



### **16.1.9.3 BIOANALYTICAL REPORTS**

Determination of Caffeine and Paraxanthine in Human Plasma (Lithium Heparin) Samples  
by LC-MS/MS (Study AA99071-08)



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**Determination of Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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: AA99071-08

Bioanalytical Final Report

Philip Morris Products S.A.  
Quai Jeanrenaud 5  
2000 Neuchâtel, Switzerland

Protocol ZRHR-REXC-03-EU

Report Date: 11-Mar-2015

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Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

## STUDY LOCATION

### TEST FACILITY

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**APPROVAL SIGNATURES**

**TEST SITE**

**Celerion:**

Bioanalytical Principal Investigator

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

11-Mar-2015

Date

Management

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

11-Mar-2015

Date





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**SPONSOR**  
**Philip Morris Products, S.A.:**

Manager Clinical Science

  
Christelle Haziza, PhD

  
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

11-Mar-2015

Date

Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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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
Bioanalytical Study Plan Amendment No. 1	23-Sep-2013	23-Sep-2013	24-Sep-2013
Critical Phase Inspection	21-Oct-2013	23-Oct-2013	28-Oct-2013
Database	19, 20-Nov-2013	20-Nov-2013	21-Nov-2013
Bioanalytical Report (Final Draft)	12-May-2014	12-May-2014	04-Sep-2014
Bioanalytical Report (Final)	10, 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.

  
Pat Curl  
Quality Assurance Auditor

15-MAR-2015  
Date



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## 1. INTRODUCTION

The purpose of this bioanalytical study (hereafter referred to as study) was to determine the concentration of caffeine and paraxanthine in human plasma (lithium heparin) 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 21-Oct-2013 and 12-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	Caffeine	d <sub>5</sub> -Caffeine
Source	(b) (4)	(b) (4)
Lot No.	J1D241*	V330P42
Purity	99.8%	99.9%
Celerion Assigned Correction Factor	0.9980	0.9990
Expiry Date	31-Aug-2012*	10-Jun-2014
Storage Conditions	Ambient temperature, protected from light, desiccant	Ambient temperature, protected from light, desiccant

\*Lot J1D241 was current when weighed on 09-Jul-2012 and stock stability was established at 902 days.



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	Analyte	Internal Standard (IS)
ID	Paraxanthine	d <sub>3</sub> -Paraxanthine
Source	(b) (4)	(b) (4)
Lot No.	FN071612-01	S-1356-086A1
Purity / Concentration	99.9% (1.00 mg/mL)	99.9%
Celerion Assigned Correction Factor	1.00	0.9990
Expiry Date	31-Aug-2015	09-Jul-2014
Storage Conditions	Ambient temperature, protected from light	Refrigerated (5 °C), protected from light, desiccant

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

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 lithium heparin as anticoagulant, was purchased from (b) (4) and collected in-house at Celerion, Lincoln, Nebraska. Human plasma stored at -20°C Human plasma (lithium heparin), free of significant interference at the retention time and mass transitions of caffeine, paraxanthine, d<sub>9</sub>-caffeine (IS), and d<sub>3</sub>-paraxanthine (IS) was used to prepare calibration standard and quality control (QC) samples.

### 2.4. Test System

#### 2.4.1. Procedure and Instruments

Procedure and Instrumentation	
Extraction Method	Liquid-liquid extraction
Chromatography system	PerkinElmer® Series 200 Micro Pump or equivalent^
MS/MS system	AB SCIEX API 4000™^
Regression Type	Weighted linear (1/concentration <sup>2</sup> )
Quantitation Method	Peak area ratio
Assay Volume	0.0500 mL
Acceptable level of hemolysis	2%

^ = Qualified systems



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#### 2.4.2. Computer Application Software

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

<sup>^</sup> = Validated systems

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

Non-zero calibration standards were spiked fresh daily at the concentration levels of 20.0, 40.0, 100, 250, 500, 1500, 3000, 4250, and 5000 ng/mL of caffeine and paraxanthine from calibration standard spiking solutions which were prepared in bulk on 03-Oct-2013 and 28-Oct-2013, and stored at -20°C for a period less than 154 days. The calibration standard spiking solutions were prepared at 1x concentrations. To achieve the required standard concentration, 0.0500 mL of standard spiking solution is added to 0.0500 mL of control blank plasma.

Quality control (QC) samples at the concentration levels of 60.0 ng/mL (low basal level + 30.0 ng/mL), 500 ng/mL (low basal level + 470 ng/mL), and 4000 ng/mL (low basal level + 3970 ng/mL) were prepared in bulk on 22-Aug-2013, aliquoted and stored at -20°C. QC samples aliquoted into clear polypropylene tubes were stored under the same conditions as the study samples were stored. The QC samples were analyzed within the established stability period of 545 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 18-Sep-2013 and were received frozen on dry ice between 22-Jul-2013 and 18-Oct-2013 from Covance Central Laboratories, 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.





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### 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 124 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	545 days in polypropylene tubes at -20 C
Short-term Stability	24 hours in polypropylene tubes at ambient temperature and in an ice water bath under white light
Cumulative Short-term Stability	53 hours in polypropylene tubes at ambient temperature and in an ice water bath under white light (total of all thaw cycles)
Freeze-thaw Stability	6 freeze (-20 C)-thaw (ambient temperature and in an ice water bath) cycles in polypropylene tubes under white light
Post-preparative Stability	162 hours in a polypropylene 96 well plate at 5 C
Processed Sample Integrity	148 hours in a polypropylene 96 well plate at 5 C
Sample Shipping Stability	3 days in polypropylene tubes at -80 C

### 2.6.4. Sample Summary

The Sponsor's protocol specifies that clinical samples will be collected from 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 8.6.

	No. of Samples
Specified in protocol/received	320/326
Analysis not required (subject discontinued from enrollment)	7
Samples analyzed in error	5
Duplicates received	326
Total number of study samples analyzed	324

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.



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### 3. SAMPLE ANALYSIS

#### 3.1. Analytical Method

The determination of caffeine and paraxanthine in human plasma (lithium heparin) samples was carried out over a calibration range of 20.0 ng/mL to 5000 ng/mL. The analytical procedure was performed at Celerion, Lincoln, Nebraska and is documented in the Method Validation Report for Celerion Study ZZ25187-02 [5]. The analytical method is documented in BAM SOP ZZ25187-02 [6]. See [Attachment 7](#).

An aliquot of human plasma (lithium heparin) containing each analyte and internal standard was extracted using a liquid-liquid extraction procedure. The extracted samples were analyzed by an HPLC equipped with an AB SCIEX API 4000™ mass spectrometer. Positive ions were monitored in the multiple reaction monitoring (MRM) mode. Quantitation was determined using a weighted linear regression analysis ( $1/\text{concentration}^2$ ) 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.

#### 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).



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Individual data of QC samples 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.
- 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. Carryover acceptance criteria is specified in the bioanalytical method for each assay.

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

Analyte	Carryover criteria (needs to be less than)
Caffeine	0.08%
Paraxanthine	0.08%

### 3.2.3. Acceptance Criteria for ISR

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

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





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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 Sample Performance

Between-analytical run precision and accuracy results for QC samples prepared 60.0, 500, and 4000 ng/mL for caffeine and paraxanthine are summarized in [Table 2](#) and [Table 3](#), respectively.

##### 4.2. Calibration Standard Performance

Back-calculated calibration curve standard concentrations are provided in [Table 4](#) and [Table 5](#) for caffeine and paraxanthine, respectively.

##### 4.3. Standard Curve Parameters

Standard curve parameters from 4 and 4 successful analytical runs are provided in [Table 6](#) and [Table 7](#) for caffeine and paraxanthine, respectively. A representative calibration curve is illustrated in [Figure 1](#) and [Figure 2](#) for caffeine and paraxanthine, respectively.

##### 4.4. Study Sample Concentrations

Study sample concentrations are provided in [Table 8](#) and [Table 9](#) for caffeine and paraxanthine, 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 caffeine and paraxanthine, 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 caffeine and paraxanthine 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.





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#### 4.5.3. Sponsor Selected Reassays

There were no Sponsor selected reassays.

#### 4.5.4. Incurred Sample Reproducibility

The method for the determination of caffeine and paraxanthine was considered reproducible, 97.2% out of 36 repeat analyses for caffeine and paraxanthine met acceptance criteria as defined in [section 3.2.3](#). Results are presented in [Table 12](#) and [Table 13](#).

### 5. CHROMATOGRAMS

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

### 6. DEVIATIONS

**6.1.** Deviation DEV-LNK-13-0561 from LNK SOP.044 V2, Section 2.6, in which Analytical Runs 3 and 6 were injected on a mass spectrometer (EQ-LNK-MS-0039) that was not validated by having a study length qualification batch on it. There was no impact as the SOP was updated effective 25-Oct-2013 as LNK SOP.044 V3 in which the requirement of a study length qualification batch was changed to an acceptable passing qualification batch.

### 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.** The following analytical run was not included in the data set.

<u>Run ID</u>	<u>Analyte</u>	<u>Reason for Non-inclusion</u>
1	Caffeine/Paraxanthine	Analytical Run 1 was reassayed as Analytical Run 4 due to an interference causing 3 of 3 QC As to fail acceptance criteria.

**8.2.** The following analytical run was not included in the data set due to instrumentation issues. The issues were resolved, and the analytical run was reinjected.

<u>Run ID</u>	<u>Analyte</u>	<u>Reason for Non-inclusion</u>
2	Paraxanthine	Analytical Run 2 was reinjected as Analytical Run 5 due to absolute response drift.



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8.3. The following samples from subjects that discontinued from enrollment were inadvertently assayed.

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000539	2	0269	0	6	656	1	OK	Analyzed in Error	Caffeine
05111520000539	5	0269	0	6	836	1	OK	Analyzed in Error	Paraxanthine
05111520000587	2	0288	0	6	1270	1	OK	Analyzed in Error	Caffeine
05111520000587	5	0288	0	6	1000	1	OK	Analyzed in Error	Paraxanthine
05111520000611	2	0299	0	6	771	1	OK	Analyzed in Error	Caffeine
05111520000611	5	0299	0	6	912	1	OK	Analyzed in Error	Paraxanthine
05111520000635	2	0309	0	6	976	1	OK	Analyzed in Error	Caffeine
05111520000635	5	0309	0	6	709	1	OK	Analyzed in Error	Paraxanthine
05111520000639	2	0312	0	6	587	1	OK	Analyzed in Error	Caffeine
05111520000639	5	0312	0	6	663	1	OK	Analyzed in Error	Paraxanthine

8.4. Analytical Run 5 consisted of reassays for paraxanthine only. The analytical run was not regressed for caffeine.

8.5. 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.

8.6. 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)



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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

## 10. CONCLUSION

In this bioanalytical study the concentration was determined in a total of 319 samples for caffeine and 319 samples for paraxanthine in human plasma (lithium heparin) 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] Determination of Caffeine and Paraxanthine in Human Plasma (Heparin) 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 AA99071-08





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- [5] Validation of an LC-MS/MS Method for the Determination of Caffeine and Paraxanthine in Human Plasma (Heparin), Celerion Study ZZ25187-02
- [6] Bioanalytical Method SOP for the Determination of Caffeine and Paraxanthine in Human Plasma (Heparin), Celerion Study ZZ25187-02



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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
Caffeine	1	Rejected	21-Oct-2013	21-Oct-2013	SUBJECTS 0001-0150 PERIOD 1	interference-ext
Caffeine	2	Accepted	28-Oct-2013	29-Oct-2013	SUBJECTS 0152-0320 PERIOD 1	OK
Caffeine	3	Accepted	06-Nov-2013	07-Nov-2013	SUBJECTS 0321-0328 PERIOD 1 + REASSAYS	OK
Caffeine	4	Accepted	31-Oct-2013	02-Nov-2013	RR FAILED BATCH 1	OK
Caffeine	6	Accepted	12-Nov-2013	12-Nov-2013	REASSAYS + ISRs	OK
Paraxanthine	1	Rejected	21-Oct-2013	21-Oct-2013	SUBJECTS 0001-0150 PERIOD 1	interference-ext
Paraxanthine	2	Rejected	28-Oct-2013	29-Oct-2013	SUBJECTS 0152-0320 PERIOD 1	variable response
Paraxanthine	3	Accepted	06-Nov-2013	07-Nov-2013	SUBJECTS 0321-0328 PERIOD 1 + REASSAYS	OK
Paraxanthine	4	Accepted	31-Oct-2013	02-Nov-2013	RR FAILED BATCH 1	OK
Paraxanthine	5	Accepted	28-Oct-2013	31-Oct-2013	SUBJECTS 0152-0320 PD1 (RI of RUN-002 Para only)	OK
Paraxanthine	6	Accepted	12-Nov-2013	12-Nov-2013	REASSAYS + ISRs	OK

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



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Table 2 Quality Control Sample Data (Between-Analytical Run Precision and Accuracy) for Caffeine

Assay Date	Run ID	QC A	QC B	QC C
		60.0 ng/mL	500 ng/mL	4000 ng/mL
29-Oct-2013	2	55.1	484	3940
		56.9	480	4170
		54.7	490	4010
02-Nov-2013	4	57.9	475	3940
		56.2	486	4030
		51.9	485	3990
07-Nov-2013	3	53.2	489	3860
		52.8	489	3800
12-Nov-2013	6	56.5	476	3900
		55.8	465	3810
Mean		55.1	482	3950
S.D.		1.94	7.95	112
%CV		3.5	1.6	2.8
%Theoretical		91.8	96.4	98.8
%Bias		-8.2	-3.6	-1.3
n		10	10	10



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Table 3      Quality Control Sample Data (Between-Analytical Run Precision and Accuracy)  
for Paraxanthine

Assay Date	Run ID	QC A 60.0 ng/mL	QC B 500 ng/mL	QC C 4000 ng/mL
31-Oct-2013	5	55.2	473	4030
		55.2	474	3920
		52.7	476	3950
02-Nov-2013	4	56.0	476	3900
		52.9	452	4020
		51.0	456	3990
07-Nov-2013	3	52.6	500	4010
		52.1	501	4000
12-Nov-2013	6	55.2	480	4140
		53.2	468	4080
Mean		53.6	476	4000
S.D.		1.66	15.9	71.7
%CV		3.1	3.3	1.8
%Theoretical		89.3	95.2	100.0
%Bias		-10.7	-4.8	0.0
n		10	10	10





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Table 4 Back-calculated Calibration Standard Concentrations for Caffeine

Assay Date	Run ID	STD B 20.0 ng/mL	STD C 40.0 ng/mL	STD D 100 ng/mL	STD E 250 ng/mL	STD F 500 ng/mL	STD G 1500 ng/mL	STD H 3000 ng/mL	STD I 4250 ng/mL	STD J 5000 ng/mL
29-Oct-2013	2	19.7	41.7	98.3	255	425	*1990	3070	4370	5330
02-Nov-2013	4	19.9	40.9	97.1	245	512	1470	3040	4300	5020
07-Nov-2013	3	19.9	41.5	92.6	247	523	1510	3040	4220	4980
12-Nov-2013	6	19.5	41.9	102	246	513	1490	2930	4160	5010
Mean		19.8	41.5	97.5	248	493	1490	3020	4260	5090
S D		0.191	0.432	3.88	4.57	45.8	20.0	61.6	91.8	164
%CV		1.0	1.0	4.0	1.8	9.3	1.3	2.0	2.2	3.2
%Bias		-1.0	3.8	-2.5	-0.8	-1.4	-0.7	0.7	0.2	1.8
n		4	4	4	4	4	3	4	4	4

Reason Deactivated

\* Rejected



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Table 5 Back-calculated Calibration Standard Concentrations for Paraxanthine

Assay Date	Run ID	STD B 20.0 ng/mL	STD C 40.0 ng/mL	STD D 100 ng/mL	STD E 250 ng/mL	STD F 500 ng/mL	STD G 1500 ng/mL	STD H 3000 ng/mL	STD I 4250 ng/mL	STD J 5000 ng/mL
31-Oct-2013	5	19.7	41.1	101	245	*406	*1880	3040	4170	5010
02-Nov-2013	4	19.7	41.4	98.3	246	517	1470	2990	4270	4970
07-Nov-2013	3	**19.0	41.1	92.7	249	519	1530	3020	4170	5040
12-Nov-2013	6	19.6	41.4	100	251	511	1490	3000	4200	4850
Mean		19.7	41.3	98.0	248	516	1500	3010	4200	4970
S.D.		0.0577	0.173	3.70	2.75	4.16	30.6	22.2	47.2	83.4
%CV		0.3	0.4	3.8	1.1	0.8	2.0	0.7	1.1	1.7
%Bias		-1.5	3.3	-2.0	-0.8	3.2	0.0	0.3	-1.2	-0.6
n		3	4	4	4	3	3	4	4	4

Reasons Deactivated

\* Rejected

\*\* Not Used (Interference)



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Table 6 Standard Curve Parameters for Caffeine

Assay Date	Run ID	Slope	Intercept	R-Squared
29-Oct-2013	2	0.00101733425	0.00369683118	0.9943
02-Nov-2013	4	0.00211900195	0.00252751614	0.9995
07-Nov-2013	3	0.00171848443	0.00372743351	0.9985
12-Nov-2013	6	0.00172075791	0.00401070004	0.9992
Mean		0.00164389464	0.00349062022	0.9979
S.D.		0.000458176268	0.000657433389	0.0024
%CV		27.9	18.8	0.2
n		4	4	4



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Table 7 Standard Curve Parameters for Paraxanthine

Assay Date	Run ID	Slope	Intercept	R-Squared
31-Oct-2013	5	0.00222751032	0.00541907992	0.9996
02-Nov-2013	4	0.00223448755	0.00857647523	0.9994
07-Nov-2013	3	0.00158350932	0.00916486349	0.9985
12-Nov-2013	6	0.00161059768	0.00997230074	0.9995
Mean		0.00191402622	0.00828317985	0.9993
S.D.		0.000366186676	0.00199328757	0.0005
%CV		19.1	24.1	0.1
n		4	4	4



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Table 8 Study Sample Concentrations for Caffeine

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000001	4	0010	0	6	1070	1	OK		Caffeine
05111520000002	4	0010	5	6	1280	1	OK		Caffeine
05111520000003	4	0011	0	6	788	1	OK		Caffeine
05111520000004	4	0011	5	6	994	1	OK		Caffeine
05111520000005	4	0014	0	6	430	1	OK		Caffeine
05111520000006	4	0014	5	6	670	1	OK		Caffeine
05111520000007	4	0015	0	6	331	1	OK		Caffeine
05111520000008	4	0015	5	6	414	1	OK		Caffeine
05111520000009	4	0016	0	6	1000	1	OK		Caffeine
05111520000010	4	0016	5	6	1760	1	OK		Caffeine
05111520000011	4	0017	0	6	1240	1	OK		Caffeine
05111520000012	4	0017	5	6	1440	1	OK		Caffeine
05111520000013	4	0020	0	6	905	1	OK		Caffeine
05111520000014	4	0020	5	6	1220	1	OK		Caffeine
05111520000015	4	0022	0	6	1620	1	OK		Caffeine
05111520000016	4	0022	5	6	2340	1	OK		Caffeine
05111520000017	4	0023	0	6	393	1	OK		Caffeine
05111520000018	4	0023	5	6	813	1	OK		Caffeine
05111520000019	4	0025	0	6	750	1	OK		Caffeine
05111520000020	4	0025	5	6	567	1	OK		Caffeine
05111520000021	4	0028	0	6	1860	1	OK		Caffeine
05111520000022	4	0028	5	6	2680	1	OK		Caffeine
05111520000023	4	0029	0	6	842	1	OK		Caffeine
05111520000024	4	0029	5	6	1130	1	OK		Caffeine
05111520000025	4	0031	0	6	613	1	OK		Caffeine



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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000026	4	0031	5	6	732	1	OK		Caffeine
05111520000027	4	0035	0	6	370	1	OK		Caffeine
05111520000028	3	0035	5	6	325	1	OK		Caffeine
05111520000029	4	0038	0	6	251	1	OK		Caffeine
05111520000030	4	0038	5	6	257	1	OK		Caffeine
05111520000031	4	0039	0	6	1090	1	OK		Caffeine
05111520000032	4	0039	5	6	1340	1	OK		Caffeine
05111520000033	4	0044	0	6	2080	1	OK		Caffeine
05111520000034	4	0044	5	6	2210	1	OK		Caffeine
05111520000035	4	0049	0	6	301	1	OK		Caffeine
05111520000036	4	0049	5	6	316	1	OK		Caffeine
05111520000037	4	0052	0	6	1220	1	OK		Caffeine
05111520000038	4	0052	5	6	1410	1	OK		Caffeine
05111520000039	4	0053	0	6	997	1	OK		Caffeine
05111520000040	4	0053	5	6	624	1	OK		Caffeine
05111520000041	4	0057	0	6	995	1	OK		Caffeine
05111520000042	6	0057	5	6	1260	1	OK		Caffeine
05111520000043	4	0060	0	6	1200	1	OK		Caffeine
05111520000044	4	0060	5	6	975	1	OK		Caffeine
05111520000045	4	0062	0	6	BLQ<(20.0)	1	OK		Caffeine
05111520000046	4	0062	5	6	1070	1	OK		Caffeine
05111520000047	4	0030	0	6	1320	1	OK		Caffeine
05111520000048	4	0030	5	6	1580	1	OK		Caffeine
05111520000049	4	0034	0	6	799	1	OK		Caffeine
05111520000050	4	0034	5	6	938	1	OK		Caffeine
05111520000051	4	0055	0	6	1730	1	OK		Caffeine
05111520000052	4	0055	5	6	1320	1	OK		Caffeine
05111520000053	4	0064	0	6	854	1	OK		Caffeine





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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000054	4	0064	5	6	527	1	OK		Caffeine
05111520000055	4	0008	0	6	1000	1	OK		Caffeine
05111520000056	4	0008	5	6	1140	1	OK		Caffeine
05111520000115	4	0001	0	6	700	1	OK		Caffeine
05111520000116	4	0001	5	6	968	1	OK		Caffeine
05111520000119	4	0004	0	6	640	1	OK		Caffeine
05111520000120	4	0004	5	6	1080	1	OK		Caffeine
05111520000123	4	0013	0	6	691	1	OK		Caffeine
05111520000124	4	0013	5	6	603	1	OK		Caffeine
05111520000127	4	0021	0	6	932	1	OK		Caffeine
05111520000128	4	0021	5	6	1090	1	OK		Caffeine
05111520000131	4	0037	0	6	617	1	OK		Caffeine
05111520000132	4	0037	5	6	534	1	OK		Caffeine
05111520000135	4	0042	0	6	448	1	OK		Caffeine
05111520000136	4	0042	5	6	413	1	OK		Caffeine
05111520000139	4	0051	0	6	1580	1	OK		Caffeine
05111520000140	4	0051	5	6	1780	1	OK		Caffeine
05111520000143	4	0063	0	6	990	1	OK		Caffeine
05111520000144	4	0063	5	6	1870	1	OK		Caffeine
05111520000147	4	0066	0	6	863	1	OK		Caffeine
05111520000148	4	0066	5	6	1020	1	OK		Caffeine
05111520000151	4	0067	0	6	994	1	OK		Caffeine
05111520000152	4	0067	5	6	1080	1	OK		Caffeine
05111520000155	4	0069	0	6	566	1	OK		Caffeine
05111520000156	4	0069	5	6	726	1	OK		Caffeine
05111520000159	4	0071	0	6	475	1	OK		Caffeine
05111520000160	4	0071	5	6	986	1	OK		Caffeine
05111520000163	4	0072	0	6	565	1	OK		Caffeine





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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000164	4	0072	5	6	587	1	OK		Caffeine
05111520000167	4	0074	0	6	749	1	OK		Caffeine
05111520000168	4	0074	5	6	1310	1	OK		Caffeine
05111520000171	4	0076	0	6	698	1	OK		Caffeine
05111520000172	4	0076	5	6	761	1	OK		Caffeine
05111520000175	4	0080	0	6	954	1	OK		Caffeine
05111520000176	4	0080	5	6	1220	1	OK		Caffeine
05111520000179	4	0083	0	6	1050	1	OK		Caffeine
05111520000180	4	0083	5	6	1440	1	OK		Caffeine
05111520000183	4	0085	0	6	1110	1	OK		Caffeine
05111520000187	4	0086	0	6	1080	1	OK		Caffeine
05111520000188	4	0086	5	6	1290	1	OK		Caffeine
05111520000191	4	0087	0	6	1000	1	OK		Caffeine
05111520000192	4	0087	5	6	777	1	OK		Caffeine
05111520000195	4	0088	0	6	2100	1	OK		Caffeine
05111520000196	4	0088	5	6	2470	1	OK		Caffeine
05111520000199	4	0090	0	6	798	1	OK		Caffeine
05111520000200	4	0090	5	6	1090	1	OK		Caffeine
05111520000203	4	0093	0	6	502	1	OK		Caffeine
05111520000204	4	0093	5	6	1000	1	OK		Caffeine
05111520000207	4	0104	0	6	2290	1	OK		Caffeine
05111520000208	4	0104	5	6	2160	1	OK		Caffeine
05111520000211	4	0105	0	6	888	1	OK		Caffeine
05111520000212	4	0105	5	6	818	1	OK		Caffeine
05111520000215	4	0106	0	6	842	1	OK		Caffeine
05111520000216	4	0106	5	6	856	1	OK		Caffeine
05111520000219	4	0107	0	6	521	1	OK		Caffeine
05111520000220	4	0107	5	6	1120	1	OK		Caffeine



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000223	4	0110	0	6	1730	1	OK		Caffeine
05111520000224	4	0110	5	6	1910	1	OK		Caffeine
05111520000227	4	0112	0	6	791	1	OK		Caffeine
05111520000228	4	0112	5	6	1020	1	OK		Caffeine
05111520000231	4	0114	0	6	935	1	OK		Caffeine
05111520000232	4	0114	5	6	1170	1	OK		Caffeine
05111520000235	4	0117	0	6	1180	1	OK		Caffeine
05111520000236	4	0117	5	6	1200	1	OK		Caffeine
05111520000239	4	0118	0	6	1230	1	OK		Caffeine
05111520000240	4	0118	5	6	1490	1	OK		Caffeine
05111520000243	4	0121	0	6	1960	1	OK		Caffeine
05111520000244	4	0121	5	6	1960	1	OK		Caffeine
05111520000247	4	0122	0	6	965	1	OK		Caffeine
05111520000248	4	0122	5	6	1110	1	OK		Caffeine
05111520000251	4	0123	0	6	939	1	OK		Caffeine
05111520000252	4	0123	5	6	1140	1	OK		Caffeine
05111520000255	4	0133	0	6	633	1	OK		Caffeine
05111520000256	4	0133	5	6	711	1	OK		Caffeine
05111520000259	2	0190	0	6	1580	1	OK		Caffeine
05111520000260	2	0190	5	6	1420	1	OK		Caffeine
05111520000263	4	0126	0	6	1020	1	OK		Caffeine
05111520000264	4	0126	5	6	803	1	OK		Caffeine
05111520000267	4	0127	0	6	329	1	OK		Caffeine
05111520000268	4	0127	5	6	431	1	OK		Caffeine
05111520000271	4	0128	0	6	1010	1	OK		Caffeine
05111520000272	4	0128	5	6	1150	1	OK		Caffeine
05111520000275	4	0129	0	6	1750	1	OK		Caffeine
05111520000276	4	0129	5	6	1340	1	OK		Caffeine



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000279	4	0130	0	6	1020	1	OK		Caffeine
05111520000280	4	0130	5	6	1430	1	OK		Caffeine
05111520000283	4	0134	0	6	876	1	OK		Caffeine
05111520000284	4	0134	5	6	1090	1	OK		Caffeine
05111520000287	4	0136	0	6	1130	1	OK		Caffeine
05111520000288	4	0136	5	6	2620	1	OK		Caffeine
05111520000291	4	0137	0	6	1110	1	OK		Caffeine
05111520000292	4	0137	5	6	1230	1	OK		Caffeine
05111520000295	4	0139	0	6	1200	1	OK		Caffeine
05111520000296	4	0139	5	6	957	1	OK		Caffeine
05111520000299	4	0140	0	6	1880	1	OK		Caffeine
05111520000300	4	0140	5	6	1420	1	OK		Caffeine
05111520000303	4	0145	0	6	2060	1	OK		Caffeine
05111520000304	4	0145	5	6	2350	1	OK		Caffeine
05111520000307	4	0147	0	6	817	1	OK		Caffeine
05111520000308	4	0147	5	6	1070	1	OK		Caffeine
05111520000311	4	0148	0	6	632	1	OK		Caffeine
05111520000312	4	0148	5	6	398	1	OK		Caffeine
05111520000315	4	0149	0	6	692	1	OK		Caffeine
05111520000316	4	0149	5	6	793	1	OK		Caffeine
05111520000319	4	0150	0	6	752	1	OK		Caffeine
05111520000320	4	0150	5	6	853	1	OK		Caffeine
05111520000323	2	0152	0	6	1220	1	OK		Caffeine
05111520000324	2	0152	5	6	1020	1	OK		Caffeine
05111520000327	2	0153	0	6	1580	1	OK		Caffeine
05111520000328	2	0153	5	6	1680	1	OK		Caffeine
05111520000331	2	0155	0	6	1340	1	OK		Caffeine
05111520000332	2	0155	5	6	1350	1	OK		Caffeine



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000335	2	0156	0	6	554	1	OK		Caffeine
05111520000336	2	0156	5	6	404	1	OK		Caffeine
05111520000339	2	0160	0	6	804	1	OK		Caffeine
05111520000340	2	0160	5	6	357	1	OK		Caffeine
05111520000343	3	0162	0	6	814	1	OK		Caffeine
05111520000344	2	0162	5	6	803	1	OK		Caffeine
05111520000347	3	0167	0	6	655	1	OK		Caffeine
05111520000348	2	0167	5	6	423	1	OK		Caffeine
05111520000351	2	0169	0	6	1540	1	OK		Caffeine
05111520000352	2	0169	5	6	1320	1	OK		Caffeine
05111520000355	2	0170	0	6	705	1	OK		Caffeine
05111520000356	2	0170	5	6	431	1	OK		Caffeine
05111520000359	2	0177	0	6	505	1	OK		Caffeine
05111520000360	2	0177	5	6	1140	1	OK		Caffeine
05111520000363	2	0181	0	6	824	1	OK		Caffeine
05111520000364	2	0181	5	6	828	1	OK		Caffeine
05111520000367	2	0183	0	6	648	1	OK		Caffeine
05111520000368	2	0183	5	6	917	1	OK		Caffeine
05111520000371	3	0185	0	6	836	1	OK		Caffeine
05111520000372	3	0185	5	6	770	1	OK		Caffeine
05111520000375	2	0187	0	6	1150	1	OK		Caffeine
05111520000376	2	0187	5	6	724	1	OK		Caffeine
05111520000379	3	0189	0	6	768	1	OK		Caffeine
05111520000380	2	0189	5	6	866	1	OK		Caffeine
05111520000383	3	0191	0	6	BLQ<(20.0)	1	OK		Caffeine
05111520000384	2	0191	5	6	812	1	OK		Caffeine
05111520000387	2	0192	0	6	923	1	OK		Caffeine
05111520000388	2	0192	5	6	1060	1	OK		Caffeine





