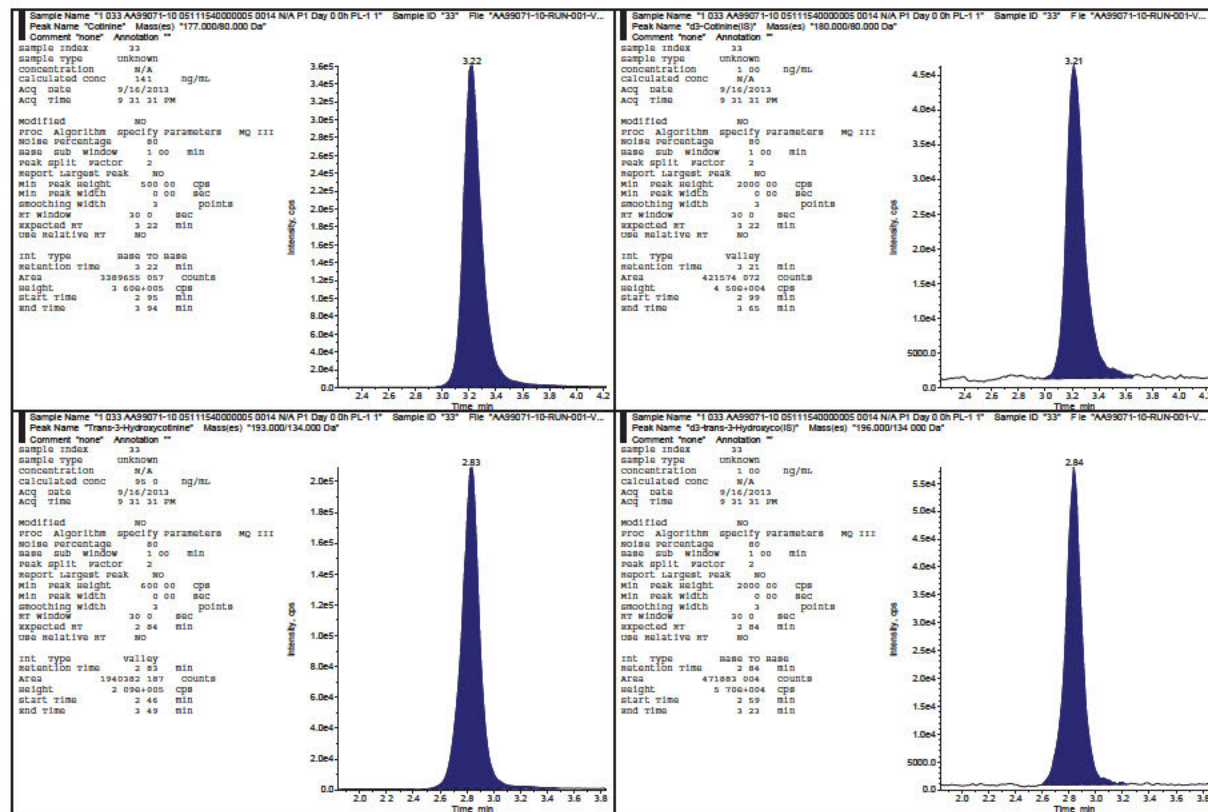


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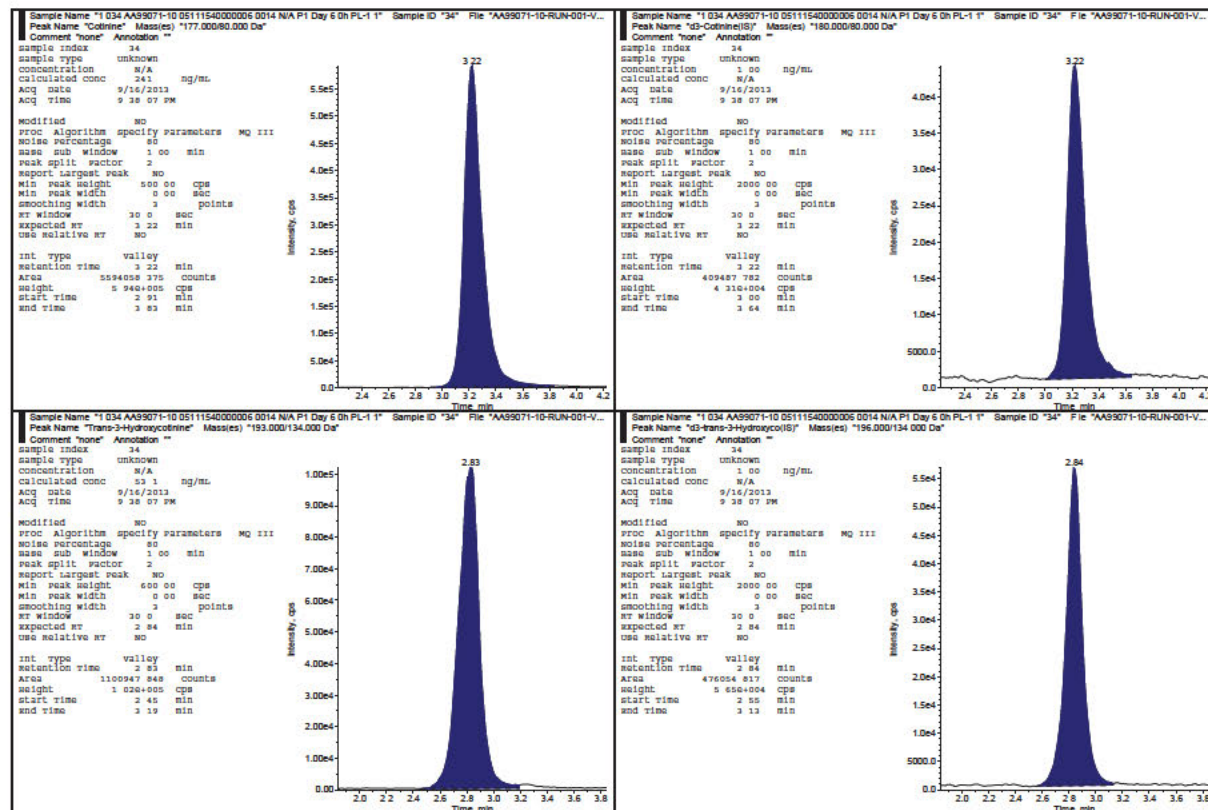


Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10



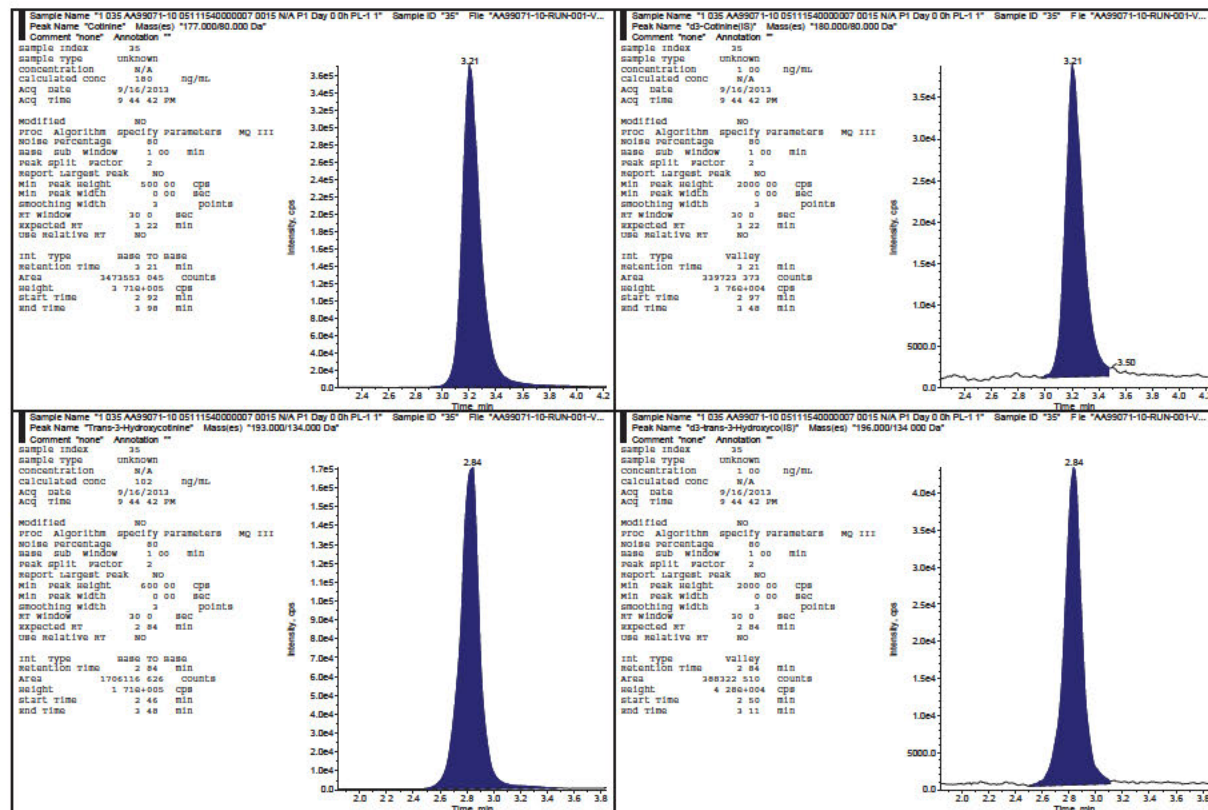


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Celerion Study AA99071-10



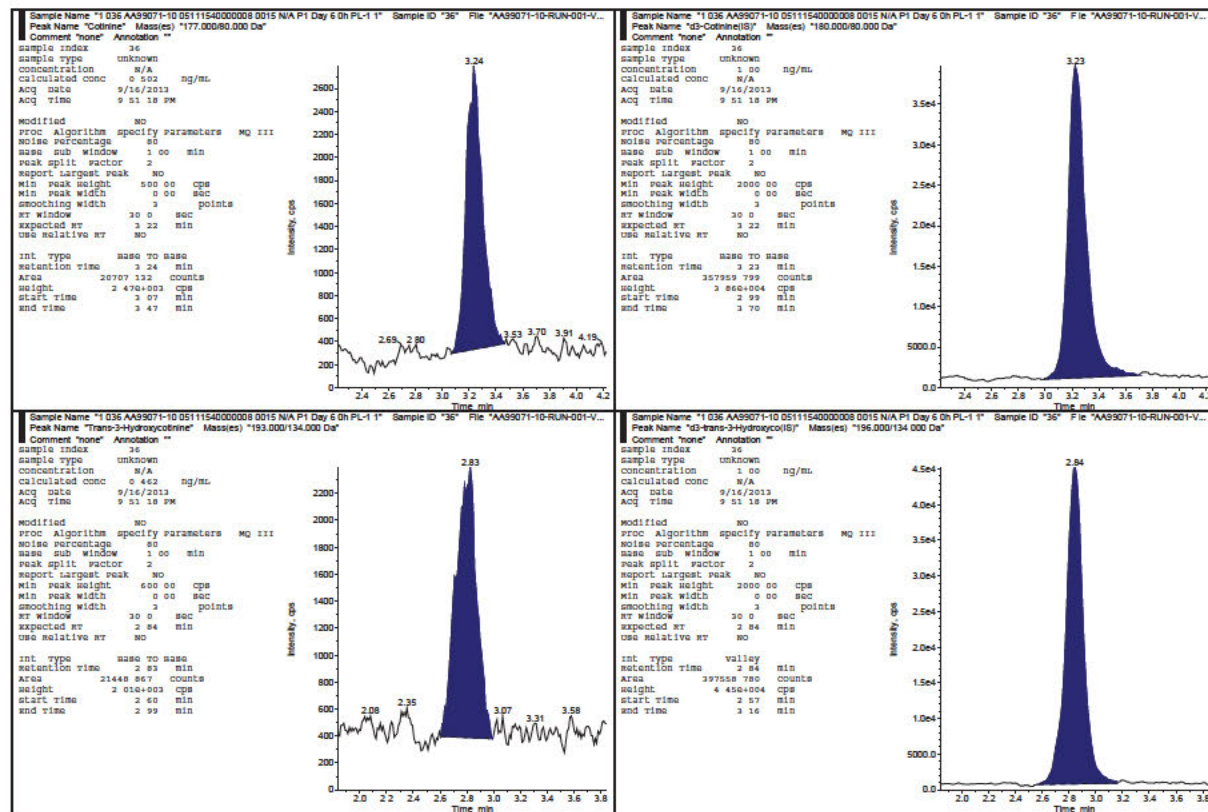


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Celerion Study AA99071-10



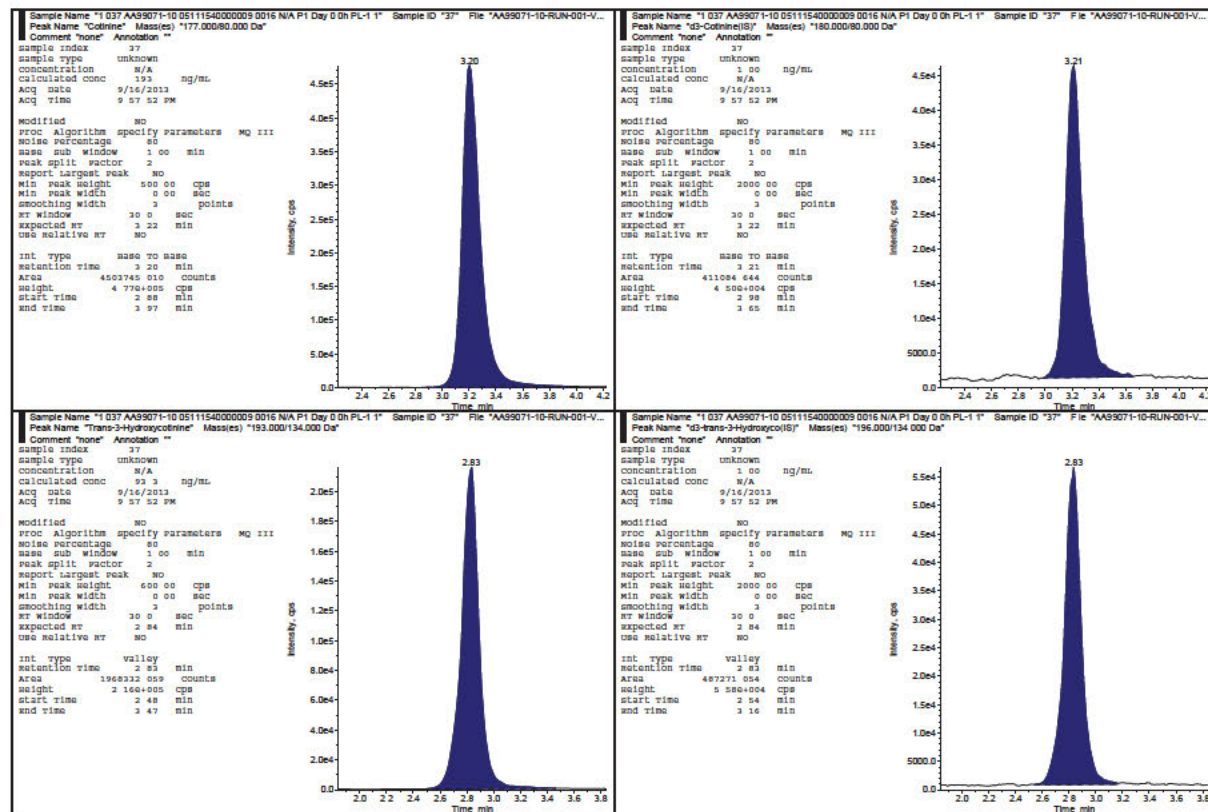


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Celerion Study AA99071-10



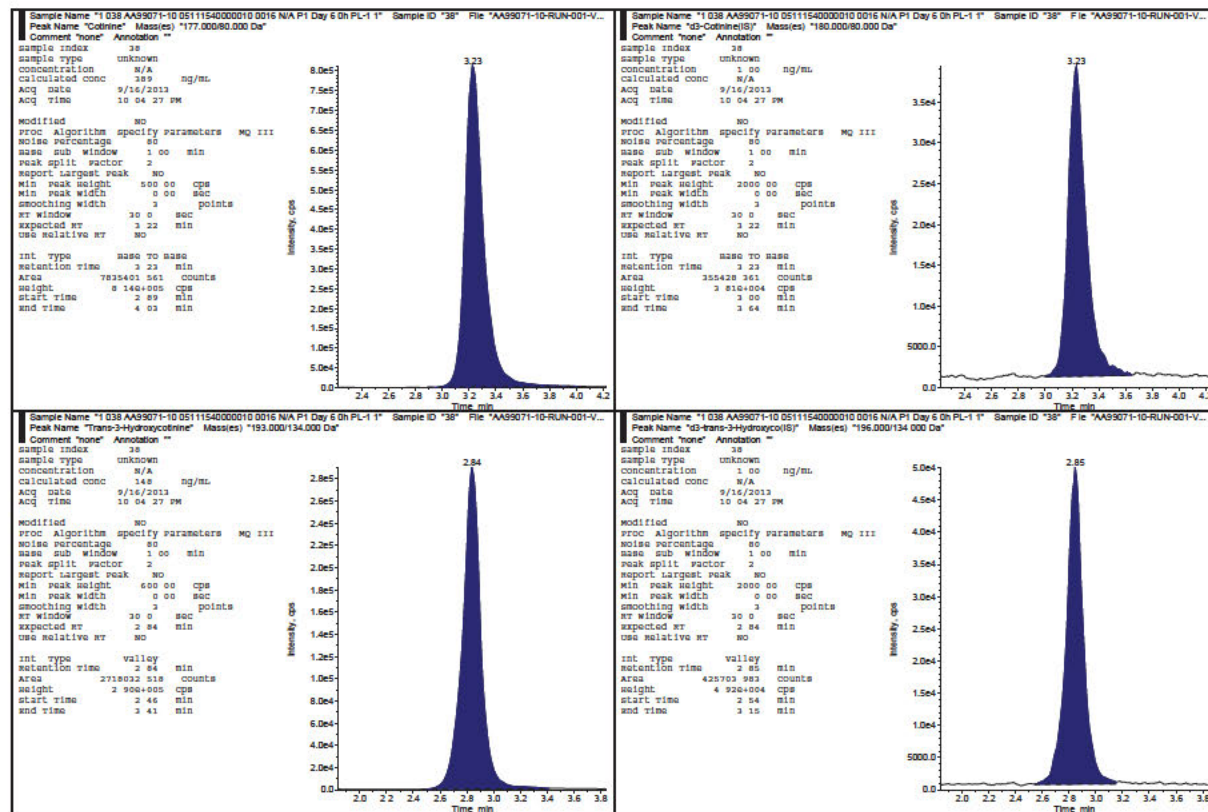


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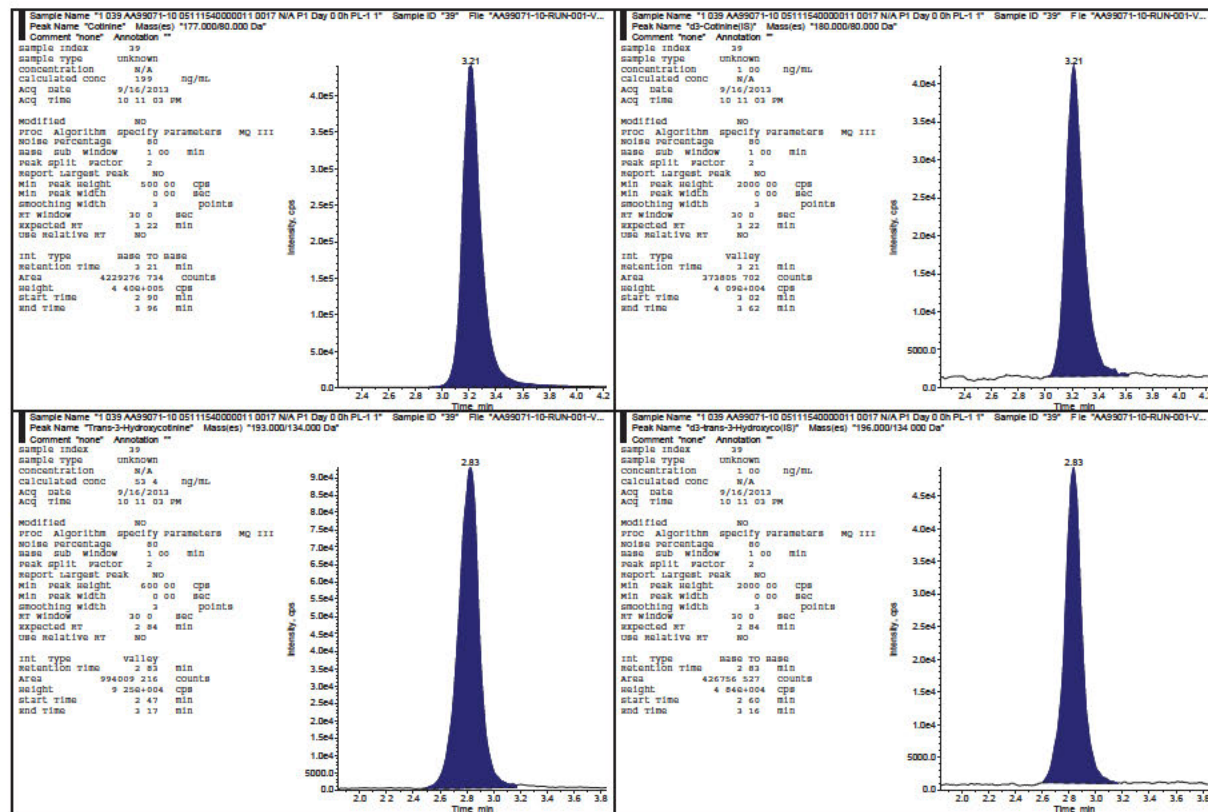


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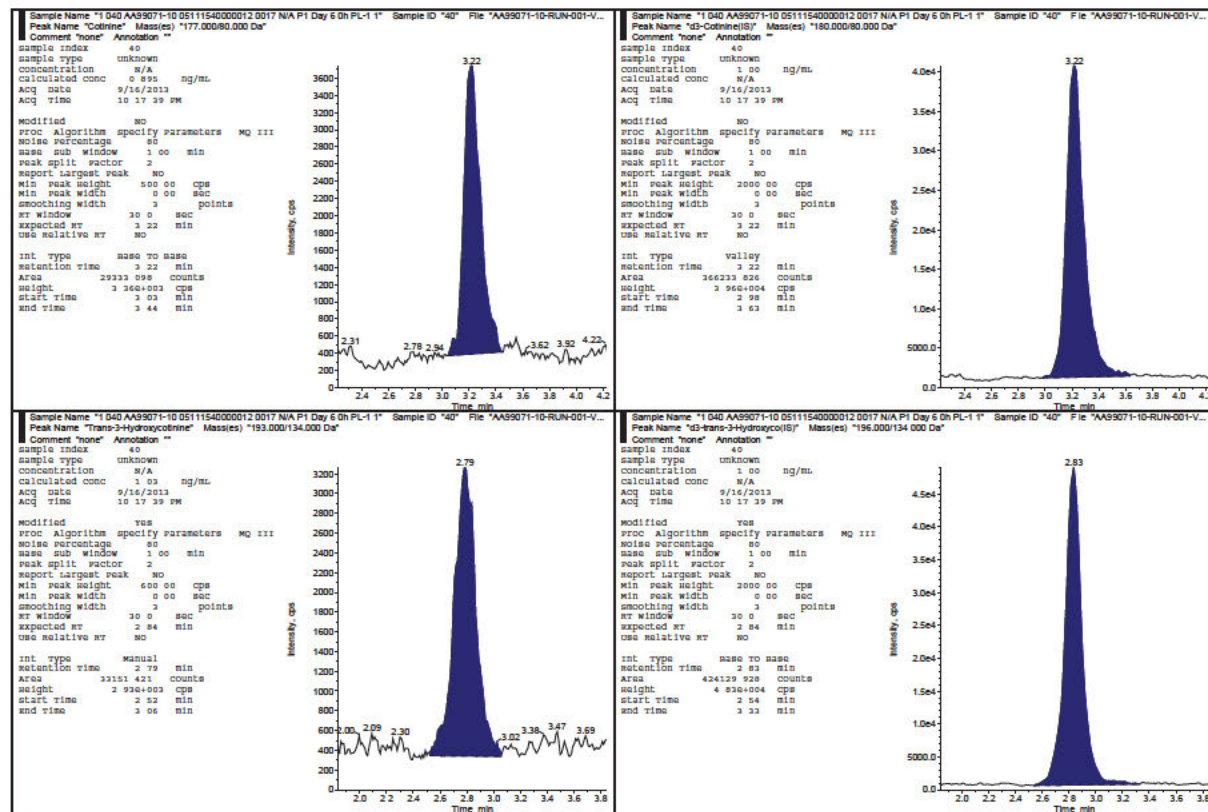


