



### **16.1.9.3 BIOANALYTICAL REPORTS**

Determination of Total 1-Hydroxypyrene (1-OHP) in Human Urine Samples by LC-MS/MS  
(Study AA99602-03)



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**Determination of total 1-Hydroxypyrene (1-OHP) in human urine 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: AA99602-03  
Bioanalytical Report No. AAA99602-03

Bioanalytical Final Report

Philip Morris Products S.A.  
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2000 Neuchâtel, Switzerland

Protocol ZRHR-REXC-03-EU

Report Date: 29 August 2014

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1-OHP in Human Urine  
Celerion Study AA99602-03

## STUDY LOCATION

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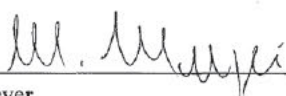
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**APPROVAL SIGNATURES**

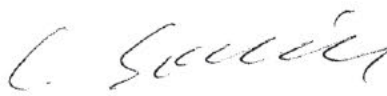
**TEST FACILITY**  
**Celerion Switzerland AG:**


Bioanalytical Principal Investigator

  
\_\_\_\_\_  
Werner Meyer

  
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Date

Test Facility Management

  
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Christine Schiebl, PhD

  
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Date





1-OHP in Human Urine  
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Date



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#### STATEMENT OF COMPLIANCE

Herewith it is confirmed, that the Celerion study AA99602-03 was performed according to the standards described in the Swiss Ordinance relating to Good Laboratory Practice, adopted 18 May 2005 [RS 813.112.1]. This Ordinance is based on the OECD Principles of Good Laboratory Practice, as revised in 1997 and adopted 26 November 1997 by decision of the OECD Council [C(97)186/Final] [1].

The OECD Principles of Good Laboratory Practice are accepted by Regulatory Authorities throughout the European Union, the United States of America and Japan.

In addition, the analysis of clinical trial samples including the validation of the applied analytical methods was conducted in accordance with the relevant standards of Good Clinical Practice and Standard Operating Procedures based on the recommendations of the EMA 'Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples' (EMA/INS/GCP/532137/2010) [2] and the EMA 'Guideline on bioanalytical method validation' (EMA/CHMP/EWP/192217/2009) [3].

This 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 audited the study. A Quality Assurance statement was then issued and is included within this document in the following page.

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 validity of the data.

Werner Meyer  
Bioanalytical Principal Investigator

29-Aug-2014


Date

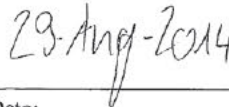
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## QUALITY ASSURANCE STATEMENT

Phase Audited	Audit Date(s)	Date Reported to Bioanalytical Principal Investigator	Date Audit Report Signed by Management
Bioanalytical Study Plan	08-Aug-2013	08-Aug-2013	09-Aug-2013
Bioanalytical Study Plan Amendment No. 1	18-Oct-2013	18-Oct-2013	18-Oct-2013
Bioanalytical Study Plan Amendment No. 2	22-Nov-2013	22-Nov-2013	22-Nov-2013
Study-based Inspection / Evaporation to dryness, reconstitution	02-Dec-2013	02-Dec-2013	03-Dec-2013
Raw Data Audit	06, 07, 10-Feb-2014	10-Feb-2014	22-May-2014
Bioanalytical Report (Final Draft)	02, 03-Jun-2014	03-Jun-2014	05-Aug-2014
Bioanalytical Report (Final)	The date of the QA review of the Final Report is identical to the signature date of the QA Statement.		

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.

  
\_\_\_\_\_  
Andrea Gabathuler  
QA Auditor

  
\_\_\_\_\_  
Date:



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## 1. INTRODUCTION

The purpose of this bioanalytical study (hereafter referred to as study) was to determine the concentration of 1-OHP in human urine samples using a validated LC-MS/MS method [4] and [5]. 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” [6]. Sample analysis was conducted between 22-Nov-2013 (experimental start) to 02-Dec-2013 (experimental end).

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 item (product name) is defined in the clinical study protocol [6].

### 2.2. Reference Items and Internal Standards

All calculations were based on the purity provided.

	Calibration standards	Quality control samples	Internal Standard (IS)
ID	1-Hydroxypyrene (1-OHP)	1-Hydroxypyrene β-D- Glucuronide (1-OHP GLU)	1-Hydroxypyrene ( <sup>13</sup> C <sub>6</sub> ) (1-OHP- <sup>13</sup> C <sub>6</sub> )
Supplier	(b) (4)	(b) (4)	(b) (4)
Lot/Batch No.	8-BHW-117-2	6-KSS-132-7	SDCK-007
CAS/IUPAC No.	5315-79-7	154717-05-2	5315-79-7 (unlabeled)
Purity	98%	98%	100%
Expiry*/Retest date	27-Jan-2016	17-Dec-2015	27-Feb-2015*
Storage conditions	5 C	-20 C	5 C

The certificate of analysis for the reference items and internal standard are presented in [Attachment 7](#). Reference items and internal standards are retained under the conditions that are specified until they become expired.

### 2.3. Blank Matrix

Human urine was collected from volunteers in-house. Human urine, free of significant interference at the retention time and mass transitions of the internal standard was used to prepare quality control (QC) samples. Human urine was stored at -20°C. UriSub<sup>®</sup>, a synthetic urine substitute, was used to prepare calibration standards, as control matrix for blanks and STD 0. UriSub<sup>®</sup> was purchased from (b) (4) stored at room temperature and was used within the given expiry date.





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## 2.4. Test System

### 2.4.1. Procedure and Instruments

Procedure and Instrumentation	
Extraction Method	Solid-phase extraction
Chromatography system	Acquity UPLC I class Binary System*
MS/MS system	Applied Biosystems/MDS SCIEX TRIPLE QUAD 6500 mass spectrometer*
Regression Type	Weighted linear regression curve (1/concentration <sup>2</sup> )
Quantitation Method	Area ratio
Assay Volume	0.500 mL

\* = Qualified systems

### 2.4.2. Computer Application Software

Software	
LC-MS/MS software	Applied Biosystems Analyst® 1.6*
LIMS	Thermo Electron Corporation Watson™ 7.3 Bioanalytical LIMS 7.3*
Laboratory Documentation System	Terrington Data Management Labnotes® 5.18, 1.21 (Web application)*
Office applications	Microsoft® Office 2007 and 2010 Package

\* = Validated systems

## 2.5. Calibration Standards and Quality Control Samples

Non-zero calibration standards at the concentration levels of 10.0, 20.0, 50.0, 100, 250, 1000, 1750 and 2000 pg/mL of 1-OHP were prepared in bulk on 18-Nov-2013 (as part of study AA98876-03 [4]), aliquoted and stored at -20°C and were used during the validated stability period [4].

Quality control (QC) samples at the concentration levels of 26.9 pg/mL (basal level), 176.9 pg/mL and 1626.9 pg/mL of 1-OHP were prepared in bulk on 31-Oct-2013 (as part of study AA98876-03 [4]), aliquoted and stored at -20°C and were used during the validated stability period [5]. The actual QC concentration was calculated by adding the basal concentration to the spiked concentrations. QC samples were stored under identical conditions as the clinical samples.

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 11-Jul-2013 and 18-Sep-2013 and were received frozen on dry ice between 16-Aug-2013 and 22-Nov-2013 from Celerion Lincoln, Nebraska, USA.



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#### 2.6.2. Sample Identification

Study samples were identified based on the Watson LIMS custom ID.

#### 2.6.3. Sample Storage and Stability

Study samples were stored from sample collection to the end of sample analysis at a nominal temperature of -20°C for a duration not exceeding 237 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 [4], [5]	1-OHP
Long-term stability	at least 237 days at nominal -20 °C in human urine at least 36 days at nominal -20 °C in Urisub® [4]
Short-term stability	19 hours at room temperature
Freeze-thaw stability	3 cycles at nominal -20 °C
Post-preparative stability	55 hours at nominal 5 °C
Processed sample integrity	126 hours at 5 °C
Sample shipping stability	19 days in a polypropylene tubes at -80 °C

#### 2.6.4. Sample Summary

The Sponsor's protocol specifies 160 subjects, 7 sampling times for 24-hour urine collections [6]. During the study nine subjects (0211, 0242, 0245, 0247, 0269, 0288, 0299, 0309 and 0312) discontinued during the clinical phase. No samples from these subjects were analyzed. Subject 0085 resigned from the study. Four samples were analyzed and reported for this subject.

	No. of Samples
Number of expected study samples/received in Zurich	1120 (primary samples) and 1120 (back-up samples) / 1117 (primary samples) and 1117 (back-up samples)
Specified "for analysis" samples in protocol/received	1120 primary samples / 1117 primary samples
Time points lost due to subject discontinuance	3
Back-up samples received	1117
Total number of study samples analyzed	1117

Following analysis, the study samples were kept frozen at -20°C and 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 total 1-OHP in human urine samples was carried out over a calibration range of 10.0 pg/mL to 2000 pg/mL (1-OHP). The method validation was performed in accordance with Celerion standard procedures, which follow the FDA guidance for the validation of bioanalytical methods [7] and the EMA guideline on bioanalytical method validation [3]. The method validation is described in AA98876-03 [4] and documented in SOP SM1-384B [8].

Human urine samples spiked with IS were treated with  $\beta$ -Glucuronidase and extracted using a solid phase extraction procedure. The extracted samples were analyzed by LC-MS/MS. Negative ions were monitored in the multiple reaction-monitoring (MRM) mode.

#### 3.2. Acceptance Criteria

##### 3.2.1. Analytical Run Acceptance Criteria

An analytical run was acceptable if all of the following criteria were met:

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

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

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

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

##### 3.2.2. Acceptance Criteria for Sample Dilution

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

##### 3.2.3. Acceptance Criteria for ISR

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





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

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

#### 4. RESULTS

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

A summary of analytical runs performed is presented in [Table 1](#). Data from rejected runs are not included in the report but remain on file at Celerion.

##### 4.1. Quality Control Sample Performance

Between-analytical run precision and accuracy results for QC samples prepared at 26.9, 177, and 1630 pg/mL are summarized in [Table 2](#) for 1-OHP.

##### 4.2. Calibration Standard Performance

Back-calculated calibration curve standard concentrations are provided in [Table 3](#) for 1-OHP.

##### 4.3. Standard Curve Parameters

Standard curve parameters from 18 successful analytical runs are provided in [Table 4](#) for 1-OHP. A representative calibration curve is illustrated in [Figure 1](#) for 1-OHP. The standard zero samples (blank samples with IS added) were not used to plot the calibration curve.

##### 4.4. Study Sample Concentrations

Study sample concentrations are provided in [Table 5](#) for 1-OHP. 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 1-OHP, 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 and of Rejected Runs

Study samples needing re-analysis according to [Attachment 5](#) and of rejected runs for 1-OHP in human urine are identified in [Table 6](#). Reassay descriptions are provided in [Attachment 5](#).

###### 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 total 1-OHP in human urine was considered reproducible, 97% out of 106 repeat analyses for 1-OHP met acceptance criteria as defined in section 3.2.3. Results are presented in Table 7.

### 5. CHROMATOGRAMS

Representative chromatograms from analytical run AA99602-03\_P1 are provided in Attachment 9.

### 6. DEVIATIONS

There were no deviations during the conduct of the study.

### 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. Schedule nominal time points

Urine was collected over 24 hours, the following relation exists:

Start day nominal	Nominal time, Nominal Day
-1	0
0	1
1	2
2	3
3	4
4	5
5	6

### 9. ARCHIVES

At a minimum the following records will be retained:

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

These documents will be kept in the archives of Celerion for at least ten (10) years, taken from the date of Bioanalytical Principal Investigator's signature on the final bioanalytical report. After this time the Sponsor will be contacted to decide if the records should be retained for a further defined time at Celerion, returned to the Sponsor or disposed of.



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## 10. CONCLUSION

In this bioanalytical study the concentration of total 1-OHP was determined in a total of 1117 human urine samples collected in the Philip Morris International Research and Development clinical study ZRHR-REXC-03-EU by a validated LC-MS/MS method [4] and [5]. 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] OECD Principles of Good Laboratory Practice (as revised in 1997), ENV/MC/CHEM(98)17, OECD, Paris, 1998. (No.1 in OECD Series on Good Laboratory Practice and Compliance Monitoring).
- [2] EMA. GCP Inspectors Working Group. Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples. EMA/INS/GCP/532137/2010 of 28 February 2012.
- [3] EMA. Committee for Medicinal Products for Human Use. Guideline on bioanalytical method validation. EMEA/CHMP/EWP/192217/2009 of 21 July 2011.
- [4] Validation of an LC-MS/MS method for the determination of total 1-hydroxypyrene (1-OHP) in human urine, Celerion Study AA98876-03, Celerion Switzerland AG.
- [5] Validation of a LC-MS/MS method for the determination of total 1-Hydroxypyrene (1-OHP) in human urine, MDS Pharma Services Switzerland AG, Validation Report VZZ00855, date of issue: 06-May-2008.
- [6] 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, Clinical Study Protocol ZRHR-REXC-03-EU, Version number: Final, Revision date: 25 April 2013.
- [7] Guidance for Industry, Bioanalytical Method Validation, U.S. Department of Health and Human Services, Food and Drug Administration, Centre for Drug Evaluation and Research (CDER), May 2001.
- [8] Determination of total 1-Hydroxypyrene (1-OHP) in human urine by LC-MS/MS, Celerion Method SOP SM1-384B, Celerion Switzerland AG, effective date 12-Nov-2013.
- [9] Determination of total 1-Hydroxypyrene (1-OHP) in human urine 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 Switzerland AG, Study Plan Bioanalysis PAA99602-03, effective date 12-Aug-2013, and amendment no.1 to the study plan, effective date 23-Oct-2013 and amendment no. 2 to the study plan, effective date 22-Nov-2013.