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000391	2	0264	0	6	678	1	OK		Caffeine
05111520000392	2	0264	5	6	928	1	OK		Caffeine
05111520000395	2	0265	0	6	711	1	OK		Caffeine
05111520000396	2	0265	5	6	928	1	OK		Caffeine
05111520000399	2	0193	0	6	1010	1	OK		Caffeine
05111520000400	2	0193	5	6	1160	1	OK		Caffeine
05111520000403	2	0195	0	6	838	1	OK		Caffeine
05111520000404	2	0195	5	6	1480	1	OK		Caffeine
05111520000407	2	0196	0	6	966	1	OK		Caffeine
05111520000408	2	0196	5	6	969	1	OK		Caffeine
05111520000411	2	0198	0	6	607	1	OK		Caffeine
05111520000412	2	0198	5	6	600	1	OK		Caffeine
05111520000415	2	0200	0	6	1590	1	OK		Caffeine
05111520000416	2	0200	5	6	1440	1	OK		Caffeine
05111520000419	2	0202	0	6	1510	1	OK		Caffeine
05111520000420	2	0202	5	6	1790	1	OK		Caffeine
05111520000423	2	0203	0	6	1360	1	OK		Caffeine
05111520000424	2	0203	5	6	927	1	OK		Caffeine
05111520000427	2	0204	0	6	1430	1	OK		Caffeine
05111520000428	2	0204	5	6	1330	1	OK		Caffeine
05111520000431	3	0206	0	6	455	1	OK		Caffeine
05111520000432	2	0206	5	6	843	1	OK		Caffeine
05111520000439	2	0210	0	6	597	1	OK		Caffeine
05111520000440	2	0210	5	6	992	1	OK		Caffeine
05111520000447	2	0216	0	6	592	1	OK		Caffeine
05111520000448	2	0216	5	6	991	1	OK		Caffeine
05111520000451	2	0218	0	6	1470	1	OK		Caffeine
05111520000452	2	0218	5	6	1650	1	OK		Caffeine





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000455	2	0220	0	6	1600	1	OK		Caffeine
05111520000456	2	0220	5	6	1590	1	OK		Caffeine
05111520000459	2	0224	0	6	1220	1	OK		Caffeine
05111520000460	2	0224	5	6	1140	1	OK		Caffeine
05111520000463	2	0228	0	6	796	1	OK		Caffeine
05111520000464	3	0228	5	6	1030	1	OK		Caffeine
05111520000467	2	0229	0	6	1130	1	OK		Caffeine
05111520000468	2	0229	5	6	944	1	OK		Caffeine
05111520000471	3	0230	0	6	497	1	OK		Caffeine
05111520000472	2	0230	5	6	489	1	OK		Caffeine
05111520000475	2	0232	0	6	1530	1	OK		Caffeine
05111520000476	2	0232	5	6	1620	1	OK		Caffeine
05111520000479	2	0234	0	6	2030	1	OK		Caffeine
05111520000480	2	0234	5	6	2290	1	OK		Caffeine
05111520000483	2	0240	0	6	1030	1	OK		Caffeine
05111520000484	2	0240	5	6	1490	1	OK		Caffeine
05111520000487	2	0241	0	6	586	1	OK		Caffeine
05111520000488	2	0241	5	6	879	1	OK		Caffeine
05111520000489		0242	0	6		2	Other	Analysis not required	Caffeine
05111520000491		0242	0	6		1	Other	Analysis not required	Caffeine
05111520000495	2	0244	0	6	1280	1	OK		Caffeine
05111520000496	2	0244	5	6	1690	1	OK		Caffeine
05111520000497		0245	0	6		2	Other	Analysis not required	Caffeine
05111520000499		0245	0	6		1	Other	Analysis not required	Caffeine
05111520000507	2	0249	0	6	1000	1	OK		Caffeine
05111520000508	2	0249	5	6	1320	1	OK		Caffeine
05111520000511	2	0251	0	6	2190	1	OK		Caffeine
05111520000512	2	0251	5	6	2130	1	OK		Caffeine



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000515	2	0252	0	6	940	1	OK		Caffeine
05111520000516	2	0252	5	6	1110	1	OK		Caffeine
05111520000519	2	0255	0	6	1100	1	OK		Caffeine
05111520000520	2	0255	5	6	1150	1	OK		Caffeine
05111520000523	2	0256	0	6	1530	1	OK		Caffeine
05111520000524	2	0256	5	6	1180	1	OK		Caffeine
05111520000527	2	0262	0	6	1440	1	OK		Caffeine
05111520000528	2	0262	5	6	1430	1	OK		Caffeine
05111520000531	2	0197	0	6	478	1	OK		Caffeine
05111520000532	2	0197	5	6	929	1	OK		Caffeine
05111520000535	2	0266	0	6	1530	1	OK		Caffeine
05111520000536	2	0266	5	6	1730	1	OK		Caffeine
05111520000543	2	0272	0	6	592	1	OK		Caffeine
05111520000544	2	0272	5	6	1080	1	OK		Caffeine
05111520000547	2	0273	0	6	1000	1	OK		Caffeine
05111520000548	2	0273	5	6	1110	1	OK		Caffeine
05111520000551	2	0276	0	6	1250	1	OK		Caffeine
05111520000552	2	0276	5	6	914	1	OK		Caffeine
05111520000555	2	0277	0	6	695	1	OK		Caffeine
05111520000556	2	0277	5	6	769	1	OK		Caffeine
05111520000559	2	0278	0	6	528	1	OK		Caffeine
05111520000560	2	0278	5	6	634	1	OK		Caffeine
05111520000563	3	0279	0	6	1060	1	OK		Caffeine
05111520000564	2	0279	5	6	1290	1	OK		Caffeine
05111520000567	2	0281	0	6	640	1	OK		Caffeine
05111520000568	2	0281	5	6	958	1	OK		Caffeine
05111520000571	2	0282	0	6	1250	1	OK		Caffeine
05111520000572	2	0282	5	6	1350	1	OK		Caffeine



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000575	2	0283	0	6	1170	1	OK		Caffeine
05111520000576	6	0283	5	6	1100	1	OK		Caffeine
05111520000579	2	0285	0	6	571	1	OK		Caffeine
05111520000580	2	0285	5	6	725	1	OK		Caffeine
05111520000583	2	0287	0	6	1240	1	OK		Caffeine
05111520000584	2	0287	5	6	1610	1	OK		Caffeine
05111520000591	2	0289	0	6	1220	1	OK		Caffeine
05111520000592	2	0289	5	6	1370	1	OK		Caffeine
05111520000595	2	0291	0	6	1650	1	OK		Caffeine
05111520000596	2	0291	5	6	2090	1	OK		Caffeine
05111520000599	2	0292	0	6	916	1	OK		Caffeine
05111520000600	2	0292	5	6	1480	1	OK		Caffeine
05111520000603	2	0296	0	6	784	1	OK		Caffeine
05111520000604	6	0296	5	6	910	1	OK		Caffeine
05111520000607	2	0298	0	6	1120	1	OK		Caffeine
05111520000608	3	0298	5	6	823	1	OK		Caffeine
05111520000615	2	0300	0	6	2780	1	OK		Caffeine
05111520000616	2	0300	5	6	2860	1	OK		Caffeine
05111520000619	2	0301	0	6	785	1	OK		Caffeine
05111520000620	2	0301	5	6	1140	1	OK		Caffeine
05111520000623	2	0306	0	6	450	1	OK		Caffeine
05111520000624	2	0306	5	6	333	1	OK		Caffeine
05111520000627	2	0307	0	6	1370	1	OK		Caffeine
05111520000628	2	0307	5	6	1930	1	OK		Caffeine
05111520000631	2	0308	0	6	454	1	OK		Caffeine
05111520000632	2	0308	5	6	782	1	OK		Caffeine
05111520000643	2	0313	0	6	1270	1	OK		Caffeine
05111520000644	2	0313	5	6	993	1	OK		Caffeine



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000647	3	0315	0	6	1030	1	OK		Caffeine
05111520000648	2	0315	5	6	947	1	OK		Caffeine
05111520000651	2	0316	0	6	1870	1	OK		Caffeine
05111520000652	2	0316	5	6	2040	1	OK		Caffeine
05111520000655	2	0317	0	6	465	1	OK		Caffeine
05111520000656	2	0317	5	6	815	1	OK		Caffeine
05111520000659	2	0318	0	6	469	1	OK		Caffeine
05111520000660	2	0318	5	6	446	1	OK		Caffeine
05111520000663	3	0322	0	6	677	1	OK		Caffeine
05111520000664	3	0322	5	6	657	1	OK		Caffeine
05111520000667	2	0320	0	6	1010	1	OK		Caffeine
05111520000668	3	0320	5	6	1670	1	OK		Caffeine
05111520000671	3	0321	0	6	804	1	OK		Caffeine
05111520000672	3	0321	5	6	898	1	OK		Caffeine
05111520000675	3	0325	0	6	430	1	OK		Caffeine
05111520000676	3	0325	5	6	755	1	OK		Caffeine
05111520000679	3	0328	0	6	1160	1	OK		Caffeine
05111520000680	3	0328	5	6	1110	1	OK		Caffeine





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Table 9 Study Sample Concentrations for Paraxanthine

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000001	4	0010	0	6	698	1	OK		Paraxanthine
05111520000002	4	0010	5	6	655	1	OK		Paraxanthine
05111520000003	4	0011	0	6	836	1	OK		Paraxanthine
05111520000004	4	0011	5	6	834	1	OK		Paraxanthine
05111520000005	4	0014	0	6	646	1	OK		Paraxanthine
05111520000006	4	0014	5	6	724	1	OK		Paraxanthine
05111520000007	4	0015	0	6	603	1	OK		Paraxanthine
05111520000008	4	0015	5	6	606	1	OK		Paraxanthine
05111520000009	4	0016	0	6	1020	1	OK		Paraxanthine
05111520000010	4	0016	5	6	1010	1	OK		Paraxanthine
05111520000011	4	0017	0	6	1370	1	OK		Paraxanthine
05111520000012	4	0017	5	6	1210	1	OK		Paraxanthine
05111520000013	4	0020	0	6	920	1	OK		Paraxanthine
05111520000014	4	0020	5	6	917	1	OK		Paraxanthine
05111520000015	4	0022	0	6	1330	1	OK		Paraxanthine
05111520000016	4	0022	5	6	1210	1	OK		Paraxanthine
05111520000017	4	0023	0	6	678	1	OK		Paraxanthine
05111520000018	4	0023	5	6	855	1	OK		Paraxanthine
05111520000019	4	0025	0	6	850	1	OK		Paraxanthine
05111520000020	4	0025	5	6	677	1	OK		Paraxanthine
05111520000021	4	0028	0	6	1000	1	OK		Paraxanthine
05111520000022	4	0028	5	6	964	1	OK		Paraxanthine
05111520000023	4	0029	0	6	543	1	OK		Paraxanthine
05111520000024	4	0029	5	6	576	1	OK		Paraxanthine
05111520000025	4	0031	0	6	857	1	OK		Paraxanthine



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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000026	4	0031	5	6	845	1	OK		Paraxanthine
05111520000027	4	0035	0	6	500	1	OK		Paraxanthine
05111520000028	3	0035	5	6	496	1	OK		Paraxanthine
05111520000029	4	0038	0	6	477	1	OK		Paraxanthine
05111520000030	4	0038	5	6	444	1	OK		Paraxanthine
05111520000031	4	0039	0	6	778	1	OK		Paraxanthine
05111520000032	4	0039	5	6	668	1	OK		Paraxanthine
05111520000033	4	0044	0	6	881	1	OK		Paraxanthine
05111520000034	4	0044	5	6	733	1	OK		Paraxanthine
05111520000035	4	0049	0	6	543	1	OK		Paraxanthine
05111520000036	4	0049	5	6	522	1	OK		Paraxanthine
05111520000037	4	0052	0	6	1050	1	OK		Paraxanthine
05111520000038	4	0052	5	6	1010	1	OK		Paraxanthine
05111520000039	4	0053	0	6	1170	1	OK		Paraxanthine
05111520000040	4	0053	5	6	964	1	OK		Paraxanthine
05111520000041	4	0057	0	6	796	1	OK		Paraxanthine
05111520000042	6	0057	5	6	780	1	OK		Paraxanthine
05111520000043	4	0060	0	6	863	1	OK		Paraxanthine
05111520000044	4	0060	5	6	823	1	OK		Paraxanthine
05111520000045	4	0062	0	6	BLQ<(20 0)	1	OK		Paraxanthine
05111520000046	4	0062	5	6	1040	1	OK		Paraxanthine
05111520000047	4	0030	0	6	1170	1	OK		Paraxanthine
05111520000048	4	0030	5	6	1110	1	OK		Paraxanthine
05111520000049	4	0034	0	6	995	1	OK		Paraxanthine
05111520000050	4	0034	5	6	870	1	OK		Paraxanthine
05111520000051	4	0055	0	6	1260	1	OK		Paraxanthine
05111520000052	4	0055	5	6	1160	1	OK		Paraxanthine
05111520000053	4	0064	0	6	861	1	OK		Paraxanthine



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000054	4	0064	5	6	750	1	OK		Paraxanthine
05111520000055	4	0008	0	6	1130	1	OK		Paraxanthine
05111520000056	4	0008	5	6	1050	1	OK		Paraxanthine
05111520000115	4	0001	0	6	714	1	OK		Paraxanthine
05111520000116	4	0001	5	6	713	1	OK		Paraxanthine
05111520000119	4	0004	0	6	948	1	OK		Paraxanthine
05111520000120	4	0004	5	6	1210	1	OK		Paraxanthine
05111520000123	4	0013	0	6	870	1	OK		Paraxanthine
05111520000124	4	0013	5	6	830	1	OK		Paraxanthine
05111520000127	4	0021	0	6	820	1	OK		Paraxanthine
05111520000128	4	0021	5	6	772	1	OK		Paraxanthine
05111520000131	4	0037	0	6	741	1	OK		Paraxanthine
05111520000132	4	0037	5	6	733	1	OK		Paraxanthine
05111520000135	4	0042	0	6	687	1	OK		Paraxanthine
05111520000136	4	0042	5	6	701	1	OK		Paraxanthine
05111520000139	4	0051	0	6	1360	1	OK		Paraxanthine
05111520000140	4	0051	5	6	1340	1	OK		Paraxanthine
05111520000143	4	0063	0	6	1180	1	OK		Paraxanthine
05111520000144	4	0063	5	6	1210	1	OK		Paraxanthine
05111520000147	4	0066	0	6	924	1	OK		Paraxanthine
05111520000148	4	0066	5	6	1020	1	OK		Paraxanthine
05111520000151	4	0067	0	6	748	1	OK		Paraxanthine
05111520000152	4	0067	5	6	868	1	OK		Paraxanthine
05111520000155	4	0069	0	6	704	1	OK		Paraxanthine
05111520000156	4	0069	5	6	818	1	OK		Paraxanthine
05111520000159	4	0071	0	6	682	1	OK		Paraxanthine
05111520000160	4	0071	5	6	918	1	OK		Paraxanthine
05111520000163	4	0072	0	6	623	1	OK		Paraxanthine



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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000164	4	0072	5	6	703	1	OK		Paraxanthine
05111520000167	4	0074	0	6	821	1	OK		Paraxanthine
05111520000168	4	0074	5	6	919	1	OK		Paraxanthine
05111520000171	4	0076	0	6	790	1	OK		Paraxanthine
05111520000172	4	0076	5	6	833	1	OK		Paraxanthine
05111520000175	4	0080	0	6	1100	1	OK		Paraxanthine
05111520000176	4	0080	5	6	1190	1	OK		Paraxanthine
05111520000179	4	0083	0	6	912	1	OK		Paraxanthine
05111520000180	4	0083	5	6	860	1	OK		Paraxanthine
05111520000183	4	0085	0	6	967	1	OK		Paraxanthine
05111520000187	4	0086	0	6	738	1	OK		Paraxanthine
05111520000188	4	0086	5	6	827	1	OK		Paraxanthine
05111520000191	4	0087	0	6	1020	1	OK		Paraxanthine
05111520000192	4	0087	5	6	968	1	OK		Paraxanthine
05111520000195	4	0088	0	6	1040	1	OK		Paraxanthine
05111520000196	4	0088	5	6	892	1	OK		Paraxanthine
05111520000199	4	0090	0	6	976	1	OK		Paraxanthine
05111520000200	4	0090	5	6	1140	1	OK		Paraxanthine
05111520000203	4	0093	0	6	767	1	OK		Paraxanthine
05111520000204	4	0093	5	6	1000	1	OK		Paraxanthine
05111520000207	4	0104	0	6	1290	1	OK		Paraxanthine
05111520000208	4	0104	5	6	1260	1	OK		Paraxanthine
05111520000211	4	0105	0	6	1190	1	OK		Paraxanthine
05111520000212	4	0105	5	6	1300	1	OK		Paraxanthine
05111520000215	4	0106	0	6	882	1	OK		Paraxanthine
05111520000216	4	0106	5	6	872	1	OK		Paraxanthine
05111520000219	4	0107	0	6	967	1	OK		Paraxanthine
05111520000220	4	0107	5	6	1190	1	OK		Paraxanthine





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000223	4	0110	0	6	1380	1	OK		Paraxanthine
05111520000224	4	0110	5	6	1340	1	OK		Paraxanthine
05111520000227	4	0112	0	6	771	1	OK		Paraxanthine
05111520000228	4	0112	5	6	814	1	OK		Paraxanthine
05111520000231	4	0114	0	6	859	1	OK		Paraxanthine
05111520000232	4	0114	5	6	986	1	OK		Paraxanthine
05111520000235	4	0117	0	6	1110	1	OK		Paraxanthine
05111520000236	4	0117	5	6	1250	1	OK		Paraxanthine
05111520000239	4	0118	0	6	1380	1	OK		Paraxanthine
05111520000240	4	0118	5	6	1480	1	OK		Paraxanthine
05111520000243	4	0121	0	6	901	1	OK		Paraxanthine
05111520000244	4	0121	5	6	909	1	OK		Paraxanthine
05111520000247	4	0122	0	6	926	1	OK		Paraxanthine
05111520000248	4	0122	5	6	909	1	OK		Paraxanthine
05111520000251	4	0123	0	6	706	1	OK		Paraxanthine
05111520000252	4	0123	5	6	866	1	OK		Paraxanthine
05111520000255	4	0133	0	6	688	1	OK		Paraxanthine
05111520000256	4	0133	5	6	713	1	OK		Paraxanthine
05111520000259	5	0190	0	6	1270	1	OK		Paraxanthine
05111520000260	5	0190	5	6	1190	1	OK		Paraxanthine
05111520000263	4	0126	0	6	776	1	OK		Paraxanthine
05111520000264	4	0126	5	6	630	1	OK		Paraxanthine
05111520000267	4	0127	0	6	624	1	OK		Paraxanthine
05111520000268	4	0127	5	6	636	1	OK		Paraxanthine
05111520000271	4	0128	0	6	868	1	OK		Paraxanthine
05111520000272	4	0128	5	6	608	1	OK		Paraxanthine
05111520000275	4	0129	0	6	920	1	OK		Paraxanthine
05111520000276	4	0129	5	6	756	1	OK		Paraxanthine



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000279	4	0130	0	6	1340	1	OK		Paraxanthine
05111520000280	4	0130	5	6	1250	1	OK		Paraxanthine
05111520000283	4	0134	0	6	719	1	OK		Paraxanthine
05111520000284	4	0134	5	6	612	1	OK		Paraxanthine
05111520000287	4	0136	0	6	1120	1	OK		Paraxanthine
05111520000288	4	0136	5	6	1850	1	OK		Paraxanthine
05111520000291	4	0137	0	6	896	1	OK		Paraxanthine
05111520000292	4	0137	5	6	797	1	OK		Paraxanthine
05111520000295	4	0139	0	6	891	1	OK		Paraxanthine
05111520000296	4	0139	5	6	905	1	OK		Paraxanthine
05111520000299	4	0140	0	6	1120	1	OK		Paraxanthine
05111520000300	4	0140	5	6	1120	1	OK		Paraxanthine
05111520000303	4	0145	0	6	765	1	OK		Paraxanthine
05111520000304	4	0145	5	6	668	1	OK		Paraxanthine
05111520000307	4	0147	0	6	899	1	OK		Paraxanthine
05111520000308	4	0147	5	6	855	1	OK		Paraxanthine
05111520000311	4	0148	0	6	862	1	OK		Paraxanthine
05111520000312	4	0148	5	6	645	1	OK		Paraxanthine
05111520000315	4	0149	0	6	764	1	OK		Paraxanthine
05111520000316	4	0149	5	6	620	1	OK		Paraxanthine
05111520000319	4	0150	0	6	1010	1	OK		Paraxanthine
05111520000320	4	0150	5	6	914	1	OK		Paraxanthine
05111520000323	5	0152	0	6	811	1	OK		Paraxanthine
05111520000324	5	0152	5	6	852	1	OK		Paraxanthine
05111520000327	5	0153	0	6	1140	1	OK		Paraxanthine
05111520000328	5	0153	5	6	919	1	OK		Paraxanthine
05111520000331	5	0155	0	6	1050	1	OK		Paraxanthine
05111520000332	5	0155	5	6	896	1	OK		Paraxanthine



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000335	5	0156	0	6	785	1	OK		Paraxanthine
05111520000336	5	0156	5	6	599	1	OK		Paraxanthine
05111520000339	5	0160	0	6	936	1	OK		Paraxanthine
05111520000340	5	0160	5	6	618	1	OK		Paraxanthine
05111520000343	3	0162	0	6	866	1	OK		Paraxanthine
05111520000344	5	0162	5	6	817	1	OK		Paraxanthine
05111520000347	3	0167	0	6	897	1	OK		Paraxanthine
05111520000348	5	0167	5	6	652	1	OK		Paraxanthine
05111520000351	5	0169	0	6	1070	1	OK		Paraxanthine
05111520000352	5	0169	5	6	917	1	OK		Paraxanthine
05111520000355	5	0170	0	6	865	1	OK		Paraxanthine
05111520000356	5	0170	5	6	684	1	OK		Paraxanthine
05111520000359	5	0177	0	6	759	1	OK		Paraxanthine
05111520000360	5	0177	5	6	876	1	OK		Paraxanthine
05111520000363	5	0181	0	6	1010	1	OK		Paraxanthine
05111520000364	5	0181	5	6	830	1	OK		Paraxanthine
05111520000367	5	0183	0	6	835	1	OK		Paraxanthine
05111520000368	5	0183	5	6	903	1	OK		Paraxanthine
05111520000371	3	0185	0	6	960	1	OK		Paraxanthine
05111520000372	3	0185	5	6	882	1	OK		Paraxanthine
05111520000375	5	0187	0	6	1080	1	OK		Paraxanthine
05111520000376	5	0187	5	6	869	1	OK		Paraxanthine
05111520000379	3	0189	0	6	1050	1	OK		Paraxanthine
05111520000380	5	0189	5	6	988	1	OK		Paraxanthine
05111520000383	6	0191	0	6	BLQ<(20 0)	1	OK		Paraxanthine
05111520000384	5	0191	5	6	722	1	OK		Paraxanthine
05111520000387	5	0192	0	6	1130	1	OK		Paraxanthine
05111520000388	5	0192	5	6	921	1	OK		Paraxanthine



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000391	5	0264	0	6	998	1	OK		Paraxanthine
05111520000392	5	0264	5	6	1170	1	OK		Paraxanthine
05111520000395	5	0265	0	6	756	1	OK		Paraxanthine
05111520000396	5	0265	5	6	828	1	OK		Paraxanthine
05111520000399	5	0193	0	6	1010	1	OK		Paraxanthine
05111520000400	5	0193	5	6	1060	1	OK		Paraxanthine
05111520000403	5	0195	0	6	861	1	OK		Paraxanthine
05111520000404	5	0195	5	6	972	1	OK		Paraxanthine
05111520000407	5	0196	0	6	1000	1	OK		Paraxanthine
05111520000408	5	0196	5	6	861	1	OK		Paraxanthine
05111520000411	5	0198	0	6	695	1	OK		Paraxanthine
05111520000412	5	0198	5	6	765	1	OK		Paraxanthine
05111520000415	5	0200	0	6	1220	1	OK		Paraxanthine
05111520000416	5	0200	5	6	1290	1	OK		Paraxanthine
05111520000419	5	0202	0	6	1130	1	OK		Paraxanthine
05111520000420	5	0202	5	6	1220	1	OK		Paraxanthine
05111520000423	5	0203	0	6	1040	1	OK		Paraxanthine
05111520000424	5	0203	5	6	644	1	OK		Paraxanthine
05111520000427	5	0204	0	6	1090	1	OK		Paraxanthine
05111520000428	5	0204	5	6	1220	1	OK		Paraxanthine
05111520000431	3	0206	0	6	693	1	OK		Paraxanthine
05111520000432	5	0206	5	6	857	1	OK		Paraxanthine
05111520000439	5	0210	0	6	780	1	OK		Paraxanthine
05111520000440	5	0210	5	6	962	1	OK		Paraxanthine
05111520000447	5	0216	0	6	850	1	OK		Paraxanthine
05111520000448	5	0216	5	6	1060	1	OK		Paraxanthine
05111520000451	5	0218	0	6	796	1	OK		Paraxanthine
05111520000452	5	0218	5	6	852	1	OK		Paraxanthine





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000455	5	0220	0	6	1270	1	OK		Paraxanthine
05111520000456	5	0220	5	6	1130	1	OK		Paraxanthine
05111520000459	5	0224	0	6	1150	1	OK		Paraxanthine
05111520000460	5	0224	5	6	1290	1	OK		Paraxanthine
05111520000463	5	0228	0	6	1160	1	OK		Paraxanthine
05111520000464	3	0228	5	6	1390	1	OK		Paraxanthine
05111520000467	5	0229	0	6	872	1	OK		Paraxanthine
05111520000468	5	0229	5	6	962	1	OK		Paraxanthine
05111520000471	3	0230	0	6	819	1	OK		Paraxanthine
05111520000472	5	0230	5	6	795	1	OK		Paraxanthine
05111520000475	5	0232	0	6	1080	1	OK		Paraxanthine
05111520000476	5	0232	5	6	1170	1	OK		Paraxanthine
05111520000479	5	0234	0	6	690	1	OK		Paraxanthine
05111520000480	5	0234	5	6	624	1	OK		Paraxanthine
05111520000483	5	0240	0	6	1300	1	OK		Paraxanthine
05111520000484	5	0240	5	6	1260	1	OK		Paraxanthine
05111520000487	5	0241	0	6	705	1	OK		Paraxanthine
05111520000488	5	0241	5	6	929	1	OK		Paraxanthine
05111520000489		0242	0	6		2	Other	Analysis not required	Paraxanthine
05111520000491		0242	0	6		1	Other	Analysis not required	Paraxanthine
05111520000495	5	0244	0	6	1190	1	OK		Paraxanthine
05111520000496	5	0244	5	6	1190	1	OK		Paraxanthine
05111520000497		0245	0	6		2	Other	Analysis not required	Paraxanthine
05111520000499		0245	0	6		1	Other	Analysis not required	Paraxanthine
05111520000507	5	0249	0	6	979	1	OK		Paraxanthine
05111520000508	5	0249	5	6	1040	1	OK		Paraxanthine
05111520000511	5	0251	0	6	916	1	OK		Paraxanthine
05111520000512	5	0251	5	6	1130	1	OK		Paraxanthine





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000515	5	0252	0	6	900	1	OK		Paraxanthine
05111520000516	5	0252	5	6	890	1	OK		Paraxanthine
05111520000519	5	0255	0	6	1030	1	OK		Paraxanthine
05111520000520	5	0255	5	6	1090	1	OK		Paraxanthine
05111520000523	5	0256	0	6	835	1	OK		Paraxanthine
05111520000524	5	0256	5	6	993	1	OK		Paraxanthine
05111520000527	5	0262	0	6	851	1	OK		Paraxanthine
05111520000528	5	0262	5	6	836	1	OK		Paraxanthine
05111520000531	5	0197	0	6	734	1	OK		Paraxanthine
05111520000532	5	0197	5	6	902	1	OK		Paraxanthine
05111520000535	5	0266	0	6	1120	1	OK		Paraxanthine
05111520000536	5	0266	5	6	1320	1	OK		Paraxanthine
05111520000543	5	0272	0	6	757	1	OK		Paraxanthine
05111520000544	5	0272	5	6	1030	1	OK		Paraxanthine
05111520000547	5	0273	0	6	740	1	OK		Paraxanthine
05111520000548	5	0273	5	6	672	1	OK		Paraxanthine
05111520000551	5	0276	0	6	945	1	OK		Paraxanthine
05111520000552	5	0276	5	6	962	1	OK		Paraxanthine
05111520000555	5	0277	0	6	766	1	OK		Paraxanthine
05111520000556	5	0277	5	6	755	1	OK		Paraxanthine
05111520000559	5	0278	0	6	658	1	OK		Paraxanthine
05111520000560	5	0278	5	6	671	1	OK		Paraxanthine
05111520000563	3	0279	0	6	924	1	OK		Paraxanthine
05111520000564	5	0279	5	6	979	1	OK		Paraxanthine
05111520000567	5	0281	0	6	761	1	OK		Paraxanthine
05111520000568	5	0281	5	6	850	1	OK		Paraxanthine
05111520000571	5	0282	0	6	1430	1	OK		Paraxanthine
05111520000572	5	0282	5	6	1280	1	OK		Paraxanthine



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000575	5	0283	0	6	1130	1	OK		Paraxanthine
05111520000576	6	0283	5	6	1070	1	OK		Paraxanthine
05111520000579	5	0285	0	6	667	1	OK		Paraxanthine
05111520000580	5	0285	5	6	820	1	OK		Paraxanthine
05111520000583	5	0287	0	6	991	1	OK		Paraxanthine
05111520000584	5	0287	5	6	1300	1	OK		Paraxanthine
05111520000591	5	0289	0	6	1020	1	OK		Paraxanthine
05111520000592	5	0289	5	6	1010	1	OK		Paraxanthine
05111520000595	5	0291	0	6	946	1	OK		Paraxanthine
05111520000596	5	0291	5	6	1040	1	OK		Paraxanthine
05111520000599	5	0292	0	6	1130	1	OK		Paraxanthine
05111520000600	5	0292	5	6	1380	1	OK		Paraxanthine
05111520000603	5	0296	0	6	717	1	OK		Paraxanthine
05111520000604	6	0296	5	6	706	1	OK		Paraxanthine
05111520000607	5	0298	0	6	1030	1	OK		Paraxanthine
05111520000608	3	0298	5	6	990	1	OK		Paraxanthine
05111520000615	5	0300	0	6	828	1	OK		Paraxanthine
05111520000616	5	0300	5	6	939	1	OK		Paraxanthine
05111520000619	5	0301	0	6	688	1	OK		Paraxanthine
05111520000620	5	0301	5	6	946	1	OK		Paraxanthine
05111520000623	5	0306	0	6	703	1	OK		Paraxanthine
05111520000624	5	0306	5	6	589	1	OK		Paraxanthine
05111520000627	5	0307	0	6	804	1	OK		Paraxanthine
05111520000628	5	0307	5	6	892	1	OK		Paraxanthine
05111520000631	5	0308	0	6	683	1	OK		Paraxanthine
05111520000632	5	0308	5	6	811	1	OK		Paraxanthine
05111520000643	5	0313	0	6	1220	1	OK		Paraxanthine
05111520000644	5	0313	5	6	1240	1	OK		Paraxanthine



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Custom ID	Run ID	Subject	Day Nominal	Hour Nominal	Concentration (ng/mL)	Split	Sample Condition	Sample Comments	Analyte
05111520000647	3	0315	0	6	1130	1	OK		Paraxanthine
05111520000648	5	0315	5	6	1120	1	OK		Paraxanthine
05111520000651	5	0316	0	6	1050	1	OK		Paraxanthine
05111520000652	5	0316	5	6	1260	1	OK		Paraxanthine
05111520000655	5	0317	0	6	864	1	OK		Paraxanthine
05111520000656	5	0317	5	6	1080	1	OK		Paraxanthine
05111520000659	5	0318	0	6	661	1	OK		Paraxanthine
05111520000660	5	0318	5	6	698	1	OK		Paraxanthine
05111520000663	3	0322	0	6	778	1	OK		Paraxanthine
05111520000664	3	0322	5	6	764	1	OK		Paraxanthine
05111520000667	5	0320	0	6	1050	1	OK		Paraxanthine
05111520000668	5	0320	5	6	943	1	OK		Paraxanthine
05111520000671	3	0321	0	6	1040	1	OK		Paraxanthine
05111520000672	3	0321	5	6	969	1	OK		Paraxanthine
05111520000675	3	0325	0	6	699	1	OK		Paraxanthine
05111520000676	3	0325	5	6	765	1	OK		Paraxanthine
05111520000679	3	0328	0	6	1240	1	OK		Paraxanthine
05111520000680	3	0328	5	6	1210	1	OK		Paraxanthine