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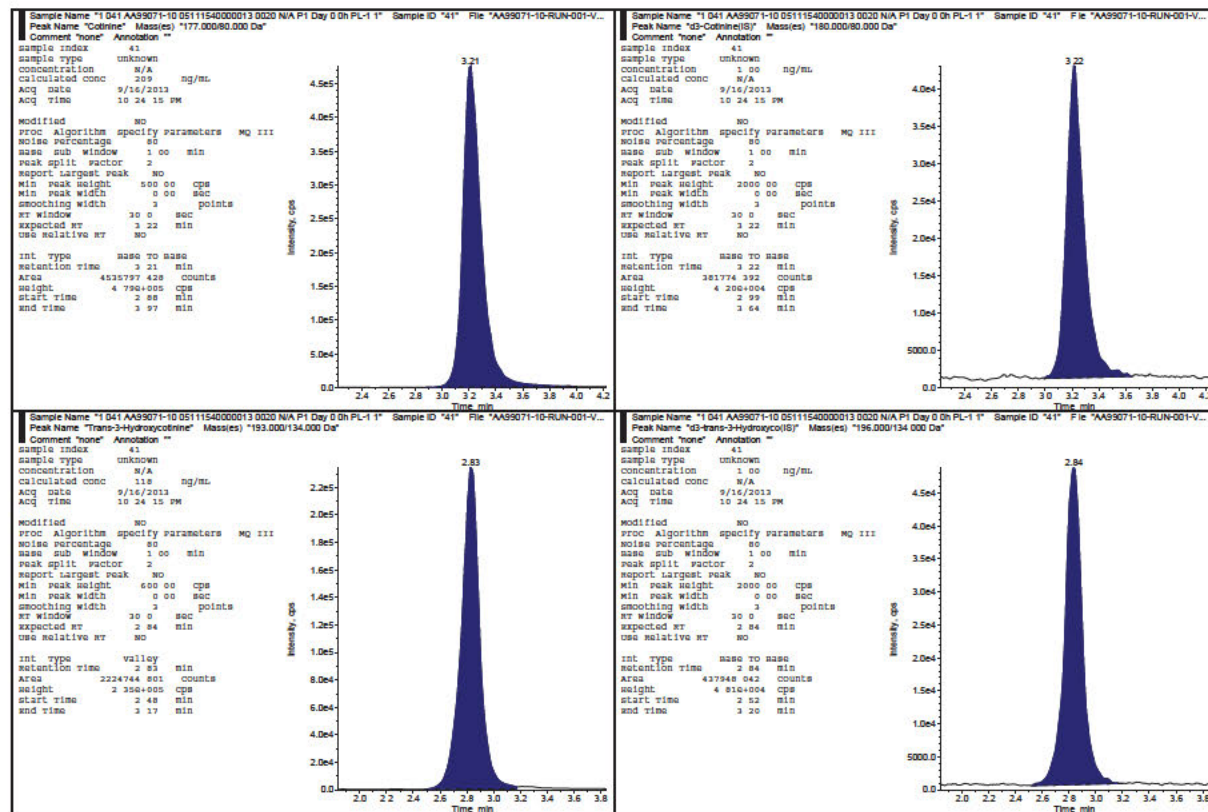


Cotinine and *trans*-3'-Hydroxycotinine in Human Plasma (K₂EDTA)
Celerion Study AA99071-10



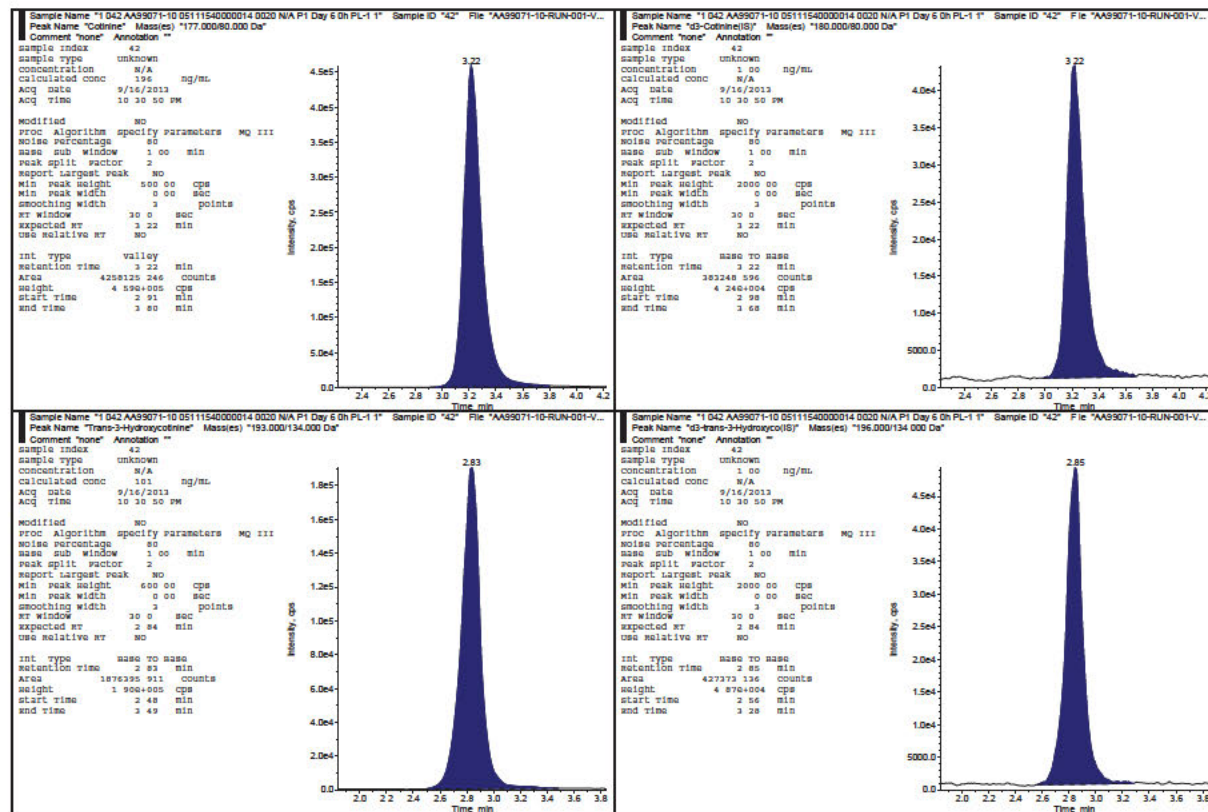


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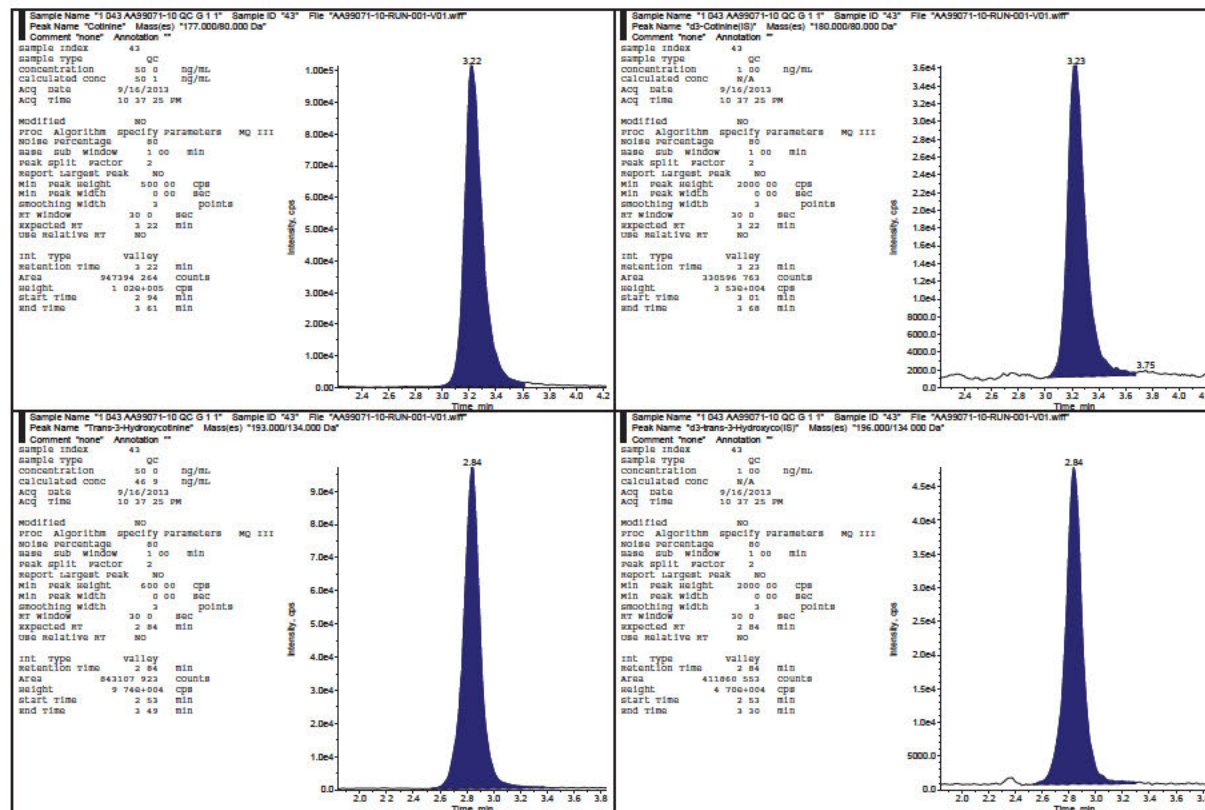


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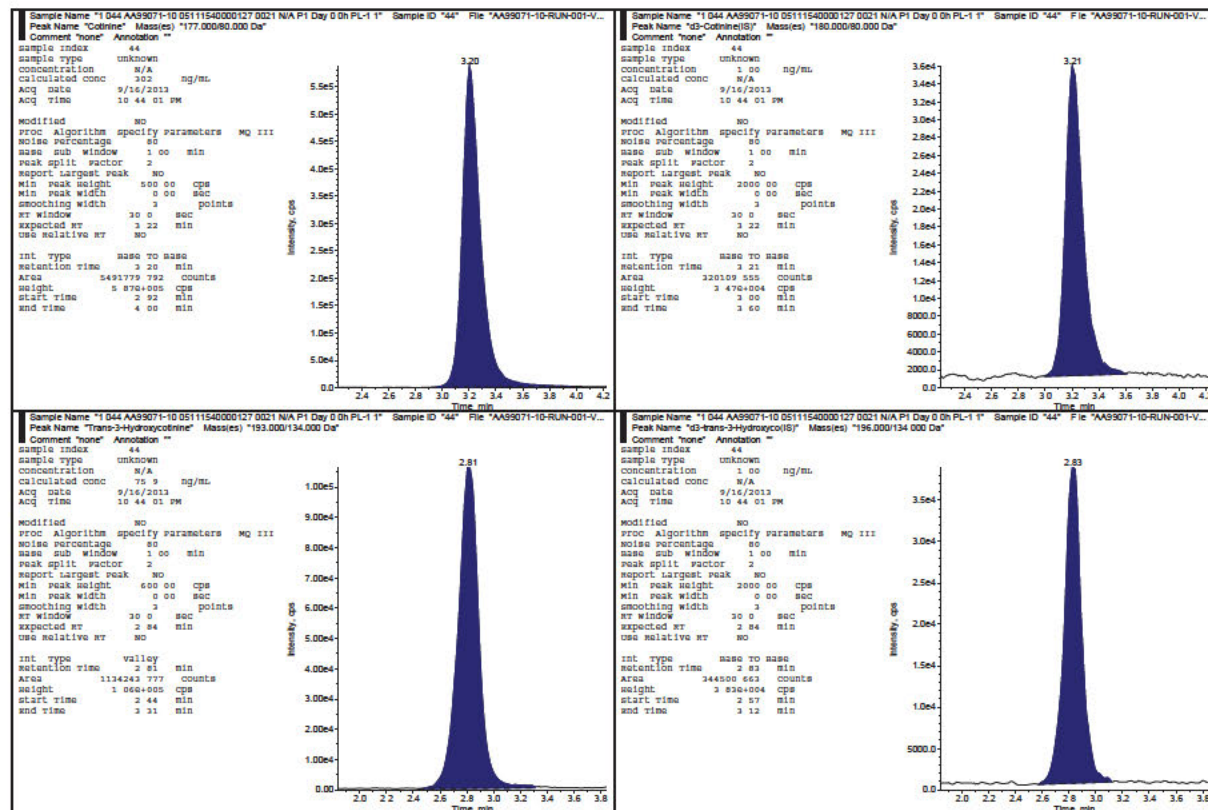


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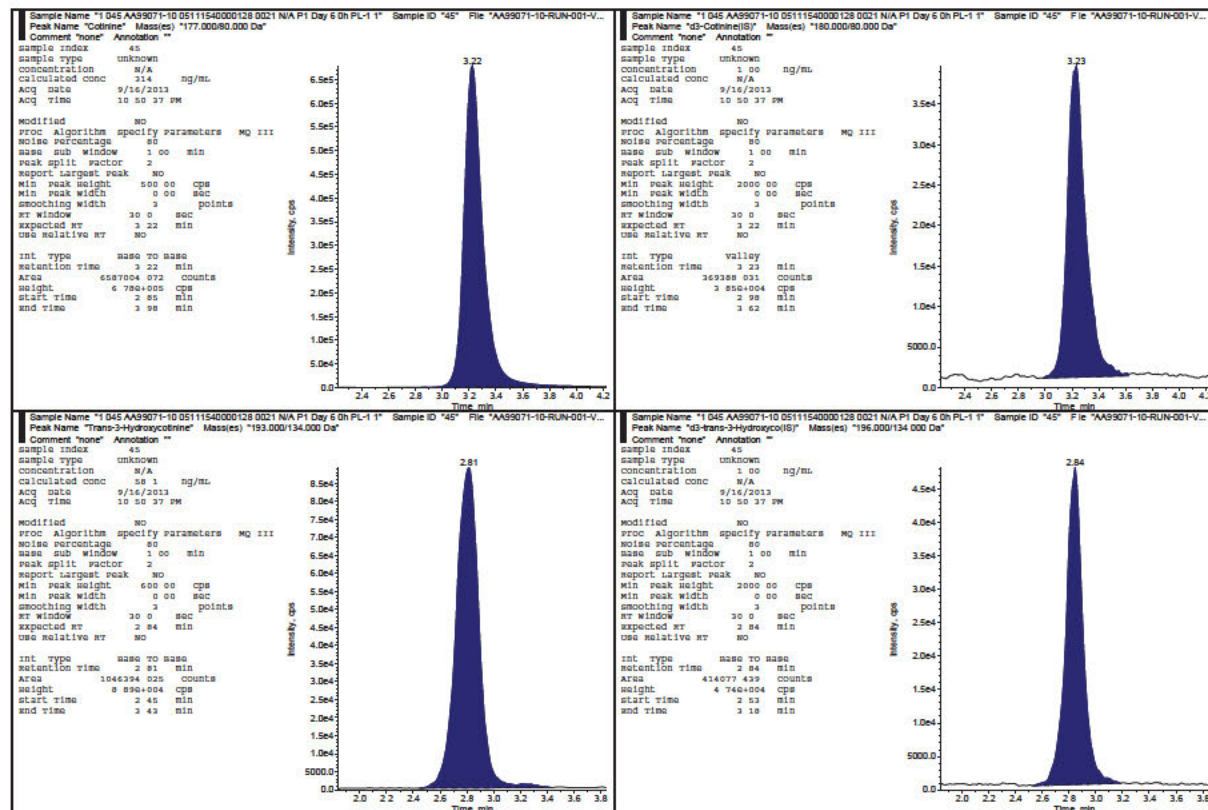


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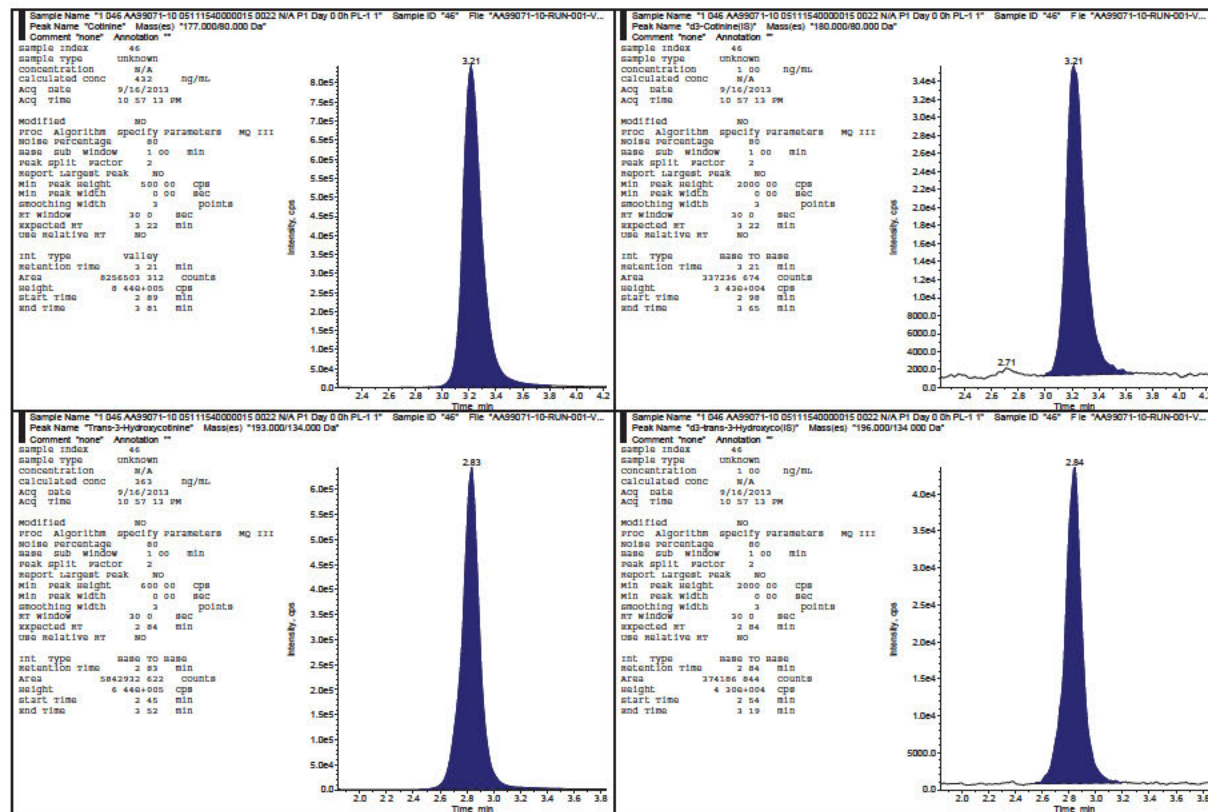


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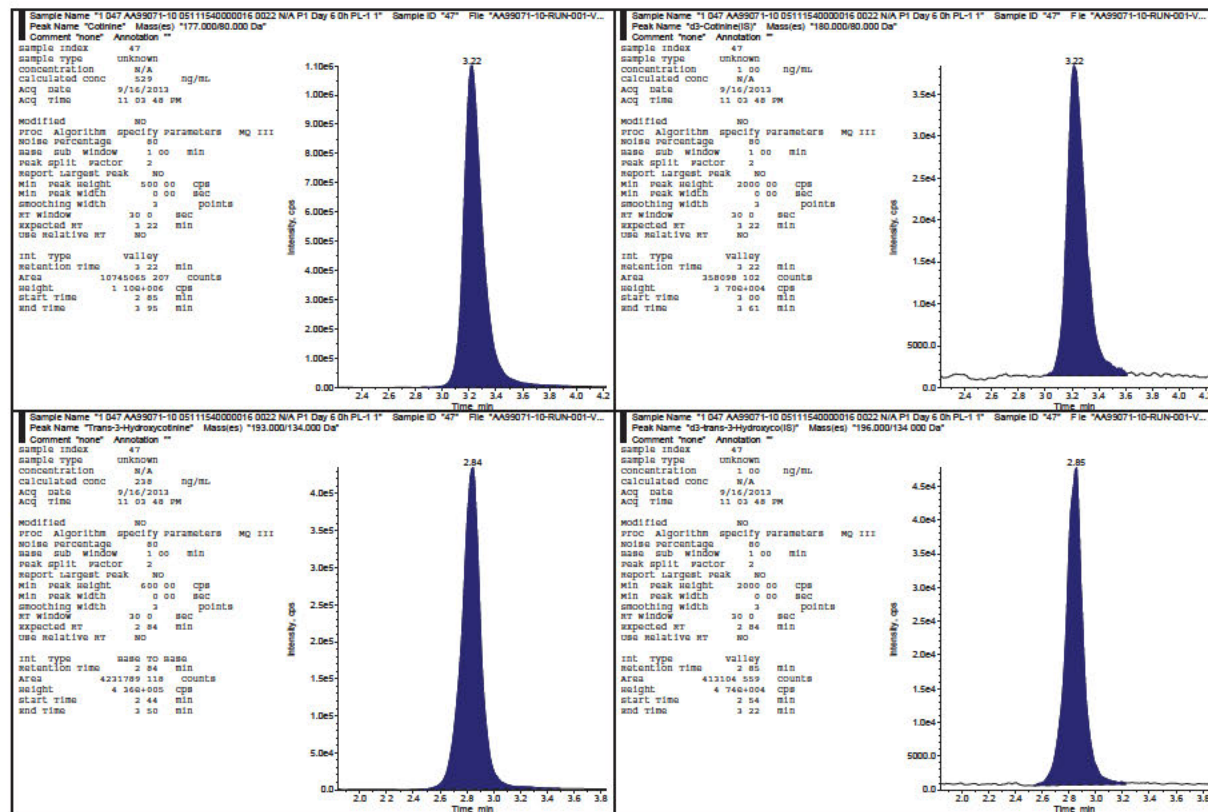


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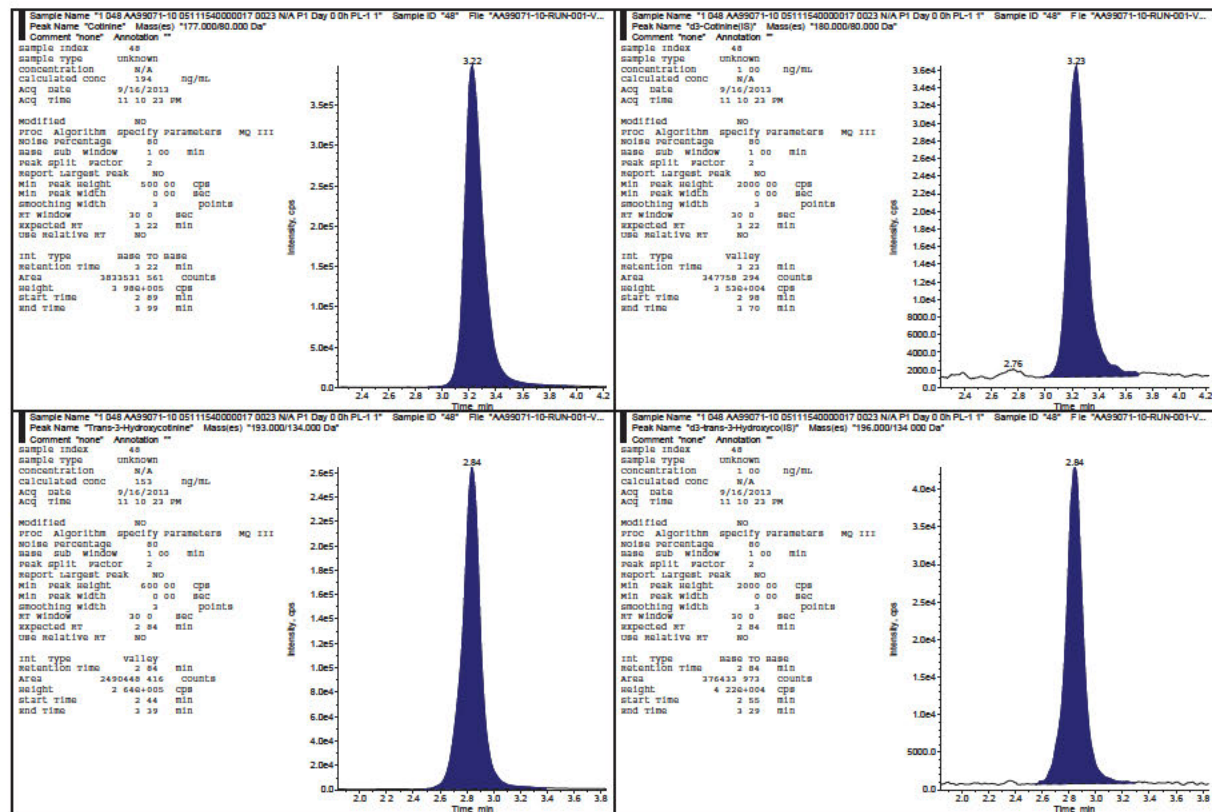