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## RESULT TABLES

Table 1 Summary of Analytical Runs Performed

Watson Run ID	Run ID	Regression Status (1-OHP)	Extraction Date	Assay Date	Description	Comment
1	AA99602-03_P1	Accepted	22-Nov-2013	22-Nov-2013	Subj 0001, 0004, 0008, 0010, 0011, 0013-0017	OK
2	AA99602-03_P2	Accepted	22-Nov-2013	22-Nov-2013	Subj 0020, 0021, 0023, 0025, 0028-0031, 0034, 0035	OK
3	AA99602-03_P3	Accepted	22-Nov-2013	23-Nov-2013	Subj 0037-0039, 0042, 0044, 0049, 0051-0053, 0055	OK
4	AA99602-03_P4	Accepted	25-Nov-2013	25-Nov-2013	Subj 0057, 0060, 0062-0064, 0066, 0067, 0069, 0071, 0074	OK
5	AA99602-03_P5	Rejected	25-Nov-2013	25-Nov-2013	Subj 0076, 0080, 0083, 0086-0088, 0090, 0093, 0104, 0105	Rejected due to Interference in blank/STD 0
6	AA99602-03_P6	Accepted	25-Nov-2013	26-Nov-2013	Subj 0106, 0107, 0110, 0112, 0114, 0117, 0118, 0121-0123	OK
7	AA99602-03_P7	Accepted	25-Nov-2013	27-Nov-2013	Subj 0126-0130, 0133, 0134, 0136, 0137, 0139	OK
8	AA99602-03_P8	Accepted	26-Nov-2013	26-Nov-2013	Subj 0140, 0145, 0147-0150, 0152, 0153, 0155, 0156	OK
9	AA99602-03_P9	Accepted	26-Nov-2013	27-Nov-2013	Subj 0160, 0162, 0167, 0169, 0170, 0177, 0181, 0183, 0185, 0187	OK
10	AA99602-03_P10	Accepted	27-Nov-2013	28-Nov-2013	ISR 1 (34 samples), 4 study samples, Subj 0085 and reassays	OK
11	AA99602-03_P11	Accepted	26-Nov-2013	27-Nov-2013	Subj 0189-0193, 0195-0198, 0200	OK
12	AA99602-03_P12	Accepted	27-Nov-2013	27-Nov-2013	Subj 0202-0204, 0206, 0210, 0216, 0218, 0220, 0224, 0228	OK
13	AA99602-03_P13	Accepted	28-Nov-2013	28-Nov-2013	Subj 0229, 0230, 0232, 0234, 0240, 0241, 0244, 0249, 0251, 0252	OK
14	AA99602-03_P14	Accepted	28-Nov-2013	28-Nov-2013	Subj 0255, 0256, 0262, 0264-0266, 272, 0273, 0276, 0277	OK
15	AA99602-03_P15	Accepted	28-Nov-2013	29-Nov-2013	Subj 0278, 0279, 0281-0283, 0285, 0287, 0289, 0291, 0292	OK
16	AA99602-03_P16	Accepted	28-Nov-2013	29-Nov-2013	Subj 0296, 0298, 0300, 0301, 0306-0308, 0313, 0316, 0317	OK
17	AA99602-03_P17	Accepted	29-Nov-2013	29-Nov-2013	Subj 0315, 0318, 0320-0322, 0325, 0328, 0072, 0022	OK
18	AA99602-03_P18	Accepted	29-Nov-2013	29-Nov-2013	Subj 0076, 0080, 0083, 0086-0088, 0090, 0093, 0104, 0105	OK
19	AA99602-03_P19	Accepted	02-Dec-2013	02-Dec-2013	ISR 2 (72 samples) and repeats	OK

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





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Table 2 Quality Control Control Sample Data (Between-Analytical Run Precision and Accuracy) for 1-OHP

Assay Date	Watson Run ID	QC BL 26.9 pg/mL	QC 150 177 pg/mL*	QC 1600 1630 pg/mL*
22-Nov-2013	1	28.9	185	1620
		27.3	180	1580
22-Nov-2013	2	29.7	171	1600
		29.2	184	1620
23-Nov-2013	3	27.3	181	1590
		28.5	167	1640
25-Nov-2013	4	28.0	182	1620
		28.0	184	1630
26-Nov-2013	6	28.4	178	1590
		27.9	~148	1600
26-Nov-2013	8	28.1	183	1610
		30.7	179	1640
27-Nov-2013	7	~33.6	179	1640
		27.8	173	1560
27-Nov-2013	9	29.0	189	1720
		30.9	187	1750
27-Nov-2013	11	26.5	182	1650
		29.3	185	1620
27-Nov-2013	12	27.9	185	1630
		27.4	174	1610
28-Nov-2013	10	29.4	186	1740
		27.6	187	1780
28-Nov-2013	13	28.8	184	1700
		26.7	180	1600
28-Nov-2013	14	29.2	186	1630
		27.3	180	1600
29-Nov-2013	15	29.3	189	1670
		29.6	188	1680
29-Nov-2013	16	30.0	182	1700
		29.4	176	1640
29-Nov-2013	17	29.1	187	1680
		27.0	176	1590
29-Nov-2013	18	27.1	183	1710
		26.2	190	1670
02-Dec-2013	19	26.9	185	1750
		29.9	191	1750
Mean		28.6	181	1650
S.D.		1.5	8	58
%CV		5.2	4.4	3.5
%Theoretical		106.1	102.5	101.4
n		36	36	36

~ bias > 15.0%, included in statistics

\*: concentrations were rounded off to 3 significant figures. QC 150 (176.9 pg/mL) and QC 1600 (1626.9 pg/mL).



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Table 3 Back-calculated Calibration Standard Concentrations for 1-OHP

Assay Date	Watson Run ID	STD 10 10.0 pg/mL	STD 20 20.0 pg/mL	STD 50 50.0 pg/mL	STD 100 100 pg/mL	STD 250 250 pg/mL	STD 1000 1000 pg/mL	STD 1750 1750 pg/mL	STD 2000 2000 pg/mL
22-Nov-2013	1	10.2	19.8	47.3	96.9	256	992	1820	2050
22-Nov-2013	2	10.2	19.4	48.1	99.8	250	980	1790	2090
23-Nov-2013	3	10.4	18.8	48.7	95.1	255	1000	1820	2070
25-Nov-2013	4	10.2	19.7	48.4	98.3	251	997	1800	2040
26-Nov-2013	6	10.3	18.9	49.5	99.9	255	987	1750	2050
26-Nov-2013	8	10.3	18.9	49.5	98.4	259	980	1740	2090
27-Nov-2013	7	10.4	18.8	46.4	97.8	262	1010	1750	2100
27-Nov-2013	9	10.2	19.9	47.5	92.1	261	1010	1790	2090
27-Nov-2013	11	10.5	18.2	48.3	96.7	259	1020	1780	2070
27-Nov-2013	12	10.1	19.8	49.4	94.0	260	960	1800	2080
28-Nov-2013	10	10.4	18.0	50.7	99.8	272	963	1760	1970
28-Nov-2013	13	10.4	18.8	49.4	95.3	254	997	1770	2120
28-Nov-2013	14	10.2	19.7	48.2	95.7	259	997	1750	2090
29-Nov-2013	15	10.1	19.5	48.8	103	249	995	1740	2030
29-Nov-2013	16	10.1	19.6	50.3	99.5	248	959	1780	2080
29-Nov-2013	17	9.79	20.9	49.9	98.1	254	982	1720	2030
29-Nov-2013	18	10.1	19.5	49.9	98.1	258	984	1730	2050
02-Dec-2013	19	10.1	19.4	50.5	100	246	983	1730	2100
Mean		10.2	19.3	48.9	97.7	256	988	1770	2070
SD		0.2	0.7	1.2	2.6	6	16	30	34
%CV		1.7	3.5	2.4	2.7	2.4	1.7	1.7	1.7
%Bias		2.3	-3.5	-2.1	-2.3	2.4	-1.2	1.1	3.3
n		18	18	18	18	18	18	18	18



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Table 4 Standard Curve Parameters for 1-OHP

Assay Date	Watson Run ID	Slope	Intercept	R-Squared
22-Nov-2013	1	0.001580	-0.0005514	0.9986
22-Nov-2013	2	0.001543	0.0004852	0.9989
23-Nov-2013	3	0.001588	0.001506	0.9978
25-Nov-2013	4	0.001473	0.0001445	0.9994
26-Nov-2013	6	0.001451	-0.0007075	0.9990
26-Nov-2013	8	0.001604	-0.001088	0.9985
27-Nov-2013	7	0.001386	0.0005922	0.9970
27-Nov-2013	9	0.001544	0.001140	0.9975
27-Nov-2013	11	0.001598	0.001109	0.9968
27-Nov-2013	12	0.001882	0.00005649	0.9981
28-Nov-2013	10	0.001838	0.0005453	0.9959
28-Nov-2013	13	0.001821	-0.0005109	0.9980
28-Nov-2013	14	0.001804	0.0003019	0.9987
29-Nov-2013	15	0.001823	-0.001401	0.9995
29-Nov-2013	16	0.001855	-0.001079	0.9992
29-Nov-2013	17	0.001771	-0.001833	0.9993
29-Nov-2013	18	0.001799	0.0007575	0.9994
02-Dec-2013	19	0.002122	0.0009067	0.9992
Mean		0.001693	0.00002079	0.9984
S.D.		0.000190	0.00096769	0.0010
%CV		11.2	4654.4	0.1
n		18	18	18



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Table 5 Study Sample Concentrations for 1-OHP

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0001	0	05113220000414	1	59.1	1	1	
0001	1	05113220000415	1	87.7	1	1	
0001	2	05113220000416	1	51.5	1	1	
0001	3	05113220000417	1	60.8	1	1	
0001	4	05113220000418	1	47.9	1	1	
0001	5	05113220000419	1	33.6	1	1	
0001	6	05113220000420	1	34.4	1	1	
0004	0	05113220000428	1	105	1	1	
0004	1	05113220000429	1	124	1	1	
0004	2	05113220000430	1	81.3	1	1	
0004	3	05113220000431	1	63.9	1	1	
0004	4	05113220000432	1	62.5	1	1	
0004	5	05113220000433	1	37.6	1	1	
0004	6	05113220000434	1	22.3	1	1	
0008	0	05113220000001	1	169	1	1	
0008	1	05113220000002	1	247	1	1	
0008	2	05113220000003	1	132	1	1	
0008	3	05113220000004	1	64.3	1	1	
0008	4	05113220000005	1	60.8	1	1	
0008	5	05113220000006	1	57.8	1	1	
0008	6	05113220000007	1	54.3	1	1	
0010	0	05113220000008	1	180	1	1	
0010	1	05113220000009	1	55.8	1	1	
0010	2	05113220000010	1	96.8	1	1	
0010	3	05113220000011	1	91.7	1	1	



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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0010	4	05113220000012	1	77.8	1	1	
0010	5	05113220000013	1	61.9	1	1	
0010	6	05113220000014	1	64.4	1	1	
0011	0	05113220000015	1	76.1	1	1	
0011	1	05113220000016	1	144	1	1	
0011	2	05113220000017	1	76.3	1	1	
0011	3	05113220000018	1	52.4	1	1	
0011	4	05113220000019	1	46.8	1	1	
0011	5	05113220000020	1	40.7	1	1	
0011	6	05113220000021	1	41.7	1	1	
0013	0	05113220000442	1	194	1	1	
0013	1	05113220000443	1	285	1	1	
0013	2	05113220000444	1	108	1	1	
0013	3	05113220000445	1	148	1	1	
0013	4	05113220000446	1	130	1	1	
0013	5	05113220000447	1	60.6	1	1	
0013	6	05113220000448	1	96.0	1	1	
0014	0	05113220000022	1	156	1	1	
0014	1	05113220000023	1	326	1	1	
0014	2	05113220000024	1	116	1	1	
0014	3	05113220000025	1	83.9	1	1	
0014	4	05113220000026	1	62.9	1	1	
0014	5	05113220000027	1	46.4	1	1	
0014	6	05113220000028	1	68.4	1	1	
0015	0	05113220000029	1	180	1	1	
0015	1	05113220000030	1	151	1	1	
0015	2	05113220000031	1	83.0	1	1	
0015	3	05113220000032	1	83.3	1	1	





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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0015	4	05113220000033	1	39.7	1	1	
0015	5	05113220000034	1	51.8	1	1	
0015	6	05113220000035	1	49.1	1	1	
0016	0	05113220000036	1	153	1	1	
0016	1	05113220000037	1	64.4	1	1	
0016	2	05113220000038	1	89.9	1	1	
0016	3	05113220000039	1	69.0	1	1	
0016	4	05113220000040	1	51.0	1	1	
0016	5	05113220000041	1	60.3	1	1	
0016	6	05113220000042	1	47.9	1	1	
0017	0	05113220000043	1	97.0	1	1	
0017	1	05113220000044	1	80.2	1	1	
0017	2	05113220000045	1	114	1	1	
0017	3	05113220000046	1	133	1	1	
0017	4	05113220000047	1	52.9	1	1	
0017	5	05113220000048	1	67.9	1	1	
0017	6	05113220000049	1	71.3	1	1	
0020	0	05113220000050	2	83.1	1	1	
0020	1	05113220000051	2	82.6	1	1	
0020	2	05113220000052	2	49.1	1	1	
0020	3	05113220000053	2	61.3	1	1	
0020	4	05113220000054	2	37.3	1	1	
0020	5	05113220000055	2	41.9	1	1	
0020	6	05113220000056	2	17.6	1	1	
0021	0	05113220000456	2	159	1	1	
0021	1	05113220000457	2	232	1	1	
0021	2	05113220000458	2	206	1	1	
0021	3	05113220000459	2	222	1	1	



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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0021	4	05113220000460	2	220	1	1	
0021	5	05113220000461	2	145	1	1	
0021	6	05113220000462	2	172	1	1	
0022	0	05113220000057	17	177	1	1	
0022	1	05113220000058	17	290	1	1	
0022	2	05113220000059	17	83.7	1	1	
0022	3	05113220000060	17	92.2	1	1	
0022	4	05113220000061	17	86.1	1	1	
0022	5	05113210000062	17	79.2	1	1	
0022	6	05113220000063	17	73.5	1	1	
0023	0	05113220000064	2	82.0	1	1	
0023	1	05113220000065	2	82.8	1	1	
0023	2	05113220000066	2	39.9	1	1	
0023	3	05113220000067	2	36.9	1	1	
0023	4	05113220000068	2	34.2	1	1	
0023	5	05113220000069	2	24.8	1	1	
0023	6	05113220000070	2	33.0	1	1	
0025	0	05113220000071	2	71.9	1	1	
0025	1	05113220000072	2	105	1	1	
0025	2	05113220000073	2	110	1	1	
0025	3	05113220000074	2	108	1	1	
0025	4	05113220000075	2	78.6	1	1	
0025	5	05113220000076	2	89.1	1	1	
0025	6	05113220000077	2	58.9	1	1	
0028	0	05113220000078	2	91.1	1	1	
0028	1	05113220000079	2	94.4	1	1	
0028	2	05113220000080	2	55.4	1	1	
0028	3	05113220000081	2	102	1	1	