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Table 10 Summary of Reassay for Analytical Reasons for Caffeine

Run Id	Reason	Sample Name
1	Fail	AA99071-08 05111520000115 0001 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000116 0001 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000119 0004 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000120 0004 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000055 0008 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000056 0008 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000001 0010 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000002 0010 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000003 0011 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000004 0011 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000123 0013 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000124 0013 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000005 0014 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000006 0014 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000007 0015 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000008 0015 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000009 0016 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000010 0016 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000011 0017 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000012 0017 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000013 0020 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000014 0020 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000127 0021 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000128 0021 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000015 0022 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000016 0022 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000017 0023 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000018 0023 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000019 0025 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000020 0025 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000021 0028 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000022 0028 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000023 0029 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000024 0029 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000047 0030 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000048 0030 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000025 0031 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000026 0031 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000049 0034 N/A P1 Day 0 6h PL-1





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Run Id	Reason	Sample Name
1	Fail	AA99071-08 05111520000050 0034 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000027 0035 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000028 0035 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000131 0037 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000132 0037 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000029 0038 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000030 0038 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000031 0039 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000032 0039 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000135 0042 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000136 0042 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000033 0044 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000034 0044 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000035 0049 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000036 0049 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000139 0051 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000140 0051 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000037 0052 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000038 0052 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000039 0053 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000040 0053 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000051 0055 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000052 0055 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000041 0057 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000043 0060 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000044 0060 N/A P1 Day 5 6h PL-1
1	LSR/Fail	AA99071-08 05111520000045 0062 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000046 0062 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000143 0063 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000144 0063 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000053 0064 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000054 0064 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000147 0066 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000148 0066 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000151 0067 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000152 0067 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000155 0069 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000156 0069 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000159 0071 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000160 0071 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000163 0072 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000164 0072 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000167 0074 N/A P1 Day 0 6h PL-1





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

Run Id	Reason	Sample Name
1	Fail	AA99071-08 05111520000168 0074 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000171 0076 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000172 0076 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000175 0080 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000176 0080 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000179 0083 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000180 0083 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000183 0085 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000187 0086 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000188 0086 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000191 0087 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000192 0087 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000195 0088 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000196 0088 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000199 0090 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000200 0090 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000203 0093 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000204 0093 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000207 0104 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000208 0104 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000211 0105 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000212 0105 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000215 0106 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000216 0106 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000219 0107 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000220 0107 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000223 0110 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000224 0110 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000227 0112 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000228 0112 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000231 0114 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000232 0114 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000235 0117 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000236 0117 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000239 0118 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000240 0118 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000243 0121 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000244 0121 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000247 0122 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000248 0122 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000251 0123 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000252 0123 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000263 0126 N/A P1 Day 0 6h PL-1



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

Run Id	Reason	Sample Name
1	Fail	AA99071-08 05111520000264 0126 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000267 0127 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000268 0127 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000271 0128 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000272 0128 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000275 0129 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000276 0129 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000279 0130 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000280 0130 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000255 0133 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000256 0133 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000283 0134 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000284 0134 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000287 0136 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000288 0136 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000291 0137 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000292 0137 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000295 0139 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000296 0139 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000299 0140 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000300 0140 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000303 0145 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000304 0145 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000307 0147 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000308 0147 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000311 0148 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000312 0148 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000315 0149 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000316 0149 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000319 0150 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000320 0150 N/A P1 Day 5 6h PL-1
2	UCR	AA99071-08 05111520000464 0228 N/A P1 Day 5 6h PL-1
2	UCR	AA99071-08 05111520000471 0230 N/A P1 Day 0 6h PL-1
2	UCR	AA99071-08 05111520000563 0279 N/A P1 Day 0 6h PL-1
2	UISR	AA99071-08 05111520000668 0320 N/A P1 Day 5 6h PL-1



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

Table 11 Summary of Reassay for Analytical Reasons for Paraxanthine

Run Id	Reason	Sample Name
1	Fail	AA99071-08 05111520000011 0017 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000012 0017 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000013 0020 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000014 0020 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000127 0021 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000128 0021 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000015 0022 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000016 0022 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000017 0023 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000018 0023 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000019 0025 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000020 0025 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000021 0028 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000022 0028 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000023 0029 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000024 0029 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000047 0030 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000048 0030 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000025 0031 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000026 0031 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000049 0034 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000050 0034 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000027 0035 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000028 0035 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000131 0037 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000132 0037 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000029 0038 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000030 0038 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000031 0039 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000032 0039 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000135 0042 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000136 0042 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000033 0044 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000034 0044 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000035 0049 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000036 0049 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000139 0051 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000140 0051 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000037 0052 N/A P1 Day 0 6h PL-1





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

Run Id	Reason	Sample Name
1	Fail	AA99071-08 05111520000038 0052 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000039 0053 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000040 0053 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000051 0055 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000052 0055 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000041 0057 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000043 0060 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000044 0060 N/A P1 Day 5 6h PL-1
1	LSR/Fail	AA99071-08 05111520000045 0062 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000046 0062 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000143 0063 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000144 0063 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000053 0064 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000054 0064 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000147 0066 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000148 0066 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000151 0067 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000152 0067 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000155 0069 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000156 0069 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000159 0071 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000160 0071 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000163 0072 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000164 0072 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000167 0074 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000168 0074 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000171 0076 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000172 0076 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000175 0080 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000176 0080 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000179 0083 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000180 0083 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000183 0085 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000187 0086 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000188 0086 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000191 0087 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000192 0087 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000195 0088 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000196 0088 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000199 0090 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000200 0090 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000203 0093 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000204 0093 N/A P1 Day 5 6h PL-1





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

Run Id	Reason	Sample Name
1	Fail	AA99071-08 05111520000207 0104 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000208 0104 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000211 0105 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000212 0105 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000215 0106 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000216 0106 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000219 0107 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000220 0107 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000223 0110 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000224 0110 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000227 0112 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000228 0112 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000231 0114 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000232 0114 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000235 0117 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000236 0117 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000239 0118 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000240 0118 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000243 0121 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000244 0121 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000247 0122 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000248 0122 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000251 0123 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000252 0123 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000263 0126 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000264 0126 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000267 0127 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000268 0127 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000271 0128 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000272 0128 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000275 0129 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000276 0129 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000279 0130 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000280 0130 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000255 0133 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000256 0133 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000283 0134 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000284 0134 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000287 0136 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000288 0136 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000291 0137 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000292 0137 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000295 0139 N/A P1 Day 0 6h PL-1



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

Run Id	Reason	Sample Name
1	Fail	AA99071-08 05111520000296 0139 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000299 0140 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000300 0140 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000303 0145 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000304 0145 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000307 0147 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000308 0147 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000311 0148 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000312 0148 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000315 0149 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000316 0149 N/A P1 Day 5 6h PL-1
1	Fail	AA99071-08 05111520000319 0150 N/A P1 Day 0 6h PL-1
1	Fail	AA99071-08 05111520000320 0150 N/A P1 Day 5 6h PL-1
2	UCR/Fail	AA99071-08 05111520000323 0152 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000324 0152 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000327 0153 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000328 0153 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000331 0155 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000332 0155 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000335 0156 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000336 0156 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000339 0160 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000340 0160 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000343 0162 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000344 0162 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000347 0167 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000348 0167 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000351 0169 N/A P1 Day 0 6h PL-1
2	UCR/Fail	AA99071-08 05111520000352 0169 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000355 0170 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000356 0170 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000359 0177 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000360 0177 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000363 0181 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000364 0181 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000367 0183 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000368 0183 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000371 0185 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000372 0185 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000375 0187 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000376 0187 N/A P1 Day 5 6h PL-1
2	UCR/Fail	AA99071-08 05111520000379 0189 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000380 0189 N/A P1 Day 5 6h PL-1





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

Run Id	Reason	Sample Name
2	Fail	AA99071-08 05111520000259 0190 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000260 0190 N/A P1 Day 5 6h PL-1
2	UCR/Fail	AA99071-08 05111520000383 0191 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000384 0191 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000387 0192 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000388 0192 N/A P1 Day 5 6h PL-1
2	UCR/Fail	AA99071-08 05111520000399 0193 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000400 0193 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000403 0195 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000404 0195 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000407 0196 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000408 0196 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000531 0197 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000532 0197 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000411 0198 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000412 0198 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000415 0200 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000416 0200 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000419 0202 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000420 0202 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000423 0203 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000424 0203 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000427 0204 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000428 0204 N/A P1 Day 5 6h PL-1
2	UCR/Fail	AA99071-08 05111520000431 0206 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000432 0206 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000439 0210 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000440 0210 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000447 0216 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000448 0216 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000451 0218 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000452 0218 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000455 0220 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000456 0220 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000459 0224 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000460 0224 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000463 0228 N/A P1 Day 0 6h PL-1
2	UCR/Fail	AA99071-08 05111520000464 0228 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000467 0229 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000468 0229 N/A P1 Day 5 6h PL-1
2	UCR/Fail	AA99071-08 05111520000471 0230 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000472 0230 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000475 0232 N/A P1 Day 0 6h PL-1



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

Run Id	Reason	Sample Name
2	Fail	AA99071-08 05111520000476 0232 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000479 0234 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000480 0234 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000483 0240 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000484 0240 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000487 0241 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000488 0241 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000495 0244 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000496 0244 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000507 0249 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000508 0249 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000511 0251 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000512 0251 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000515 0252 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000516 0252 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000519 0255 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000520 0255 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000523 0256 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000524 0256 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000527 0262 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000528 0262 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000391 0264 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000392 0264 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000395 0265 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000396 0265 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000535 0266 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000536 0266 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000539 0269 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000543 0272 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000544 0272 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000547 0273 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000548 0273 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000551 0276 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000552 0276 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000555 0277 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000556 0277 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000559 0278 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000560 0278 N/A P1 Day 5 6h PL-1
2	UCR/Fail	AA99071-08 05111520000563 0279 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000564 0279 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000567 0281 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000568 0281 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000571 0282 N/A P1 Day 0 6h PL-1





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

Run Id	Reason	Sample Name
2	Fail	AA99071-08 05111520000572 0282 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000575 0283 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000579 0285 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000580 0285 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000583 0287 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000584 0287 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000587 0288 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000591 0289 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000592 0289 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000595 0291 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000596 0291 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000599 0292 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000600 0292 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000603 0296 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000607 0298 N/A P1 Day 0 6h PL-1
2	ISP/Fail	AA99071-08 05111520000608 0298 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000611 0299 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000615 0300 N/A P1 Day 0 6h PL-1
2	Fail	AA99071-08 05111520000616 0300 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000619 0301 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000620 0301 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000623 0306 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000624 0306 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000627 0307 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000628 0307 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000631 0308 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000632 0308 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000635 0309 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000639 0312 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000643 0313 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000644 0313 N/A P1 Day 5 6h PL-1
2	UCR/Fail	AA99071-08 05111520000647 0315 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000648 0315 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000651 0316 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000652 0316 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000655 0317 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000656 0317 N/A P1 Day 5 6h PL-1
2	UISR/Fail	AA99071-08 05111520000659 0318 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000660 0318 N/A P1 Day 5 6h PL-1
2	Fail	AA99071-08 05111520000667 0320 N/A P1 Day 0 6h PL-1
2	UISR/Fail	AA99071-08 05111520000668 0320 N/A P1 Day 5 6h PL-1
3	LSR	AA99071-08 05111520000383 0191 N/A P1 Day 0 6h PL-1



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

Table 12 Incurred Sample Reproducibility Assessment for Caffeine

Subject	Period	Time Point	Analyte	Units	Original Value	Reassay Value	Mean Value	% Difference	Reproducible?	Event?	% of Passing ISR Samples
0022	1	Day 5 6h	Caffeine	ng/mL	2340	2380	2,360	1.69	Pass	No	97.2
0028	1	Day 5 6h	Caffeine	ng/mL	2680	2150	2,420	21.90	Fail	No	
0035	1	Day 0 6h	Caffeine	ng/mL	370	378	374	2.14	Pass	No	
0038	1	Day 0 6h	Caffeine	ng/mL	251	247	249	1.61	Pass	No	
0049	1	Day 0 6h	Caffeine	ng/mL	301	310	306	2.94	Pass	No	
0057	1	Day 0 6h	Caffeine	ng/mL	995	993	994	0.20	Pass	No	
0013	1	Day 5 6h	Caffeine	ng/mL	603	590	597	2.18	Pass	No	
0071	1	Day 0 6h	Caffeine	ng/mL	475	457	466	3.86	Pass	No	
0104	1	Day 0 6h	Caffeine	ng/mL	2290	2240	2,270	2.20	Pass	No	
0118	1	Day 5 6h	Caffeine	ng/mL	1490	1510	1,500	1.33	Pass	No	
0127	1	Day 5 6h	Caffeine	ng/mL	431	428	430	0.70	Pass	No	
0136	1	Day 5 6h	Caffeine	ng/mL	2620	2540	2,580	3.10	Pass	No	
0148	1	Day 0 6h	Caffeine	ng/mL	632	643	638	1.72	Pass	No	
0153	1	Day 5 6h	Caffeine	ng/mL	1680	1630	1,660	3.01	Pass	No	
0156	1	Day 0 6h	Caffeine	ng/mL	554	497	526	10.84	Pass	No	
0162	1	Day 0 6h	Caffeine	ng/mL	814	801	808	1.61	Pass	No	
0177	1	Day 5 6h	Caffeine	ng/mL	1140	998	1,070	13.27	Pass	No	
0185	1	Day 0 6h	Caffeine	ng/mL	836	801	819	4.27	Pass	No	
0189	1	Day 0 6h	Caffeine	ng/mL	768	744	756	3.17	Pass	No	
0189	1	Day 5 6h	Caffeine	ng/mL	866	784	825	9.94	Pass	No	
0196	1	Day 0 6h	Caffeine	ng/mL	966	881	924	9.20	Pass	No	
0203	1	Day 0 6h	Caffeine	ng/mL	1360	1210	1,290	11.63	Pass	No	
0206	1	Day 0 6h	Caffeine	ng/mL	455	446	451	2.00	Pass	No	
0228	1	Day 5 6h	Caffeine	ng/mL	1030	1010	1,020	1.96	Pass	No	



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

Subject	Period	Time Point	Analyte	Units	Original Value	Reassay Value	Mean Value	% Difference	Reproducible?	Event?	% of Passing ISR Samples
0230	1	Day 5 6h	Caffeine	ng/mL	489	455	472	7.20	Pass	No	
0255	1	Day 0 6h	Caffeine	ng/mL	1100	1040	1,070	5.61	Pass	No	
0276	1	Day 5 6h	Caffeine	ng/mL	914	839	877	8.55	Pass	No	
0282	1	Day 0 6h	Caffeine	ng/mL	1250	1220	1,240	2.42	Pass	No	
0298	1	Day 5 6h	Caffeine	ng/mL	823	821	822	0.24	Pass	No	
0300	1	Day 5 6h	Caffeine	ng/mL	2860	2670	2,770	6.86	Pass	No	
0315	1	Day 0 6h	Caffeine	ng/mL	1030	955	993	7.55	Pass	No	
0322	1	Day 0 6h	Caffeine	ng/mL	677	634	656	6.55	Pass	No	
0320	1	Day 5 6h	Caffeine	ng/mL	1670	1450	1,560	14.10	Pass	No	
0321	1	Day 5 6h	Caffeine	ng/mL	898	1000	949	10.75	Pass	No	
0325	1	Day 0 6h	Caffeine	ng/mL	430	433	432	0.69	Pass	No	
0328	1	Day 0 6h	Caffeine	ng/mL	1160	1130	1,150	2.61	Pass	No	





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Table 13 Incurred Sample Reproducibility Assessment for Paraxanthine

Subject	Period	Time Point	Analyte	Units	Original Value	Reassay Value	Mean Value	% Difference	Reproducible?	Event?	% of Passing ISR Samples
0022	1	Day 5 6h	Paraxanthine	ng/mL	1210	1240	1,230	2.44	Pass	No	97.2
0028	1	Day 5 6h	Paraxanthine	ng/mL	964	778	871	21.35	Fail	No	
0035	1	Day 0 6h	Paraxanthine	ng/mL	500	500	500	0.00	Pass	No	
0038	1	Day 0 6h	Paraxanthine	ng/mL	477	494	486	3.50	Pass	No	
0049	1	Day 0 6h	Paraxanthine	ng/mL	543	547	545	0.73	Pass	No	
0057	1	Day 0 6h	Paraxanthine	ng/mL	796	810	803	1.74	Pass	No	
0013	1	Day 5 6h	Paraxanthine	ng/mL	830	823	827	0.85	Pass	No	
0071	1	Day 0 6h	Paraxanthine	ng/mL	682	671	677	1.62	Pass	No	
0104	1	Day 0 6h	Paraxanthine	ng/mL	1290	1370	1,330	6.02	Pass	No	
0118	1	Day 5 6h	Paraxanthine	ng/mL	1480	1550	1,520	4.61	Pass	No	
0127	1	Day 5 6h	Paraxanthine	ng/mL	636	663	650	4.15	Pass	No	
0136	1	Day 5 6h	Paraxanthine	ng/mL	1850	1900	1,880	2.66	Pass	No	
0148	1	Day 0 6h	Paraxanthine	ng/mL	862	884	873	2.52	Pass	No	
0153	1	Day 5 6h	Paraxanthine	ng/mL	919	928	924	0.97	Pass	No	
0156	1	Day 0 6h	Paraxanthine	ng/mL	785	768	777	2.19	Pass	No	
0162	1	Day 0 6h	Paraxanthine	ng/mL	866	845	856	2.45	Pass	No	
0177	1	Day 5 6h	Paraxanthine	ng/mL	876	822	849	6.36	Pass	No	
0185	1	Day 0 6h	Paraxanthine	ng/mL	960	925	943	3.71	Pass	No	
0189	1	Day 0 6h	Paraxanthine	ng/mL	1050	1020	1,040	2.88	Pass	No	
0189	1	Day 5 6h	Paraxanthine	ng/mL	988	943	966	4.66	Pass	No	
0196	1	Day 0 6h	Paraxanthine	ng/mL	1000	1000	1,000	0.00	Pass	No	
0203	1	Day 0 6h	Paraxanthine	ng/mL	1040	1050	1,050	0.95	Pass	No	
0206	1	Day 0 6h	Paraxanthine	ng/mL	693	662	678	4.57	Pass	No	
0228	1	Day 5 6h	Paraxanthine	ng/mL	1390	1370	1,380	1.45	Pass	No	





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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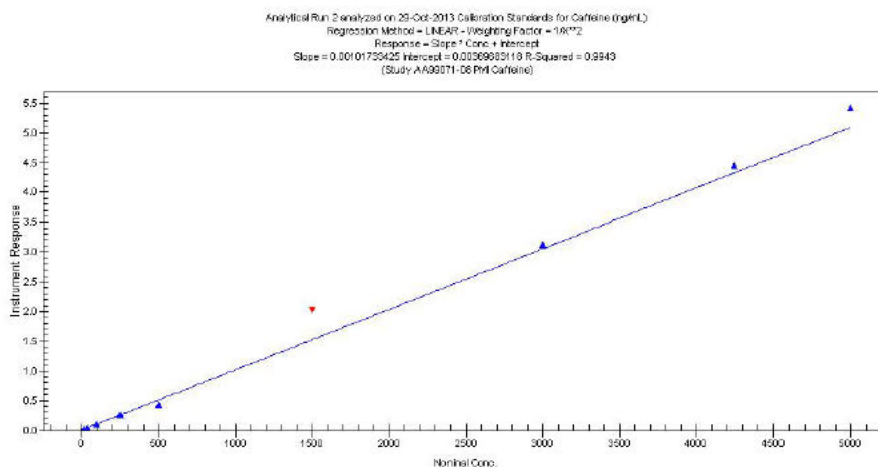
Subject	Period	Time Point	Analyte	Units	Original Value	Reassay Value	Mean Value	% Difference	Reproducible?	Event?	% of Passing ISR Samples
0230	1	Day 5 6h	Paraxanthine	ng/mL	795	782	789	1.65	Pass	No	
0255	1	Day 0 6h	Paraxanthine	ng/mL	1030	1030	1,030	0.00	Pass	No	
0276	1	Day 5 6h	Paraxanthine	ng/mL	962	943	953	1.99	Pass	No	
0282	1	Day 0 6h	Paraxanthine	ng/mL	1430	1440	1,440	0.69	Pass	No	
0298	1	Day 5 6h	Paraxanthine	ng/mL	990	995	993	0.50	Pass	No	
0300	1	Day 5 6h	Paraxanthine	ng/mL	939	921	930	1.94	Pass	No	
0315	1	Day 0 6h	Paraxanthine	ng/mL	1130	1090	1,110	3.60	Pass	No	
0322	1	Day 0 6h	Paraxanthine	ng/mL	778	726	752	6.91	Pass	No	
0320	1	Day 5 6h	Paraxanthine	ng/mL	943	960	952	1.79	Pass	No	
0321	1	Day 5 6h	Paraxanthine	ng/mL	969	1040	1,000	7.10	Pass	No	
0325	1	Day 0 6h	Paraxanthine	ng/mL	699	699	699	0.00	Pass	No	
0328	1	Day 0 6h	Paraxanthine	ng/mL	1240	1220	1,230	1.63	Pass	No	



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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## FIGURES

Figure 1 Calibration Curve for Caffeine in Control Matrix, Watson Run ID 2<sup>1</sup>

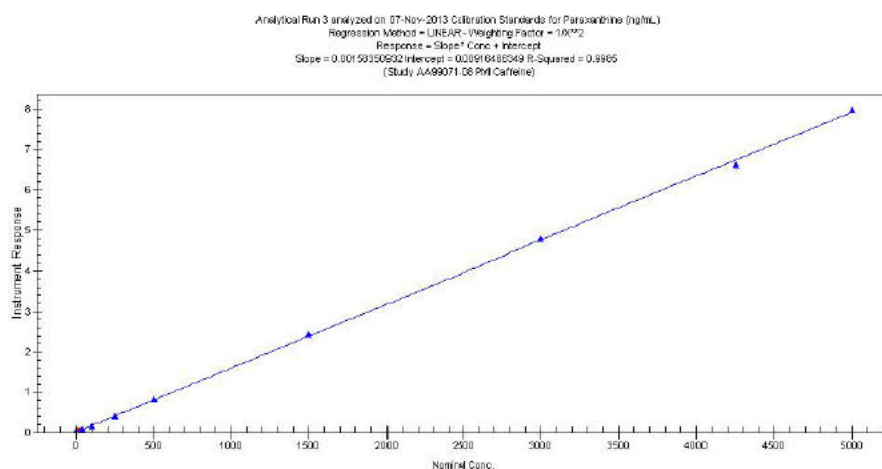


<sup>1</sup> Note: Though included on the figure above, the Standard 0 (blank sample extracted with internal standard) was not used as a standard to calculate the calibration curve parameters.



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Figure 2 Calibration Curve for Paraxanthine in Control Matrix, Watson Run ID 3<sup>2</sup>



<sup>2</sup> 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





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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



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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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



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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#### Attachment 2 Temperature Definitions at Celerion

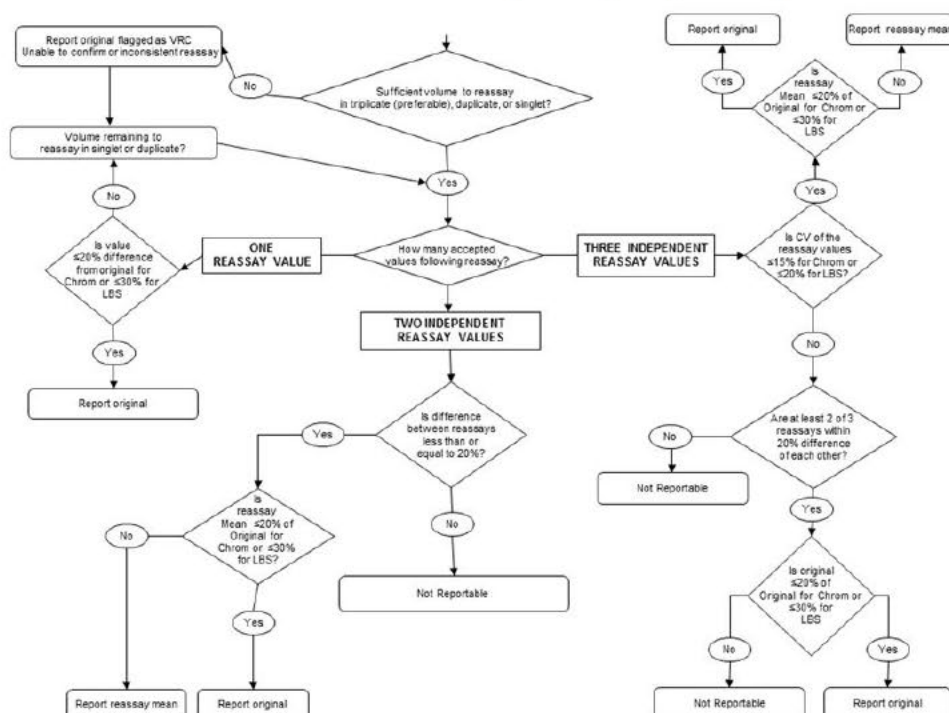
Values for temperatures are nominal temperatures representing the following temperature ranges:

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



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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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.



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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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

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

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



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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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).



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Attachment 6 Certificates of Analysis



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
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Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

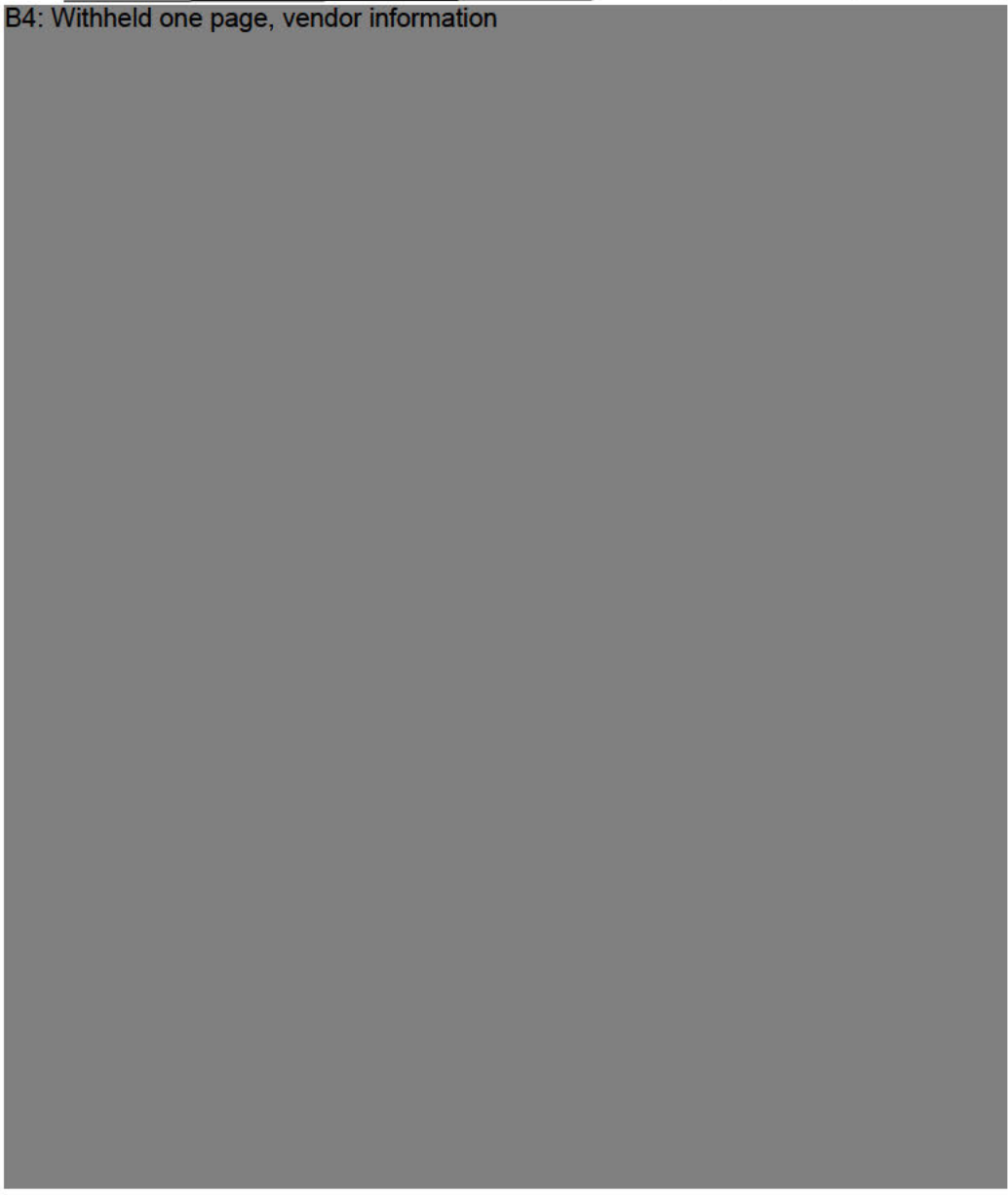
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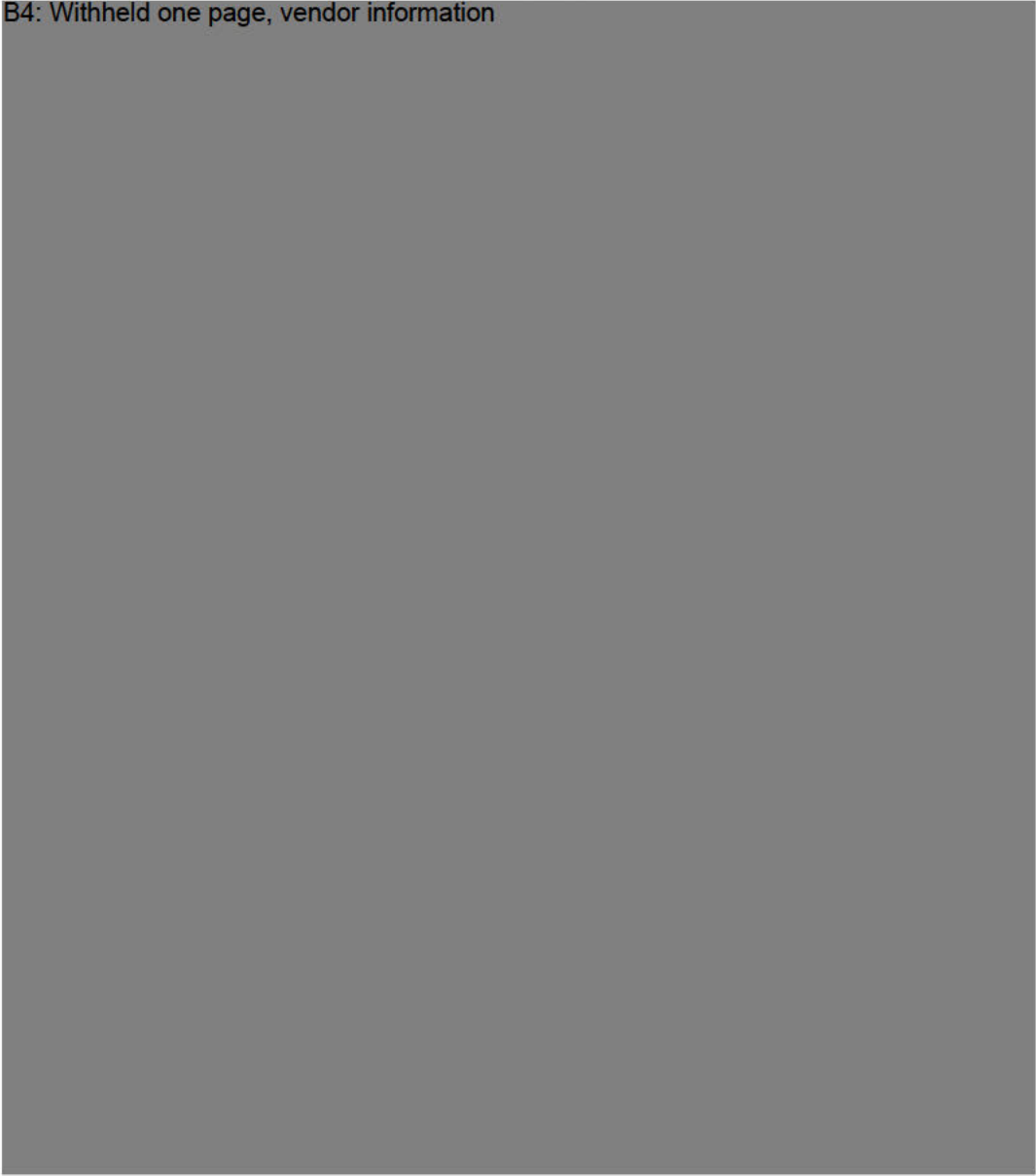
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Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