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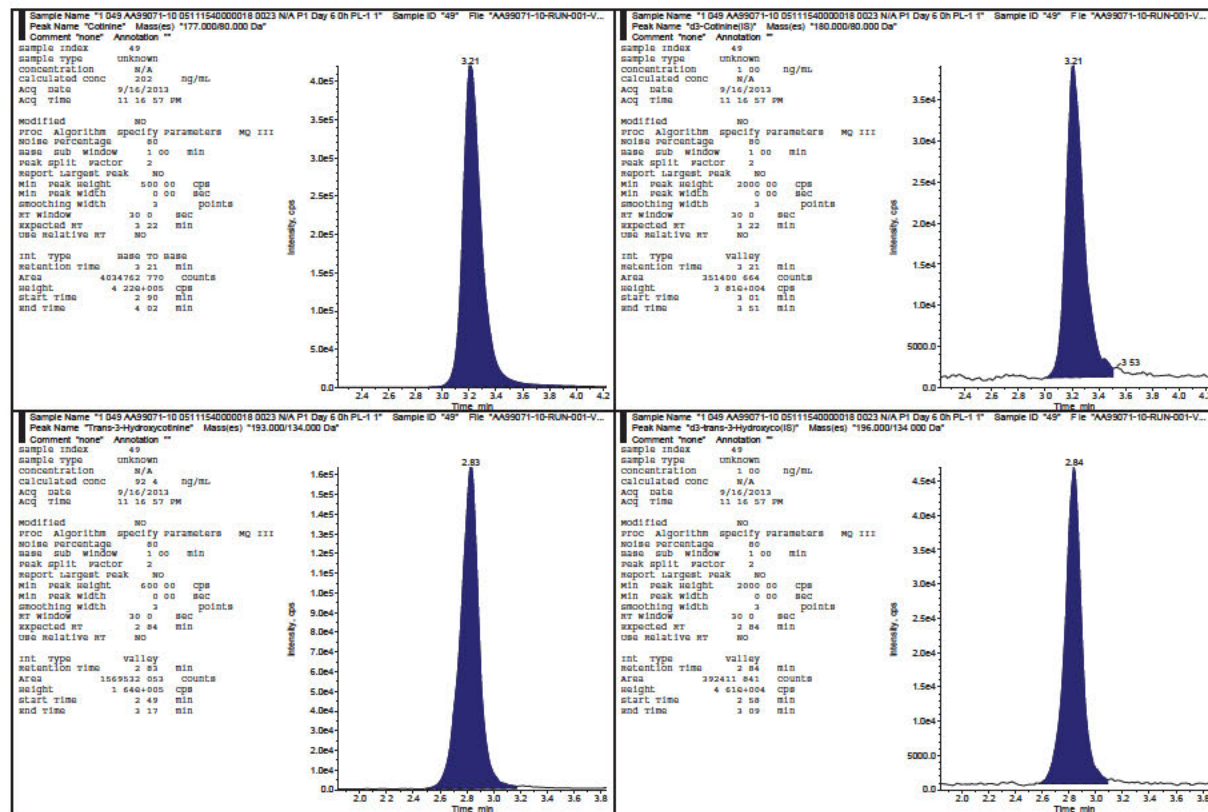


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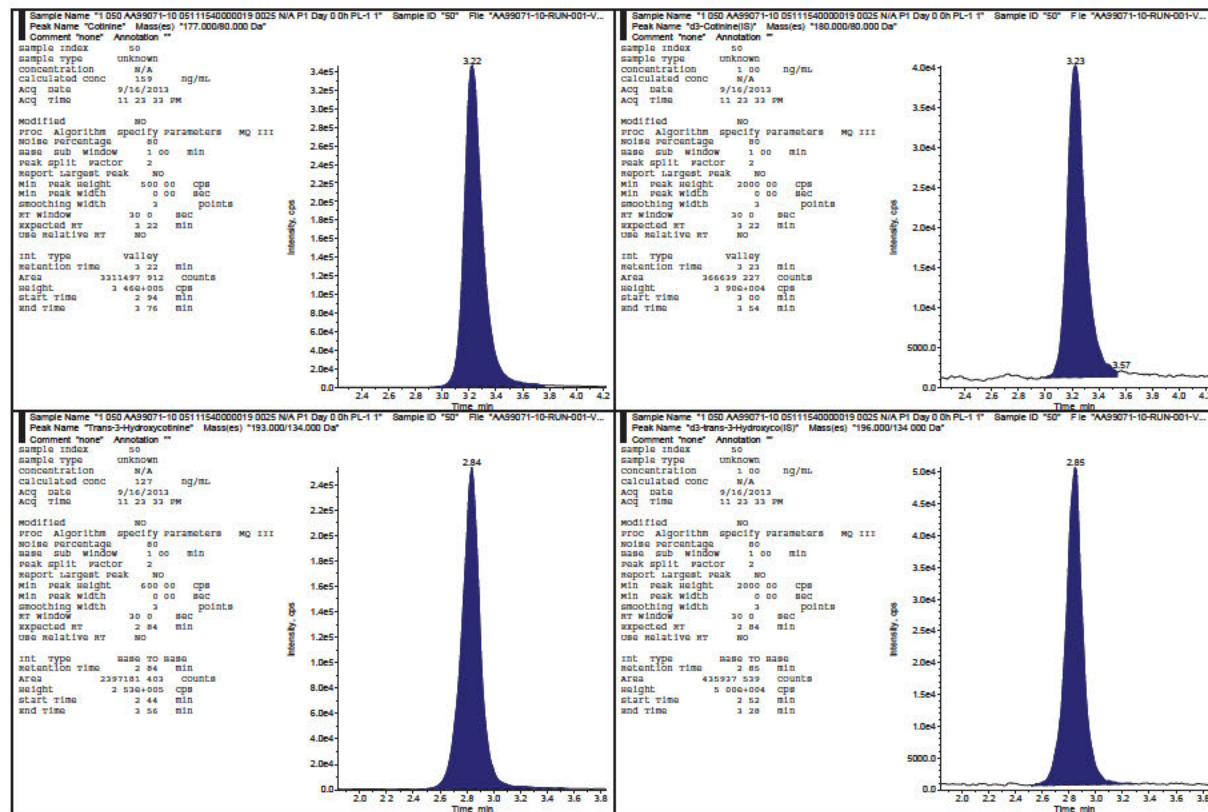


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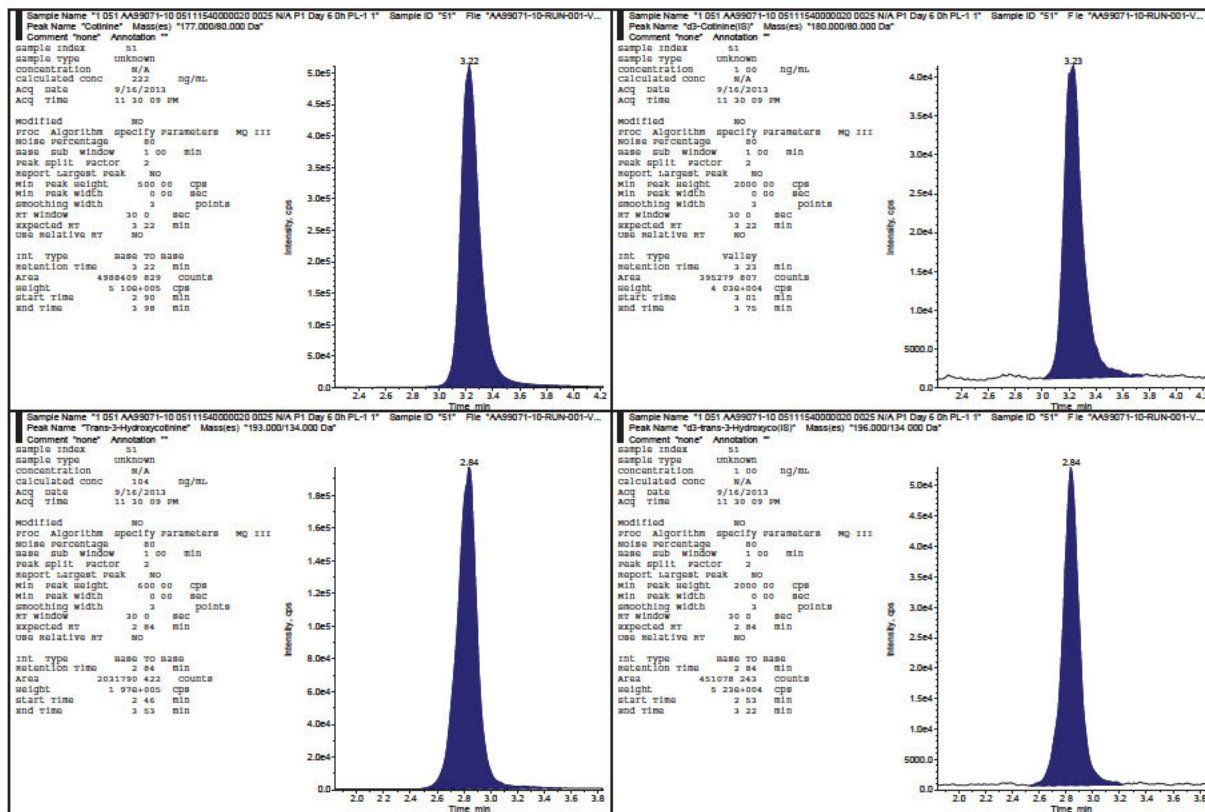


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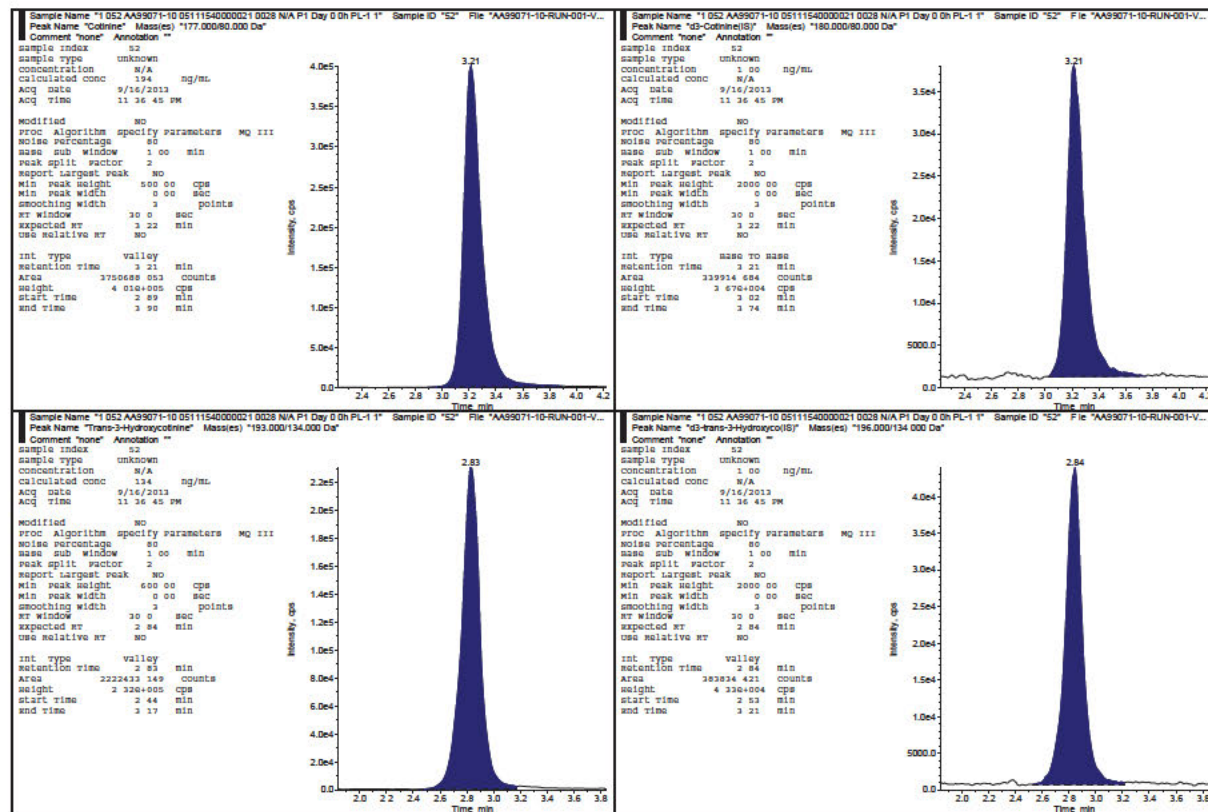


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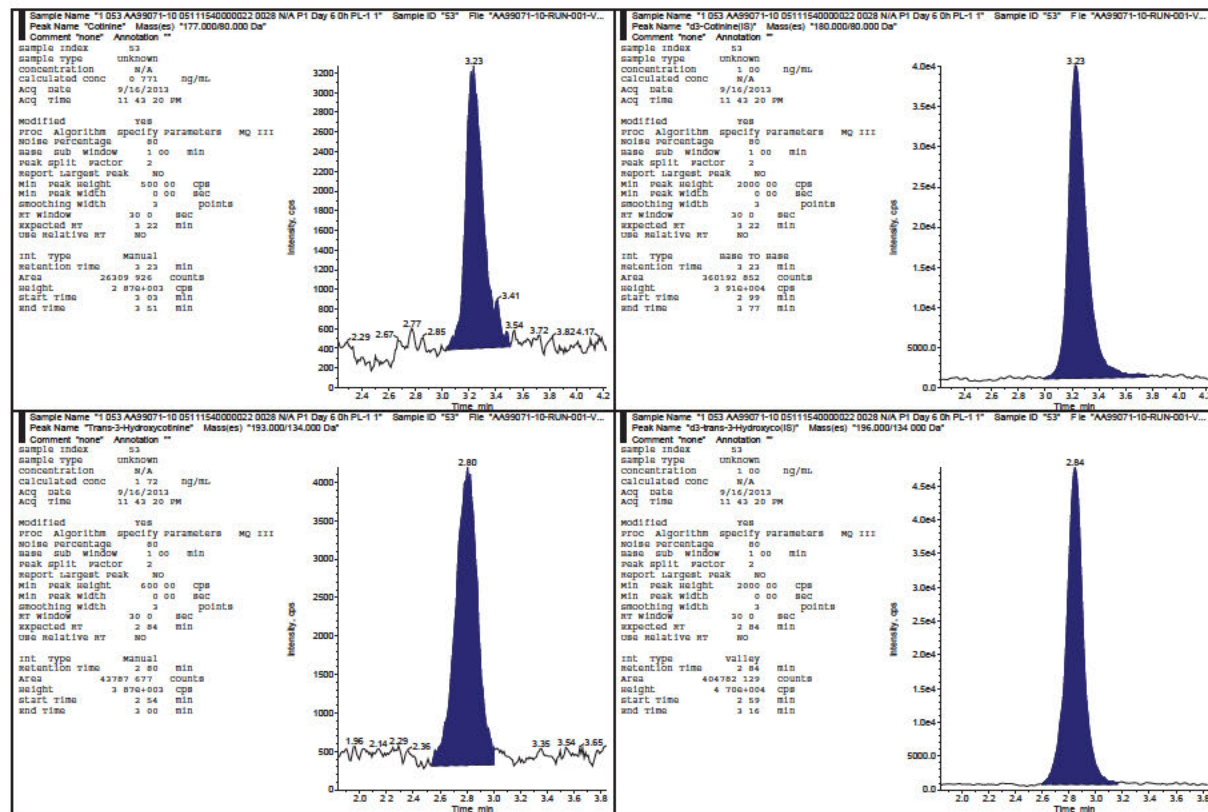


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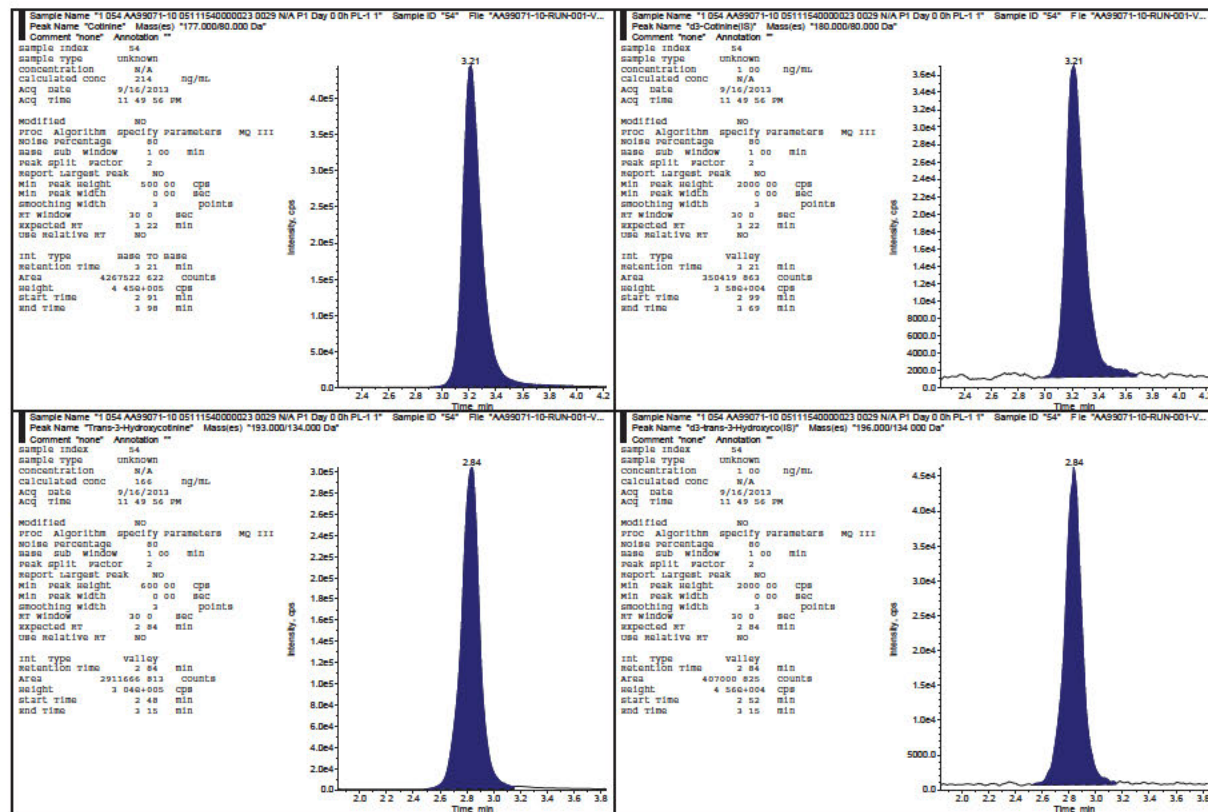


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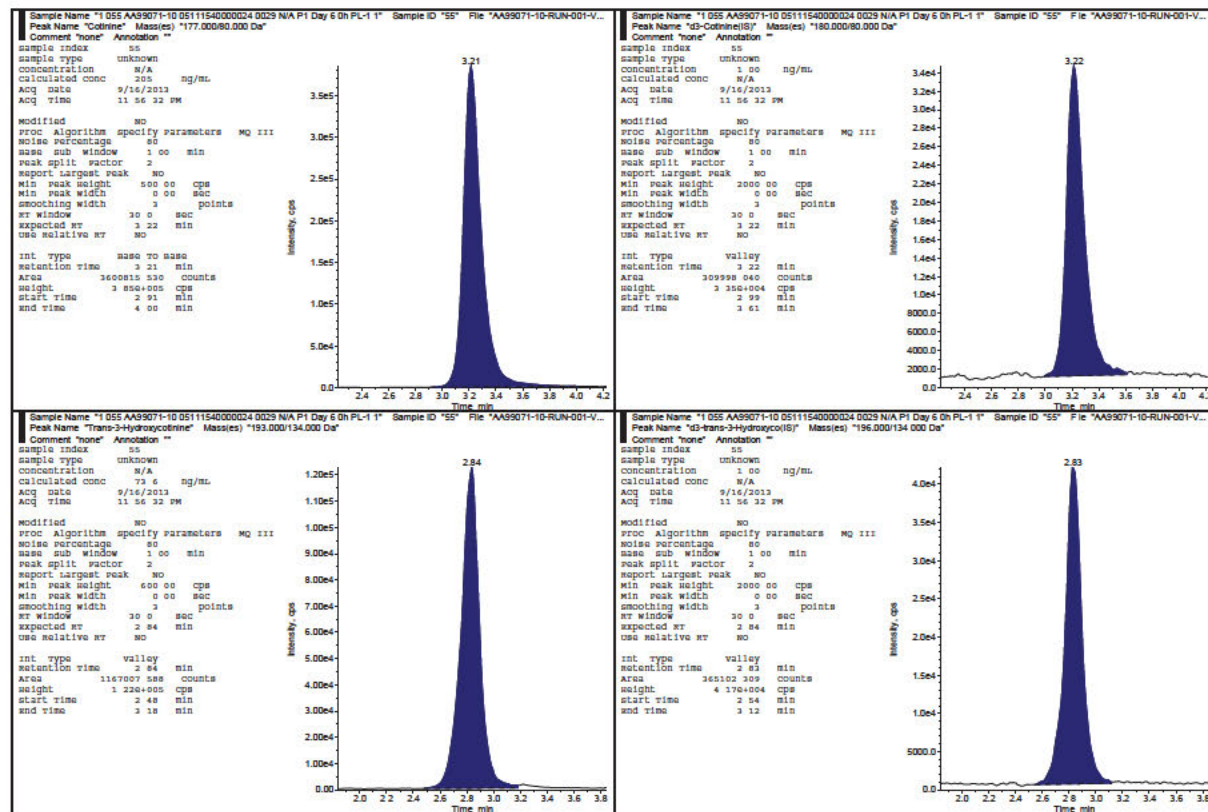


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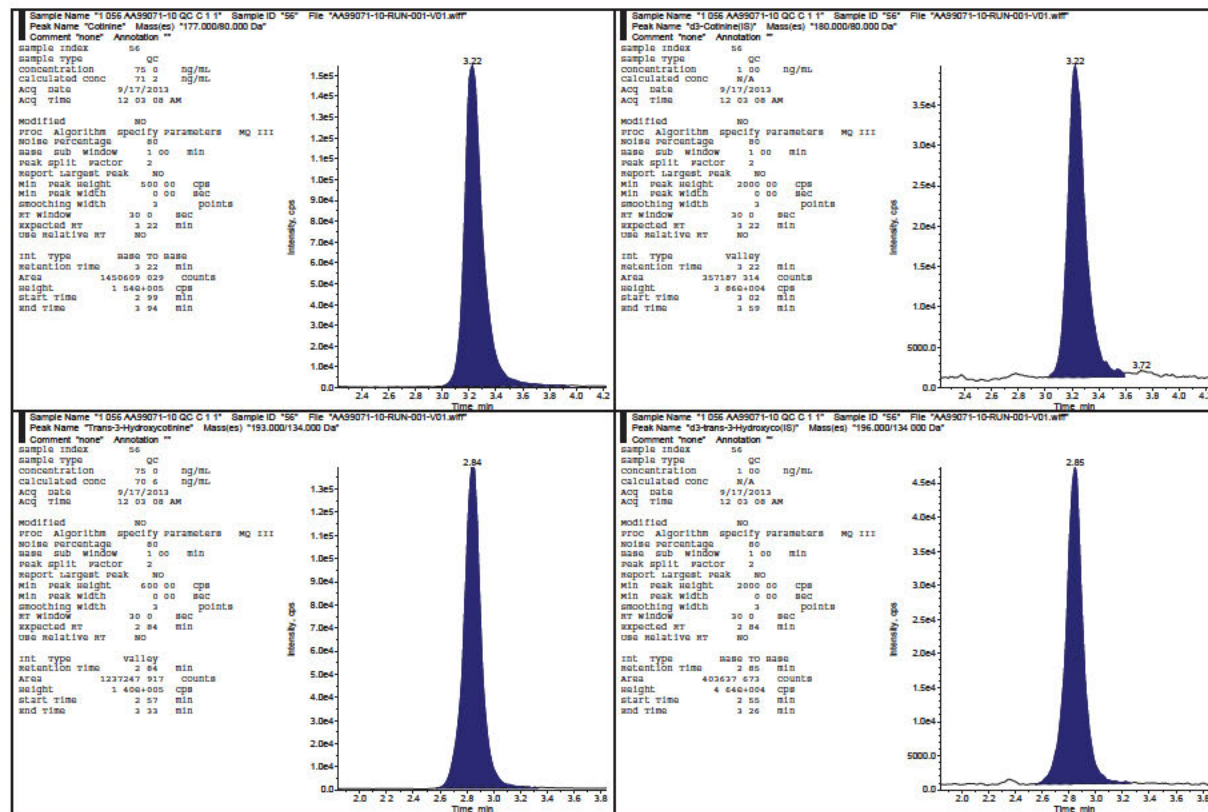