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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0028	4	05113220000082	2	49.3	1	1	
0028	5	05113220000083	2	53.7	1	1	
0028	6	05113220000084	2	39.0	1	1	
0029	0	05113220000085	2	91.1	1	1	
0029	1	05113220000086	2	38.9	1	1	
0029	2	05113220000087	2	72.8	1	1	
0029	3	05113220000088	2	93.1	1	1	
0029	4	05113220000089	2	60.5	1	1	
0029	5	05113220000090	2	72.4	1	1	
0029	6	05113220000091	2	67.6	1	1	
0030	0	05113220000092	2	116	1	1	
0030	1	05113220000093	2	177	1	1	
0030	2	05113220000094	2	106	1	1	
0030	3	05113220000095	2	56.2	1	1	
0030	4	05113220000096	2	52.2	1	1	
0030	5	05113220000097	2	73.9	1	1	
0030	6	05113220000098	2	70.0	1	1	
0031	0	05113220000099	2	117	1	1	
0031	1	05113220000100	2	252	1	1	
0031	2	05113220000101	2	85.2	1	1	
0031	3	05113220000102	2	87.4	1	1	
0031	4	05113220000103	2	49.7	1	1	
0031	5	05113220000104	2	40.7	1	1	
0031	6	05113220000105	2	38.5	1	1	
0034	0	05113220000106	2	144	1	1	
0034	1	05113220000107	2	123	1	1	
0034	2	05113220000108	2	104	1	1	
0034	3	05113220000109	2	84.3	1	1	



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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0034	4	05113220000110	2	81.6	1	1	
0034	5	05113220000111	2	107	1	1	
0034	6	05113220000112	2	35.2	1	1	
0035	0	05113220000113	2	175	1	1	
0035	1	05113220000114	2	192	1	1	
0035	2	05113220000115	2	145	1	1	
0035	3	05113220000116	2	118	1	1	
0035	4	05113220000117	2	99.3	1	1	
0035	5	05113220000118	2	136	1	1	
0035	6	05113220000119	2	150	1	1	
0037	0	05113220000470	3	218	1	1	
0037	1	05113220000471	3	215	1	1	
0037	2	05113220000472	3	192	1	1	
0037	3	05113220000473	3	177	1	1	
0037	4	05113220000474	3	163	1	1	
0037	5	05113220000475	3	165	1	1	
0037	6	05113220000476	3	168	1	1	
0038	0	05113220000120	3	246	1	1	
0038	1	05113220000121	3	251	1	1	
0038	2	05113220000122	3	149	1	1	
0038	3	05113220000123	3	70.6	1	1	
0038	4	05113220000124	3	80.7	1	1	
0038	5	05113220000125	3	61.7	1	1	
0038	6	05113220000126	3	65.6	1	1	
0039	0	05113220000127	3	109	1	1	
0039	1	05113220000128	3	130	1	1	
0039	2	05113220000129	3	113	1	1	
0039	3	05113220000130	3	48.1	1	1	



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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0039	4	05113220000131	3	51.4	1	1	
0039	5	05113220000132	3	54.7	1	1	
0039	6	05113220000133	3	36.9	1	1	
0042	0	05113220000484	3	133	1	1	
0042	1	05113220000485	3	203	1	1	
0042	2	05113220000486	3	181	1	1	
0042	3	05113220000487	3	182	1	1	
0042	4	05113220000488	3	325	1	1	
0042	5	05113220000489	3	116	1	1	
0042	6	05113220000490	3	137	1	1	
0044	0	05113220000134	3	159	1	1	
0044	1	05113220000135	3	255	1	1	
0044	2	05113220000136	3	222	1	1	
0044	3	05113220000137	3	173	1	1	
0044	4	05113220000138	3	134	1	1	
0044	5	05113220000139	3	116	1	1	
0044	6	05113220000140	3	92.4	1	1	
0049	0	05113220000141	3	144	1	1	
0049	1	05113220000142	3	76.1	1	1	
0049	2	05113220000143	3	166	1	1	
0049	3	05113220000144	3	94.8	1	1	
0049	4	05113220000145	3	121	1	1	
0049	5	05113220000146	3	91.2	1	1	
0049	6	05113220000147	3	59.6	1	1	
0051	0	05113220000498	3	47.7	1	1	
0051	1	05113220000499	3	48.3	1	1	
0051	2	05113220000500	3	26.5	1	1	
0051	3	05113220000501	3	28.4	1	1	



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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0051	4	05113220000502	3	20.8	1	1	
0051	5	05113220000503	3	15.7	1	1	
0051	6	05113220000504	3	29.9	1	1	
0052	0	05113220000148	3	170	1	1	
0052	1	05113220000149	3	192	1	1	
0052	2	05113220000150	3	124	1	1	
0052	3	05113220000151	3	91.2	1	1	
0052	4	05113220000152	3	46.9	1	1	
0052	5	05113220000153	3	52.6	1	1	
0052	6	05113220000154	3	65.4	1	1	
0053	0	05113220000155	3	142	1	1	
0053	1	05113220000156	3	146	1	1	
0053	2	05113220000157	3	141	1	1	
0053	3	05113220000158	3	132	1	1	
0053	4	05113220000159	3	132	1	1	
0053	5	05113220000160	3	80.9	1	1	
0053	6	05113220000161	3	118	1	1	
0055	0	05113220000162	3	184	1	1	
0055	1	05113220000163	3	226	1	1	
0055	2	05113220000164	3	193	1	1	
0055	3	05113220000165	3	191	1	1	
0055	4	05113220000166	3	97.4	1	1	
0055	5	05113220000167	3	171	1	1	
0055	6	05113220000168	3	192	1	1	
0057	0	05113220000169	4	58.4	1	1	
0057	1	05113220000170	4	64.0	1	1	
0057	2	05113220000171	4	65.1	1	1	
0057	3	05113220000172	4	45.6	1	1	



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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0057	4	05113220000173	4	51.3	1	1	
0057	5	05113220000174	4	34.8	1	1	
0057	6	05113220000175	4	31.4	1	1	
0060	0	05113220000176	4	170	1	1	
0060	1	05113220000177	4	173	1	1	
0060	2	05113220000178	4	136	1	1	
0060	3	05113220000179	4	153	1	1	
0060	4	05113220000180	4	253	1	1	
0060	5	05113220000181	4	106	1	1	
0060	6	05113220000182	4	69.5	1	1	
0062	0	05113220000183	4	48.7	1	1	
0062	1	05113220000184	4	88.9	1	1	
0062	2	05113220000185	4	40.5	1	1	
0062	3	05113220000186	4	40.4	1	1	
0062	4	05113220000187	4	21.9	1	1	
0062	5	05113220000188	4	32.0	1	1	
0062	6	05113220000189	4	27.7	1	1	
0063	0	05113220000512	4	148	1	1	
0063	1	05113220000513	4	173	1	1	
0063	2	05113220000514	4	106	1	1	
0063	3	05113220000515	4	55.4	1	1	
0063	4	05113220000516	4	76.6	1	1	
0063	5	05113220000517	4	63.1	1	1	
0063	6	05113220000518	4	59.5	1	1	
0064	0	05113220000190	4	64.5	1	1	
0064	1	05113220000191	4	151	1	1	
0064	2	05113220000192	4	83.9	1	1	
0064	3	05113220000193	4	85.0	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0064	4	05113220000194	4	78.8	1	1	
0064	5	05113220000195	4	53.9	1	1	
0064	6	05113220000196	4	103	1	1	
0066	0	05113220000526	4	82.4	1	1	
0066	1	05113220000527	4	114	1	1	
0066	2	05113220000528	4	52.2	1	1	
0066	3	05113220000529	4	72.4	1	1	
0066	4	05113220000530	4	49.5	1	1	
0066	5	05113220000531	4	26.2	1	1	
0066	6	05113220000532	4	24.2	1	1	
0067	0	05113220000540	4	139	1	1	
0067	1	05113220000541	4	267	1	1	
0067	2	05113220000542	4	154	1	1	
0067	3	05113220000543	4	182	1	1	
0067	4	05113220000544	4	78.1	1	1	
0067	5	05113220000545	4	92.5	1	1	
0067	6	05113220000546	4	86.1	1	1	
0069	0	05113220000554	4	101	1	1	
0069	1	05113220000555	4	131	1	1	
0069	2	05113220000556	4	110	1	1	
0069	3	05113220000557	4	96.4	1	1	
0069	4	05113220000558	4	78.3	1	1	
0069	5	05113220000559	4	54.0	1	1	
0069	6	05113220000560	4	48.4	1	1	
0071	0	05113220000568	4	130	1	1	
0071	1	05113220000569	4	126	1	1	
0071	2	05113220000570	4	73.7	1	1	
0071	3	05113220000571	4	76.2	1	1	





1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0071	4	05113220000572	4	41 0	1	1	
0071	5	05113220000573	4	22 7	1	1	
0071	6	05113220000574	4	45 3	1	1	
0072	0	05113220000582	17	89 7	1	1	
0072	1	05113220000583	17	89 8	1	1	
0072	2	05113220000584	17	69 1	1	1	
0072	3	05113220000585	17	106	1	1	
0072	4	05113220000586	17	131	1	1	
0072	5	05113220000587	17	71 4	1	1	
0072	6	05113220000588	17	131	1	1	
0074	0	05113220000596	4	205	1	1	
0074	1	05113220000597	4	221	1	1	
0074	2	05113220000598	4	145	1	1	
0074	3	05113220000599	4	193	1	1	
0074	4	05113220000600	4	110	1	1	
0074	5	05113220000601	4	56 4	1	1	
0074	6	05113220000602	4	59 1	1	1	
0076	0	05113220000610	18	85 6	1	1	
0076	1	05113220000611	18	67 3	1	1	
0076	2	05113220000612	18	161	1	1	
0076	3	05113220000613	18	119	1	1	
0076	4	05113220000614	18	104	1	1	
0076	5	05113220000615	18	16 8	1	1	
0076	6	05113220000616	18	52 2	1	1	
0080	0	05113220000624	18	90 3	1	1	
0080	1	05113220000625	18	96 3	1	1	
0080	2	05113220000626	18	99 4	1	1	
0080	3	05113220000627	18	121	1	1	





1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0080	4	05113220000628	18	101	1	1	
0080	5	05113220000629	18	58.4	1	1	
0080	6	05113220000630	18	105	1	1	
0083	0	05113220000638	18	163	1	1	
0083	1	05113220000639	18	150	1	1	
0083	2	05113220000640	18	101	1	1	
0083	3	05113220000641	18	99.4	1	1	
0083	4	05113220000642	18	72.9	1	1	
0083	5	05113220000643	18	48.2	1	1	
0083	6	05113220000644	18	34.4	1	1	
0085	0	05113220000652	10	127	1	1	
0085	1	05113220000653	10	163	1	1	
0085	2	05113220000654	10	119	1	1	
0085	3	05113220000655	10	87.3	1	1	
0086	0	05113220000666	18	328	1	1	
0086	1	05113220000667	18	352	1	1	
0086	2	05113220000668	18	390	1	1	
0086	3	05113220000669	18	236	1	1	
0086	4	05113220000670	18	160	1	1	
0086	5	05113220000671	18	117	1	1	
0086	6	05113220000672	18	287	1	1	
0087	0	05113220000680	18	200	1	1	
0087	1	05113220000681	18	167	1	1	
0087	2	05113220000682	18	175	1	1	
0087	3	05113220000683	18	169	1	1	
0087	4	05113220000684	18	189	1	1	
0087	5	05113220000685	18	93.9	1	1	
0087	6	05113220000686	18	53.0	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0088	0	05113220000694	18	121	1	1	
0088	1	05113220000695	18	126	1	1	
0088	2	05113220000696	18	131	1	1	
0088	3	05113220000697	18	80.9	1	1	
0088	4	05113220000698	18	92.0	1	1	
0088	5	05113220000699	18	37.9	1	1	
0088	6	05113220000700	18	39.1	1	1	
0090	0	05113220000708	18	71.3	1	1	
0090	1	05113220000709	18	79.4	1	1	
0090	2	05113220000710	18	91.0	1	1	
0090	3	05113220000711	18	108	1	1	
0090	4	05113220000712	18	97.6	1	1	
0090	5	05113220000713	18	48.4	1	1	
0090	6	05113220000714	18	58.4	1	1	
0093	0	05113220000722	18	156	1	1	
0093	1	05113220000723	18	170	1	1	
0093	2	05113220000724	18	103	1	1	
0093	3	05113220000725	18	104	1	1	
0093	4	05113220000726	18	71.6	1	1	
0093	5	05113220000727	18	50.1	1	1	
0093	6	05113220000728	18	41.0	1	1	
0104	0	05113220000736	18	71.9	1	1	
0104	1	05113220000737	18	77.0	1	1	
0104	2	05113220000738	18	49.6	1	1	
0104	3	05113220000739	18	53.4	1	1	
0104	4	05113220000740	18	33.2	1	1	
0104	5	05113220000741	18	22.6	1	1	
0104	6	05113220000742	18	34.3	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0105	0	05113220000750	18	126	1	1	
0105	1	05113220000751	18	136	1	1	
0105	2	05113220000752	18	186	1	1	
0105	3	05113220000753	18	166	1	1	
0105	4	05113220000754	18	120	1	1	
0105	5	05113220000755	18	78.4	1	1	
0105	6	05113220000756	18	48.7	1	1	
0106	0	05113220000764	6	56.3	1	1	
0106	1	05113220000765	6	78.8	1	1	
0106	2	05113220000766	6	46.0	1	1	
0106	3	05113220000767	6	51.1	1	1	
0106	4	05113220000768	6	49.6	1	1	
0106	5	05113220000769	6	22.7	1	1	
0106	6	05113220000770	6	23.0	1	1	
0107	0	05113220000778	6	213	1	1	
0107	1	05113220000779	6	150	1	1	
0107	2	05113220000780	6	126	1	1	
0107	3	05113220000781	6	186	1	1	
0107	4	05113220000782	6	89.8	1	1	
0107	5	05113220000783	6	82.1	1	1	
0107	6	05113220000784	6	55.9	1	1	
0110	0	05113220000792	6	175	1	1	
0110	1	05113220000793	6	192	1	1	
0110	2	05113220000794	6	128	1	1	
0110	3	05113220000795	6	162	1	1	
0110	4	05113220000796	6	114	1	1	
0110	5	05113220000797	6	67.5	1	1	
0110	6	05113220000798	6	81.8	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0112	0	05113220000806	6	135	1	1	
0112	1	05113220000807	6	139	1	1	
0112	2	05113220000808	6	76.2	1	1	
0112	3	05113220000809	6	52.0	1	1	
0112	4	05113220000810	6	48.2	1	1	
0112	5	05113220000811	6	28.2	1	1	
0112	6	05113220000812	6	38.4	1	1	
0114	0	05113220000820	6	136	1	1	
0114	1	05113220000821	6	279	1	1	
0114	2	05113220000822	6	233	1	1	
0114	3	05113220000816	10	187	2	1	
0114	4	05113220000824	6	115	1	1	
0114	5	05113220000825	6	70.8	1	1	
0114	6	05113220000826	6	87.4	1	1	
0117	0	05113220000834	6	145	1	1	
0117	1	05113220000835	6	217	1	1	
0117	2	05113220000836	6	218	1	1	
0117	3	05113220000837	6	296	1	1	
0117	4	05113220000838	6	189	1	1	
0117	5	05113220000839	6	136	1	1	
0117	6	05113220000840	6	94.9	1	1	
0118	0	05113220000848	6	193	1	1	
0118	1	05113220000849	6	229	1	1	
0118	2	05113220000850	6	226	1	1	
0118	3	05113220000851	6	211	1	1	
0118	4	05113220000852	6	232	1	1	
0118	5	05113220000853	6	141	1	1	
0118	6	05113220000854	6	201	1	1	