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#### Attachment 7 Bioanalytical Method Summary





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08



## BIOANALYTICAL METHOD SUMMARY (BMS)

Doc No: FOR\_QM000496 – CR204A2

Version N°: 2.0

Page 1 of 2

Biomarker: Caffeine		Matrix: Plasma	
MVR/SOP no. & date: ZZ25187-02 / 06-Oct-2014		CRO/Laboratory: Celerion-Lincoln	
LLOQ: 20.0 ng/mL		ULOQ: 5000 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 liquid/liquid extraction procedure. The extracted samples were analyzed by a HPLC equipped with an AB SCIEX API 4000 <sup>TM</sup> mass spectrometer. Positive ions were monitored in the multiple reaction monitoring (MRM) mode. Quantitation was determined using a weighted linear regression analysis (1/concentration <sup>2</sup> ) of peak area ratios of the analyte and internal standard.			
Selectivity/Sensitivity/Matrix effect:		No significant matrix effect was observed in any of the 6 human plasma (heparin) lots that were fortified at the concentration of the LLOQ (20.0 ng/mL) and in any of the 6 lots that were fortified at the concentration of the high QC (4000 ng/mL) sample	
Accuracy:		Intra-batch: -10.5 to 8.0% R.E. Inter-batch: -6.0 to 3.6% R.E.	
Precision:		Intra-batch: 1.1 to 8.0% C.V. Inter-batch: 4.3 to 7.9% C.V.	
Recovery:		81% at 50.0 ng/mL in human plasma 81% at 500 ng/mL in human plasma 87% at 4000 ng/mL in human plasma	
Freeze and thaw stability:		6 freeze/cycles in polypropylene tubes at -20°C under white light	
Short-term temperature stability:		53 hours in polypropylene tubes at ambient temperature and in an ice water bath under white light	
Long-term stability:		545 days in polypropylene tubes at -20°C	
Stock solution stability:		902 days at 2000 µg/mL in 40:60 methanol:H <sub>2</sub> O in a polypropylene container at -20°C	
Post-preparative stability:		162 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"	



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08



PMI RESEARCH &amp; DEVELOPMENT

## BIOANALYTICAL METHOD SUMMARY (BMS)

Doc No: FORL\_QM000496 - CR204A2

Version N°: 2.0

Page 2 of 2

<b>BMS completed by:</b>		
<b>Name:</b>	<b>Date:</b>	<b>Signature:</b>
Erica Nachi	03-Mar-2016	<i>Erica Nachi</i>



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08



## BIOANALYTICAL METHOD SUMMARY (BMS)

Doc No: FOR\_QM000496 – CR204A2

Version N°: 2.0

Page 1 of 2

Biomarker: Paraxanthine		Matrix: Plasma	
MVR/SOP no. & date: ZZ25187-02 / 06-Oct-2014		CRO/Laboratory: Celerion-Lincoln	
LLOQ: 20.0 ng/mL		ULOQ: 5000 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 liquid/liquid extraction procedure. The extracted samples were analyzed by a HPLC equipped with an AB SCIEX API 4000™ mass spectrometer. Positive ions were monitored in the multiple reaction monitoring (MRM) mode. Quantitation was determined using a weighted linear regression analysis (1/concentration <sup>2</sup> ) of peak area ratios of the analyte and internal standard.			
Selectivity/Sensitivity/Matrix effect:		No significant matrix effect was observed in any of the 6 human plasma (heparin) lots that were fortified at the concentration of the LLOQ (20.0 ng/mL) and in any of the 6 lots that were fortified at the concentration of the high QC (4000 ng/mL) sample	
Accuracy:		Intra-batch: -9.5 to 4.0% R.E. Inter-batch: -3.3 to -0.6% R.E.	
Precision:		Intra-batch: 0.7 to 4.7% C.V. Inter-batch: 1.9 to 6.5% C.V.	
Recovery:		59% at 50.0 ng/mL in human plasma 61% at 500 ng/mL in human plasma 63% at 4000 ng/mL in human plasma	
Freeze and thaw stability:		6 freeze/cycles in polypropylene tubes at -20°C under white light	
Short-term temperature stability:		53 hours in polypropylene tubes at ambient temperature and in an ice water bath under white light	
Long-term stability:		545 days in polypropylene tubes at -20°C	
Stock solution stability:		41 days at 100 µg/mL in 40:60 methanol:H <sub>2</sub> O in a polypropylene container at -20°C	
Post-preparative stability:		162 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"	



Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08



## BIOANALYTICAL METHOD SUMMARY (BMS)

Doc No: FDR\_QM00496 – CR204A2

Version N°: 2.0

Page 2 of 2

<b>BMS completed by:</b>		
<b>Name:</b>	<b>Date:</b>	<b>Signature:</b>
Erica Nash	03-Mar-2015	<i>Erica Nash</i>





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08

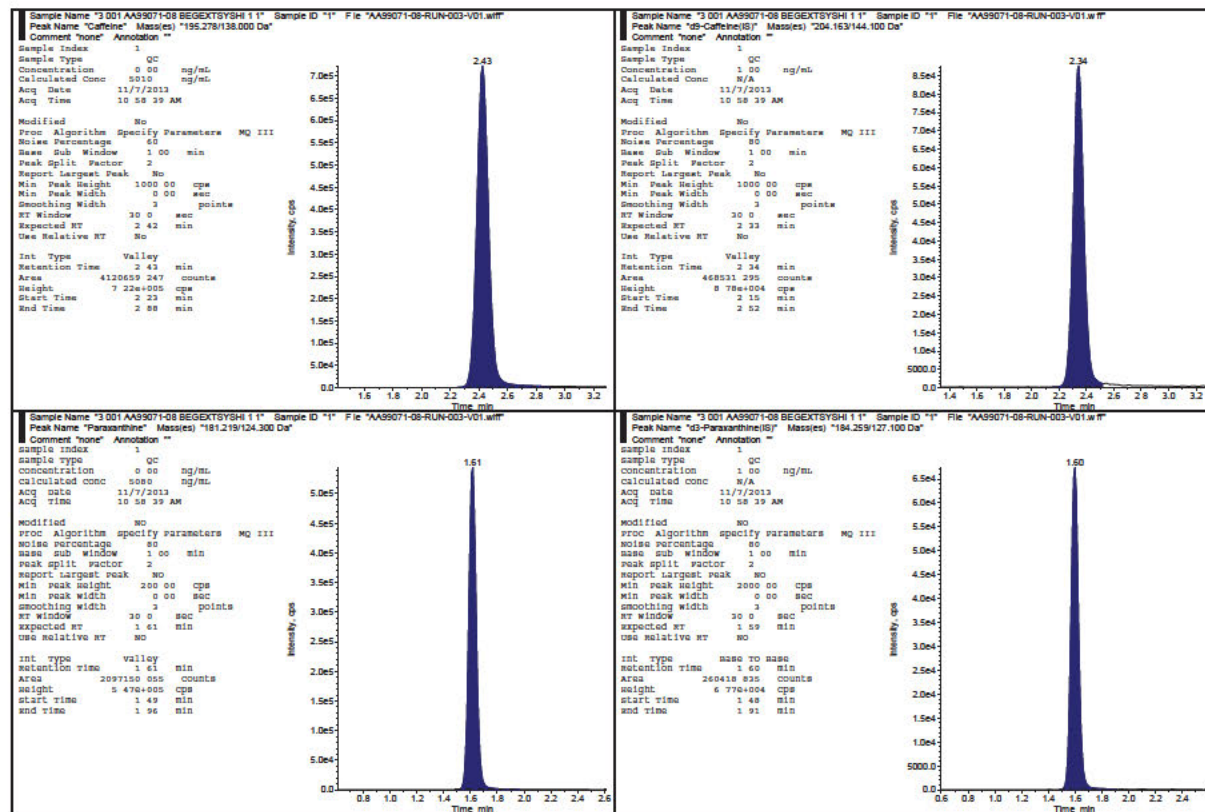
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Attachment 8 Chromatograms

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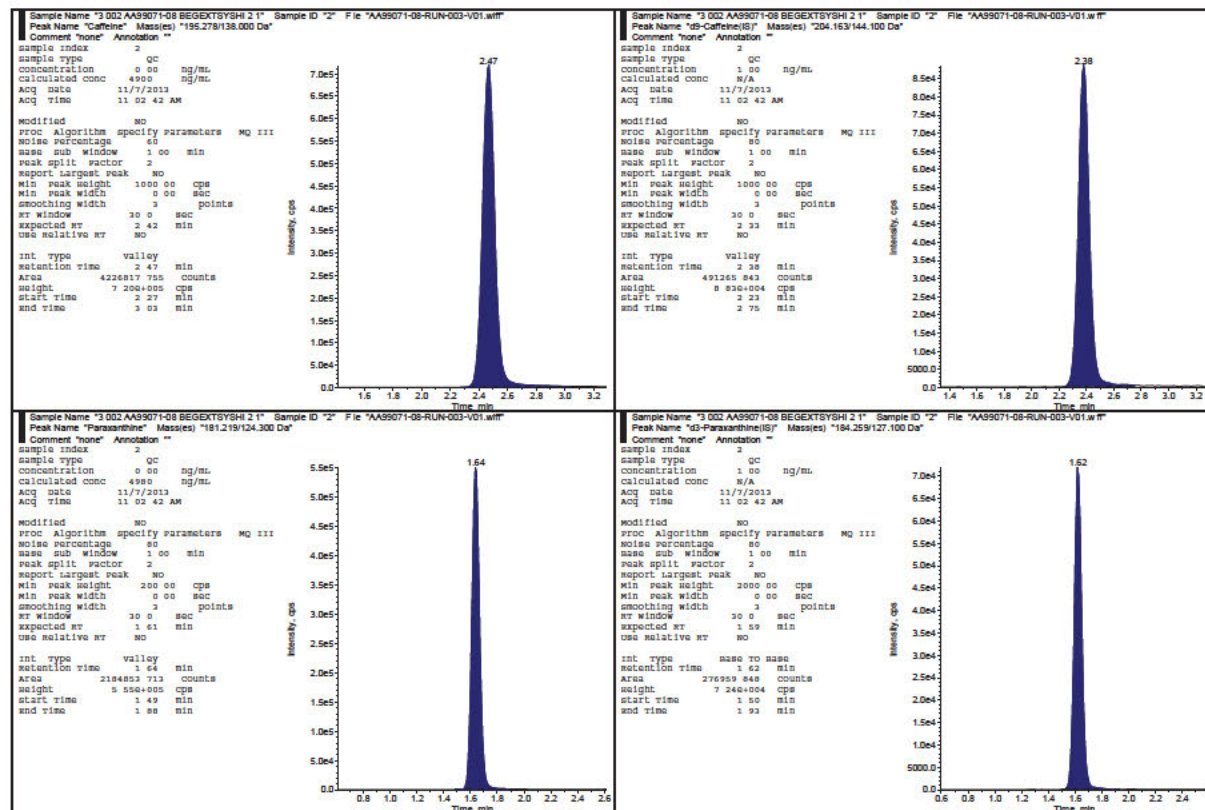


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Celerion Study AA99071-08



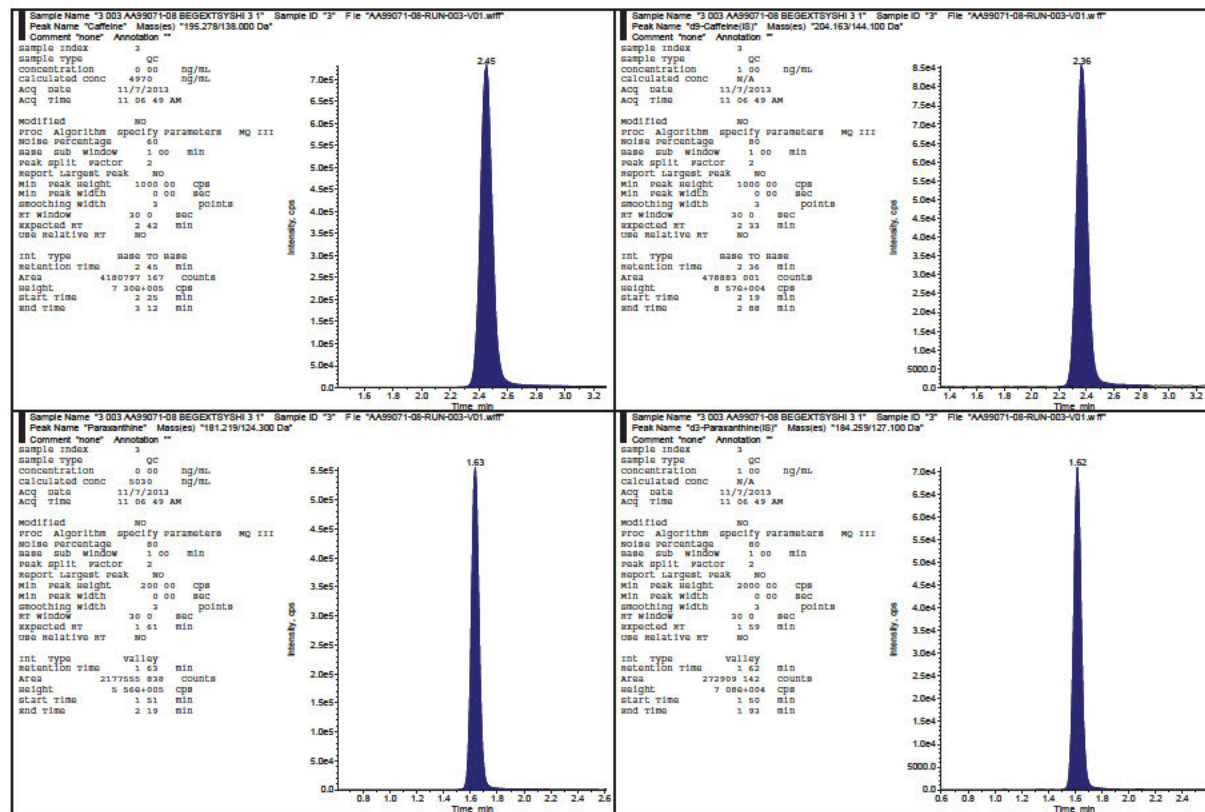


Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08





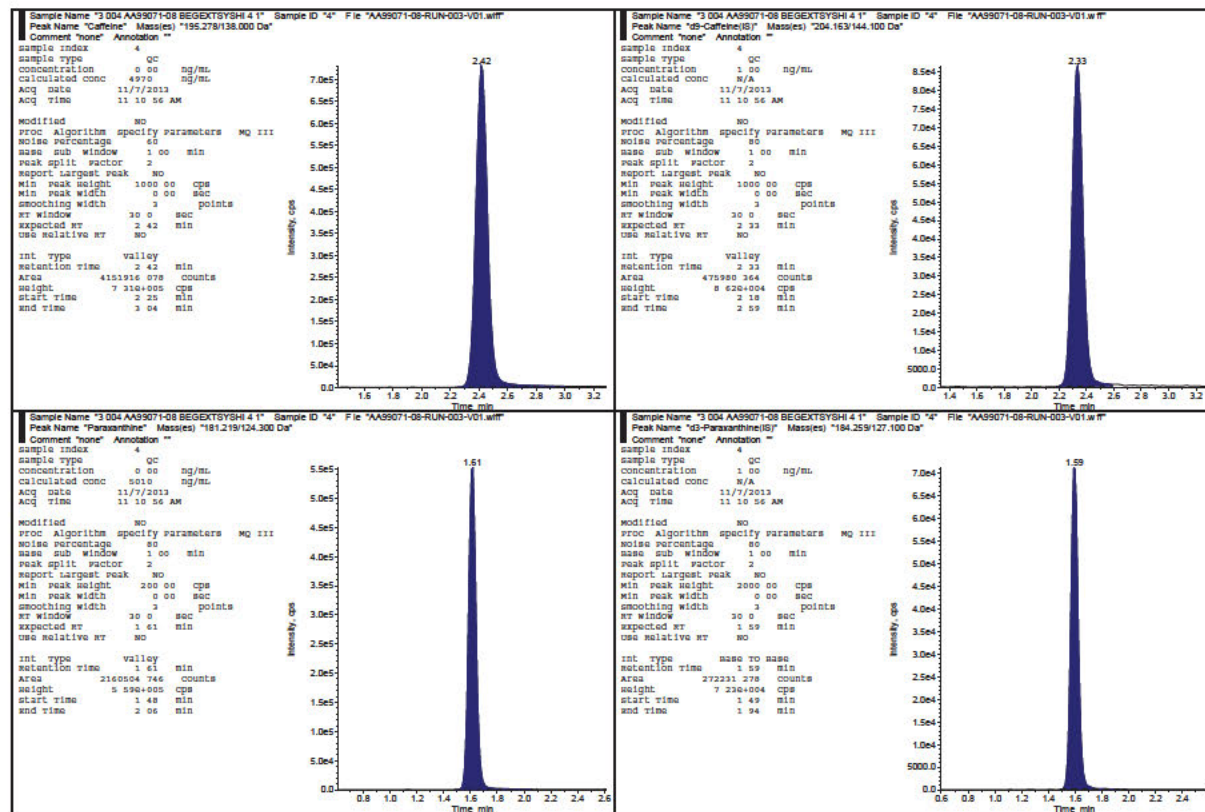
Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08





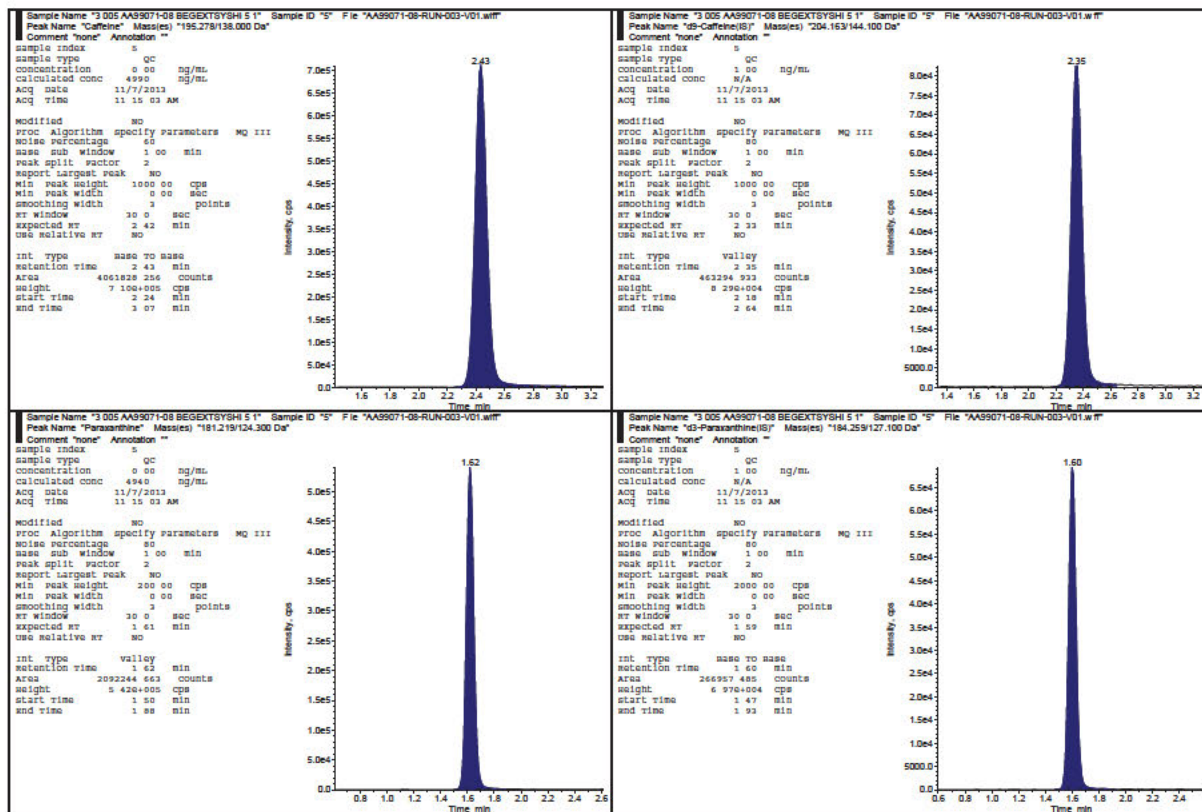


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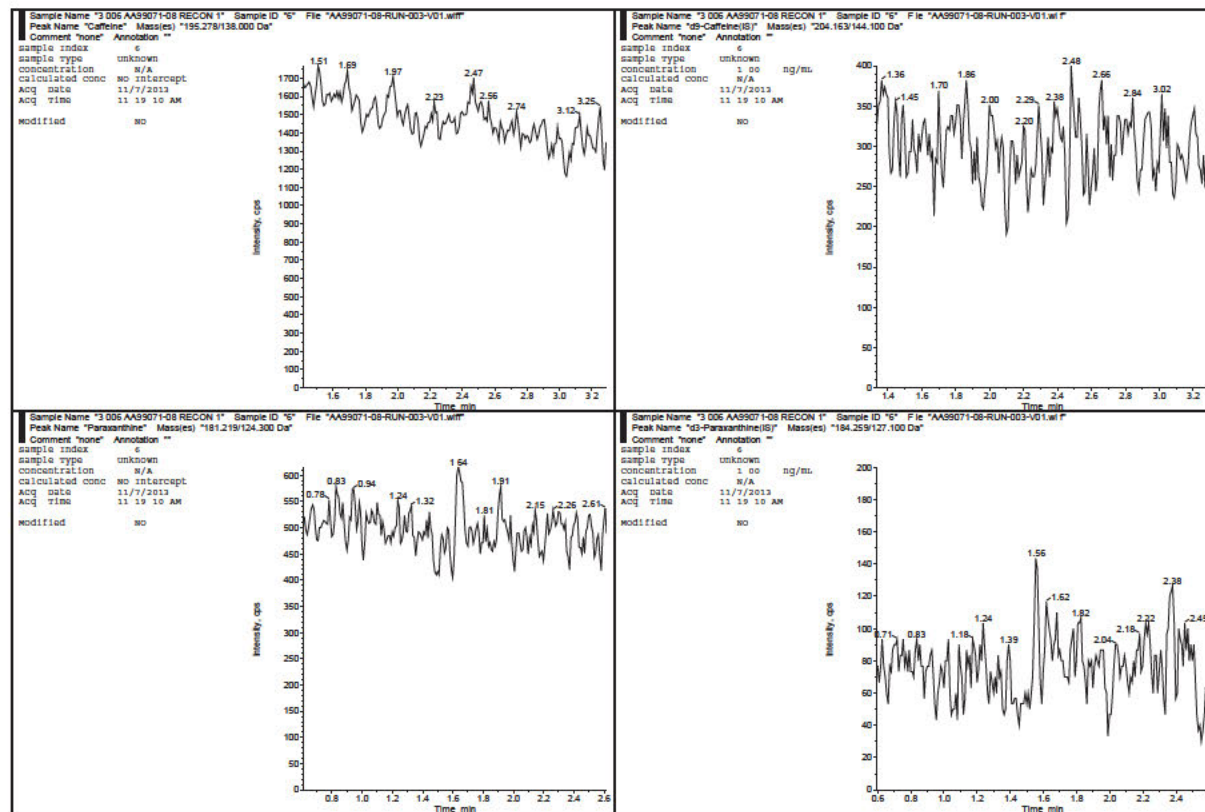


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Celerion Study AA99071-08



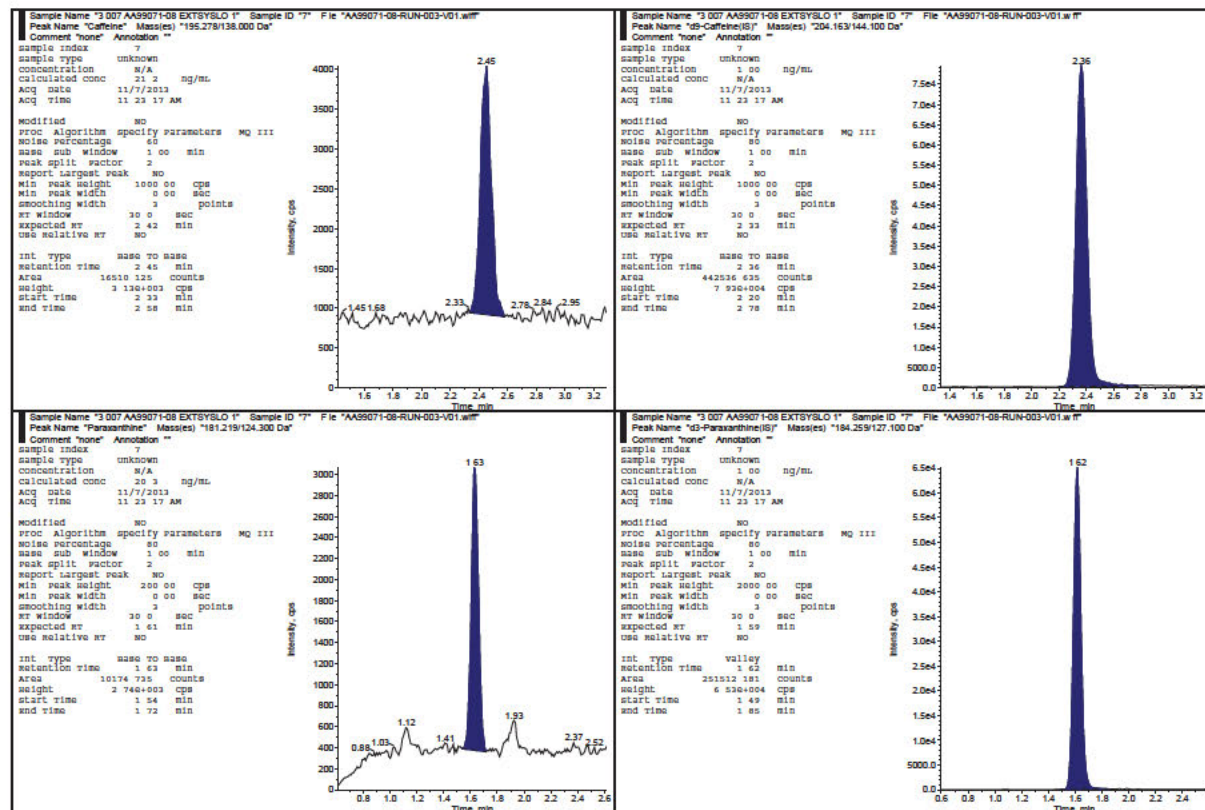


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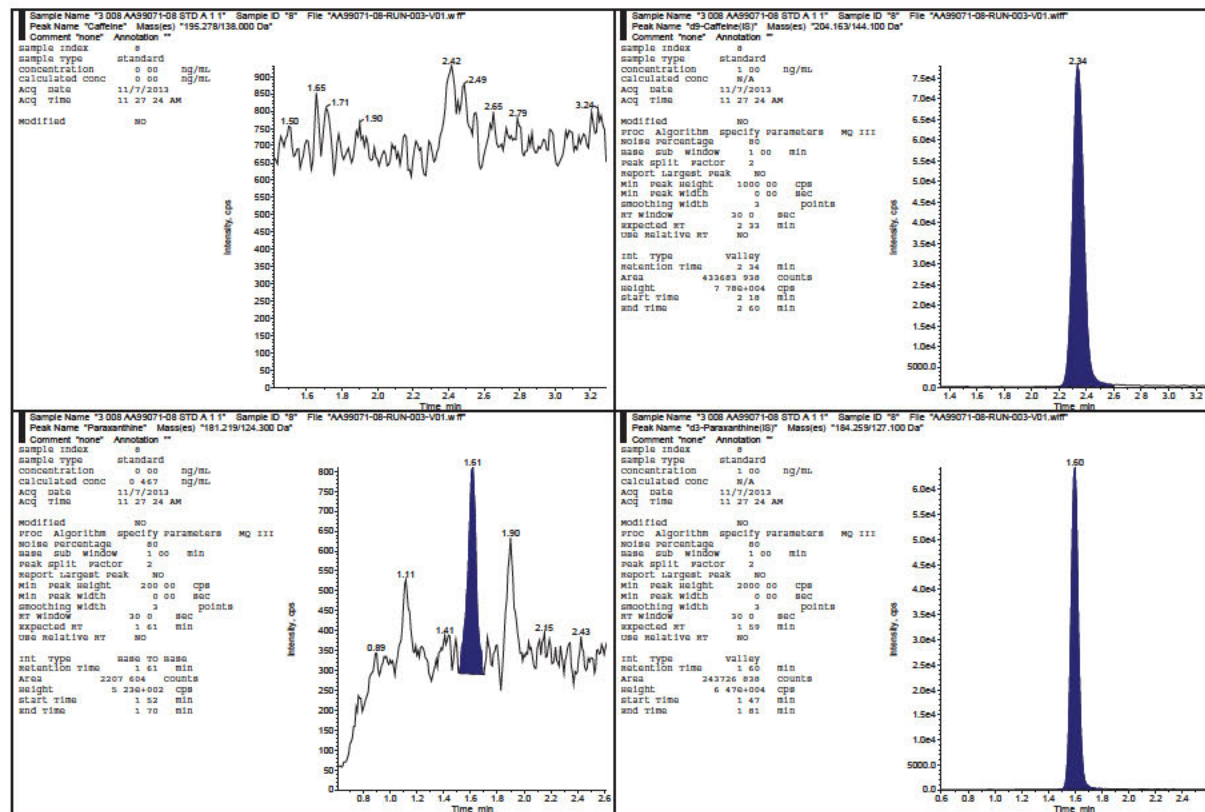
Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08







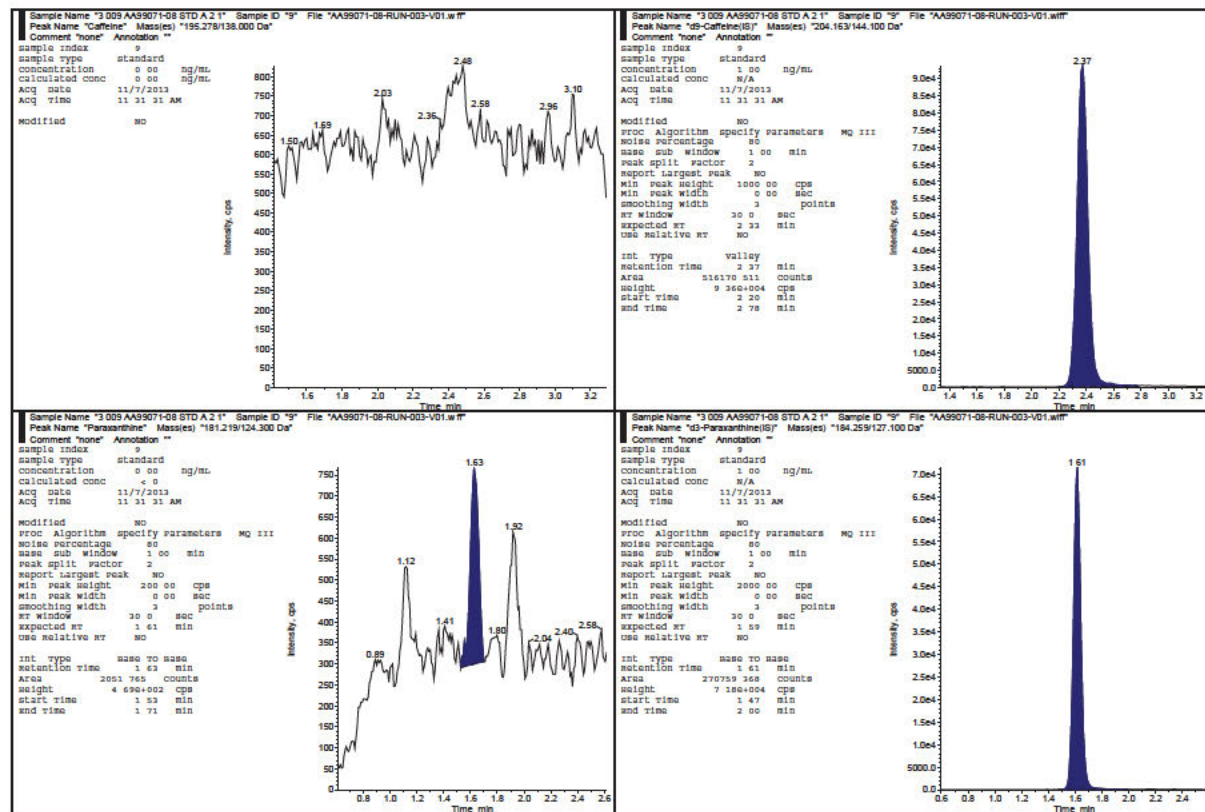
Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08