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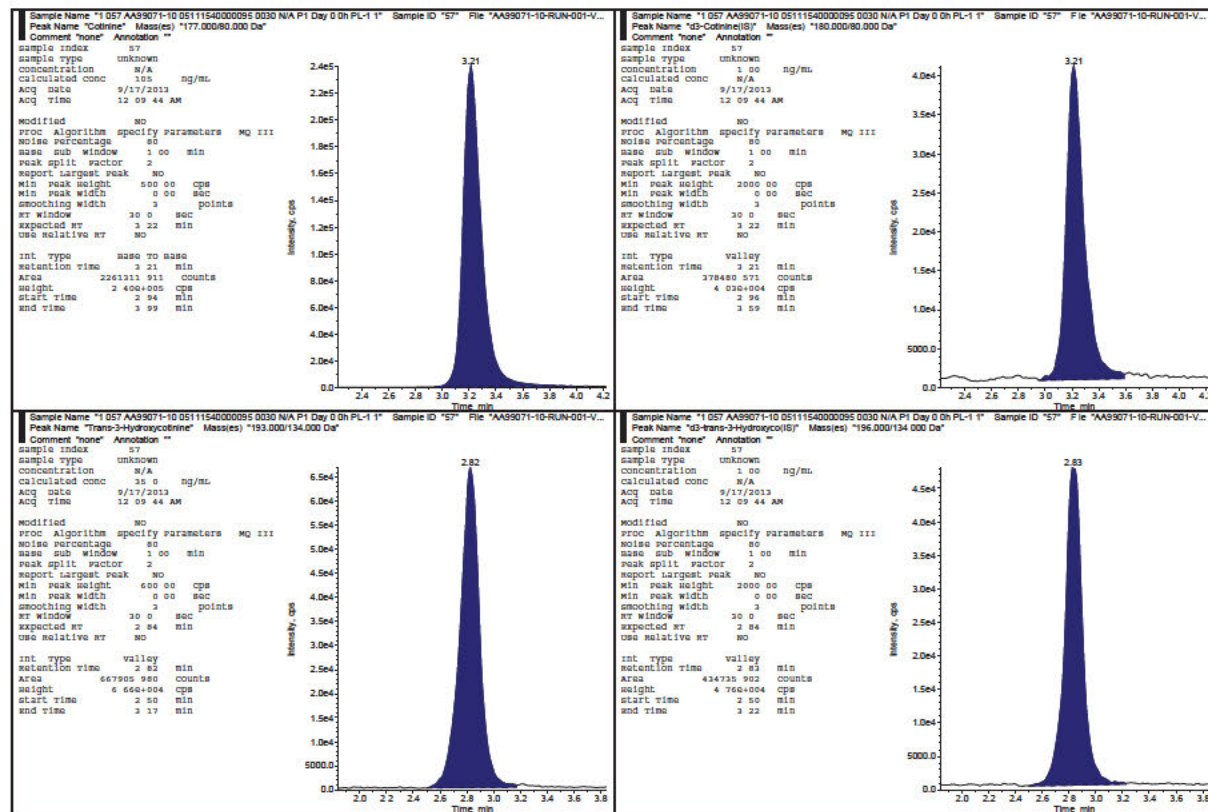


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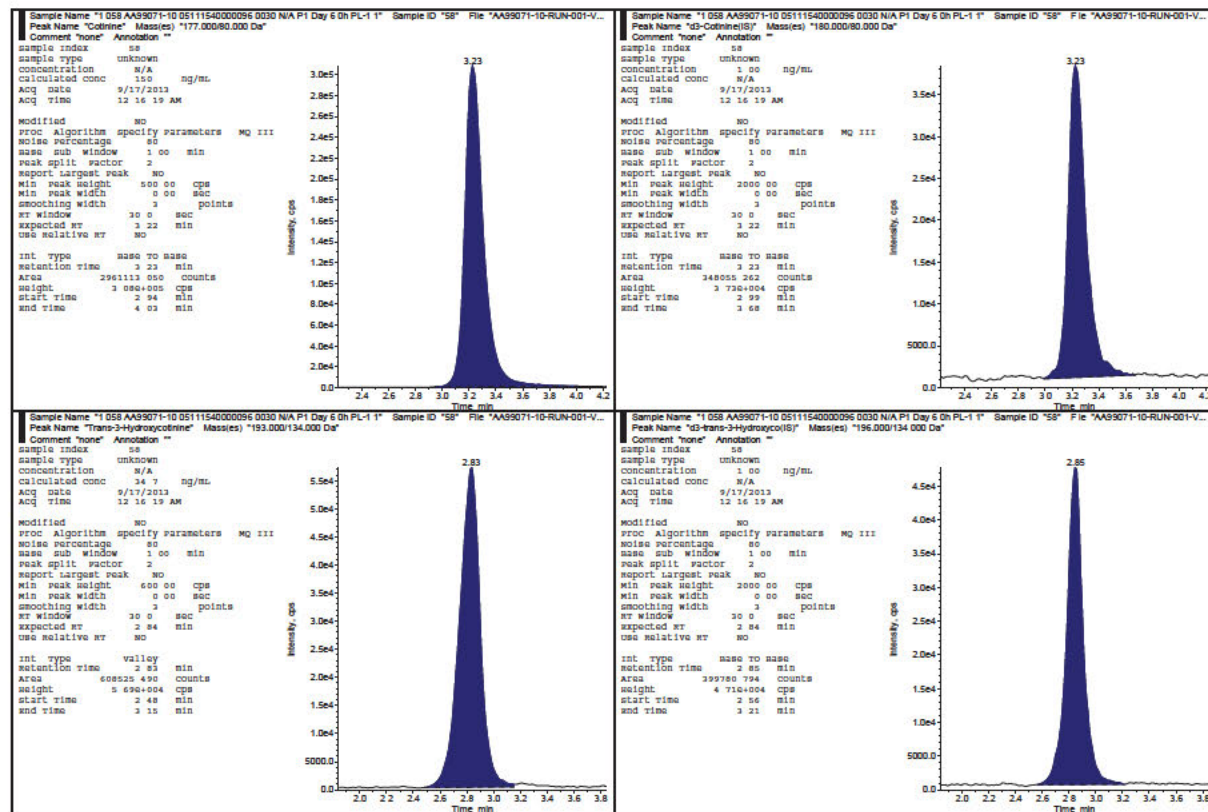


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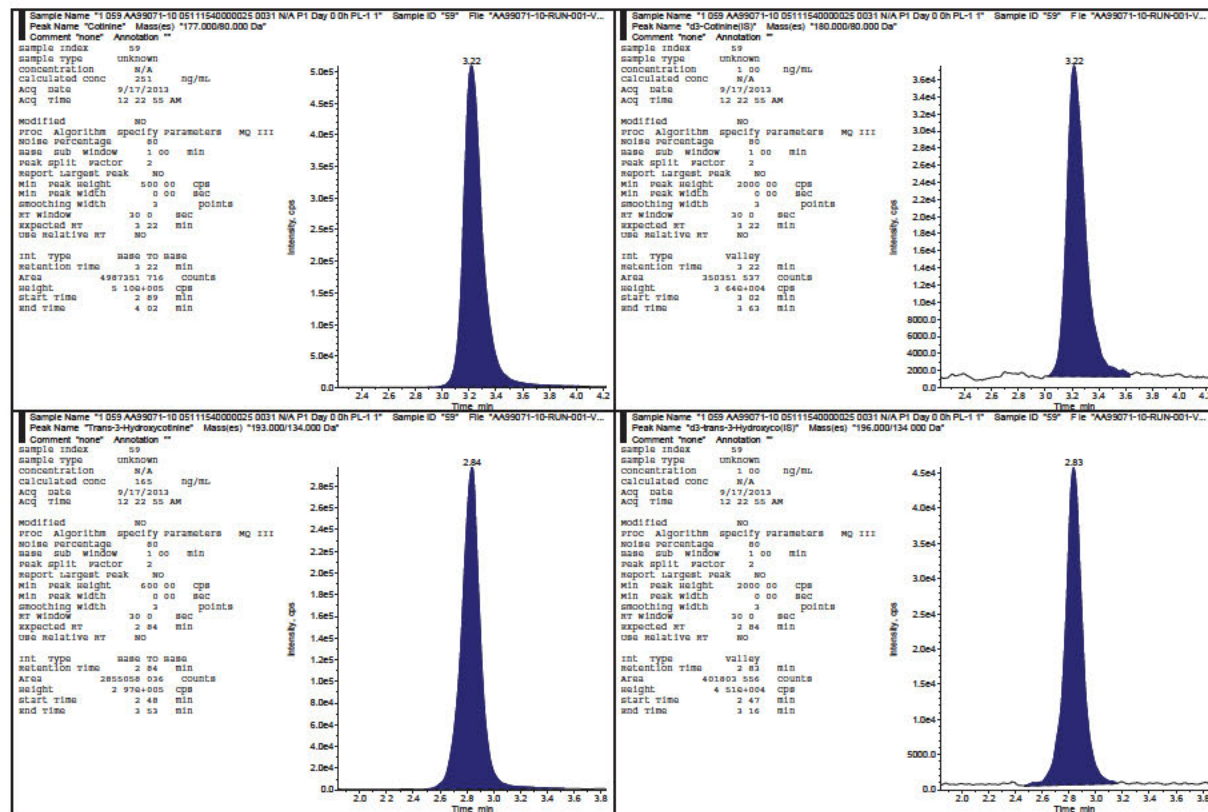


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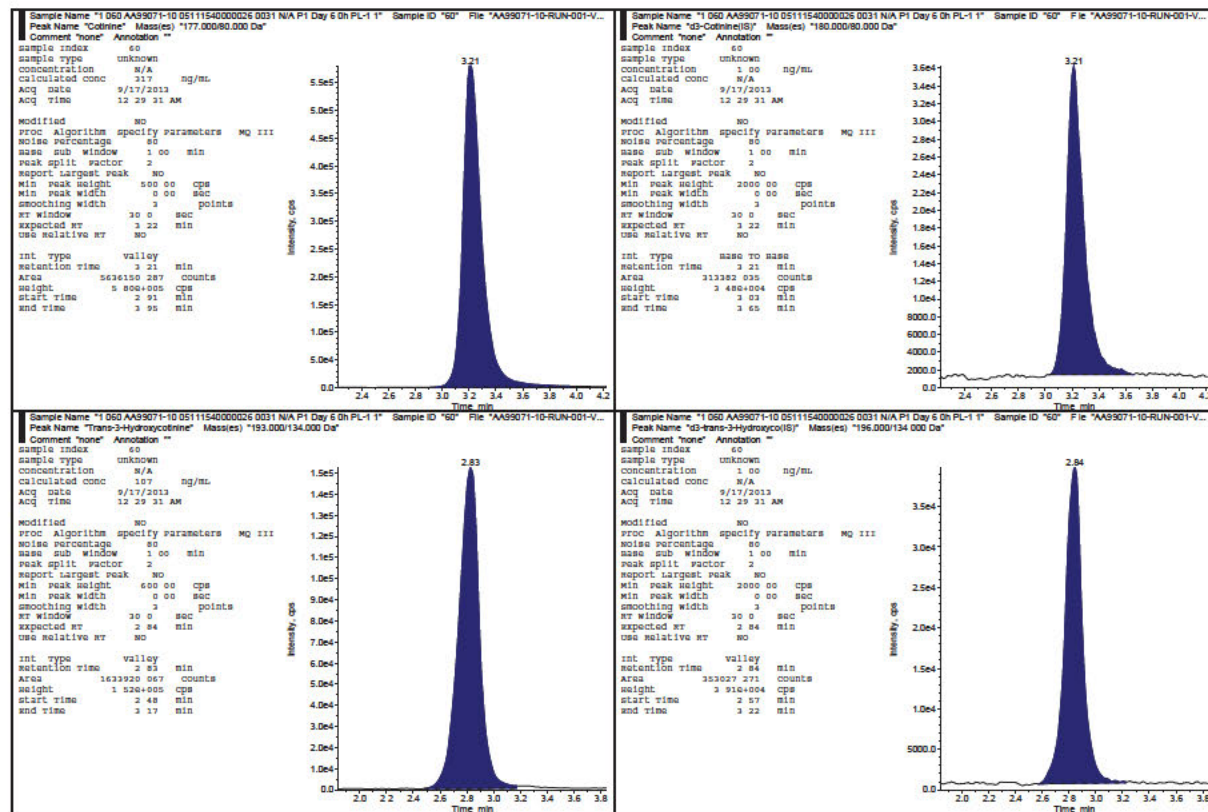


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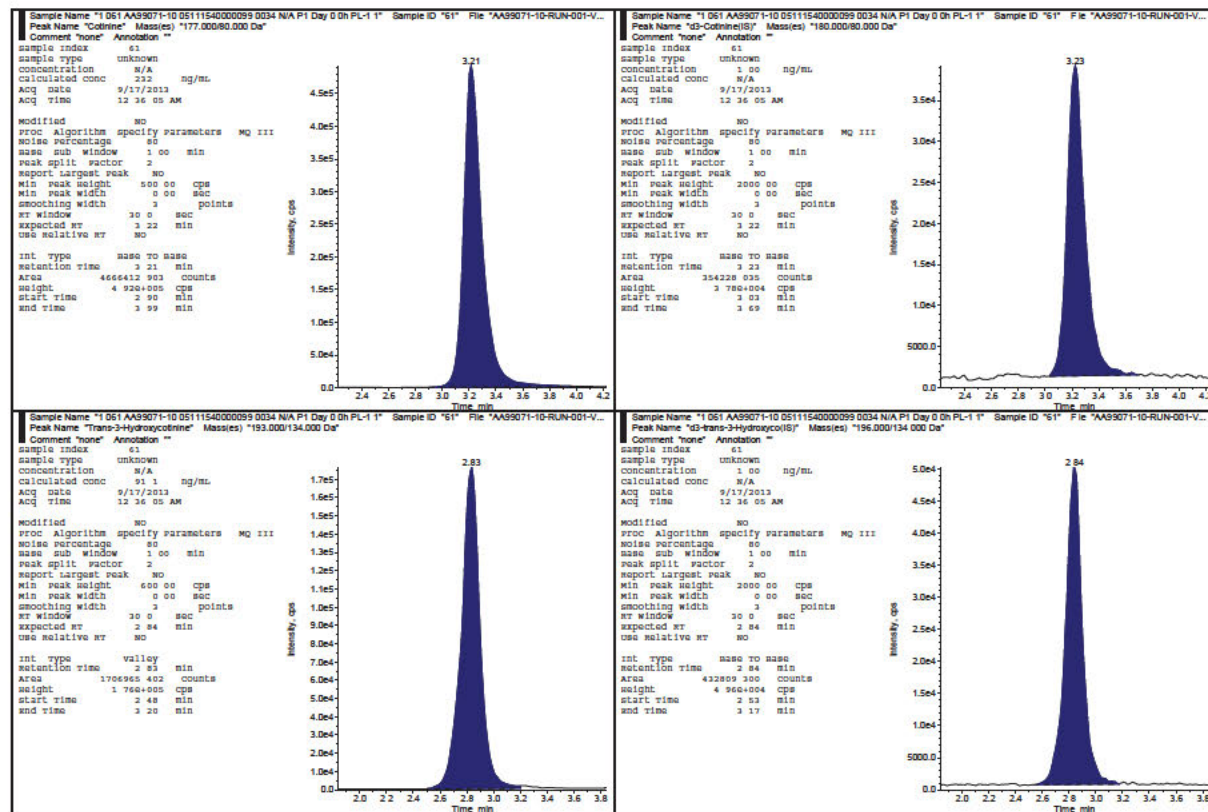


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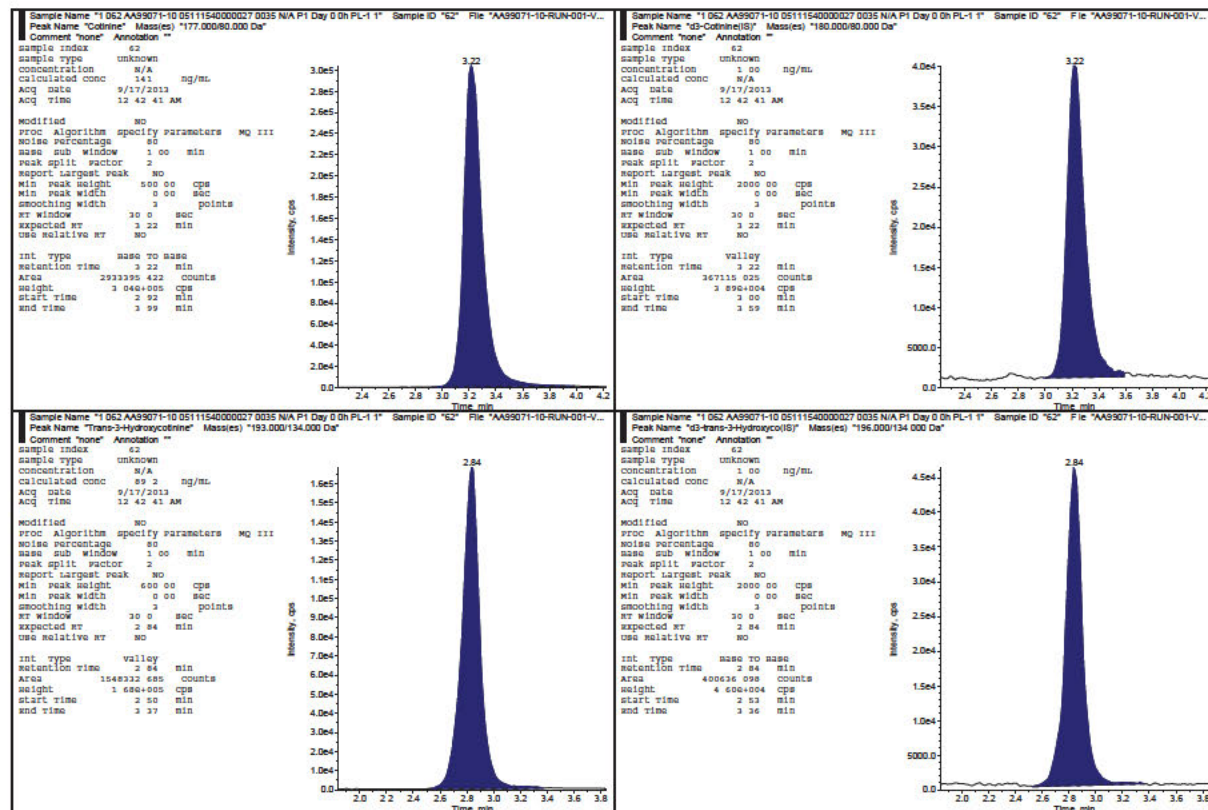


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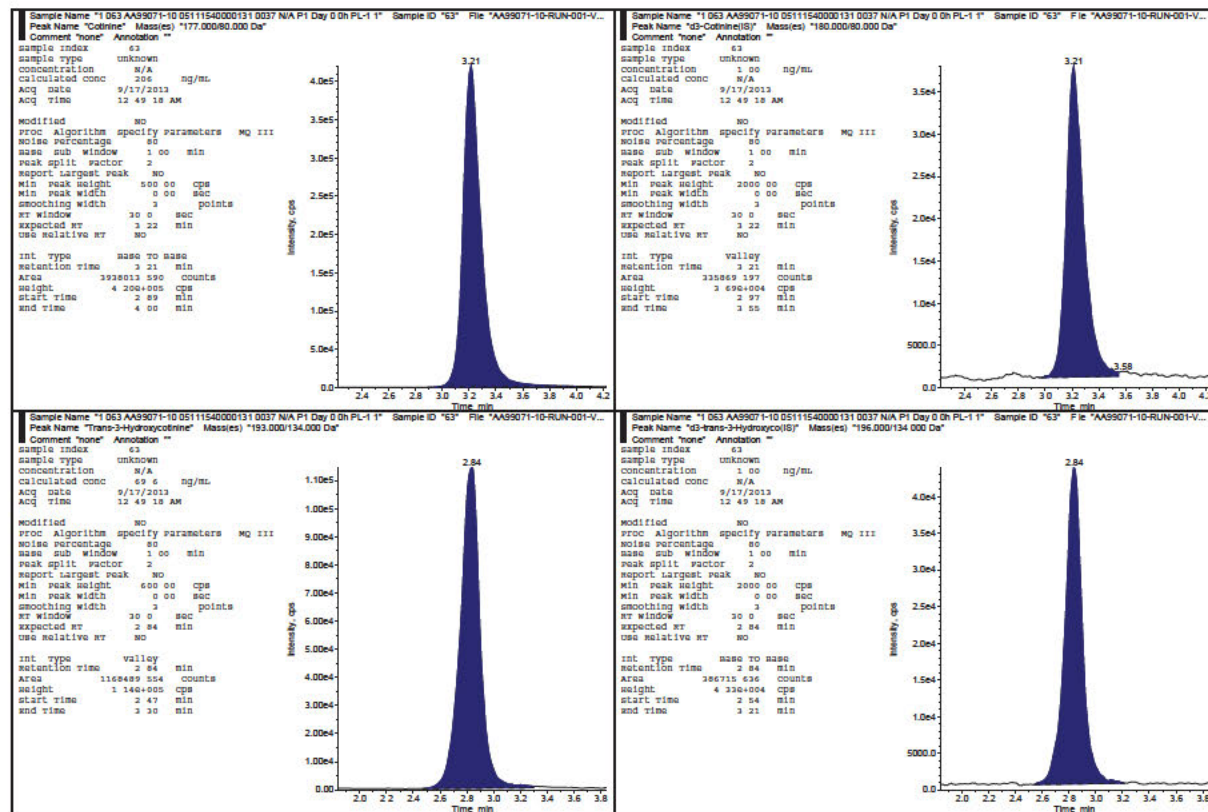