1-OHP in Human Urine  
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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0121	0	05113220000862	6	127	1	1	
0121	1	05113220000863	6	180	1	1	
0121	2	05113220000864	6	99 8	1	1	
0121	3	05113220000865	6	118	1	1	
0121	4	05113220000866	6	107	1	1	
0121	5	05113220000867	6	72 9	1	1	
0121	6	05113220000868	6	72 1	1	1	
0122	0	05113220000876	6	59 7	1	1	
0122	1	05113220000877	6	46 7	1	1	
0122	2	05113220000878	10	31 1	1	1	
0122	3	05113220000879	6	39 1	1	1	
0122	4	05113220000880	6	23 6	1	1	
0122	5	05113220000881	6	22 7	1	1	
0122	6	05113220000882	6	22 3	1	1	
0123	0	05113220000890	6	105	1	1	
0123	1	05113220000891	6	105	1	1	
0123	2	05113220000892	6	78 6	1	1	
0123	3	05113220000893	6	51 3	1	1	
0123	4	05113220000894	6	61 6	1	1	
0123	5	05113220000895	6	35 3	1	1	
0123	6	05113220000896	6	34 6	1	1	
0126	0	05113220000918	7	108	1	1	
0126	1	05113220000919	7	99 3	1	1	
0126	2	05113220000920	7	83 3	1	1	
0126	3	05113220000921	7	61 3	1	1	
0126	4	05113220000922	7	73 1	1	1	
0126	5	05113220000923	7	39 8	1	1	
0126	6	05113220000924	7	39 7	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0127	0	05113220000932	7	234	1	1	
0127	1	05113220000933	7	83.4	1	1	
0127	2	05113220000934	7	35.7	1	1	
0127	3	05113220000935	7	44.5	1	1	
0127	4	05113220000936	7	34.4	1	1	
0127	5	05113220000937	7	37.3	1	1	
0127	6	05113220000938	7	37.7	1	1	
0128	0	05113220000946	7	367	1	1	
0128	1	05113220000947	7	316	1	1	
0128	2	05113220000948	7	178	1	1	
0128	3	05113220000949	7	92.5	1	1	
0128	4	05113220000950	7	124	1	1	
0128	5	05113220000951	7	75.5	1	1	
0128	6	05113220000952	7	73.7	1	1	
0129	0	05113220000960	7	149	1	1	
0129	1	05113220000961	7	164	1	1	
0129	2	05113220000962	7	95.4	1	1	
0129	3	05113220000963	7	73.9	1	1	
0129	4	05113220000964	7	71.9	1	1	
0129	5	05113220000965	7	52.8	1	1	
0129	6	05113220000966	7	34.5	1	1	
0130	0	05113220000974	7	176	1	1	
0130	1	05113220000975	7	159	1	1	
0130	2	05113220000976	7	110	1	1	
0130	3	05113220000977	7	76.9	1	1	
0130	4	05113220000978	7	87.9	1	1	
0130	5	05113220000979	7	66.8	1	1	
0130	6	05113220000980	7	36.2	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0133	0	05113220000988	7	108	1	1	
0133	1	05113220000989	7	157	1	1	
0133	2	05113220000990	7	115	1	1	
0133	3	05113220000991	7	25.8	1	1	
0133	4	05113220000992	7	35.6	1	1	
0133	5	05113220000993	7	21.0	1	1	
0133	6	05113220000994	7	37.9	1	1	
0134	0	05113220001002	7	182	1	1	
0134	1	05113220001003	7	157	1	1	
0134	2	05113220001004	7	87.4	1	1	
0134	3	05113220001005	7	71.2	1	1	
0134	4	05113220001006	7	66.6	1	1	
0134	5	05113220001007	7	43.1	1	1	
0134	6	05113220001008	7	36.8	1	1	
0136	0	05113220001352	7	428	1	1	
0136	1	05113220001353	7	336	1	1	
0136	2	05113220001354	7	278	1	1	
0136	3	05113220001355	7	264	1	1	
0136	4	05113220001356	7	240	1	1	
0136	5	05113220001357	7	89.8	1	1	
0136	6	05113220001358	7	85.3	1	1	
0137	0	05113220001016	7	139	1	1	
0137	1	05113220001017	7	108	1	1	
0137	2	05113220001018	7	104	1	1	
0137	3	05113220001019	7	85.7	1	1	
0137	4	05113220001020	7	69.3	1	1	
0137	5	05113220001021	7	44.7	1	1	
0137	6	05113220001022	7	47.0	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0139	0	05113220001030	7	292	1	1	
0139	1	05113220001031	7	328	1	1	
0139	2	05113220001032	7	206	1	1	
0139	3	05113220001033	19	258	1	1	
0139	4	05113220001034	19	258	1	1	
0139	5	05113220001035	7	172	1	1	
0139	6	05113220001036	7	149	1	1	
0140	0	05113220001044	8	82.1	1	1	
0140	1	05113220001045	8	95.8	1	1	
0140	2	05113220001046	8	81.1	1	1	
0140	3	05113220001047	8	94.2	1	1	
0140	4	05113220001048	8	106	1	1	
0140	5	05113220001049	8	78.8	1	1	
0140	6	05113220001050	8	52.7	1	1	
0145	0	05113220001058	8	139	1	1	
0145	1	05113220001059	8	158	1	1	
0145	2	05113220001060	8	128	1	1	
0145	3	05113220001061	8	109	1	1	
0145	4	05113220001062	8	58.4	1	1	
0145	5	05113220001063	8	44.6	1	1	
0145	6	05113220001064	8	39.9	1	1	
0147	0	05113220001072	8	99.0	1	1	
0147	1	05113220001073	8	96.8	1	1	
0147	2	05113220001074	8	65.5	1	1	
0147	3	05113220001075	8	54.7	1	1	
0147	4	05113220001076	8	36.9	1	1	
0147	5	05113220001077	8	36.9	1	1	
0147	6	05113220001078	8	19.8	1	1	





1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0148	0	05113220001086	8	472	1	1	
0148	1	05113220001087	8	430	1	1	
0148	2	05113220001088	8	392	1	1	
0148	3	05113220001089	8	290	1	1	
0148	4	05113220001090	8	288	1	1	
0148	5	05113220001091	8	205	1	1	
0148	6	05113220001092	8	183	1	1	
0149	0	05113220001100	8	116	1	1	
0149	1	05113220001101	8	80 6	1	1	
0149	2	05113220001102	8	48 1	1	1	
0149	3	05113220001103	8	44 3	1	1	
0149	4	05113220001104	8	48 1	1	1	
0149	5	05113220001105	8	26 6	1	1	
0149	6	05113220001106	8	23 6	1	1	
0150	0	05113220001114	8	333	1	1	
0150	1	05113220001115	8	221	1	1	
0150	2	05113220001116	8	187	1	1	
0150	3	05113220001117	8	162	1	1	
0150	4	05113220001118	8	77 8	1	1	
0150	5	05113220001119	8	55 5	1	1	
0150	6	05113220001120	8	64 8	1	1	
0152	0	05113220001128	8	119	1	1	
0152	1	05113220001129	8	79 9	1	1	
0152	2	05113220001130	8	65 2	1	1	
0152	3	05113220001131	8	60 4	1	1	
0152	4	05113220001132	8	50 3	1	1	
0152	5	05113220001133	8	30 0	1	1	
0152	6	05113220001134	8	29 6	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0153	0	05113220001142	8	103	1	1	
0153	1	05113220001143	8	125	1	1	
0153	2	05113220001144	8	74 4	1	1	
0153	3	05113220001145	8	57 5	1	1	
0153	4	05113220001146	8	55 4	1	1	
0153	5	05113220001147	8	27 1	1	1	
0153	6	05113220001148	8	20 4	1	1	
0155	0	05113220001156	8	85 0	1	1	
0155	1	05113220001157	8	86 9	1	1	
0155	2	05113220001158	8	68 5	1	1	
0155	3	05113220001159	8	83 1	1	1	
0155	4	05113220001160	8	50 4	1	1	
0155	5	05113220001161	8	36 8	1	1	
0155	6	05113220001162	8	30 1	1	1	
0156	0	05113220000904	8	166	1	1	
0156	1	05113220000905	8	227	1	1	
0156	2	05113220000906	8	195	1	1	
0156	3	05113220000907	8	185	1	1	
0156	4	05113220000908	8	176	1	1	
0156	5	05113220000909	8	180	1	1	
0156	6	05113220000910	8	120	1	1	
0160	0	05113220001170	9	145	1	1	
0160	1	05113220001171	9	179	1	1	
0160	2	05113220001172	9	148	1	1	
0160	3	05113220001173	9	123	1	1	
0160	4	05113220001174	9	237	1	1	
0160	5	05113220001175	9	94 1	1	1	
0160	6	05113220001176	9	68 3	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0162	0	05113220001184	9	133	1	1	
0162	1	05113220001185	9	187	1	1	
0162	2	05113220001186	9	133	1	1	
0162	3	05113220001187	9	111	1	1	
0162	4	05113220001188	9	106	1	1	
0162	5	05113220001189	9	49.5	1	1	
0162	6	05113220001190	9	43.2	1	1	
0167	0	05113220001198	9	138	1	1	
0167	1	05113220001199	9	209	1	1	
0167	2	05113220001200	9	101	1	1	
0167	3	05113220001201	9	85.9	1	1	
0167	4	05113220001202	9	68.6	1	1	
0167	5	05113220001203	9	50.1	1	1	
0167	6	05113220001204	9	35.8	1	1	
0169	0	05113220001212	9	102	1	1	
0169	1	05113220001213	9	81.0	1	1	
0169	2	05113220001214	9	136	1	1	
0169	3	05113220001215	9	78.1	1	1	
0169	4	05113220001216	9	75.9	1	1	
0169	5	05113220001217	9	22.7	1	1	
0169	6	05113220001218	9	33.5	1	1	
0170	0	05113220001226	9	250	1	1	
0170	1	05113220001227	9	174	1	1	
0170	2	05113220001228	9	119	1	1	
0170	3	05113220001229	9	123	1	1	
0170	4	05113220001230	9	84.8	1	1	
0170	5	05113220001231	9	80.5	1	1	
0170	6	05113220001232	9	64.1	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0177	0	05113220001240	9	213	1	1	
0177	1	05113220001241	9	204	1	1	
0177	2	05113220001242	9	88 1	1	1	
0177	3	05113220001243	9	59 4	1	1	
0177	4	05113220001244	9	65 6	1	1	
0177	5	05113220001245	9	40 7	1	1	
0177	6	05113220001246	9	44 2	1	1	
0181	0	05113220001254	9	1180	1	1	
0181	1	05113220001255	9	504	1	1	
0181	2	05113220001256	9	244	1	1	
0181	3	05113220001257	9	134	1	1	
0181	4	05113220001258	9	125	1	1	
0181	5	05113220001259	9	77 0	1	1	
0181	6	05113220001260	9	48 2	1	1	
0183	0	05113220001268	9	207	1	1	
0183	1	05113220001269	9	183	1	1	
0183	2	05113220001270	9	83 8	1	1	
0183	3	05113220001271	9	99 8	1	1	
0183	4	05113220001272	9	67 7	1	1	
0183	5	05113220001273	9	42 2	1	1	
0183	6	05113220001274	9	40 7	1	1	
0185	0	05113220001282	9	238	1	1	
0185	1	05113220001283	9	120	1	1	
0185	2	05113220001284	9	102	1	1	
0185	3	05113220001285	9	106	1	1	
0185	4	05113220001286	9	74 4	1	1	
0185	5	05113220001287	9	56 9	1	1	
0185	6	05113220001288	9	51 7	1	1	