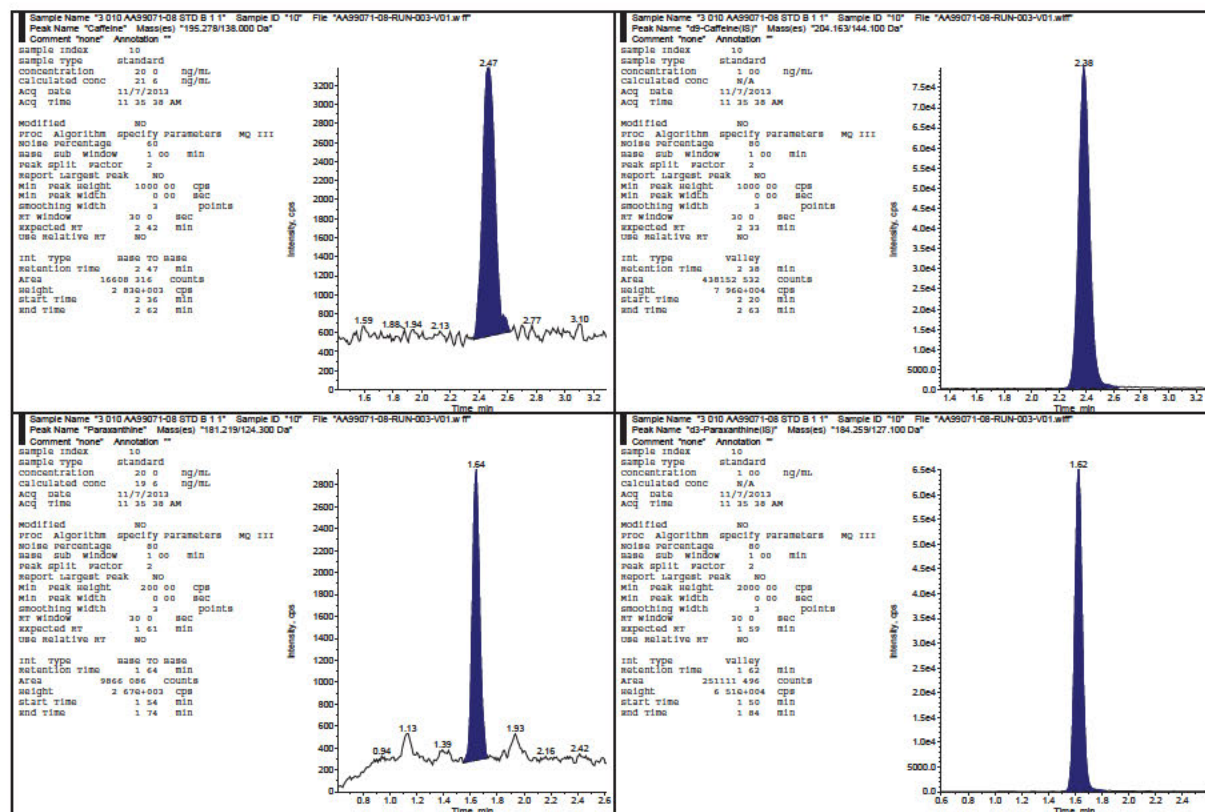


Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08





Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08



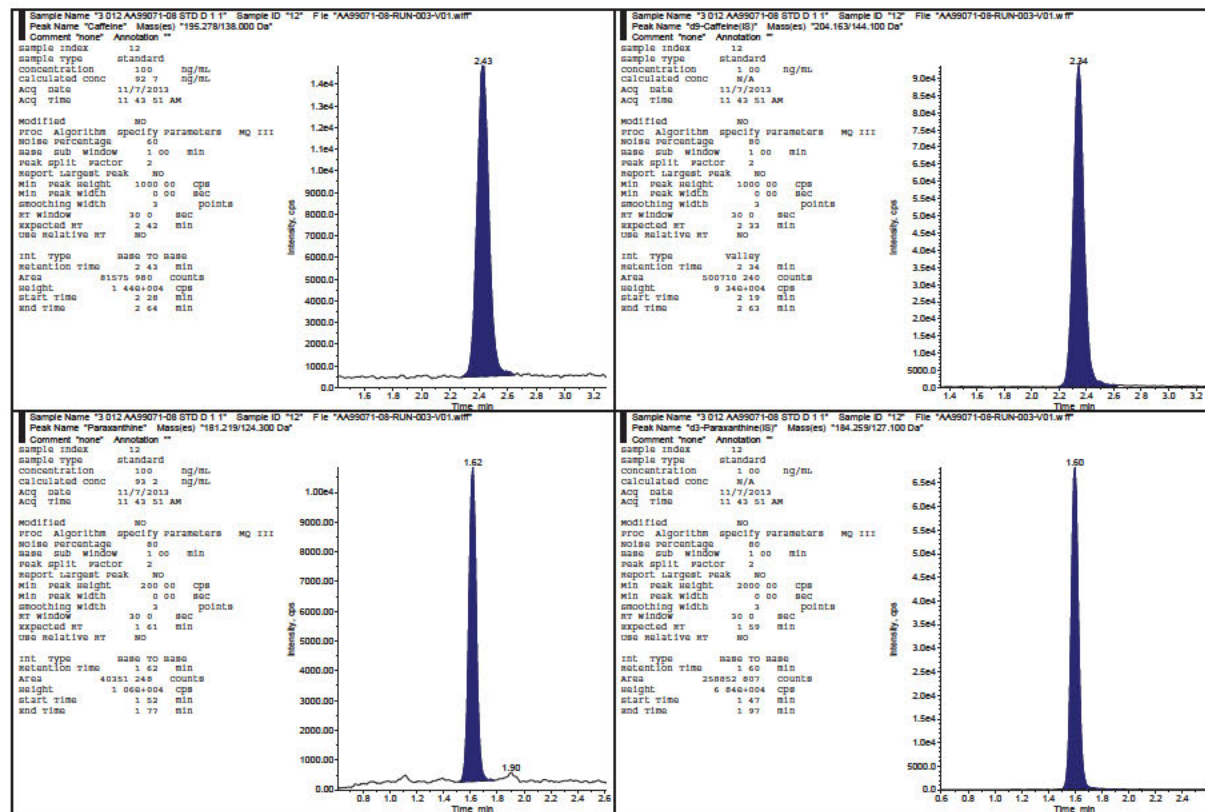


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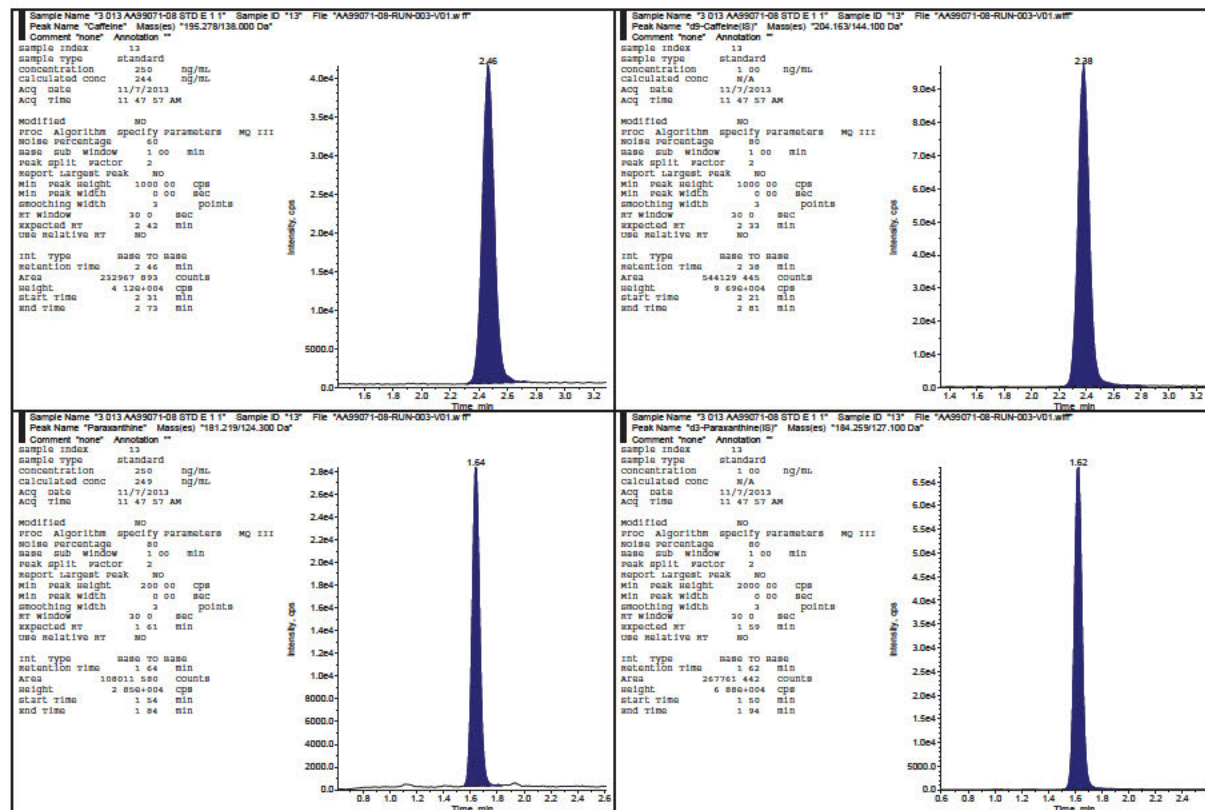
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Celerion Study AA99071-08







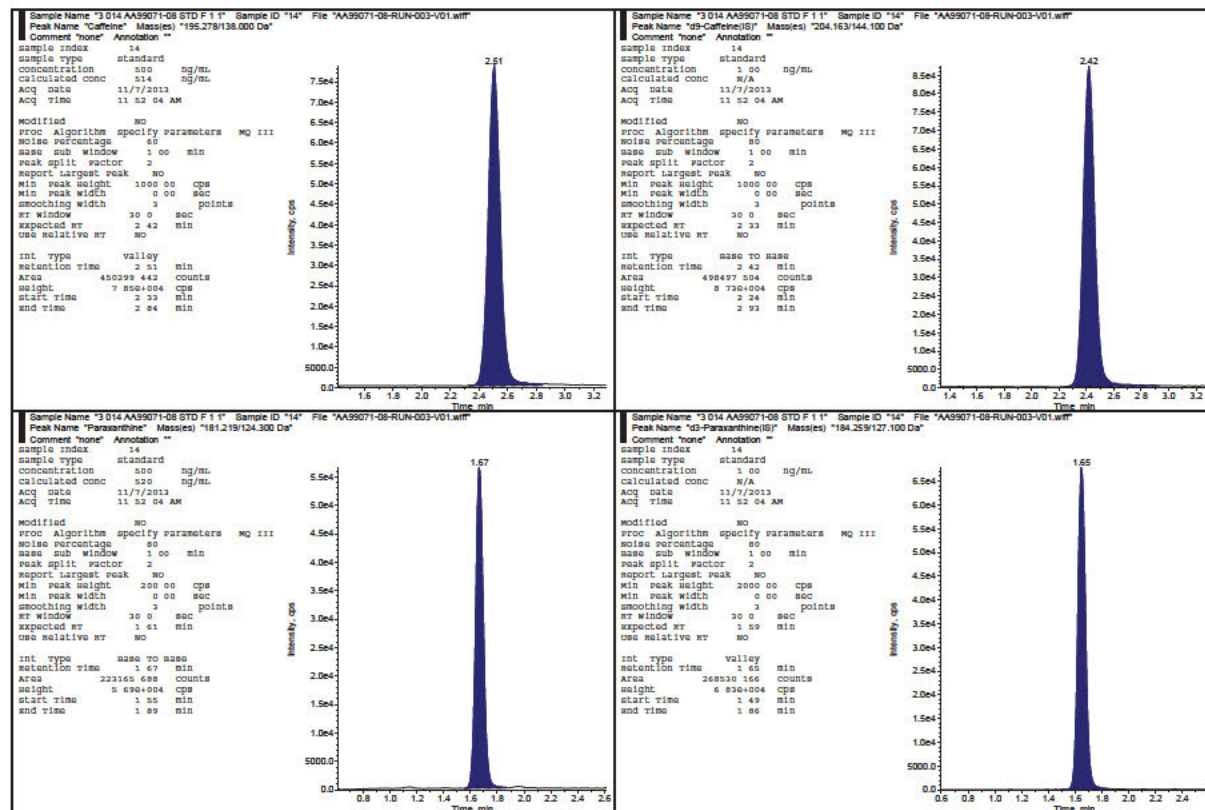
Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08





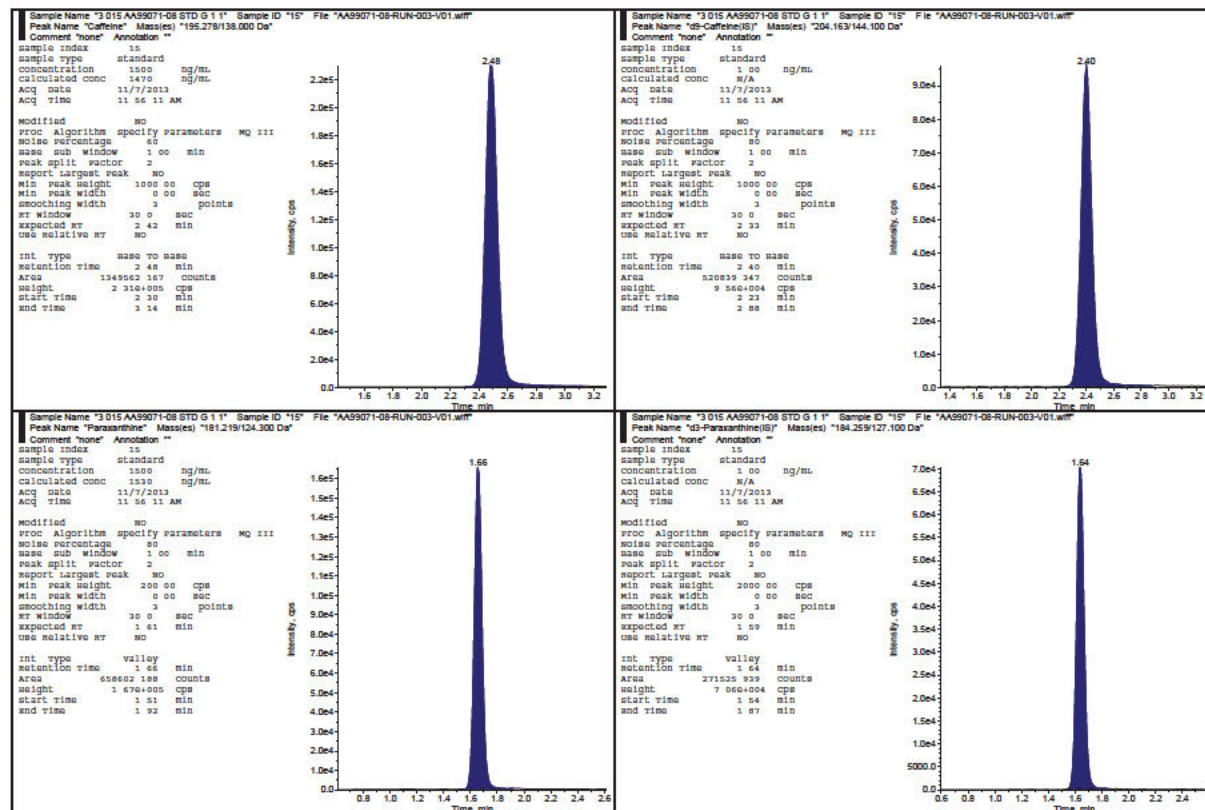


Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08



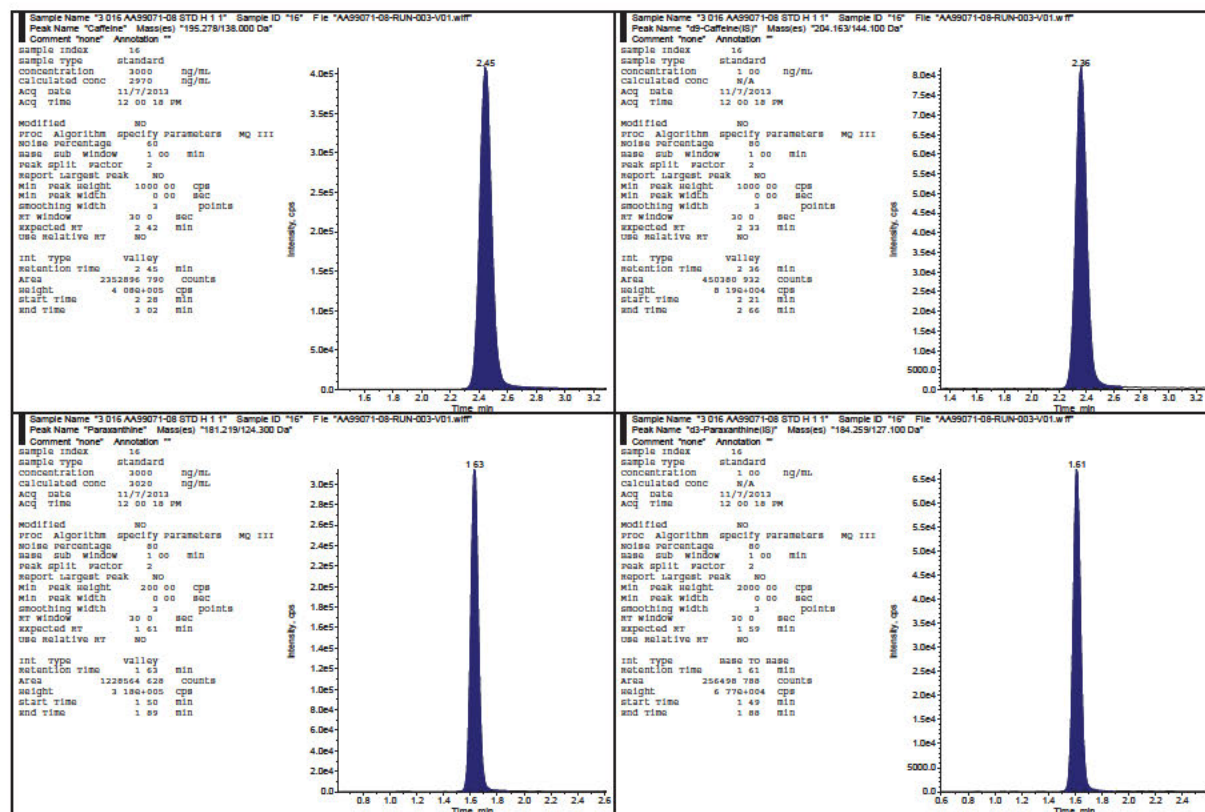


Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08



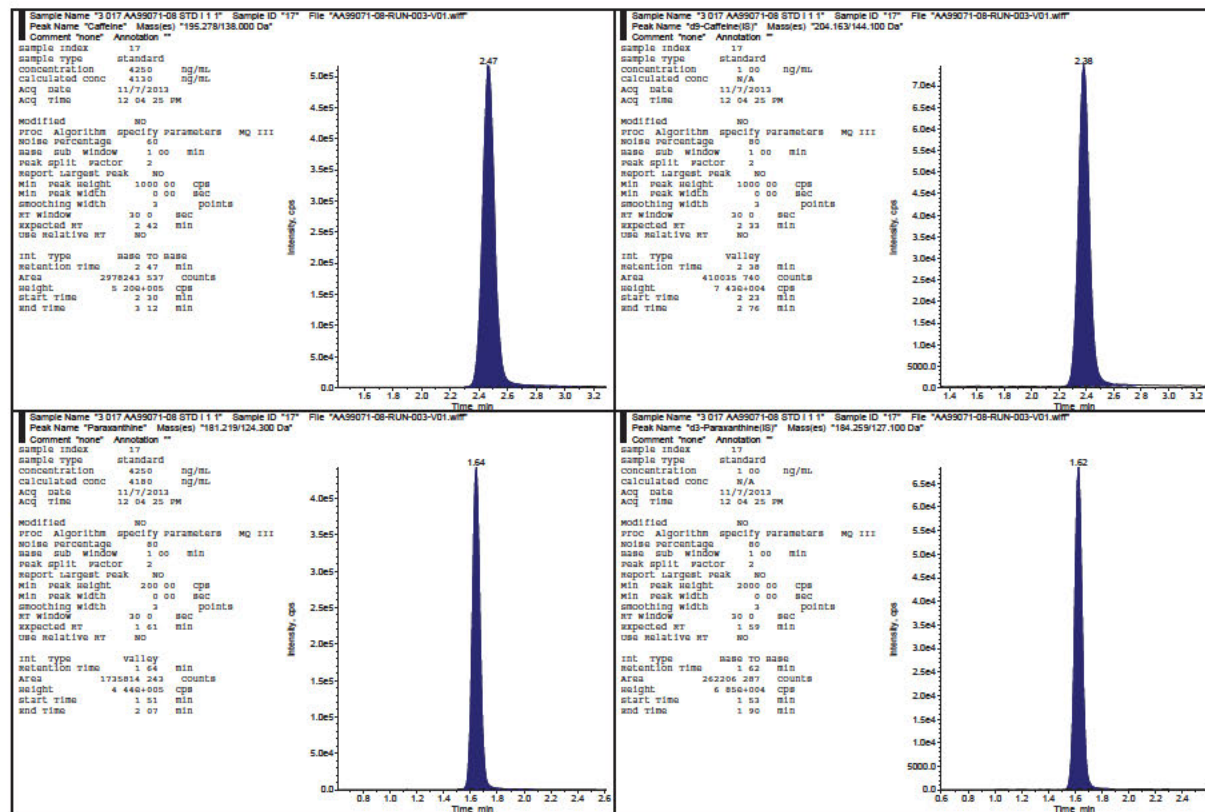


Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08





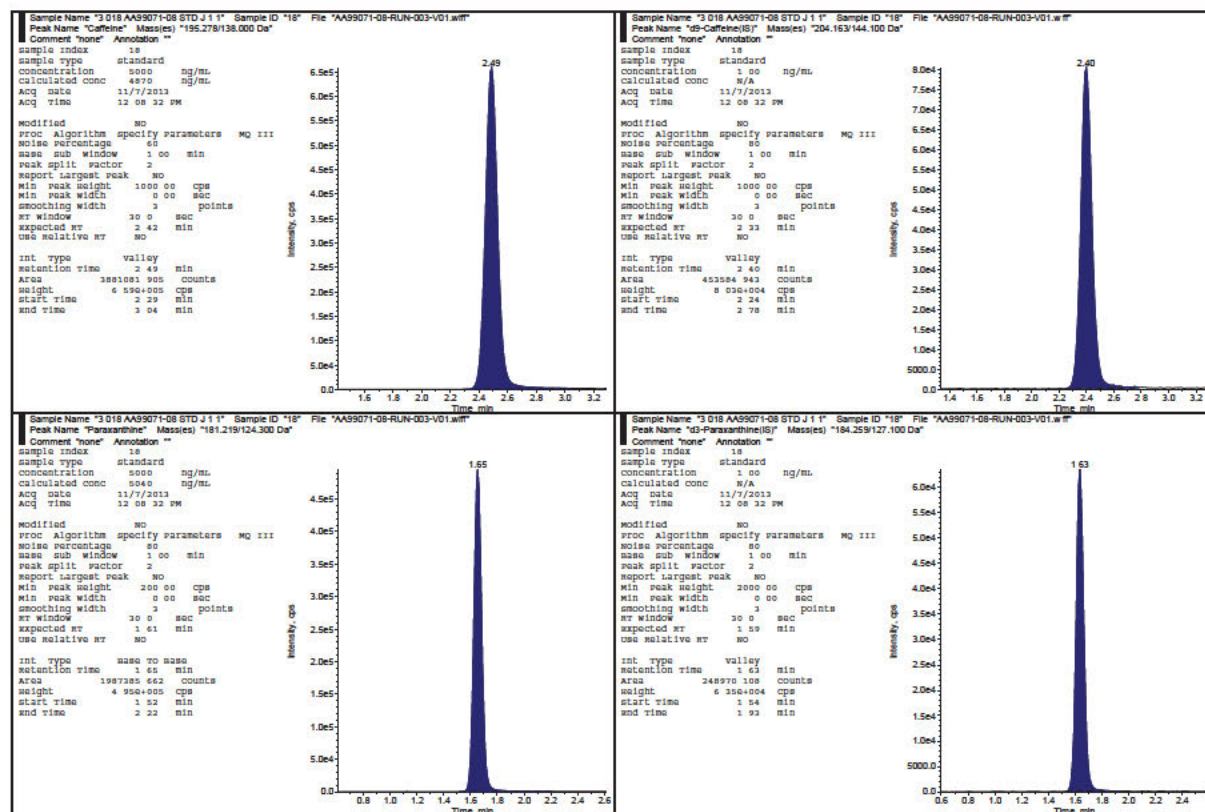
Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08







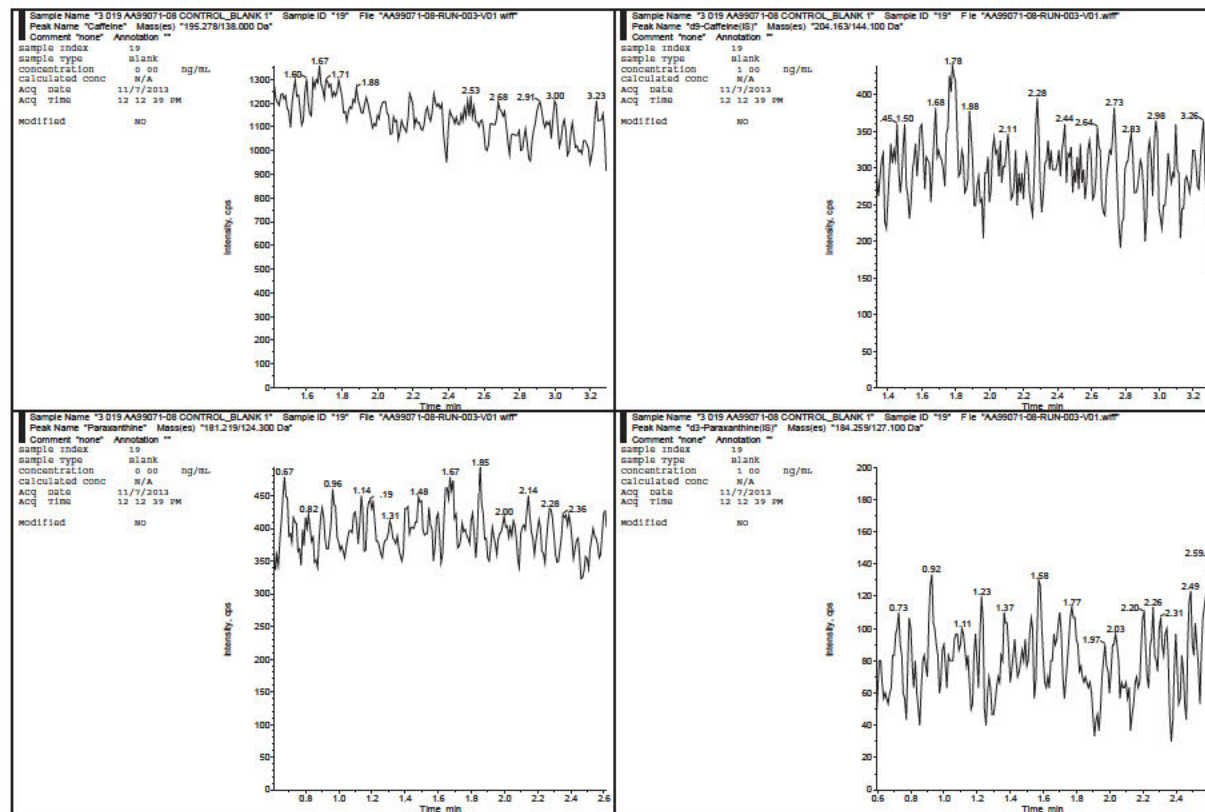
Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08