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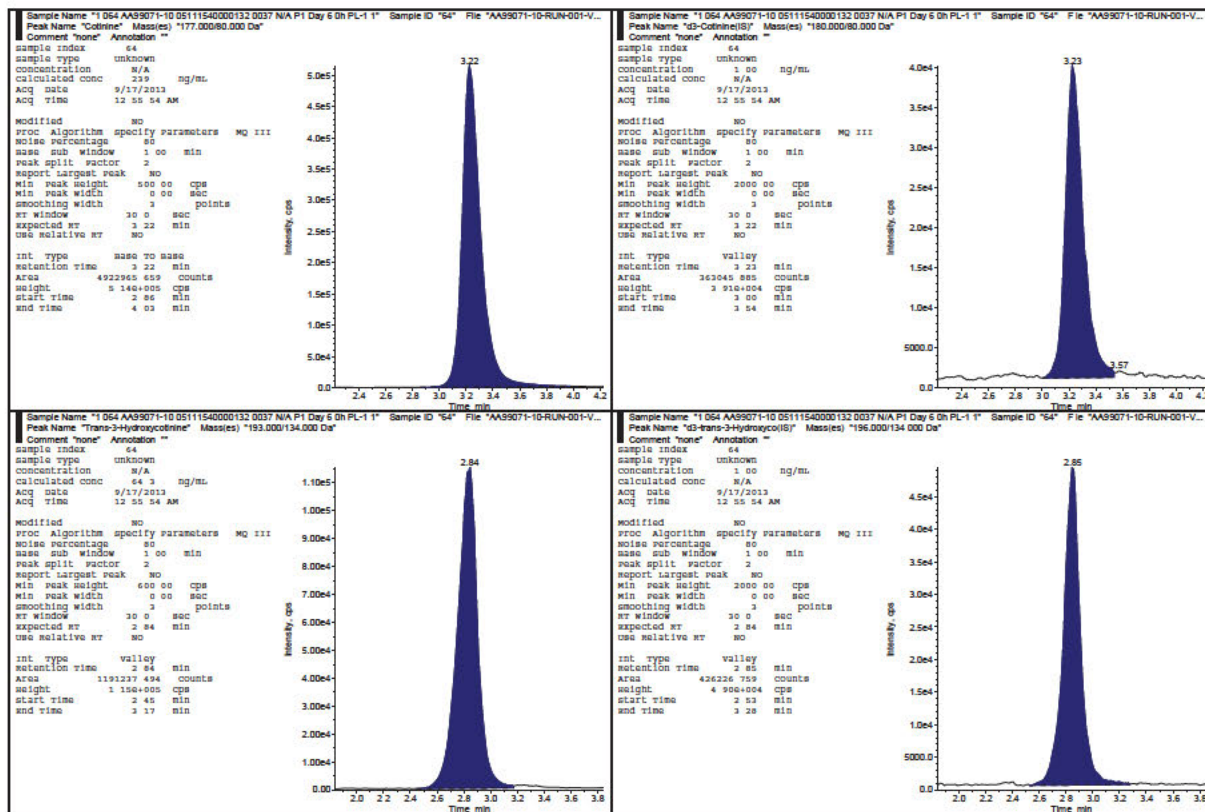


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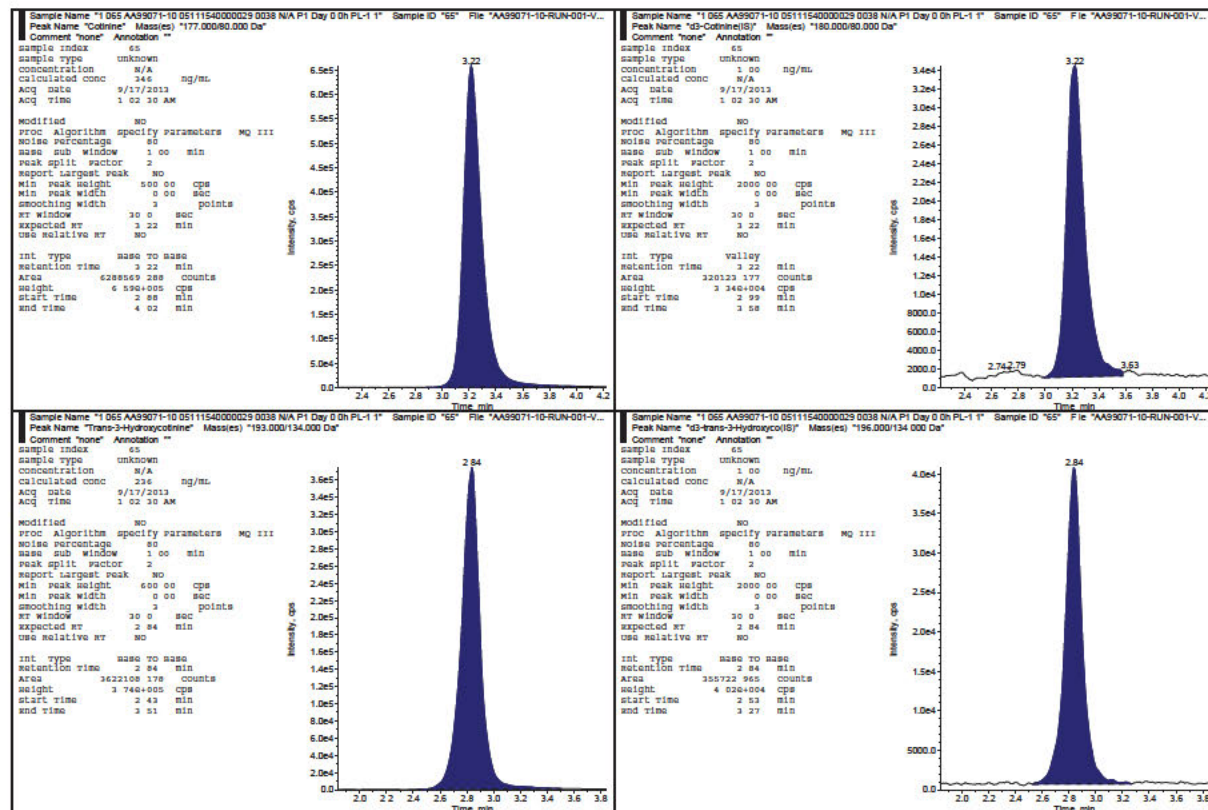


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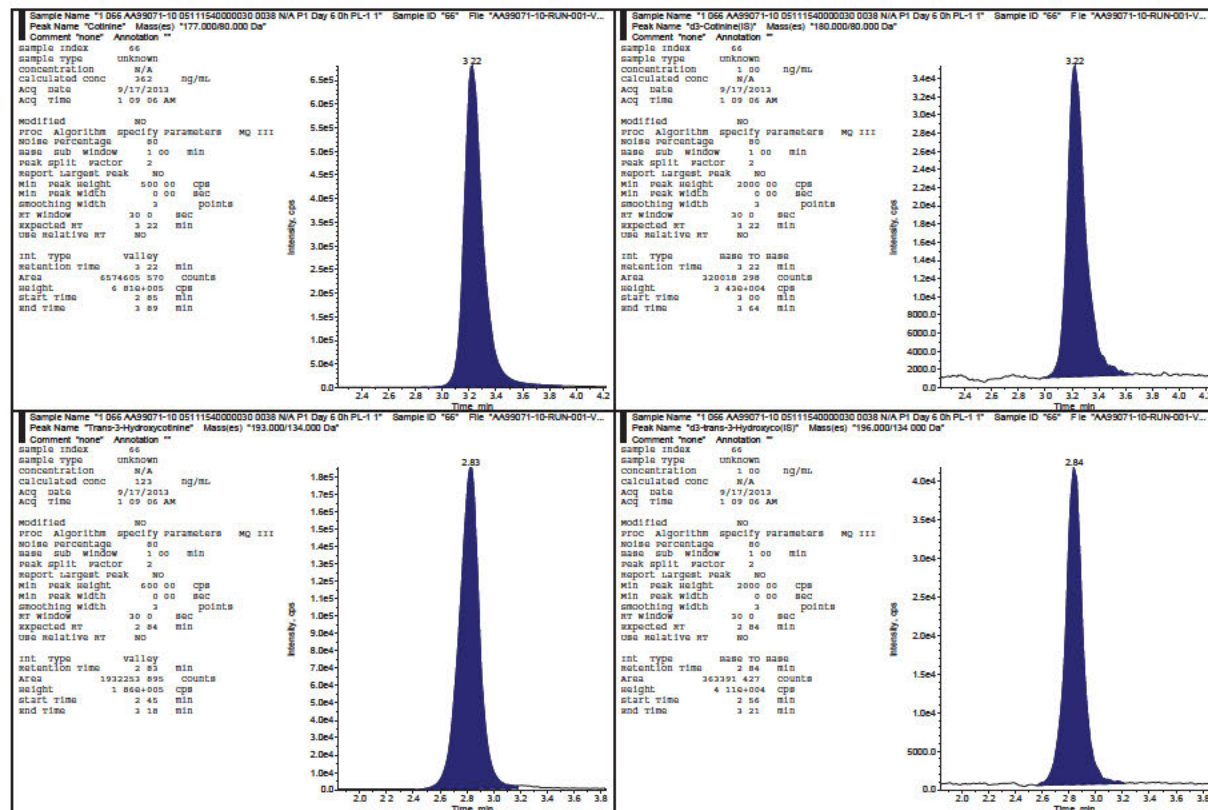


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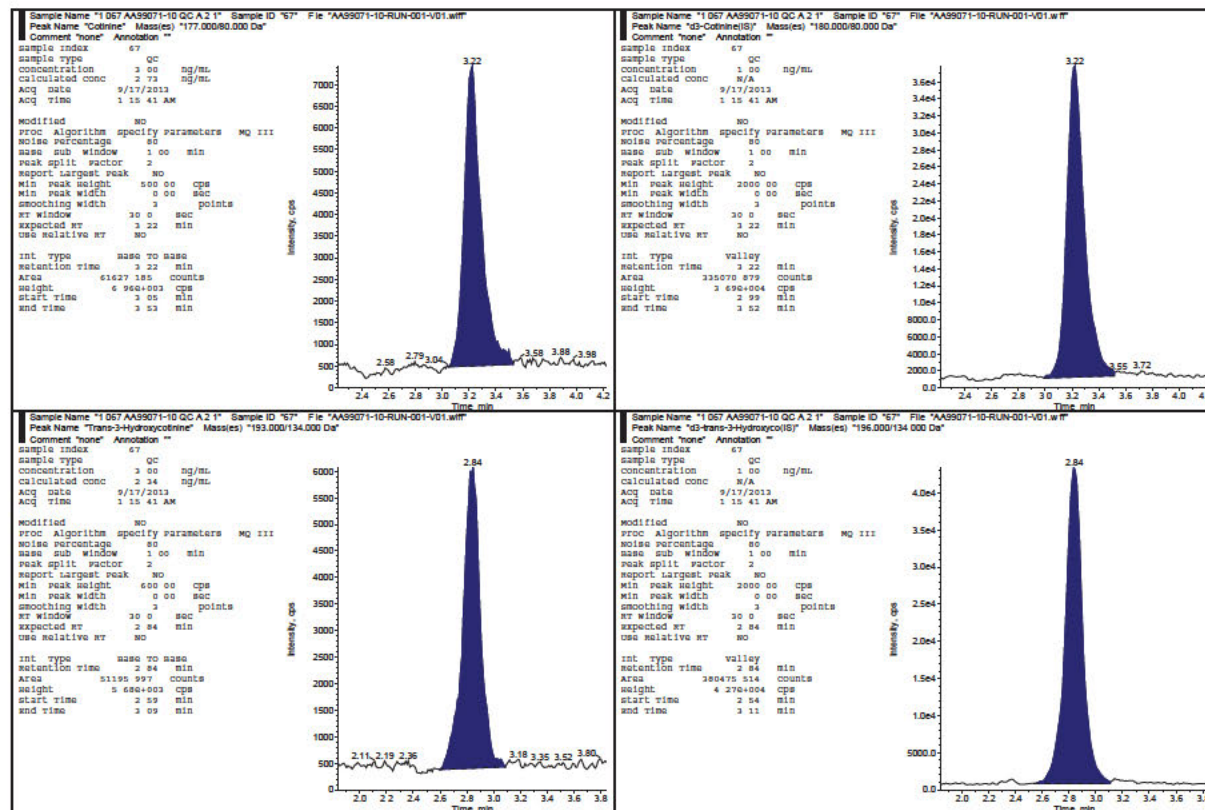


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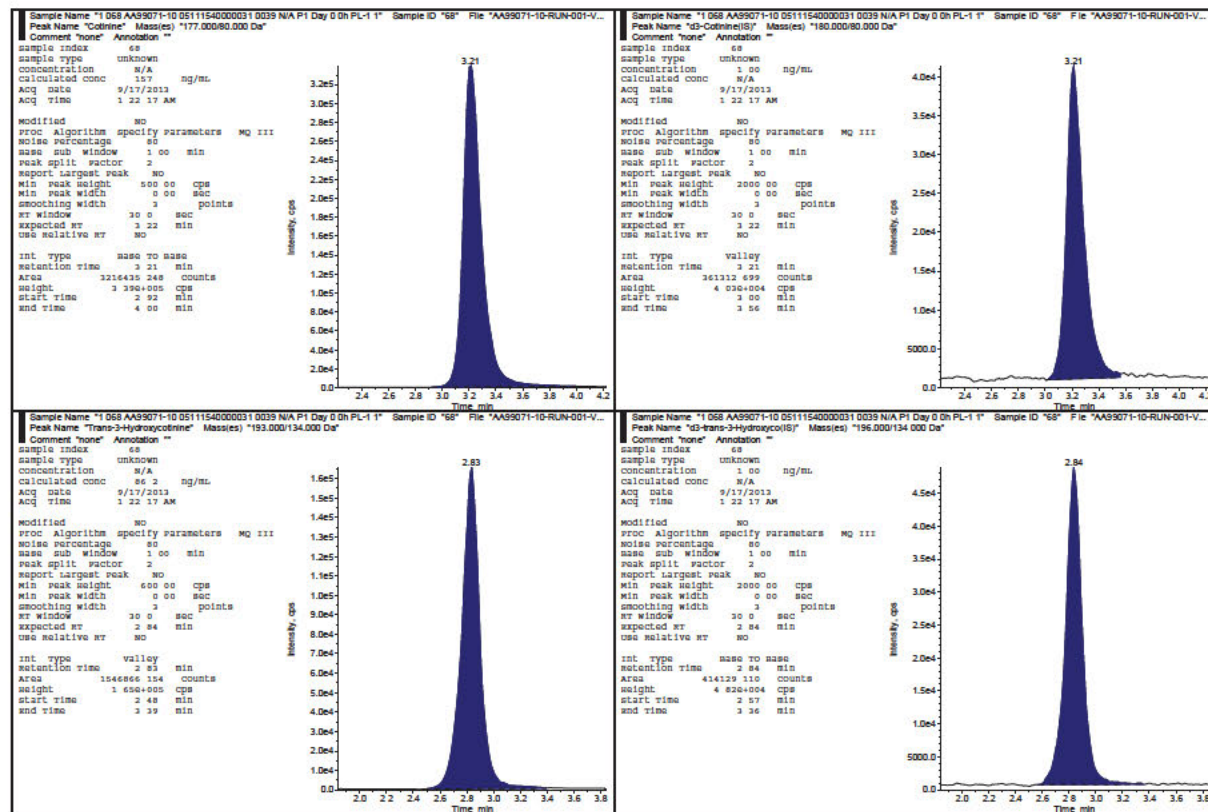


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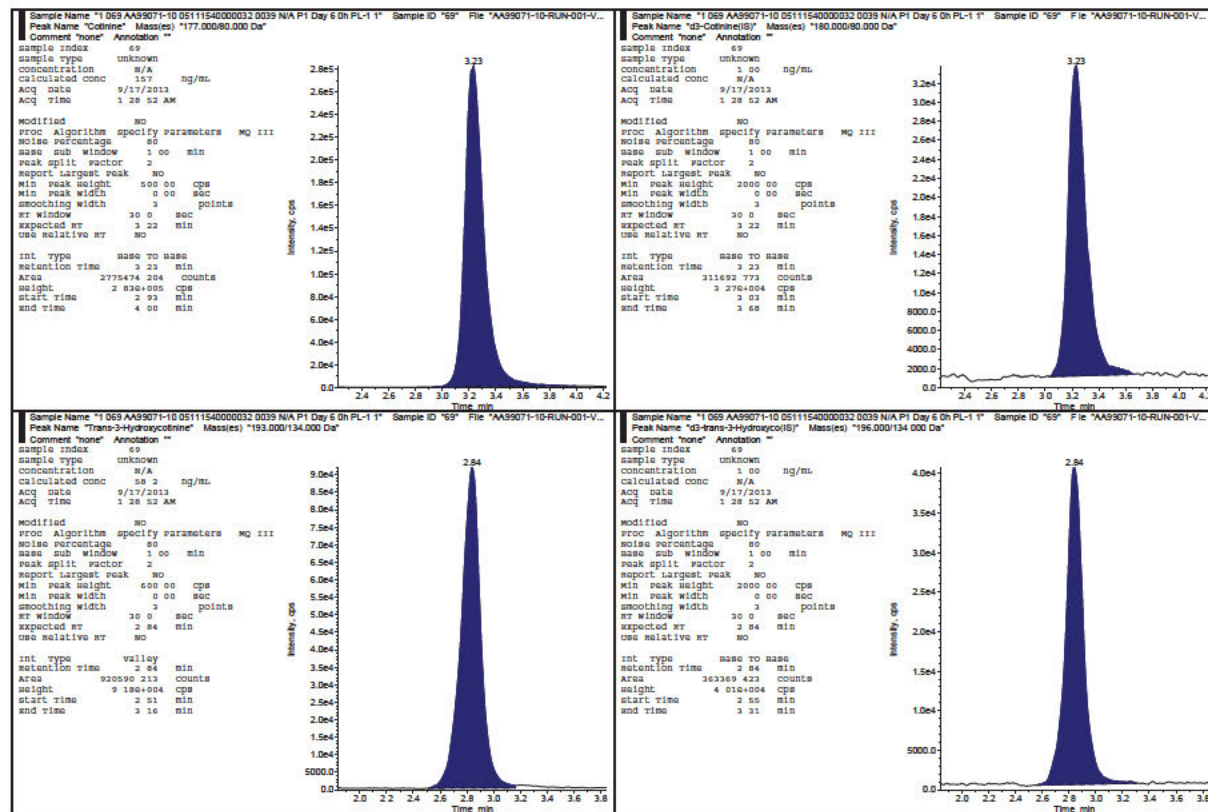


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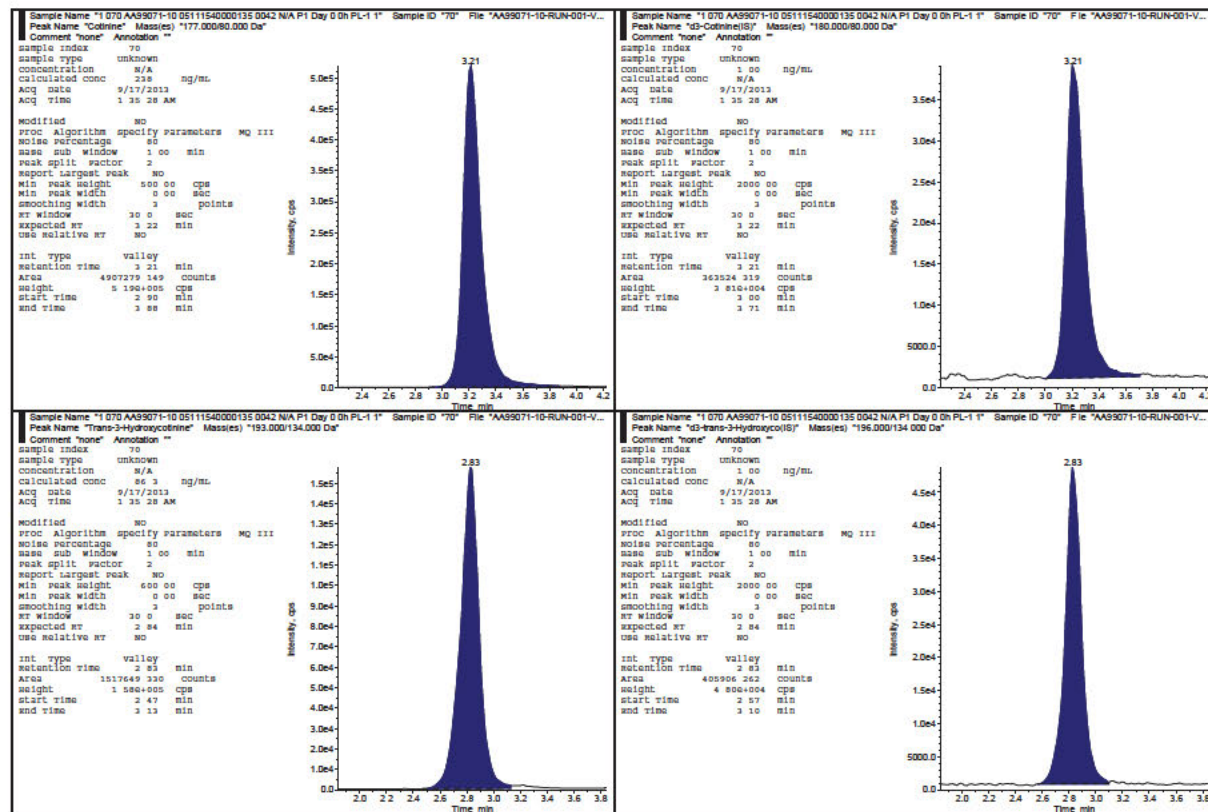


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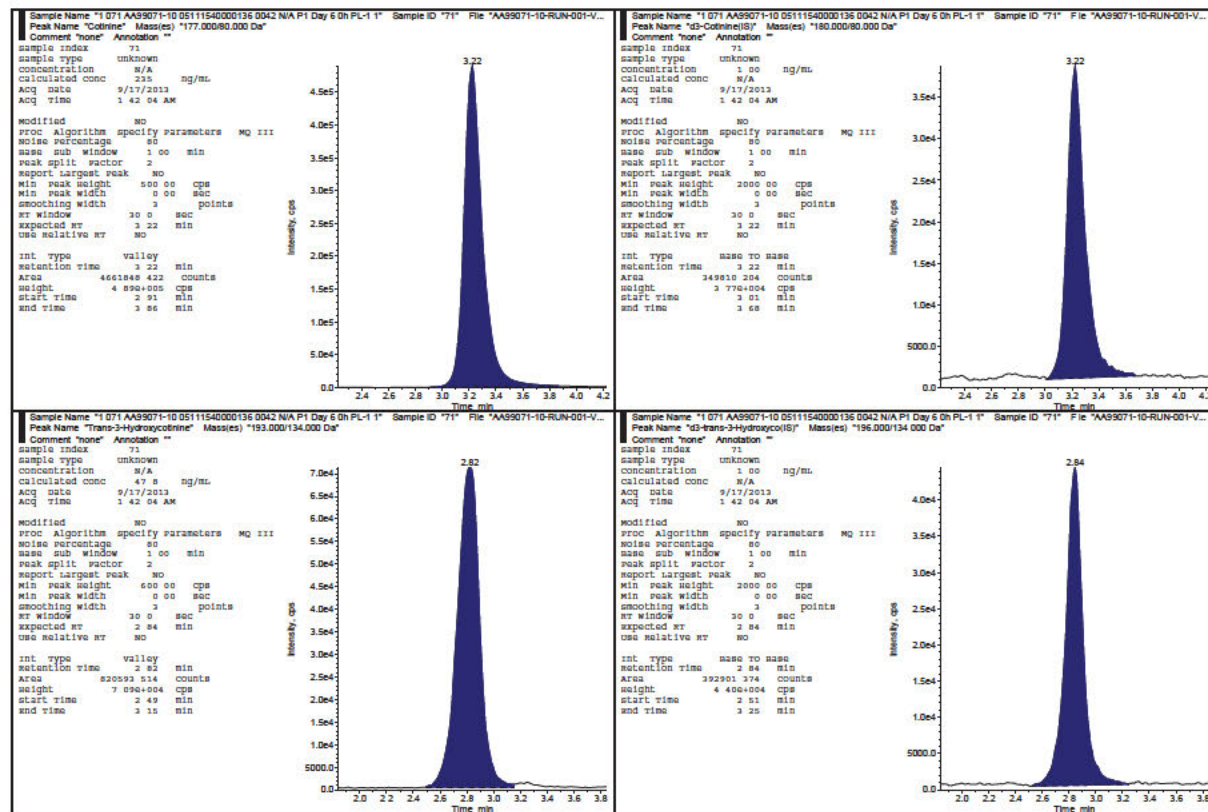