1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0187	0	05113220001296	9	168	1	1	
0187	1	05113220001297	9	125	1	1	
0187	2	05113220001298	9	97.6	1	1	
0187	3	05113220001299	9	180	1	1	
0187	4	05113220001300	9	204	1	1	
0187	5	05113220001301	9	120	1	1	
0187	6	05113220001302	9	67.4	1	1	
0189	0	05113220001366	11	85.8	1	1	
0189	1	05113220001367	11	81.0	1	1	
0189	2	05113220001368	11	52.8	1	1	
0189	3	05113220001369	11	59.9	1	1	
0189	4	05113220001370	11	30.8	1	1	
0189	5	05113220001371	11	37.1	1	1	
0189	6	05113220001372	11	30.2	1	1	
0190	0	05113220001310	11	129	1	1	
0190	1	05113220001311	11	132	1	1	
0190	2	05113220001312	11	125	1	1	
0190	3	05113220001313	11	78.3	1	1	
0190	4	05113220001314	11	60.8	1	1	
0190	5	05113220001315	11	40.4	1	1	
0190	6	05113220001316	11	53.8	1	1	
0191	0	05113220001324	11	73.4	1	1	
0191	1	05113220001325	11	68.9	1	1	
0191	2	05113220001326	11	76.2	1	1	
0191	3	05113220001327	11	76.4	1	1	
0191	4	05113220001328	11	71.3	1	1	
0191	5	05113220001329	11	52.6	1	1	
0191	6	05113220001330	11	36.3	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0192	0	05113220001338	11	217	1	1	
0192	1	05113220001339	11	226	1	1	
0192	2	05113220001340	11	76.9	1	1	
0192	3	05113220001341	11	110	1	1	
0192	4	05113220001342	11	66.7	1	1	
0192	5	05113220001343	11	36.5	1	1	
0192	6	05113220001344	11	43.5	1	1	
0193	0	05113220001394	11	135	1	1	
0193	1	05113220001395	11	326	1	1	
0193	2	05113220001396	11	98.5	1	1	
0193	3	05113220001397	11	70.4	1	1	
0193	4	05113220001398	11	94.0	1	1	
0193	5	05113220001399	11	66.1	1	1	
0193	6	05113220001400	11	49.6	1	1	
0195	0	05113220001408	11	79.0	1	1	
0195	1	05113220001409	11	95.0	1	1	
0195	2	05113220001410	11	83.9	1	1	
0195	3	05113220001411	11	73.3	1	1	
0195	4	05113220001412	11	64.3	1	1	
0195	5	05113220001413	11	53.3	1	1	
0195	6	05113220001414	11	16.6	1	1	
0196	0	05113220001422	11	37.8	1	1	
0196	1	05113220001423	11	45.1	1	1	
0196	2	05113220001424	11	41.1	1	1	
0196	3	05113220001425	11	23.8	1	1	
0196	4	05113220001426	11	24.9	1	1	
0196	5	05113220001427	11	42.0	1	1	
0196	6	05113220001428	11	13.3	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0197	0	05113220001436	11	94.6	1	1	
0197	1	05113220001437	11	199	1	1	
0197	2	05113220001438	11	112	1	1	
0197	3	05113220001439	11	127	1	1	
0197	4	05113220001440	11	53.8	1	1	
0197	5	05113220001441	11	47.2	1	1	
0197	6	05113220001442	11	30.7	1	1	
0198	0	05113220001450	11	132	1	1	
0198	1	05113220001451	11	294	1	1	
0198	2	05113220001452	11	189	1	1	
0198	3	05113220001453	11	294	1	1	
0198	4	05113220001454	19	256	1	1	
0198	5	05113220001455	11	262	1	1	
0198	6	05113220001456	11	174	1	1	
0200	0	05113220001464	11	53.0	1	1	
0200	1	05113220001465	11	89.4	1	1	
0200	2	05113220001466	11	65.4	1	1	
0200	3	05113220001467	11	55.5	1	1	
0200	4	05113220001468	11	63.8	1	1	
0200	5	05113220001469	11	59.5	1	1	
0200	6	05113220001470	11	33.1	1	1	
0202	0	05113220001478	12	207	1	1	
0202	1	05113220001479	12	343	1	1	
0202	2	05113220001480	12	202	1	1	
0202	3	05113220001481	12	138	1	1	
0202	4	05113220001482	12	105	1	1	
0202	5	05113220001483	12	75.4	1	1	
0202	6	05113220001484	12	33.4	1	1	



1-OHP in Human Urine  
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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0203	0	05113220001492	12	132	1	1	
0203	1	05113220001493	12	181	1	1	
0203	2	05113220001494	12	99 4	1	1	
0203	3	05113220001495	12	81 2	1	1	
0203	4	05113220001496	12	59 5	1	1	
0203	5	05113220001497	12	44 4	1	1	
0203	6	05113220001498	12	28 8	1	1	
0204	0	05113220001506	12	54 5	1	1	
0204	1	05113220001507	12	103	1	1	
0204	2	05113220001508	12	103	1	1	
0204	3	05113220001509	12	71 6	1	1	
0204	4	05113220001510	12	78 5	1	1	
0204	5	05113220001511	12	67 9	1	1	
0204	6	05113220001512	12	64 3	1	1	
0206	0	05113220001520	12	118	1	1	
0206	1	05113220001521	12	181	1	1	
0206	2	05113220001522	12	112	1	1	
0206	3	05113220001523	12	102	1	1	
0206	4	05113220001524	12	102	1	1	
0206	5	05113220001525	12	57 3	1	1	
0206	6	05113220001526	12	40 2	1	1	
0210	0	05113220001534	12	176	1	1	
0210	1	05113220001535	12	158	1	1	
0210	2	05113220001536	12	97 3	1	1	
0210	3	05113220001537	12	89 7	1	1	
0210	4	05113220001538	12	102	1	1	
0210	5	05113220001539	12	76 6	1	1	
0210	6	05113220001540	12	25 3	1	1	





1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0216	0	05113220001562	12	145	1	1	
0216	1	05113220001563	12	175	1	1	
0216	2	05113220001564	12	94 6	1	1	
0216	3	05113220001565	12	57 3	1	1	
0216	4	05113220001566	12	50 4	1	1	
0216	5	05113220001567	12	45 4	1	1	
0216	6	05113220001568	12	24 4	1	1	
0218	0	05113220001576	12	145	1	1	
0218	1	05113220001577	12	255	1	1	
0218	2	05113220001578	12	83 7	1	1	
0218	3	05113220001579	12	174	1	1	
0218	4	05113220001580	12	125	1	1	
0218	5	05113220001581	12	58 7	1	1	
0218	6	05113220001582	12	58 9	1	1	
0220	0	05113220001590	12	87 2	1	1	
0220	1	05113220001591	12	156	1	1	
0220	2	05113220001592	12	57 7	1	1	
0220	3	05113220001593	12	88 5	1	1	
0220	4	05113220001594	12	58 4	1	1	
0220	5	05113220001595	12	33 5	1	1	
0220	6	05113220001596	12	BLQ<(10 0)	1	1	
0224	0	05113220001604	12	124	1	1	
0224	1	05113220001605	12	251	1	1	
0224	2	05113220001606	12	163	1	1	
0224	3	05113220001607	12	156	1	1	
0224	4	05113220001608	12	144	1	1	
0224	5	05113220001609	12	138	1	1	
0224	6	05113220001610	12	107	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0228	0	05113220001618	12	171	1	1	
0228	1	05113220001619	12	326	1	1	
0228	2	05113220001620	12	134	1	1	
0228	3	05113220001621	12	71.9	1	1	
0228	4	05113220001622	12	79.9	1	1	
0228	5	05113220001623	12	57.6	1	1	
0228	6	05113220001624	12	28.2	1	1	
0229	0	05113220001632	13	115	1	1	
0229	1	05113220001633	13	120	1	1	
0229	2	05113220001634	13	123	1	1	
0229	3	05113220001635	13	142	1	1	
0229	4	05113220001636	13	134	1	1	
0229	5	05113220001637	13	122	1	1	
0229	6	05113220001638	13	74.6	1	1	
0230	0	05113220001646	13	133	1	1	
0230	1	05113220001647	13	290	1	1	
0230	2	05113220001648	13	201	1	1	
0230	3	05113220001649	13	163	1	1	
0230	4	05113220001650	13	141	1	1	
0230	5	05113220001651	13	139	1	1	
0230	6	05113220001652	13	108	1	1	
0232	0	05113220001660	13	62.1	1	1	
0232	1	05113220001661	13	68.8	1	1	
0232	2	05113220001662	13	39.6	1	1	
0232	3	05113220001663	13	38.5	1	1	
0232	4	05113220001664	13	38.4	1	1	
0232	5	05113220001665	13	28.3	1	1	
0232	6	05113220001666	13	16.1	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0234	0	05113220001674	13	200	1	1	
0234	1	05113220001675	13	288	1	1	
0234	2	05113220001676	13	106	1	1	
0234	3	05113220001677	13	128	1	1	
0234	4	05113220001678	13	88.6	1	1	
0234	5	05113220001679	13	61.2	1	1	
0234	6	05113220001680	13	37.5	1	1	
0240	0	05113220001688	13	185	1	1	
0240	1	05113220001689	13	185	1	1	
0240	2	05113220001690	13	94.7	1	1	
0240	3	05113220001691	13	80.6	1	1	
0240	4	05113220001692	13	84.2	1	1	
0240	5	05113220001693	13	76.3	1	1	
0240	6	05113220001694	13	46.1	1	1	
0241	0	05113220001702	13	89.9	1	1	
0241	1	05113220001703	13	117	1	1	
0241	2	05113220001704	13	65.5	1	1	
0241	3	05113220001705	13	72.9	1	1	
0241	4	05113220001706	13	43.5	1	1	
0241	5	05113220001707	13	38.5	1	1	
0241	6	05113220001708	13	30.7	1	1	
0244	0	05113220001730	13	105	1	1	
0244	1	05113220001731	13	103	1	1	
0244	2	05113220001732	13	58.8	1	1	
0244	3	05113220001733	13	63.1	1	1	
0244	4	05113220001734	13	41.8	1	1	
0244	5	05113220001735	13	43.3	1	1	
0244	6	05113220001736	13	24.7	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0249	0	05113220001772	13	236	1	1	
0249	1	05113220001773	13	234	1	1	
0249	2	05113220001774	13	120	1	1	
0249	3	05113220001775	13	91 0	1	1	
0249	4	05113220001776	13	94 5	1	1	
0249	5	05113220001777	13	50 7	1	1	
0249	6	05113220001778	13	50 9	1	1	
0251	0	05113220001786	13	112	1	1	
0251	1	05113220001787	13	92 2	1	1	
0251	2	05113220001788	13	59 9	1	1	
0251	3	05113220001789	13	65 0	1	1	
0251	4	05113220001790	13	39 9	1	1	
0251	5	05113220001791	13	34 9	1	1	
0251	6	05113220001792	13	19 4	1	1	
0252	0	05113220001800	13	174	1	1	
0252	1	05113220001801	13	205	1	1	
0252	2	05113220001802	13	97 9	1	1	
0252	3	05113220001803	13	82 3	1	1	
0252	4	05113220001804	13	62 3	1	1	
0252	5	05113220001805	13	52 5	1	1	
0252	6	05113220001806	13	43 8	1	1	
0255	0	05113220001814	14	145	1	1	
0255	1	05113220001815	14	156	1	1	
0255	2	05113220001816	14	70 0	1	1	
0255	3	05113220001817	14	77 9	1	1	
0255	4	05113220001818	14	51 9	1	1	
0255	5	05113220001819	14	62 7	1	1	
0255	6	05113220001820	14	42 5	1	1	



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0256	0	05113220001828	14	159	1	1	
0256	1	05113220001829	14	227	1	1	
0256	2	05113220001830	14	98.6	1	1	
0256	3	05113220001831	14	103	1	1	
0256	4	05113220001832	14	76.2	1	1	
0256	5	05113220001833	14	88.2	1	1	
0256	6	05113220001834	14	42.6	1	1	
0262	0	05113220001842	14	93.1	1	1	
0262	1	05113220001843	14	128	1	1	
0262	2	05113220001844	14	100	1	1	
0262	3	05113220001845	14	133	1	1	
0262	4	05113220001846	14	160	1	1	
0262	5	05113220001847	14	136	1	1	
0262	6	05113220001848	14	57.0	1	1	
0264	0	05113220001856	14	45.9	1	1	
0264	1	05113220001857	14	73.2	1	1	
0264	2	05113220001858	14	51.4	1	1	
0264	3	05113220001859	14	38.5	1	1	
0264	4	05113220001860	14	47.2	1	1	
0264	5	05113220001861	14	26.5	1	1	
0264	6	05113220001862	14	17.1	1	1	
0265	0	05113220001380	14	162	1	1	
0265	1	05113220001381	14	220	1	1	
0265	2	05113220001382	14	149	1	1	
0265	3	05113220001383	14	112	1	1	
0265	4	05113220001384	14	117	1	1	
0265	5	05113220001385	14	92.9	1	1	
0265	6	05113220001386	14	64.4	1	1	





1-OHP in Human Urine  
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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0266	0	05113220001870	14	170	1	1	
0266	1	05113220001871	14	146	1	1	
0266	2	05113220001872	14	102	1	1	
0266	3	05113220001873	14	61.2	1	1	
0266	4	05113220001874	14	62.7	1	1	
0266	5	05113220001875	14	57.2	1	1	
0266	6	05113220001876	14	56.5	1	1	
0272	0	05113220001898	14	324	1	1	
0272	1	05113220001899	14	369	1	1	
0272	2	05113220001900	14	168	1	1	
0272	3	05113220001901	14	158	1	1	
0272	4	05113220001902	14	163	1	1	
0272	5	05113220001903	14	70.0	1	1	
0272	6	05113220001904	14	95.8	1	1	
0273	0	05113220001912	14	172	1	1	
0273	1	05113220001913	14	191	1	1	
0273	2	05113220001914	14	105	1	1	
0273	3	05113220001915	14	78.4	1	1	
0273	4	05113220001916	14	81.8	1	1	
0273	5	05113220001917	14	50.1	1	1	
0273	6	05113220001918	14	50.1	1	1	
0276	0	05113220001926	14	65.7	1	1	
0276	1	05113220001927	14	67.3	1	1	
0276	2	05113220001928	14	77.3	1	1	
0276	3	05113220001929	14	62.3	1	1	
0276	4	05113220001930	14	67.8	1	1	
0276	5	05113220001931	14	60.3	1	1	
0276	6	05113220001932	14	63.3	1	1	



1-OHP in Human Urine  
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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0277	0	05113220001940	14	104	1	1	
0277	1	05113220001941	14	123	1	1	
0277	2	05113220001942	14	76 4	1	1	
0277	3	05113220001943	14	63 4	1	1	
0277	4	05113220001944	14	50 7	1	1	
0277	5	05113220001945	14	29 7	1	1	
0277	6	05113220001946	14	32 3	1	1	
0278	0	05113220001954	15	150	1	1	
0278	1	05113220001955	15	149	1	1	
0278	2	05113220001956	15	201	1	1	
0278	3	05113220001957	15	153	1	1	
0278	4	05113220001958	15	176	1	1	
0278	5	05113220001959	15	116	1	1	
0278	6	05113220001960	15	104	1	1	
0279	0	05113220001968	15	323	1	1	
0279	1	05113220001969	15	196	1	1	
0279	2	05113220001970	15	136	1	1	
0279	3	05113220001971	15	91 1	1	1	
0279	4	05113220001972	15	109	1	1	
0279	5	05113220001973	15	62 9	1	1	
0279	6	05113220001974	15	68 8	1	1	
0281	0	05113220001982	15	457	1	1	
0281	1	05113220001983	15	425	1	1	
0281	2	05113220001984	15	235	1	1	
0281	3	05113220001985	15	172	1	1	
0281	4	05113220001986	15	224	1	1	
0281	5	05113220001987	15	115	1	1	
0281	6	05113220001988	15	140	1	1	