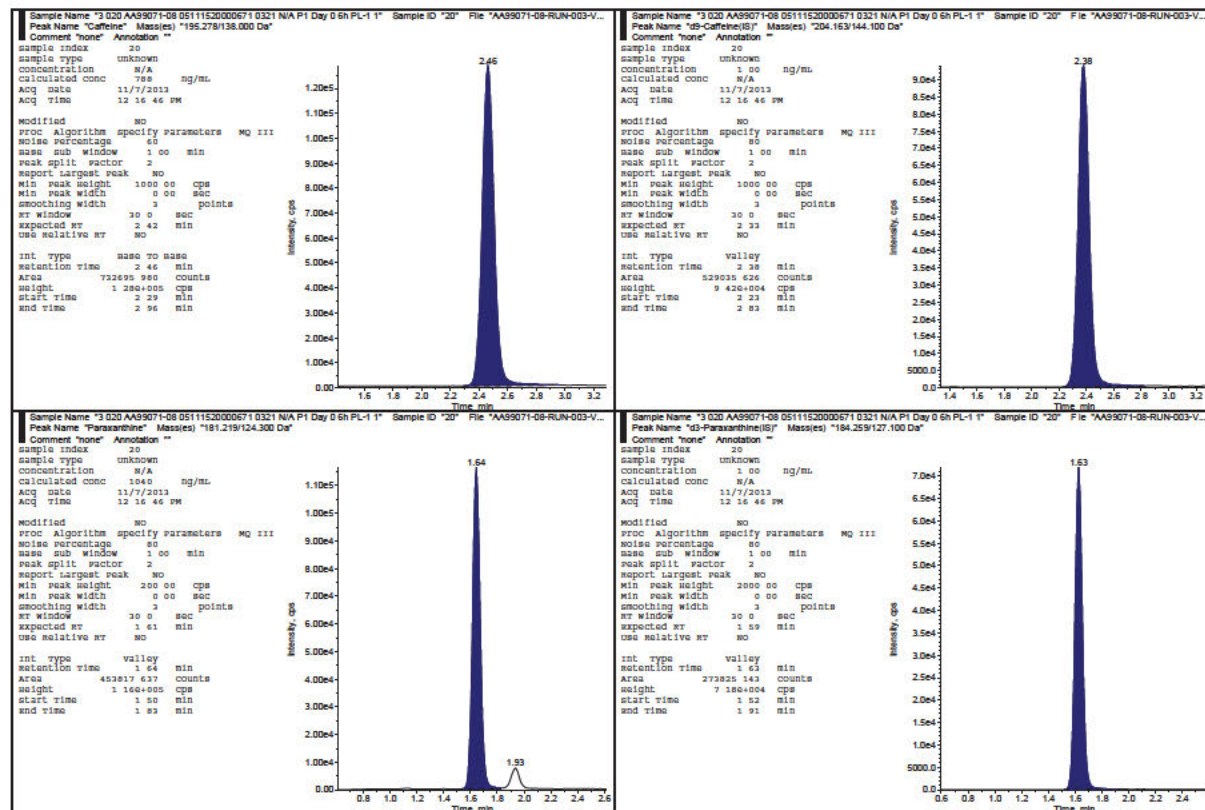


Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08



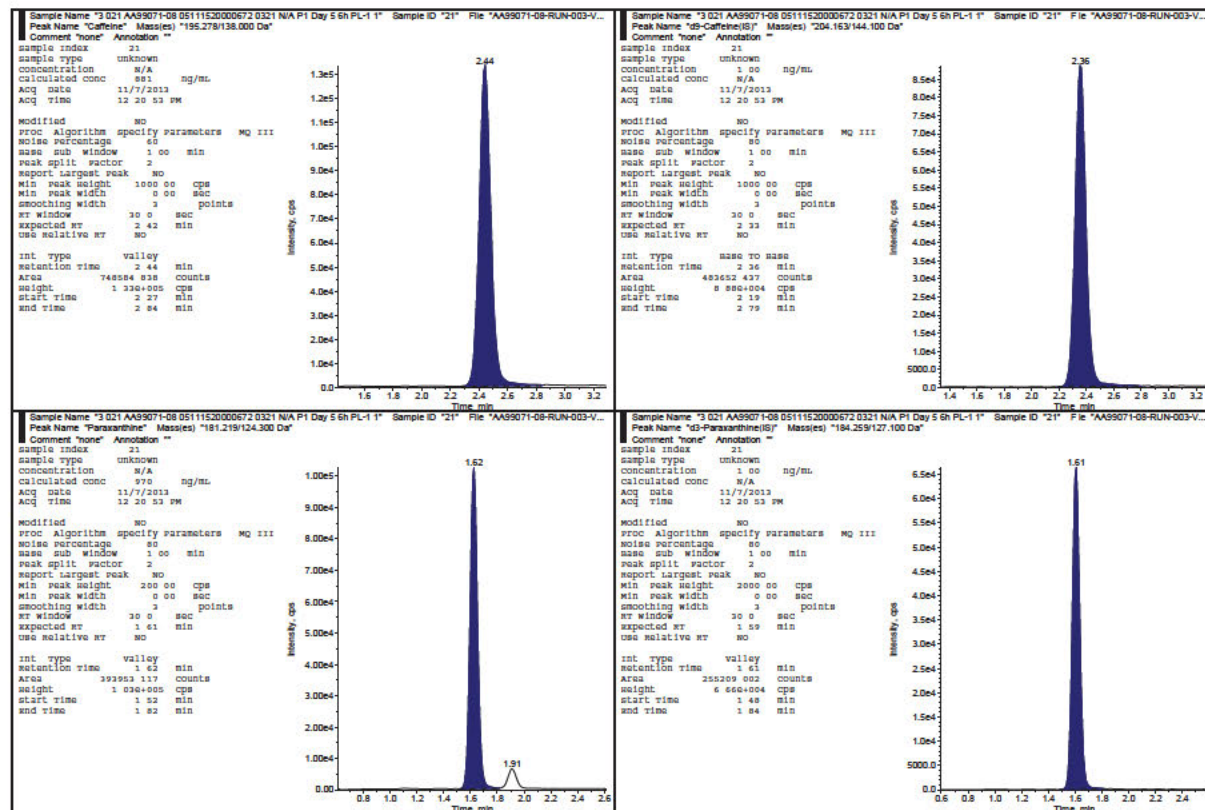


Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08



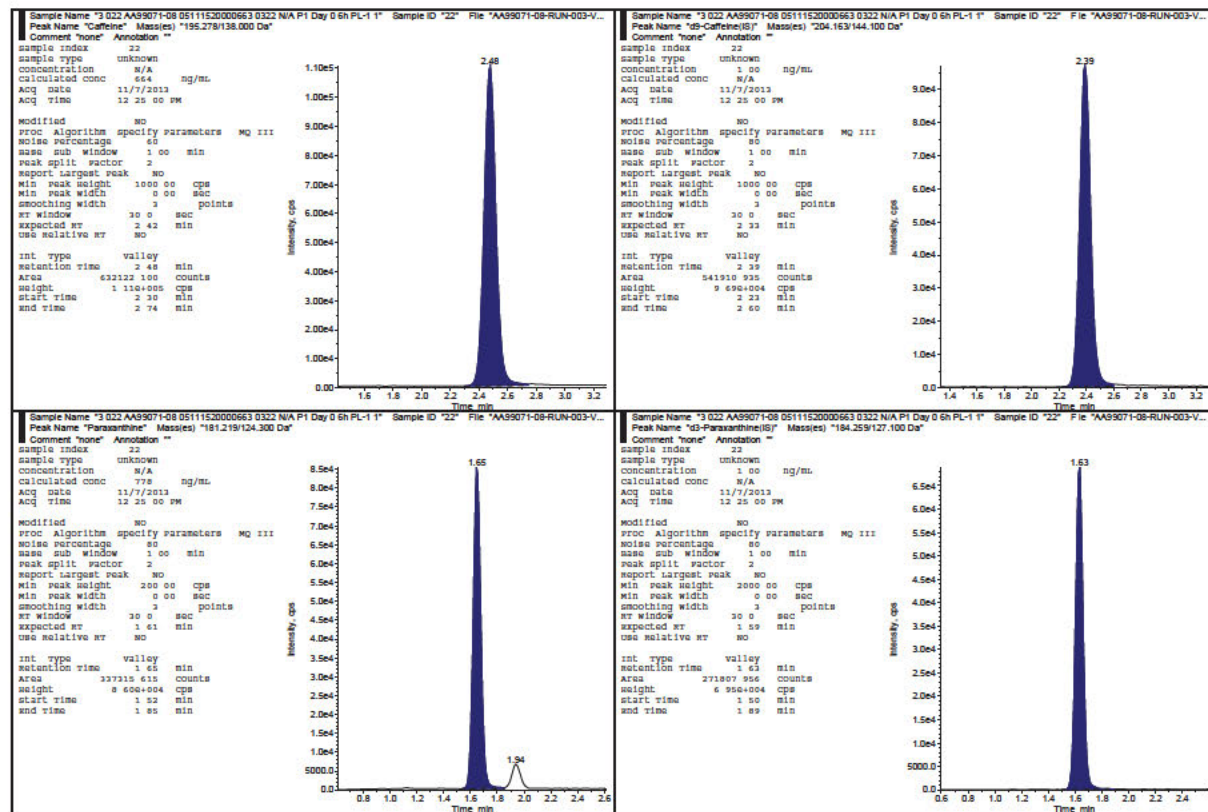


Caffeine and Paraxanthine in Human Plasma (Lithium Heparin)  
Celerion Study AA99071-08





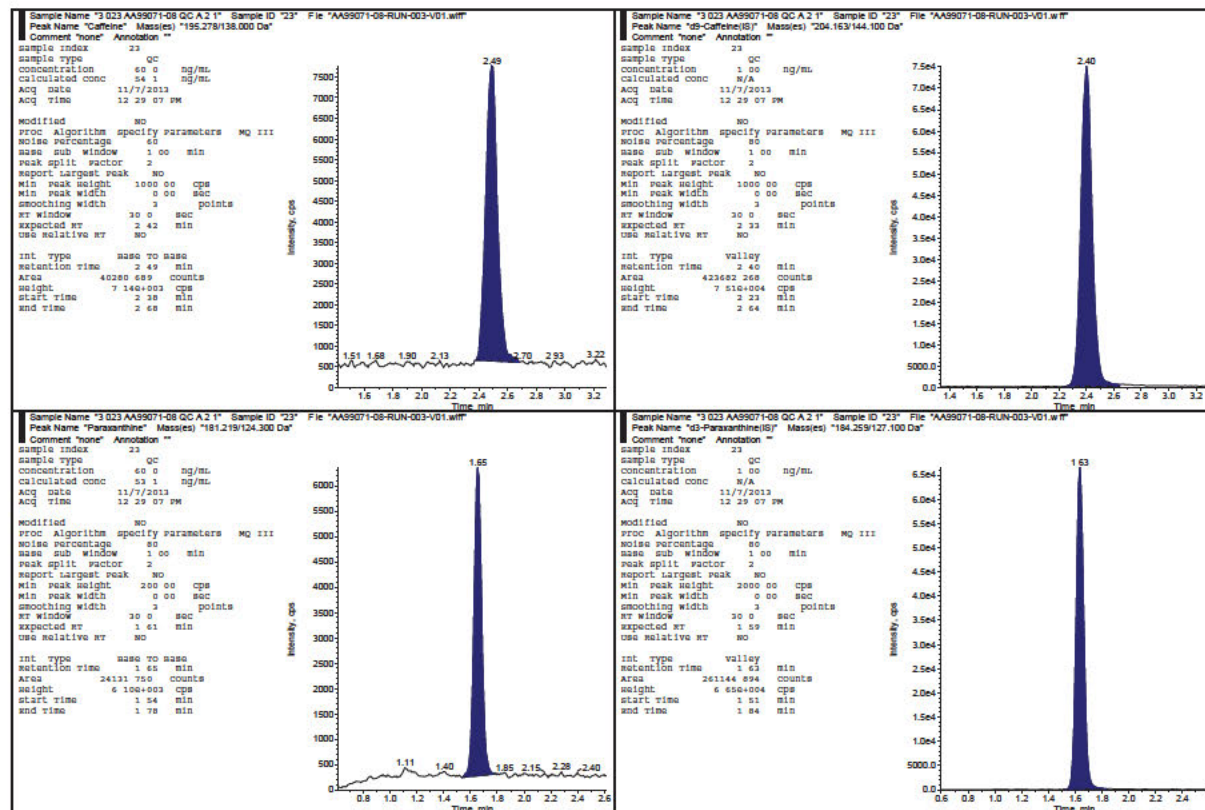
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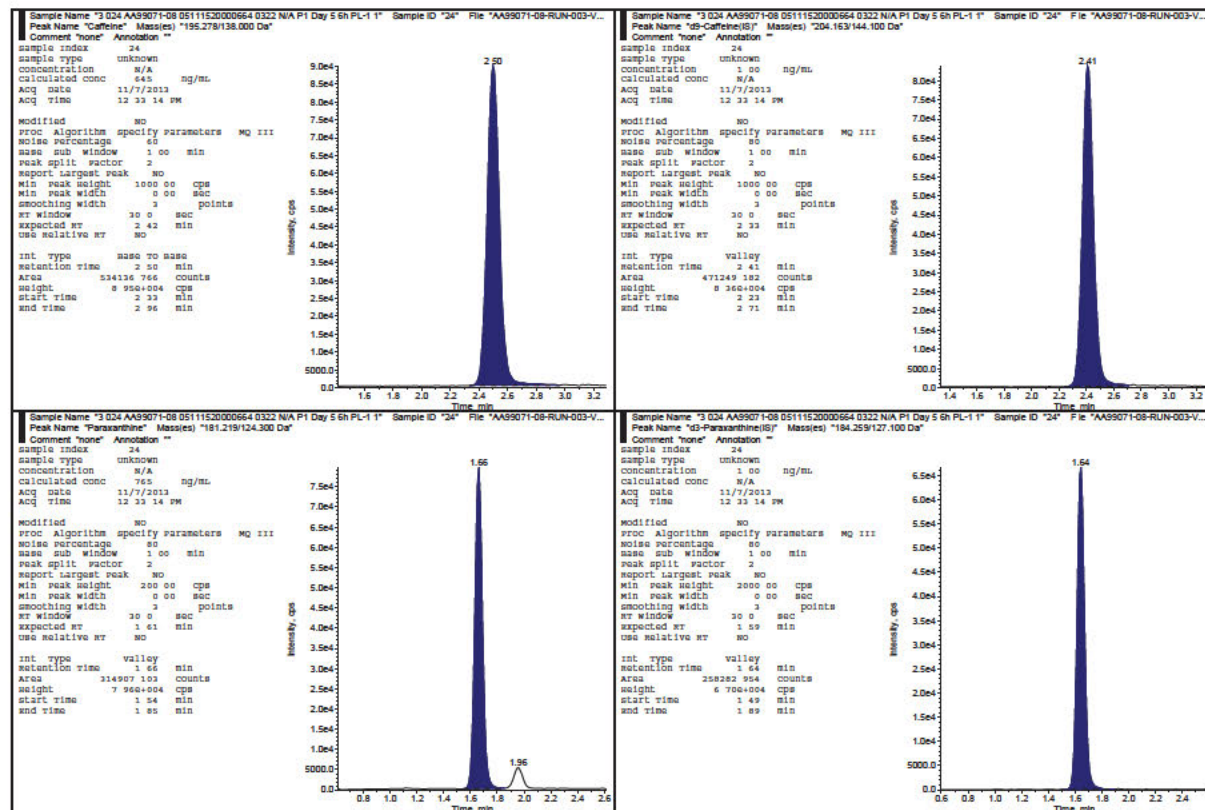
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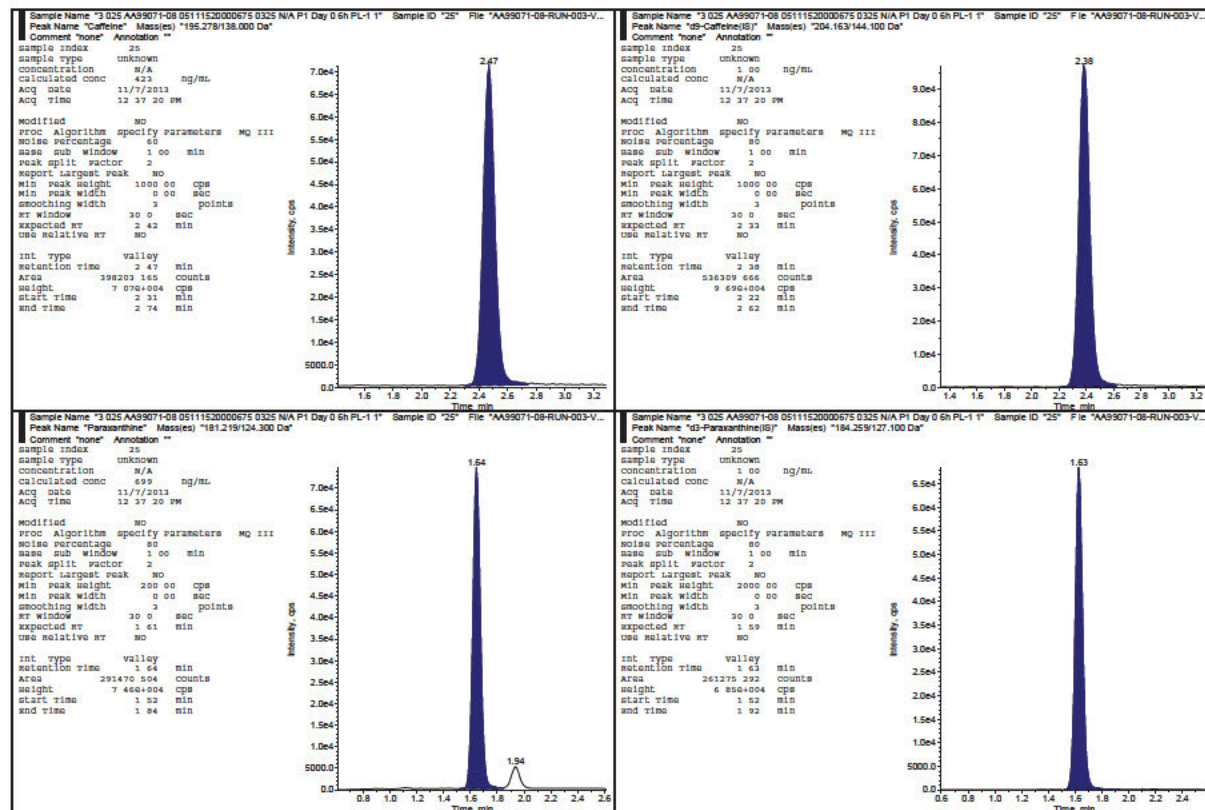


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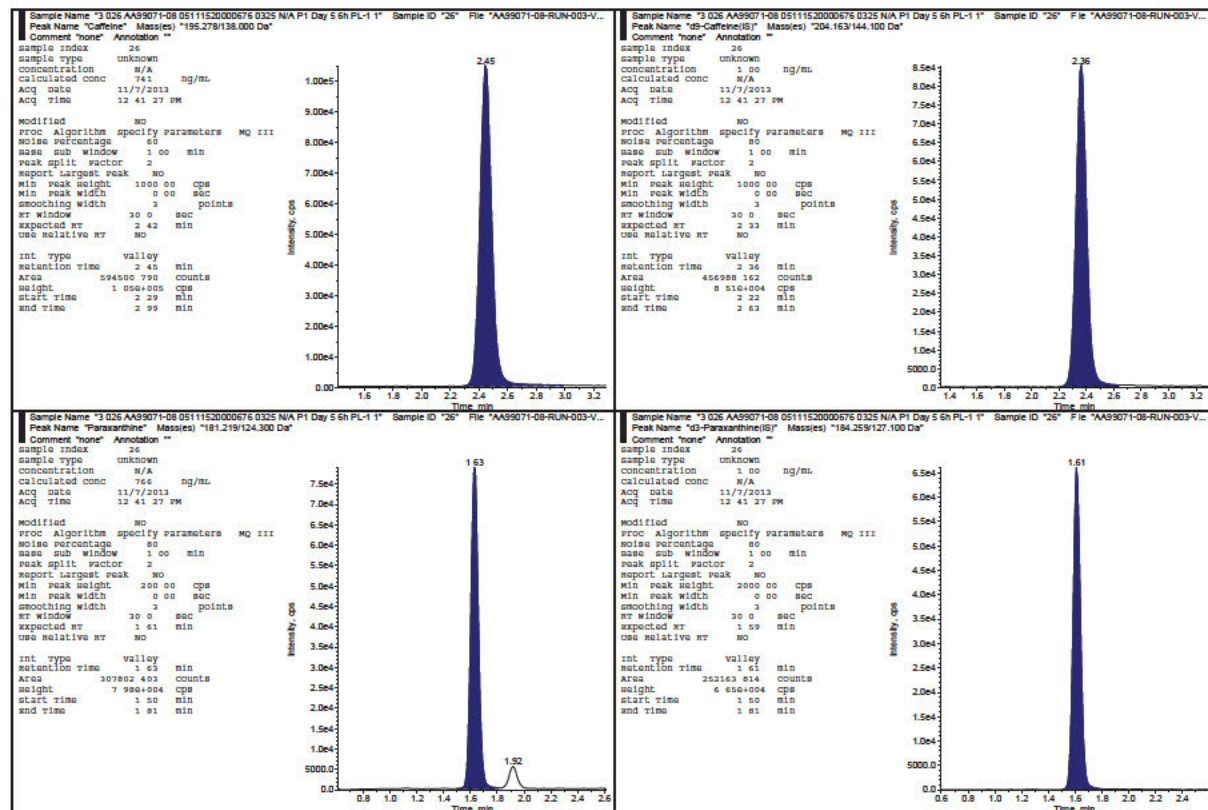


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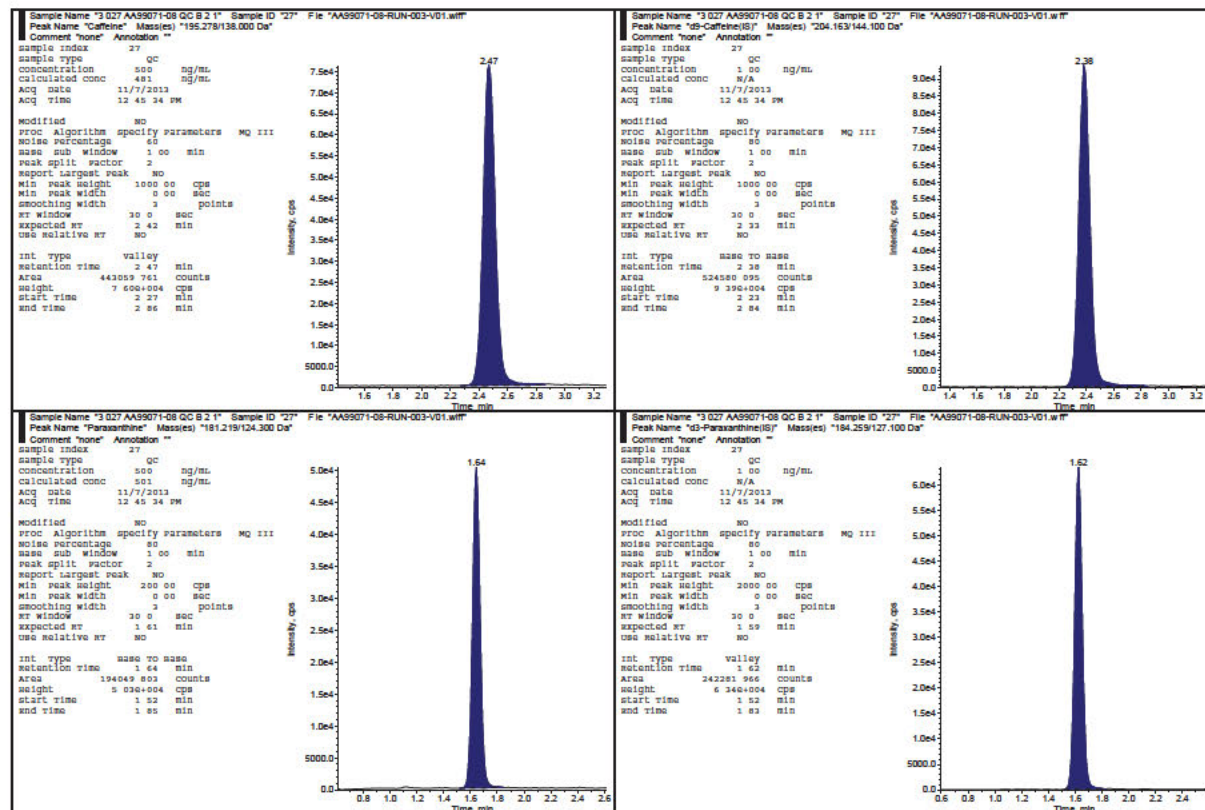


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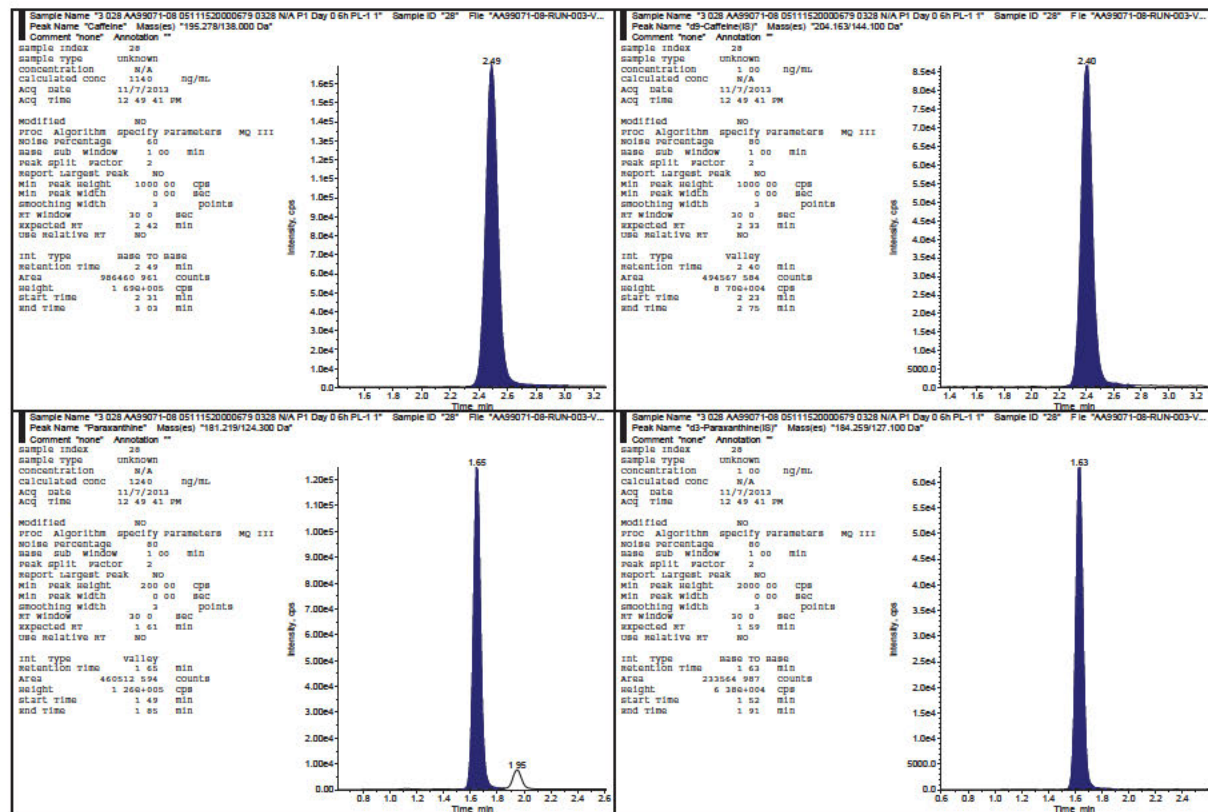
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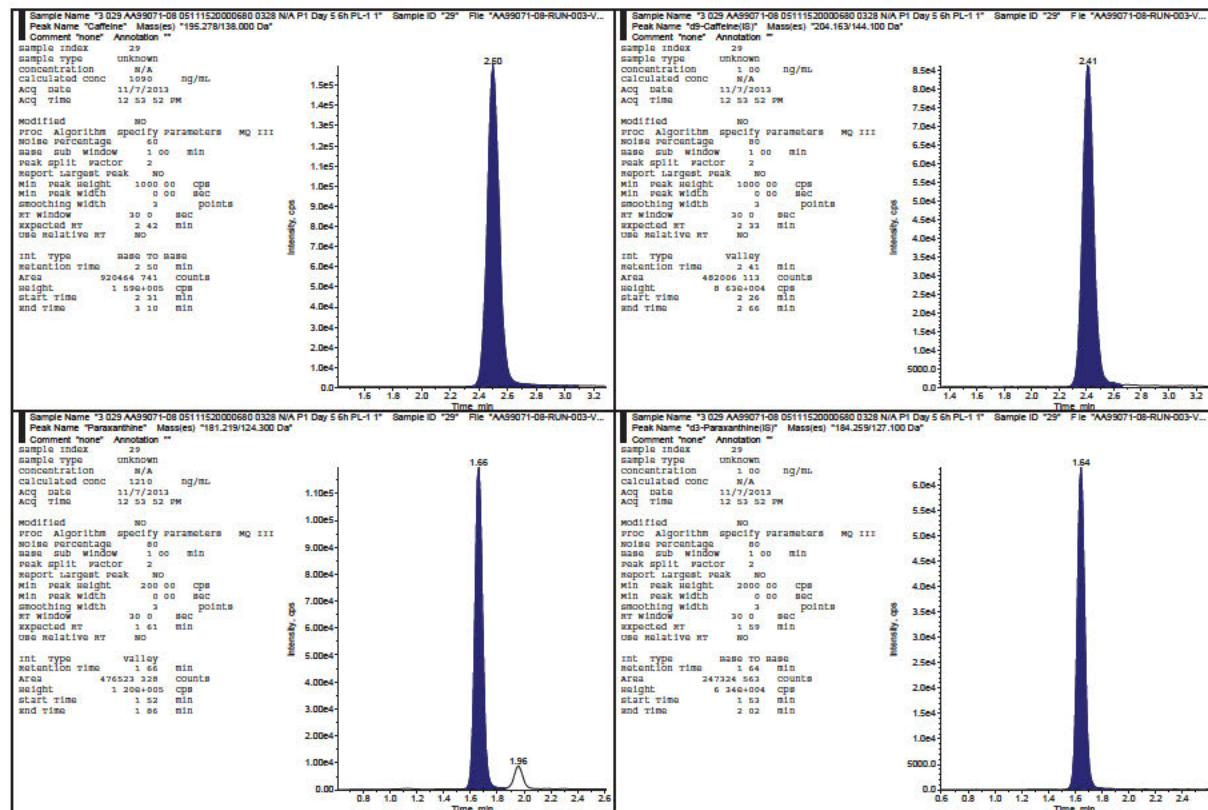
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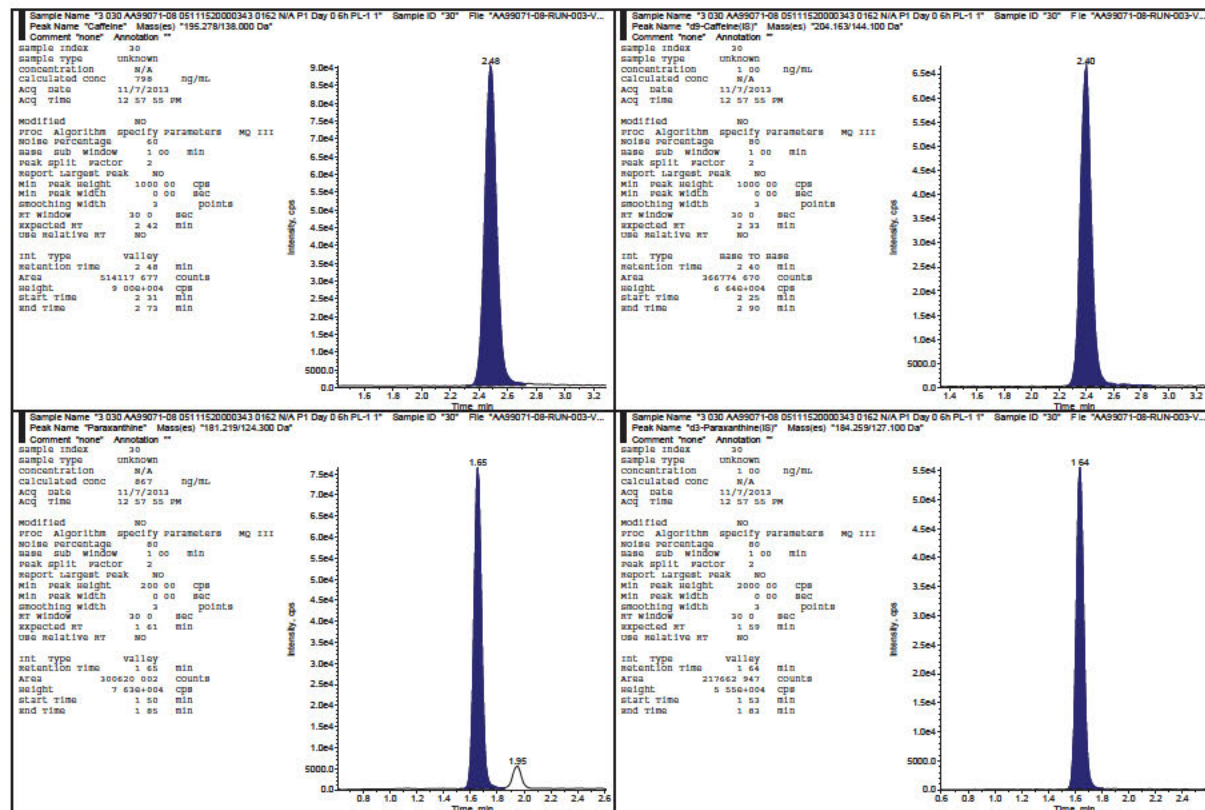