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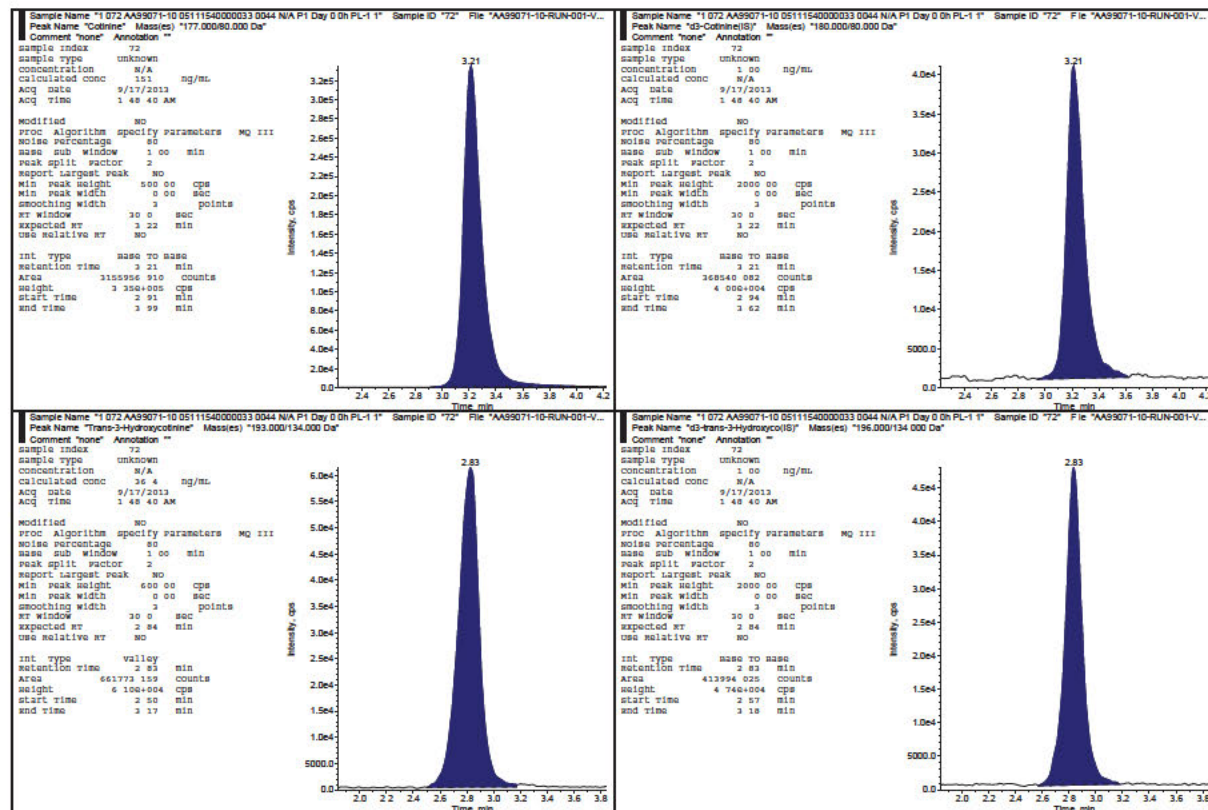


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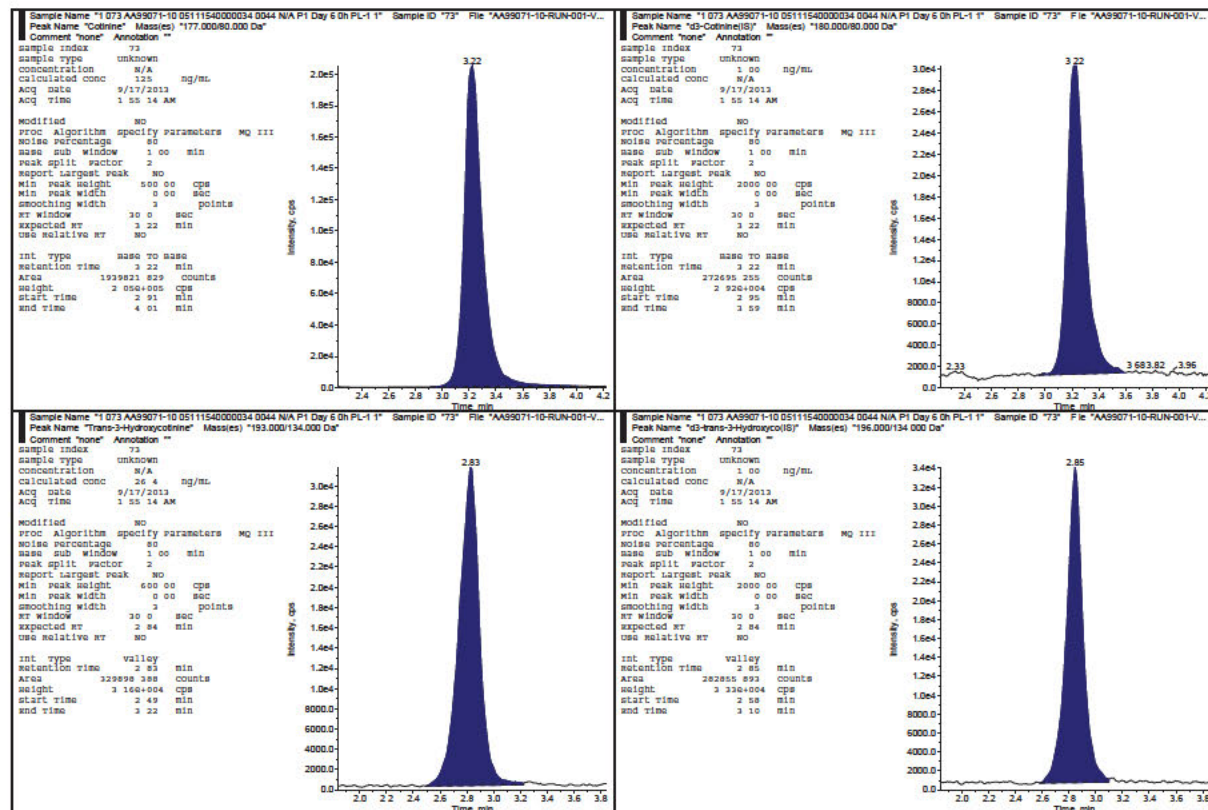


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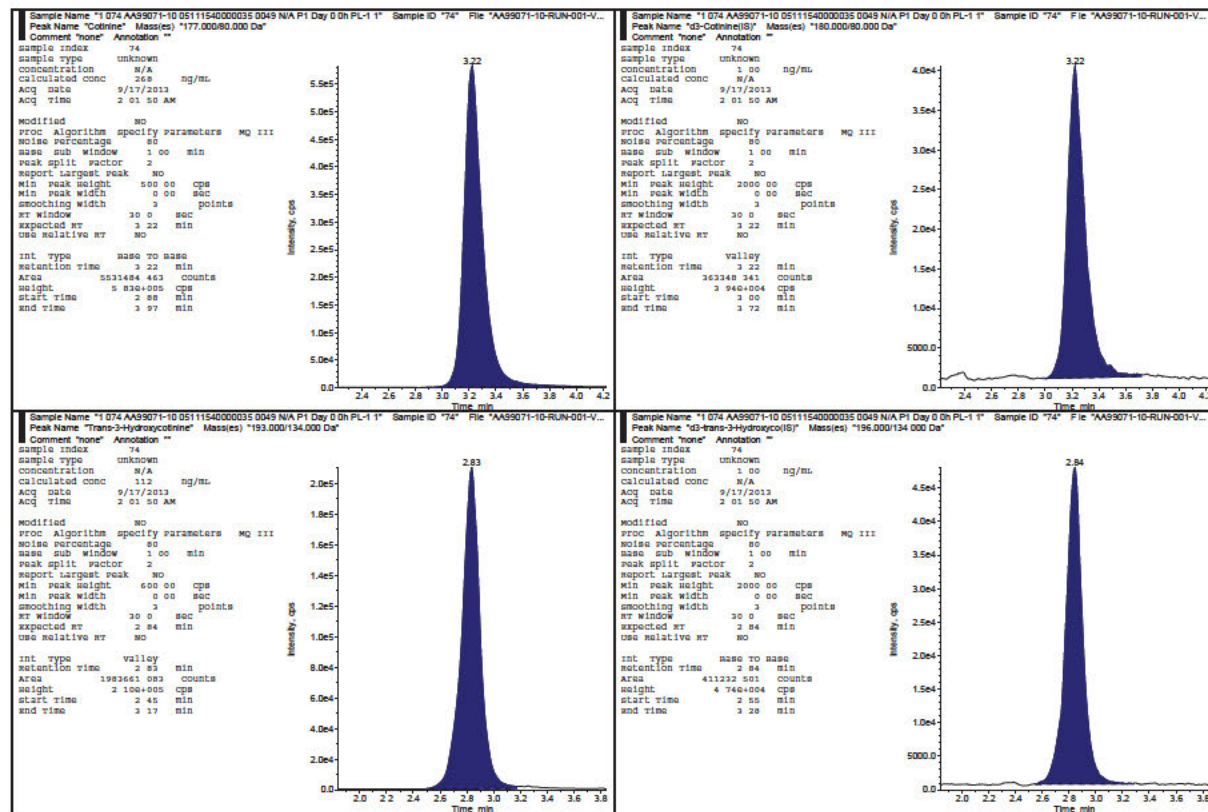


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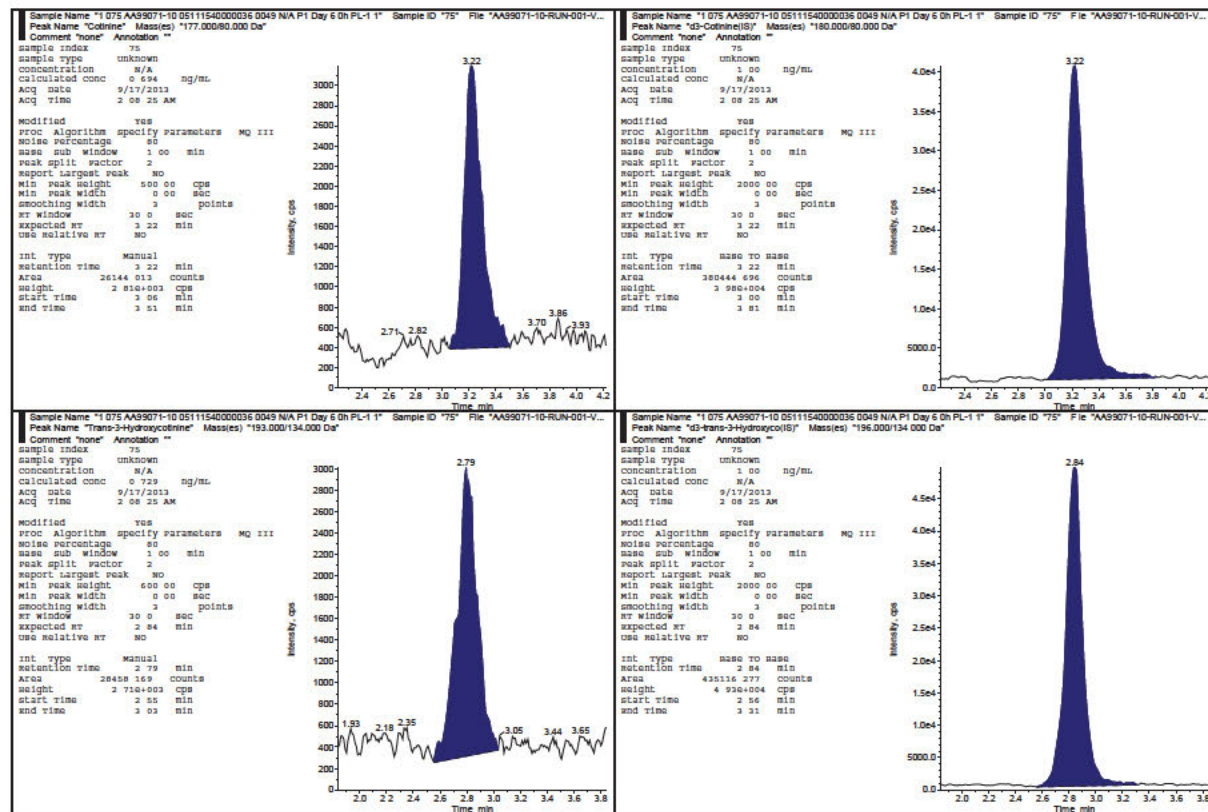


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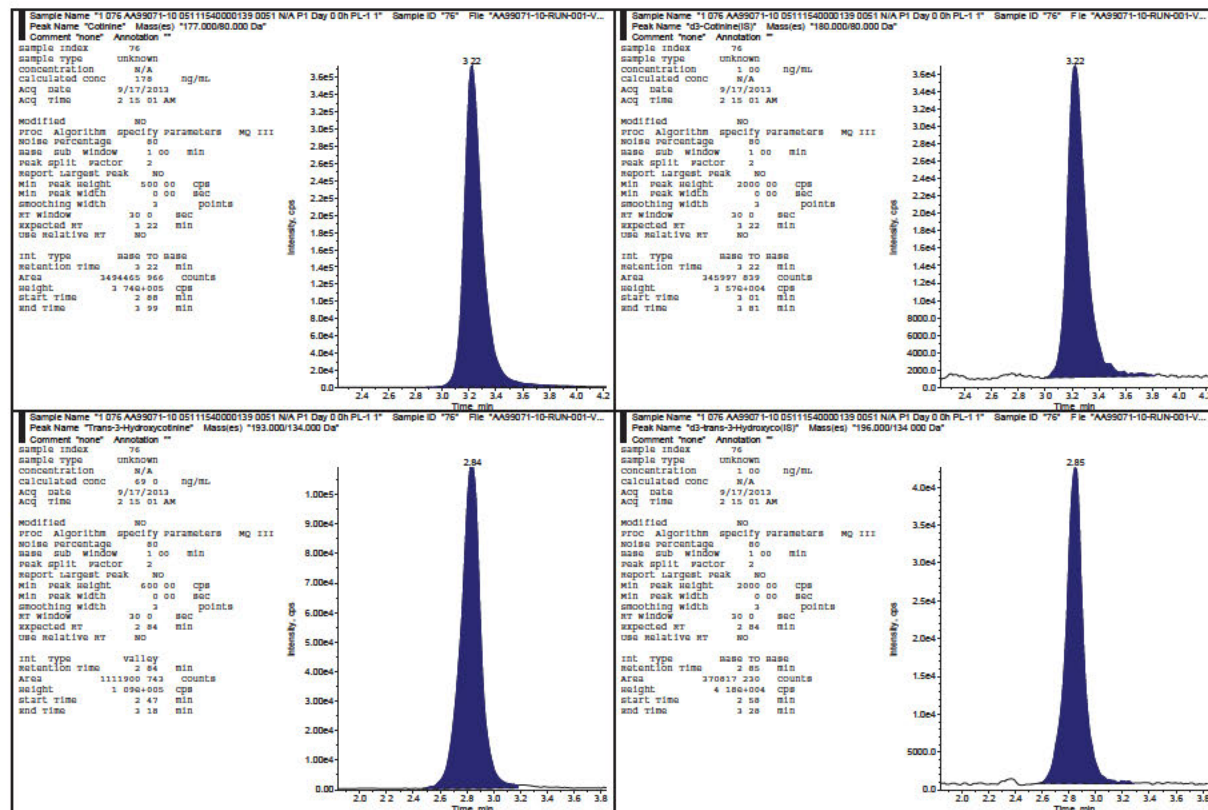


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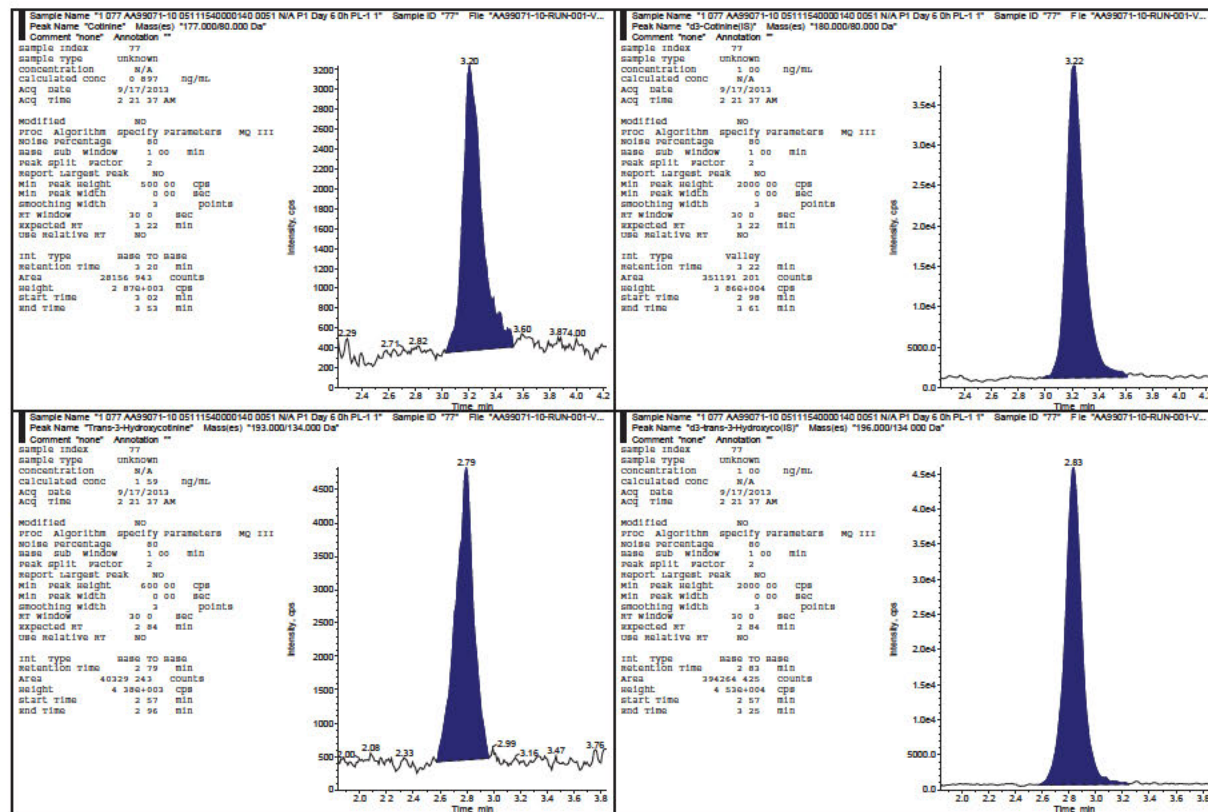


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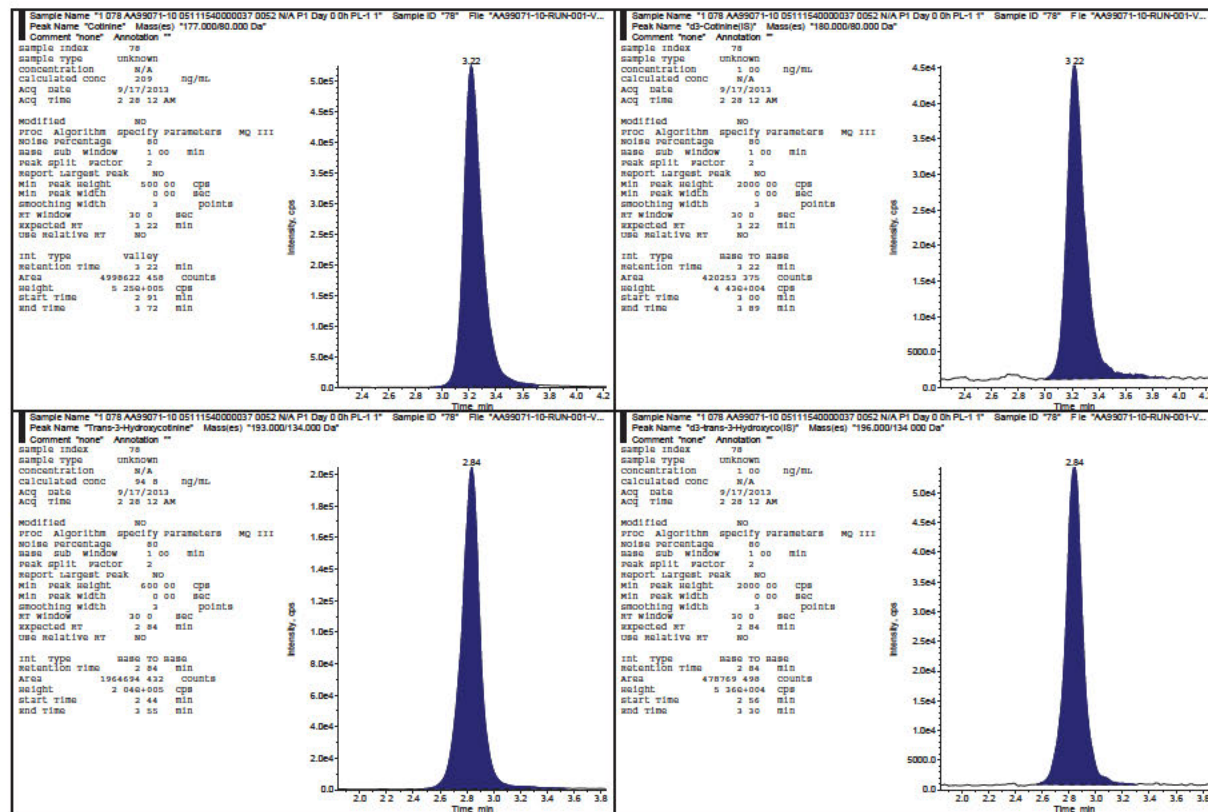


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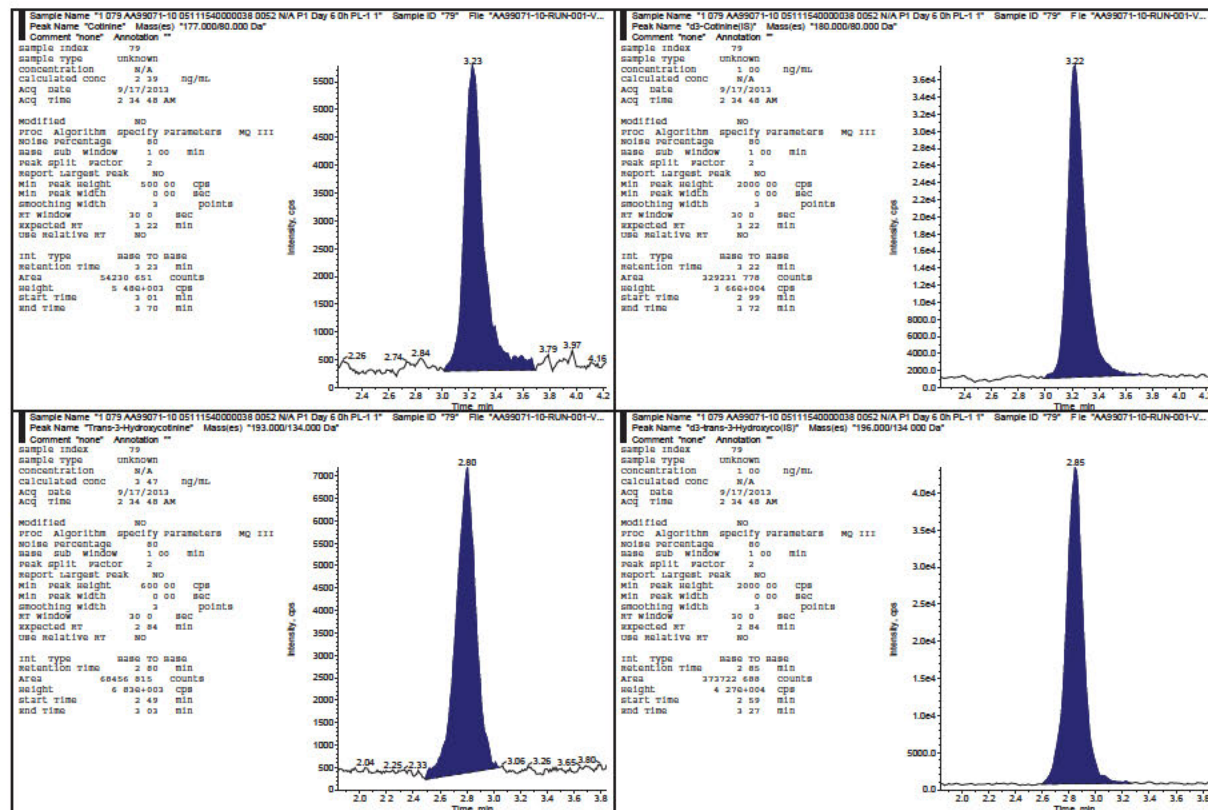