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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0282	0	05113220001996	15	63.8	1	1	
0282	1	05113220001997	15	92.0	1	1	
0282	2	05113220001998	15	48.0	1	1	
0282	3	05113220001999	15	35.9	1	1	
0282	4	05113220002000	15	33.9	1	1	
0282	5	05113220002001	15	26.2	1	1	
0282	6	05113220002002	15	21.2	1	1	
0283	0	05113220002010	15	152	1	1	
0283	1	05113220002011	15	107	1	1	
0283	2	05113220002012	15	98.2	1	1	
0283	3	05113220002013	15	112	1	1	
0283	4	05113220002014	15	100	1	1	
0283	5	05113220002015	15	68.1	1	1	
0283	6	05113220002016	15	50.3	1	1	
0285	0	05113220002024	15	108	1	1	
0285	1	05113220002025	15	180	1	1	
0285	2	05113220002026	15	174	1	1	
0285	3	05113220002027	15	201	1	1	
0285	4	05113220002028	15	130	1	1	
0285	5	05113220002029	15	86.3	1	1	
0285	6	05113220002030	15	153	1	1	
0287	0	05113220002038	15	125	1	1	
0287	1	05113220002039	15	119	1	1	
0287	2	05113220002040	15	104	1	1	
0287	3	05113220002041	15	49.9	1	1	
0287	4	05113220002042	15	67.8	1	1	
0287	5	05113220002043	15	43.7	1	1	
0287	6	05113220002044	15	45.7	1	1	



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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0289	0	05113220002066	15	143	1	1	
0289	1	05113220002067	15	118	1	1	
0289	2	05113220002068	15	102	1	1	
0289	3	05113220002069	15	84 0	1	1	
0289	4	05113220002070	15	71 4	1	1	
0289	5	05113220002071	15	43 7	1	1	
0289	6	05113220002072	15	39 0	1	1	
0291	0	05113220002080	15	198	1	1	
0291	1	05113220002081	15	189	1	1	
0291	2	05113220002082	15	85 6	1	1	
0291	3	05113220002083	15	89 3	1	1	
0291	4	05113220002084	15	69 0	1	1	
0291	5	05113220002085	15	113	1	1	
0291	6	05113220002086	15	34 5	1	1	
0292	0	05113220002094	15	129	1	1	
0292	1	05113220002095	15	186	1	1	
0292	2	05113220002096	15	173	1	1	
0292	3	05113220002097	15	74 0	1	1	
0292	4	05113220002098	15	98 1	1	1	
0292	5	05113220002099	15	43 7	1	1	
0292	6	05113220002100	15	53 0	1	1	
0296	0	05113220002108	16	206	1	1	
0296	1	05113220002109	16	192	1	1	
0296	2	05113220002110	16	122	1	1	
0296	3	05113220002111	16	173	1	1	
0296	4	05113220002112	16	117	1	1	
0296	5	05113220002113	16	116	1	1	
0296	6	05113220002114	16	98 5	1	1	



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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0298	0	05113220002122	16	170	1	1	
0298	1	05113220002123	16	227	1	1	
0298	2	05113220002124	16	273	1	1	
0298	3	05113220002125	16	118	1	1	
0298	4	05113220002126	16	163	1	1	
0298	5	05113220002127	16	124	1	1	
0298	6	05113220002128	16	176	1	1	
0300	0	05113220002150	16	67.7	1	1	
0300	1	05113220002151	16	71.0	1	1	
0300	2	05113220002152	16	45.2	1	1	
0300	3	05113220002153	16	37.5	1	1	
0300	4	05113220002154	16	51.2	1	1	
0300	5	05113220002155	16	29.0	1	1	
0300	6	05113220002156	16	33.0	1	1	
0301	0	05113220002164	16	188	1	1	
0301	1	05113220002165	16	251	1	1	
0301	2	05113220002166	16	94.4	1	1	
0301	3	05113220002167	16	77.5	1	1	
0301	4	05113220002168	16	120	1	1	
0301	5	05113220002169	16	78.4	1	1	
0301	6	05113220002170	16	78.1	1	1	
0306	0	05113220002178	16	222	1	1	
0306	1	05113220002179	16	236	1	1	
0306	2	05113220002180	16	126	1	1	
0306	3	05113220002181	16	87.7	1	1	
0306	4	05113220002182	16	96.8	1	1	
0306	5	05113220002183	16	62.8	1	1	
0306	6	05113220002184	16	82.9	1	1	





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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0307	0	05113220002192	16	264	1	1	
0307	1	05113220002193	16	245	1	1	
0307	2	05113220002194	16	131	1	1	
0307	3	05113220002195	16	91.6	1	1	
0307	4	05113220002196	16	104	1	1	
0307	5	05113220002197	16	64.0	1	1	
0307	6	05113220002198	16	61.4	1	1	
0308	0	05113220002206	16	104	1	1	
0308	1	05113220002207	16	179	1	1	
0308	2	05113220002208	16	80.4	1	1	
0308	3	05113220002209	16	71.3	1	1	
0308	4	05113220002210	16	63.0	1	1	
0308	5	05113220002211	16	45.6	1	1	
0308	6	05113220002212	16	66.6	1	1	
0313	0	05113220002248	16	133	1	1	
0313	1	05113220002249	16	124	1	1	
0313	2	05113220002250	16	177	1	1	
0313	3	05113220002251	16	76.1	1	1	
0313	4	05113220002252	16	134	1	1	
0313	5	05113220002253	16	109	1	1	
0313	6	05113220002254	16	91.3	1	1	
0315	0	05113220002262	17	128	1	1	
0315	1	05113220002263	17	173	1	1	
0315	2	05113220002264	17	98.2	1	1	
0315	3	05113220002265	17	117	1	1	
0315	4	05113220002266	17	96.0	1	1	
0315	5	05113220002267	17	72.3	1	1	
0315	6	05113220002268	17	85.9	1	1	



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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0316	0	05113220002276	16	61.4	1	1	
0316	1	05113220002277	16	74.7	1	1	
0316	2	05113220002278	16	52.3	1	1	
0316	3	05113220002279	16	44.3	1	1	
0316	4	05113220002280	16	51.9	1	1	
0316	5	05113220002281	16	24.8	1	1	
0316	6	05113220002282	16	24.5	1	1	
0317	0	05113220002290	16	100	1	1	
0317	1	05113220002291	16	82.9	1	1	
0317	2	05113220002292	16	76.5	1	1	
0317	3	05113220002293	16	67.8	1	1	
0317	4	05113220002294	16	52.5	1	1	
0317	5	05113220002295	16	45.1	1	1	
0317	6	05113220002296	16	38.7	1	1	
0318	0	05113220002304	17	144	1	1	
0318	1	05113220002305	17	152	1	1	
0318	2	05113220002306	17	175	1	1	
0318	3	05113220002307	17	160	1	1	
0318	4	05113220002308	17	155	1	1	
0318	5	05113220002309	17	134	1	1	
0318	6	05113220002310	17	178	1	1	
0320	0	05113220002318	17	251	1	1	
0320	1	05113220002319	17	265	1	1	
0320	2	05113220002320	17	118	1	1	
0320	3	05113220002321	17	93.1	1	1	
0320	4	05113220002322	17	100	1	1	
0320	5	05113220002323	17	77.5	1	1	
0320	6	05113220002324	17	72.9	1	1	



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Subject	Day Nominal	Custom ID	Watson Run ID	Concentration (pg/mL)	Split	Dilution Factor	Sample comment
0321	0	05113220002374	17	120	1	1	
0321	1	05113220002375	17	96 3	1	1	
0321	2	05113220002376	17	93 2	1	1	
0321	3	05113220002377	17	84 3	1	1	
0321	4	05113220002378	17	93 4	1	1	
0321	5	05113220002379	17	63 8	1	1	
0321	6	05113220002380	17	77 7	1	1	
0322	0	05113220002332	17	148	1	1	
0322	1	05113220002333	17	195	1	1	
0322	2	05113220002334	17	140	1	1	
0322	3	05113220002335	17	130	1	1	
0322	4	05113220002336	17	109	1	1	
0322	5	05113220002337	17	96 8	1	1	
0322	6	05113220002338	17	79 4	1	1	
0325	0	05113220002346	17	703	1	1	
0325	1	05113220002347	17	488	1	1	
0325	2	05113220002348	17	714	1	1	
0325	3	05113220002349	17	432	1	1	
0325	4	05113220002350	17	429	1	1	
0325	5	05113220002351	17	227	1	1	
0325	6	05113220002352	17	305	1	1	
0328	0	05113220002360	17	80 7	1	1	
0328	1	05113220002361	17	99 4	1	1	
0328	2	05113220002362	17	68 6	1	1	
0328	3	05113220002363	17	75 9	1	1	
0328	4	05113220002364	17	76 4	1	1	
0328	5	05113220002365	17	54 0	1	1	
0328	6	05113220002366	17	60 7	1	1	



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Table 6 Summary of Reassay for Analytical Reasons for 1-OHP

Watson Run ID	Reason	Sample Name (Custom ID Subject Treatment Period Matrix-Split Nominal Time)
5	Rejected run	05113220000610 0076 N/A P1 URN-1 Day 0
5	Rejected run	05113220000611 0076 N/A P1 URN-1 Day 1
5	Rejected run	05113220000612 0076 N/A P1 URN-1 Day 2
5	Rejected run	05113220000613 0076 N/A P1 URN-1 Day 3
5	Rejected run	05113220000614 0076 N/A P1 URN-1 Day 4
5	Rejected run	05113220000615 0076 N/A P1 URN-1 Day 5
5	Rejected run	05113220000616 0076 N/A P1 URN-1 Day 6
5	Rejected run	05113220000624 0080 N/A P1 URN-1 Day 0
5	Rejected run	05113220000625 0080 N/A P1 URN-1 Day 1
5	Rejected run	05113220000626 0080 N/A P1 URN-1 Day 2
5	Rejected run	05113220000627 0080 N/A P1 URN-1 Day 3
5	Rejected run	05113220000628 0080 N/A P1 URN-1 Day 4
5	Rejected run	05113220000629 0080 N/A P1 URN-1 Day 5
5	Rejected run	05113220000630 0080 N/A P1 URN-1 Day 6
5	Rejected run	05113220000638 0083 N/A P1 URN-1 Day 0
5	Rejected run	05113220000639 0083 N/A P1 URN-1 Day 1
5	Rejected run	05113220000640 0083 N/A P1 URN-1 Day 2
5	Rejected run	05113220000641 0083 N/A P1 URN-1 Day 3
5	Rejected run	05113220000642 0083 N/A P1 URN-1 Day 4
5	Rejected run	05113220000643 0083 N/A P1 URN-1 Day 5
5	Rejected run	05113220000644 0083 N/A P1 URN-1 Day 6
5	Rejected run	05113220000666 0086 N/A P1 URN-1 Day 0
5	Rejected run	05113220000667 0086 N/A P1 URN-1 Day 1
5	Rejected run	05113220000668 0086 N/A P1 URN-1 Day 2
5	Rejected run	05113220000669 0086 N/A P1 URN-1 Day 3
5	Rejected run	05113220000670 0086 N/A P1 URN-1 Day 4
5	Rejected run	05113220000671 0086 N/A P1 URN-1 Day 5
5	Rejected run	05113220000672 0086 N/A P1 URN-1 Day 6
5	Rejected run	05113220000680 0087 N/A P1 URN-1 Day 0
5	Rejected run	05113220000681 0087 N/A P1 URN-1 Day 1
5	Rejected run	05113220000682 0087 N/A P1 URN-1 Day 2
5	Rejected run	05113220000683 0087 N/A P1 URN-1 Day 3
5	Rejected run	05113220000684 0087 N/A P1 URN-1 Day 4
5	Rejected run	05113220000685 0087 N/A P1 URN-1 Day 5
5	Rejected run	05113220000686 0087 N/A P1 URN-1 Day 6
5	Rejected run	05113220000694 0088 N/A P1 URN-1 Day 0
5	Rejected run	05113220000695 0088 N/A P1 URN-1 Day 1
5	Rejected run	05113220000696 0088 N/A P1 URN-1 Day 2
5	Rejected run	05113220000697 0088 N/A P1 URN-1 Day 3
5	Rejected run	05113220000698 0088 N/A P1 URN-1 Day 4
5	Rejected run	05113220000699 0088 N/A P1 URN-1 Day 5
5	Rejected run	05113220000700 0088 N/A P1 URN-1 Day 6
5	Rejected run	05113220000708 0090 N/A P1 URN-1 Day 0
5	Rejected run	05113220000709 0090 N/A P1 URN-1 Day 1





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Watson Run ID	Reason	Sample Name	
		(Custom ID Subject Treatment Period Matrix-Split Nominal Time)	
5	Rejected run	05113220000710 0090 N/A P1 URN-1	Day 2
5	Rejected run	05113220000711 0090 N/A P1 URN-1	Day 3
5	Rejected run	05113220000712 0090 N/A P1 URN-1	Day 4
5	Rejected run	05113220000713 0090 N/A P1 URN-1	Day 5
5	Rejected run	05113220000714 0090 N/A P1 URN-1	Day 6
5	Rejected run	05113220000722 0093 N/A P1 URN-1	Day 0
5	Rejected run	05113220000723 0093 N/A P1 URN-1	Day 1
5	Rejected run	05113220000724 0093 N/A P1 URN-1	Day 2
5	Rejected run	05113220000725 0093 N/A P1 URN-1	Day 3
5	Rejected run	05113220000726 0093 N/A P1 URN-1	Day 4
5	Rejected run	05113220000727 0093 N/A P1 URN-1	Day 5
5	Rejected run	05113220000728 0093 N/A P1 URN-1	Day 6
5	Rejected run	05113220000736 0104 N/A P1 URN-1	Day 0
5	Rejected run	05113220000737 0104 N/A P1 URN-1	Day 1
5	Rejected run	05113220000738 0104 N/A P1 URN-1	Day 2
5	Rejected run	05113220000739 0104 N/A P1 URN-1	Day 3
5	Rejected run	05113220000740 0104 N/A P1 URN-1	Day 4
5	Rejected run	05113220000741 0104 N/A P1 URN-1	Day 5
5	Rejected run	05113220000742 0104 N/A P1 URN-1	Day 6
5	Rejected run	05113220000750 0105 N/A P1 URN-1	Day 0
5	Rejected run	05113220000751 0105 N/A P1 URN-1	Day 1
5	Rejected run	05113220000752 0105 N/A P1 URN-1	Day 2
5	Rejected run	05113220000753 0105 N/A P1 URN-1	Day 3
5	Rejected run	05113220000754 0105 N/A P1 URN-1	Day 4
5	Rejected run	05113220000755 0105 N/A P1 URN-1	Day 5
5	Rejected run	05113220000756 0105 N/A P1 URN-1	Day 6
6	ISP	05113220000823 0114 N/A P1 URN-1	Day 3
6	ISP	05113220000878 0122 N/A P1 URN-1	Day 2
7	ISP	05113220001033 0139 N/A P1 URN-1	Day 3
7	ISP	05113220001034 0139 N/A P1 URN-1	Day 4
11	ISP	05113220001454 0198 N/A P1 URN-1	Day 4

ISP, please see [Attachment 5](#) for reassay descriptions.