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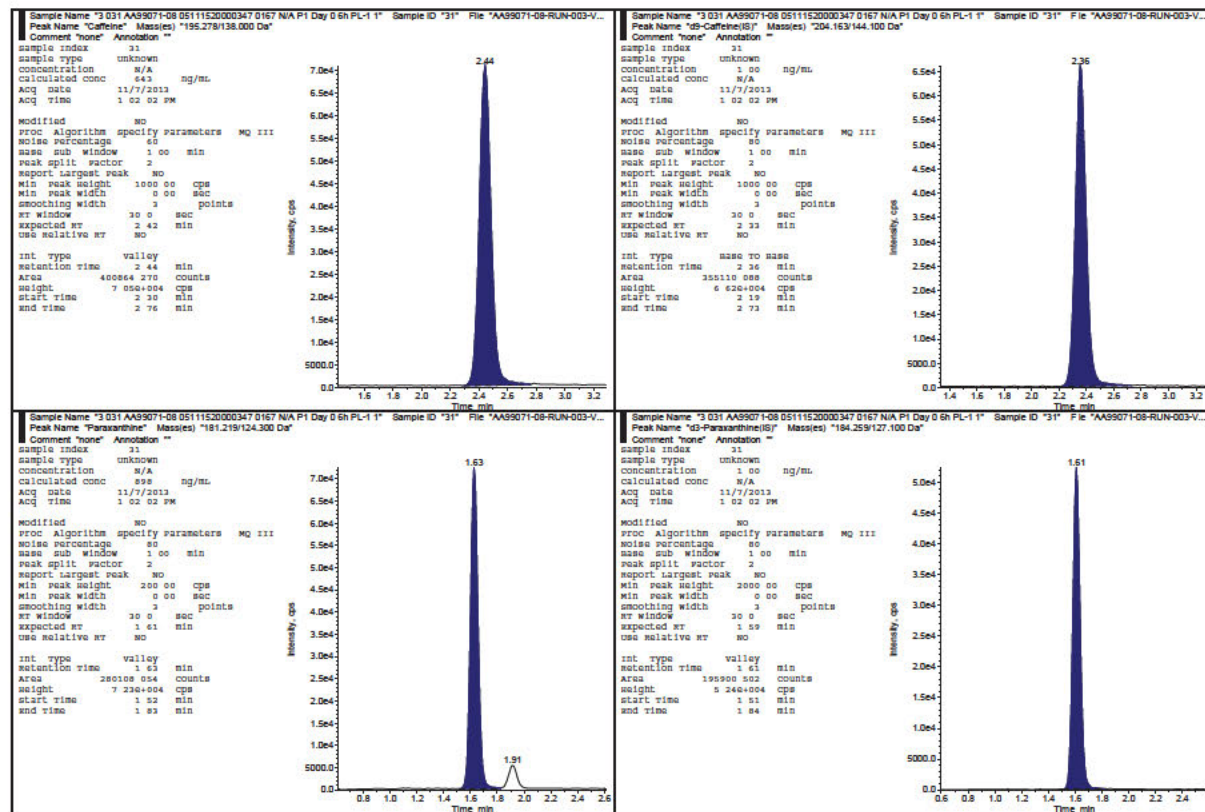


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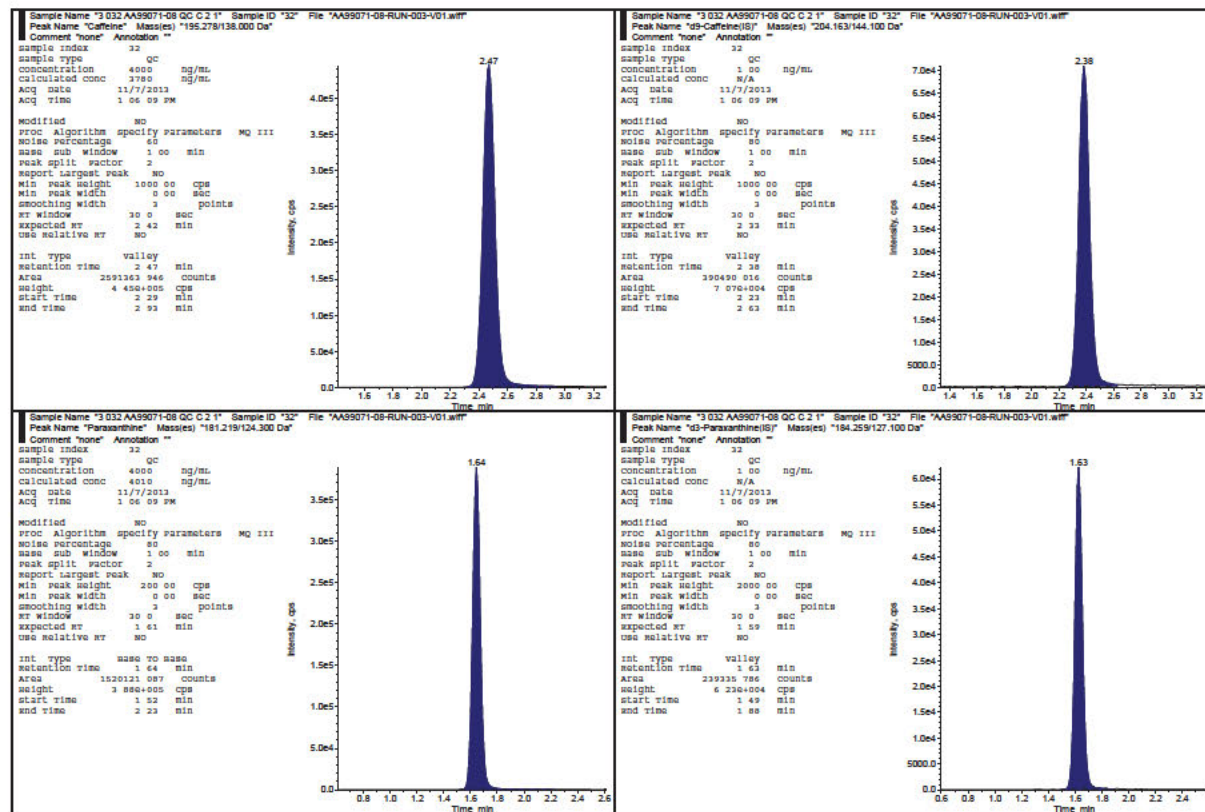


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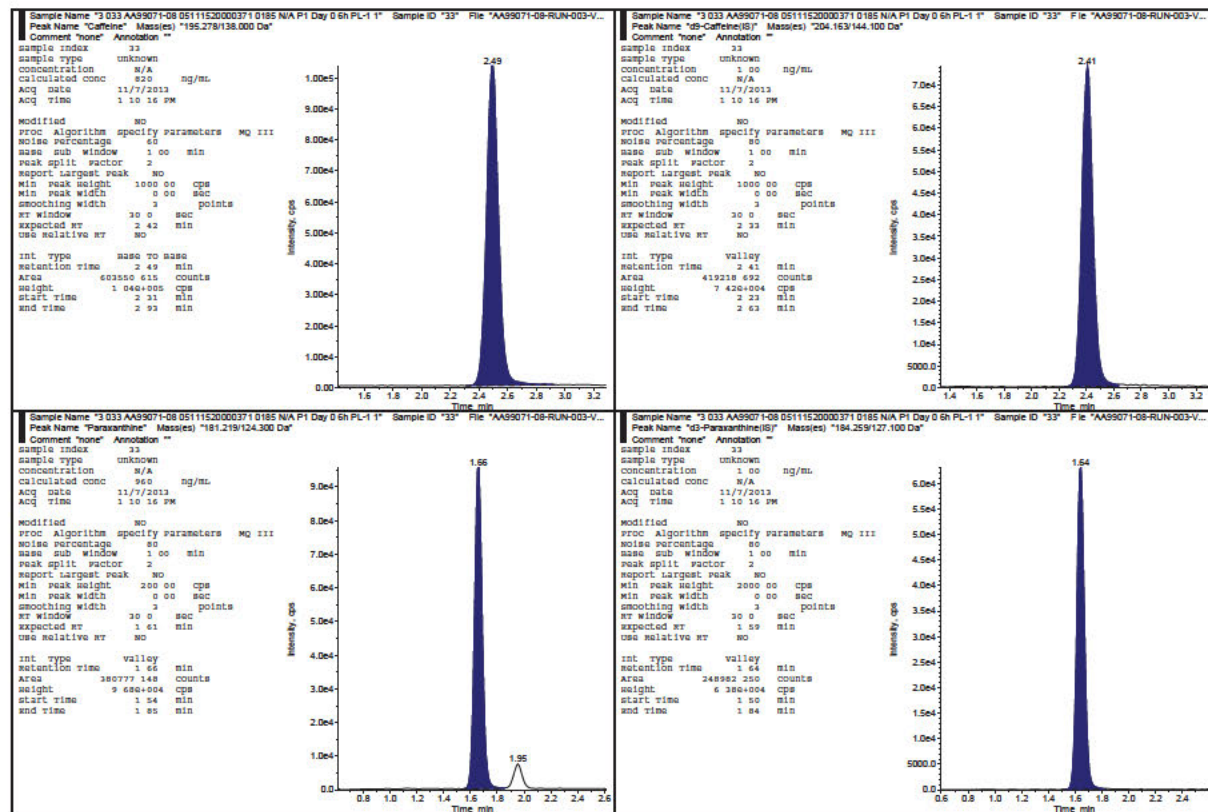
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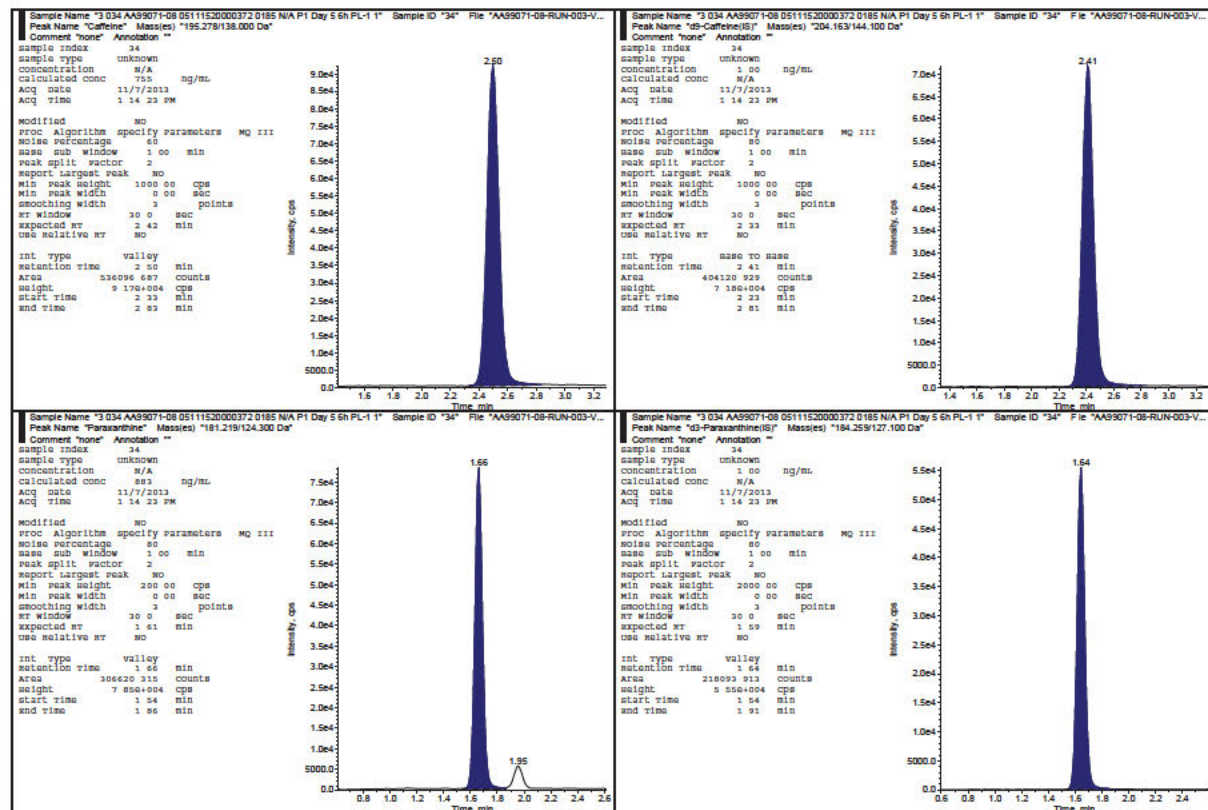
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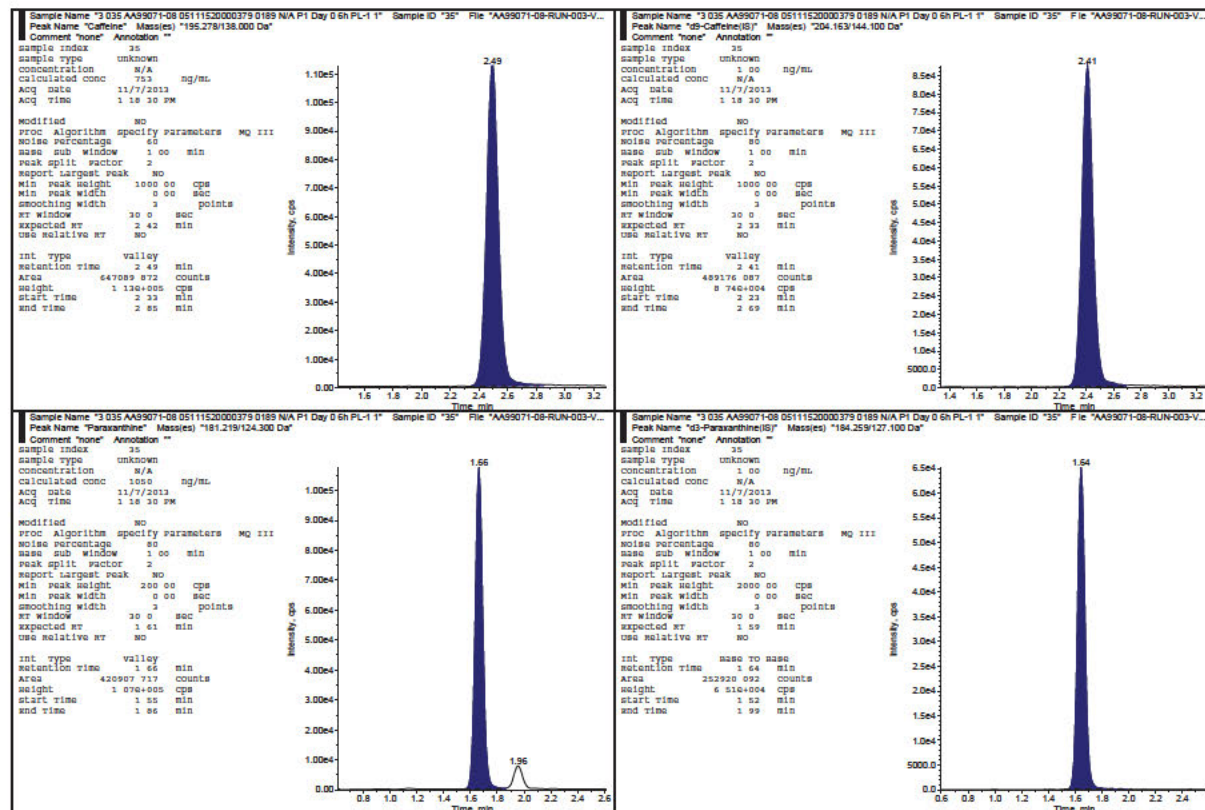


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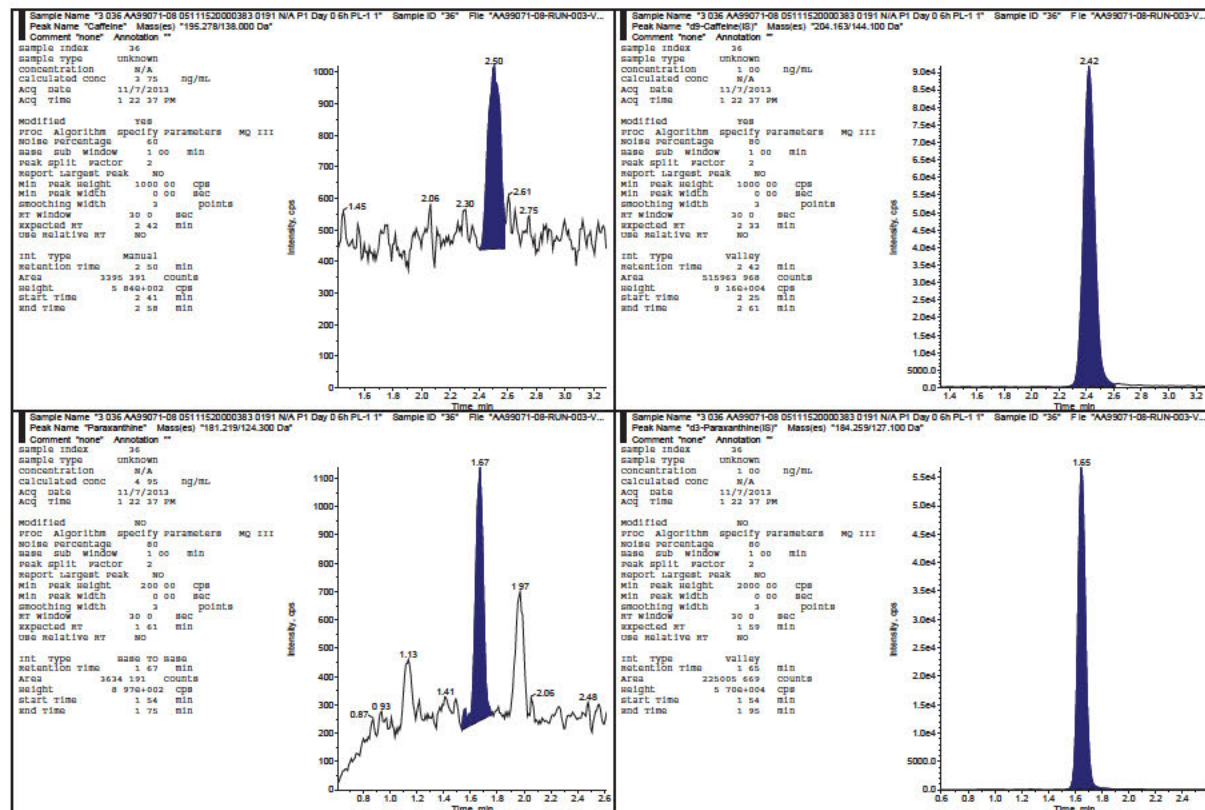


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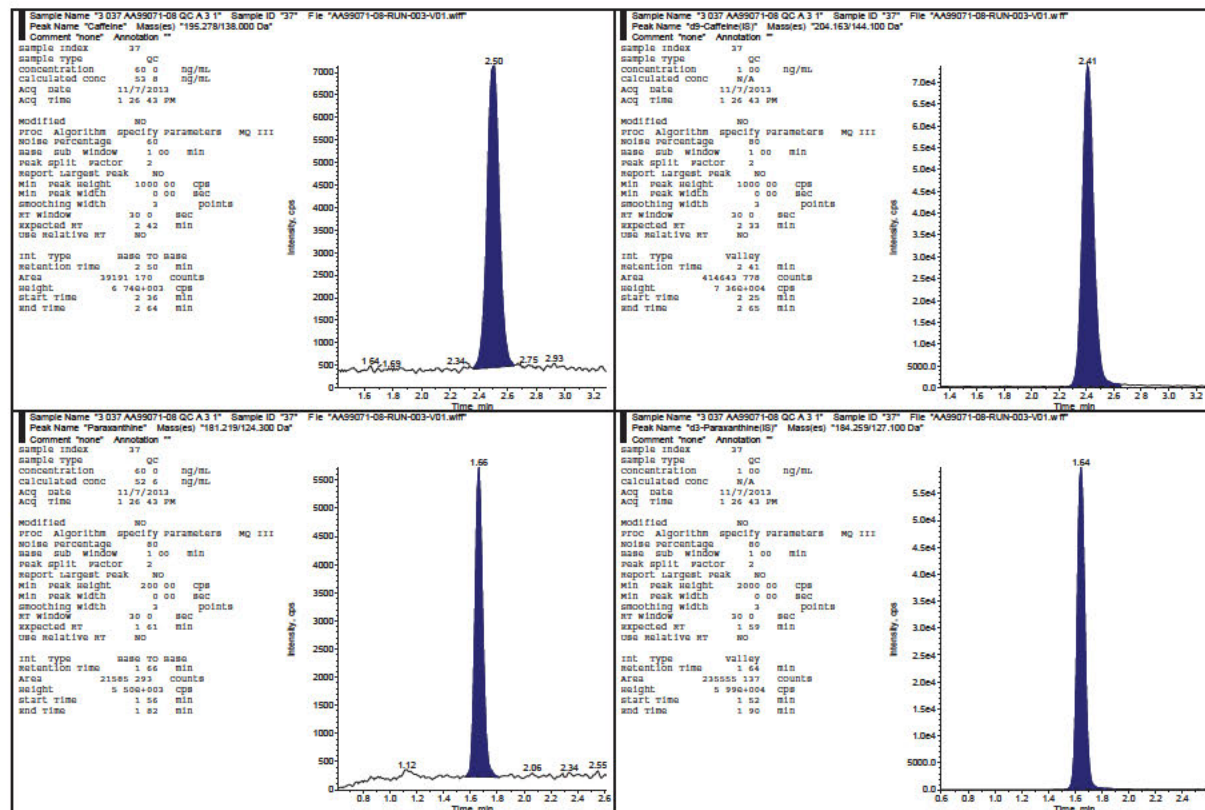


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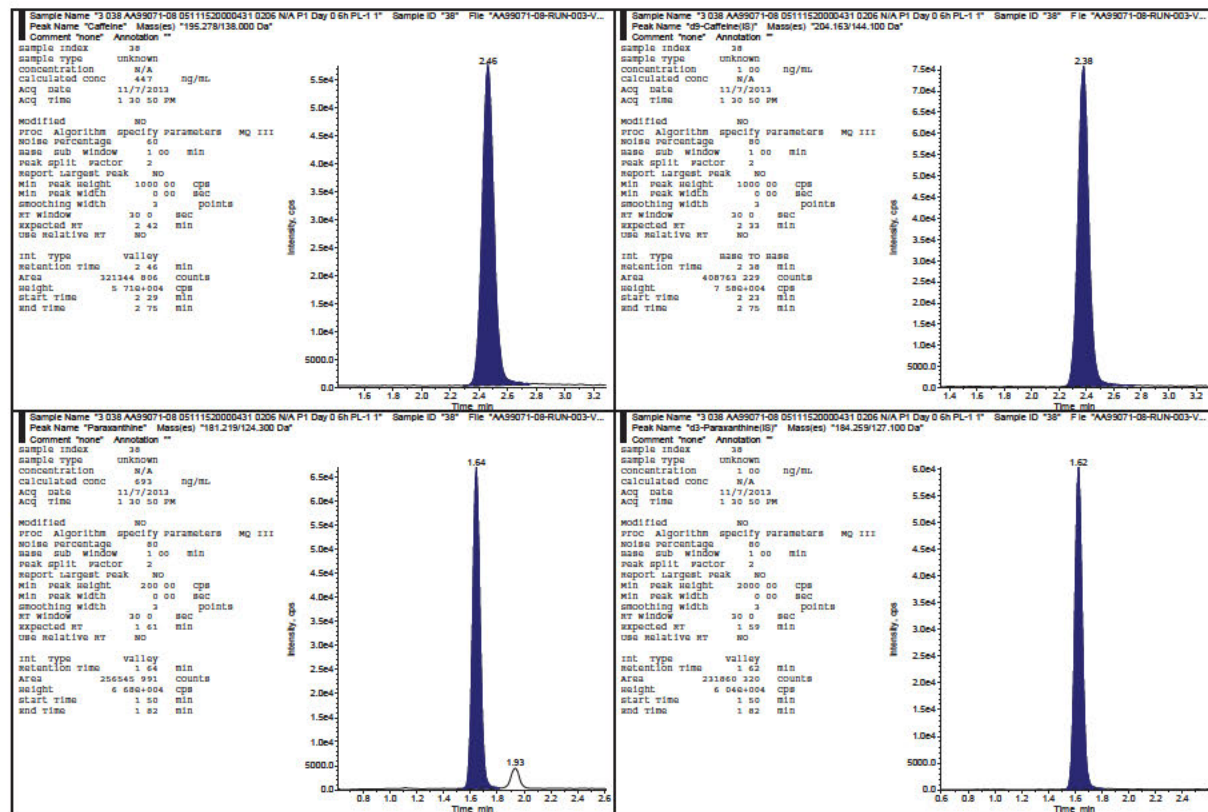
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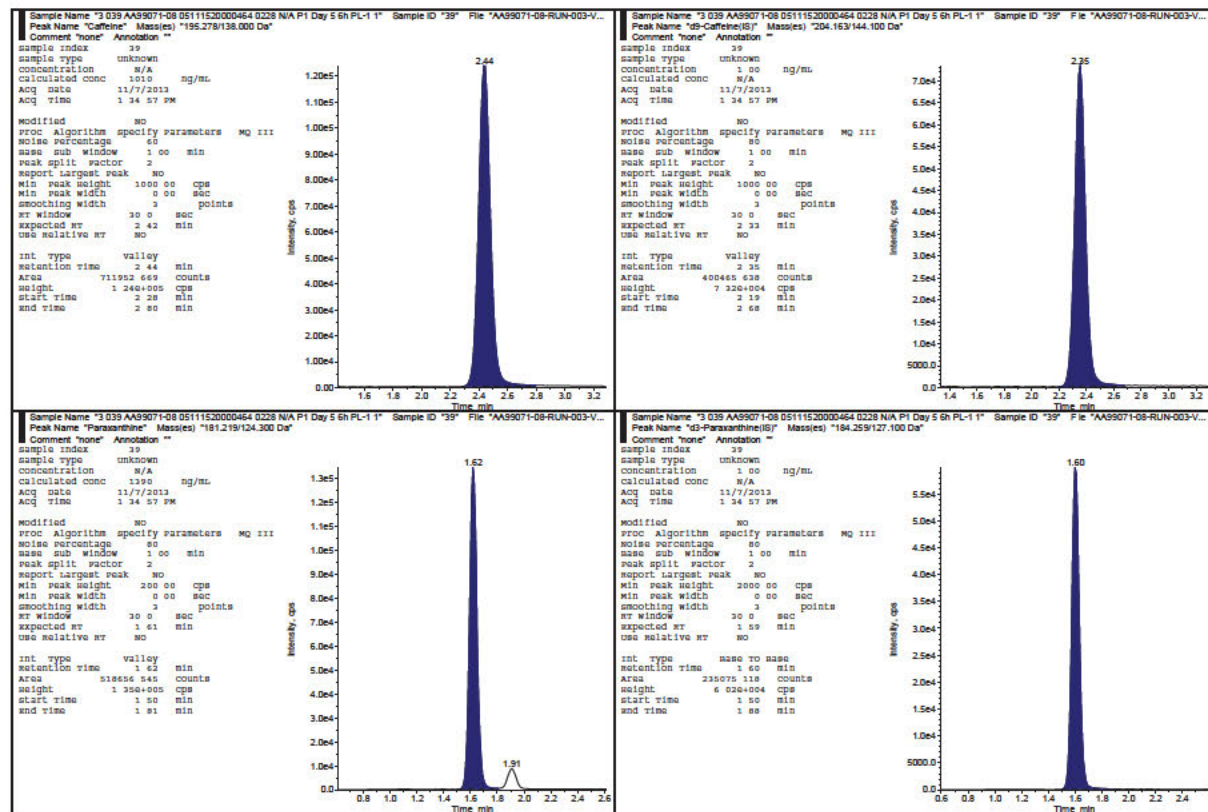
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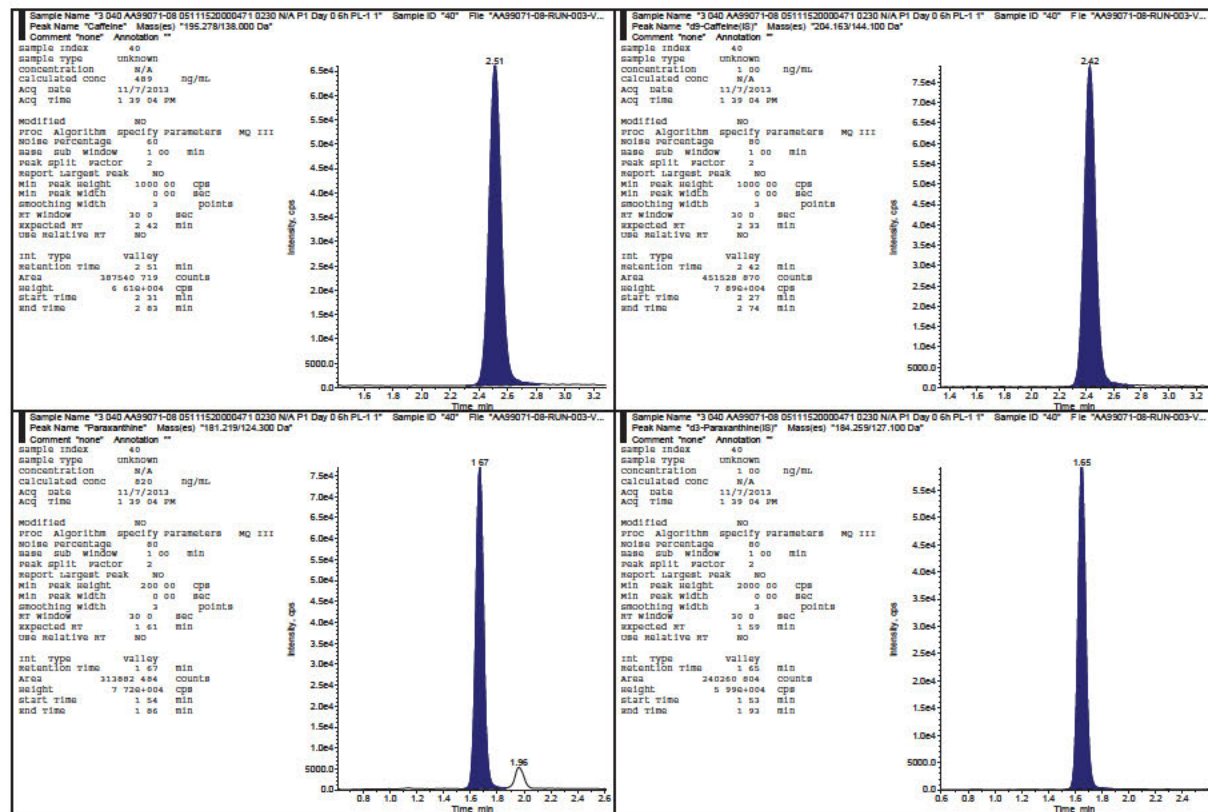


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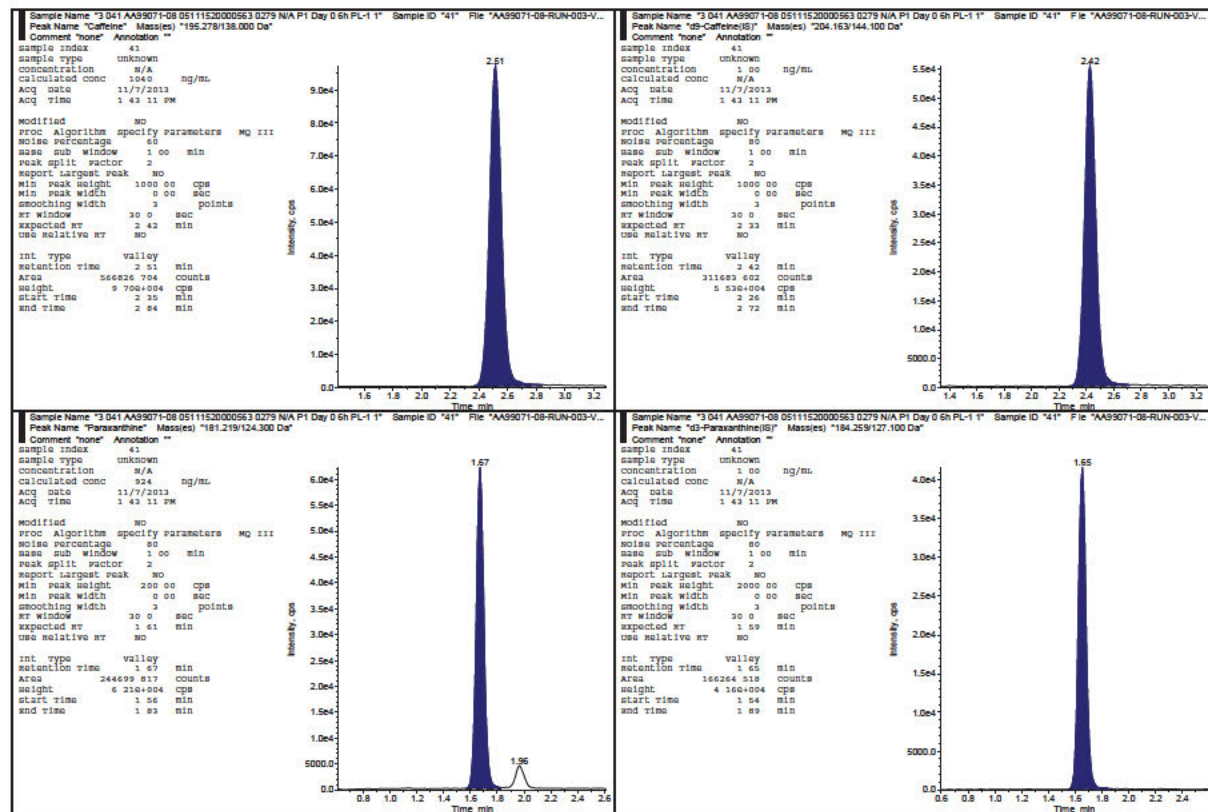