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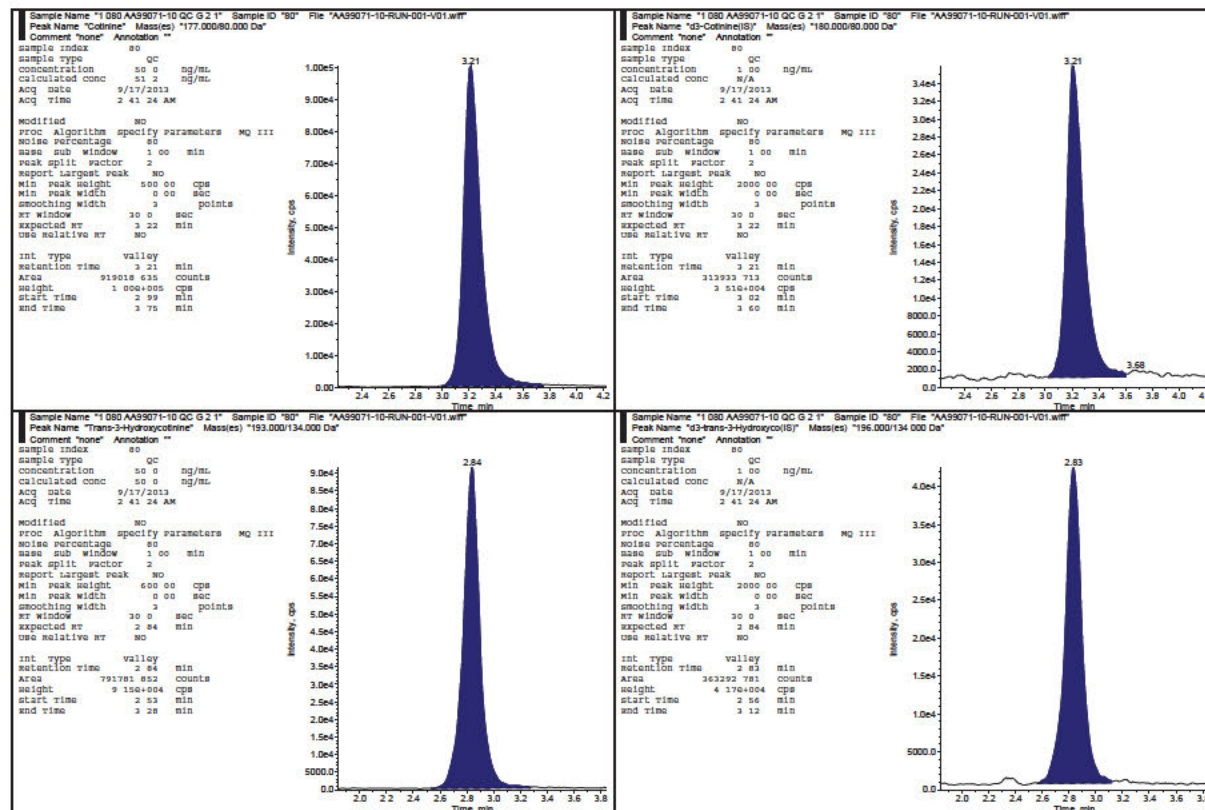


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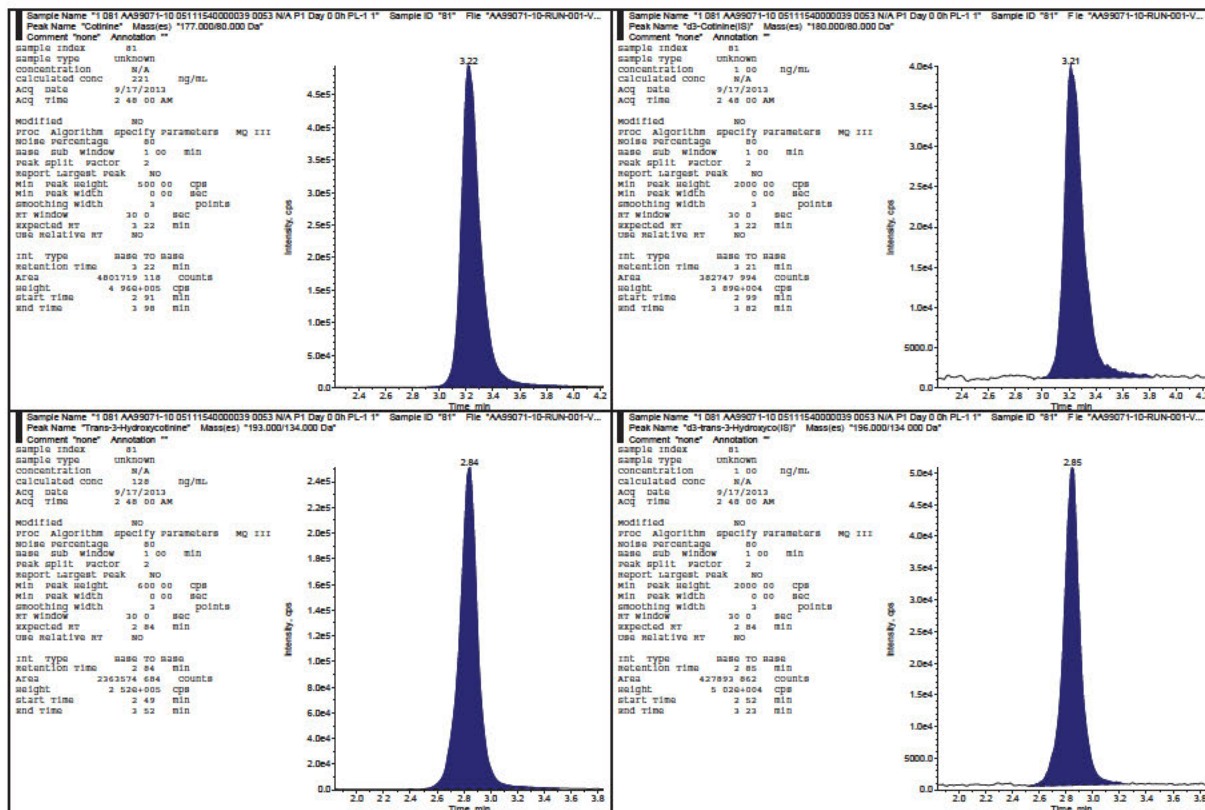


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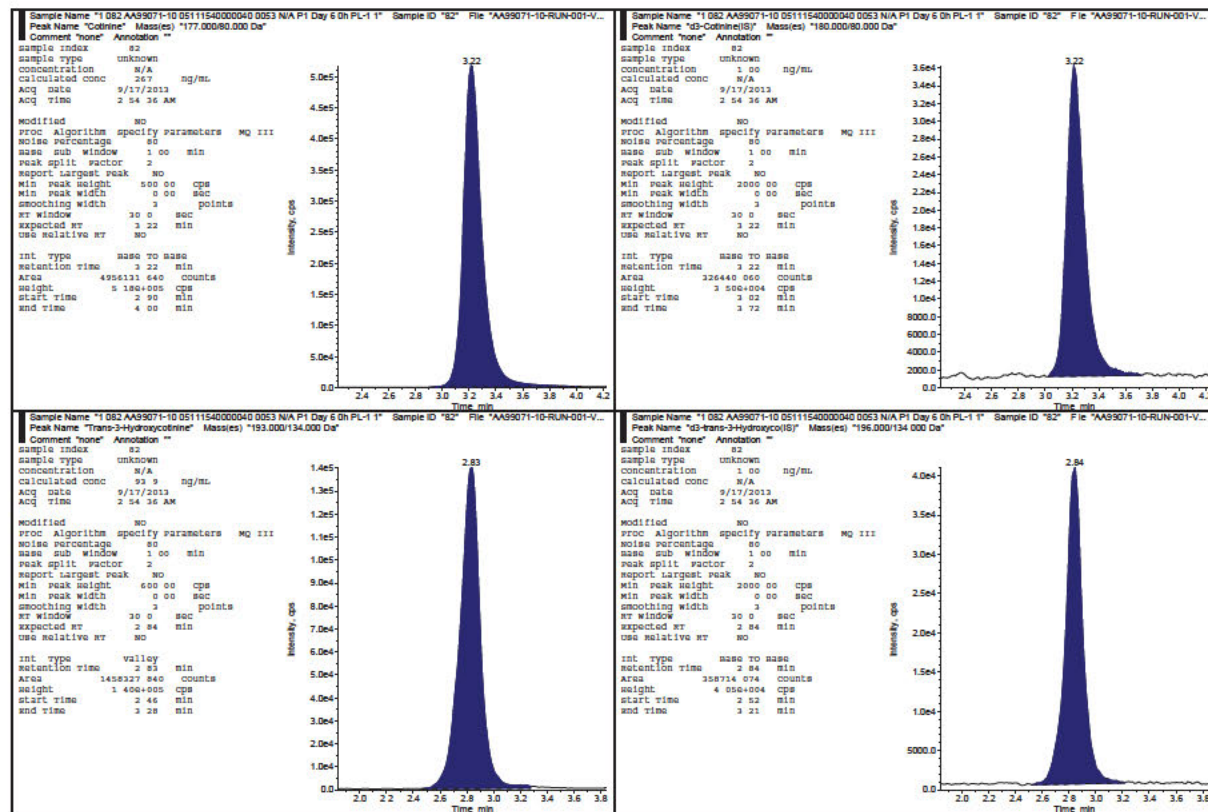


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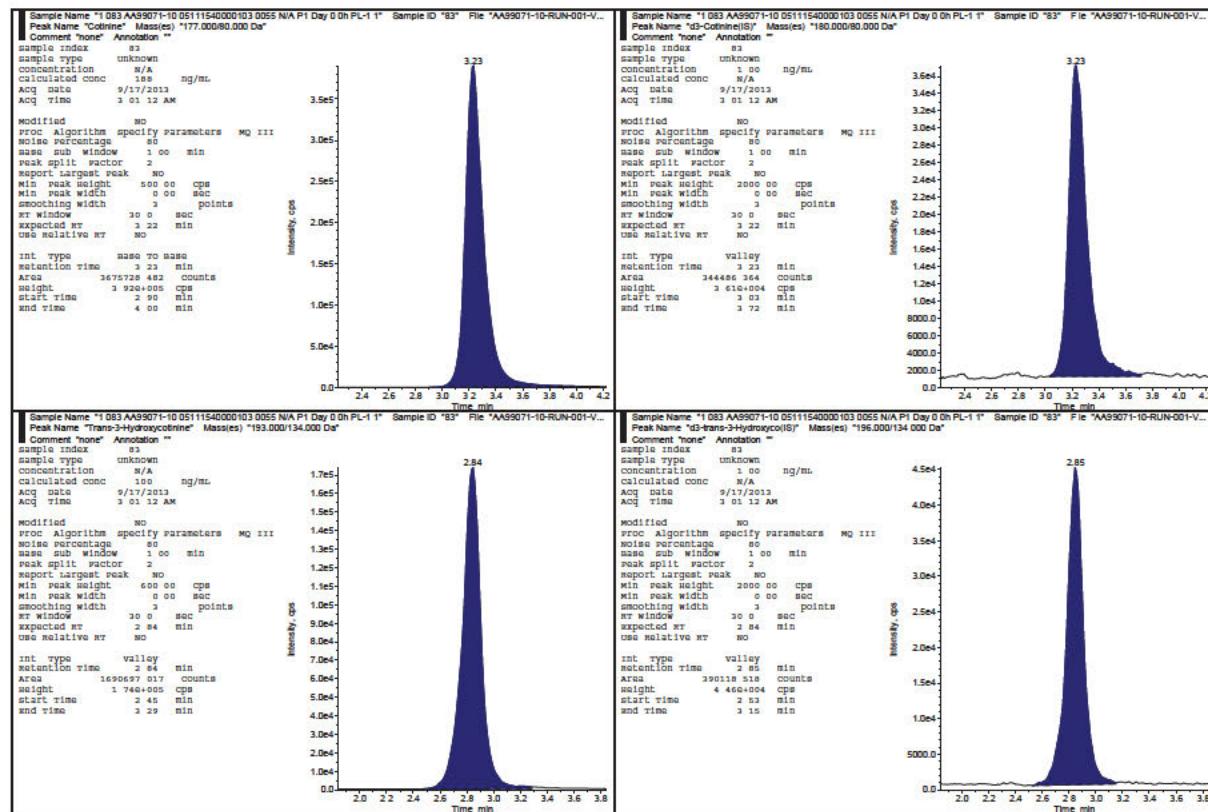


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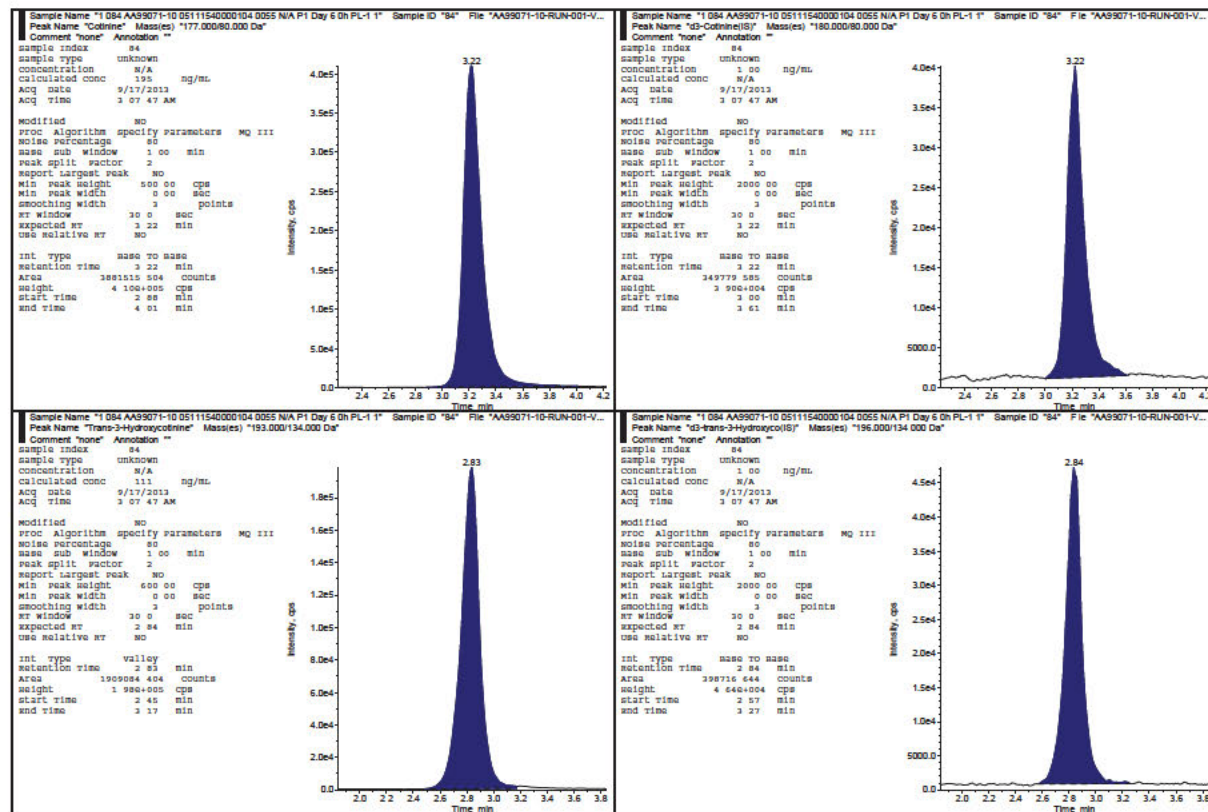


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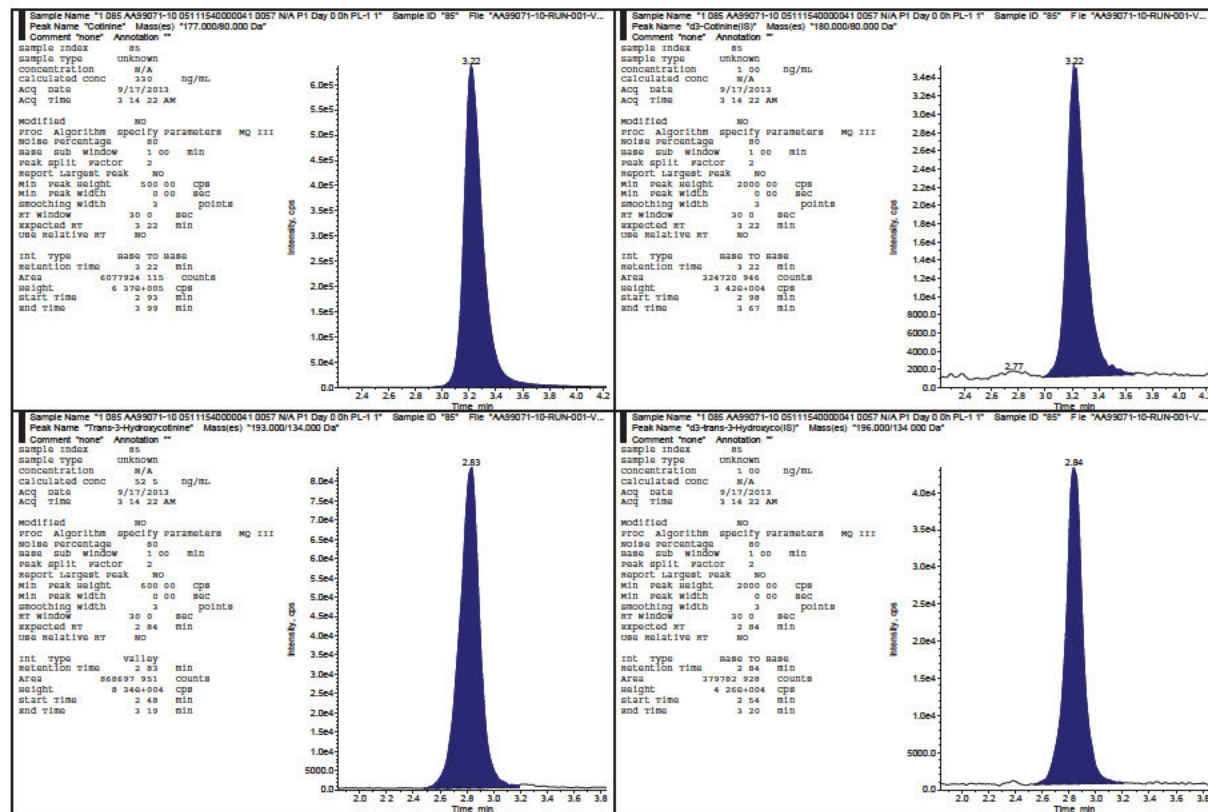


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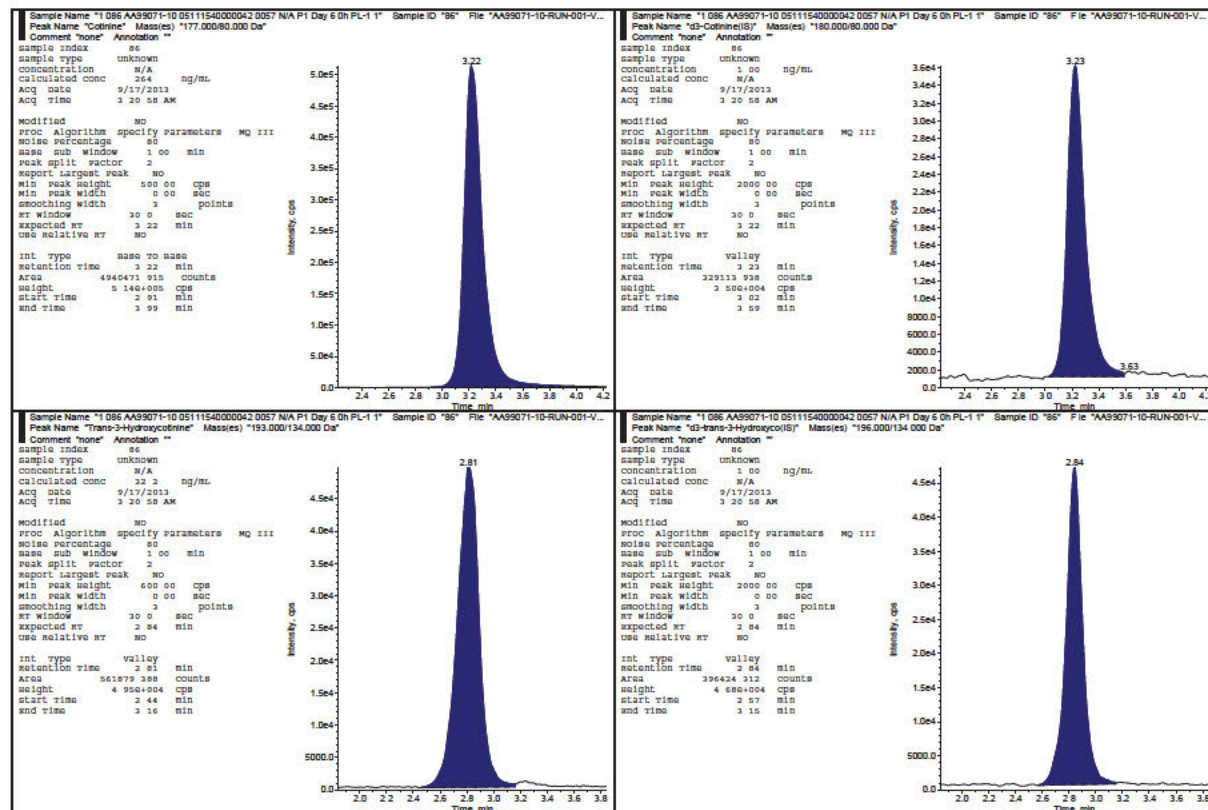


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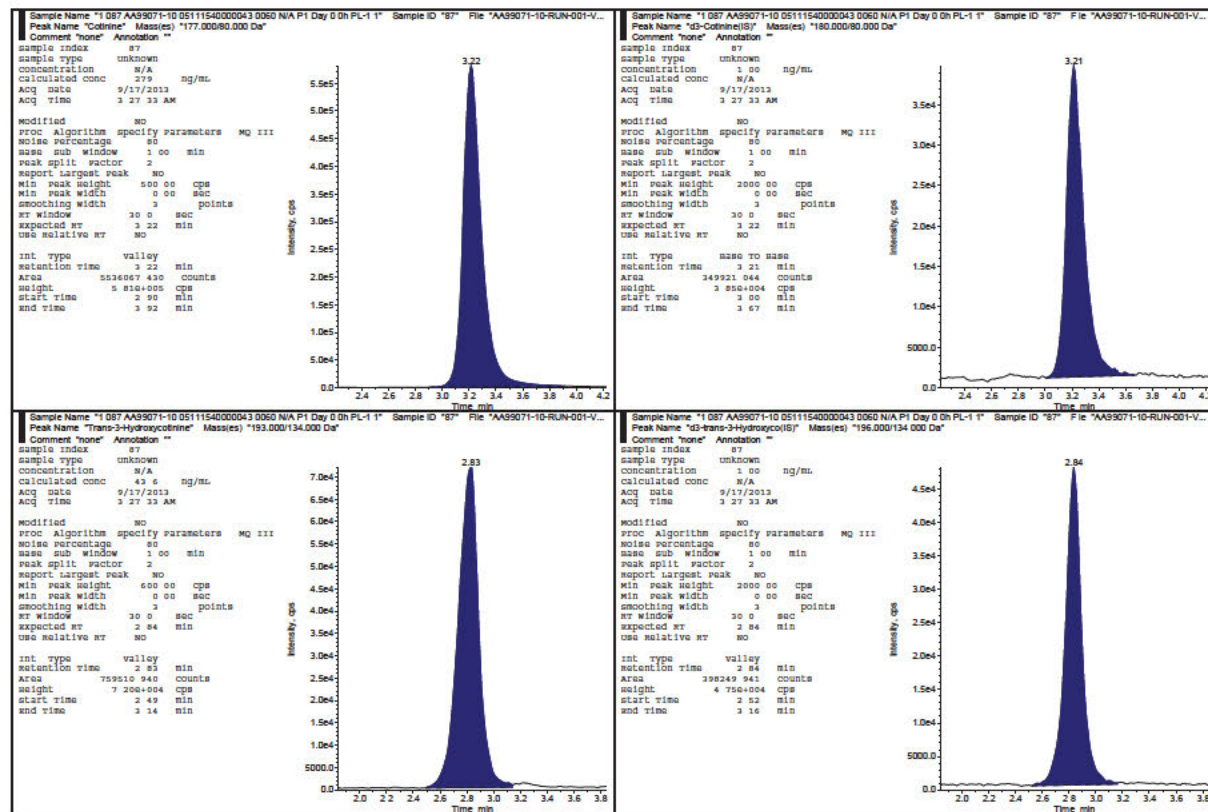