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Table 7 Incurred Sample Reproducibility Assessment for 1-OHP

Subject	Day Nominal	Custom ID	Original analysis		ISR analysis		%Diff	Match
			Result (pg/mL)	Watson Run ID	Result (pg/mL)	Watson Run ID		
0001	5	05113220000419	33.6	1	33.8	10	0.5	Yes
0004	5	05113220000433	37.6	1	40.4	10	7.2	Yes
0008	1	05113220000002	247	1	254	10	2.9	Yes
0011	5	05113220000020	40.7	1	39.5	10	3.1	Yes
0013	1	05113220000443	285	1	304	10	6.5	Yes
0014	1	05113220000023	326	1	345	10	5.6	Yes
0015	4	05113220000033	39.7	1	37.8	10	4.9	Yes
0020	4	05113220000054	37.3	2	40.9	10	9.2	Yes
0021	1	05113220000457	232	2	244	10	4.9	Yes
0022	1	05113220000058	290	17	227	19	24.5	No
0023	3	05113220000067	36.9	2	36.6	10	0.9	Yes
0030	1	05113220000093	177	2	181	10	2.5	Yes
0031	1	05113220000100	252	2	272	10	7.6	Yes
0034	6	05113220000112	35.2	2	37.3	10	5.8	Yes
0035	1	05113220000114	192	2	197	10	2.5	Yes
0038	1	05113220000121	251	3	262	10	4.3	Yes
0039	6	05113220000133	36.9	3	40.3	10	8.8	Yes
0042	4	05113220000488	325	3	319	10	1.7	Yes
0044	1	05113220000135	255	3	273	10	6.7	Yes
0049	6	05113220000147	59.6	3	63.6	10	6.5	Yes
0051	0	05113220000498	47.7	3	49.7	10	4.2	Yes
0052	4	05113220000152	46.9	3	51.1	10	8.6	Yes
0057	5	05113220000174	34.8	4	36.4	10	4.5	Yes
0057	6	05113220000175	31.4	4	31.0	10	1.2	Yes
0060	4	05113220000180	253	4	261	10	3.1	Yes
0062	5	05113220000188	32.0	4	33.5	10	4.7	Yes
0063	1	05113220000513	173	4	171	10	1.2	Yes



1-OHP in Human Urine  
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Subject	Day Nominal	Custom ID	Original analysis		ISR analysis		%Diff	Match
			Result (pg/mL)	Watson Run ID	Result (pg/mL)	Watson Run ID		
0067	1	05113220000541	267	4	274	10	2.6	Yes
0072	2	05113220000584	69.1	17	75.0	19	8.1	Yes
0074	1	05113220000597	221	4	228	10	3.0	Yes
0083	6	05113220000644	34.4	18	31.6	19	8.5	Yes
0086	2	05113220000668	390	18	404	19	3.4	Yes
0087	0	05113220000680	200	18	190	19	5.1	Yes
0088	5	05113220000699	37.9	18	38.8	19	2.3	Yes
0104	4	05113220000740	33.2	18	34.5	19	3.8	Yes
0105	2	05113220000752	186	18	199	19	6.7	Yes
0112	6	05113220000812	38.4	6	37.3	10	2.8	Yes
0114	1	05113220000821	279	6	305	10	8.9	Yes
0117	3	05113220000837	296	6	315	10	6.1	Yes
0118	4	05113220000852	232	6	266	10	13.6	Yes
0122	3	05113220000879	39.1	6	41.7	10	6.4	Yes
0123	6	05113220000896	34.6	6	34.4	10	0.8	Yes
0127	2	05113220000934	35.7	7	37.1	19	3.7	Yes
0128	0	05113220000946	367	7	382	19	4.0	Yes
0130	6	05113220000980	36.2	7	34.8	19	4.1	Yes
0133	4	05113220000992	35.6	7	37.2	19	4.5	Yes
0134	6	05113220001008	36.8	7	42.0	19	13.2	Yes
0136	0	05113220001352	428	7	434	19	1.4	Yes
0139	1	05113220001031	328	7	357	19	8.7	Yes
0145	6	05113220001064	39.9	8	38.6	19	3.1	Yes
0147	5	05113220001077	36.9	8	36.2	19	2.2	Yes
0148	0	05113220001086	472	8	480	19	1.7	Yes
0150	0	05113220001114	333	8	358	19	7.5	Yes
0155	6	05113220001162	30.1	8	30.0	19	0.3	Yes
0156	1	05113220000905	227	8	239	19	5.4	Yes
0160	4	05113220001174	237	9	235	19	0.7	Yes
0167	6	05113220001204	35.8	9	36.9	19	3.2	Yes



1-OHP in Human Urine  
Celerion Study AA99602-03

Subject	Day Nominal	Custom ID	Original analysis		ISR analysis		%Diff	Match
			Result (pg/mL)	Watson Run ID	Result (pg/mL)	Watson Run ID		
0169	6	05113220001218	33.5	9	38.2	19	13.2	Yes
0170	0	05113220001226	250	9	244	19	2.4	Yes
0177	5	05113220001245	40.7	9	40.3	19	0.8	Yes
0181	0	05113220001254	1180	9	1190	19	1.1	Yes
0185	0	05113220001282	238	9	228	19	4.5	Yes
0189	6	05113220001372	30.2	11	32.0	19	5.7	Yes
0191	6	05113220001330	36.3	11	37.1	19	2.3	Yes
0192	1	05113220001339	226	11	240	19	6.0	Yes
0193	1	05113220001395	326	11	BLQ (10.0)	19	-	No
0197	6	05113220001442	30.7	11	33.2	19	7.7	Yes
0198	1	05113220001451	294	11	307	19	4.6	Yes
0200	6	05113220001470	33.1	11	33.6	19	1.3	Yes
0202	1	05113220001479	343	12	348	19	1.5	Yes
0202	6	05113220001484	33.4	12	30.0	19	10.7	Yes
0206	6	05113220001526	40.2	12	42.9	19	6.7	Yes
0218	1	05113220001577	255	12	272	19	6.6	Yes
0220	5	05113220001595	33.5	12	36.4	19	8.3	Yes
0228	1	05113220001619	326	12	353	19	7.7	Yes
0230	1	05113220001647	290	13	298	19	2.7	Yes
0234	1	05113220001675	288	13	281	19	2.3	Yes
0234	6	05113220001680	37.5	13	37.0	19	1.1	Yes
0241	6	05113220001708	30.7	13	31.9	19	4.1	Yes
0249	0	05113220001772	236	13	245	19	4.0	Yes
0251	5	05113220001791	34.9	13	37.4	19	7.0	Yes
0252	1	05113220001801	205	13	216	19	5.3	Yes
0255	6	05113220001820	42.5	14	45.0	19	5.6	Yes
0256	1	05113220001829	227	14	235	19	3.1	Yes
0264	3	05113220001859	38.5	14	39.7	19	3.2	Yes
0265	1	05113220001381	220	14	235	19	6.3	Yes
0272	1	05113220001899	369	14	387	19	4.7	Yes



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Subject	Day Nominal	Custom ID	Original analysis		ISR analysis		%Diff	Match
			Result (pg/mL)	Watson Run ID	Result (pg/mL)	Watson Run ID		
0277	6	05113220001946	32.3	14	32.3	19	0.2	Yes
0278	2	05113220001956	201	15	215	19	6.3	Yes
0279	0	05113220001968	323	15	318	19	1.5	Yes
0281	0	05113220001982	457	15	457	19	0.0	Yes
0282	4	05113220002000	33.9	15	38.7	19	13.2	Yes
0289	6	05113220002072	39.0	15	37.8	19	3.2	Yes
0291	6	05113220002086	34.5	15	34.9	19	1.2	Yes
0292	5	05113220002099	43.7	15	46.8	19	6.8	Yes
0298	2	05113220002124	273	16	287	19	5.0	Yes
0300	6	05113220002156	33.0	16	34.0	19	2.8	Yes
0301	1	05113220002165	251	16	254	19	1.2	Yes
0307	0	05113220002192	264	16	270	19	2.1	Yes
0316	3	05113220002279	44.3	16	41.9	19	5.5	Yes
0317	6	05113220002296	38.7	16	37.0	19	4.5	Yes
0318	6	05113220002310	178	17	294	19	49.1	No
0320	1	05113220002319	265	17	272	19	2.6	Yes
0321	5	05113220002379	63.8	17	66.0	19	3.3	Yes
0325	2	05113220002348	714	17	747	19	4.5	Yes
0328	5	05113220002365	54.0	17	55.0	19	1.7	Yes
n							106	103
Matches (%)								97

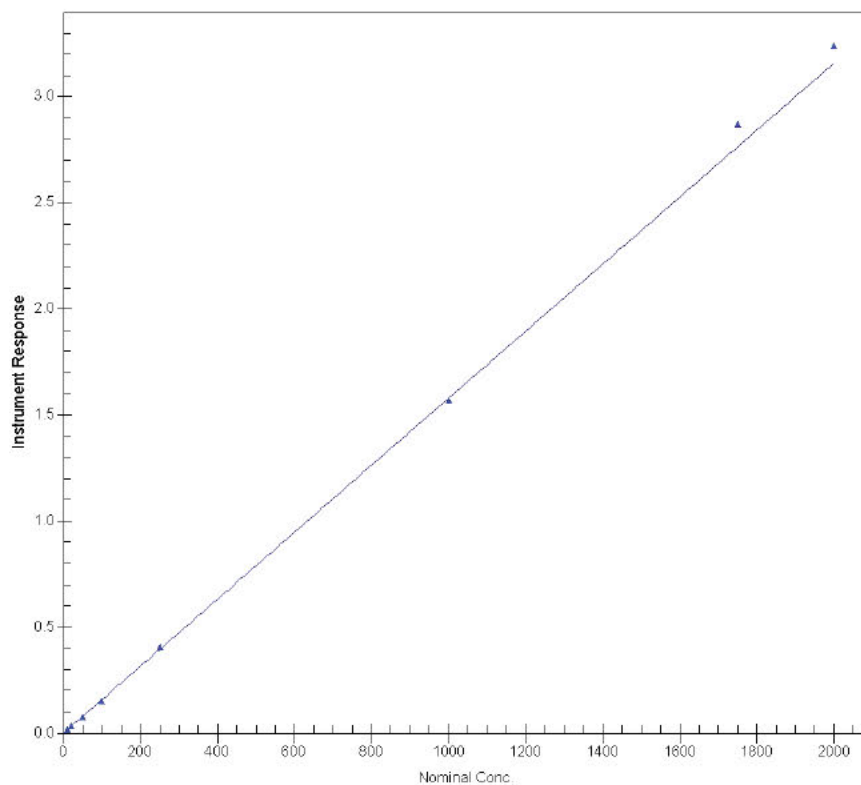


1-OHP in Human Urine  
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## FIGURES

Figure 1 Calibration Curve for 1-OHP in human urine, Watson Run ID 1

Analytical Run 1 analyzed on 22-Nov-2013 Calibration Standards for 1-OHP (pg/mL)  
Regression Method = LINEAR - Weighting Factor =  $1/X^{**2}$   
Response = Slope \* Conc + Intercept  
Slope = 0.00157986903 Intercept = -0.000551416468 R-Squared = 0.9986  
(Study ZRHR-REXC-03-EU; 1-OHP)







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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	Stmospheric 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
EMA	European Medicines Agency
EQB	Exceeding quadratic bounds
EXT	Extraction
FDA	Food and Drug Administration (U.S. Department of Health and Human Services)
fg	Femtogram
g	Gram
GLP	Good laboratory practices
h	Hour
HDPE	High density polyethylene
HPLC	High performance liquid chromatography
HSR	High standard removed

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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
LC-MS/MS	Liquid chromatography-tandem mass spectrometry
LLOQ	Lower limit of quantitation
LNK	Celerion, Lincoln site
M	Molar
mg	Milligram
mL	Millilitre, milliliter
mol	Mole
MRM	Multiple reaction-monitoring
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
RI	Reinjection
RIA	Rarioimmunoassay



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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
USP	US pharmacopeia
$\bar{x}$	Mean



1-OHP in Human Urine  
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#### Attachment 2 Temperature Definitions at Celerion

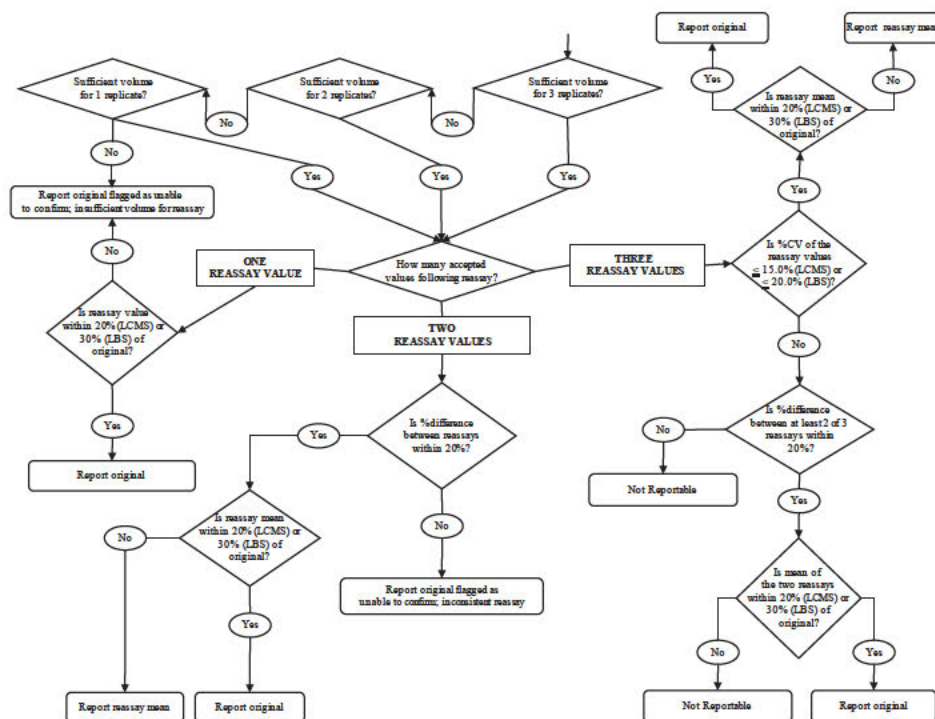
Values for temperatures are nominal temperatures representing the following temperature ranges:

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



1-OHP in Human Urine  
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### Attachment 3 Procedure for VCR and SSR Reassays and Reporting of Reassay Results



To compare reassays:

$$\frac{|\text{Reassay Value 1} - \text{Reassay Value 2}|}{\text{Mean of Reassay Value 1 and 2}} \times 100\%$$

To compare to original:

$$\frac{|\text{Mean of Reassays} - \text{Original Value}|}{\text{Original Value}} \times 100\%$$

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.