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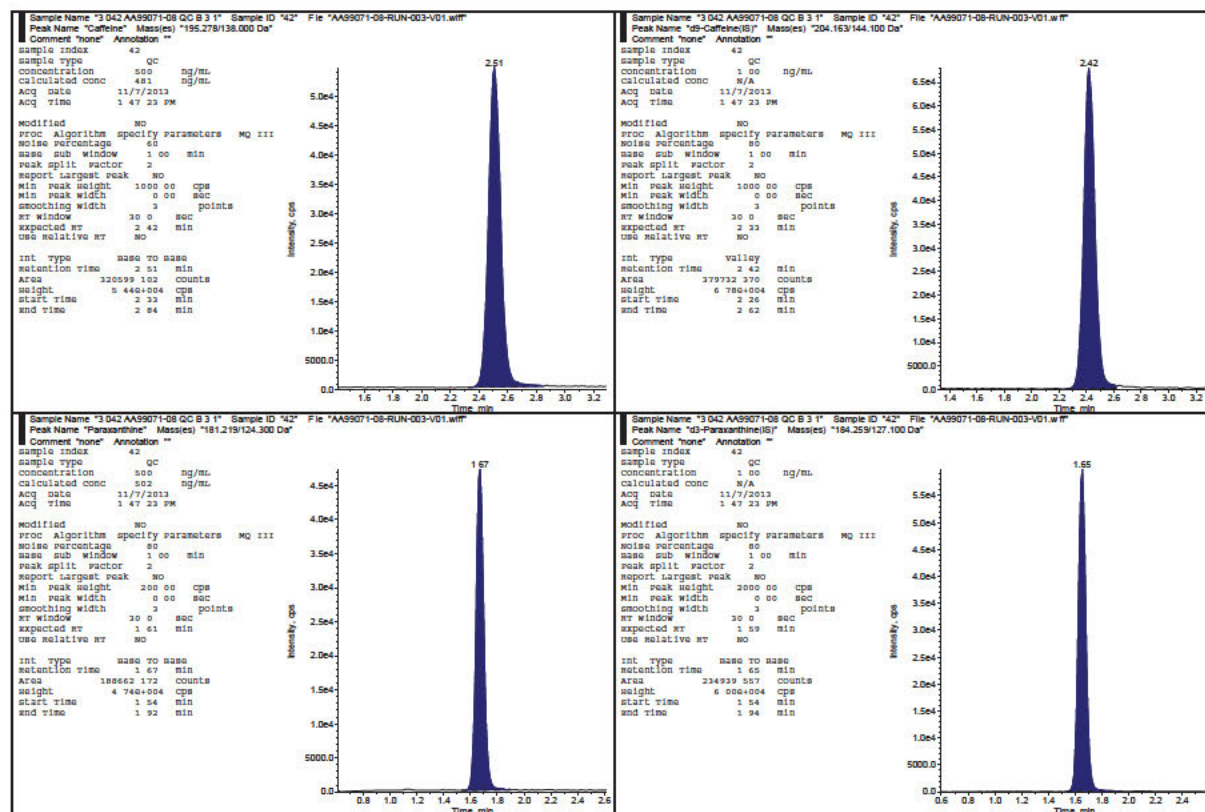


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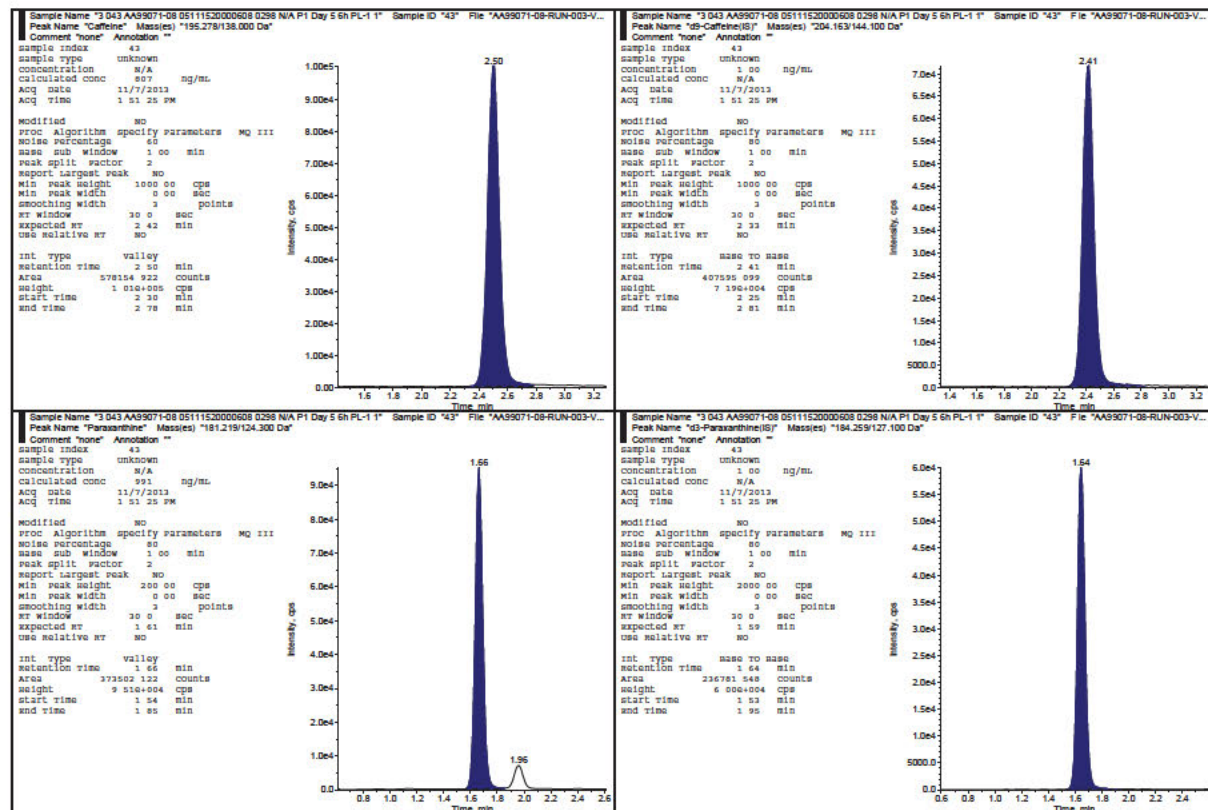
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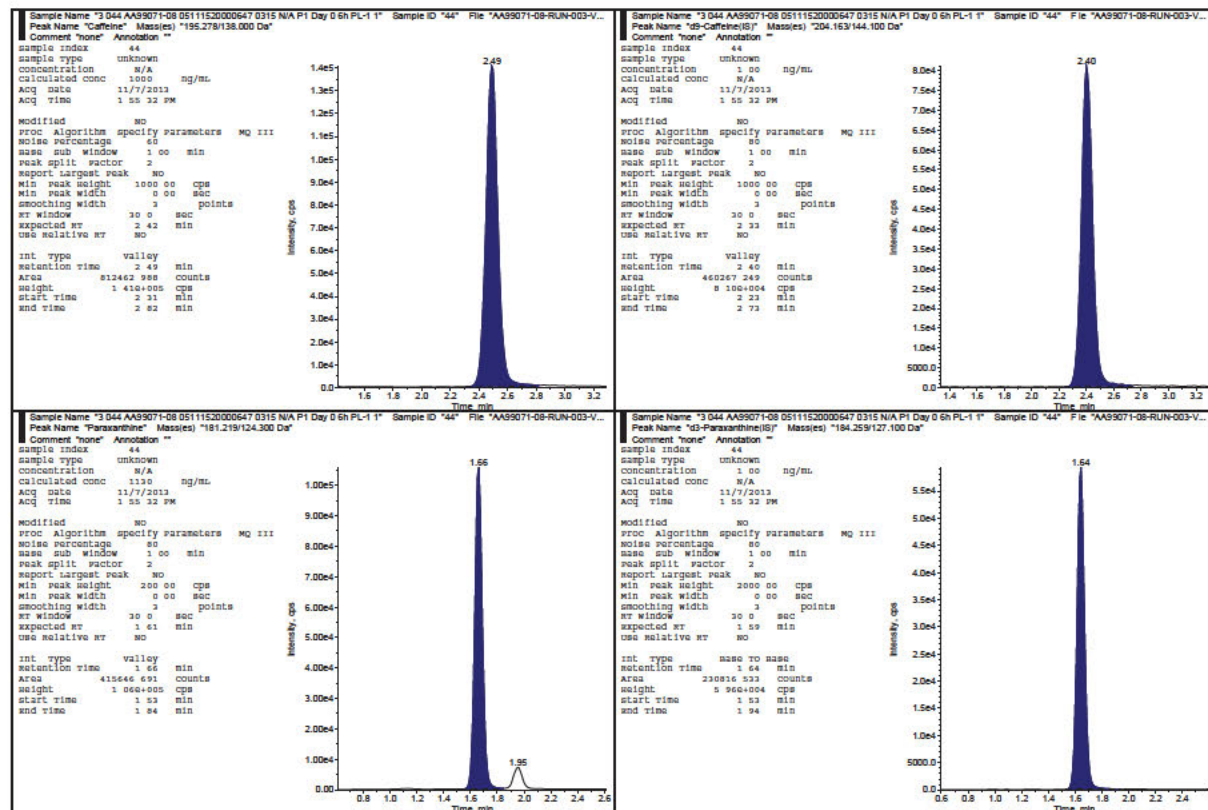
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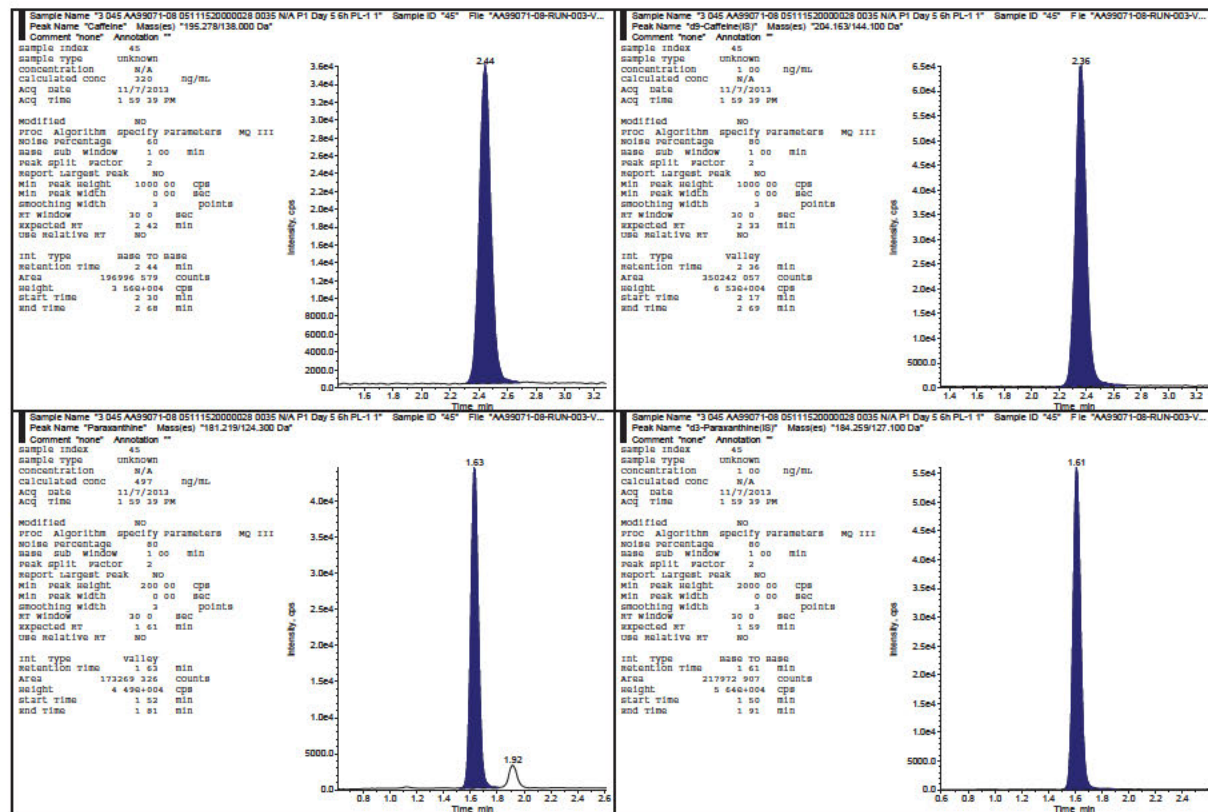


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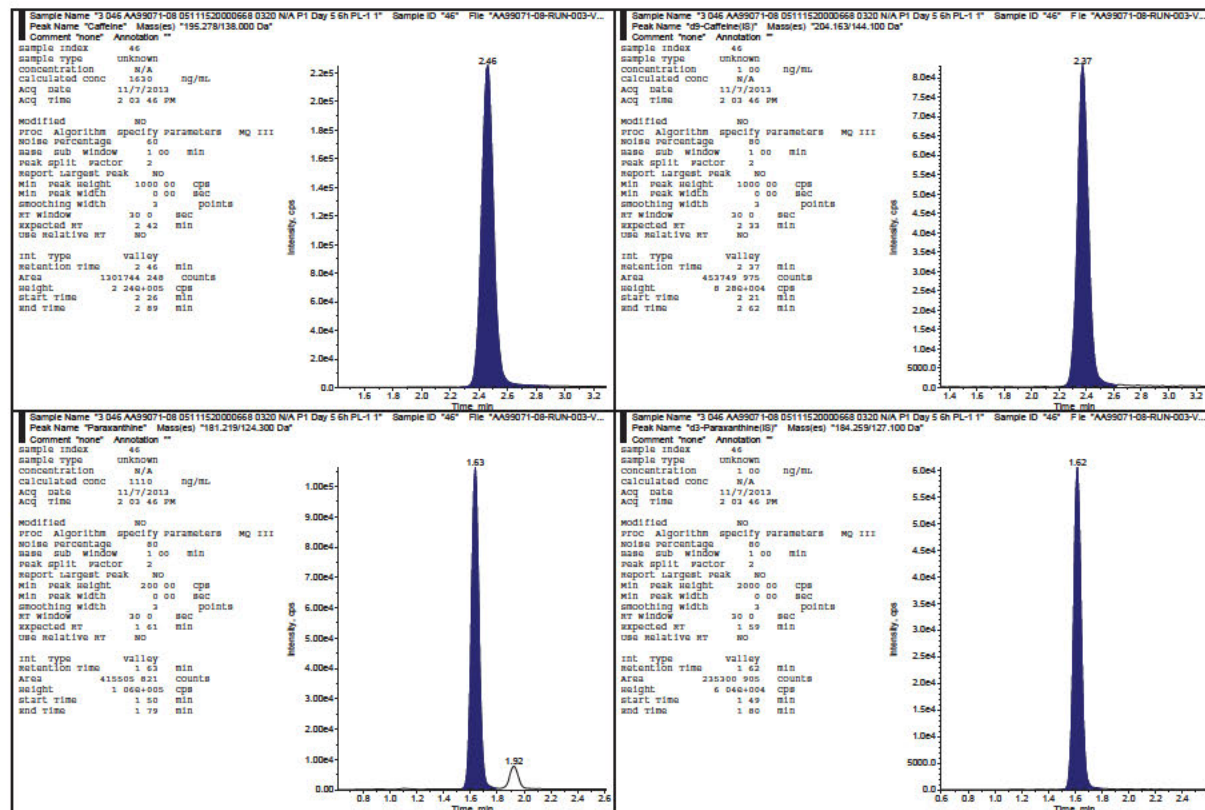


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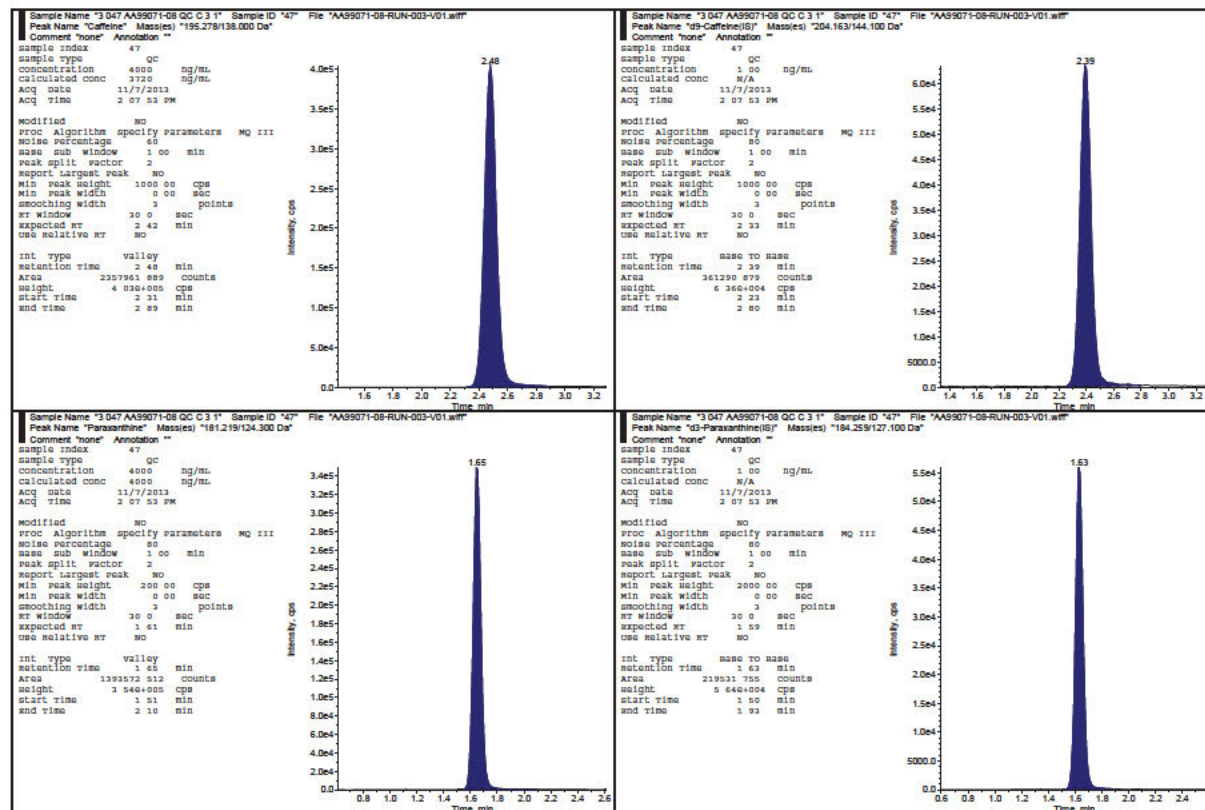


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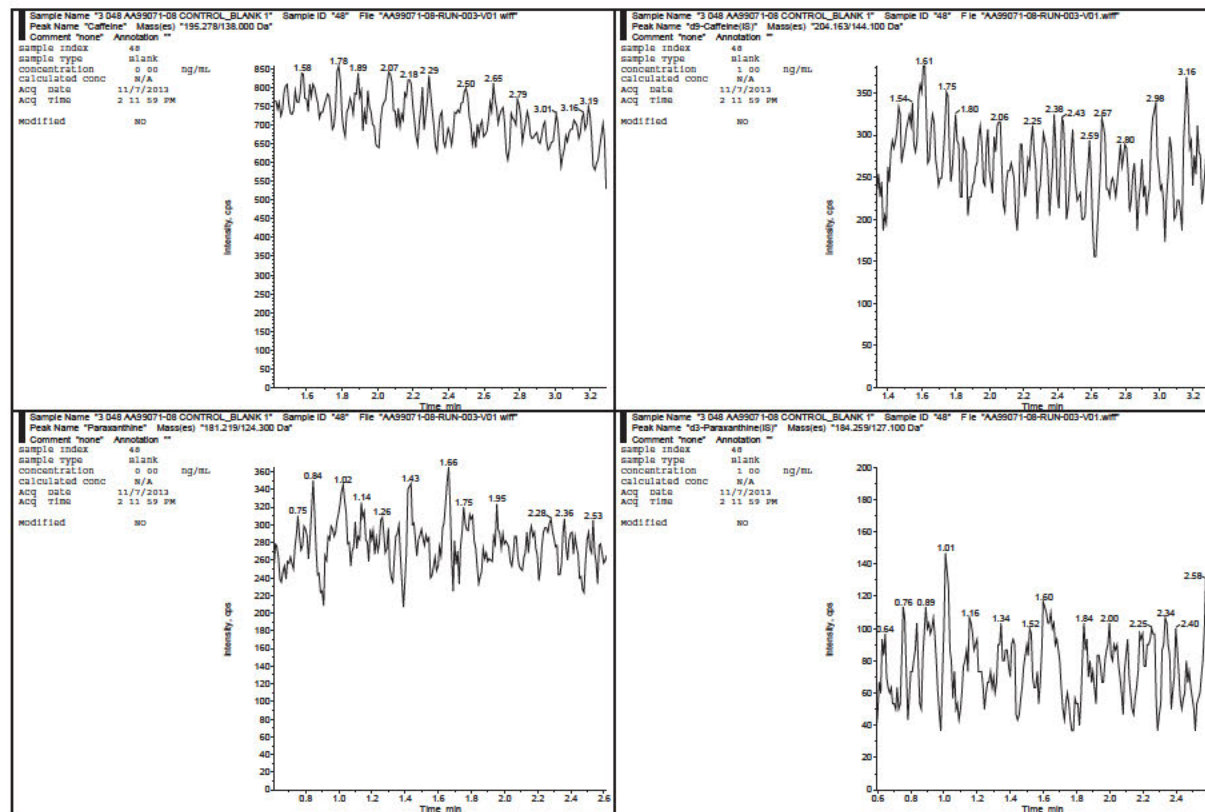
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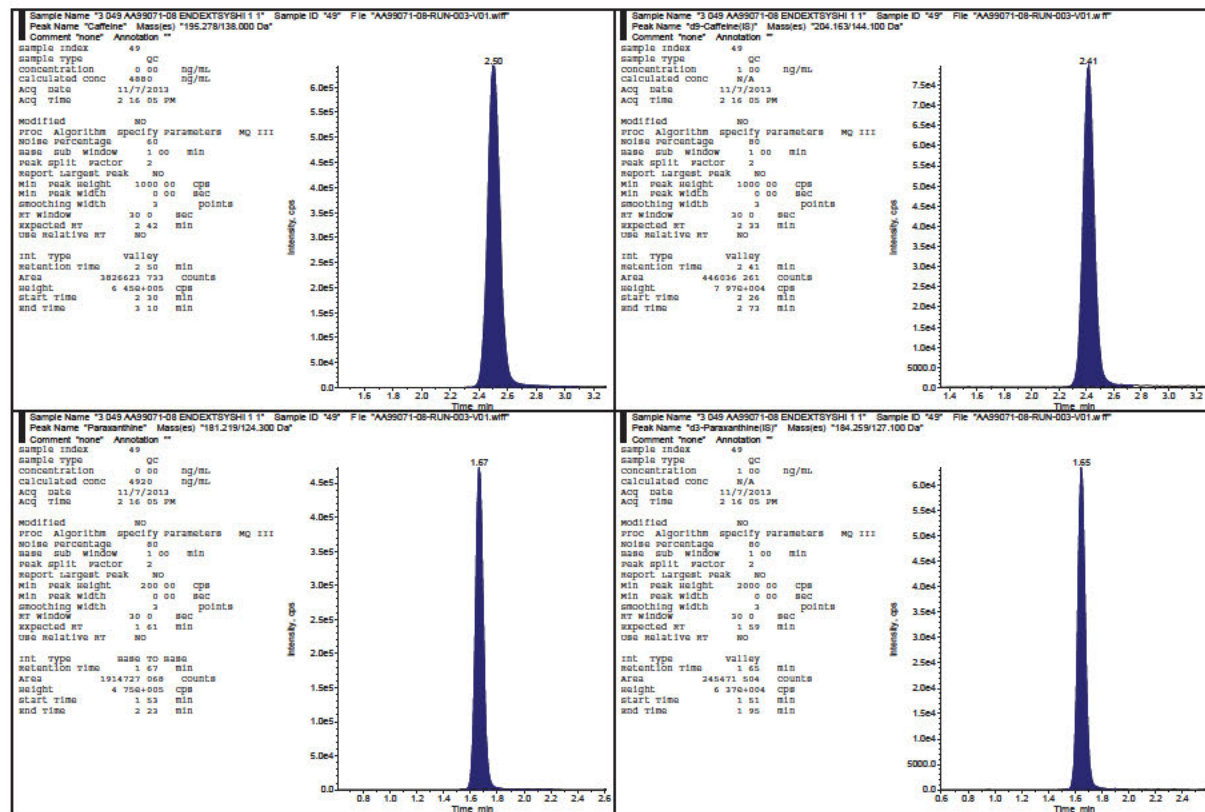
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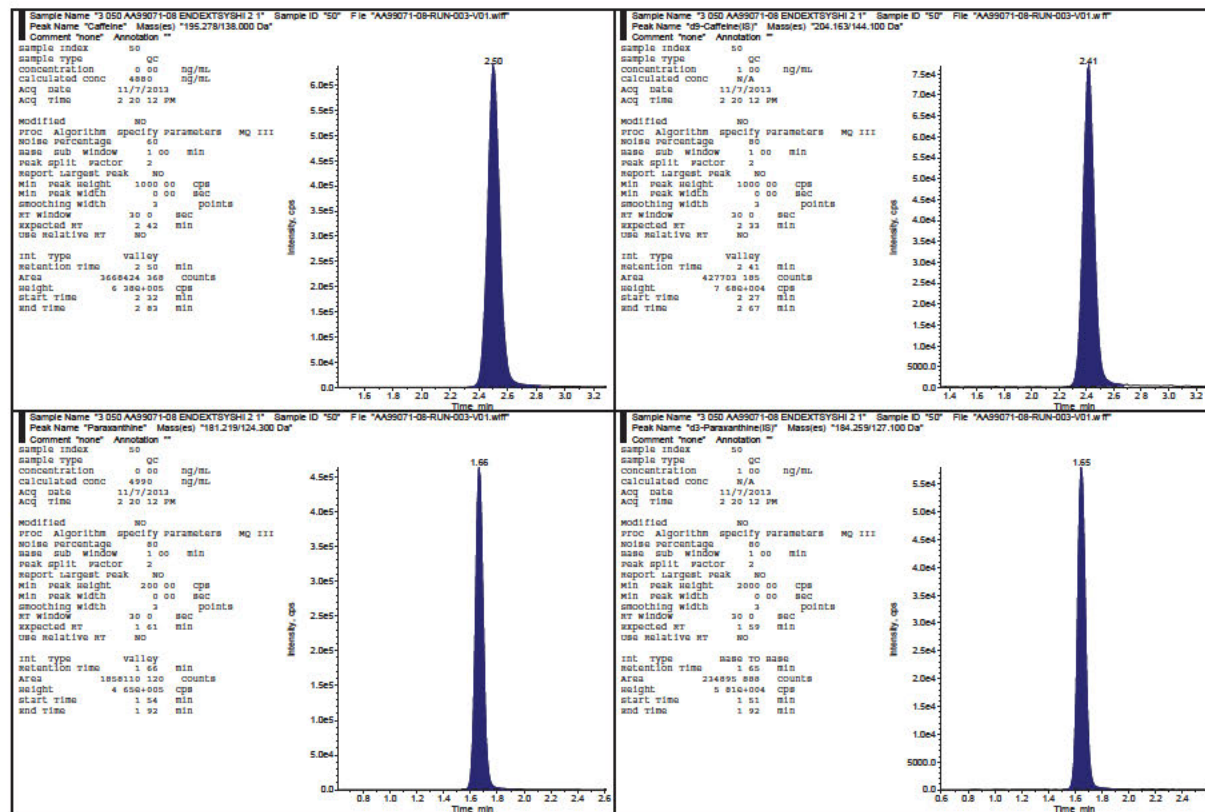


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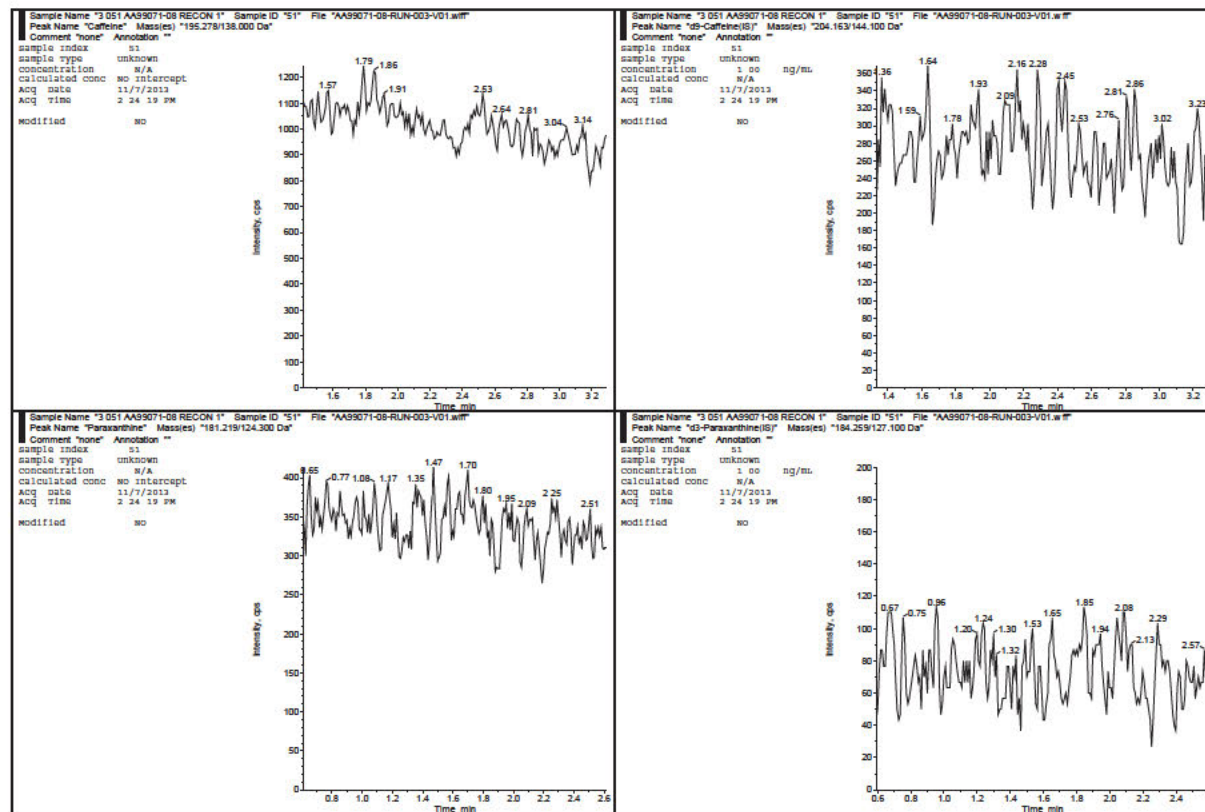


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