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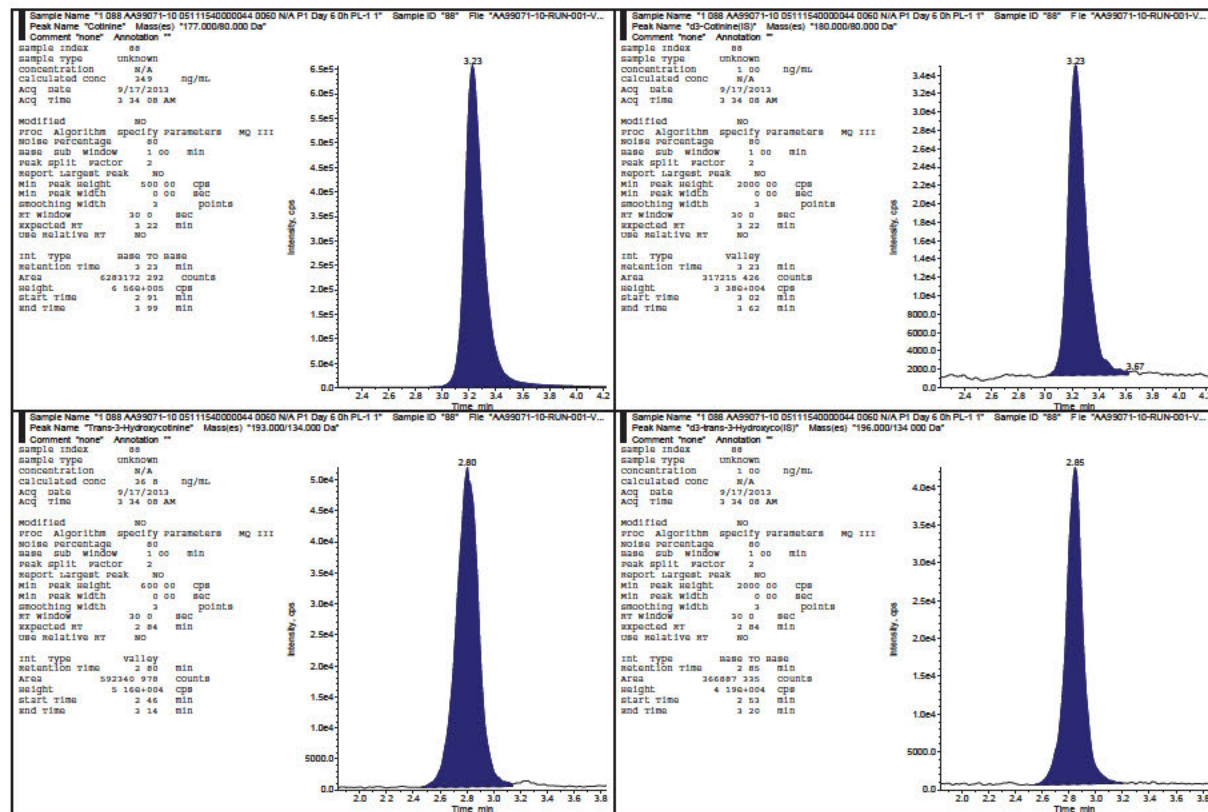


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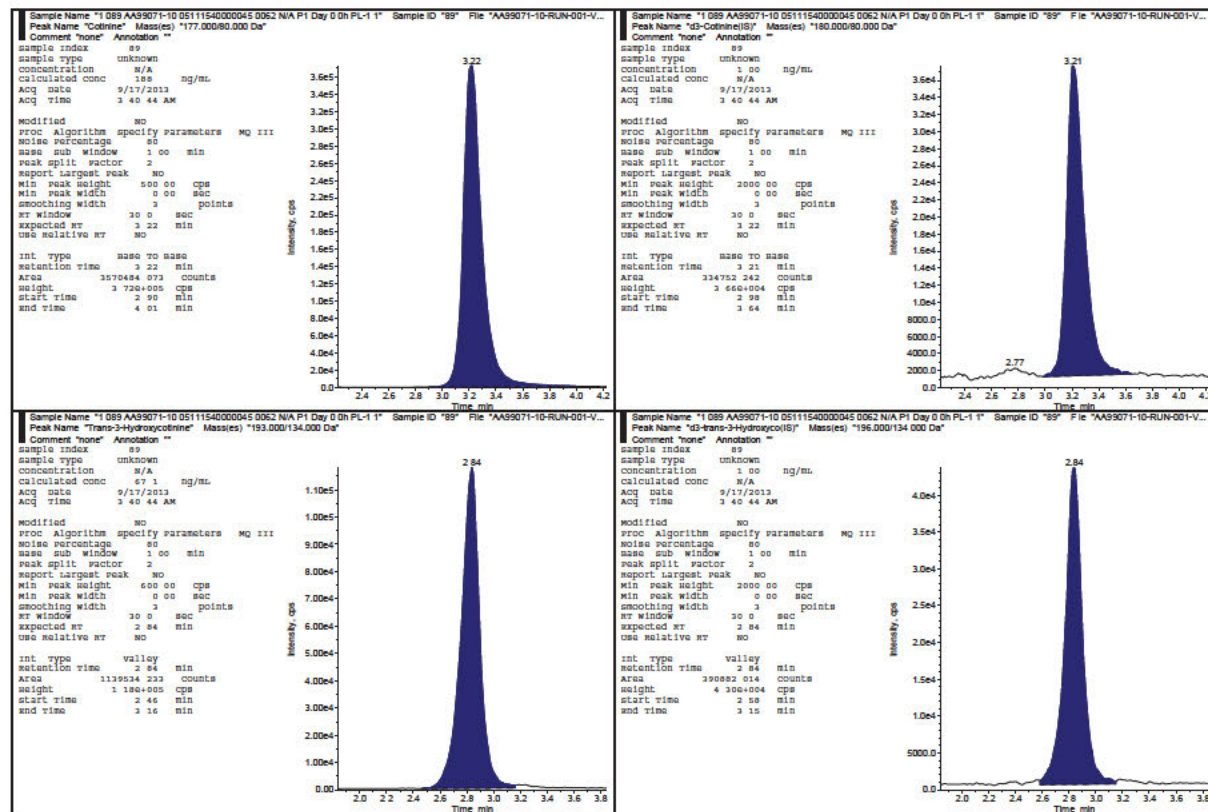


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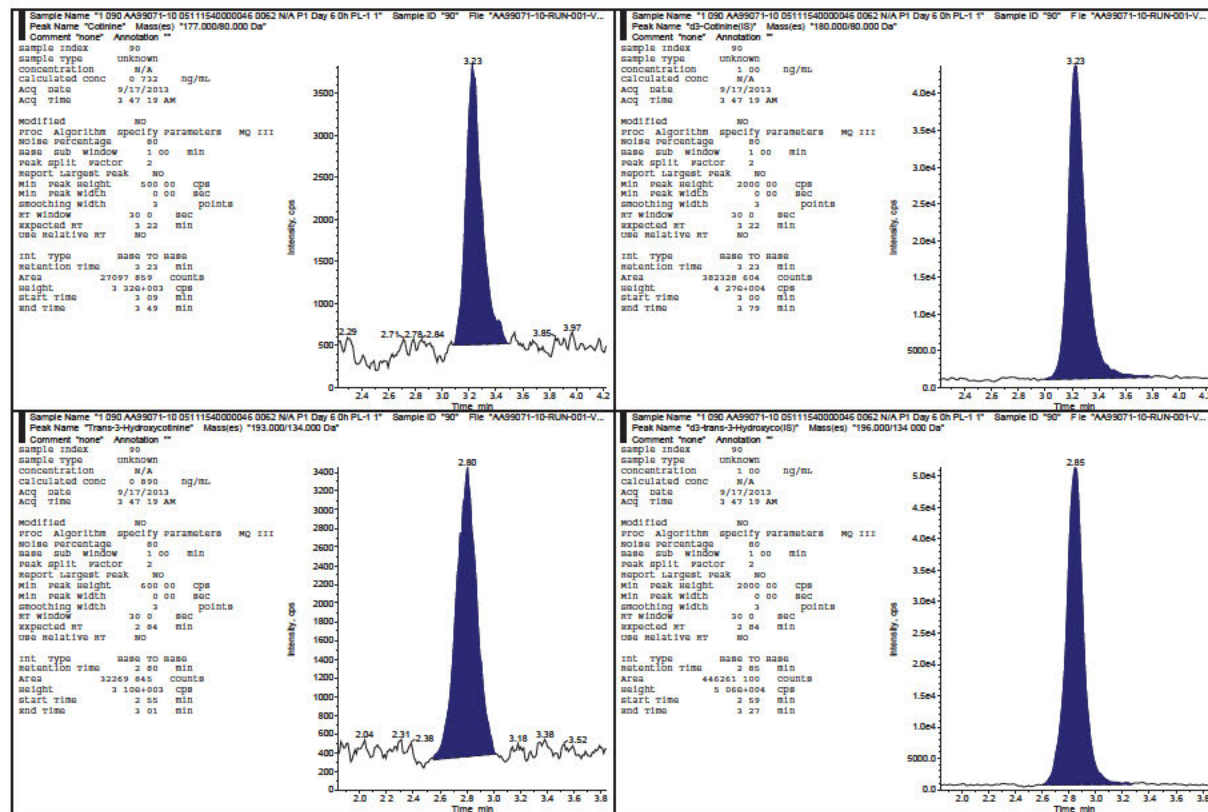


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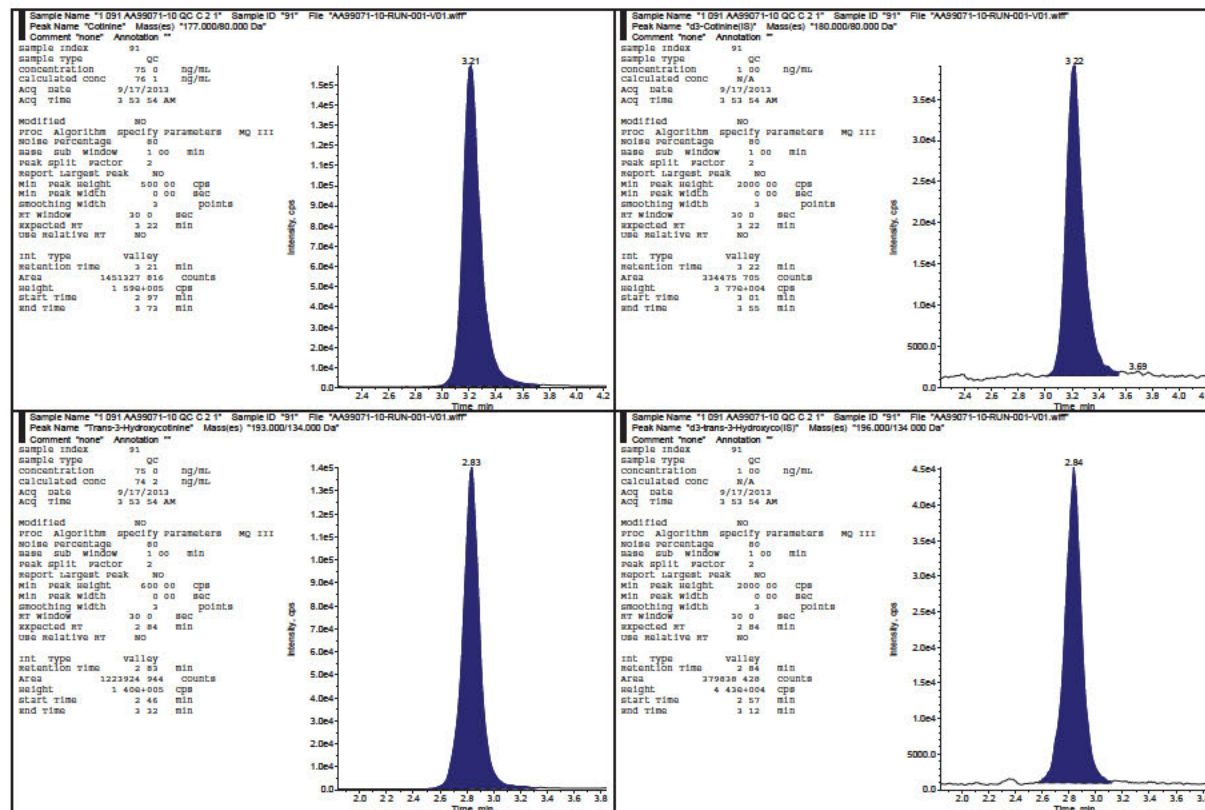


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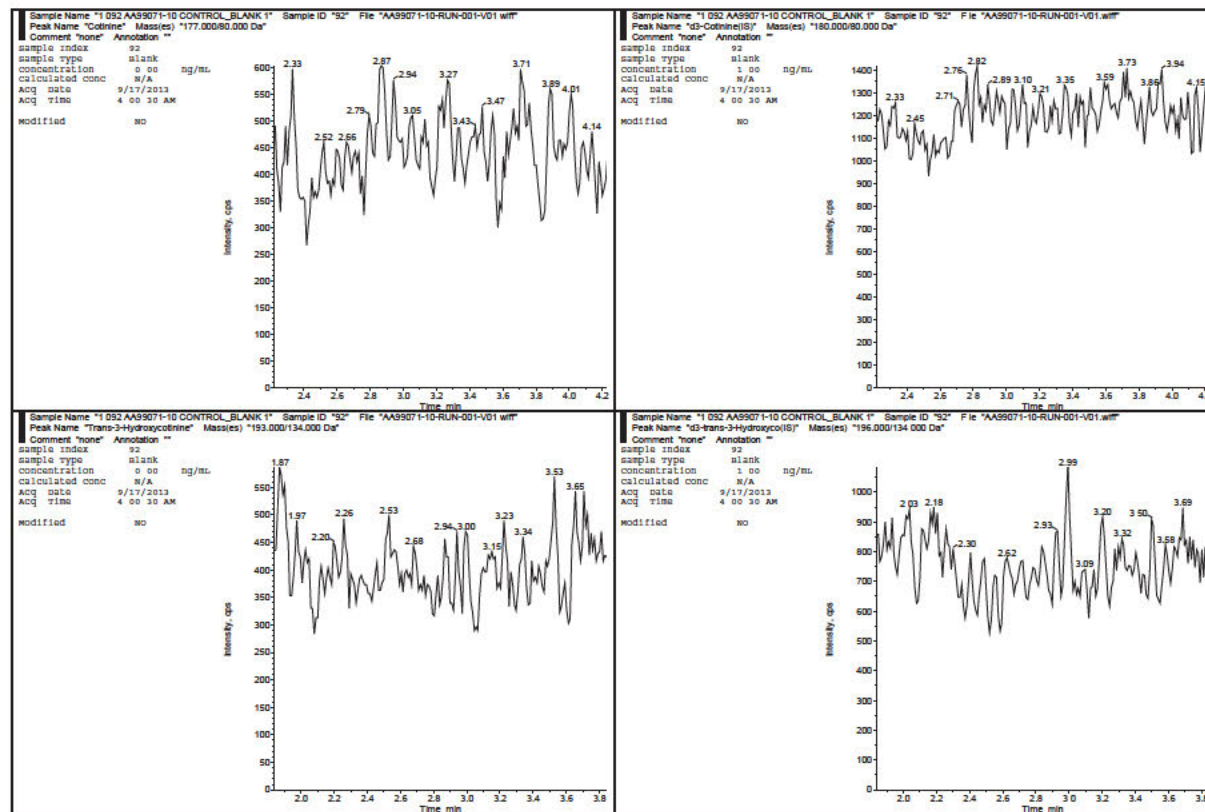


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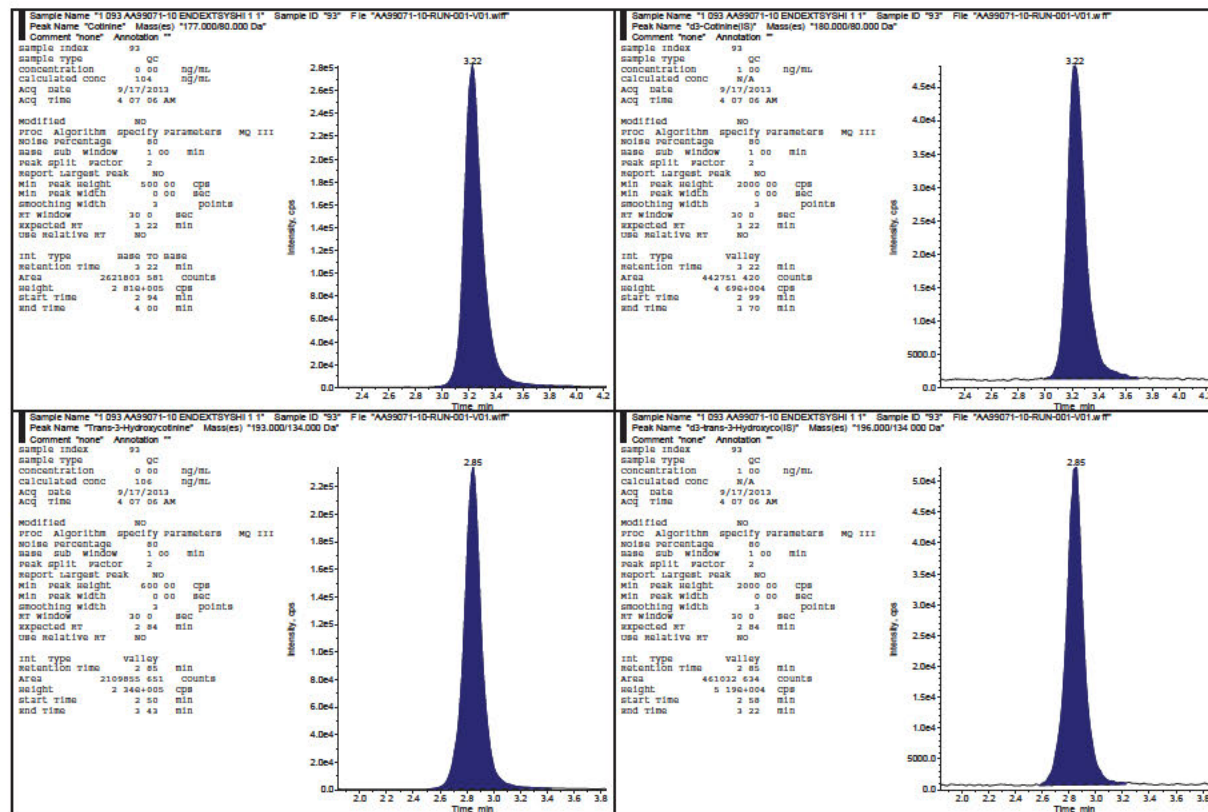


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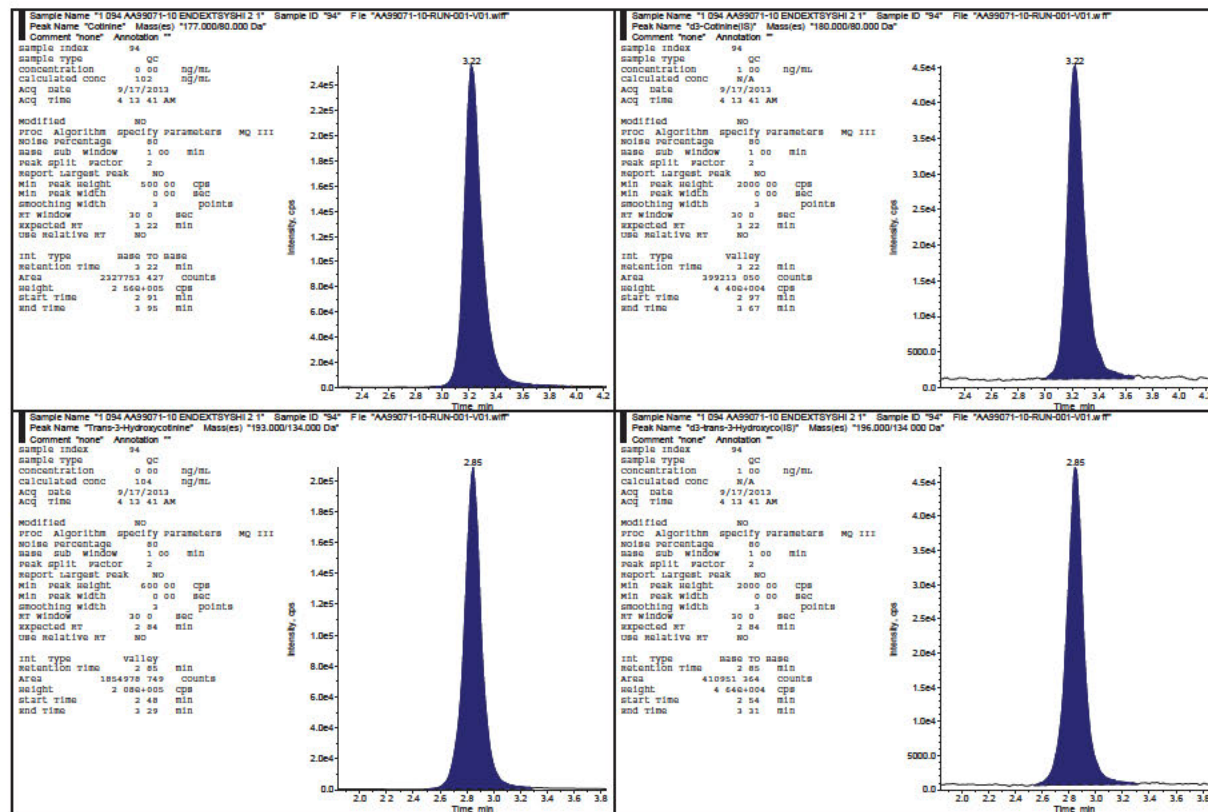


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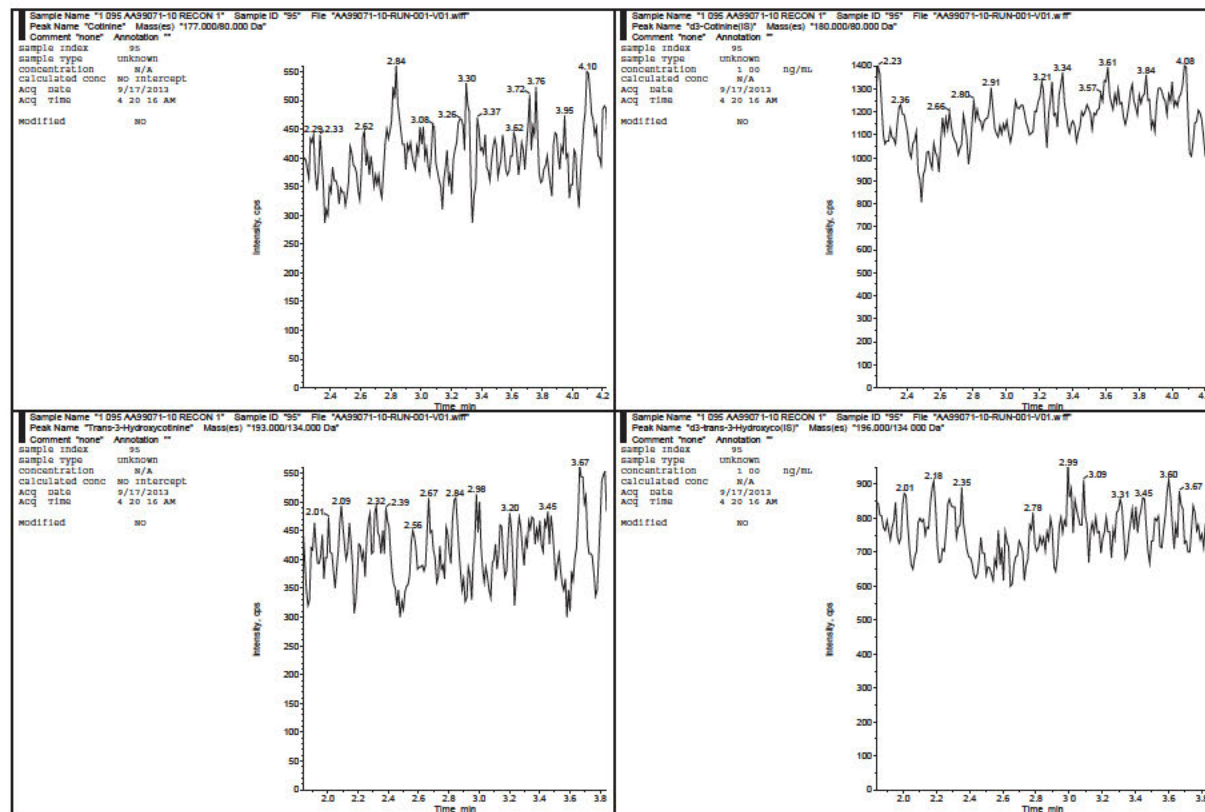


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