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## Attachment 4 General List of Calculation Formulae

$$\text{Mean:} \quad \bar{X} = \frac{1}{n} \sum_{i=1}^n X_i$$

$$\text{Standard Deviation (SD):} \quad s = \sqrt{\frac{1}{n-1} \sum_{i=1}^n (X_i - \bar{X})^2}$$

$$\text{Precision (RSD, CV):} \quad \text{CV \%} = (\text{SD} / X_{\text{Mean}}) * 100$$

$$\text{Accuracy (\% Theoretical):} \quad \text{Accuracy \%} = (X / X_{\text{Nominal}}) * 100$$

$$\text{Accuracy of Mean \%} = (X_{\text{Mean}} / X_{\text{Nominal}}) * 100$$

$$\text{Inaccuracy (\% Bias, \% RE):} \quad \text{Bias \%} = ((X - X_{\text{nominal}}) / X_{\text{nominal}}) * 100$$

$$\text{Bias of Mean \%} = ((X_{\text{Mean}} - X_{\text{nominal}}) / X_{\text{nominal}}) * 100$$

X = value (e.g. analyte concentration, OD value, cpm value, peak signal)  
n = number of values X



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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 (TVR)	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).



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## Attachment 6 Statement of GLP Compliance (Swissmedic)

The Swiss GLP Monitoring Authorities		
	Schweizerische Eidgenossenschaft Confédération suisse Confederazione Svizzera Confederaziun svizra Swiss Confederation	Federal Department of Home Affairs DHA Federal Office of Public Health FOPH  Federal Department of the Environment, Transport, Energy and Communications DETEC Federal Office for the Environment FOEN
		 Swiss Agency for Therapeutic Products

### Statement of GLP Compliance

According to Article 14 paragraph 3 Ordinance on Good Laboratory Practice [OGLP, SR 813.112.1]

The notification authority for chemicals confirms that the following test facility was inspected with respect to the compliance with the Swiss Ordinance on Good Laboratory Practice, adopted on 18th May 2005 [OGLP, SR 813.112.1]. This Ordinance is based on the OECD Principles of Good Laboratory Practice, as revised in 1997 and adopted on 28th November 1997 by decision of the OECD Council [C(97)186/Final].

Unequivocal name and address of the test facility:	Area of expertise according to article 3 paragraph 1 letter d OGLP:
Celerion Switzerland Ltd Allmendstrasse 32 8320 Fehraltorf, Switzerland	8. analytic and clinical chemistry testing.

Inspection authority: Swiss Agency for Therapeutic Products (Swissmedic)

Date of inspection: 13 to 14 May 2013

Date of decision: 27 June 2013

Based on the above mentioned decision it can be confirmed that the above mentioned test facility is able to conduct studies according to the aforementioned area of expertise in compliance with the principles of GLP. The above mentioned test facility is listed in the register and GLP list according to the Article 14 OGLP and is inspected on a regular basis according to Article 6 paragraph 2 OGLP.

Swiss Federal Office of Public Health  
Consumer protection directorate  
Notification authority for chemicals  
CH-3003 Bern



*Dag Kappes*

Bern, 14 August 2013, The Head, Dr. Dag Kappes.

The notification authority for chemicals is the coordination and decision authority for the good laboratory practice (GLP) for the FOEN, the FOPH and Swissmedic.

Swiss Federal Office of Public Health, Consumer protection directorate, Notification authority for chemicals, CH-3003 Bern.

[www.glp.admin.ch](http://www.glp.admin.ch), Phone: +41 (0)31 322 73 05, Fax: +41 (0)31 323 54 85



1-OHP in Human Urine  
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1-OHP in Human Urine  
Celerion Study AA99602-03

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1-OHP in Human Urine  
Celerion Study AA99602-03


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1-OHP in Human Urine  
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Attachment 8 Summary of the Method Validation Data

 PMI RESEARCH & DEVELOPMENT


BIOANALYTICAL METHOD SUMMARY (BMS)

Doc No: FOR\_QM000466 – CR204A2 Version N°: 2.0 Page 1 of 2

Biomarker: Total 1-hydroxypyrene (1-OHP)		Matrix: Human urine
MVR/SOP no. & date: SOP SM1-384A / 11-Oct-2013 and SM1-384B / 12-Nov-2013		CRO/Laboratory: Celerion Switzerland
LLOQ: 10.0 pg/mL		ULOQ: 2000 pg/mL
Validation	<input type="checkbox"/> Full <input checked="" 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 urine containing the analyte and internal standard (assay volume of 500 µL) was treated with β-Glucuronidase and extracted by a solid phase extraction procedure. The extracted samples were analyzed by an UPLC I class equipped with an Applied Biosystems/ MDS SCIEX TRIPLE QUAD 6500 mass spectrometer. Negative ions were monitored in the multiple reaction monitoring (MRM) mode. Quantification was performed using the peak area ratios of analyte versus IS for each pair of analyte and IS. The calibration curve fitting was done by 1/concentration <sup>2</sup> -weighted linear regression.		
Selectivity/Sensitivity/Matrix effect:	Comments: No significant interference at the retention time and mass transition of 1-OHP- <sup>13</sup> C <sub>6</sub> (IS) in all six human urine lots. Matrix effect within acceptance for all seven human urine lots spiked near the low (26.9 pg/mL) and high (1627 pg/mL) concentration level.	
Accuracy:	Intra-run: -4.4 – -0.7% R.E. Inter-run: -0.8 – 13.4% R.E.	
Precision:	Intra-run: 2.9 – 6.2% C.V. Inter-run: 4.1 – 11.0% C.V.	
Recovery:	N/A	
Freeze and thaw stability:	N/A	
Short-term temperature stability:	N/A	
Long-term stability:	19 days at -80°C in UV shielded polypropylene tubes	
Stock solution stability:	N/A	
Post-preparative stability:	N/A; processed sample integrity up to 116 hours at 5°C demonstrated	
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"	
BMS completed by:		

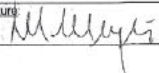


1-OHP in Human Urine  
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 PMI RESEARCH & DEVELOPMENT

BIOANALYTICAL METHOD SUMMARY (BMS)

Doc No: FOR\_QM000495 - CR204A2 Version N°: 2.0 Page 2 of 2

Name: Werner Meyer	Date: 22 NOV 2013	Signature: 
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1-OHP in Human Urine  
Celerion Study AA99602-03



PMI RESEARCH &amp; DEVELOPMENT

## BIOANALYTICAL METHOD SUMMARY (BMS)

Doc No: FOR\_QM000486 - CR204A2

Version N°: 2.0

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Biomarker: 1-Hydroxypyrene		Matrix: Urine
MVR/SOP no. & date: AA00499-01 / 03-May-2013		CRO/Laboratory: Celerion-Lincoln
LLOQ: 10.0 pg/mL		ULOQ: 2000 pg/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 urine containing the analyte and internal standard was pH-adjusted, incubated with $\beta$ -Glucuronidase from <i>Helix pomatia</i> , Type H-1, and extracted using a solid phase extraction procedure. The extracted samples were analyzed by an HPLC equipped with an AB SCIEX API 4000 <sup>TM</sup> or AB SCIEX API 5000 <sup>TM</sup> mass spectrometer. Negative ions were monitored in the multiple reaction monitoring (MRM) mode. Quantitation was determined using a weighted linear regression analysis ( $1/x^2$ ) of peak area ratios of the analyte and internal standard.		
Selectivity/Sensitivity/Matrix effect:	No significant matrix effect was observed in any of the 8 human urine lots that were fortified at low concentration or in any of the 8 human urine lots that were fortified near the concentration of the high QC samples.	
Accuracy:	Intra-batch: 1.4 to 5.7% R.E. Inter-batch: 3.4 to 7.0% R.E.	
Precision:	Intra-batch: 1.4 to 5.7% CV Inter-batch: 2.8 to 5.5% CV	
Recovery:	98% recovery at 23.6 pg/mL in human urine 88% recovery at 224 pg/mL in human urine 90% recovery at 1474 ng/mL in human urine	
Freeze and thaw stability:	6 freeze/cycles in silanized tubes 5 freeze/cycles in high density polyethylene tubes	
Short-term temperature stability:	24 hours in high density polyethylene tubes at ambient temperature under UV filtered light. 25 hours in silanized tubes at ambient temperature under white light	
Long-term stability:	411 days in silanized tubes at -20°C 209 days in high density polyethylene tubes at -20°C 209 days in high density polypropylene tubes at -20°C	
Stock solution stability:	731 days at approximately 100 $\mu$ g/mL in methanol in polypropylene tubes at -20°C	
Post-preparative stability:	172 hours in injection vials with glass inserts at 5°C	



1-OHP in Human Urine  
Celerion Study AA99602-03



PMI RESEARCH &amp; DEVELOPMENT

## BIOANALYTICAL METHOD SUMMARY (BMS)

Doc No: FOR\_QM000466 - CR204A2

Version N°: 2.0

Page 2 of 2

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"	
BMS completed by:		
Name:	Date:	Signature:
Erica Nachi	14-MAR-2013	<i>Erica J Nachi</i>





1-OHP in Human Urine  
Celerion Study AA99602-03



PMI RESEARCH &amp; DEVELOPMENT

## BIOANALYTICAL METHOD SUMMARY (BMS)

Doc No: FOR\_QM000495 - CR204A2


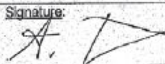
Version N°: 2.0

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Biomarker: Total 1-Hydroxypyrene (1-OHP)	Matrix: Human urine
MVR/SOP no. & date: VZZ00855 / 06-May-2008 SM1-291B / 06-Mar-2007	CRO/Laboratory: Celerion Switzerland
LLOQ: 10.0 pg/mL	ULOQ: 2000 pg/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 urine containing the analyte and internal standard (assay volume of 1000 µL) was first enzymatically hydrolysed using β-glucuronidase (type H1 from Helix Pomatia) prior to being extracted using a solid phase extraction procedure. The extracted samples were analyzed using a Perkin Elmer Series 200 Micropump HPLC equipped with an Applied Biosystems/ MDS SCIEX API 4000 triple quadrupole mass spectrometer. Negative ions were monitored in the multiple reaction monitoring (MRM) mode. Quantification was performed using the peak area ratios of analyte versus IS for each pair of analyte and IS. The calibration curve fitting was done by 1/concentration <sup>2</sup> -weighted linear regression.	
Selectivity/Sensitivity/Matrix effect:	No significant matrix effect was observed in ten human urine lots that were spiked at the concentration of low QC and at the concentration of the high QC sample
Accuracy:	Intra-run: -13.0 – 5.1% R.E. Inter-run: -8.8 – 0.8% R.E.
Precision:	Intra-run: 1.3 – 11.8% C.V. Inter-run: 2.6 – 10.5% C.V.
Recovery:	86.9% recovery at 29.1 pg/mL 78.7% recovery at 204 pg/mL 83.7% recovery at 1450 pg/mL
Freeze and thaw stability:	3 cycles at nominal -20°C
Short-term temperature stability:	19 hours at room temperature
Long-term stability:	237 days at nominal -20°C
Stock solution stability:	239 days at approximately 500 µg/mL in methanol at nominal -20°C (1-OHP) 237 days at approximately 500 µg/mL in methanol/Millipore water (50:50 v/v) at nominal -20°C (1-OHP-glucuronide) (post deconjugation assessment) 132 days at approximately 500 µg/mL in methanol/Millipore water (50:50 v/v) at nominal -20°C (1-OHP-glucuronide) (analysis without deconjugation)
Post-preparative stability:	55 hours at nominal 5°C



1-OHP in Human Urine  
Celerion Study AA99602-03

 PMI RESEARCH & DEVELOPMENT	
BIOANALYTICAL METHOD SUMMARY (BMS)	
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<b>Accreditation/ GLP compliance/ QA statements:</b>	<b>Date:</b> 06-May-2009 GLP compliance: Herewith it is confirmed, that the MDS PS study ZZ00855 was performed in compliance with the Swiss Ordinance relating to Good Laboratory Practice, adopted 18 May 2005 [RS 813.112.1]. This Ordinance is based on the OECD Principles of Good Laboratory Practice, as revised in 1997 and adopted 26 November 1997 by decision of the OECD Council [C(97)188/Final].
<b>BMS completed by:</b>	
<b>Name:</b> Anna-Lena Steck	<b>Date:</b> 11 AUG 2014 <b>Signature:</b> 



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Attachment 9 Chromatograms

Representative chromatograms from analytical run AA99602-03\_P1.

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